

# Advances in Mitral Valve Therapy



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## Introduction



The graphic is a purple and white promotional banner for a webinar. At the top, it features the HeartValveSurgery.com logo. The central white section contains the title 'Patient Webinar Advances in Mitral Valve Therapy' and the start time 'The Webinar will begin at 5:00 PM CST'. The bottom purple section is titled 'Webinar Speakers' and lists three individuals with their photos and titles: Dr. Charles Davidson (Cardiologist, Northwestern Medicine), Dr. Clyde Yancy (Cardiologist, Northwestern Medicine), and Adam Pick (Patient & Website Founder, HeartValveSurgery.com).

**Adam Pick:** Hi, everybody. My name is Adam Pick, and I'd like to welcome you to the webinar titled, "Advances in Mitral Valve Therapy". If I have yet to meet you, I'm a patient and I'm also the founder of [HeartValveSurgery.com](http://HeartValveSurgery.com). Our mission at the website is simple: we want to educate and empower patients with heart valve disease. This webinar, which has had 503 registrations from patients - in countries all over the world - is designed to support that mission.

During the webinar, all participants will be in what we call listen-only mode. That being said, you may submit questions during the webinar. Simply post your questions in the control panel that's on the top-right part of your screen. We will do our best to address your questions during the live "Q&A" section of the webinar. As we close the webinar, we're going to ask you to complete a very quick five-question survey.

I am thrilled to introduce the featured speakers for this session. Dr. Charles Davidson is the medical director of the Bluhm Cardiovascular Institute, and the clinical chief of cardiology at Northwestern Medicine. Dr. Davidson has several areas of expertise, including valvular heart disease, coronary angioplasty, and adult congenital heart disease.

Dr. Clyde Yancy is the chief of the division of cardiology and professor at Northwestern University Feinberg School of Medicine. Most recently the medical director for Baylor Heart and Vascular Institute, and the chief of cardiothoracic transplantation for Baylor University Medical Center in Dallas, Dr. Yancy is the immediate past president of the American Heart Association.



I could go on-and-on about the careers of Dr. Davidson and Dr. Yancy and their achievements in cardiac care. Instead, I will tell you that this Northwestern team is celebrated by our community, and for a very, very good reason. Since launching this website, the Northwestern Memorial Hospital has successfully treated over 100 patients from our community, including Janet Ruddock, Robert

Winter, Sarah Bloomfield, Ron Rovin, Gene Cook, Sharon Knickerbocker, and the list goes on.

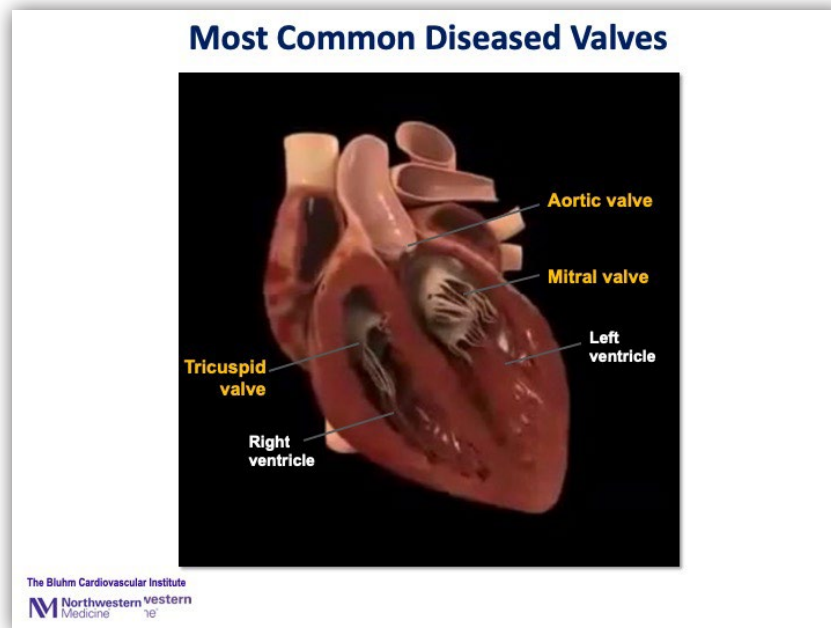


Specific to this discussion, I have to shine a light on the MitraClip success stories of [Michelle Golden](#), on the left, and [Charlotte Cummings](#) on the right. Michelle was about to go onto a heart transplant list, and Charlotte could barely walk prior to receiving the MitraClip. Now, Michelle is back camping, and Charlotte is doing what she loves, walking the Windy City of Chicago.

Personally, I am humbled that Dr. Davidson and Dr. Yancy are taking time away from their very busy practices at Northwestern to share their experiences and clinical research during this educational webinar. To start, I'd like to introduce you to Dr. Charles Davidson.

## About Your Heart Valves

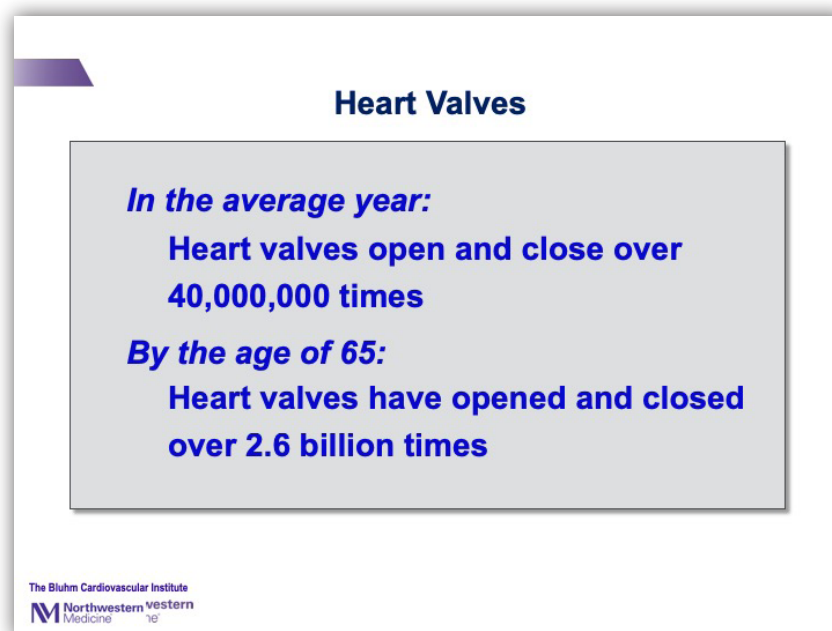
**Dr. Davidson:** Welcome everybody. Thanks for joining us today. Today, we're going to go through the mitral valve, and the anatomy and physiology of it, and then we're going to speak to some therapies, and also talk about some of the symptoms and heart failure treatments that can also be used in conjunction with mitral valve disease.



The heart has four valves. It's essentially a muscle pump. There's two valves on the right side of the heart and two valves on the left side of the heart. The mitral valve is the regulator of blood flow from the top part of the heart, the left atrium, to the bottom part of the heart, the left ventricle.

The diagram is just showing the left ventricle and the right ventricle. The left ventricle pumps the blood out to the rest of the body. The right ventricle pumps blood to the lungs. We're going to focus mostly on the left side of the heart today, since the mitral valve is between the left atrium and the left ventricle.


As you can see, as blood comes back from the lungs, it goes into the left atrium, goes through the mitral valve into the left ventricle, and then out through the aortic valve.



**Heart Valves**

*In the average year:*  
**Heart valves open and close over  
40,000,000 times**

*By the age of 65:*  
**Heart valves have opened and closed  
over 2.6 billion times**

The Bluhm Cardiovascular Institute  
 Northwestern Medicine

In the average year, our heart valves open-and-close over 40 million times. By the age of 65, your heart valves would have opened and closed over 2.6 billion times. I guess it depends how much you exercise throughout your lifetime, but this is an average number.



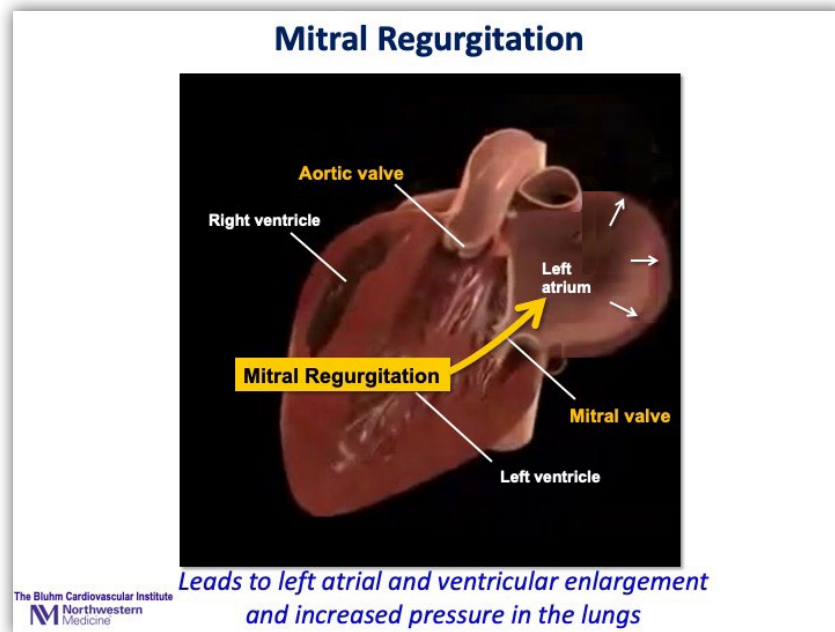
## Burden of Mitral Valve Disease

- **5,000,000 Americans with moderate or severe mitral regurgitation, ~10% risk over 75 years**
- **Worldwide, ~20,000,000 with rheumatic valve disease**

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There are five million Americans with [moderate or severe mitral regurgitation](#) and about 10% are at risk for treatment over the age of 75 years. Worldwide, there's about 20 million patients with [rheumatic valve disease](#), which is a disease that affects the mitral valve primarily, causing mitral stenosis, or blockage of the mitral valve. That is not what we're going to speak about today. But, it is a very prevalent disease throughout the world - particularly in third world countries.

## Mitral Valve Regurgitation



**Dr. Davidson:** A mitral regurgitation occurs when the mitral valve does not close properly, and then blood, instead of going forward out to the aortic valve, regurgitates or leaks back into the left atrium. What this causes is a fluid overload on the left side of the heart. As a result, the left ventricle can begin to dilate. Atrial arrhythmias, like [atrial fibrillation](#), can occur as a result of this. Eventually heart failure can occur when the disease becomes more advanced.

What are the consequences of mitral regurgitation? Just to reiterate: it causes weakening of the left ventricular muscle because of the extra blood flow in there. It's like a balloon: it gets too much water in it, it stretches out, and then, even if you fix it, it may not completely come back to normal - especially if you fix it at too late a stage in the disease. It causes elevated blood pressure in the lungs known as pulmonary hypertension. That can then transmit back to the right-sided valve called the tricuspid valve, which can also leak, and atrial fibrillation and risk of stroke from blood clots that can occur in the left atrium, particularly in the left atrial appendage.

## Mitral Regurgitation

### **Consequences:**

- **Weakening of the left ventricular muscle (heart failure)**
- **Elevation of blood pressure in the lungs (pulmonary hypertension)**
- **Tricuspid valve regurgitation**
- **Atrial fibrillation ... and risk of strokes from blood clots in the left atrium**

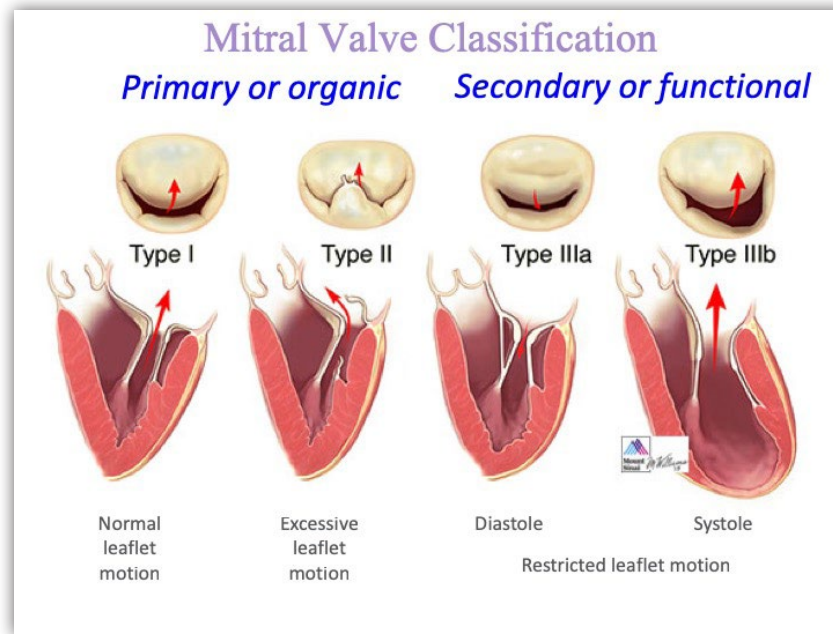
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When you come to a physician, what should they be doing?

Obviously, a physical examination should be part of any physician's exam. Usually, what that physician will hear is a murmur. With that, if the mitral regurgitation is becoming more severe, they will develop some water or fluid in the lungs. You can get edema or swelling in the legs or in the feet. Typically, at that point, some other tests would be ordered – those are EKG; chest X-ray – but all of those really don't diagnose mitral regurgitation very well.

The gold standard test is [echocardiography](#), or a transthoracic echocardiogram. That's essentially an ultrasound of the heart.

## Types of Mitral Regurgitation



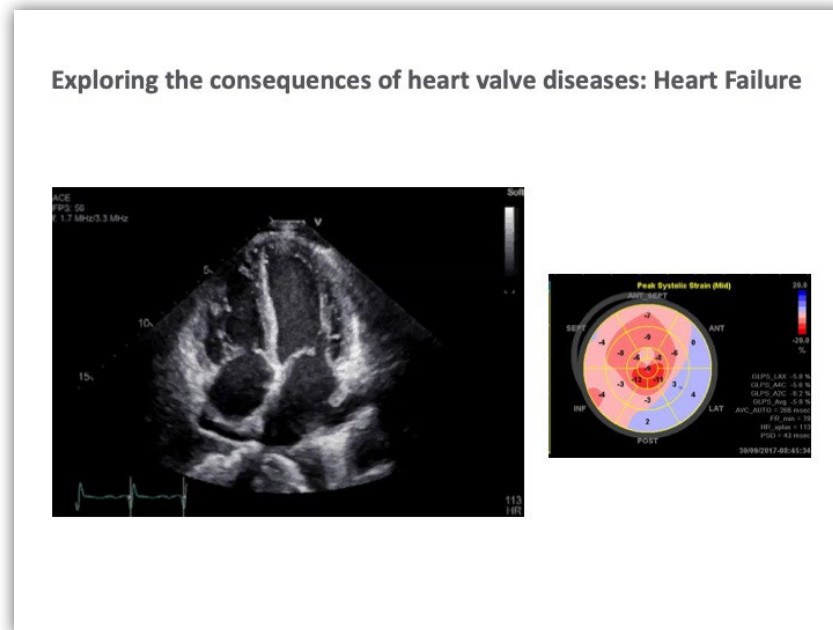
**Dr. Davidson:** Mitral regurgitation can occur in two different classifications. One is primary or organic. That means there is an intrinsic problem with the mitral valve. The valve may not have been born normally. It may have had [mitral valve prolapse](#) that progressed to the [leaflets of the valve](#), or not necessarily constructed properly at birth. Over time, the leaflets can wear out or cause disruption of the connections of the mitral valve apparatus that cause leaking.

The secondary or functional type of mitral regurgitation, which is what we're going to talk a lot about today in the subject of the COAPT clinical trial. This occurs with patients that have had previous heart attack or have heart failure where there's been stretching of the mitral annulus and therefore causing mal-coaptation of the leaflets and regurgitation of blood into the left atrium.

You can quantify the amount of mitral regurgitation by echocardiography in patients. That measurement is what's called an ERO greater than 40. More leak results in less survival.

We do know that there are gradations of mitral regurgitation, and even in a severe range, the likelihood of survival becomes less with more severe mitral regurgitation. More leak equals worse survival.

## Heart Failure & Mitral Regurgitation



**Dr. Yancy:** Adam, thank you for the opportunity to participate today. I'm delighted that so many people have an interest in what it is we're planning to do today. That was a great overview of the mitral valve. The reason that it's so important is because this problem with the mitral valve can lead to another situation known as heart failure. Let me just take a few minutes to let you know what heart failure is. That will set up Dr. Davidson's next discussion about how we address the mitral valve to treat those people with heart failure.

What you see here is an image, a moving image, on the left of your screen. This is a heart that is terribly weakened. It's probably lost over 70% of its function. The walls are moving very sluggishly. When this occurs, the person in whom this happens feels short of breath, accumulates fluid in the ankles, and the abdomen, and the lungs, and in general doesn't feel well. If we weren't able to interrupt this process, the concern is that it can go on, and unfortunately, heart failure, when not treated well, can lead to hospitalization, and even worse.

## Definition of HF<sup>1</sup>

- Complex, progressive, clinical syndrome
- Results from structural or functional impairment of ventricular filling or contractility
- Major clinical manifestations
  - Dyspnea and fatigue
  - Fluid retention
- Patient presentation is variable
- HF is not synonymous with cardiomyopathy or LV dysfunction, which describe possible structural or functional *bases for the development of HF definition*

1. Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147-e239.

When we think about a definition, I want everyone to appreciate that this is not a rare circumstance. If there were indeed 500 people that are interested in today's seminar, at least 100 of us are likely to develop heart failure while we're still alive – mitral valve disease being just one cause. This definition makes it very clear that the condition can be derived from a variety of different sources. Heart failure can occur because of high blood pressure, it can be because of valvular heart disease, it can be because of blocked blood vessels in the heart. Ultimately, it leads to weakness of the heart, retaining fluid, and shortness of breath, which is very much an important consideration.

## Heart Failure (HF)

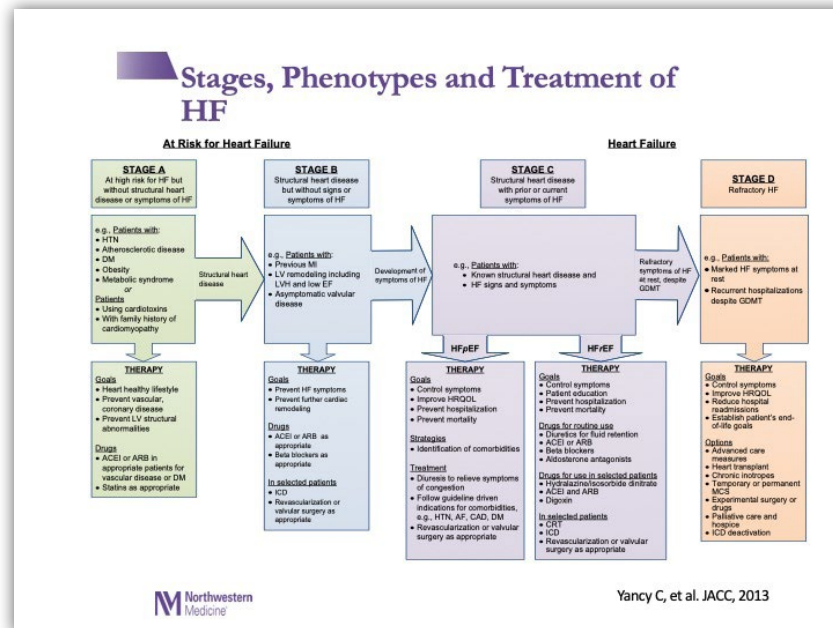
- 5.7 million people in the United States have heart failure
  - 825,000 new HF cases annually
  - Projected to increase by 46% from 2012 to 2030 resulting in >8 million people HF
- One in 9 deaths in 2009 included heart failure as contributing cause
- About half of people who develop heart failure die within 5 years of diagnosis.
- Heart failure accounts for an estimated \$32 billion in direct and indirect costs each year.

CDC Available: [http://www.cdc.gov/dhbsp/data\\_statistics/fact\\_sheets/fs\\_heart\\_failure.htm](http://www.cdc.gov/dhbsp/data_statistics/fact_sheets/fs_heart_failure.htm).  
Accessed: September 27, 2014. Go AS, et al. *Circulation*. 2014;129:e28-e292.

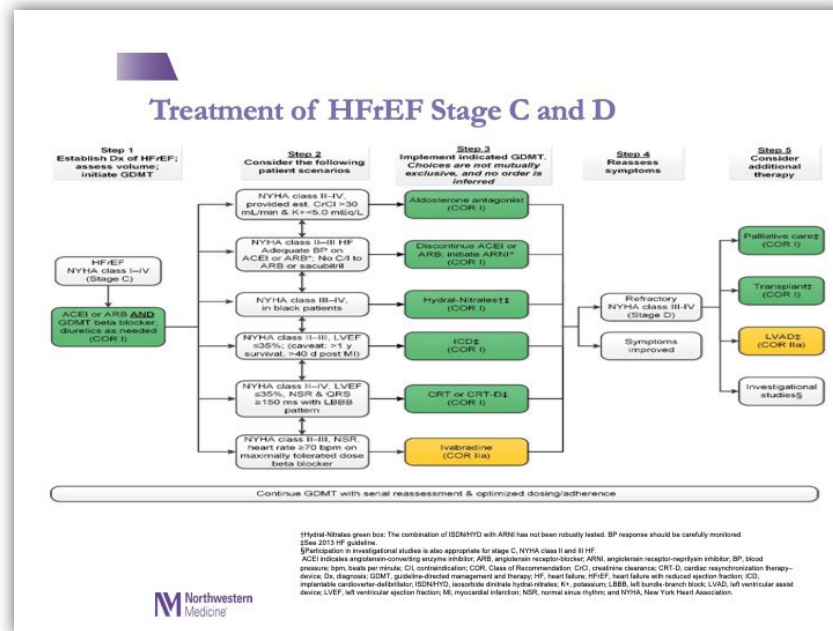
Realize that just like there are statistics that Dr. Davidson shared with you about mitral valve disease, there are statistics that are just as worrisome about heart failure. Millions of people have this condition on a regular basis, it does cause death. We, as tax payers, really do pay a very large toll for the cost of heart failure, both direct and indirect. So, there are reasons that we should be concerned – public health reasons, economic reasons, and importantly, quality of life and duration of life.



# Treating Heart Failure



**Dr. Yancy:** I share this diagram with you to let you know that many of you, I'm confident, have heard the diagnosis of heart failure within your family circle - from physicians, from friends, from nurses. I want you to appreciate that what we used to say about heart failure 15 or 20 years ago is no longer accurate. We now have very appropriate and proven strategies to treat this condition. That's important in the context of what Dr. Davidson is going to tell you. As physicians, we follow this template - you see before you - that is embedded in a concept that's known as the guideline. A guideline is really a set of directives to help physicians know how to approach the condition.



I'm sharing this with you today - as patients - so you know that we're not guessing when we treat you for heart failure. We're not playing a hunch, nor are we using therapies that are not proven. This graphic demonstrates that there is a strategy in the way we think about heart failure. There are proven therapies to treat it.

Those proven therapies fall in a number of categories. The first thing we have to do is take a picture of your heart. If it looks like the picture that I just shared with you, we know that there are certain therapies that we necessarily have to use. We use what we would call an "algorithm" that's before you to make the right decision to help you as much as possible.

**Translated Into Clinical Apps**

**TreatHF App**



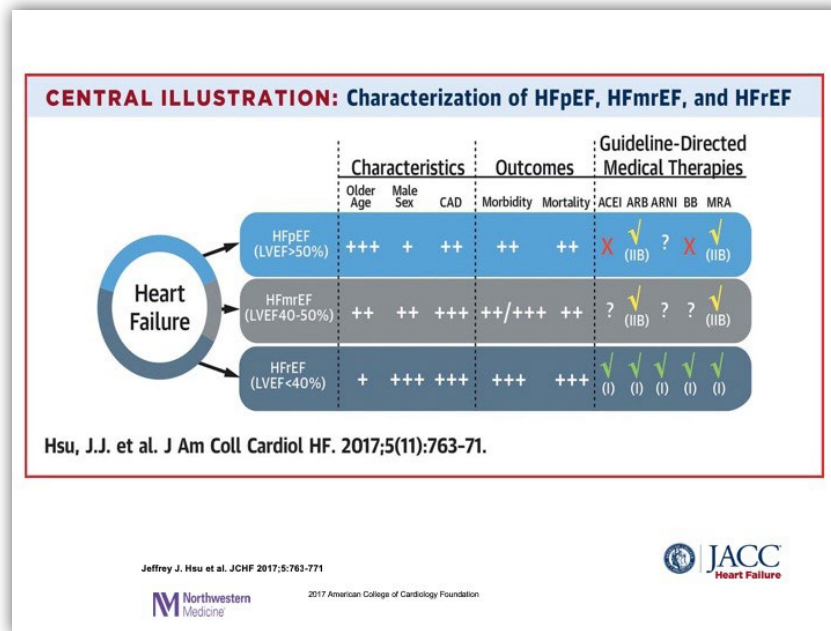
This App helps clinicians confirm which therapies are suggested for their symptomatic heart failure patients with reduced ejection fraction (HFrEF) and provides guidance on the use of each therapy.

- Enter patient indications
- Review individualized next steps for medical therapy
- Email or print a summary of the next steps
- Reference detailed information on:
  - Initiation, titration, and monitoring of each medication
  - Guidance for optimizing your overall medication strategy




One of the things that we talk about in today's world is... Is there an app for that? Well, guess what? There is an app for this. Over the years, we've helped to develop some of these guideline statements. One of those times we actually developed this TreatHF app. It's in the app store. We make this easily and freely available to physicians and care providers so that on the phone can be these guidelines - these directives on how best to care for heart failure when it occurs. That's incredibly important because any other therapies that happen need to happen after you've been treated as well as possible.

Let me be certain that I help you appreciate the fact that not all heart failure is the same. The heart failure that Dr. Davidson is going to describe for you is where the heart muscle is weakened. But sometimes, the heart muscle is exactly intact. It is sufficiently strong enough. But, unfortunately, the way in which it works - it's too stiff, it's too thick, and so symptoms can still develop. Occasionally it's somewhere in between - it's not too weak, it's not too strong, it's in between. There are symptoms that happen there. For the heart muscle that is very vigorous that leads to symptoms. Many times that's an older woman with high blood pressure. For the person that has a heart that's very weak - it's someone with a heart valve problem. Or, someone that's had a heart attack. Or, someone that's had a specific heart muscle disease.



The reason we have such a focus on the mitral valve is that this valve can lead to weakening of the heart muscle. At that point in time, there are therapies we can use to treat the condition. If those therapies don't work well, we can go onto other therapies. Dr. Davidson is going to describe - probably the most important issue in trying to prevent heart failure from occurring - and that is because of early diagnosis and taking appropriate strategies to intervene sooner than later.


## About the MitraClip

**Chronic Primary Mitral Regurgitation**  
*What to do for High-risk Patients*

**Current Recommendations**

Percutaneous MV repair may be considered for severely symptomatic patients (NYHA class III-IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy, but a prohibitive surgical risk because of severe comorbidities

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IIb	B

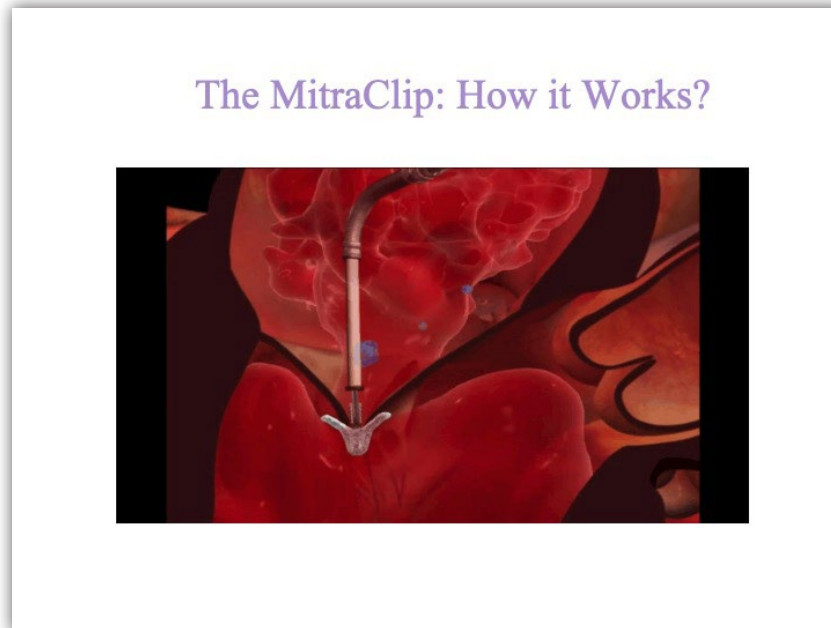


MitraClip System

**Dr. Davidson:** I think the most important point here is that “prevention” is the best option here. Then the next step, if the patient develops heart failure, is going to be medical therapy. When medical therapy is ineffective, often the mitral valve is implicated.

Traditionally... When the mitral valve was leaking severely, the only treatments were medical therapy. If ineffective, there was surgical [mitral valve repair](#) or [replacement](#). A few years back, patients that had degenerative disease, that means a problem with the valve from birth, there was an approval for a device for patients that were at high-risk for surgery. This device is called the [MitraClip](#), which is essentially a staple that pulls together the leaflets of the valve that are not coming together. It improves the leak. That was shown to be effective in high-risk patients that had degenerative mitral regurgitation.

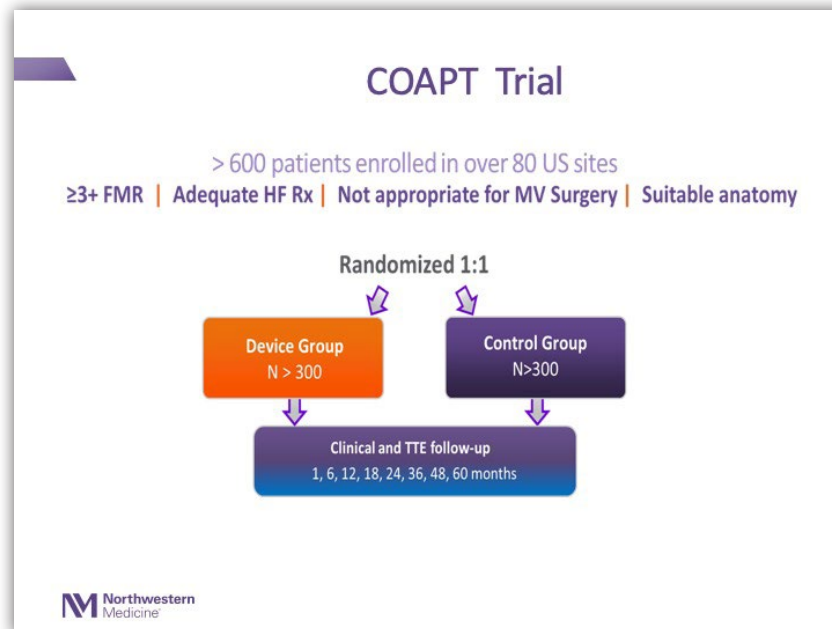
## How Does the MitraClip Work?



**Dr. Davidson:** Let me just show you how a MitraClip works. To watch this animation video, [click here](#). This is done from a leg vein. We cross from the right side of the heart to the left side of the heart, and then this tube is maneuvered across the mitral valve. We use echocardiography, transesophageal cardiology and general anesthesia. Then, we capture the leaflets where the leak is occurring, and then we pull together those leaflets with this staple-like device called a MitraClip. We can then examine it in the transesophageal echo, and under fluoroscopy to make sure the device is in the right spot. Once we do, we release the MitraClip and make sure that the leak has improved. We can place one of these, two of these, or even three of these as necessary. The majority of patients receive one to two. If done correctly, we can get an excellent result.

This mirrors a surgical procedure or surgical operation called the Alfieri stitch. It is now done percutaneous or through a leg vein. Patients are typically able to go home the next day. They can get up in bed and are eating usually later in the day.

## The COAPT Trial



**Adam Pick:** When it was understood that this worked for people with degenerative mitral valve disease, the question became, “What happens with people with weak heart muscles that are not doing well with medical therapy and have a leaking mitral valve?” As we knew before, the only thing that could be done was medical therapy. In this COAPT study that was recently completed and published late last year, over 600 patients were enrolled in 80 centers. We were one of the participating sites in this study. The patients had severe 3+ functional mitral regurgitation and were all on guideline directed medical heart failure therapy. The patients were all seen by a heart failure specialist, and they were all deemed not necessarily appropriate for mitral valve surgery due to either comorbidities, advanced age, or severe LV, or left ventricular dysfunction. The patients also had to have the anatomy that was thought to be suitable for a Mitraclip to be applied.

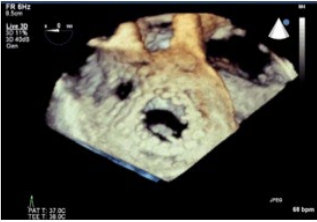
In the COAPT trial, half the patients received the device and half received standard medical therapy. These patients are followed up with. I’m going to present you some of the data that we now have available.

**Patient with Severe Functional MR  
and enrolled in COAPT Trial**

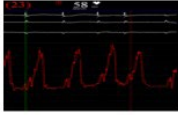
70 yo with prior MV ring for functional MR

She had recurrence of MR with severe symptoms (recurrent hospitalizations, BNP > 400) despite GDMT


Enrolled in COAPT trial and randomized to Mitraclip



Poor leaflet coaptation



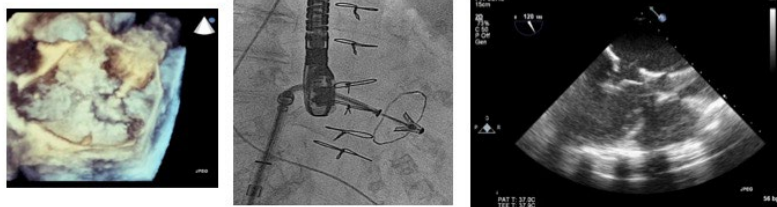
Prominent V waves (35mm)

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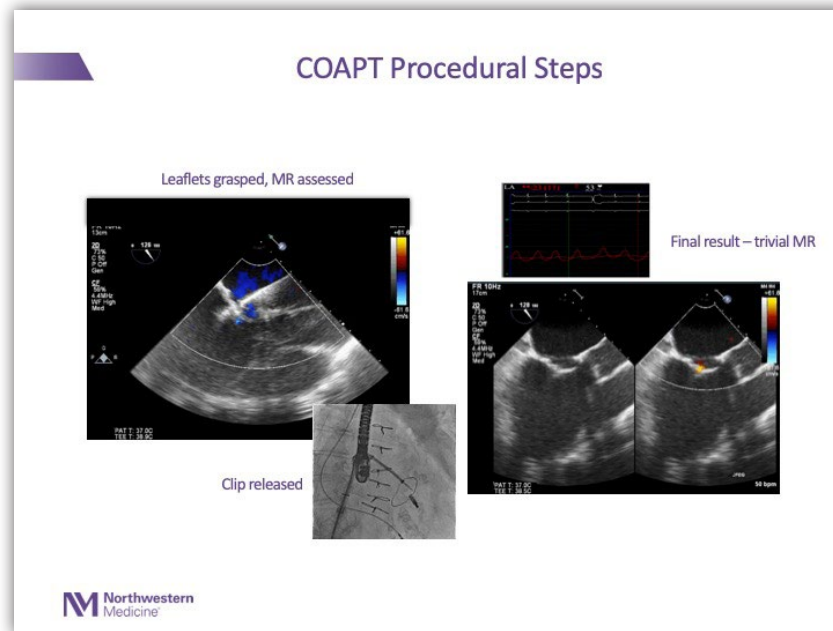
Just to give you a flavor of this... Here's a patient that we had with severe functional mitral regurgitation that agreed to be in the COAPT trial. It was a 70-year-old that had actually a prior mitral valve ring for functional mitral regurgitation that then developed further mitral regurgitation. The patient had some blood tests that showed that they were in heart failure despite medical therapy. The patient got enrolled in the COAPT trial and was then randomized to MitraClip therapy.



## MitraClip procedure, TEE and fluoroscopy



As you can see on that right-hand moving image that the valve leaflets do not coapt well. That black in the middle should not appear as leaflets come together. This produces a leak in the mitral valve. We call this “poor leaflet coaptation”.




That's the echocardiogram on the far left. There's fluoroscopy on the right that we used to guide the MitraClip across the ring. The ring is that metal wire. You can see that the MitraClip is going right through. Then, if you go over to the far right image, you'll see the MitraClip. That's that big white thing moving between: that is us trying to capture the leaflets under echocardiography. It's a little bit like playing a video game.

On that upper left image, you can see that the leaflets have been grasped. The color - the blue, and red, and orange - are the amounts of leaking left. There's a minimal amount of leaking in this valve. The clip is then released. The final result shows minimal leak.

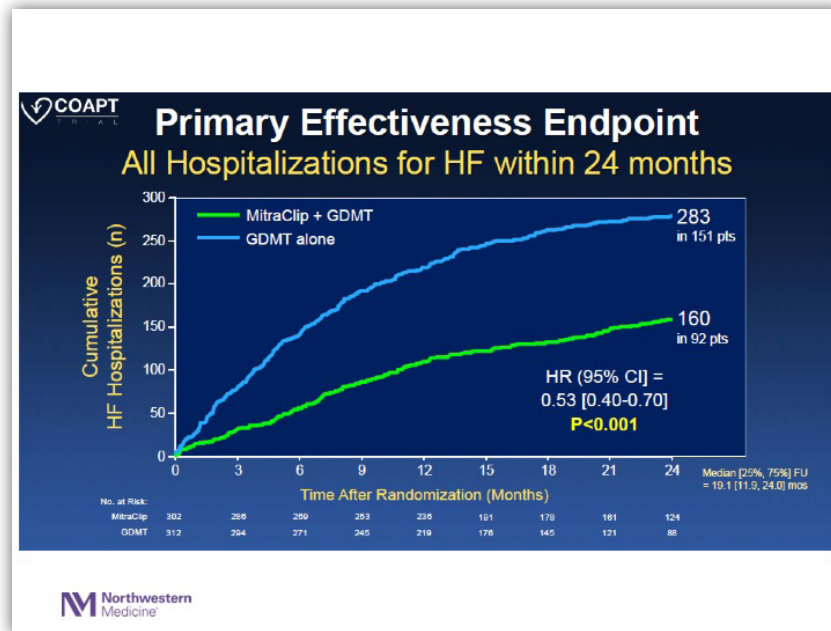
**COAPT trial results – Published NEJM Sept 2018**  
 Baseline characteristics details

- Mean age 72 yo, 2/3 male
- ~55% AF
- 2/3 high; 1/3 not high risk surgical risk
- 60% ICM, 40% NICM
- 1/3 with prior CRT, 1/3 with prior ICD
- Mean LVEF 31% (>80% EF ≤ 40%)

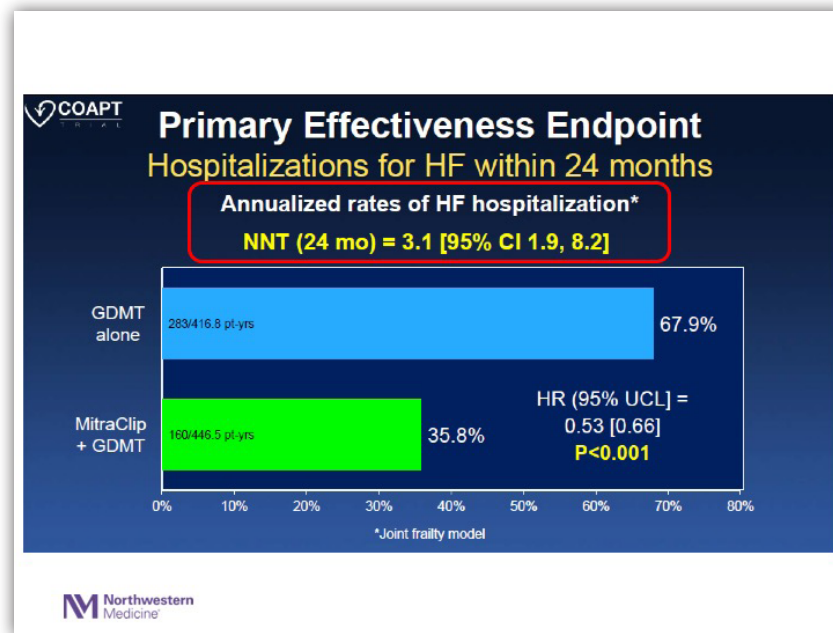
Medication Use at Baseline		
	MitraClip + GDMT (n=302)	GDMT alone (n=312)
Beta-blocker	91.1%	89.7%
ACEI, ARB or ARNI	71.5%	62.8%
Mineralocorticoid receptor antagonist	50.7%	49.7%
Nitrates	6.3%	8.0%
Hydralazine	16.6%	17.6%
Diuretic	89.4%	88.8%
Chronic oral anticoagulant	46.4%	40.1%
Aspirin	57.6%	64.7%
P2Y12 receptor inhibitor	25.2%	22.8%
Statin	62.6%	60.6%



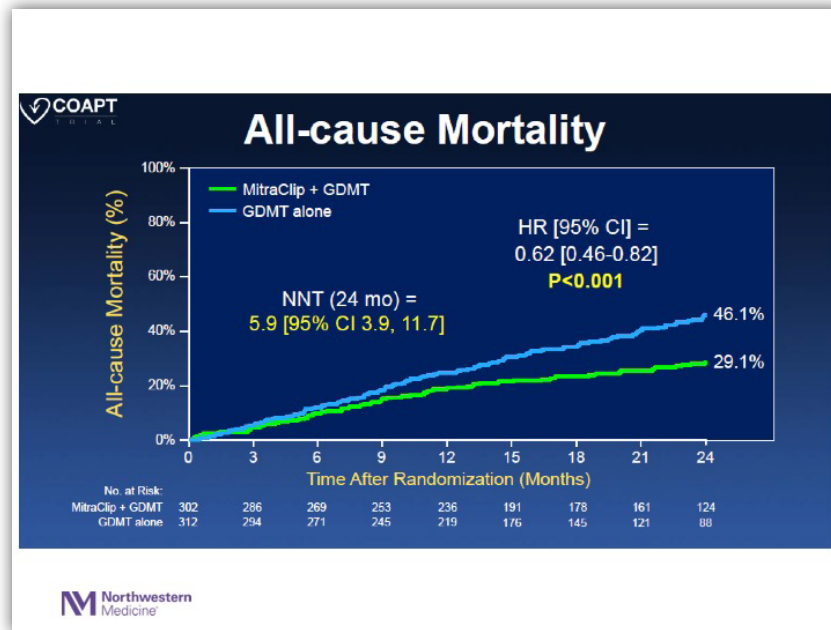
These results were published and presented at our national meeting in September and published in the New England Journal of Medicine. This is just what the patient looked like. Average age was 72. Most of them were high-risk. About a third had prior defibrillators placed in. The mean ejection fraction was 30%. Normally the ejection fraction is over 50%. These are people with severely dysfunctional ventricles.



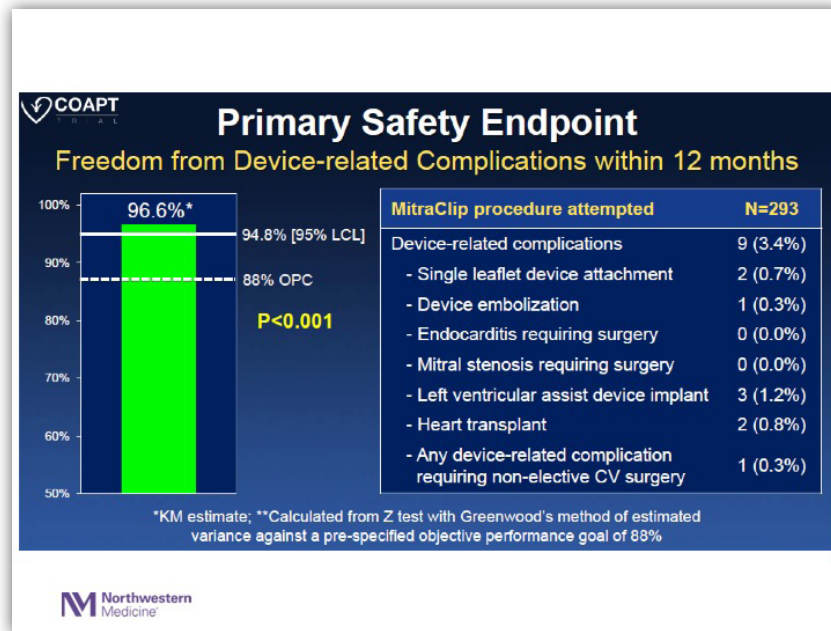
This was one of the few “home runs” you might ever see in cardiology. This is showing in the top blue bars, patients that got guideline medical therapy and how many heart failure hospitalizations they had within two years. There’s about 283 and 151 patients. If you look at the group that got MitraClip plus therapy, it was only 160 hospitalizations. That was a massive reduction - close to a 50% reduction in heart failure hospitalizations.



When we talk about these things, we ask, “How many patients would you need to treat to prevent a hospitalization?” Here it’s approximately three patients you need to treat to prevent one hospitalization. This is a huge treatment effect when you think about quality of life improvement.



That was exciting. We improved people’s quality of life. But, could we actually improve patients’ survival? The exciting part of the COAPT trial was that we did improve patient survival. Forty-six percent (46%) died within two years if they just got guideline therapy. With the MitraClip, mortality was down to 29%. That means that only six patients have to be treated to save one life, which is a huge treatment effect for anything we do in cardiovascular disease.




The next question in the COAPT trial was, “Is it safe?” As you can see on the right side, there were very minimal complications. There were only a handful of the 293 patients that had any device-related complications throughout the procedures – and through 12 months follow-up.

**COAPT**

### 24-Month Event Rates (ii)

	MitraClip + GDMT (n=302)	GDMT alone (n=312)	HR [95% CI]	P-value
MV intervention or surgery*	4.0%	9.0%	0.61 [0.27, 1.36]	0.23
- MitraClip	3.7%	6.6%	0.99 [0.38, 2.58]	0.99
- Mitral valve surgery	0.4%	2.5%	0.14 [0.02, 1.17]	0.07
PCI or CABG	2.8%	4.3%	0.62 [0.24, 1.60]	0.32
Stroke	4.4%	5.1%	0.96 [0.42, 2.22]	0.93
Myocardial infarction	4.7%	6.5%	0.82 [0.38, 1.78]	0.62
New CRT implant	2.9%	3.3%	0.85 [0.31, 2.34]	0.75
<b>LVAD or heart transplant</b>	<b>4.4%</b>	<b>9.5%</b>	<b>0.37 [0.17, 0.81]</b>	<b>0.01</b>
- LVAD	3.0%	7.1%	0.34 [0.13, 0.87]	0.02
- Heart transplant	1.4%	3.6%	0.35 [0.09, 1.32]	0.12

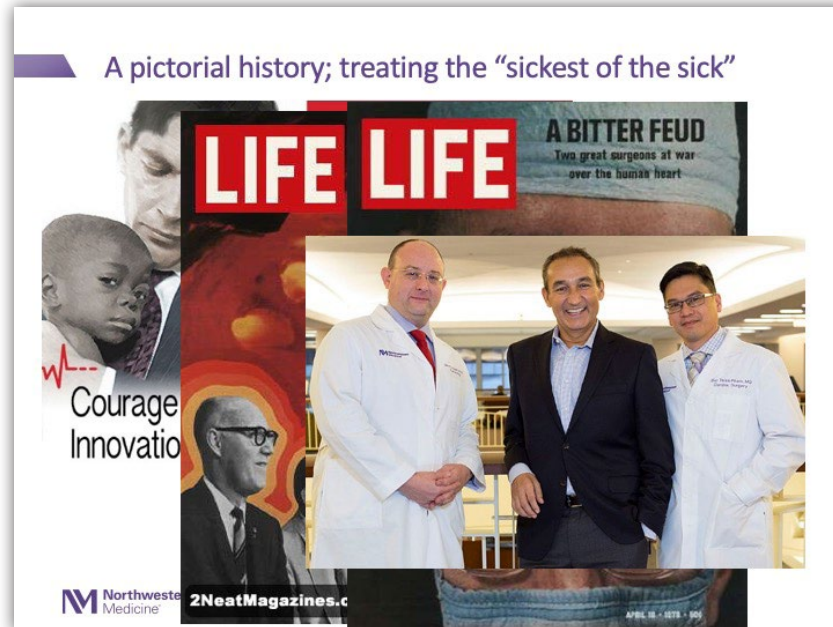
\*Unplanned. Kaplan-Meier time-to-first event rates



This is a busy slide. But, I want to highlight the bottom part of it. What's exciting here, is that patients are on guideline therapy: 9.5% went on to having either a VAD, a ventricular assist device, or heart transplant. But, with MitraClip there was over 50% reduction – only 4.4%. If you look at the number for transplant, it was 3.6% down to 1.4%. For VAD, it went from 7.1% down to 3.6%. All of these were significant improvements in the combined heart transplant and ventricular assist device alone.



## What Happens If Mitral Valve Repair Does Not Work?



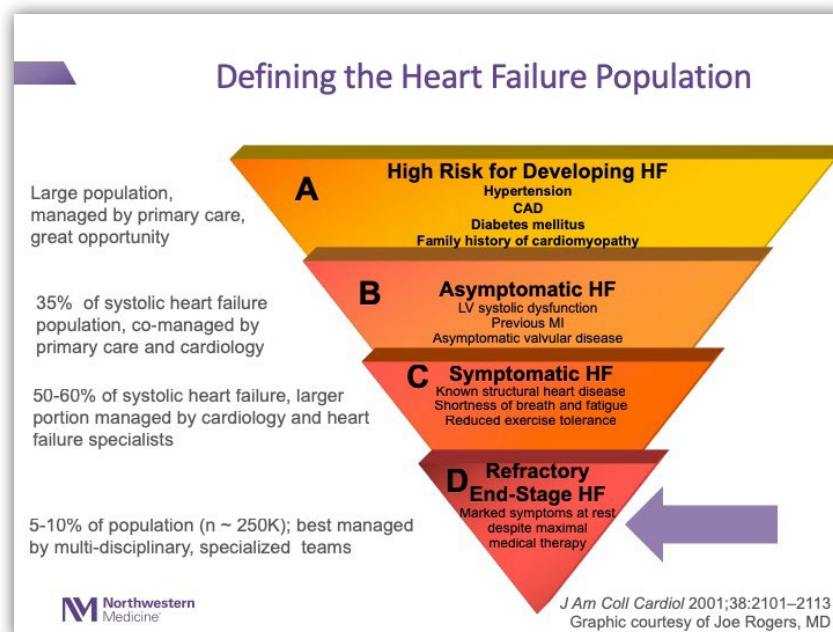
**Dr. Yancy:** 51 years ago we witnessed the first heart transplant. Think about that. It's been 51 years that we've been talking about this. We're still having to deal with this very dramatic operation for patients who have heart failure that can't be treated any other way. That's an important reason why the MitraClip approach to the mitral valve is a necessary discussion to have for everyone because there's an alternative we didn't have before.

Heart transplant was not easy. But some brave souls continued. There was ongoing discussion about what's the right thing to do. Surgeons in Texas were

famously trying to develop an artificial heart, in part enabled by the permission from Lyndon Johnson, then president, who had heart failure. President Johnson was dying of heart failure and wanted someone to develop an artificial heart to save his own life. These two famous surgeons ended up focusing on developing an artificial heart and had a famous feud. But, their progress has made great inroads and allowed us to treat many people today with technologies that are incredibly effective.

This is public information... But, the picture you see of the man smiling the most is the CEO of United Airlines, who has received an LVAD. An LVAD is a mechanical heart, and a transplant through Northwestern, supported by the medical director of our transplant program, Dr. Allen Anderson, the doctor to his right. The surgeon, [Dr. Doug Pham](#), is the gentleman to his left. This is an example of the heroic things that we can do now for people that have advanced heart failure that's not otherwise treatable.

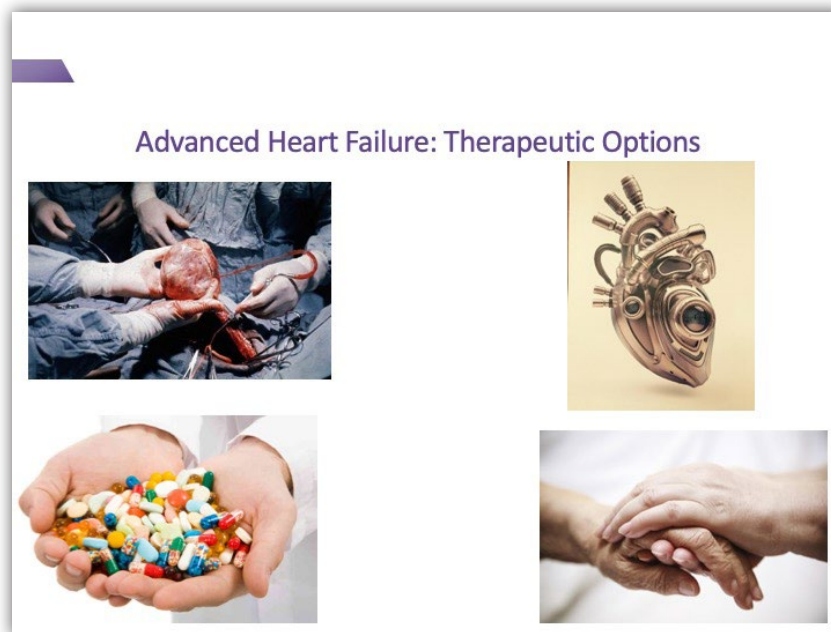
We know that they're only a few people with heart failure that end up with this kind of advanced disease, part of which is driven by the valve disease that Dr.



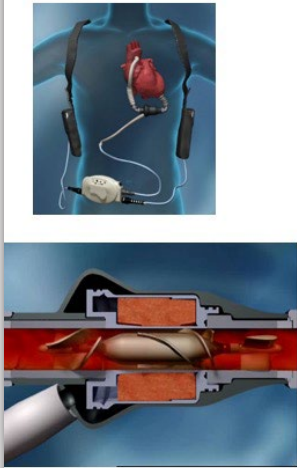
Davidson has shared with you.

You'll see that that number really is a fairly small number, measured in the several 100,000 range, an even smaller number that's attributable to this leaking heart valve. But, this is the circumstance we get when all else fails that we have to do transplants or VADs.

These are all the different therapies. You've already heard about the valve repair



that we can do through the skin, which is a stunning development. We can do the transplant, as I've shared with you. We can do the mechanical heart. Then, in the lower left, we can do medical therapy with pills – that's what I do. I give people lots of pills. Then, you can see the hand-holding, that's hospice. That's helping people at a very important stage of life.



**Patients for Whom VAD  
is the Best Choice**

- Patients awaiting transplant who are unstable on maximally tolerated treatments
- Patients who are not transplant candidates
  - Older
  - Pulmonary hypertension
  - Nutritionally challenged
  - Recent malignancy

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Medicine

This is what the mechanical heart looks like. I won't dissect all of the things you see here. But, there's a device that we can implant that is a near permanent install. It is driven by an external battery pack that is rechargeable. We've kept patients alive for many years on these devices. The devices continue to get better and better, with fewer and fewer complications. But, they're not yet perfect tools.

## Next-Generation Mitral Valve Therapies

### SUMMARY: Mitral Valve Disease Challenges and Innovation

- Mitral Regurgitation is associated with increased mortality
- Mitral valve disease may lead to heart failure which requires specific other therapies
- The COAPT trial demonstrated improved survival and quality of life in patients undergoing transcatheter mitral valve repair compared to *ideal* medical therapy for heart failure.
- MitraClip is the new standard of care for patients with functional mitral regurgitation. However, many patients are not eligible due to anatomy
- In patients with previous bioprosthetic mitral valve replacement or repair with valvular degeneration, transcatheter mitral valve in valve is a potential option.






**Dr. Davidson:** Let's talk about what we went over today and what maybe next for mitral valve devices and other valves.


"Mitral valve disease challenges and innovation" is how I summarize this. Mitral regurgitation is associated with higher mortality rates. The more leaking, the more severe the mortality rates and more frequent. Mitral valve disease can lead to heart failure, which requires other therapies. The COAPT trial demonstrated improved survival and quality of life in patients undergoing transcatheter mitral valve repair compared to medical therapy for heart failure. Remember, all of these patients were maximized on medical therapy already.

The MitraClip may be the new standard of care for patients with functional

mitral regurgitation. However, many patients are not necessarily eligible due to anatomy. Patients should be carefully selected, as they were in this trial. It's not one size fits all. In patients with previous bioprosthetic mitral valve replacement, or repair with valvular degeneration, the mitral transcatheter valve therapy is a potential option. Even with prior surgery, there may be options for transcatheter mitral therapies.

### BCVI Transcatheter Valve Trials

- PARTNER:  
– 1A, 1B, 2A, 2B and 3

  
- Cardioband Tricuspid  
– EFS

  
- Trialign Tricuspid Annulus Repair  
– US EFS



\*\*Investigational Use Only\*\*

These are investigational trials that we're performing at Northwestern. The PARTNER trials were all aortic valve replacements, from a [transcatheter approach](#) from the femoral artery. These are being done thousands a year throughout the US and are now commercially available for patients who are intermediate or high risk. This Sunday, there will be a very [exciting trial presented, which will be the PARTNER 3 trial](#), looking at patients that are low risk that were compared to transcatheter valve versus surgical aortic valve replacement. We're all anticipating these results that have been in The New England Journal of Medicine as well that day. The hope is that it will be the same as surgery as far as results. If that's the case, it can really open up this to a larger population of patients.



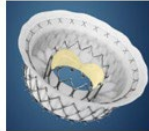
Now, Cardioband Tricuspid is essentially a ring that's placed around the mitral valve, almost like a surgical ring. This is also done from a leg vein, under


ultrasound guidance. We've now done the most of these that have been done in the United States and are really getting some very nice results. Once again, these are offered to patients that may not be good surgical candidates and are having leakage on their tricuspid valve. We previously participated in the Trialign tricuspid valve, which is another device that mirrors surgical treatment by putting pledgets to hold together the annulus and improve mitral regurgitation.

The Cardioband Mitral is a similar type of ring but now placed on the mitral side. A lot of these valves that you're seeing developed now for the mitral are also applicable to the tricuspid and vice-versa. There's a whole plethora of new devices becoming available. Everyone is really energized by the fact that we've seen such great results from the COAPT trial and other repair techniques that

**BCVI Transcatheter Valve Trials**

- Cardioband Mitral
  - Pivotal
- CARDIAQ
  - Pivotal MV Replacement- Transseptal
- APOLLO
  - Pivotal MV Replacement - Transapical


**\*\*Investigational Use Only\*\***

mirrors surgery may be available and may be also helpful.

In the more severe stages of mitral regurgitation, we're doing two trials at Northwestern: one is the cardiac, which is a mitral valve replacement, from a transcatheter approach, done transeptally - again from the vein in the leg across the septum of a heart. Then there's the APOLLO trial, which is a transapical approach, which comes up from the apex, the tip of the heart, and replaces the valve. These are more severe stages of mitral regurgitation that may not be eligible for the MitraClip.




## Questions & Answers

**Adam Pick:** Now we can move into the live “Questions & Answers” section. Since we posted the webinar announcement, my inbox has received great questions from our patient community.

### Mitral Calcification

Rose asks, “Hi Adam, I’m scheduled to have open heart surgery on May 14<sup>th</sup> due to severe mitral calcification. Is there any procedure that can be utilized to repair or replace my mitral valve without undergoing open heart surgery?”



The first question comes from Rose and it’s about mitral calcification. She says, “Hi Adam, I’m scheduled to have open-heart surgery on March 14th, due to severe mitral calcification. Is there any procedure that can be utilized to repair or replace my mitral valve without undergoing open-heart surgery?”

**Dr. Davidson:** This is called mitral annular calcification. It can cause either leaking or blockage in the valve, and usually causes both. Unfortunately, this is an unmet need for all of the techniques we talked about today. The mitral annular calcium and calcification of the valve is not treated very well by the MitraClip technique because there's also some blockage in the valve and that might cause further blockage - and, the banding techniques don't tend to anchor very well into it as well. Even the valve replacement by the catheter approach are not quite strong enough valves to hold open that calcium at this point. At this point in time, surgery still remains the only viable option for severe mitral calcification causing mitral regurgitation or mitral stenosis.

**Dr. Yancy:** Charlie, if I can add to that. Adam, please make certain that Rose knows that as we did the studies to understand if we can get to the mitral valve through the skin and make the repair happen, over half the patients that we evaluated to be a part of the study were no longer able to go forward. Either they responded to medical treatments for their heart failure or the structure of their valve. That's why you have to have a really good conversation with your cardiologist and understand what are the risks, what are the benefits, and what's best for your condition.

## Watchful Waiting

Ricardo asks, "What signals for a patient that the 'Watchful Waiting' period is nearing its end? Are there key measurements in an echocardiogram summary that alerts the patient of this?"

**Adam Pick:** Ricardo asks, “What signals are there for a patient that the “Watchful Waiting” period is nearing its end? Are there key measurements in an echocardiogram summary that alerts the patient to this?”

**Dr. Davidson:** This is an outstanding question and there’s actually a whole algorithm related to this. The first question you need to know is, “What’s the cause of the mitral regurgitation?” If it’s functional mitral regurgitation, we try to treat with medications first - except maybe secondary and then surgery. If they’re not eligible for a MitraClip or something experimental. If it’s primary degenerative mitral regurgitation, then there are a number of parameters that we utilize on echocardiography related to the amount of leaking that we can quantify related to the left ventricular function - related to pulmonary artery pressures. There are parameters that we look at in a patient that is asymptomatic but has severe mitral regurgitation.

Those should be carefully evaluated, and I will say, not all echocardiograms are created equally. You want to be examined at a center that does a lot of this work. It’s not just the cardiologist that’s doing the intervention or the surgeon, but it’s the whole team around him or her. Echocardiography, getting good quantitative measure of the amount of leak and the amount of LV dysfunction, is extremely important in order to make this decision very carefully and thoughtfully so surgery is offered at the right time - no sooner and no later.

**Dr. Yancy:** Let me agree with Charlie that this is a brilliant question. This concept of “Watchful Waiting” is not exactly something we embrace as much anymore because over the years we’ve learned that we can wait too long. If we wait too long, the outcomes may not be as good as we’d wish. There are key measurements that are completely vetted, evidence-based, improvement and be accurate. We just have to make certain that people who have mitral valve disease have an opportunity to be evaluated by someone with real expertise, studied in a lab that can get really high quality images so that a team can make this decision. You don’t want to wait too long because it can only lead to a more challenging circumstance.

**Dr. Davidson:** It is a great question. Stenotic valves typically present with

symptoms. A leaking valve, when symptoms occur, is often to the point that there's actually been significant damage done to the heart. The echocardiogram becomes the best measure to follow these patients because often we want to get to them before symptoms develop - based on dilation of the heart, LV function, pulmonary artery pressures and the like.

## Re-Operations

Lisa asks, "I had a mitral valve repair 3 years ago but within months I was back to moderate regurgitation. Recently, my surgeon brought up the MitraClip solution to reduce regurgitation. Will the MitraClip prevent me from a possible open heart re-repair in the future? Or, could the MitraClip be a long-term solution?"



**Adam Pick:** Lisa asks, "I had a mitral valve repair three years ago, but within months I was back to moderate regurgitation. Recently, my surgeon brought up the MitraClip solution to reduce regurgitation. Will the MitraClip prevent me from a possible open-heart re-repair in the future or could the MitraClip be a long-term solution?"

**Dr. Yancy:** Adam, this really is an important question because there's a lot that Lisa has embedded here. We need to understand why the surgeon believes something else needs to be done. This actually could be heart failure getting worse, and treating the heart failure might be the better option. This could be something else about the valve. It's really important to have a very comprehensive look. I think neither or Dr. Davidson can give Lisa a direct response. I wish we wish we could. We want to let her know that it's important to have a global evaluation because there may be other strategies that would help slow the process down or maybe restore her quality of life. It's really key that a team takes a comprehensive look at everything that's going on.

**Dr. Davidson:** It's an excellent point. If I was advising Lisa, I'd say she ought to be seen by heart failure specialist. Get all the best medications that you can get, see how this mitral regurgitation responds. If it does not respond appropriately to medication, the MitraClip could be an option. You'd have to see what the leaflets looks like, how much blockage there is, but it is a possibility. The first place to start would be to optimize medical therapy and then look at catheter-based options. If those are not working properly. It could be a long-term solution. Best we know, it is a durable solution at this point.

## Rheumatic Fever

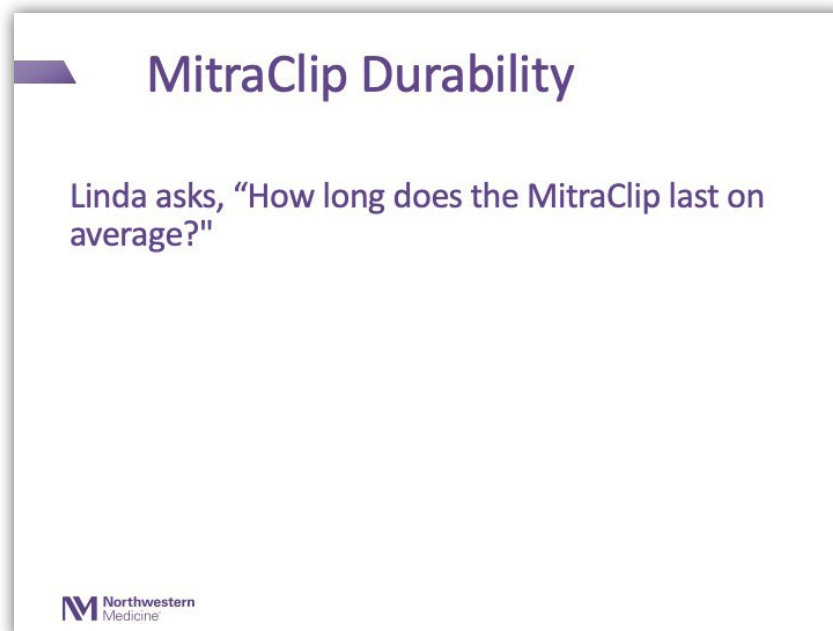
Cathy asks, “Are there options for valve replacement for someone like me who has severe mitral regurgitation due to having rheumatic fever as a child?”



**Adam Pick:** Cathy asks, “Are there options for valve replacement for someone like me, who has severe mitral regurgitation due to having rheumatic fever as a child?”

**Dr. Yancy:** Cathy, one of the things that we understand about rheumatic fever, particularly when it's been lifelong, is that the valve will develop calcium. This gets back to the same conversation that we just had - specifically being that a team has to look very carefully at the anatomy of the valve, and determine if it's approachable. Severe mitral regurgitation independently is something that needs an intervention. It's a real exercise of a lot of people coming together to decide what's that right next intervention. Whether or not replacement, like we've talked about today, is appropriate for her situation really is going to depend on how the valve looks.

**Dr. Davidson:** Typically, with mitral regurgitation from rheumatic fever, there's a fair amount of mitral stenosis as well, which makes the catheter-based options not that feasible. Often when mitral regurgitation occurs as a result of rheumatic fever, mitral valve replacement becomes the best option. Now, isolated mitral stenosis, which is not what the question is, can be often treated with balloons when it occurs from rheumatic fever. But, this sounds like it's going to be more of a surgical approach.

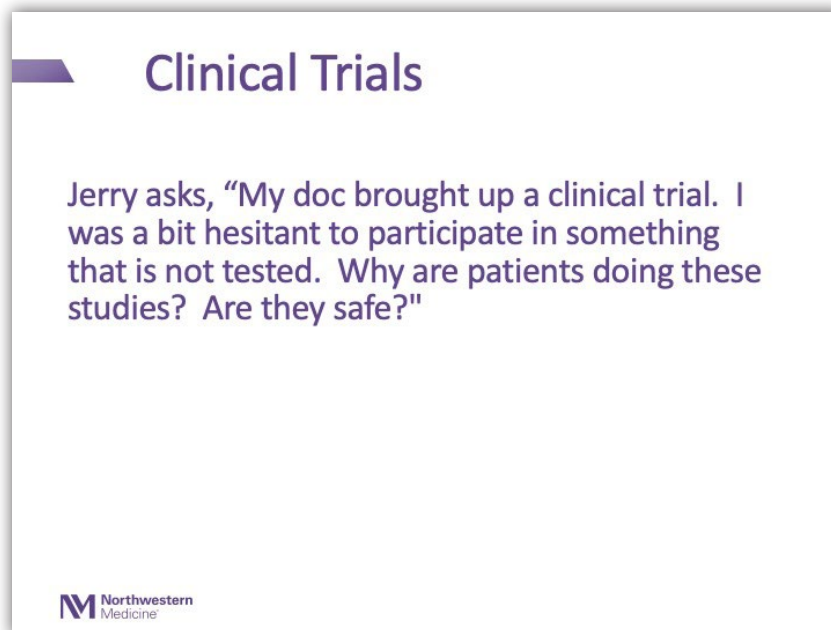


**Adam Pick:** Linda asks, "How long does the MitraClip last on average?"

**Dr. Davidson:** It's a great question. As I showed in the COAPT trial, we have two-year data that looks very durable. There doesn't seem to be any detriment on the functionality of the valve or in the amount of regurgitation recurring at that point in time. The original trial that was done called the Everest trial, also had data out for a few years. We do not have ten-year data on this yet; we barely have any five-year data that's well collected. I think time will tell. The only analogy I could make that might be useful is what we know with the surgical clip. We know that that's generally a durable approach if it works initially. We would be optimistic that this would mirror that. But, data beyond two years,


three years is not well collected at this point in time. This is a “to be continued” situation.

**Dr. Yancy:** Charlie, this really does give us the opportunity to emphasize that this is a percutaneous through-the-skin procedure. You’re saving yourself a trip to the operating room. When you’re thinking about risk-benefits and lifestyle, being able to avoid a surgery is not a trivial issue. Again, there’s a conversation that’s important to be had here. Even if you’re delaying surgery, which I don’t think this is, but even if it was that maybe a benefit rather than going to surgery earlier on.



## Clinical Trials

Jerry asks, “My doc brought up a clinical trial. I was a bit hesitant to participate in something that is not tested. Why are patients doing these studies? Are they safe?”

 Northwestern  
Medicine

**Adam Pick:** Jerry asks a question, “My doc brought up a clinical trial. I was a bit hesitant to participate in something that is not tested. Why are patients doing these studies? Are they safe?”

**Dr. Yancy:** I really would like to address this question. I’ve done a lot of work with the FDA and I’m still working with the FDA to find better ways to do clinical trials. Jerry, you really bring up an unbelievably important point. The only way people like Dr. Davidson and I know how best to care for patients is through getting data under controlled circumstances, so we can understand what works best, what doesn’t work as well. The advantage of being in a trial other than the notion of contributing



to knowledge is this... We make absolutely certain that every patient in a trial receives whatever the standard of care for that condition happens to be at that time.

The nurse coordinators that govern a trial are really tasked to be certain that if it's an indicated therapy. It's remarkable, Jerry, that in virtually every cardiovascular trial that comes forward, the group that's in the control arm, not getting the indicated therapy, or the tested therapy, actually does much better than the group in the regular population. That is patients come into trials and don't receive better care; they receive almost ideal care. That raises the bar, but that means when something's been proven to be beneficial, like the MitraClip, it's been against a very good standard of care.

I can't vouch for every trial that's ever been done. But, in general, the patients who enter a trial receive excellent care. If they're in the control group or the reference group, their outcomes are better than had they not been. A great question and one that many of us are working on to improve this going forward.

**Dr. Davidson:** Specifically device trials, and I've been doing those for close to 30 years now, it's important to have a "heart team" approach to these patients. When someone comes in with any problem related to a heart valve disease, they're evaluated by cardiology, which includes a heart-failure cardiologist. This involves an interventional cardiologist, a cardiac surgeon, and an echocardiographer, and often a radiologist to do our CAT scan imaging of these. All of us look at the patient and try to offer what are the best options. We look at medical therapy. We look at catheter-based therapies that are approved, and then those that might be investigational.

If you notice, most of these trials that we talked about are starting with high-risk patients for surgical therapies. Often the surgical therapies are known to be at a certain high risk of mortality and therefore we know the disease has a higher risk of mortality, and we're looking for options for these patients that are not necessarily commercially available. Through the work that Dr. Yancy and others at the FDA, we are now seeing early feasibility trials in the United States. Often these trials were being done in South America or Eastern Europe, patients were

being tested there and the results would come out and we didn't know how well the data were collected. What we're trying to understand here is under the best of circumstances, with the right patients, what type of results can we get? Clearly, with these trials, you should have a discussion with your physician. How many have been done? What do the results look like thus far? Understand what the risks and benefits might be for your particular situation.

**Dr. Yancy:** Jerry, the last thing I'll tell you is that there are many, many types of clinical trials. In today's world, we're using the electronic health record a lot more than we did before. We're using machine learning a lot more than we did before. We're using certain blood tests to help us to figure out who exactly is at risk and how best can we study the smallest number of people to get the biggest amount of information. Don't hesitate to raise a few additional questions about trials; they're not all the same, and we continue to change the model to make it better for the patient.

**Adam Pick:** Great question, Jerry. Thanks Dr. Davidson, Dr. Yancy. We're going to go on to another question, but before, I just want to pass along to Dr. Davidson and the entire Northwestern team, [Paul Powers is on the line](#) and he just posted, "Dr. Davidson and the Northwestern team saved my life with the first-ever mitral valve-in-valve in March of 2016. Thanks so much." Can you maybe talk a little bit about what a mitral valve-in-valve is?

**Dr. Davidson:** Thanks for joining us today Mr. Powers. He was the first one we did on that. He'd had a previous mitral valve replacement that was degenerating, not work well. We know that the surgical valves in the mitral position, typically around ten years, can start having some difficulty. His was having it and the option for him was a second operation or a mitral valve-in-valve. It's done a lot like that MitraClip. We come up through a femoral vein, through a vein in the groin, crossover from the right side to the left side of the heart.

What we used in him was a valve that is constructed for the aortic valve. That one I showed you from the PARTNER trial, the SAPIEN valve. We placed it across the degenerative mitral valve that was placed surgically, and such that becomes a new functioning valve, connecting the left atrium, the left ventricle. I remember

coming up to see him later in the afternoon and he was up eating lunch. I'm thinking, "Well, that's probably better than a second operation in the chest."

I'm thrilled to hear that he's still doing well and thankful that he let us go at this for our first case. Since then, we've done a lot of them. It's become much more common. You have to start somewhere. We've done a lot of these in the aortic position but none in the mitral valve and valve. Now it's being done [mitral valve-in-valve and aortic valve-in-valve procedures](#).

## The Future of Mitral Therapy

Adam asks, "With all of the advances we have discussed today... What is the future of mitral valve therapy? Will transcatheter devices replace the need for surgical intervention in the future?"



**Adam Pick:** With all the advances we have discussed today, "What do you think is the future of mitral valve therapy? Could these transcatheter devices replace the need for surgical intervention in the future?"

**Dr. Davidson:** That's a terrific question. Aortic valve disease, we've made huge strides in ten years, going from the extreme-risk patients to now down to low-risk patients. At Northwestern, over 75% of our aortic valve replacements are doing via catheter approach; only about 20% are done from surgery at this point. The mitral valve is much more complex than the aortic valve, as we tried

to show you today. The anatomy of that area is much more difficult and the pathology is not as homogeneous as various causes of mitral valve disease.

I would say possibly, but this is more of a long-term play. This is not going to be, flick the switch and five years from now we're going it all transcatheter. I don't think it's going to be a one size fits all as well with this. There's going to be repair techniques. There's going to be replacement techniques. There may be combinations of transcatheter repair techniques.

In the short term, these therapies will be applied primarily to high-risk patients. As we learn more, gather more information, the technology improves and then we'll eventually migrate to a lower-risk group. I do think this is quite a while before we'll see this. If you want to use the word "replace", I don't know if that will ever occur, but even transform to a 50% or more, it's going to be quite a while for that to occur.

**Dr. Yancy:** One other perspective is that not everyone develops aortic stenosis. Meaning that there's a way to avoid it. Not everyone develops mitral insufficiency. That means there's a way to avoid it. The kind of mitral insufficiency we're talking about today is largely due to underlying heart failure first. We really are rushing towards treatments and strategies that can prevent heart failure from ever occurring. If you don't ever have heart failure, then you won't have this kind of mitral valve disease. That's not something that far down the road.

We really are developing the right steps to prevent that part of cardiovascular disease from happening. It's a big burden. It's a big effort because so many people at risk, but that will take shape as we go forward. We are fascinated about the biology of some of these heart valve conditions, some of that maybe because of genetics, some of that may be because of the environment, some of that maybe because of diet or lifestyle issues. As we keep exploring not only these brilliant strategies that Dr. Davidson explained about using some of the invasive approaches, going through the skin to repair and replace valves, the group with which I work most closely is really focused on how can we interrupt

this process at the very, very beginning. It takes a lot of effort, a lot of work, but we're committed to trying to get those answers.

**Adam Pick:** Fantastic!!! With that response, we are going to conclude the Q&A section of the webinar. I want to go ahead and extend an incredibly, extraordinary thank you to Dr. Yancy and Dr. Davidson for sharing their expertise with us today. It's been an excellent session. As we end the webinar, I'd like to thank you, all the attendees, for your participation in this community event.

It's always great to get together with you online, in real time!

## HeartValveSurgery.com Resources for Patients

Since 2006, [HeartValveSurgery.com](http://HeartValveSurgery.com) has developed several resources to help you better understand your diagnosis, your treatment options and your recovery.

Listed below, please find resources created exclusively for patients and caregivers. We hope they educate and empower you.

- [Adam's Free Patient eBooks](#) - Download 7 free eBooks about heart valve disease and treatment options for aortic, mitral, pulmonary and tricuspid valves.
- [Heart Valve Learning Center](#) - Visit the Heart Valve Learning Center to access over 1,000 pages of educational information about valvular disorders.
- [Patient Community](#) - Meet people just like you in our patient community. There's nothing better than connecting and learning from patients who are sharing their stories in our community.
- [Surgeon Finder](#) - Find and research patient-recommended heart surgeons that specialize in heart valve repair and heart valve replacement procedures.
- [Heart Hospitals](#) - Learn about medical centers that have dedicated teams and resources that specialize in heart valve therapy.
- [Adam's Heart Valve Blog](#) - Get the latest medical news and patient updates from our award-winning blog.
- [Educational Videos](#) - Watch over 100 educational videos filmed by the Heart-ValveSurgery.com film crew about heart valve surgery.