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TRANSCRIPT - GR 05 24 24 "***Malpass Lecture - "Health Equity in Cystic Fibrosis: A Global Issue"***" Cynthia Brown, MD from Indiana School of Medicine

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Internal Medicine Grand Rounds

- Well, thank you all for joining us for the first annual Charles Malpass lecture. I want to extend our gratitude to the Department of Medicine leadership for making as possible and to Dr. Malpas and family, for Charl or Charlie, as he was known to his family, was an extraordinary individual, who touched countless lives. We are honored to have so many with friends, and calling from around the country, joining us today in person, and he last left the lasting like legacy as an educator, clinician, colleague, husband and father as an educator he was known for having a USB. Drive with numerous Powerpoints, that he was ready to drop at any moment, and for innovations in broncos could be teaching like skittles in our airway dummies.
- The scenes are still there today to remind us of all the ways you've styled, and teaching ourselves.
- His patients knew they could rely on him even in the dark. His hours and his colleagues knew that he was always there as an advocate for them. Someone who would be linked to the next hand would listen to their challenges, and be there for support. But I also know that in the fall 2,022 Carl joins joining myself, Eric Davis and Max Davis, for the initial mile which had recently reopened from Covid. On the first time that preliminary vision. Together we all started out together in a very nice, so I thought, we're respectable 8 min, 30 s mile Charles ran with us somewhere between the half mile, Mark and the mile mark waiting for us and cheering for us.
- And it was really that moment that someone was through Metrics will be came out. He was someone who put himself to be his best, whether he, and as a career as a father, as a runner, as a human being, but he also was there to to hear for us to do the same thing, that we have to be our best sell and everything that we did
- today. We honor that memory with this lecture, and we are pleased to welcome Dr. Cindy Brown, who knew Charles as a fellow fellow to come and give this lecture.
- He is going well, educator as a teacher and as someone who see desire to see other, just for bad cells for those of you not know, Cindy. She hails from a small state south of Oklahoma, where she unfortunately went to school. But I won't hold that again before going to the John Thompson University, I was reminded, educating members of our faculty here today and later coming to the University of Virginia as her first faculty job, where she educated myself, Charles, and many other fellows before going off Indiana University, where she is currently the professor of clinical Medicine, and leads the adults to think by roses he's also the Medical Director of Clinical Research Center at Indiana University.
- Please join me in welcoming Dr. Brown, whose entire day I will note in Uva colors as he presents the first annual Charlest memorial lecture.
- Thank you so much for inviting me, Aaron Kyle, when I got the email, and in January asked for me to do this I would just like to sort of start by acknowledging you know

how meaningful and how humble I am to be here, I've given, you know, like many of you lectures in many different spaces, and for me this has been the most we are racking one put together. Because and I'm just more nervous here than I probably been in a really long time. So I also wanted to just acknowledge the Charles is meaning to me as well. I remember him first at the house staff, when we were just hoping and praying that he would go in pioneering medicine, and n terminology, or Gi, or any of the other things that you consider. And then he stayed on as a fellow, and Charles were my fellow, so I was very privileged, and I just kind of remember being on round thinking to myself how probably was the least smart person on ground. But I was always cha challenged by trials. Immediately kind of pops into my mind is and and what you know at that point is that he is 5 steps ahead of you, waiting for you to catch up, and when you do finally catch up to whatever the joke, the the piece of knowledge.

- That's a week September tenth. Okay?
- So, as Kyle mentioned, I left here, I went to Indiana University, where I direct our adults to, as you all know, particularly an adult with a large disease in the United States since 2,014, more than half of the population.
- So we're we're probably about 57% of the population living with the specific United States or adult here and and around the world. So we'll go next.
- I'm just gonna kind of walk you through some of the things that we're grappling with. With the shy line on where we are today today. Discuss inequities in this regard in the Us.
- And also look at sort of the world. It's really easy to get up in your bubble about cystic viruses around.
- But first of all, because I know there's probably a lot of phenomenologists in the room, but I don't know how how long it's been since many of you some basics.
- So when I started my residency now previous.
- Well, the symptoms of the disorder caused by genetic animal. So what this has as you can see, this is a large Panion transport, bipartite as well.
- More than 2,000 genetic variants have been described.
- Manifestations of the disease primarily are when you don't transmit your blood with imperative distillery. Parents and broncosis, chronic pause and severe cases, respiratory and sympathy.
- What you may not know is that we first they were dying about malnutrition highlight where we are. We are in a good space in the United States. Like many Northern European and Westernized countries where we're seeing an increasing survival over time.
- The first, as I mentioned the first pathologic description, was actually 1938. At that time children barely barely live beyond the age of 2 years as of 2022, which is the last provider.
- I will believe this with important sort of things that happened along the way. So with most children, we're dying in the forties and fifties of Mount Cushion, we started to see increases in survivability. Illness began to catch up, and some of the common medications that we think about things. I also like to highlight. That I do think contributed to care is the initiation of the Cf. Foundation. Cf. Foundation is started to standardize what we consider.
- Get them on pretty much with pay credit.

- So I mentioned Cftr modulator therapies. That's the one we consider highly effective Cft but same to your moderator therapies. The accommodation therapies combines directors.
- What it did was bind to cf pure protein that was able to be transferred to the cell surface, and that core open, that Flora Channel opened a while more, for I just get the problem with the most patients with Cf was that you know these amendment F. 508. That's a misinterpretation that leads to a confirmational change not permitted adequate cell service.
- So when you think about the homes. I guess patient with them. By the way, they have less than 1% of. So that's then you combine it with a potential to increase correct.
- So okay, so we haven't had these very long back in 2011 is the first publication of our and with brand name in the United States. This was a truly landmark trial.
- You could see with the for for a small population within 2 weeks, one increase by 10% of sweat chloride and drop Laura into what's the indeterminate range? That's what this dotted line is, so to say, somebody has cystic fibrosis. So we're showing that we are actually affecting the
- There's a way that they work.
- However, the problem is with this using potgenator, I have to. Only we're only able to get drug out about 78%. We see that population.
- So then we go into some of these other drugs and other mutations. So electroceth was approved in 2019 very big deal in Cf I don't know if you know this, but Francis Collins he was up on stage. He plays he played the guitar, and he said, so he's up there playing the guitar, singing. I think the name of the song is and he has started this song. I mean earlier had to add somebody as the Cftr modulated.
- So this is the shown to be effective, for any patient has even one copy of the F. 508 mutation and then, as the FDA.
- And you can see if you had one. This is data from people who had 1 5 away with the second mutation being what's called a minimal function mutation. So a mutation that would not be predicted to have any chloride activity. So again, here we are in 2 weeks seeing it almost 15% improvement. Fb. One increased over the life of the trial and an over 40, and this Wi-fi. And this is approved very rapidly by the FDA. Quickly rolled out. Many of our patients are, of course, benefiting from it, but this part of the first only 90% of there's a 10% who we have to look at other if you look, 43 have to being introduced. But in 2022 it dropped to 15 in my own institution. Well, what this translated to was we used to have an inpatient pulmonary service. We would have 7 to 10 cf. Patients admitted at any one time by 2020, they said. We have to disband the pulmonary service inpatient pulmonary service. We don't have enough patients in their pulmonary, it would be a service that was like 60 to 70% cf, and they said, There's just not enough for house to do.
- Why, it's happening abundance. He's so you can see, in 2,019 in the year before the birth. There's about 300 pregnancies, and every year you're gonna be more likely to to operate and be able to carry a child. But anywhere there's mucus anywhere. There's an excellent plan.
- Cctr works. So throughout the female reproductive tech, we think improving fertility issues, yeah dramatically down. And the vast majority of those were actually retrans. So not a lot of people getting new transplants right now.
- And I already mentioned the survival statistic of 56 years. So this has been transformative. But we're not done. So what's next?

- It doesn't do anything about paying bigger jeans. It just makes what's their work better.
- So we have to. For this last 10% is going to be the bigger hurdle for us to get
- so lots of problems, how do you deliver? How do you deliver? It belongs the people who need it the most still have so much mucus. If you didn't inhale therapy, you may not even get the genes where you want it to be messenger. Rna. Gene editing engine transfer therapy. But then we're probably, I would think, probably 10 years plus for supervisors to have, you see.
- So I'd like to kind of hit on some health equity issues that we see in the United States specifically on people in the population. What we are seeing is that the population of individuals.
- So you know, you can see in the under 18 group almost a quarter of the population identifies as a minoritized group of individuals in the United States, and it's been going up every year with the largest kind of country. So we have an increase.
- We're starting to recognize it more. We're starting to make sure that coming up on newborn screening. But it's it's missed a lot. And you'll you. I can think of one individual that I follow my clinic. She is a young African American woman who was diagnosed at the age of 18, her first interaction with the healthcare system, which was a pediatric, you know, large Cs Center pediatric. So when she was admitted dehydration, and told she had barter syndrome with metabolic alpha. 2.
- And that should trigger, can you see so the minute like that that should trigger a sweat. She was not diagnosed with asthma, which was never asthma, and she was always been and then developed diabetes before the age of 10. It was.
- Everything was there, just waiting for somebody to see it. Age of 18, when a physician who in the community had scanned her, saw the Bronchiectasis and the the report. Also, you probably should consider cystic, and that triggered her origin.
- What happens it we we do see these patients get more likely to be diagnosed a little bit later. Age outcomes Megan Mcgarrett at Ucsf. Has done quite a bit of this work, but she has shown that both Hispanic and black patients they have worse imaging findings.
- Exactly. Our Hispanic patients have higher mortality mutations that should predict that they do that so the the more minor mutations they have, a higher mortality, despite hiring identify as Hispanic versus non Hispanic, starting the the mortality device around page 10.
- So imagine when screening being something that's been transformative helping us identify patients earlier.
- I maybe it shouldn't surprise us. However, our new zoom don't do a great job, always identifying the minority population.
- So these have choices, and how they do no more screening. So. And I'm not a pediatrician. So I'll just preface this. This is my understanding. If there's a pediatrician to the room, I may say something completely. Well, I know what we do in Indiana, so we'll start with the heel stick we look at for what's called irt. I mean our reactive trip signage. This is a pancreatic enzyme. If this is abnormally high then they will duplex who is using genetic screening panels. Most of the genetic screening panels pick up in the mid 100, very few do a 23 g panel anymore. (135) 113-9165. So they're just screening for some of the most common mutations.
- If you if you're white, that's great, and it'll get 97% of mutations of other people. But you can see that if you even just one variant, the the black non Hispanic, Hispanic

patients are lower. And this, this is kind of a little bit confusing graph. But let me walk you through it.

- So of the total population of individuals who are white nominating 84 screening panel, and I know they account for 70% of false negative. So white patients Ca, account for 85% of the positive newborn screens, but they're under represented above the false positive as well as delay diagnosis. Whereas why? Why? Non hispanic patients account for about 3.6% of the positive one screens but are overrepresented and delay diagnosis. And you can see similar graphics there. So more ethnically diverse states have a lower likelihood of identifying 2 variants on their new one. On this 139 newborn screen panel you can see the hay in Puerto Rico, or the 2 places that do absolutely worse with newborns training. Be able to identify 2 2 mutations. I highlighted Virginia here. Pretty high up there and then Indiana. Probably no surprise, for on that lower half to take medicine.
- and patients who are minoritized have a lower likelihood of why, non Hispanic population is eligible.
- Hi. However, only 62% of black patients and 2 thirds of patients are eligible for service. I don't think about so. This data was presented last year at the North American. Yeah Conference by the side, Georgine Hergen, wrote Rhoderic Child. So if even if you're eligible you have a mutation that makes you eligible. If you identify the minority, you're less likely to be prescribed.
- The Alex. Has Aiba, and there's a delay in prescribing. So even when you, when you're part of the group that's lucky enough to be able to get it. You still don't.
- You can see here, if you look at, say, around one year of the live population about only about 75% more on.
- Let me. So now, I'm gonna yeah, I have an idea and talk a little bit more, please.
- So what's happened in low Louise? Yeah.
- Jonathan, woe from the Uk. Has published a lot of data in this year. This shows where we have diagnosed populations of individuals with cf, they don't know. Most of them are gonna be in us. Uk, Canada. So we have some of the larger populations 400,000 people have been diagnosed with. Here, however it is suspected to be underdiagnosed significantly.
- And I really want to highlight India. This is a genetic estimates of disease in India is is between carrier state should be between one and 2,000 to one and 30,000, so that this is based on a one and 30,000 estimate so if you're kind of given the size, the population in the Indian subcontinent continent, if it was a 130,000 residents. This there would be 45,000 additional people in India alone.
- And it's not no right like it's really a disease that's not known in India.
- I have. I showed you survival statistics. I wanted to kind of compare and contrast United States with other countries, but many of these countries can't tell you what the medium, but what they can tell you is amongst the people who've been diagnosed with cystic fibrosis. So you look if you look here, we have Australia, us Uk, France, Canada, we're all over the age of 20. We use it starts to dump down South Africa, 17 Poland and Brazil, only 13,
- Russia, 1239, Us. Population in India immediately.
- So these are all like releasing individuals, probably not in a very young basis.
- So thinking about Cf. And low and middle income countries. Even knowing about the disease. The country doesn't know if this is not a widespread disease. So the first cf, awareness day in India for the first time was 2021.

- Problem is, you have to get over a knowledge barrier. The second problem is, it's hard to diagnose cytochism.
- Not every place has a capability of doing a swipe chloride. Even in the United States you have to get come into a referral Cs center typically to be able to even do a swipe in India. Very few centers that can do that just gene testing is even harder to come by and a lot of countries. So one thing that said is, you know, maybe we can use this phenomenon of autogenic wrinkling to sort of this quick and dirty screening test that you can do in clinic. You have somebody who's malnourished, maybe sick has respiratory symptoms that you're concerned. We could see how long it takes for palms to wrinkle and you can see the the average time to ring for a patient with Cf. Is 3 min versus healthy or carrier, which was, I think, that the carrier was over 10 min, and they, healthy, quick, and dirty, test potentially referral into a more tiered person, where you might be able to get a situation. Maybe you just initiate there.
- Then we get to the lack of global expertise. We have well organized CFC foundation is sponsoring some global partnerships. So Sami announcer, who is at University of Michigannshe has she has taken her Cfo, Egypt and Turkey to train people there on what is best now. But even things like enzymes, airway parentsnsodium, chloride, like, what are the things that you can do to improve outcomes even in the absence of the these very expensive pair.
- So this is data. So the nutrition coming over this nutritional is really important improving nutrition. So, and even in the United States. What we've shown your nutritional status at age 2 will predict what you're where your life functions. You're gonna have a poor language. 86.
- This is some. This is the work that some of the work that Dr. Nasser did in Turkey. In this group you can see with just sort of baseline interventions they were able to get weightnwait percentiles and Bmi up in this group of patient by just instituting good high quality. So even in the absence of some annotation being able to provide high quality. Overall tools appear is very important, and you can see also, they were even able to start moving their needle on as well.
- And then I mentioned lack of access to standard therapies. We take for granted we have access, not just to modulators, but to inhale antibiotics to door days, butnmixing it with some water, and it may be tap water. You don't know. Nobody's had. Nobody has to still water right? So you're mixing your salt together, you may be inhaling things that may even microorganisms into your lungs. And then, you know, finally, I do want to talk about lack of access to modulator therapies.
- I do want to show that because I want to, even before getting into the modulated therapies, I want to compare
- Canada which actually, Canada is better than us specific members. Here generally you saw that they they had a higher Median patient age. They also have a higher Median predictive survival than the United States. But compared to South Africa, and we'll getnfor their populations before modulators. And you can see, I I touted that we have been a situation where the population is over 50%.
- There is more we are, you know, Canada is more non Hispanic white than South Africa. But you can see some of these standard therapies in South Africa. You're more likely to be on hypotonic saline than say Canada, becausenone thing like their days, they're much less likely to be on and individuals in South Africa who more likely to require. I'll do it in addition, if you look, the red groups, Canada, the green groups for South Africa and across all aid groups. Individuals in South Africa had lower lung function and higher percentage.

- So kind of again. How do I?
- We have to get the basics right before we even get to modulators?
- But I'm gonna kind of with modulators from 12 to 27.
- That looks really awesome.
- But if you look, and when we kind of when you drill down, these are all patients that are primarily in Europe, us Canada, Asia. If you go to the rest of the world.
- the entire rest of the world. Beyond these groups only 914 of the diagnosed population have access to pstr modulated therapies, which is 5% of the diagnosed population. And this giant chunk of patients that we think are undiagnosed. So we are really in a, you know, a huge equity gap here and it come. A lot of this does come back to reimbursement for the medication.
- So the cost of Alex has either is over 300,000. The list price is over $300,000 per year. We're talking about a medication that can be prescribed as early as age 2 and prescribed throughout the lifetime normal lifespan for an individual just perfect shows in blue areas where people have access. And there's a reimbursement agreement in place. Red shows that there's no reimbursement agreement in place, and the hash line shows that areas where there's something going on. And you can see that Brazil has an agreement. It's not yet been pulled out for Alexa as either, until you're 18 and pull them. We're only going to pay if you're over age 12. And interestingly, in the Uk. The Nice, which is their cost effectiveness group has recently said guys, but the price is not cost effective for quality of life. You're spending. So maybe we need to reevaluate new prescriptions even in the Uk.
- And this is the draft guidance from that. So, even when considering the condition, severity, and its effect on quality and length of life, the most likely cost effectiveness estimates for all these are all different. Cf, 2 tier long delayers.
- They're above the range that not considers acceptable using. So it's possibility that the Uk may run into access issues as well.
- And this again kind of highlights the list price of over 270 even for me, which was, of course, that well, and also like to show the patent expiry dates. We're still quite a bit ways away from patent integration.
- And we'll go into that here in a second. Dr. Bottle really has dug in deep. He's like I said. He's a leading help. And people, I say, well, it's we need charges because of the money that goes into R&D, he would do all the Sec filings and create this graph. So this is all data that he pub that was publicly available, and the reported revenue from 2,012 to now is over 45 billion is 18 billion. So there are probably additional.
- But the argument that it's well, this is the money we needed to spend in order to recoup our costs is us.
- So is there an alternative? Because this is really not that hard to make so much cheap. I think it's even 4,000 a month. It's actually probably is that maybe you kind of think it's actually a little over. I think it's more like 15 a year. So it's I mean, it's really much more effect affordable in Argentina. We can do you one better we. So so the people in South Africa said, I know we have to pay for this out of pocket, so can we make it last longer. So Alexis Iva is extensively metabolized by the Cytokine system and the sip. 3, a inhibitors. So if you if you combine Alex Iva with a really strong. Sip. 4. A inhibitor, 3. A sub. 3, a inhibitor. You only have to take it twice a week. So, and then I then I said, you know we can show it works. So this, the the top group shows a change in sweat fluoride one month. If you are on the standard unchanged dose versus the the modulator sparing dose. Okay? So maybe the the

sweat fluid went down has a slightly sleeve steeper slope. But you are still getting a 15 point reduction in sweat, fluoride in the live testing.

- And this shows the change in lung function. Now, the right. You can see the people who are on the standard dose had higher lung function to begin with, and when these patients who are either on the modulator sparing dose unchanged, or maybe they started on a regular dose, and then went to a modulator sparing dose. You can see that the the Delta is similar between groups, even though the people who are on standard dose started a much higher fee one. So people around the world are getting really creative in ways to get around and patent and get drugs to their patients. But it's a big, it's a big deal, and there's a lot of organization around this around the world.
- So I'm gonna kind of circle back to the United States. Right? We talked about it being a really expensive drug.
- The Iser, which is our cost effectiveness. Group says, you know, really probably based upon everything we know. Cost effective is this should cost more on the order of it. What else? What can we do?
- I'm in. There are increasing use of patient prescription drug affordability boards. So people like these are high cost medications. It's happening in Medicare with things like Eliquis, you know, but it's happening. And yeah, in fact, Colorado had included Tricia in their first drug, and they were able to keep it on formulary. But it's coming up.
- And then in the background.
- Initially, vertex was like, Yep, we're giving everybody great patient assistance. Nobody's gonna go without phone. And so for the first 4 years most patients got about $150,000 in patient assistance. And then last year they said, You know what? Never mind, we're only gonna Max, we're gonna maximize per year. So patients are running into. And there are other programs we utilize. Have you utilize health? Well, health? Well, used to put in as much as $15,000 for covid per year for patients with. Cf, well, we're running out of money in that now. Really early. In fact health will close down last year for the first time for new enrollments. It's already closed down. So it's open from January until just recently. So it's closing down as well. So I it's gonna it's gonna happen we are gonna run into drug portability after on their medication list so they will exclude it, and then they expect patient assistance programs to kick in. And so we we have now have had an individual for 3 months now going between perfect saying, the company has to pay for this, the company, the interest company saying, No, we don't and the last thing they said is, you know, he should probably import it from Canada. That was that was, we can buy it from a cheaper price from Canada, and we'll import it from Canada for him.
- So I'm gonna in here.
- The the Cftr modulator therapies have been nothing short of transformative
- hands down. The best thing I've seen in cystic fibrosis in 20 years, however, affordability data access is a huge issue, and even when we take that out of the picture, we are vastly under diagnosing and under treating individuals in both in the United States and around the world. In addition, if you think about sort of the the next step, we still have that 10%. So we need to all stick with this until we have equitable and adequate healthcare. So thank you very much. With that also.
- Heck, thanks.
- Okay.

- I will do the Chief President's job of starting the questions. Thank you for a great talk. I'm wondering you alluded to sickle cell and genetic therapy. So we've seen some advances there, but this therapies are pretty expensive as well. I'm just curious if anyone has done any cost cost assessment analysis. Comparing for Cf. Gen. Editing versus sort of cft, or modulated therapy over the lifespan with sort of extended.
- I think you know, I think that we're gonna see this a lot, though, with genetic diseases. And I mean, reality is is if we have an effective gene therapy for Cf, and you pay 3 million dollars for one time. Then it's gonna be cheaper than these drugs.
- So interestingly, one of the sickle cell drugs, one of the 2 approved therapies is actually a gene therapy from birth. Now in the sickle cell. Hate saved as well.
- Michael Jordan.
- Thank you. That talk that was great. I was really struck by
- Argentina had done. There's 3 companies that make the modulators. We're not going to be able to do that. What do you see is the kind of low seeing fruits for fixing that problem right now for people who are those are obviously expensive drugs that are globally available, right? Like population living with arthritis in humora is a lot different than the population. However, I think if if it's proven that we can make those drug price negotiations work for drugs, other drugs and I guess what? Well, it's just shocking, and it's like so scary to make a patient speak up. So most of losing their mess me, thinking about the fact that I have never my crew made a new diagnosis of Cf, and I think that newborn screening is a big part that. But you show data that shows that newborn screening is not as effective for minoritized patients. Do you think that we're missing diagnoses in that population for folks in their like teen or young adult years. And how do we better?
- What non Hispanic population? The oldest patient I've diagnosed with sisic is 62, maybe 65. It's only 62 65 every every year. I in our clinic we have between 5 and 10 adult diagnoses. And sometimes it's it's it's one of the things. When I'm lecturing about non. Cf, rocky accesses, every patient should have a swipe, alright period when you have a disease that has a potentially, dramatically effective therapy you want to know right? Like may may be 20 years ago, and everybody was gonna end up on hypertonic saline and then chest wall oscillation, anyway, and there was nothing else. But if people who are diagnosed later in life actually are more likely to have a modulator responsive mutation, at least one, because they they were the ones that used to be called.
- They often have some degree of residual function, and those are ones that often even respond to potential. So every patient gets a swit chloride when I see them this real quick on that. So people don't sweat. So what did? What's your suggestion that they all get genetics in part of the challenge with the genetic testing, it's based off these cohorts where we just historically thought, Cf isn't like people. How do we get.
- I believe, represented cohorts we have. We're not just looking at 140 mutations that occur.
- And if you, when you didn't have the opportunity and kind of go in. But when you go at X, us percolates to the top even in most cohorts, but it's like 50%, not full gene sequencing is really right. So most of these are screening panel, and we get the most common mutation on screening panels. And I will do that as a start, because a screening panel is cheaper than full gene sequencing so. But if my screening panel is negative, then I request to do sequencing deletion, deletion, and

duplication. And you know, I mean, like, there it kind of can can continue on with different things. Look for deep traumatic mutations like. There's different things you can do. If your suspicion is high enough, you can keep it so moving forward like 2030 years. Since you have a therapy for this kid set up one. Now, what do you anticipate into a long term health? I anticipate it to be excellent. So we're gonna have when they project out what Cf looks like, say, 2040 the population being diagnosed. But the percentage that are adults are dramatically higher. With an estimate less than 10 to 20 sort of significant lung disease. Most most people will have normal lung function. Even now, most 8, the average lung function for an 18 year old living with it's, you know, most individuals enter. Don't leave a normal one option. It's a group of people. It's a group of people who have already had damp the the pre, the pre modulator damage. So they're living with a lot of sustained bronchiectases that are going to be the ones that continue to be problematic. But I think we're gonna when when these trucks were coming out I was liking it. Antiretrovirals came out for HIV kind of dating myself.

- But the patients like it was transformative for these patients. But then all these other things popped up right? So what are we going to see. What are we going to see in people who've lived with Cf for?
- Are we gonna see heart disease because they have been told to eat a high, fat, high calorie diet for their lives, and they have increased information.
- They may end up with kidney disease because they've gotten, you know, 45 courses of immune glycosides. And are, we gonna see, you know, Covid with kidney disease. And then the things we don't know like cancer, we know, there's a 6 times increased risk of colon cancer. But are there other cancers that are gonna start popping up that we haven't considered with the police updated? There was actually a just past week American Grass Society, the other development and drug. And I guess there, you know, the orphan disease has a tax break for the company to do it as a financial. And apparently they have a something called an Ira right? And that's what makes the $200,000 probably cost. It's maybe like $5,000 to make it.
- So, a new law actually set up before you can actually use the one compound multiple indications, you get a lot of money, but then don't use it. What one indication, you know, apparently the great thinking for that is that we can't have a better pricing. But the bad part is that there was about 2 pharmacy companies that drop the phase, 3 clinical trial to move on. So there's a little delicate balance. I think we should probably all have to pay for at least some partial press control, nowhere to see sort of more tax.
- Have you had any? Travel on a foundation before they're talking about that. Any thoughts on that congrats with faces?
- No, I I don't think no, I haven't really like thought too much about that but session.
- But you can't charge $300,000 for something that cost $5,000 to me.
- So these are things like that.