Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/bridging-distances-in-pah-bringing-best-practices-to-the-people-through-telemonitoring/24051/

Released: 10/11/2024
Valid until: 10/11/2025
Time needed to complete: 60 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Bridging Distances in PAH: Bringing Best Practices to the People Through Telementoring

Announcer:
Welcome to CME on ReachMD. This activity titled, Bridging Distances in PAH: Bringing Best Practices to the People Through Telemonitoring, is jointly provided by Global Education Group and Iridium Continuing Education, and is supported by educational grants from Actelion Pharmaceuticals US Incorporated, a Janssen Pharmaceutical Company at Johnson & Johnson, and Merck Sharp & Dohme LLC. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Kolaitis:
Hello, and welcome to our program titled, Bridging Distances in PAH: Bringing Best Practices to the People Through Telemonitoring. I'm Dr. Nicholas Kolaitis, Assistant Professor of Medicine in the Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine at the University of California San Francisco. I'm joined today by my esteemed colleagues, Dr. Jean Elwing, Professor of Medicine in the Division of Pulmonary, Critical Care, and Sleep Medicine at the University of Cincinnati in Cincinnati, Ohio, and Dr. Katharine Clapham, Assistant Professor of Cardiology, Associate Professor of the Pulmonary Hypertension and Dyspnea Clinic, and Director of Pulmonary Research at the University of Utah in Utah.

Our disclosures are on the screen.

This educational activity is supported by an independent educational grant from both Merck Sharp & Dohme LLC, and Actelion Pharmaceuticals US, a Janssen Pharmaceutical Company of Johnson & Johnson.

The learning objectives for today's program are to summarize the best practices for decreasing the diagnostic interval in PAH, to evaluate the scientific evidence supporting the use of current and emerging therapeutics for PAH, discerning their current and potential roles in treatment and management of this disease, to explain how to implement newly refined risk assessment tools into practice even when practicing in remote settings, and to integrate telehealth and telementoring practices. This way we ensure consistent remote access to specialized multidisciplinary teams for the optimal care of PAH communication.

Dr. Elwing, would you like to start off our conversation today by summarizing what clinicians need to know about delayed diagnoses in PAH?

Dr. Elwing:
Oh, thank you, Nick. Thank you for asking that very important question, and thank you for inviting me to share this conversation with you. So we know that pulmonary arterial hypertension is a progressive disease, and it is not cured. We do, however, have many treatments that have more than doubled survival in our patients now reaching 10 to 15 years, but it's still high risk and they still face poor prognosis, especially when the diagnosis is delayed. So I'd like to talk to you a little bit about that because I think it's such an important thing people be aware of that our patients go through multiple visits, on average, five primary care physician visits and three specialist visits before they reach their diagnosis, and that takes over 2 years in many of our patients to reach that final diagnosis of pulmonary arterial hypertension. And they're treated for other conditions during that time, which delays the time to getting the right management.

Dr. Kolaitis:
Thank you, Dr. Elwing. I'm now going to discuss some of the challenges in diagnosing PAH, because once we understand the challenges, we can understand where we need to act to change practice.

As you know, patients with pulmonary arterial hypertension often present with very nonspecific symptoms. They might present with insidious onset dyspnea and fatigue, but more of the advanced findings that we associate with pulmonary arterial hypertension such as chest pain or syncope or fluid retention don't occur until patients are at significant risk of death due to very advanced disease. And early on, our patients may present with just shortness of breath of unclear etiology, which leads to a diagnostic challenge, because pulmonary arterial hypertension is such a rare disease that many frontline providers don't think of it in their differential when a patient presents with dyspnea.

Another challenge that we're faced with is that many patients live very far away from accredited centers, or Centers of Excellence, who know how to manage patients with pulmonary arterial hypertension. Take, for example, a patient that lives in rural Montana, and their nearest center is Salt Lake City. That means that there are over 550 miles driving away from the Center of Excellence, which is over 9 hours. And so these PAH care center deserts leads to a further delay in diagnosis, because the frontline providers and the community, the medical community in some of these places, doesn't have an awareness of the existence or of the importance of diagnosing pulmonary arterial hypertension early.

In addition to that, many patients with PAH face multiple issues related to social determinants of health. As we talked about, distance from a center is an important thing. Care in these centers is highly specialized, and if patients have transportation issues, this could lead to delayed diagnosis because they don't end up coming to the center due to these transportation issues. Medical literacy is really important, not only in our diagnosis, but in our care for these patients because some of our therapies are very complex and hard to tolerate. Housing and access to reliable refrigeration is important for some of our patients because some of our meds need to be refrigerated. The cost of treatment, it can be quite burdensome for patients, and so financial resources impacts how care is delivered. Additionally, the diagnosis of pulmonary hypertension is associated with loss of ability to work, and so income can be affected and mental health can be affected as well. So all these different factors come together, and they can delay diagnosis, they can delay treatment, and they can impact our care in these patients.

Dr. Elwing, I want to talk about the geographic barriers that we have present.

Dr. Elwing:
So one thing that has come about in the recent several years is the use of telehealth. And telehealth has its strengths and its weaknesses, but the one place I think has a great role is reaching our patients that are having difficulty finding us and traveling to us. And there's many advantages that I'd like to point out, one is it's cost savings for our patients. They have less cost with driving, taking care of their vehicle, staying overnight at a facility that may be quite expensive for them. So that's one. The second is quality. We love our primary care providers, but our patients that have PAH need to see a specialist that focuses on this illness because it is so very complicated, and it's one way they can improve their quality of care by having that backbone or their primary care physician, but adding a specialist in that may only be accessed in some occasions virtually. And more timely appointments, earlier diagnosis. We talked about the delay in diagnosis that is real and ongoing in our patients. Anything we can do to reach patients earlier, we want to do, and we can reach patients earlier if we can go through means of virtual visits to discuss with them, evaluate, and get that diagnosis secured more quickly. And education. We have a lot of ways we can reach people virtually, and we can utilize that for our PAH patients to teach them about disease, teach others about this disease, and support them through virtual support groups.

And through all of these efforts, we can personalize their care. If some people need more attention to titration of medications or follow-up of their heart failure, we can do that because we have that way to touch patients more easily through this virtual means. So we hope adding this all together gives us better outcomes.

Do you agree with that, Nick?

Dr. Kolaitis:
I agree completely, and I think that was a great recap of where we are with telemedicine and how it can help our patients.

Dr. Elwing, as we begin Part 2 of this program, could you walk us through the diagnostic process in PAH?

Dr. Elwing:
I would love to. And I think this is a really important thing to talk about, because this is where patients get delayed and have worse outcomes. So increasing the awareness of the symptoms associated with this condition is so very important.

So as you mentioned in a previous session, the initial symptom of pulmonary arterial hypertension is often dyspnea. It starts with

dyspnea on exertion and then progressively worsens over time. And as disease progresses, patients start to have additional symptoms, like chest pain, lightheadedness, they might start to retain some fluid in their lower extremities, some lower extremity edema. And then in really advanced situations, they start to feel presyncopal and syncopal. So sort of that whole myriad of symptoms can be associated with this condition. But early on, the most common thing is some shortness of breath with activity.

And when a patient presents with those symptoms, the physical exam can really help to discern what those symptoms are coming from. And in our PAH patients, on cardiac exam will oftentimes hear a loud P2 from the closure of that pulmonic valve and a tricuspid regurgitant murmur over the left midsternal border, and that's a systolic murmur. And when our patients start to retain some fluid, we can appreciate that, of course, by edema, but also hepatojugular reflux or jugular venous distention. And then if we palpate over the anterior chest, we might feel an RV heave. And in late stage, we'll appreciate things consistent with right heart failure, like ascites. And of course, we do not want to meet people when they're having syncope and they have right heart failure with ascites. And I'm sure, Nick, you've met many patients in that situation, and you wish you could have turned back the time to get them diagnosed and sent to you when they were just dyspneic.

Dr. Kolaitis:
Absolutely.

Dr. Elwing:
Yeah, it's really heartbreaking. And so how can we change that? Well, knowing what the symptoms are will help. And putting that together with our colleagues, our primary care physicians, those out there, doing ER and urgent care, doing their history and their physical and their basic assessment, and then thinking about pulmonary hypertension, doing basic tests and imaging and getting patients to the point of a right heart catheterization for diagnosis.

Now, those tests can be done by many different providers, but the people who are doing the most in terms of the labor to get patients to us are primary care providers, urgent care providers, ER providers. And they're doing the basic tests that prompt the thought, could this be PAH? They do blood work, and the common things that are looked at are blood counts, metabolic panels looking at renal function, liver function. And one thing that oftentimes tips us off is the BNP or NT-proBNP. EKGs that show some RV changes and imaging telling us, hmm, this could be pulmonary hypertension, because you have lack of certain changes, no infiltrates, interstitial lung disease, or things of that nature on the imaging of the chest, but changes on the echo that say, hey, the pulmonary pressures may be up, the right heart must be having a little bit more stress, it's enlarged, it's dysfunctional. And that'll prompt us to get to someone like me or you to say, hey, what else do we need to do to sort out is this PAH? Or is this another condition that we need to understand so this patient can be treated properly?

And when I see a patient, I'm sure you too, Nick, we do a very deep dive into the previous evaluation. We look at all the things that have been sent to us, and then we do additional blood work, additional imaging, sometimes more testing to look at exercise capacity, and a right heart catheterization. And the right heart catheterization, of course, is the litmus test. That tells us, is there high pressures? And if it's high, is it from the heart? Or is it from the lungs? And then, of course, we have still some work to do to figure out, is it PAH? Or is it another form of pulmonary hypertension that's from the precapillary nature, meaning it's from the blood vessels in the lungs? So is that similar to what you do, Nick?

Dr. Kolaitis:
Absolutely. And I think that, you know, this multimodal assessment is absolutely necessary to figuring out what's causing the pulmonary hypertension as well as what the best way to treat it is. And having this done in a center where the providers are aware of pulmonary hypertension and how to best manage it is really the standard of care.

Dr. Elwing:
So this disease is relentless, and if we don't diagnose it and we don't treat it. It progresses, and sometimes very rapidly. And the way we get to the best management is through the things we talked about. We need access to specialists. We need frequent monitoring, and we can do that by face-to-face visits and virtual visits. And we need to optimize medications. This is not a disease where you start a medication and then leave it alone. We're constantly changing, tweaking, optimizing. And of course, we need support. It's not just us; it's a team that makes these patients have good outcomes: us, our nurses, our RTs, our nutritionists, our social workers, and all the staff we work with in our hospitals for optimal care and optimal outcomes.

Dr. Kolaitis:
Dr. Elwing, I was wondering, you know, access to care is challenging because of geographic barriers and distance and also social determinants of health that might limit a patient's ability to come to your center. So are you using telehealth? And how do you think telehealth might play a role in improving the diagnosis of pulmonary arterial hypertension?\

Dr. Elwing:
Well, Nick, I think we both know there's too few PAH specialists. There's too few rare lung disease specialists and rare disease specialists. So it helps us expand our reach, touch more patients, hopefully improve more lives through the things we've learned from all of the people we've spent our careers sharing knowledge with. And I think that's where telehealth has really played a role, at least in my mind, and I do use telehealth especially for rapid follow-up, people that need extra attention with right heart failure and medication management, and discussing results. People want to be able to have some time to say, hey, what does that rate heart cath look like? Am I making progress? What risk am I at or worsening? And I think that's been a very, very important role of telehealth. We do you use it in so many ways every day. We do synchronous visits, asynchronous visits, remote monitoring. And each of those are different, and each have an important role.

Nick, are you doing mostly synchronous virtual visits? Are you doing electronic medical record electronic visits? Are you doing anything like that?

Dr. Kolaitis:
We're actually doing all sorts of things. So synchronous modalities are used all the time. For example, earlier today I had a whole clinic that was a synchronous modality of clinic visits. The asynchronous review occurs before and after I see every patient where we review the data, sometimes in a multidisciplinary review with our radiologists or cardiologists or our interventional radiologists as well. So we can do an asynchronous modality and do it in a multimodal assessment with a multidisciplinary group.

And we're using remote monitoring more and more. There are remote monitoring tools to assess things like 6-minute walk distance. There are remote monitoring tools for, you know, activity. And you know, in other lung diseases, we are frequently using remote monitoring to measure breathing tests. Our clinic, in our lung transplant clinic for example, developed a remote monitoring tool that monitors our patients' lung testing via spirometry and home spirometry on a regular basis. And so this allows us to expand our care outside of the individual prescribed visit to a continuous care model throughout the course of a patient's disease.

Now, let's turn to discuss the best practices for assessing risk in telehealth. Dr. Elwing, when do you think we should do a risk assessment in patients with PAH?

Dr. Elwing:
Well, I would say at every interaction with the patient that's a scheduled visit. And if we're seeing a patient intermittently by video visit, also during those times if we think there's been a change in status. Nick, are you doing risk assessment at most every visit for your PAH patients?

Dr. Kolaitis:
Yeah, I'm doing it at baseline and at every follow-up visit as well. We actually use some of the risk prediction algorithms in our HER and have built a scoring system using that.

Dr. Elwing:
Yeah, we did too, and I think it's been very helpful because not only can you assess at that point in time, but also you can track more easily. And it really is very helpful when you're following these patients for years, and many of them are doing well, and then all of a sudden things start to change. So you can pick up subtle changes in their status by really monitoring in a standardized way. And I'm going to talk a little bit about that. So we recommend, as a group of PAH providers, to risk assess at baseline and every visit thereafter every 3 to 6 months, even when patients seem stable because we may miss things with our routine questions. And we want to prevent patients from getting worse. We want to augment therapy so that's why we take every opportunity to reevaluate in a standard way.

Dr. Kolaitis:
Why do you think it's so important to perform risk assessment so frequently in patients with PAH?

Dr. Elwing:
So let's talk about what risk tools we can use. There's several out there. And I'm sure, Nick, you have the same approach: use one of them. That's my recommendation. And whatever you use, use it consistently because it's hard to use one tool and then another tool and then another tool, and you can't track that easily over time. What do you recommend when you teach about risk stratification?

Dr. Kolaitis:
Although our risk prediction tools might say that somebody's low risk, you know, if there's some other sign with them that makes you concerned, something else that keeps you up at night when you're thinking about that patient, don't just use the risk prediction tool; it should be used in conjunction with your clinical assessment to assess the patient's overall risk.

Dr. Elwing:

Oh, very true. And the whole picture, and sometimes more, right? Additional testing when things don't seem exactly right.

Dr. Kolaitis:
Yep.

Dr. Elwing:
So one tool I'd like to mention is the ERS/ESC 2022 guidelines tool for risk assessment. And that looks at patients on their initial evaluation and uses a 3-strata approach. And that tells us in groups of patients that are in registries, if you have certain features, what your risk of having a poor outcome in that first year would be. And your low-risk patients having less than 5% mortality in that first year. And the high-risk patients having more than 20% mortality in that first year. So very, very significant differences in these groups.

And we really look at the things we've discussed already in this series. We look at signs of heart failure. We look at how fast things are progressing. If patients are passing out, which is a very poor prognostic sign. We look at their functional class, which we need to assess at each visit. And their walk distance, which we look at in terms of their functionality and exercise tolerance. And we can use other testing, like exercise testing, BNP which is a biomarker for us in terms of volume and stress on the right heart, echo looking at several parameters, cardiac MRI, and hemodynamics. And what we need to do is look at that big picture when we first see patients and see where they land in terms of their risk. And as you said, Nick, this is not 100% perfect, but it gives us an idea. Does this patient need two medications that are oral and started at the same time? Or do we need to talk to them about parenteral therapy? A very different approach, a very different discussion. And we both talked about the importance of this and the fact that it is something we use routinely, but when looked at amongst PAH providers, only about 50% of the time it's being used.

So our message, I think, from both of us, is think about risk stratification and not just think about it, actually use it and use it consistently, and it will be very helpful in terms of your understanding of how the patient is doing. Do you have anything else to say about that?

Dr. Kolaitis:
Yeah, I mean, I think it's probably a good idea that we go through some of the risk prediction tools. And so maybe you could tell us a little bit about some of these tools.

Dr. Elwing:
Oh, very good. So I did mention the ERS/ESC 2022 guidelines and their initial 3-strata model. And on follow-up, they use a 4-strata model that helps separate out patients a little bit more. And I'm going to talk to you about that.

You can choose to use the ESC/ERS guidelines or, and many times in the US, we use REVEAL, and that's based on the REVEAL registry. And when I meet a new patient, I use REVEAL 2.0. As you said, Nick, I have it in the EHR, and I'm able to plug those numbers in and get a risk assessment and have that be in their computer profile to look at going forward. And then on follow-up, I try to use something a little less invasive, and I use REVEAL Lite 2. And you can see that here, it looks at parameters that are easy to obtain, their walk, their BNP, their renal function, their functional class, their heart rate, and their blood pressure. And even when you're seeing someone virtually, you can get several of these factors quickly from their outside labs, talking with them, and maybe even doing a virtual 6-minute walk.

What about you, Nick, what are you using on follow-up?

Dr. Kolaitis:
Yeah, so I do the same approach. I'll use REVEAL 2.0 at my initial assessment, and then I use REVEAL Lite 2 on my follow-up assessment. This is more of a sort of just familiarity with the practice, rather than why we've chosen REVEAL over the ERS/ESC calculator. But you know, we just have a lot more historical familiarity with it at our center.

I think the other reason I like the REVEAL personally is that you can put people into low, intermediate, or high risk with either 2.0 or REVEAL Lite 2. But the scoring system is also a continuous scoring system. So even within the categories, a 1-point increase in REVEAL score is associated with poorer outcomes. And so rises or changes and even 1 point on the REVEAL are associated with these bad outcomes, and so it could inform my treatment decisions. And so I like the idea generally of risk assessment tools that are using a more continuous distribution for their scores rather than categories. This being said, the category models do work well. And I think you'll tell us a little bit about the 4-strata model going forward.

Dr. Elwing:
Yes. And I think that that is a very important point, that just because you're in that intermediate risk, which many patients are, about 70%, doesn't mean everyone in that intermediate risk is going to do as well as other people. So the lower part of intermediate risk actually has a much better outcome than those with the higher score. And you can see here at baseline and at follow-up, those patients who have low-intermediate risk track more with the low-risk patients, and those with the high-intermediate are closer to the high-risk

patient. So really, we need to look at them differently, treat them a bit differently, and a bit more aggressively in our high intermediate-risk patients, knowing that if we don't act appropriately for them as an individual PAH patient, we won't have as good outcome as we would like. And the goal always, of course, is driving patients to low risk. That's always our goal when we risk assess patients.

And you know, when we look at the different ways to risk assess I talked earlier about the 4-strata model and that was recommended by the 2022 ERS/ESC guidelines, and that gives you that low-risk group, a high-risk group, and in the intermediate as low-intermediate and a high-intermediate. And their risk calculator is very simple. It looks at functional class, walk distance, and BNP or NT-proBNP. You get those values, plug them in, and then you get a score.

Dr. Kolaitis:
And actually, what I like to do is, when I'm sitting in clinic with them, I will open up these risk calculators online and I will plug their values in while with them. And so what that does is it allows me to then say to a patient, look, objectively this is your risk score, and that helps me have conversations with them about treatment decisions.

Dr. Elwing:
A very, very important point. And that's one thing I think patients should be aware of, these risk assessments. And providers should be aware that these are available in some of our electronic medical records, but also online that we can plug in the numbers quite quickly. So a very important point.

The other thing I think we should mention is the importance of an accurate – as much as it can be – functional assessment, looking at functional class I through IV in our patients, and knowing that when we use this tool face to face, it might be a little bit easier because we're watching our patients walk to the visit, we're watching them get up to the examination table, but when we're seeing them virtually, we're going to have to ask them a little bit more questions. And the same rules apply virtually or in person, that the functional class I person is easy; they have no limitations. The functional class IV person is short of breath with any activity, and that II and III are the ones we really have to tease out. And the functional class II patient is slightly limited. They're going to be able to do all their routine activities, but when they need to go up the stairs, they need to carry groceries, they need to do their laundry and carry it up the stairs from the basement, they're going to be winded. And the functional class III patient is going to be short of breath with routine stuff around the house, day-to-day activities, dressing, bathing, those kind of things. So we really have to spend a little bit of time to hone in on their functional status and then plug them into the functional class we really believe they are to make these risk tools work as effectively as possible.

Anything to add on that, Nick?

Dr. Kolaitis:
No, I think that that's great. And I think, you know, we can be using these remotely as well. Patients can do their self-assessments of these, and that can help us in terms of treatment decisions because the patients know better than anybody how they're feeling.

Dr. Elwing:
Oh, very true. Very true.

Dr. Kolaitis:
With regards to telehealth, how do you think risk assessment can be implemented remotely? We talked about this, but what extra tools could we use besides just asking patients how they feel?

Dr. Elwing:
Well, we do have some ways to assess functionality in terms of exercise tolerance, and one we could do, a smartphone-based 6-minute walk test, but that requires access to a smartphone, ability to download apps, and access to the internet most of the time because it uses GPS. So you need a little bit of resources to be able to do that. You could use a test called the Incremental Shuttle Walk Test, where you have cones 9 meters apart, and you have increasing rate of walking from cone to cone, and you see how the patient fares with that. Or you could use some simpler tools like pedometers, accelerometers, actigraphy. And many of those can be very simple. The step counters can be something that is used without any access to WiFi, or something you could download once you get home to your home internet. So really, I think you have to ask the patient what resources they have, how comfortable they are with this technology we're asking them to use, and then figure out what might work for them.

Is there anything else you use, Nick?

Dr. Kolaitis:
Those are the ones we use. But I'm really interested to learn about tele echocardiography. Maybe you could tell me a little bit about that.

Dr. Elwing:

Oh, boy. Are you using this?

Dr. Kolaitis:
Not yet.

Dr. Elwing:
So I'm not either, but I think this is going to be important tool for us in the future. When a patient is not able to access an echo lab or we're seeing them at a remote location, this is something we could use to see those very important images, the 4-chamber view of their heart and quickly assess their RV based on this limited echo technology. And I'm sure it will get better and better over time, but I think this will be something we could add to our physical exam. We'll listen to their heart, and then we'll look at their heart briefly, get a few of the very important images, and that will help us understand how much improved is their right heart and if we need to further optimize their medications. So in addition to the risk assessment.

Dr. Kolaitis:
We will now move on to discuss the best practices in personalizing care in PAH.

Dr. Elwing:
What do you think about the success of telehealth? How can we use it successfully? And when it's not successful, how do we pivot and say we need to do this a different way?

Dr. Clapham:
Yeah, I think at first understanding all these factors might take some time or some initial interactions to really grasp what the barriers are to successful telehealth. So we might start off planning for a virtual visit using video, and then realize, oh, the internet connection isn't good enough, or the person has trouble interfacing with the virtual platform. And so sometimes if that happens we are able to pivot and think about alternative strategies. Like, for example, if your internet at home doesn't work well, do you have access to a hotspot from a library? Or are there other ways we could work around that? Or do we need to think of a different type of visit? A telephone visit? Are there ways that we can be flexible there? And if those strategies don't work, we may end up needing ultimately to return to the in-person visit.

Dr. Elwing:
No, very important point. And I think we have to personalize this, right? Like we try to manage patients in a way that fits that individual and their needs.

So what are some of the strategies you have used to enhance patient outcomes with telehealth? How do you think it really plays a role? And where is it most valuable?

Dr. Clapham:
So in our practice, we frequently use telehealth to monitor therapies, to talk about side effects of new medications, and a lot of that can be done effectively remotely. We also use, you know, telehealth to figure out how to make best use of our in-person visits. So if we know that we need certain testing, we'll try to collect as much of it as we can at once and we'll also coordinate it with a clinic visit so that we can make the best use of the time. And telehealth often enables us to figure out what we need at that in-person visit and how to get it done. So that's how we've used it in our practice.

I think it's also exciting that there are some new monitoring strategies for how patients are doing from a risk perspective. Like I said, a lot of our testing we end up doing in the office but I think as our telehealth tools grow, it is more possible to do some of this risk assessment remotely. And one example that we've discussed in this course has been remote exercise testing. So there are several different strategies people have looked at to try to figure out how we can get at someone's exercise capacity remotely. And they've looked at how well this correlates with the 6-minute walk test that we usually do in the office. And so there was a study called the PHRET study where people looked at four different types of remote exercise testing and then correlated that to the 6-minute walk. And three of the tests just involved using a timer, but one of the tests incorporated an app that guided patients through a 6-minute walk test. So the patients were really able to complete these exercises at home. The completion rate of the test was high. And the correlation with the standard 6-minute walk test was pretty good too. The one that correlated the best with the 6-minute walk test was the 6-minute walk app, but only about half the patients were able to complete that test. So that is maybe a marker of some of the barriers that may exist to employing these telehealth tools that the more complicated the technology, the more difficult it is to employ.

But I think that with, you know, education of patients up front and learning how to use these technologies, we could probably move the needle on that and have people use it more successfully. So I think that's an exciting, up and coming tool that we personally haven't, you know, integrated into our practice yet, but I think would be very useful to us in the future.

Dr. Elwing:
I agree. And one thing that strikes me when you describe this is that we really have to be thinking ahead. In addition to exercise, what are some of the other tools that you may implement or utilize with telehealth? What are some things that worked for you or something you're interested in trying?

Dr. Clapham:
Sure. Well, I think there's great opportunities for coordination of care and also consulting over distances through telehealth. So being able to, for example, you know, we see patients that are based in surrounding states who are followed more closely by providers nearer to them. So they might have either a primary care doctor or cardiologist or a pulmonologist who follows them, but may not, you know, be expert in pulmonary hypertension and is looking for advice. And so that ability to communicate with the team that's kind of on the ground is one really great use of telehealth. So whether that's you have video conference or even just a phone call, I think you can save a lot of time and heartache that way through better communication across distances.

I think that another way that we have taken advantage of technology and the care of our patients is through patient resources that are available online. So the Pulmonary Hypertension Association, for example, has an excellent website with many resources available for patients and providers to learn about the disease and look for support groups and lots of information. So that's another very useful tool.

I think coming down the line, other things that I think are interesting are we've talked about in the course using point of care testing, potentially to look for some of the lab values that we use to risk stratify patients and monitor their progress. That would be really neat to see that in action. And also to use - we've talked about using maybe tele echo, where images could be obtained at someone's home and then interpreted remotely. And I know that some centers are doing this, where not necessarily that the echoes are performed at home, but they're performed at a center that's much closer to the patient, and then the PH expert is able to interpret those images remotely and give an opinion.

So I think those are some of the ways that we are using telehealth well and that are coming in the future.

Dr. Elwing:
And what about like, surveys, quality of life assessment and like psychological testing or support, are you using anything like that?

Dr. Clapham:
Yeah, I think it's pretty easy to obtain, for example, a functional class through an interview over telehealth which is a key part of our risk assessment. So that's a routine, you know, question that we're asking. That's probably the main survey that we use. Have you used other surveys in your practice?

Dr. Elwing:
So you know, we oftentimes don't think of this as telehealth but we do surveys before the patient comes in. We use EmPHasis-10. We use a social determinants of health survey, and then a survey just of their symptoms. And truly, it is telehealth; we just have integrated into our face-to-face visits, but now I'm also adding that to my virtual visits to try to make that assessment a little bit more robust. And I find that it is really enlightening sometimes when you see patients' surveys and you're like, Wow, you have really changed over the last few years, and that helps them also to know, because we all get used to how we feel, and we may forget, of course, how bad we felt 3 years ago when we first met each other. So yeah, I have been utilizing those tools, and I think I'll use them a little bit more.

What does a virtual care team look like for PAH patients? Katie, will you help me with that?

Dr. Clapham:
Definitely. Yeah, I think we know through our experience in caring for patients with pulmonary arterial hypertension that it really involves a team, and we need expertise from different realms including the cardiology side, the pulmonology side, but we also need pharmacist's knowledge about medications, and we need help coordinating testing and coordinating transportation and appointments. We need to think about what are the barriers to receiving care, like cost to get into appointments and need for social support when you're dealing with a difficult disease that a social worker can be helpful with. And then, of course, incorporating the primary care physician too into the whole plan. So there are a lot of parts of the puzzle that need to come together for good, comprehensive pulmonary arterial hypertension care. And so if we can do some of that coordination virtually, that really helps bring those pieces together.

Dr. Elwing:
Definitely, and everyone has a role to play, and getting them to work together is sometimes tricky. But how are you approaching that? How are you helping clinicians collaborate to provide that optimal care to our patients?

Dr. Clapham:
So it's always nice when we can be together in person, but a lot of the time that's not possible. We have different schedules and

different responsibilities that we have to attend to, so I think getting people on the phone is probably the main way that we do that. I was just thinking about one of my patients who's followed by a cardiologist in another state and it was hugely helpful just to have a conversation over the phone as opposed through the EHR. And then I think an ideal scenario would be to even have multiple people at a telehealth visit, where you could have multiple people on the line. I definitely have seen that in action with patients who want to engage family members who want to be involved in their care or know how to help. And so it's makes it a lot easier to dial in a sister or a child or a relative who might live far away into a virtual visit than it is to an in-person one. So that's been super helpful I would say.

I do have a multidisciplinary meeting with my pulmonology team, cardiology team, and also the addiction team on a weekly or biweekly basis. So we do have the chance to put our heads together about complicated diagnostic dilemmas, or to review imaging or to talk about how we can best support the patient from more than one side. So we do also engage in that outside of the visit in a way that I think has been really beneficial to our patients care too.

Dr. Elwing:
Yeah, another way, we're using telehealth, and we don't even really realize it, and don't appreciate all the ways it helps us in our daily life with our patients. How do you think AI is going to influence telehealth? And do you think it will change anything?

Dr. Clapham:
Yeah, I think it's really interesting to see the tools that people are coming up with.

I've seen examples of this, for example, for EKG interpretation and using AI to assist physicians with that. That's been kind of in a pilot phase. But I think there's a lot of potential for AI to help us in several ways.

I think, for example, AI could allow us to collect many variables from the EHR, rather than sort of hunting and digging through charts to find all of the relevant information. AI could maybe potentially efficiently collect those things so that we can spend time thinking about the information rather than finding the information in the chart. I think that AI could also help us maybe think of things that are important to understanding patients' diseases or risks that we don't even realize yet are important. You know, the science has not yet identified these features as being important in the disease process, but AI might be able to help us uncover that through looking at many, many variables and through many patients.

And then I think also providing sort of a friendly interface to help us in decision-making is another role that AI could play. There is an AI tool for helping guide decision-making about what diabetes medication you might want to start someone on, and the AI can present you with information like, what is the cost of this medication to the patient, what are the pros and cons of this medication, the side effects, the benefits and the risks, and provide all that information in an easy to understand and digest format to help us make the best decision for our patient. And so you could imagine something similar for pulmonary arterial hypertension, where the data like the 6-minute walk test and the NT-proBNP and the functional class data might be presented in a way that could bring to your attention, you know what their risk score is, and maybe prompt you to act in a way that it would be – it might take more time to arrive at where you might not instinctively arrive at but the AI can sort of help you get there.

Dr. Elwing:
Having all the information we have in our electronic medical record, and have it work for us instead of us just entering data. What do you think about delay in diagnosis, and how AI could possibly decrease that time from symptom to PAH?

Dr. Clapham:
I think one way that I could imagine that working is if the AI is to look for signs in the EHR that are warning signals that something like PAH might be a possibility. And again, some of that might be things that we know like NT-proBNP levels or features of right heart dysfunction on echo, but that might even be things we don't know yet. Maybe the AI could recognize patterns in lab values or vital signs that we are not using currently in clinical practice to make these diagnoses. So I think there's a couple of ways that it might help us with that.

Dr. Elwing:
No, I'm hopeful for that also, that we are going to be able to harness some of what information we have and make it usable for us.

In terms of education, where are you learning about these different things you've started, these practices you've implemented? Are you learning it from your peers? Are you learning it from reading journal articles or websites? What's your best resource to teach you about telemedicine?

Dr. Clapham:
I found scientific meetings to be a helpful way to learn about what's up and coming. So attending the pulmonary hypertension meetings, the PHA meeting is actually coming up soon, and so it's interesting to learn about what cutting-edge technologies people have in mind

and are looking at. So I found probably meetings, peers, and reading scientific journals are probably the way that I learn about these things. How about you, Jean, what would you say?

Dr. Elwing:
No, I would say the same thing. And I have learned a lot from discussing this with you and seeing your approaches. I love that you're using these meetings with the addition of your addiction specialist for your patients who have drug and toxin-associated pulmonary hypertension, I think that's so important and impactful. And I've taken away a lot of information you've discussed, and I'm going to implement it. So I really appreciate that. So it was a great discussion.

Dr. Clapham:
Thank you.

Dr. Elwing:
Next, we'll be discussing evolving treatments in PAH with Dr. Kolaitis, and we're looking forward to his discussion.

Dr. Kolaitis:
Dr. Elwing, there's various agents that have been used to target pulmonary arterial hypertension, and I think it's important to talk about these different agents to understand the pathway forward. Historically, we've had three major pathways that we've been targeting, and it's a very exciting time in PAH because we recently had a fourth pathway where we have a drug that was approved for treatment. So I'm going to first talk about the three pathways that we know, and then talk about this new pathway.

So the nitric oxide pathway is a pathway we know. As you pointed out, there's the phosphodiesterase inhibitors in this pathway. You can also use exogenous nitric oxide or a soluble guanylate cyclase stimulator. And the point of this pathway is to increase nitric oxide production. And increased nitric oxide production with these agents leads to vasodilation. Then there's the prostacyclin pathway. And in this pathway, we have prostacyclin analogs and prostacyclin receptor agonists. These medicines are vasodilators as well, leading to potent vasodilation. These medicines come in IV, inhaled, and oral forms. They also come in a subcutaneous form. And these are typically our most effective therapies. And then there's the endothelin pathway. The endothelin pathway is a vasoconstricting pathway, so if we can block this pathway with endothelin receptor antagonists, this could lead to vasodilation.

Now, up until recently, these three pathways really targeted vasodilation, and we're excited that we now have a new pathway, which is the activin pathway. And with activin inhibition, we might be rebalancing some of the pro- and anti-proliferative factors that lead to pulmonary hypertension, not through direct vasodilation, but potentially through the heart of the disease, what's actually driving the disease.

And so how do you approach treatment? Dr. Elwing, you very nicely pointed out that in a low-intermediate-risk patient, we typically start with an ERA, an endothelin receptor antagonist, and a phosphodiesterase-5 inhibitor. And the high-risk patient, we'll typically put them on parenteral prostacyclin therapy.

Now, if patients at follow-up are still not meeting their goals, we have to escalate therapy. And so this is one approach that's been described, is that maybe if at follow-up a patient remains higher risk, then you might add on the activin inhibition at that point in time.

I'd like to think a little bit back though, and why is it that we target initial, intermediate- or low-risk patients with upfront combination therapy with two drugs? Why don't we treat them with one? And really, this comes from a landmark study in pulmonary arterial hypertension called the AMBITION trial. This trial looked at patients that were either on monotherapy or on a combination of an endothelin receptor antagonist plus a PDE5 inhibitor. At the time, it was tadalafil plus ambrisentan versus monotherapy with either tadalafil or ambrisentan. And so this was upfront combination therapy with two drugs versus monotherapy. And you can see here that there was a 50% reduction in risk of clinical failure events. And so for this reason, the standard of care is that patients go on upfront combination therapy.

Now, this has typically been our practice, and I think that it's a really exciting time in PAH because in addition to this knowledge that we need to treat patients more aggressively, we now have new pathways under investigation and new pathways that are active.

Dr. Elwing, I'd like to talk about some recently published trials but before I do is there anything you want to add about these pivotal trials in terms of initial treatment therapy?

Dr. Elwing:
So the AMBITION study that you mentioned changed everything about how we approach a new PAH patient. And really, I think this is the key to getting patients to expert centers. Because this is what we do best: we see a patient, we assess, and then we initiate that therapy that is indicated based on how ill the patient is. And I believe that we really need to be aware of this and offer our new PAH patients that upfront combination therapy to give them that opportunity to reach that low-risk status or stay at low-risk status.

Dr. Kolaitis:
And when you're starting somebody on initial combination therapy with a PDE5 inhibitor and an endothelin receptor antagonist, how many pills are you actually giving them? Because you're giving them two medicines.

Dr. Elwing:
Right. Very important. We could do sildenafil first, which would be then three tablets a day if we start at the 20 mg by mouth three times daily dose, in addition to the endothelin receptor antagonist. So four tablets there. If we would choose tadalafil, that would be two tablets plus the endothelin receptor antagonist. But you're going to tell me about something really exciting that was recently published.

Dr. Kolaitis:
Yeah. So I want to talk about two new recent trials that came out, which are our two most recent trials that led to two new FDA approvals for medications in the United States.

So the first trial that I want to talk about is called the A DUE trial. So this was a phase 3 trial of patients with pulmonary arterial hypertension, and it was looking at a fixed-dose combination tablet of an endothelin receptor antagonist, macitentan, and a PDE5 inhibitor, tadalafil, in a once-daily single tablet. And so what they did here was they had patients that were treatment naïve, and they randomized them to either fixed-dose combination therapy or monotherapy with either an endothelin receptor antagonist or a PDE5 inhibitor. If a patient had been on a prior therapy, they then randomized them to either fixed-dose combination therapy or the monotherapy. And they looked at pulmonary vascular resistance as their primary outcome at 16 weeks. And what they showed was that fixed-dose combination therapy had a greater reduction in the pulmonary vascular resistance as compared to monotherapy. This is not surprising based on what we see from the AMBITION trial, but this ultimately led to the approval of a single tablet combination therapy, reducing our pill burden for patients.

Dr. Elwing:
And I think it's also very helpful, because from AMBITION, we learned that there was a delay in worsening. And from this study, we learned about the short effects, that reduction in pulmonary vascular resistance with combination therapy in that 16-week period. So I think it really expanded our understanding of upfront combination therapy.

Dr. Kolaitis:
So, you know, we talked a little bit about a modified treatment algorithm earlier, and we're highly anticipating the 2024 World Symposium on Pulmonary Hypertension Treatment Algorithm to be published. But I'd like to go back a couple years to the 2022 ESC/ERS guidelines. And one of the things that was recommended in that guideline was that patients with cardiopulmonary comorbidities should get started on an initial monotherapy with either a PDE5 inhibitor or an endothelin receptor antagonist. So Dr. Elwing, maybe you could tell me a little bit about your thoughts on this proposal that patients with cardiopulmonary comorbidities should get a single agent versus upfront combination therapy.

Dr. Elwing:
The way I approach that in my mind is, if I believe a patient has pulmonary arterial hypertension, I treat them according to the guidelines and the knowledge we have from our studies, including AMBITION and A DUE. So I would rarely, rarely implement that one therapy, even if patients have some cardiopulmonary comorbidities. If the comorbidities are such that I think they're driving the shortness of breath or the exercise limitation, of course I'm going to address those and then come back and look if I still believe pulmonary arterial hypertension is a major player and it's contributing in the patient's outcomes, and then I'm going to treat it as aggressively as I would other patients. So I look at it a little bit differently than those 2022 ERS/ESC guidelines. I really want to take out those comorbidities, address them, treat them, optimize them, and then see what I'm left with.

Dr. Kolaitis:
I would agree completely. I think, you know, if the patient truly has PAH, they need upfront combination therapy. And there's been some post-hoc analyses to some of these trials showing that patients with cardiopulmonary comorbidities that were included in the trials still respond well to treatment.

Dr. Elwing:
Absolutely.

Dr. Kolaitis:
So now we've talked about PDE5 inhibitors, we talked about endothelin receptor antagonists, we've talked about when to use parenteral prostacyclins, but there's a new pathway that recently became available and this is really exciting. So I'd like to walk us first through the pathway, and then a little bit about through what the trial showed.

So when we talk about pulmonary hypertension, one of the pathways that might be involved is the BMPR2 pathway. And so in this pathway, you have sort of an increase and a decrease of the pro-proliferative and anti-proliferative factors. So if you have high amounts of the pro-proliferative factors, activins and GDFs, these combine the ALK and the ActIIA receptors, leading to phosphorylation of P-SMAD, leading to activation of the Gremlin and Noggin pathway, which then leads to anti-proliferation. So this is essentially, in patients with PAH, turned on, where there's a rise in the pro-proliferative factors and a decrease in anti-proliferative factors. If you then bind these activins and GDFs, and block them from binding the receptors, you don't get phosphorylation of P-SMAD, you don't get activation of Gremlin1 and Noggin, and you don't get inhibition of the anti-proliferative factors. So then those anti-proliferative factors are actually free to do their job and prevent proliferation. And so this is a novel mechanism that was studied in PAH.

And so I'd like to walk us through this recent trial design. And so this is the results from the STELLAR trial, which was a study of 323 patients with pulmonary arterial hypertension, and they were randomized to either this novel activin inhibitor, sotatercept, or placebo on top of background therapy. And what they looked at was change in 6-minute walk distance at 24 weeks. You can see that the population was on average around 50 years. And they were actually on therapy for quite a long time, about 9 years since diagnosis. And most patients were on triple therapy, with a high number of patients actually on our most aggressive form of therapy, prostacyclin infusion therapy.

The trial improved 6-minute walk distance. It also was successful at meeting multiple other endpoints, including clinical worsening reduced by 84%, a fourfold increase in multicomponent improvement, improved pulmonary vascular resistance, improved biomarkers, and improved patient-reported outcomes. And from a safety signal, it was consistent with the phase 2 results. And some post-hoc analyses – or sorry, some open-label extension data, there might be a signal for some increased bleeding that we need to be aware of, but it seems like the drug is fairly well tolerated.

And so it's an exciting time, because we have two new drugs that have been approved in pulmonary hypertension, one that actually reduces the burden of treatment, and one that's a novel pathway.

So Dr. Elwing, I'd like to go back to the simplified treatment algorithm that was proposed, and what are your thoughts on this simplified treatment algorithm?

Dr. Elwing:
No, I think this applies to most of our PAH patients. Everybody gets upfront combination therapy. Our sickest patients are offered parenteral therapy, and if we're not reaching the goal of low risk, we reassess, make sure that we've addressed all their other medical problems, and then add therapy, augment therapy, change therapy if we need to. And we have to be a little bit relentless. We want low risk. We've got to be a little bit greedy there and keep offering and modifying therapy until we reach that for our patients.

Is that kind of what you do also?

Dr. Kolaitis:
I agree. I would do the same. And I think that, you know, as I talked about in a prior session, we use our risk assessment tools to help us. But if there's something that's concerning you about that patient, err on the side of making sure that we get them to the low risk status even in your heart of hearts.

I think, in addition to these recently published trials and these exciting new therapies, the world of pulmonary arterial hypertension is exciting for other reasons. We have new trials that are also ongoing. There's a trial of inhaled seralutinib which was a trial of a medication that was shown to be effective in a phase 2 trial, This inhibits the PDGFR-alpha and beta receptors, as well as the CSF1R receptor and the c-Kit kinase inhibitor. And there's also a cell therapy trial which recently completed enrolling that we're looking for the results soon. And there's a liposomal version of inhaled treprostinil being studied that will offer a easier to use therapy for a drug that we already have approved.

We have also reached the end of our time today. I would like to thank doctors Jean Elwing and Katie Clapham for the robust discussion today. We would also like to thank Merck and Janssen for their support of this program. We would like to ask the learners to please fill out this evaluation and post-test to receive CME credit. This provides us with valuable feedback that will be used for the planning of upcoming programs. Please follow Iridium CE on X, Facebook, and LinkedIn, so you will not miss any updates.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Education Group and Iridium Continuing Education and is supported by educational grants from Actelion Pharmaceuticals US Incorporated, a Janssen Pharmaceutical Company of Johnson & Johnson, and Merck Sharp & Dohme LLC. To receive your free CME credit or to download this activity, go to reachmd.com/cme. Thank you for listening.