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Advancing Cystic Fibrosis: Addressing Disparities, Challenging Perceptions, and Innovating Patient-Centered Care

Announcer:
Welcome to CME on ReachMD. This activity, titled “Advancing Cystic Fibrosis: Addressing Disparities, Challenging Perceptions, and Innovating Patient-Centered Care” is jointly provided by Global Education Group and Iridium Continuing Education and is supported by an independent educational grant from Vertex Pharmaceuticals Incorporated.

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Dr. McColley:
Hello, and welcome to our program titled Advancing Cystic Fibrosis: Addressing Disparities, Challenging Perceptions, and Innovating Patient-Centered Care. I'm Dr. Susanna McColley, Professor of Pediatrics in Pulmonary and Sleep Medicine at Northwestern University Feinberg School of Medicine, and Director of Interdisciplinary Research Partnerships at Stanley Manne Children's Research Institute, Ann and Robert H. Lurie Children's Hospital of Chicago in Chicago, Illinois. I'm joined today by my esteemed colleagues, Alex Wilson, Manager of Cystic Fibrosis Clinical Research at National Jewish Health in Denver, Colorado; Gregory Sawicki, Director of the Cystic Fibrosis Center and Safety and Quality at Boston Children's Hospital and Associate Professor of Pediatrics at Harvard Medical School in Boston, Massachusetts; and Denis Hadjiliadis, Paul F. Harron Jr. Professor of Medicine Pulmonary, Allergy, and Critical Care at the Perlman School of Medicine, University of Pennsylvania, and Director of the Adult Cystic Fibrosis Program and member of the Lung Transplantation and Palliative Care Programs at the Hospital of the University of Pennsylvania in Philadelphia, Pennsylvania.

Our disclosures are displayed on the screen.

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Alex, I was hoping you’d start off our conversation today by setting the stage and providing some background information about cystic fibrosis.

Dr. Wilson:
Sure. Cystic fibrosis, or CF, is the most common life-limiting genetic disease in the United States, affecting nearly 40,000 children and adults. It should be noted that CF affects people of all racial and ethnic backgrounds, and globally. There have been great strides in the treatment and available therapies for people with CF, allowing for greater quantity and quality of life. In fact, the 2023 CF foundation patient registry report highlights the median age of survival for people with CF born between 2019 and 2023 is 61 years.

The cause of cystic fibrosis is a mutation in the cystic fibrosis transmembrane conductance regulator or CFTR gene. This gene encodes for CFTR protein, a chloride channel that drives salt and fluid secretions in tissues such as the airways, gastrointestinal, and reproductive tracts, as well as sweat glands. With normal CFTR function, the salt and fluid secretion is balanced, allowing thin, watery

secretions to move normally in those tissues. In cystic fibrosis, CFTR is either not present at all, the gate does not open or is faulty, or low amount of CFTR is present at the epithelial cell surface. This ultimately results in thick, dehydrated, and sticky secretions such as mucus in the airways.

While CF is typically thought of as a pulmonary disease, it is truly a multi-organ system disease. It impacts the upper and lower airways resulting in chronic sinusitis, nasal polyps, chronic respiratory infections, resulting in frequent exacerbations and ultimately, bronchiectasis. Gastrointestinal impacts are numerous and can significantly impact quality of life. These include exocrine pancreatic insufficiency resulting in malabsorption particularly of fats and fat soluble vitamins. Hepatobiliary impacts include abnormal bile production, elevated liver transaminases, and potentially CF-related liver disease, which can result in cirrhosis or portal hypertension. People with cystic fibrosis may be at higher risk of kidney stones. Impaired glycemia is common, and CF-related diabetes can occur in many. And people with cystic fibrosis are at increased risk of colorectal cancer and potentially other GI cancers. They should be screened earlier than those without CF particularly if they have a family history of GI cancers. Other GI impacts are gastroesophageal reflux disease and rectal prolapse. Stress incontinence and muscle weakness may occur as side effects of frequent cough or inactivity, respectively. Delayed puberty may occur. Low bone density, osteopenia, or osteoporosis can present early and at any stage of life. So you see, there are many impacts that those living with CF and their caretakers must manage.

Newborn screening for CF has resulted in earlier diagnosis and better outcomes for many with CF. This is important so that caretakers can take immediate steps to treat and care for a child with CF. In 2010, newborn screening for cystic fibrosis was recommended nationwide. In the current era, the majority but not all diagnoses of CF are made by newborn screen. In 2022, 60% of those newly diagnosed with CF were detected by newborn screening. Clear and prompt communication of a positive newborn screen is crucial so that referrals to specialists can be made and confirmatory testing be done. Cystic fibrosis specialists, often at a pediatric CF care center will complete a sweat chloride test and genetic screening.

Clinical presentations at this age include poor growth or malnutrition, secondary to exocrine pancreatic insufficiency, steatorrhea, and potentially poor pulmonary health. It is important to know though that some infants may be asymptomatic at the time of positive screen.

There are times that a diagnosis of cystic fibrosis can be delayed. While newborn screening has resulted in better outcomes, it does have false negatives. There are plenty of people who present with cystic fibrosis as teenagers and adults and even into late adulthood. Later diagnosis may result from a non-classic phenotype such as pancreatic sufficient at birth resulting in positive newborn screen, CF genetic variants that are not included in current CF mutation panels, delayed follow-up after positive newborn screening, and bias among healthcare providers about what racial and ethnic groups may have CF, and a lack of healthcare provider cultural humility resulting in suboptimal communication with patients and families, leading to mistrust of healthcare teams. The main point here, though, is that when someone is diagnosed with cystic fibrosis, prompt referral to a CF center for specialized care is recommended.

So a multi-organ system disease requiring specialized care and impacting psychosocial aspects of both the person with CF and their caretakers requires a multidisciplinary team. The person with CF is the center of this team. The cystic fibrosis care team consists of the following providers: a CF pulmonologist, access to specialists familiar with cystic fibrosis such as a psychologist, gastroenterologist, and endocrinologist are often available. CF care teams also include nurses, respiratory therapists, clinical dieticians, social workers, and clinical coordinators, often a nurse coordinator. Pharmacists, physical therapists, and clinical research coordinators are often closely involved with the CF clinical care teams.

Telemedicine is a helpful tool for those with less access to a cystic fibrosis center. It is recommended for people with CF to visit their CF care team four times a year, but at minimum annually for lung function testing and a sputum microbiology culture. This can be difficult for many reasons, including but not limited to living in a rural area making travel to a cystic fibrosis center costly and time consuming, busy school and work schedules, or busy personal lives in general. For this reason, telehealth can be an effective tool for people with CF and their caretakers to close the communication gap, allowing for contact between primary care providers and CF clinics. Some CF clinics may also be able to accept remote sputum collection and shipping to a microbiology lab and even home spirometry using remote systems.

Dr. McColley:
Thanks so much for that, Alex. We know that disparities affect patient outcomes in those with cystic fibrosis. Can you discuss some of these disparities and their impact?

Dr. Wilson:
Yes, I can definitely discuss that. So unfortunately, as you mentioned, there are fairly significant health disparities in people with CF. I'll review briefly several related to demographic, socioeconomic, and environmental effects of discrimination or exclusion. A person's race or ethnicity may delay diagnosis based on which CFTR variants are being detected in certain newborn screening programs. Black and

Hispanic people with cystic fibrosis do have worse pulmonary outcomes and have increased mortality rates. Female sex is associated with decreased life expectancy compared to male sex. Women are at increased risk of acquiring Pseudomonas aeruginosa at an earlier age, and sex hormones, progesterone and estrogen, for some reason result in worse clinical outcomes. A person's gender identity results in disparities based on multiple factors, including bias by and suboptimal communication with healthcare providers, mental health of a person identifying as LGBTQIA+, and potentially the use of sex hormone therapy. Socioeconomic status as a measure of power, resources, and education is a determinant of health status. Those with absence of health insurance, a marker of socioeconomic status, have increased mortality. Lastly, disparities in where a person lives may impact a person's health outcomes. Those living in areas with higher air pollution tend to have more frequent pulmonary exacerbations.

As noted earlier, prompt identification and treatment of CF results in better growth and long-term outcomes in infants with CF. A concern arises with the misperception that cystic fibrosis is primarily a disease impacting those who are white. There are different distributions of CFTR variants from racial and ethnic minority groups compared to white people with CF. Most newborn screening programs detect most of the CFTR variants of non-Hispanic white groups, while other programs leave out CFTR variants more commonly associated with minority racial and ethnic groups. So if newborn screening programs do not detect CFTR variants of all ethnicities and races equally, then infants will be missed on newborn screening, delaying identification of CF and therefore care.

A recent literature review revealed widespread patterns of inequitable treatment across pediatric specialties. These identified studies indicate that children from minoritized racial and ethnic groups received poorer healthcare services related to non-Hispanic white children. A lack of attention to health literacy of anyone, but in this case people with CF and their caretakers and lack of access to appropriate translation and interpretation services contributes to disparities. Bias among and communication with healthcare providers or lack thereof can lead to mistrust with healthcare teams. As care providers and researchers, we need to aim to be aware of cultural nuances and aim to make appropriate services available so that all people can have equitable access to care.

This next slide is really underlining the importance of universal screening of unmet needs, tobacco health exposure, and mental health screening, including people with

CF. We also need to aim to ensure equitable access to treatment and therapies and equitable access to participation in clinical trials. There is a robust clinical trial network aimed at improving access to therapies for all people with CF who do not qualify for certain types of therapies that are currently available. Ultimately, this network aims to cure cystic fibrosis, in addition to providing alternative therapies for chronic infection, nutrition, inflammation, and targeting the defect of CFTR mutation.

Dr. McColley:
Thank you for that great discussion. I'd now like to discuss the patient case. This patient is named Jayden. He was a full-term black boy who had a positive newborn screening test for cystic fibrosis that showed one CFTR variant detected. The primary care physician advised the family that cystic fibrosis is very unlikely and a sweat test to be sure was not urgent. At 6 weeks of age, Jayden presents for a sweat test and is found to be only slightly over birth weight, so hasn't gained significant weight since birth, and his sweat test is consistent with the diagnosis of cystic fibrosis. Because if you have a positive newborn screening test and a positive sweat test, that confirms the diagnosis. So his family is confused and upset. So how can the CF team establish a relationship with the family? And how can the primary caregiver perhaps also be included in going back and discussing the diagnosis in this family who's quite surprised?

This does come up a lot, and it's not limited to people from minoritized racial and ethnic groups, many families are actually told that if their child only has one variant, they're probably a carrier and not affected by the disease. And sometimes that does delay diagnosis, so it's important for people to understand that infants who have one variant on newborn screening tests, have about a 1 in 10 chance of having cystic fibrosis. So still, you know, most of them won't, but remember this is a disease where the prevalence is about 1 in 4,400 people in the United States, so it's vastly increased risk compared to the general population.

The other thing that we've heard from many families is that there is less familiarity in their communities about cystic fibrosis. So I think that when you meet a family like this, it's important to just listen and let them talk through their confusion, disappointment, if they're angry, it's perfectly appropriate to validate those feelings of anger. Many parents will also feel like they wish they'd known sooner, maybe the baby would be growing better.

So segueing from that into hope and treatment and the fact that most children who are – before we had newborn screening, most babies and children who were started on pancreatic enzymes began to gain weight quickly. That there are lots of treatments for cystic fibrosis, that life expectancy is now in the early 60s for kids diagnosed right now. So to go from listening, supporting, to the basic things about care and hope and not trying to give way too much information on that first visit,but rather get the essential treatment started and then have a quick follow-up visit. And this is also an area where collaboration between the CF provider and the primary care provider can be very important, sort of talking it through and making sure that people get the same positive messaging.

Dr. Wilson:
For this kiddo who is having poor growth, what would be the essential treatments?

Dr. McColley:
We're going to talk about CF therapies, and we're going to start with therapies that are focused on treating symptoms. Chest physiotherapy is a manual way to get sticky secretions out from the airway wall to being within the airway lumen so that they can be coughed out. Bronchodilators, of course, are widely used for many pulmonary diseases and widen the airways to increase airflow through them. There are inhaled therapies that are more specific to cystic fibrosis, including dornase alfa, hypertonic saline, and inhaled mannitol that help make thick, sticky secretions looser and more able to be cleared from the airways. Pancreatic replacement therapy is essential because most people with cystic fibrosis do not have active enzymes secreted from their pancreas into the intestine to absorb food. And in fact, pancreatic enzyme replacement therapy was the first treatment to be used that allowed kids to gain weight and survive at least for some years with cystic fibrosis. And then we had antibiotics, which are used both to treat and to prevent flares related to chronic respiratory infections in the airway.

One of the advances in cystic fibrosis during the past decade plus have been new therapies for cystic fibrosis that focus on the underlying genetic defect. These are gene variant-specific therapies, and the first one to be approved was ivacaftor. This is a single, small molecule treatment given orally twice a day, and it works for people who have specific types of CFTR variants that are at the cell surface so fluoride can pass through them to rehydrate the airway. That was approved initially in 2012 for a single gene variant, lots of research led it to be approved for many variants, but it's a small percentage of the population that can be treated with that medicine alone. In 2015, combination ivacaftor and lumacaftor was approved for people who have two copies of the most common CFTR variant called F508del. And then another drug combination that had some additional benefits for that same population was approved in 2018. In 2019 we had FDA approval of elexacaftor-tezacaftor-ivacaftor, which works for people who have just one F508del variant, as well as some other types of variants that respond to that medicine. So we have really expanded usage of these very effective medicines.

Now, I talked a bit about modulators and proteins and what the proteins do, so I'm just going to back up and talk a little bit more about that. So using the case of ivacaftor, there is a protein that sits at the cell surface, that channel if you will, but the channel is closed, and so these CFTR potentiators help the channel stay open so that chloride ion can flow to the cell surface. The common F508del variant is misfolded protein, and it actually never gets to the cell surface. It is caught inside the cell and it gets broken up and cleaned up because it's not a useful protein. So these corrector therapies, lumacaftor, tezacaftor, and elexacaftor, actually help the protein folding get to the cell surface. When it gets there, it's not very active, and so ivacaftor can open that channel so that you have the correction of the chloride channel defect. F508del, I've said a couple of times, is the most common gene variant but many others exist. In fact, hundreds of CFTR variants cause cystic fibrosis. And this is just a list from the United States of the percentage of people with CF who have one or two copies of a gene variant. So you see F508del here at the top, about 85% of people after that, it falls off greatly. But the important thing to remember is that there are many variants that cause cystic fibrosis. Many are responsive to treatments, but many are actually not picked up with standard newborn screening tests or even with panels that can be used to confirm a diagnosis by a laboratory.

CFTR modulators, as I noted before, are suitable for people who have different types of CFTR mutations or variants. It's not limited to what we talked about earlier. But keep in mind that because of the protein configuration differences so these correct the proteins. And so we've talked about ivacaftor again, many variants, some of which are so rare that uniquely in cystic fibrosis, some of these therapies were actually approved by the Food and Drug Administration based on in vitro testing. And then going all the way over to the triple combination therapy of elexacaftor-tezacaftor-ivacaftor, there are many more people who are eligible, and have good results with that treatment.

So I'm going to go through a couple of the studies that have been published, and the first was the pivotal trial of ivacaftor. And this was a remarkable study, because for the first time in a CF trial, we saw a very large increase in lung function measured by forced expiratory volume in 1 second within 2 weeks of starting therapy. And this persisted, not only through the 3 months of these clinical trials, but actually well beyond in open-label extension trials. When you look at lumacaftor with ivacaftor, you see that there is a similar pattern; however, it's a much lower increase in FEV1. So this medicine was helpful but it was not the same boost that people who were ivacaftor eligible got. And very similar results for ivacaftor and tezacaftor. If, however, you look at the ivacaftor-elexacaftor-tezacaftor data, what you see is again a very large improvement in forced expiratory volume in 1 second within 2 weeks of starting the medication that persists for a long time.

Now, one of the things about these CFTR modulators is, although they're very effective and many people can take them, some people are not eligible for them, and this is primarily people who have a variant that has what's called a stop codon in it, and so it tells the cell to not make any protein. So you can only modulate a protein if there is a protein in the cell. So there are many new types of therapies that are under study. None of these are approved yet. Messenger RNA can be delivered to the cells through inhalation to

make protein. So there are studies going on with this type of therapy. There are also CFTR gene transfer vectors to give DNA delivery to cells, and this is an area that has been under research for decades. But as more is learned about gene therapy, there are more promising systems that are being studied. And then finally, in this era of CRISPR/Cas gene editing therapies that actually repair the CFTR variant are also under study.

This is just a cartoon showing a little bit about how these work. So if you have an incomplete CFTR protein that says stop and you can give messenger RNA, you can have a readthrough so that you get a full length protein to restore CFTR function.

Getting back to modulators now there's been rapid evolution of uses these drugs are approved, and so as I noted before, by far the one that is used by most people in the United States who are eligible for a modulator is this combination elexacaftor-tezacaftor-ivacaftor that's shown in the green bar on this slide.

Now, one of the issues with health disparities in CF is that because of differences in gene variant distributions across ancestral populations, minoritized people with cystic fibrosis are less likely to be eligible for CFTR modulator therapy than white non-Hispanic people with CF. And this is capitulated by particularly the decreased frequency of F508del in these populations, although it is still the most common gene variant in these populations because it is so prevalent worldwide. Even more concerning is that eligible minoritized people with CF are still less likely to be prescribed the therapy and have delays in the therapy compared to white non-Hispanic people with CF. These are epidemiologic observations from the Cystic Fibrosis Foundation patient registry, and we don't know the causes for that, but it certainly requires those of us who take care of people with CF to be clear in our communication and make sure that everyone who could benefit from a therapy is offered that therapy.

Dr. Wilson:
Thanks so much for that information, Dr. McColley. Now that we know more about the treatments, can you take us through the current treatment guidelines?

Dr. McColley:
Yes, I'm happy to do that. And I'm also happy to say that guidelines are being updated frequently as the field changes. There are a number of different specific guidelines for people with CF with different circumstances. We have guidelines for indications and what the evidence is for using different medications, for airway clearance techniques, for respiratory support for people who have advanced lung disease and need that, and for lung transplantation.

One of the things that we have discussed in this program is that it's very important to make sure that social determinants of health are screened for. And we think about the traditional social determinants of health that are non-medical factors that affect health, and on average, they affect health more than medical care does. We have strong evidence that these things are very important in cystic fibrosis respiratory outcomes and require targeted interventions, screening for unmet social needs, making referrals to community organizations to help address them, screening for tobacco smoke exposure, and counseling using evidence-based guidelines, ensuring equitable access to treatment as we discussed with ETI, prescriptions, screening and treating for depression and other mental health concerns, and then supporting socioeconomically disadvantaged and minoritized people with CF to participate in clinical trials.

Let's dive into a patient case.

Dr. Wilson:
So let's meet Bri. Bri is a 34 year old non-Hispanic, white woman recently diagnosed with cystic fibrosis. She has had barriers to regular medical care during childhood. Bri has a history of asthma, frequent sinus infections, nasal polyps, chronic cough, and a recent episode of pancreatitis. And Bri is concerned about the costs of therapies for her cystic fibrosis. Bri has asked her pulmonologist if there are any natural therapies to treat her cystic fibrosis. How would you approach this conversation with Bri?

Dr. McColley:
My approach to these things are twofold. The first thing is really to ask if they had any specific ideas about that or have read anything. And then I generally talk about how to safely use products that may not be really studied or approved for cystic fibrosis safely. The most important thing being clear communication and knowledge that many herbs and other therapies actually can have negative interactions with some medicines that can be essential to preserve health. Now, in your practice I'm sure that this comes up a lot, so tell me what your approach is.

Dr. Wilson:
Yes, this has come up frequently, and I think really starting the conversation and asking which therapies they might want to be more natural, and then also the reasons for wanting a more natural therapy, just to get that better understanding and get that good communication going forward. If it's an over-the-counter treatment, there are websites and resources, consumerlabs.com that providers

can utilize to see what the interactions with other medications might be. And then to have a good discussion about whether the goals are to only have a natural therapy, or if they have other goals that we can compromise. Maybe there are some treatments that they can do more natural, and then the other ones that might be really important for their overall health. As an example for pancreatic enzyme replacement therapy to ask them, let's stick with this, let's stick with an enzyme that we know is effective and doesn't have large interactions. And then maybe we can consider trying some other things and meeting them halfway. Sitting down with them and talking through the rationale for using the natural versus the provider recommended treatments. And sometimes it can be a perceived concern about cost for the treatments, and truly sometimes sitting down and doing a dollars and cents comparison of what the over-the-counter natural treatment might cost compared to the potentially insurance covered medication might relieve some of that anxiety for that cost concern, if that's their rationale for wanting to do natural. And then also asking again what their definition of natural is, and seeing if that is even something that's feasible for them to obtain and then to maintain.

Dr. McColley:
Let's now discuss how telemedicine can help support people with CF and their families. Dr. Sawicki?

Dr. Sawicki:
Thank you, Dr. McColley. So as many people know, over the last several years telemedicine has been increasing in frequency and availability across the healthcare landscape. For people with cystic fibrosis, clinicians who work with people with cystic fibrosis as well as their families, telemedicine can serve a key role in providing optimal and high quality CF care. It is also a crucial part in facilitating the education of health professionals who are involved in the care of people with cystic fibrosis.

When thinking about telemedicine, there are several different elements that could be considered. One referred to as telementoring is a system in which specialists use telecommunication technology to deliver training, education, and support to other community-based healthcare providers. In the cystic fibrosis care model, this may be in the form of outreach to those who may not be affiliated directly with a cystic fibrosis accredited care center. There also is an aspect of telemedicine which is referred to as telemonitoring in which people with cystic fibrosis as patients or their family members can really be monitored remotely by means of audio, video, or other technologies. This could include telecommunications for direct patient care and visits, such as using these technologies to specifically have a visit or hold a visit using a telehealth modality. But could also be around monitoring of symptoms and other key health indicators for people with cystic fibrosis.

So in general, as seen on this slide, there are many benefits that telemedicine may have to bridge gaps in access to care for those with cystic fibrosis. It also can be used to augment the care that is received at CF care centers. Telemedicine may reduce the burden of time that is spent by people with CF, their caregivers, and families, particularly when those individuals may live far away from a care center. Telemedicine may also limit exposure to potential infectious disease in clinics or hospital settings. And in the cystic fibrosis care model, where infection control predominates, this is an important consideration, particularly during seasons when other illnesses may be present in a CF clinic. Telemonitoring may also allow people at home to monitor key health indicators, as I mentioned previously. For cystic fibrosis, this could include monitoring of oxygen saturation, but also more importantly monitoring of respiratory function. For those who are living in remote areas further from care centers, perhaps even rural areas not anywhere near urban CF care centers, this could improve access. And it can also reduce the financial burden of travel that may be required to get to a care center if some of the visits can be done in a remote fashion.

I think one of the most interesting and innovative advances in telemedicine for cystic fibrosis over the last several years has been the monitoring of lung function, also known as home spirometry. On this slide, you see an example of a possible device that is now available to monitor lung function. These are handheld devices that have become more frequently used and utilized by pulmonary clinics throughout the country. There's been an explosion of research into the feasibility and acceptability of these devices, and is now well established that home spirometry devices are quite valid as compared to the spirometry that is done in conventional clinic settings or in pulmonary function laboratories, particularly if these devices are done with direct supervision from someone from a clinical setting. That said, although there is some feasibility data that suggests unsupervised spirometry is valid, the feasibility in unsupervised settings is still less clear, particularly for children with cystic fibrosis, as they may have more difficulty with using these devices without appropriate coaching.

And as much as there is great promise in the use of these devices, we still have data from studies and other research initiatives that adherence to remote monitoring protocols is often poor. We can give devices to individuals. We can train them to use these devices, but we have to develop systems in which people are either prompted to use devices on a regular basis or taught when to use these devices to help augment their care. And much research is still ongoing in thinking about how to best implement such devices into routine CF care.

But we do know that during the COVID-19 pandemic, over the past several years, home monitoring in CF care using home spirometry

devices has definitely increased. This graph from a publication shows the number of home spirometers which were shipped out to patients and families with cystic fibrosis in the United States by the USCF Foundation. During the lockdown periods of early 2020, it was clear that people with CF could not be coming to clinic as frequently as they needed to and so the CF Foundation, with encouragement from the CF community, helped obtain and purchase devices to be distributed through the CF Care Network. And as you can see on this graph, within the first year of this program, nearly 20,000 home spirometers were sent out to individuals with CF throughout the United States. In certain centers, people then monitored how these devices were being used, and what was clear was that people were using them very differently. Very few people were using them on a daily basis. About 20% ended up using them on a weekly basis, but the vast majority were using them on a monthly or right before clinic visit basis, which I think intuitively makes more sense. And obviously care centers and clinicians were directing and counseling patients and families as to their local practices. As the pandemic waned, we have now seen that people still have these devices, and there definitely are varying programs around the country in terms of implementation and use, but sustaining these kind of programs longer term certainly will take innovation and a discussion across care centers to think about what the best practices should be.

Turning now to telementoring, where we think about how clinicians can work in networks with each other to increase the capacity to treat people with CF throughout the country, there are several models that are out there to think about how telementoring can work best. Project ECHO's model of 'all teach, all learn' is one such model. In this model, an expert hub team is developed with expertise from specialists in a variety of disciplines. This allows for access for patients, but also allows for access for care teams and clinicians throughout the communities develop what are known as local learning loops that can then feed back to provide optimal care to patients and promote best practices across larger networks.

Particularly in remote areas, telementoring can provide multiple benefits to patients, as seen in this slide. It allows for the leveraging of the expertise of a multidisciplinary care team to support clinicians and families with a personalized approach. The functions include video consultations, help with monitoring, help with provision of education, and help with self-management, as would be the case with home spirometry as an example. Digital technology can be leveraged, including smartphones, apps, web platforms, and home devices, as I previously discussed. And all of this can be integrated into electronic medical records. The benefits really can be increased accessibility to healthcare, supporting adherence to therapy, early detection of exacerbations particularly if home spirometry is incorporated into more frequent use, and then increasing support and understanding for patient's needs.

Dr. McColley:
Thank you so much for that terrific presentation, Dr. Sawicki. I'd now like to discuss a patient case.

Dr. Sawicki:
Thanks. Dr. McColley, our case here is of Carlos. He is a 16-year-old Latino boy who lives in a rural area who presents to his primary care physician with shortness of breath, constant cough, inability to gain weight, and frequent sinus infections. He's undergone genetic testing that shows a CFTR variant of T1036N and had a sweat test with a sweat chloride level of greater than 60. You note that he also has had delayed puberty and recognize that he comes from a family with low socioeconomic status. Both parents work and are not able to take him for frequent appointments at the CF care center where he received the diagnosis, and you, as a pediatrician, are asked to think about what would be the best way to provide care for an individual and family such as that caring for Carlos.

Dr. McColley:
This is a very high-risk youth because of delayed puberty, weight gain issues, lots of respiratory symptoms, who's going to need quite a bit of monitoring. And so some of the things that you talked about, Greg, are really pertinent here. This is a teenager who could benefit from more frequent visits, but many of them could be done virtually. And of course, technology can be an issue in rural areas but telemedicine can be done successfully on smartphones. Spirometry can be done using smartphone technology. And so frequent check-ins along with having ways to help support the family in some visits to the CF center, even if that is sort of more off hours, early in the day, late in the day, could really help. We always worry, of course, about monitoring microbiology and making sure that the medication is being administered, that the family understands how to do that and has access to those things. So those are my initial thoughts.

Dr. Sawicki:
In addition to that, I think one of the roles of a primary care community physician would be to really understand how much the family knows about the diagnosis. It's one thing for the diagnosis to be made and this to be in a chart to say that a sweat test was done, but to understand have they made the link between all this testing that was done in an actual name of a condition, what they understand about the condition? Because that partnership, I think, would then allow for a discussion to say, you know, what's the role of the primary care doctor or the clinic for the health center? What's the role of the CF care team? And allow the clinicians to encourage, you know, visits with a social worker or a dietitian or a respiratory therapist as well. I think that we often see situations where diagnoses can be made but if there's a lack of true understanding how all of this comes together, it sets a family up for missing appointments, for instance, because

they don't recognize the importance of the connection between the inability to gain weight and cystic fibrosis, or the cough and CF and they may be told, you know, by family members that they're all not related, or 'Oh, every kid coughs that way.' And so I think there's a real role here for education.

Dr. McColley:
Let's now discuss caregiver support in cystic fibrosis.

Dr. Hadjiliadis:
As we all know, despite all the advances that we have had in cystic fibrosis, this is still a burdensome disease. There's a lot of burden to parents of young children living with cystic fibrosis, but there's also a lot of burden even in adults with cystic fibrosis, and this might be related to their partners, their relationships, or even their parents. And sometimes when they are parents, there is also burden in a different way when they have strain for taking care of their kids.

The challenges that the caregivers face are a lot. Caregiver burden can be defined as the level of multifaceted strain perceived by the caregivers from caring for a family member or a loved one over time. The challenges for caregivers can include many different aspects of life. Those include emotional strain, include financial strain, and also demands on time. You have to go to clinic, you have to have unplanned hospital stays or other things that might be required, and you also have to adhere to a very complicated regimen. And even though things have improved, it is estimated that many times, parents have to spend up to 75 minutes helping children with their regimen every day.

These lead to a lot of problems in the caregiver support and there's consequences for both the caregiver and the person that is living with CF. So the financial issues are significant. You have less resources that you need. You might have multiple responsibilities that conflict with each other, taking care of other children, your work, that means that you might have fewer social activities, and that creates caregiver burden. That leads to inability to provide the care that you need. You also have decreased quality of life, and as a result, you end up having a lot of physical and psychological health deterioration for the caregiver. The consequences can be bad for self-perception of the caregiver. It can create problems for the person with cystic fibrosis, and also create a lot of strain in many different aspects, and leads to worse outcomes.

There is different things that we can do to try and help caregivers of persons living with CF. First of all, we have to understand better how the impact of caregiving leads to problems in the care of the persons with CF. Screening caregivers for unmet needs is important because those needs might change. At different times there might be financial strain, at other times it might be a time strain, or there might be other competing priorities. In situations where there's anxiety or depression, you can provide support and resources from that perspective. And if there's access to palliative care when appropriate for persons with CF, this might help indirectly the person with CF, but also the caregiver. So those are important things to think about.

There's a lot of different resources. Obviously the most important one is the Cystic Fibrosis Foundation, including the local chapters. One aspect of the Cystic Fibrosis Foundation compass helps a lot in providing resources, especially when it has to do with insurance, financial challenges, and other things that are related to life with CF. And by helping the person with CF, also helps you with caregiver by taking away some of the burden.

I want also highlight the NOAACF, which is an organization that helps the African American community living with CF. Another foundation is the Take a Breather Foundation, which provides breathers for families of persons living with CF, similar to what Make A Wish does. And some other foundations are CFRI, the Boomer Esiason Foundation that provide a lot of educational and research support, but they also have resources for persons living with CF. And there's CF News Today, Bonnell Foundation, and many others. And I would encourage anybody that's looking for resources to also look at their state and regional foundations which might be useful, and they might have specific areas where they provide help.

Dr. McColley:
Thanks for telling us about online resources. Now let's talk about patient-centered care.

Dr. Hadjiliadis:
Thank you so much, Dr. McColley. Anybody that lives with a chronic disease, there's different needs and they come from a different background, we need to know as healthcare providers how to provide the best care that fits their values, their wishes, and provides information that's culturally appropriate. We're going to go back to the same things that we spoke about before. So looking for unmet social needs is one of the more important things that we can do as providers for cystic fibrosis. In different parts of this talk, we've talked about food insecurity, for example, that's a very important issue to look for. Anxiety and depression, anybody living with a chronic disease is prone to have that so if we screen, we're more able to find it. Tobacco smoke exposure, and this can happen in parents. It can happen in partners. And providing information on smoking cessation and education on how this leads towards outcomes might help

the person and their family indirectly. We also know that this is associated with lower socioeconomic and educational status, which many times leads towards worsening disease.

There are some best practices to improve patient care for cystic fibrosis, and those include making referrals to community organizations that help alleviate the needs of persons with CF. We can do our best to try and have equitable access to treatment. This is especially true when we think about lung transplantation and the highly effective modulator therapies, because those can be very unique and important for people, either living with advanced cystic fibrosis or to prevent progression of disease and ensure quality of life.

And also another aspect that's very significant is making sure there's equitable enrollment in clinical trials, so that we learn more about people that are underrepresented otherwise and we treat them appropriately.

Dr. McColley:
Thank you for that important information. Now that we've discussed patient-centered care, let's explore how to transition patients from pediatric care, like what I do, to adult CF care like you do.

Dr. Hadjiliadis:
Thank you for the segue, Dr. McColley. As we all know, this has been the new phase of CF compared to the time that many of us started practicing. Thanks to the excellent job that all the pediatricians have done, cystic fibrosis now a disease that affects a lot more adults than children, the last data suggests that they are close to 60% but it's continuing to increase compared to the total population. So one of the more significant times when there can be complications, lung function lost, lost to follow-up, and problems is during the late adolescence and the early adult will then transition happen. So it is extremely important to be able to get patients safely from the pediatric to the adult care. And there are many different ways to do that, but it's best to have a well-defined process.

So the first part is the pediatrician meets with a parent and the family, usually at the latest that should happen in early adulthood but as we said, sometimes it can happen a little earlier to start talking about the transition. When the time gets closer, then the patient and the family meet with the adult team to discuss the process and make sure that there's less anxiety about this transition. And then, usually, the transition happens somewhere between the age of 16 and 21 based on the local circumstances, the ability to see people less than 18. What other, you know, things that happen. It usually happen – It should happen with a protocol between the pediatric center and the adult center. But any point there's a lot of disengagement or a problem with the transition process, sometimes you go back and you try to reestablish contact and start from an earlier, you know, stage until you hopefully achieve a successful transition.

A program that was developed a few years ago, it's called the CF RISE, and that facilitates transition for patients from pediatric to adult CF care, and includes mostly a focus on responsibility and independence for the person that's being transitioned. It has educational material. It has knowledge assessments, has a responsibility checklist, and educational resources for everybody to be able to do that transition as smoothly as possible.

Cystic fibrosis is a multi-system disease that would require educating the patients about the possible areas where cystic fibrosis might be affecting them. And all of us know that the airways are the more common, more morbid area for persons that live with cystic fibrosis, and there's a lot of infectious bronchiectasis exacerbations. But nobody should forget issues that have to do with areas like CF-related diabetics, osteoporosis, infertility in males, muscle weakness, stress incontinence, a lot of GI issues related to pancreatic insufficiency, obstructions like DIOS, pancreatitis for some patients, liver disease. So all those things are areas where the person needs to know what might be the complications. And, you know, educating them early and appropriately also based on, you know, what their conditions are.

Dr. McColley:
Denis, thank you very much for that discussion. Transition can really be a key point in management of cystic fibrosis. And I would say many of us in pediatrics actually talk about adult CF care at the time of diagnosis because it gives families the information that they should expect their baby to live into adulthood.

Speaking of another important issue with families, let's now talk about structural competency and cultural humility and how training can support CF care in those areas.

Dr. Hadjiliadis:
As we all know, we are seeing increased diversity in our population with persons with CF. This is not surprising because we see that in the United States population. So right now, there's basically about 2/3 of the population or more that is white and non-Latino, but it's expected that by 2050 that percentage of population will be close to 50%. As a result, we see more people of African American, especially Latinos, but even from other places that traditionally we didn't even think that cystic fibrosis was very common.

So developing structural competency among the healthcare team is needed to be able to mitigate disparities and create better outcomes in underserved populations. Structural barriers to healthcare are very embedded, institutional racism, classism, sexism, homophobia,

ableism, and intersections of these aspects of identity can lead to significantly higher prevalence of chronic health outcomes. And the structural competency is a concept that's developed to overcome those barriers. It's defined the trainability to understand how a host of issues defined clinically as symptoms, attitudes, or diseases also represent the downstream implications of a number of upstream decisions about such matters, healthcare and food delivery systems, zoning laws, urban and rural infrastructure, medicalization, or even about the very definition of illness and health. So this definition tries to go into the root of all those problems where we have significant, you know, issues that are very different to untangle. And many times as healthcare providers, we see the tail end of this, but we need to know about that to be able to do our best to help treat our patients.

Cultural humility cultivates person-centered care. So cultural humility is a component of the structural competency and is an approach to caring for a person and their families. So that means that you have to have self-reflection and assessment. You have to appreciate patients' expertise on their social and cultural background. You have to be open to establishing a power balance relationship with patients. That means listening, you know, to their side of things and how they view their life and what's important to them. And also means that you have to learn from patients all the time. You have to be able to do that and reassess your values, beliefs, and bias, and be able to adjust based on this.

Components of cultural humility and training work together to help patient care. And there's five R's of cultural humility that drive interactions between the clinics and the caregivers. So one is reflection. That's the approach of trying to look at every encounter with humility and understand there is the respect, treat every person with respect and strive to preserve dignity and respect. Regard: hold every person in their highest regard, to try and avoid any unconscious bias to interfere with any interactions. Relevance: expect cultural humility to be relevant and apply the practice to every encounter. And resiliency: embody the practice of cultural humility to enhance personal resilience and global compassion. There's many steps to take into this. So you have to engage the patients. Familiarize with persons, their families, and their treatment. You can endorse collaboration in interviews and assessments, and you can integrate culturally relevant information and themes. You can gather culturally relevant collateral information, select culturally appropriate screening and assessment tools. And then determine the readiness and the motivation for change, provide culturally responsive management and incorporate all those cultural factors into the treatment plan on how you approach, you know, every patient.

Dr. McColley:
Let's discuss the patient case that brings some of these concepts to real life.

Dr. Hadjiliadis:
Imran is a 10-year-old, devout Muslim boy with cystic fibrosis, has been losing weight for the past 6 months. He has short stature, has malnutrition and declining lung function. Imran admits that he stopped taking his enzyme replacement therapy without his parents' knowledge 6 months ago when he learned that it was porcine derived. How will you approach this situation with Imran and his parents?

Dr. McColley:
The interesting thing with this is that a child has made a decision based on religion without really engaging parents. And of course, any of us who are parents know that a 10-year-old, although they need a lot of supervision, does a lot of things independently, and particularly when he's not at home. So I think this is one of those situations that starts with asking questions, and the best question is also why you made that decision. In pediatrics, it's also important to be prepared to calm family tension, because a family that finds out that their kid has not been following something that they thought they were can be very upset by that, and that's normal.

In this case, I'll finally comment that it is important for healthcare providers to know some of the tenets of Islam, and that, like many Abrahamic religions there is a focus on health that can supersede other, for example, dietary restrictions. And so one of the things that's happened a lot in my own practice is discussions with teenagers about why they should not observe fasting during Ramadan because they have increased nutritional needs.

Dr. Hadjiliadis:
I'm going to add here that we can make the religious community of Imran's an ally of ours. So utilizing the Imam in this case and how, you know, this is appropriate, might provide even more validity to us saying that this is something that's okay because it's medically, you know, oriented.

Dr. McColley:
That's an excellent point. And indeed, I have done that in the past as well.

Dr. Hadjiliadis:
I think that would be, you know, the most important approach is engage, you know, Imran, engage the parents. Maybe have them separately, also to see, you know, where they're coming from and see what their concerns are as we do that.

Dr. McColley:
We've reached the end of this episode. I want to thank all of the esteemed faculty for this engaging discussion. We'd also like to thank Vertex for their support of this program. Be sure to claim your CME credit by filling out the evaluation and post-test. Also be sure to follow Iridium on X, Facebook, and LinkedIn for more continuing medical education programs.

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