[Researcher\_1] 0:05

Thank you very much. Just one other point, we obviously this meeting is going on to almost five o'clock. So if you do need to take a phone call or you know, grab a drink or whatever, just feel free to go and do that and just rejoin us at your leisure. Don't, don't feel like you have to hang around. Alright, so to start with, it'd be good to get an idea of who's in the call with us and where we all fit in the kind of CF patient care pathway. So I'll kind of describe the information that we want. So I'm [Researcher\_1]. As I said, I'm a methodologist at the Newcastle MIC.. And I don't really have any interactions or exposures to people with CF outside with this project. But I'd hoped that you might be able to let us know where you fit in the care pathway as we go around. So if I start with CFG1\_1, do you wanna give us that information if that's okay,

CFG1\_1 1:12

yeah, I'm good. I'm CFG1\_1 and I'm a CF physician in the adult unit. I know some some people here, certainly [Researcher\_2] and [CFG1\_4], I know. So I work at the adult units, we cater for about 450 patients, and I'm also involved in the --- CF project with --- running.

[Researcher\_1] 1:34

Thank you very much, [CFG1\_2 ].

CFG1\_2 1:40

Hi, I'm [Clinician\_2]. So I work into a paediatric network clinic and into the adult services as well. And I'm also doing some research in my spare time in health therapy use and co-adherence alongside modulators. So I see people with CF clinically and have done for about 20 odd years and I'm the person who tries to get the samples that you would like to to be testing.

[Researcher\_1] 2:25

Thank you very much,.

CFG1\_3 2:28

Hi, I'm [CFG1\_3] . I'm a clinical CNS at the adult CF Centre.

[Researcher\_1] 2:37

Thank you very much. Sorry, how long have you been in the role for?

CFG1\_3 2:40

Oh, sorry for two years and previous to that I was a CF nurse.

[Researcher\_1] 2:46

Thank you very much..

CFG1\_4 2:55

Couldn't turn on my mic. Yeah. Um, I'm [CFG1\_4]. I'm an adult CF physician, we care for about 600 patients. I'm also a professor of practice and respiratory medicine.. So I've got quite a mixed experience in CF across clinical and research. diagnostics is mostly actually to do with the diagnosis of CF not to do with infection diagnostics as such, and involved to kind of clinical trials in CF.

[Researcher\_1] 3:40

Thank you very much, [CFG1\_5].

CFG1\_5 3:44

So I'm a consultant pharmacist in paediatric CSL D, which obviously includes CF and I have worked with children with CF for the last 22 years I think now. And so I see children, inpatients outpatients work with them clinically. More recently, I've been involved with doing some research, using pharmacokinetic modelling to determine dosing of an antifungal medicine. And also want to take this further so particularly interested in this diagnostic pathways that you're looking at.

[Researcher\_1] 4:27

Wonderful. Thank you very much. And finally,[CFG1\_6].

CFG1\_6 4:32

Hi, so my name is [CFG1\_6] , and I'm a recently retired senior biomedical scientist. I had a very big involvement with lung transplantation. And so I actually do a lot of combination testing to try and get drugs to use for time of transplant. On the back of that mould, so become an expert in cystic fibrosis, attend the the weekly MDT. And so for many years, I've done an awful lot of work for cystic fibrosis research, where that's just collection strains for testing your antibiotics or getting samples for project students and things like that. So we do have a very big repository. And our lab is set of pathogens. And we develop the the the NTm, agar, which is currently been circulated for use in CF, and other other purposes. And so that's kind of my background. So currently, and. So the Witten party we convened a couple of years ago, just just before COVID. And it was to update the laboratory standards for processing of CF samples. And so the document first came out in 2010. And it was very much out of date, we spent the last two years as a group, redefining those standards. And that document is now all written and finished, just went off for proofreading over the summer. And that's due to come out very, very soon. So we have rewritten what we want, expect people to do. If they have a sample from a patient who has got CF.. It's a new new subject altogether. And that's where I am

[Researcher\_1] 6:37

wonderful. Thank you very much for that [CFG1\_6]. So we've got coverage from we've got CNS, we've got BMS, we've got consultants, pharmacists here. I presume everyone is involved in an MDT and to some extent, where do you all fit in in the care pathway for patients with CF in relation to each other?

CFG1\_6 6:59

I would say for me as a biomedical scientist, I was the first one, invited along to an adult MDT many years ago. And for me as a lab, lab scientist, it was a real eye opener. When you go to an MDT, you hear about the patients how they are compliant or non compliant, about what the issues are. And I just think it is a great insight, as it just helped to put things into perspective when I work with CF samples. And so I carried that on until I retired. I don't think anyone in our centre is actually doing that. Now, obviously, the consultant microbiologist goes along. And but for us, it was more just a communication became very much easier because we all knew each other very, very well. So any questions or anything, we could just email each other, or ring each other, this sort of thing? So that's kind of where I fit in with, with that side of things yeah.

CFG1\_2 7:49

Do you mean sort of, professionally, [Researcher\_1]? So where on professional sits into the MDT. So I've worked across a few different CF centres. And I guess the physio role is that fairly similarly across them in there, our focus tends to be on making sure that there's up to date lung function and giving some context to that. Thinking about sampling, why there are samples, why there aren't samples, have we done induced sputums if we can't get samples, those sorts of things. In more recent years, and sort of the last decade or so, physios have tended to take on more of a prescribing role as well. So kind of taking some of the actions from MDT, making prescriptions, considering what might be the most appropriate thing alongside our MDT colleagues. So I guess again, for example, with that focus on inhaled antibiotics, working alongside the consultant, the pharmacist, nursing team to kind of really think about what is going to be the best choice for this patient in terms of both their microbiology but also adherence and other things that might be needed. So I guess we've got a role in terms of monitoring, we've got a role in terms of treatment choice and a role in terms of that physiological monitoring versus treatment monitoring as well. And then bringing that together in MDT, I think, it's fair to say, and it probably will come out in the rest of the discussion that there's a lot of overlap across MDT roles within CF teams, and I think that's what makes it such cohesive care. We don't tend to get a lot of gaps down the middle of professions, but we do get quite a bit of overlap, which sometimes, I guess can be a little bit confusing in terms of boxing out who does what, if that makes sense.

[Researcher\_1] 9:51

Thank you very much. So now if anyone else have other comments to add there?

CFG1\_5 10:02

I can add to that as well. I mean, I think kind of what [CFG1\_2 ] described is kind of our experiences as well. I mean, I think from a again, I'll talk about it from a general pharmacy kind of point of view. I think the role of the pharmacy within the MDT has changed somewhat actually, in the last kind of four or five years really, in particularly, I think, since the modulators have come about. So traditionally, obviously, pharmacy has been seen as a supply, supply kind of profession, you know, you go down to your dispensary, and that's where you get your pills from. And I think, like I said, More more recently, we're very much integral to the MDT. So we work within the teams as inpatients and more and more so with out-patients to help patients to get the most from their medicines. So not dissimilar to sort of [CFG1\_2 ] in terms of from a prescribing point of view, from a monitoring point of view, still very much involved in the supply kind of point of view. And actually kind of some of our biggest work at the moment is trying to link up into primary care as well. So linking in sort of tertiary, secondary and primary care to make sure that people can get hold of their medicines in the first place. Because if people can't get hold of the medicines, they can't take them. And obviously, have a role in education as well. I think that's the other thing. So kind of educating families, and other members of the MDT on medicines as well.

[Researcher\_1] 11:38

Thank you very much. Have any other comments? A Sorry.

CFG1\_1 11:52

Go on, and he's gonna answer this.

CFG1\_4 11:53

I mean, I don't know what you want us to say really, as, as the sort of consultant clinicians and some consultant physicians in responsible for the care. I mean, I guess we have an overarching responsibility. We prescribe, we coordinate, we manage, across the team. And obviously, as part of our day to day work, conduct ward rounds, do clinics. And usually, although it's not always the physician, manage the team. And also try to bring together research, governance, clinical work, and all of those important aspects. So I mean, that's sort of a very sort of overarching viewpoint, I suppose. But, yeah, from day to day management to the sort of wider strategic direction of the departments.

[Researcher\_1] 12:52

Thank you very much, [CFG1\_4].

CFG1\_5 13:07

Sorry, you got your hand raised there, [Facilitator\_1].

[Facilitator\_1] 13:11

Yeah, I was just going to ask from, from my perspective, obviously, my responsibilities to ensure sort of like involvement of the CF community and ensure their insights and experiences kind of inform the work and inform the project. So I was just going to ask how much of people's work they felt was patient led maybe. Because I think you develop such long standing relationships with your patients, you obviously really get to know them, I'm sure that they think of you as family members. So I just wondered how much of your work you felt was patient led.

CFG1\_2 13:59

[Facilitator\_1]. Do you mean in terms of the way we now sort of structure care or more from a day to day viewpoint of kind of interacting with people with CF or both?

[Facilitator\_1] 14:13

We're probably a bit of both, really, but I guess it really may be more on the kind of like day to day aspects, you know, when it's sort of like around decision making about what treatment or you know, to adopt when to react to something went to perhaps change direction, try something new. Those kinds of things. Really.

CFG1\_2 14:37

Yeah. I mean, I think I think [CFG1\_5] , brought in that aspect of kind of education. I think over time, kind of education has become much broader in terms of it's become more communication education. So, so real kind of batting back into in terms of, you know, I'm being very led by people with CF. So building foundations on what we can offer and the both the monitoring we can offer the treatments we can offer, the even down to the sort of service we can offer really, and then kind of opening your up and responding to what people tell us works for them and how they feel they want things to be. So I think it is quite ladder. I'm thinking of an example recently, you know, where we we've got someone who, who really, from a standards point of view, and from a good clinical care point of view, we really want to have very regular communication with them, we want to offer them much more treatment and much more monitoring. And actually, that doesn't work for them in terms of them feeling that then they've got CF here in their face, whereas they would like it to be more in the background of their life. And so sort of balancing those needs. So in terms of how much that's led by people with CF, I think that probably varies from centre to centre with culture and ethos. But overall, I think it's really very lead. Within the framework of some standards of what we offer, what's actually accepted is extremely led by people with CF. I don't know if that answers the question, but that's how it feels to me. Yeah, I think

[Facilitator\_1] 16:29

I think you touched on it. It's sort of almost that negotiation, isn't it between each say maybe what's best for their health at that moment in time, but also what fits in with their lifestyle and what they're wanting to manage in their, you know, home like their lives away from clinic basically.

CFG1\_2 16:46

Yeah. Yeah, the whole thing around care is definitely a conversation, isn't it? I think that's how I describe it best. It's an ongoing, lifelong conversation of, you know, kind of offering and outlining the optimum and what we might like as clinicians, and then balancing it with what works for the person. So yeah, just having that continual conversation really.

[Researcher\_1] 17:11

Thanks. Great. Thanks very much, [CFG1\_2 ]. We do have some more questions about patient perspectives later on. So I'll come back to that a bit. If that's okay. We'll get on with the what the current practice is. So the first question is literally that what is the current practice for diagnosing formerly pulmonary infection or exacerbations in cystic fibrosis?

CFG1\_1 17:38

So can you say that again? I didn't, I didn't.

[Researcher\_1] 17:41

What is the current practice for diagnosing pulmonary infection or exacerbation in cystic fibrosis?

CFG1\_1 17:48

Oh, I can I can start that one off. It's there's two answers. There's scientific answer. And there's a pragmatic answer. The pragmatic answer is what the patient wants. They come in, they give you the right things, you give them orals or IVs. It's considered pulmonary exacerbation. The scientific answers the standard one about decline in lung functions, sputum changing colour. The number of times that is actually the case when you're giving people antibiotics is it's very little [CFG1\_4]'s smiling

CFG1\_4 18:24

It's a little bit more than that. I mean, around a basic framework, I do agree with you to a certain extent that we are definitely swayed, and it carries on from what [Facilitator\_1] says, by what the patient comes in with. And usually there is a strong feel before they come in as to whether or not they think they are exacerbating and whether or not they need a treatment that might treat that exacerbation. So then there's, there's there's that kind of approach the patient has, as they walk in the door as to what they feel they need from the consultation, which is probably quite unique in CF for lots of reasons to be honest, you know, the long standing relationship with the team, but obviously growing up with the condition, some of the nuances and subtleties about what a pulmonary exacerbation is, which sometimes is not that clear cut such as lethargy, but then there are... Yeah, I mean, you know, we try to be objective, we do try to, to look more closely at the information that we're receiving. And see if it does look like there is strong enough evidence for a pulmonary exacerbation to warrant some form of treatment. So for instance, objective markers, you know, FEV1, saturations maybe, but then really a lot of it is subjective, what the patient's reporting, symptoms changing, cough changing, sputum changing, volume, changing colour, you know, but Ultimately, there are some subtleties that the patient will tell you how they're feeling. And then it's hard to say 'no' sometimes in that context

[Researcher\_1] 20:10

definitely. [CFG1\_2 ] got your hand up as well.

CFG1\_2 20:12

Yeah, I agree and caveat it with that. I think we are definitely seeing that in the face of modulators that some of that nuance around how accurate it feels. People with CF are now when they feel they've got an exacerbation is maybe not as good as it was... and the team actually, you know, in terms of actually is this an exacerbation or isn't it, and people saying, well, I feel absolutely amazing. I'm definitely not got an exacerbation. You do lung function and it's 400 mils down. And it's like, right, what do we do with this now? you know, because actually you feel you've not got an exacerbation, I wouldn't have said you had an exacerbation. Now we've done some lung function. It tells me something different. So I think we're all feeling our way a little bit in the brave new world of modulators, and actually what what is an exacerbation now? What does it mean?, when do we treat it? What is being too reactive versus not reactive enough for long term health?, I think is just a little bit more uncertain than it previously was.

[Researcher\_1] 21:21

Thank you very much, [CFG1\_2 ].

CFG1\_4 21:26

Just to add, it is probably worth at this point, stating that, you know, within the research arena, there are very, there have been developed very strict criteria for what a pulmonary exacerbation is, you know, there are many different criteria that have been developed, but the one that's most often use used as the Fuchs criteria, you know, which is four out of the total 10 different elements. So, you know, in the research arena, there are strict criteria, but the reality is, that's not really what happens day to day in the clinic.

[Researcher\_1] 22:02

It sounds like just from these few comments that there isn't such thing as a standard pathway in CF, is about right.

CFG1\_4 22:15

Standard pathway to

[Researcher\_1] 22:17

Yeah, like a care pathway, or how, you know, it's Is there a sort of standardised process? Or is it very much on patient variation?

CFG1\_4 22:25

I mean, there are recommendations Yes, I don't think it's a strict pathway, there are recommendations. But I wouldn't say there's a strict pathway. There's a lot of discretion involved in terms of and individuality in terms of decision making. You know, once you've decided they probably are exacerbating, then you're trying to decide how severe it is and how sick they are and how appropriate it is to treat them with oral antibiotics or IV antibiotics and how appropriate it is to treat at home versus Hospital and the nuances around that with the background, the support of the individual, the family they're with. So there's so many different things that come into play there. Because you know, on the one hand, you could have an extremely sick patient who you're happy to treat at home. Because they're extremely well supported. They're very knowledgeable. They know what they're doing, but they're actually clinically very sick versus someone who's relatively mild, but has got no idea what they're doing and you don't really have a clue what they're doing. So it's much better to have them in and keep an eye on them and optimise their physiotherapy and as well as you know, monitor their treatment response. So that's the thing. It's very variable.

[Researcher\_1] 23:40

Sounds very patient LED. I think there were a lot of nodding heads during that. That description there. Obviously, we've got secondary care, tertiary care covered pretty well in this focus group. Where do patients mostly present is it in the community or a GP or as a clinic in a&e? How do they how do they normally present

by text message?

CFG1\_4 24:04

That's far too old school surely. WhatsApp and TikTok. Absolutely.

CFG1\_2 24:14

I mean, I'm sort of saying it in a jokey way. But But actually, you know, I think the CF team is key in to to people with CF and you know, aside from exacerbations, largely people present with their primary care complaints to us as a CF team, everything comes via us and we farm it back out to the GPs wherever appropriate. You know, it's kind of like really, I think, you know, your skin problem probably needs to go back to your GP at this point. So it very much is direct care to us. We our first point of contact, it does tend to be that perhaps people will present by by a text or an email or or, or however kind of that centre has got contact setup. And we're finding more and more certainly we use a lot of virtual monitoring, virtual care. So sometimes the the contact is actually, you know, checking a spirometry, and it's down. And there's no a note on it saying, oh, yeah, you know, this isn't so great. I'm probably gonna need to hear from you. So, so very much I think the contact comes in directly to us and is managed by us as a specialist team.

[Researcher\_1] 25:35

Yeah, thank you, [CFG1\_2 ]. We're all in agreement with that are we? Yep.

CFG1\_4 25:39

So I don't even think we really talk about it as primary, secondary and tertiary, you know, there's, you know, we're their specialist care centre. This is we, therefore, are usually their first port of call. As [CFG1\_2 ] says, sometimes it really is inappropriate, because it is much more like a GP community thing. But for the vast majority of things that will be asked they come to you first, and usually, mostly it is appropriate.

[Researcher\_1] 26:05

Why do you think they come to you? Is it because of the rapport that you built up with the team? Or is it the responsiveness? What do you think it is that draws them to come to you when they think there's a problem, even if, as [CFG1\_2 ] was saying they have a skin condition or something?

CFG1\_2 26:19

I think in the case of those sorts of sorts of things, it's often a mixture of responsiveness. So actually, they can speak to a specialist team almost instantaneously in many cases, or someone from that team. Whereas particularly at the moment, you know, it's challenging to hear from anyone within primary care, because there's massive challenges there, there's massive challenges everywhere, but the way our care is set up means that there is access. So there is that aspect, but equally, I think people understand and know that the majority of the things that they have an issue with are related to their CF and that is appropriate and needs to come via the specialists team. And that is drilled into people from paediatrics. You know, if you're unsure if this is related to your CF, come to us. And I think that's even more important now with more unusual treatments like the precision medicines, you know, because certainly, you know, non specialists clinicians can't necessarily keep up with all of the things that we might need to think about. And we do see issues where people have presented to non specialist clinicians and are put on something that interacts with that modulator or whatever else so so it's the right way. It's the way care's setup, people access care that way.

[Researcher\_1] 27:49

So we touched very briefly on the effect of modulators on presentation. How do patients present with infection or with an exacerbation? How do they present to you? In terms of the mode or in terms of that, sorry, this year, the signs and symptoms what does it look like? Well,

CFG1\_4 28:09

the most common symptoms are an increase in cough and increase in sputum or change in sputum. But other symptoms include breathlessness, tiredness, and maybe fever, although that's relatively unusual. They will probably have their own spirometer they may have even checked it and that might be down but mostly it's cough and sputum change, really.

[Researcher\_1] 28:32

And in terms of the diagnostics that are used, what are the diagnostics used for a CF pulmonary infection?

CFG1\_4 28:39

Well, the key one is spirometry. in terms of objective measurement.

[Researcher\_1] 28:45

Does anyone have any others? Try and build a list.

CFG1\_2 28:50

Yeah, I'd agree largely spirometry and then the other thing might be sputum sampling. So you know sometimes you do see someone for a routine clinic and I guess it gets its whether you mean infection or exacerbation, you know, exacerbations will mostly be picked up by spirometry, we may sometimes pick up infections like a new Pseudomonas growth that actually they haven't yet had a lung function response to that but we would still treat it. So. So sputum sampling, cough syrup sampling, that that sort of thing remains important.

[Researcher\_1] 29:31

Are there any other diagnostic tests that are used in this process, is there any indication from say routine blood sampling or anything like that? Anything like MRI or imaging? X rays?

CFG1\_1 29:44

I think I think there's a there's a role for surveillance. And you know, very often we see people a bit of a drop in spiral and not right coming in for antibiotics, but giving them in a little more than what they're required. And then about two months down the line, they've grown something so something new... I know that's a bit more chronic disease then then acute, but one leads to the other and then you know it's just catch 22. Which one comes first? the infection and then all the bugs, the chances are the bug which has been lying there, It's just they've not coughed it up and then we've not captured it.

CFG1\_4 30:16

You mentioned MRI. Wow, I'd love it. If we could just do an MRI each time. There's a lot you can detect in CF with MR. We're way off that. I mean, we do do chest X rays, they're not that helpful, unless there's something atypical or concerning going on. I mean, there is some evidence out there about CRP in the value of it, in terms of indication for treatment or not and length of treatment, but to be honest, it's not that robust. So there are of course point of care CRP monitors that GPs use and things... We don't use them, although there is some research behind it. There's some interesting work research work looking at other biomarkers breath condensate, urinary biomarkers of an exacerbation. None of them have shown consistent data to use. So it all comes back to symptoms. And FEV1 really, I would say,

[Researcher\_1] 31:11

Does anyone else have any other input on diagnostic tests that are used in this in this area?

CFG1\_4 31:20

Sorry the only other thing to add is there is like a validated symptom diary out there. Cystic Fibrosis symptom diary. I think it's got another couple of letters to it. It's by Chris Goss. But there is a validated symptom diary, which goes with exacerbations as well. But it's similar to what we just asked.

[Researcher\_1] 31:45

So is that is a used by the patient? Or is it used in both care team?

CFG1\_4 31:50

It's mostly used in research to be honest. Again, but people have tried to validate it in the context of remote monitoring systems to see how well it works. how well it performs. If a patient an individual with CF is doing it on a daily basis, can it be an early marker of an exacerbation to indicate early treatment? I don't think it's been shown to be particularly effective at that. But but it is out there

[Researcher\_1] 32:22

when talking about infection, what type of infections are most common in terms of bacterial viral or fungal but other common culprits or species in particular that come up repeatedly?

CFG1\_4 32:36

I'm at risk of talking too much. But can I just clarify something with you? You talked about infection. Someone else mentioned this. It's very different infection to exacerbation. So there's, you know, most people with CF have some form of infection at all times. Because they have a pathogen in their airways. That's extremely common. That's not the same as them exacerbating so we predominately talking about exacerbations are we predominately talking about airways? pathogens?

[Researcher\_1] 33:06

Yeah, I was gonna say we'd like to get coverage of both. In this case, it's infection as opposed to say colonisation. Yeah, good, good idea to get coverage of exacerbation, you know, beyond just whether it's infection or so and so on.

CFG1\_4 33:29

So, I won't keep talking too much, but the most common pathogen Pseudomonas aeruginosa, certainly in adults, and that will be a chronic pathogen, but that will also likely be a cause of an acute infective exacerbation where they have a sort of sudden flare of that, but that's one of the most common pathogens.

CFG1\_6 33:58

We do see a lot of people being referred for transplantation have got Pseudomonas enterobacter, Burkholderia,... still quite not it's a lesser pathogen now, but we'll see people are coming for for transplantation or colonised for that. So it's been a chronic illness for years and suddenly their lungs don't work anymore. So we do see that with sudo still, for us, bring the most common pathogen we see in adults.

But NTM is also on the increase,, so M abscesses complex as you know, it's on the increase in the CF population. And this is kind of a worldwide thing and that's even though changing current practices of culture and when you put it back that culture method and you find even more so the prevalence is much is very much increasing in in CF patients now.

CFG1\_5 34:50

Staphylococcus and haemofolous in younger kids. I'd say probably more staph than haemafolus.

CFG1\_2 34:58

We see issues with viral, you know, viral issues as well. And then it's quite fascinating because you, you can get this sort of almost cascade effect where, you know, people have one thing maybe viral and then it's followed by something else. So sort of disrupts what's going on essentially, in the in the lung, that microbiome all seems to change. I think it's worth following on from next point as well just say, you know, sometimes it can be this sort of stability really, where people are just, they are just growing a bacteria and they seem relatively stable with it, whereas other people will, will grow a bacteria and have massive problems. So it's quite hard to predict, it's very individual, it can be individual at different times. So that trying to tease out what is, what is the growth that we're seeing, that's clinically significant, and what isn't, sometimes is quite challenging for each individual, how aggressive we are with it. And overall, I think we're very aggressive with most things. But it can be difficult to tease out whether that's always warranted, I guess.

[Researcher\_1] 36:25

And with these instances of coinfection, is there some sort of prioritisation against those? Is there anything that goes 'oh, We need to sort this out first, before we deal with something else?' Or is it all done at once?

CFG1\_2 36:39

That, again, is quite individual. I think it depends on what they've grown before. Has that caused an issue before? We're very twitchy about NTMs, especially abscessus because of the issues around transplantation... But But yeah, I mean, essentially, if there's a new growth of, of pseudomonas, we'll treat it aggressively. But, yeah, if they're going multiple things at once again, it's sometimes difficult to tease out which of these is causing the biggest issue and sometimes you treat one to exclude whether it's that or not, and then if they don't get better, you treat the next thing. Sometimes it's balancing treatment for both at once. But I think it does hark back to this is very individual, and it's how have they responded before if we know that? And what is our feeling when we tease apart all the results about which might be causing the biggest issue? I think that's fair to say.

[Researcher\_1] 37:42

Thank you very much for that [CFG1\_2 ]. Obviously, we talked a good amount about bacteria that came up, I think there was a mention of fungal infection in the chat as well. How have we decided what this is? Presumably, it's all done by culture is it? Is it just done in a lab with a standard culture or is anything else any other diagnostics that are used to determine what the species is?

CFG1\_6 38:08

So for bacteria and fungi, so traditional culture based methods, so we grow bacteria or fungi and then identify them. So, what the CF Trust recommends, if you have a CF sample and you go CF pathogen, you should always use MALDI-Tov or molecular method. Never use a biochemical biochemical test because they get it wrong a lot and fungi still traditional - what it looks like under the microscope and if we can't identify this, we refer to an expert who can, and we're still usually and but that's there's no sort of molecular work going on in terms of trying to diagnose infections from CF Samples directly ... so for NTm culture certainly [hospital] a lot of people using it now, we use a specialist agar for absessus, there's a specialised agar for ----- for example and for staph Aureus so we're going to try and target the pathogens with the right agar medium, right growth conditions and the same applies to fungi.

[Researcher\_1] 39:08

Thank you [CFG1\_6]. So you mentioned specific pathogens there or specific agar would you plate those up from a sample you know altogether or would you kind of expect you know this patient's always has the same infection so we'll plated up on there do like breath all the time or does it depend No.

CFG1\_6 39:29

Have a standard SOP and I think all labs have a standard SOP and no matter what, the sample gets the full the full works every single time, we don't pick and choose to see this person always absessus then were still going to culture for abscessus again in case it's gone away. So it's really important for monitoring purposes for surveilence that we do culture for all the pathogens that you expect to be able to look for for CF. So don't pick and choose... even cough swabs get as much as we could possibly do and They don't get fungal culture, but they do get NTm culture as seen in our centre, because they're not very good quality samples. But with the new modulators, a lot of people aren't actually producing any sputum anymore. So it's hard to get anything other than a cough swab. But no, we do the whole process for every sample. And we don't, we don't differentiate.

[Researcher\_1] 40:19

What are the time to results for these existing diagnosis? What kind of impacts that

CFG1\_6 40:25

I talked about? Positive culture results? So

[Researcher\_1] 40:28

for culture, yes, but some of the other things that we touched on as well. Obviously, spirometry, i presume that's pretty instantaneous. But what are the sort of time to results in each of these diagnostic cases.

CFG1\_6 40:41

So from a lab perspective, if we receive a sample on a Monday, for example, you you should know, within 48 hours, three days, if you've grown pseudomonas or enterobacter. So we cook ours for 10, actually five days before we're sure there's nothing there, we often get sort of very delayed, slow growning pseudomonas at day four, for example. So our team expects a negative result on day five, for routine processing. And they'll expect a negative result for everything at day 21. So we're kind of the you know what to expect, based on the culture, incubation period of the sample, we sort of get an interim report to see what 's going on end of day five, but NTm culture is ongoing. So five days to 21 days for negative result in a positive within 24 hours, haemofolus or staph aureus. And we always let the consultant know, if a patient grows a new Staph aureus or a new Pseudomonas or new NTm, we automatically ring the consultant or the CF team, if they’re not available.

[Researcher\_1] 41:48

Thank you very much, [CFG1\_6]. Oh, [CFG1\_4] ,

CFG1\_4 41:51

I was just going to add, although it's fair to say for some of the mycobacterias, it can be up to six to seven weeks. So we would, you know, it can take a long time, from these culture based methods. And some of the unusual fungal species can take up to 28 days. So you know, -------, for instance. So it's slow, is the bottom line. Some of the molecular techniques in theory are obviously a lot quicker. But mostly, they're not clinically based, the clinical utility of some of them. So there's a lot of research in that field. But But But otherwise, traditional cultures are, relatively speaking quite slow for some of the atypical species.

[Researcher\_1] 42:40

Thank you very much, [CFG1\_4] . In terms of, well, I guess the next question leading off on that one, where does the treatment or the say if it's a bacterial infection, where's the treatment come in this process? If we're talking 28 days to get some of the culture positive results back? Is it largely empirical or is that based on the information as it comes in?

CFG1\_4 43:05

It's largely initially empirical or based on previous cultures. So what the patient is chronically infected with what the previous cultures have shown, depends how sick they are, depends how much time you think you've got. But often you are treating someone based on symptoms and a change. By definition, there's usually some change in their clinical or level of clinical stability. So you usually end up giving an intervention. Occasionally, you will wait depending on the indication and the sort of context. But if you're suspicious for an NTm, or a fungus, you'd usually in treat empirically with antibiotics for their other co-pathogen, which will be a bacteria, and then you'll wait and see. And then you'll continue to monitor and decide if maybe it is the fungus or the micro bacteria that needs treating, but there is a lot of empirical treatment definitely.

[Researcher\_1] 43:59

So on the back of that as well, then, in terms of treatment efficacy, or determining treatment efficacy, is that done at all based on diagnostic tests? Are you re-culturing after antibiotics? Or are you just doing it based on patient's symptoms?

CFG1\_4 44:17

The vast majority of times the goal is not to clear / eradicate the pathogen because it's established and a chronic infection, if you're talking about. So there are very important interventions to try and attempt to eradication once you first isolate a bacteria such as pseudomonas, and we know that really does impact long term outcomes. And so we're very aggressive about trying to eradicate a pathogen when it first appears particularly somewhere where its very strongly evidenced based such as Pseudomonas. Otherwise, if it's a chronic pathogen, the goal is very different. Absolutely the imperative is to get the patient back to baseline. And what do we mean by that? Usually, we mean spirometric baseline within 10%, let's say of their baseline FEV1 and their symptoms to have resolved. And we know that about a quarter exacerbations in about a quarter of exacerbations patients do not return to their baseline. And their trajectory over the long term is worse. So it's a real key measure of treatment response. Definitely.

[Researcher\_1] 45:19

Thank you very much, opening it up. Are there any other comments on the assessment or treatment in any way? Does anyone else do something different in their, in their hospital or in the team? That's pretty much how it is.

CFG1\_6 45:37

When we do get told on the CF bench that we've got some of them with a new pseudomonas. You kind of watch out for that patients next sample coming through the door, because you're aware they're on treatment, and kind of monitoring that process. And if we do grow pseudomonas, during that treatment time we do let a consultant know ASAP. Usually for another set of drugs to use. So the CF team on looking at the samples, they can look out for these patients just have a really good eye on them so you don't miss that pseduo, it's kind of broke through again.

[Researcher\_1] 46:11

Any other comments there as well, sorry?

CFG1\_2 46:13

Yeah, I think otherwise, it's As [CFG1\_4] said, I think it depends, again, it's those two pathways of is this, you know, an exacerbation? In which case we wouldn't re-culture unless there was another specific reason to, it would go on spirometry and symptoms versus is that a new infection? As in is it a new growth of bacteria in which case we would quite aggressively, for want of a better word, really try and re-sample at the end. You know, we we really want to know, have we eradicated effectively? So So I think, again, two different pathways where Re-culturing is really very important on the one side, but for exacerbation, probably less so.

[Researcher\_1] 47:02

In terms of antibiotic susceptibility testing, is that done at all in any anyone's cases? Does anyone know of that being done routinely or on the off chance?

CFG1\_6 47:13

So the policy is, and this is in the new CF guidelines as well. So we always always do sensitivity testing on Staph aureus, no matter how often we isolate, every single time, we do a sensitivity profile on it.. with pseudomonas and -----bacter and Berkholderia complex. And we will do sensitivity testing on the first and the second and the third isolates, but once it starts to become a chronic infection, we get the heads up from the consultant who'll say. We're not doing any more sensors on this because I said chronic infection and we'll just because the CF team don't find them very useful at all. And so once you get past that stage we dont do senses, but do that once a year for people who've got chronic CF, but we don't really know what we're doing. We'll just use it as an eyeball where it looks like a year on but not routinely. Probably first, second, third, and then we'll probably stop when we're told this is chronic. Let's just stop doing sensitivity.

[Researcher\_1] 48:16

Thank you very much. Anyone else have anything to add?

CFG1\_6 48:21

And the same goes with NTm. So for getting a new M absesses complex, we do our own sensitivity test in [city]and using the standard methodologies by the reference lab. So we'll do these sensitivities anyway. In case they do decide to treat the don't always treat M abscesses complex infections depends on the patient etc. And whether it's going to be beneficial or not. But they do sort of use them as a bit of a guide to treatment of absessus complex. Thank you [CFG1\_6].

CFG1\_4 48:56

I was I mean I think that's fairly typical across most centres and microbiological units. For the reason [CFG1\_6] says it's it's the recommendations and standard of care. So, yeah, for new new growths then sensitivity susceptibilities are undetermined. But beyond that, I didn't realise it was the third actually [CFG1\_6], I must admit beyond that, then we don't do them, because they really don't seem to have any clinical relevance or have limited clinical relevance. Put it that way. Annually, though, they all go to the reference lab and are typed properly to look for epidemic strains, to look for patterns, the epidemiological patterns of the strain of the of the particular species. And I think it's the same for us with staph, as [CFG1\_6] said and Burkholderia and some of the rarer ones achromobacter arratia. So we do get sensitivities initially, but beyond that less so, the reality is it doesn't tend to predict clinical response in the context of a, of a chronic infection. So for a long time, that's what CF physicians have been saying. And the and the research shows, although there is some growing research suggesting that maybe in some situations, we might need to start looking at that, or some of the multi level susceptibility testing that I think is beginning to come out of research, but as a clinical tool, no.

CFG1\_6 50:31

That's what we find. And again, we are kind of led by the consultant who will say this is chronic, let's stop doing it, but we will always check before we stop doing sensitivities. And again, we want to do strain typing as you do because we're looking for the transmissible strains. I forgot what i was gonna say next after that. And oh, yeah, so once you start getting chronic pseudomonas, for example, you can pick off colonies and gets totally different biograms from lots of different colony types. And really, it gives you a very confusing picture. So you can see how everything is pan-resistant or the next one's fully sensitive. And it just means that you've got a chronic infection sort of doesn't really help guide treatment at all.

[Researcher\_1] 51:18

Thank you. Sorry. How confident are you in the tools that you use to make a diagnosis? When you see something like a culture result, are you fairly happy that that's correct. And you will act on that? Or is, is there a little bit of apprehension there? Or do you want to do additional testing? What are you confident in in terms of the tools that you use to to make a diagnosis of exacerbation and infection?

CFG1\_2 51:54

perhaps I can talk about when we're not confident. So I think you know, there are really big issues with people who don't produce sputum. And that issue has become more difficult since modulators and cough swabs, you know, generally are a good positive predictor, but not a great negative predictor. So, you know, if it's clear, then I don't think we're confident it's clear. I think we also have issues around kind of, where is this potential growth or infection? Is that clinically relevant? So even if we're getting good sputum, you know, is there a problem with the sinuses? So certainly something we're really aware of is, you know, post eradication, we've eradicated from the lung but what is going on in the sinuses? And then is that why we're getting regrowth and, and those sorts of problems? So it's, it's complicated, but I think, definitely, as the physio trying to get good samples, and you're sort of seeing the output of that, and when something comes back negative, and you know, what sort of sampling What's your thinking? Dunno lung function still down? I'm not quite happy with them. I'm not sure really what's going on. And actually, that sample wasn't great. So so we do use a lot of induced samples. At the centre here, we're able to because we're a smaller centre. But there are challenges to extensively using induced samples. Obviously, the research is pretty good even for using induced cough swabs rather than a plain cough swab and the excellent - I always love that it was entitled "spit" trial. It's just a wonderful trial in all ways, you know, really sort of guided us on that. But again, the practicalities of that, particularly during kind of the COVID response, the practicalities of induced cough swabs induced sputum. It's tricky. And particularly as we've moved to maintain some level of virtual consultations as well, relying on samples that have maybe been done and delivered to the GP rather than us directly getting samples and seeing the quality of all the potential quality of those. It's definitely challenging. So, yeah, so in terms of what isn't great, I think, I think those sorts of sampling issues are definitely a problem.

CFG1\_6 54:37

So I don't want to want to sound negative at all but. And when you're a scientist and reading CF cultures, if you don't have experience, it's very easy, very easy to miss an atypical pathogen. And this is not I'm not gonna say it happens in [city] specifically, but I do know it does happen around the country and if you have, For example, where the CF section in with the sputum section, you'll have trainees on there, and you can guarantee they're gonna miss some pathogens. And we know this is the issue, a training issue. And I think if patients go to a good CF centre with a good lab who understands the needs, then you will get very good results. But that's not true in every microbiology lab in the country, unfortunately, that is the case. And one of the kind of recommendations of the CF Trust is. If, if, if a lab gets a CF sample, if they don't have a CF unit and trained BMS is they should not be looking at that sample at all, because the chances are they're going to miss the atypical helicobacters. You know, some patients will even be missed, you know, because of inexperienced biomedical scientists. So don't Don't be negative, but is it a fact.

CFG1\_2 55:53

And again, that can be more of an issue now with samples coming via GPs, sometimes where patients dropped in a sample locally, that can be an issue, because sometimes they can end up somewhere where you didn't expect them to end up. All patients are, you know, tempted to post in samples, and then that delay does cause some uncertainty as well with with samples being sent in.

[Researcher\_1] 56:20

Did you have anything more to add, there?

CFG1\_4 56:25

I've just I've just got a couple of additional things just to quickly add. So, so we've heard a lot about when we're not very confident in terms of getting the sample or knowing whether or not there is or isn't something there. But sometimes when we have a positive result from the lab, and we're confident in the lab, we don't always know whether or not we should treat it. We don't always know whether or not it's actually, you know, just it could be a transient phenomenon. And we don't want to over treat as well, we have a very low threshold in CF to treat any bacteria that's identified if it's new, but there are quite a few in which there is not that much evidence of damage. So bugs such as stenotrophomonas, perhaps we should perhaps we shouldn't there's some even rarer ones that we just really don't know, because the evidence base is not there. So that's a problem. And just to continue on, from what [CFG1\_2 ] said, yeah, we've looked at our postal sputum results over the last two years and compared it to a much smaller percentage of postal sputum results before the pandemic. And without doubt, delay to lab. So transit time directly correlates with the appearance of unusual bacteria and unusual Pseudomonas species species. So the one we're particularly worried about in CF is Pseudomonas aeruginosa. But you get all sorts of weird and wonderful Pseudomonas species if you leave your sputum sample hanging around or in the Royal Mail for too long, such as Pseudomonas Putida, and stuff, and that is a contamination almost certainly.

[Researcher\_1] 58:12

I think that brings us on to a good point, actually. So the next section is on the unmet needs within the care pathway. And it sounds like we've covered a few things on culture times, the types of methods that are used, the transit times in inducing contamination. Maybe we can go around, everyone gets their input, what are the kinds of unmet needs at the moment in the CF care pathway?

CFG1\_1 58:39

Shall I start us off, I think one thing, one thing we lack is bedside is bedside testing, or quicker or quicker markers. I know there's there was some talk about Pseudomonas a while ago, and doing sort of breath condensates and doing a big thing with swabs and bedside bedside kits which give which given indication, but also the same with viral with viral infections. And I think lateral flows have now come to the forefront. And I know, certainly the joint team [city]are looking at some of viral contaminants to these to the swabs we're getting. So I think bedside tests quite useful. How useful it'll be with kaftrio will be up for debate.

[Researcher\_1] 59:37

I think there was some comments back from the the patient focus group around kaftrio so maybe we'll come back to that as well. Did someone else have another comment there? Sorry, [CFG1\_2 ]?

CFG1\_2 59:46

Yeah, I think following on from that as well more acceptable testing, like asking teenage girls for sputum is really challenging. And you know, when I was a teenage girl, I'd been mortified to have to provide someone with a sputum sample. I mean, on the whole, I think people with CF are really resilient about the types of invasive testing that we ask them to do. But actually, sometimes it can be things that we take for granted that are almost the straw that broke the camel's back. And actually, for a number of people having to provide sputum samples is maybe 'distressing' is taking it too far, but certainly doesn't feel comfortable, and I think leads to under-sampling. So we know that there are a number of people where we don't have samples, or sufficient samples to be confident about what's going on. And that's not because there's no sputum there. That's because it's not a comfortable way to test.

[Researcher\_1] 1:00:53

[CFG1\_5] ?

CFG1\_5 1:00:54

Yeah, I mean, I was, I mean, obviously, we've we've been talking about the fact that our patients are drying up somewhat. So obviously, trying to find an alternative to sputum is one thing. And I think the other thing that we probably should think about as well as that other biomarkers to help us to monitor infection out there just a greater, greater, more efficient way of doing that, if we're not going to be able to grow things and or get sputum, what are the biomarkers can we use to monitor and diagnose infection?

[Researcher\_1] 1:01:28

Right, [CFG1\_3] do you have anything more to add?

CFG1\_3 1:01:30

Now, pretty much what everybody else has said so far, really,

[Researcher\_1] 1:01:34

in terms of not necessarily as the diagnostic tools, but the whole pathway as a whole. Maybe how the patients interact with you. Is there something else in there that you might, maybe he's not working quite how you'd like?

You're perfectly happy. Everything comes out 100% every time? Yep. Yeah. Okay. Fair enough. And [CFG1\_6], from a lab perspective is anything from from your side of things, where it's possibly not quite as we'd want it.

CFG1\_6 1:02:07

What I find, or what i've discovered is that everybody seems to do things a little bit differently depending on where you work. So for example, some people do with 21 Day culture for fungi, and we are doing five days, and well, 10 must be better than five, I think there's not consistency between the laboratories. So the bigger centres do, obviously, you know, take the lead on what should be done, but you can't tell people what to do or how to do it. So I would say that for a patient, you know, the quality of care will depend on where you go. And that could be also down to the laboratory who process your samples, as there isn't any consistency, and hopefully, when the new guidelines come out, we want people actually to follow them. But we can't enforce those rules on people. And that's all I can say about that. I just feel its a shame we can't make them more consistent throughout the country. We do this, this is how we do it, all do the same thing, then you know we are all getting the same treatment no matter where you live in the country.

[Researcher\_1] 1:03:08

So equity of care, I think it's quite important isnt it.

CFG1\_4 1:03:10

Can I make a comment [Researcher\_1]? Yeah, sure. unmet need. I think a massive unmet need is knowing how long to treat. So one detecting treatment, but then to detecting treatment response and effective treatment response. Because actually, we're almost certainly very frequently overtreating, which is obviously it has consequences - consequences to the patient, consequences to healthcare system, consequences to the wider bacterial resistance out there in the community, is a really hard nut to crack. There was an excellent study recently published, called 'stop2' trying to sort of challenge the long standing two week of treatment rule in cystic fibrosis, whether or not it really has succeeded to do that, I don't know. But we don't have if we had a biomarker that can tell us there's an infection and a biomarker and tell us there's no longer an infection, and we can just give three days of treatment in this instance, that's a lot better than giving 14 days of standard.

[Researcher\_1] 1:04:14

So thet'd be about, say a theranostic type approach to determine whether the treatments effective and how it whether you can shorten that length of that course of antibiotics. Okay. Does anyone have any other unmet needs?

CFG1\_2 1:04:30

[Researcher\_1], do you mean absolutely across the pathway? I mean, well, you know, the risk of being very predictable here. I mean, I think we still have a massive issue in terms of supporting people in the right way to be able to take their treatment. There are very few people who, you know, well, there are a significant number of people who are unable to take their treatment in the way in which is prescribed because they are humans, and none of us take our treatment in the same way. So we do need to solve the human condition in speaking about this. So, I know it is a bit ridiculous, but, you know, in 10 years, so kind of the study I originally published around adherence was that, you know, people took 36% of their prescribed inhaled treatment. And, you know, a year ago, the starting point for the CFL sub trial was about 36% of treatment. So in a decade, we have come not very far in terms of helping people and supporting people. And in terms of kind of focusing this back to your focus, you know, if, if we have studies that, that show the way in which this, these treatments may be effective, and then we have only a very small number of people who are actually able to take them in that way. And I think there's a whole thing around, you know, behavioural interventions with that. But equally, you know, it's not easy to take, if we think about inhaled treatment, it's still not easy to take some of the quickest treatments to take, and then we're scuppered because actually, they should be taken three times a day. So I can go for inhaled Casten, which will take less than a minute, brilliant, I think I might even feel like doing that. But then it's three times a day. And I know if it was me, I would not be doing it three times. So nor do any of my patients, or very few of them. But then equally, what else can I go for? Well, I can go for quince there. It's only twice a day, it doesn't have to be refrigerated, but it's going to take me six or seven minutes. And it tastes like the devil. So I'm not going to take that either. Or I could go for Toby and you know, kind of, again, you know, twice a day, I need to fridge if it's going to be over 25 degrees, and blah, blah, blah. So, you know, I think the practicalities of taking treatment remain a challenge, right down to paediatrics if we are giving flu clocks at any point, it again tastes absolutely hideous. So we've got all these issues about the practicalities of stuff. And then equally I don't think we are implementing evidence based behavioural change support equitably either. So I think it's multifaceted. But I think if we could support people to take their treatments better. And that takes a whole structural approach, then actually, we might see different outcomes.

[Facilitator\_1] 1:07:31

Thank you very much, [CFG1\_2 ]. Are there any other comments at the moment? So I've been writing them down. Well, I hope hopefully writing them down as we went along there. So I think it'd be good to maybe take some of these in turn and kind of discuss them as a group. So if we were a working group as a commissioner or say, we're advising NICE, how might we address these unmet needs? Would that be through change into the pathway or new diagnostic? And if it is something like a diagnostic or pathway change? What would those changes actually need to be in order to be effective? So I think one of the first things that came up, I think from CFG1\_1 was like bedside testing, quicker markers for viral infection and lateral flow testing. How might we kind of address this need in a clinic?

CFG1\_1 1:08:23

I think the first thing, [Researcher\_1] is there's no, there's no data to support any of this. Now, these are, at the moment pie-in-the-sky small, they're small studies, I think it's very difficult to address anything without the actual data. So the first thing that needs to be done is studies to show it's effective. And second, is that you can rely on this clinically.

[Researcher\_1] 1:08:47

And what do you think the issues might be for moving something like testing to the bedside? Or having people do lateral flow tests for various viral infections?

CFG1\_1 1:08:58

Are there any studies now that are going to come through with funding? It's the arguments for funding, the studies easy to set up. Its the funding structures which limit these things.

[Researcher\_1] 1:09:08

In terms of bringing this into a clinic? So if we're moving something to a bedside testing environment, what are the kind of impact on the care pathway and who's involved? And who's going to sort of action, all of this? How might that be impacted?

CFG1\_2 1:09:23

I think we do need to think about where we're at with virtual clinics, etc. So actually, for many of our patients, that isn't a bedside time. So you know, in terms of implementing, you're then left with self testing, which has implications, you know, certainly in terms of spirometry. Self testing means that we do need to have a system where we can assess technique and understand what's happening when the person is doing that test. So we can do that with spirometry as long as we invest in the right system. But for other the sorts of testing can we do that? So for example, sputum testing at home, as we've mentioned, A - you've got less idea about the quality of that sample, going into the lab, the lab obviously will have to make their own assessment. But certainly going into the lab, you've got less idea about it. And then you've got the issues of how to get it there. If it's bedside testing, it's thinking about the, the technique that's used at home and how that's done and an equally again, kind of when and how it's implemented as something else that we're asking people to do in the home potentially. So So I think, that just needs to be thought about carefully in terms of the days of people coming through once every eight to 12 weeks, and physically being in front of you in a clinic room or on the wards. I mean, I was just looking this week at our, you know, home and hospital life, e-numbers, and they are nowhere near what they once were. So, you know, again, kind of when does that happen? And if we're moving it into the home, how does that happen in terms of either self, or members of the team going out, which will vary from centre to centre because of geographical footprints as to whether that's even feasible?

[Researcher\_1] 1:11:18

[CFG1\_5] ?

CFG1\_5 1:11:21

I'm I possibly thinking about this a little bit too, simplistically, but like, if I'm sort of just thinking about like a lateral flow test, similar to like a COVID-19 test, that's easy to do, it's reproducible, then actually, I think that would be a really nice thing, from a surveillance point of view. And I think [CFG1\_2 ] mentioned, you know, getting teenage girls to like, give sputum is just really not very nice, don't like doing it. So actually, if you could have a test, which was so much, you know, which patients much preferred than actually one, you might get more surveillance testing. And, you know, it might just be sort of generally easier. But I guess in terms of, I guess, it depends on what equipment you need, doesn't it? I mean, if it can be something as simple as the COVID test, then that would be great. But if you then need equipment, then it's a completely useless thing to be able to use at home in the first place.

[Researcher\_1] 1:12:16

And taking something like a COVID test, for example, if we're comparing that to say a sputum culture or whatever the standard test would be, what kind of what are the what's the kind of balance there between the convenience, the easy access, and perhaps the drawback on maybe accuracy or confidence in the results? And what what do you think the acceptable limit is on that?

CFG1\_5 1:12:41

Is this question to me or just all of us?

[Researcher\_1] 1:12:50

It's open, but you're unmuted, so go for it.

CFG1\_5 1:12:53

I mean, it there's no use having a test that's 50% of the time accurate is there? So I mean, personally, I think I would aim high and just say, actually, I'd like it to be accurate 95% of the time. I think there's no point saying we only want it to be accurate 70% of the time, otherwise, I think it's just not very helpful.

CFG1\_4 1:13:18

Yeah, I mean, it depends what we're trying to do with this test. So so to diagnose a viral precipitant of a pulmonary exacerbation, I think it's quite possible and quite realistic, isn't it to have a COVID like test? And maybe you'd have a panel of respiratory viruses. That would be on the lateral flow. And, you know, it'd be a quick way of doing it to confirm that. I don't see how else it would help in terms of the context of pulmonary exacerbation for someone like an adult who've got chronic infections, chronic pseudomonas, what's the lateral flow going to do? Unless I misunderstood? You know, is it going to say there Pseudomonas there? Well, we know that Pseudomonas there... It, you know, and we know from the data that [CFG1\_2 ]'s already been quoting this spit CF data, you know, cough swabs, throat swabs are not very accurate for lower airways infections. Definitely not. We've known that for years but the Spit CF study shows it really nicely, so I'm just not sure or is it? Are we looking for a marker in the airways that says, that is a pulmonary exacerbation? Some sort of protein, something else? If that's what we're talking about, which is a bit more kind of pie in the sky, but you know, could be game changing, then that's brilliant, but I I don't think I know of anything yet that's been found. That would show that I don't know some sort of thing. inflammatory markers. Like I said, there are some studies looking at urine biomarkers and stuff for exacerbations. But they've never been that promising. They've never really shown consistent results. That's the only thing. So yes, a quick I think for kids, perhaps, particularly viruses can, I mean, it probably does happen in adults as well. But viruses do cause quite a high proportion of pulmonary exacerbations for children in particular. So maybe then you would treat with antibiotics. But what?... that's the next question, would you then treat that virus with an antibiotic because you're worried about secondary exacerbation? So really, what you want is an all encompassing biomarker that says this person is at risk of deterioration. And it's highly likely it's a bacterial cause for that deterioration, and they need to treatment or this person is having a viral exacerbation, they're at low risk of bacterial exacerbation. They don't need treatment. You know, again, in the modulator era, we're seeing a lot of people who present with mild symptoms that do not need treatment, whereas historically, we would have given them treatment. But paradoxically, we're seeing some people present a bit late and have quite bad exacerbations, because as as others were saying earlier in the call, that they don't know their symptoms so well anymore.

[Researcher\_1] 1:16:19

I think we found that [Facilitator\_1] didn't we in in our patient review, so we'll pick up on that again, as well, I think later on. So we also discussed about acceptability of testing. We mentioned sputum was one that seemed to come up quite a lot, I think from from our patient perspective, as well, there were talk about bronchoscopy, and that was something that that was a big no no, for a lot of the patients. One of them was very, very against blood testing, which is obviously going to cause some inconvenience at hospital. How do you think we might address the sort of acceptability of testing? Is this based on the number of times? is it based on using a different test entirely? Do you as the care team have to have to adapt to what diagnostic tests you would perform, and maybe even take a bit of an impact on the information that you might get back based on patient acceptability?

CFG1\_2 1:17:17

I think nirvana is is definitely a test where we don't need sputum. You know, I think the only thing that's less acceptable than sputum is actually faecal testing. It's certainly our dietitians that have a worse time than me in terms of getting samples, it has to be said. So, you know, I think even those who, who are okay with it, I think often, you know, when you dig down into it, they're okay, not okay. You know, is kinda like, you know, I'm doing this because i know I need to. Even I think, you know, the very nonchalant, often men who are like, ah, it's not a problem when you when you dig down, actually, I think having to do this, it's seen as another thing that people without CF, tend to not have to do... it is quite a big deal. So, so yeah, I think the Nirvana would be something like breathm or whatever where you, you just don't have to do that. I guess. What would be great is when we're doing here we go, here is proper pie in the sky. So you know, when someone's doing spirometry, let's have something in the system that actually from breath can then say, oh, yeah, you know, we've, we've, we've spotted this or we've spotted that bacteria. I mean, that would be great. Because it also condenses down the number of tests you're having to do - brilliant. But without pie in the sky, I would say you know, anything that A - reduces the number of sputum samples that we need. And ideally kind of reduces the need for it. And I guess this, this comes back to maybe [CFG1\_6]'s point as well about inconsistency and certainly, i've worked across a number of different centres over a period of time. And in some centres, you do have to provide multiple samples for a viral swab a MC NS and AFB and it's kind of like, No, you know, I want all those separately, we want this many separate samples. Whereas in other centres and other labs, it's kind of like, send us one sample, send us what you've got, and we'll just test it for everything we possibly can. So I think there's something about consistency to reduce the number of samples that we need to send. And then there's definitely something about does it have to be that at all? Could it be something non-sputum based, which is more long term ambition, I suppose. And then there is something in the care pathway about how we do sampling as well, I think, you know, so I think we become very immune to it. So you know, I'm often quite conscious, particularly I've got new members of staff. And sometimes you observe what's going on and, and I know I've done it as well, where you are almost standing over the person while they're doing a sputum sample, thinking nothing of it. But actually, that, that how watched and how observed people are is actually, you know, something that I think we do need to think about in terms of, you know, how we do these tests. So often leaving the room, leaving people to do it, and then be able to pot their own samples without you having to come into contact with it, can feel more comfortable for some people. So I think there's something easy about when I say easy, it's, when you ask people to do something different. It's never easy. But there's something easier about how the person who's taking samples has an awareness and does them, there's something about can we make the process better in itself, and then there's something about could it be a totally different test.

[Researcher\_1] 1:21:04

It's quite funny that you picked up on, on the kind of leaning over, you know, leering over the person while they're doing the testing, because I think that's something again, that came up in in our patient focus group was, there was a bit of anxiety around like the need to perform, when they're called into the clinic. It's like, Oh, I'm gonna have to give a sputum to them, or the Mr. So and so is going to be angry at me, or I need to make sure that my spirometry is good, that I've done a good breath sample, otherwise, um, you know, someone's going to tell me off for that. There was a lot of anxiety about coming into the clinic based on this kind of need to perform. Yeah, and the idea of a bit of like, over over bearing kind of parent association with some of the, the patients as well.

CFG1\_2 1:21:51

Part of that is, you know, that's the way our clinic rooms are set up, you know, they're often set up where when you come in, you aren't necessarily sitting down as the clinician, especially if you're in a busy clinic, and you're the physio, you know, because it is like, hang on, why haven't you seen that patient yet? Oh, let's go in and see this patient, you need to get their spirometry done. So you know, you are often in and out of rooms quite quickly. So without consciously thinking about how the room set out, and whether there's a chair to sit on, and whether that chair is the one by the desk, that's always a bit higher than the person with CF, who's on the lower visitor chair. And even if you don't mean to be unless you very consciously think about it, you're often leering over. The other thing to physically do cough swabs well, is that actually, the easiest way, particularly if you're short, like me to do a good cough swab is to get the person sitting and you stand, I want to do it, now you're standing over, because that way, you can get the cough swab without touching the mouth and the throat and everywhere else. If you're below the person, it's very hard to do that, and to see where you need to see. So So there's definitely something about the technicalities of doing a good cough swab, that mean that you are leering over the person, coupled with what I mentioned about I think we become clinically immune to how it feels because it's so normal to us. So we're like, well, it's just sputum, isn't it? Like, it's a great part of my job when I get sputum, whereas it doesn't feel like that for the person.

[Researcher\_1] 1:23:32

Does everyone else have a similar kind of thought line of thought? Yeah. And in terms of how do you think that the kind of layout or the way in which the way in which the clinics are set up, but also the kind of way that you interact with patients might affect, you know, adherence to the treatment or adherence to testing at home? How do you think it all kind of impacts them? It's an open question, sorry.

CFG1\_4 1:24:09

The pandemics changed things quite a lot. I mean, we're all doing slightly different things. But in terms of amount of remote versus face to face case, but I think we've all got some sort of mixture of that probably some sort of hybrid. Maybe that's certainly what we have. And it's interesting because in some ways, it enhances adherence and engagement in some ways it it does the opposite. And it depends on the individual. Because some you know, some for some people, it works really well. They're feeling more in control of things, they are checking their spirometry at home, they have more autonomy of of what they're doing with themselves. So actually, then they're more engaged when it does come to their clinic appointments and you know, they have some data ensure that they really do engage and take part of it but for others it becomes less, it becomes definitely de-prioritised. Their clinic visit, for instance, had a patient who was in <another country> on holiday the other day, and I was talking to them when they were sun-bathing and all that sort of stuff. So there's that element. And then there's the face to face clinics, the traditional face to face clinics, which is still very important, and we all still do. And the setup of those, it is very, it's it's a very kind of well organised, strict approach which patients know and have known for a very long time. But I know for a fact that yes, there's often a lot of anxiety in coming up to clinic and performing spirometry, performing sputum. And the most important thing to say about these interactions, which is where probably virtual remote, in theory could be better, is a one off measurement is not that useful in the history of that person of how they're really doing, you know, snapshot measurement to base every single decision on is not that useful, really. So you know, that's where probably some of the remote monitoring things could, could improve that because if they have home spirometry, for instance, they can do it more frequently. And you get a much better picture of what's really going on.

[Researcher\_1] 1:26:19

Any other comments to add from the group? no? Okay, so thinking about the test characteristics of diagnostics, at the moment, the kind of scope that they used in, the test performance, the accuracy, the cost, the time to results, the type of sample that they're using, who performs the test, where it can be done, whether it's at home or in a clinic, taking all of these kinds of characteristics, what are your thoughts on the sort of the top three characteristics that are really important in this area, the CF infection and exacerbation kind of area, what are the top three characteristics that someone really needs to meet, if they're going to bring a diagnostic into this area, maybe we can do a whole a whole roundtable, just get everyone's views. [CFG1\_2 ] do you want to start us off?

CFG1\_2 1:27:10

At the risk, again, of being boring, I think it needs to be acceptable to the person. Because tests can be wonderful. But actually, if you spend a lot of your time having to persuade and almost coerce people into doing that test, then it's not helpful, especially in an area where you do need that long term relationship with people. So acceptable would be my top one. My second one would be accurate. Because what you don't want is that you reassure someone that everything's absolutely fine. And then they go for their transplant assessment or whatever. And hey, ho, hey, presto, they've grown something brand new that you've missed, and, you know, that precludes them from transplant or whatever else or hasn't been treated. So I think, accurate in terms of, you know, really spotting what is there, when it's there. But also, I think, as [CFG1\_4] mentioned earlier, not spotting things that are irrelevant or not there. Because, you know, that too just means that we already have patients who are highly treated, we don't want them to be over treated needlessly. And number three, I suppose the acceptable that I said is number one was more to the person with CF, I guess, number three would be acceptable to the clinical teams in terms of you know, that they, you can realistically fit them into the pathway and do the test. You know, if the test requires a person to come through once a week, that's not acceptable to the person, but it's also not acceptable to us really and it is not going to work, you know, so, so something that is acceptable to the team in terms of all aspects. So, you know, size, cost, ability to use it, how complicated it is to use, and train new people to use it. So I think they're my three acceptable to the person, accurate, acceptable to the team.

[Researcher\_1] 1:29:29

That's all about how it's integrated into the, into the current care pathway. I Imagine with the last one there? the sort of feasibility of it. Yeah, yeah. Great.

CFG1\_3 1:29:41

So I agree with [CFG1\_2 ] about it being acceptable for the patients, but I also think that it needs to the results need to come in a timely fashion, because sometimes there can be a delay in results coming through

[Researcher\_1] 1:29:54

what do you think the impact of that would be? What's an acceptable time?

CFG1\_3 1:29:57

So for an example that I've had recently is that a patient dropped off sputum on Friday to us and I still haven't got a result today. And that patient is at home on an antibiotic, but it might not be the right antibiotics make them feel better, and I hope, hopefully it'll be back by tomorrow. But that's that from that point of view, and timely.

[Researcher\_1] 1:30:22

What sort of impact do you think of that delay?

CFG1\_3 1:30:26

Well, patients, well, he's still, he's been on antibiotics for four days. And they're clearly not the right ones for him, but I can't get him up here to be assessed by us up here. This has been a sputum that was dropped off by his wife. So you could he could have a different antibiotic, if I just knew what we were treating.

[Researcher\_1] 1:30:43

Great. Thank you very much for that. [CFG1\_6]. I see you are unmuted, do you want to go next?

CFG1\_6 1:30:49

Yeah, so I think from a laboratory point of view, we need to be more communicative to the team. And I appreciate your frustration of not getting the results, but it's probably still cooking, it's probably nowhere near finished. I think hopefully, if the people in the lab find something new, they will tell your consultant who will then feed it back to you. Yes, exactly. That's that could be improved. I think the communication between the laboratories, the consultant, and microbiologist and the CF team. So you got to have that link. I think that really tight link with the laboratories, which I think also improving the standards of education within labs, who actually do the processing of the samples, I think consistency of what we do. So like I said, it depends on where you live in a country where you get everything done, or you get the minimum work done, and there's just across the board, it's just not consistent. And I think that could be improved, I believe, by education and discussions and focing standards on people, I suppose is another way to put it

[Researcher\_1] 1:31:56

to open that out, in terms of interconnectivity with, you know, patient management systems, is that something that's integral really to the successfulness of a test coming into the pathway?

CFG1\_1 1:32:11

No, every hospital is different, it is impossible to integrate anything into into the electronic system, good luck in even trying to do that. I can't get a spirometry result from new way on to our flow sheets. Its a manual process.

CFG1\_4 1:32:30

Hearing what [CFG1\_6] was saying about communicating with her team and the consultants is really great to hear. But it sounds like you know, it's very much dependent on a manual system. And you know, and I'm sure you have a really robust system whereby you do check it. But as CFG1\_1 says, you know, it's highly variable and errors happen and things slip through the net, if you had a really robust automated system. I mean, for instance, we used to rely on our micro staff to tell us of new growths of Pseudomonas in particularly, but you know, the systems keep changing over. Staff members keep changing over, that system is now not in place. Currently, you get lots of junior doctors and others doing clinics. And you try to put in a robust system in place for reporting and checking. But you know, humans are humans, things slip through the net, unfortunately. So a very robust automated process with good IT would be amazing. One day, maybe in the NHS, but who knows?

[Researcher\_1] 1:33:44

Brilliant. So [CFG1\_4], [CFG1\_5] , and CFG1\_1, what are your sort of top three characteristics? are the same as what everyone said? Was there anything different or anything that maybe haven't touched on yet?

CFG1\_5 1:33:55

Yeah, I mean, it's like one of those games, isn't it? where you go round, and if your last everybody's already said your thoughts!

My, my, my number one thing I still think is, is the sample itself, I still think that the biggest thing we've got to think about is an alternative to sputum samples. Acceptability Totally agree, all of that. But I think we've got to think of other things, whether it's an alternative sample for detection of bugs or an alternative biomarker for the bugs, that's my biggest thing, I think. And I think that everything that we do going forward because I'm thinking even like, you know, from a clinical trials point of view, you know, how do you prove from my point of view, like the efficacy of a new anti-microbial, if, for example, you can't grow anything to prove, for example, that it works, how do you do it? Everything hinges on that, and even for existing stuff that we have, we can't necessarily do more research on those things to prove that they're any good, if we can't grow anything, or we can't get the samples to grow in the first place.

CFG1\_1 1:35:13

I mean, for me, it's 'is this thing easy'. And being effective in, in what we want to do, but also being efficacious. High Sensitivity, high specificity, you don't want to have false positive and even worse, false negatives, it's easy to undo something as against missing something and then catching up.

[Researcher\_1] 1:35:36

So you think sensitivity outweighs specificity in this case,

CFG1\_1 1:35:41

both sensitivity and specificity have to be have to be high. But that's only in an ideal world, but I think test has to be sensitive, I think.

CFG1\_4 1:35:52

Yeah, I mean, I was gonna say sensitivity and specificity really needs to be thought about. And these be very high for both to be quite honest. I mean, one thing we haven't really talked about is kind of molecular-micro and microbiome and understanding that properly. I mean, you know, that that can be extremely quick. It doesn't need a culture, it doesn't need a growth, you don't need very much of a sample, you but the you know, and it's amazing research and science, but it's the interpretation is currently very challenging in the clinical arena, you know, if we could crack that, you know, then you have a quick you can, you can use a molecular data, molecular micro for bacteria, for viruses, for mycobacteria, for fungi, you know, you had an integrated system, whereby you had, you know, this overarching view of what's going on on one sample be it breath condensate, be it a swab. And you could then, you know, assimilate that and, and, and manage to correlate that with the risk of exacerbation and therefore, the need for treatment. Of course, that's ultimately what we would love. Now, you know, I think we're a long way off that, unfortunately, because it's lovely is the research in microbiome data is no one's really convincingly showed me the true clinical utility of it yet. But something like that, you know, is exactly what we'd love. Because, you know, I think that would just tell us potentially so much, and it doesn't rely on culture and sputum sample necessarily.

[Researcher\_1] 1:37:27

Brilliant. Thank you, [CFG1\_4] . Are there any other comments on characteristics? Oh, yeah, sorry.

CFG1\_6 1:37:30

The only problem is, I think it is molecular techniques, you can use in the laboratory, direct PCR for pseudomonas, for example, they do that a lot in Ireland, it's all down to resources. Sure, no, you know, you can get a big batch of samples. And if, you've got like an hour to get them processed, what you don't have time in labs won't necessarily have the money to invest on these new techniques, which are very doable, it's just going to be resources at the end of the day, I think, to bring these things into practice,

CFG1\_4 1:38:02

I think [Researcher\_1] and the CF trust are gonna get us that money, aren't you?

[Researcher\_1] 1:38:07

I'll let [Facilitator\_1] answer that one! yep, done deal, there we go.

So in the last couple of minutes, as mentioned, previously, we had a patient focus group similar to this about two, or three weeks ago, maybe a bit longer. And there's there's tonnes and tonnes of output from that it was really fantastic, a great experience, I wanted to maybe pass some of these back to you, just to get your thoughts on, and maybe do a bit of a back and forth on that, I think that'd be quite interesting. So we asked, we gave them a similar task towards the end of our focus group on the patient rankings of TPP characteristics, so the accuracy, the time to results and so on. And the kind of order that they came back in was accuracy came as the top thing, almost certainly in relation to their confidence in the result, and that they were getting the treatment that was necessary. So accuracy, I think there was a, there was also a discussion about the kind of burden as I think [CFG1\_2 ] picked up on earlier, where you know, CF is like having another full time job, I think is one of the quotes that I've used too many times now from that patient focus group, and this kind of burden having to do this test, and then it not provide the result that you want, or it's not good enough, or there's not enough sample type. So I think that all came under the kind of umbrella of accuracy. And that was their, their kind of top thing and other that other than that was the time to results. So they surprisingly, they were they were very, has a lot of thoughts about the empirical use of antibiotics. And they thought that something with a minimal time to result might actually minimise the empirical use of antibiotics, which is which is really well thought out, I think. Under that was the speed that it takes to do the test. So again, as I mentioned, this kind of minimization on the lives of the patient, the impact that it has the they don't want to be doing this, you know, a test every day or a test every week, if it doesn't seem like it's actually doing anything for them. Underneath that was the convenience. So they almost universally preferred something to be done at home, where they wouldn't have to come into the clinic. And as few times as possible, I think was the other kind of outcome there. And then, as we've mentioned, in this focus group as well, acceptability. So as we talked, you know, different patients noted sort of different preferred sample types, and we're all over having a new test for blood, you know, based on their blood, if they could just do a little finger prick. Some of them were completely against it. But sputum is one of those ones that was very dividing as well, I think amongst the patients. So taking those kinds of ideas, what are your thoughts on the kind of outputs that they that they gave?

CFG1\_2 1:40:59

Think that's really important, because I think it comes back to that, actually, you know, if if things aren't focused on what's acceptable to people with CF, then it's impossible to implement them, you know, we only implement by consent, we can't force people to either come through for a test or do a test at home. Everything we do is by collaboration and consent with people with CF. So I think I think they have highlighted, generally the same things that that we are, it's quite nice to see everyone on a similar page, that's sort of what you hope when you spend a lot of time with the group of people that you work with. I guess the one thing I would say is that I think we need to bear in mind that the people with CF, who you will engage at focus groups are people who tend to be more engaged, because otherwise, they wouldn't be at the focus group. And I think that's one thing that's quite tricky sometimes is to hear the voices of people who are less engaged with their treatment or less engaged with with monitoring. And so actually, what's acceptable to the cohort who engage with those sorts of things, versus the cohort, who probably have more of a concern that maybe don't engage with with monitoring Well, currently, it's really difficult to gain those views, isn't it? So I think we have to always accept when we're doing exercises like this, that we are only seeing a very small part. It's like catchphrase, isn't it? remember, catchphrase? So you're seeing the bits that have come up on the screen. And we're all making an assumption from that bit of picture that, you know, we think is showing one thing and when the screen comes back, and all the bits are there, you're seeing something else. And I guess that's true as well for the clinicians. And I'm very conscious that as someone who works into a network clinic as well as a specialist centre. Equally, I think you're getting views here, mostly from people engaging with specialist centred care, and picking paediatrics we do need to acknowledge that actually the landscape for people who are providing network care within non specialist centres, they might have different views about what's important. And I think as we see adult care develop, and we are needing to make stronger links with our, you know, community colleagues, although as we've said, care is vary based around around the specialist team, equally with the geography and people having more virtual consultations, it may be that we, we start to work out alongside our primary care colleagues more so. So I think it might be important to think about which bit of the picture we're currently seeing both from people with CF or you're seeing both from people with CF and, and clinicians.

[Researcher\_1] 1:44:06

[CFG1\_4] Did you have something to add there?

CFG1\_4 1:44:11

No, not really. I was pleasantly surprised. I mean, mostly what you said about the patients were similar to what we'd spoken about, I think similar themes anyway, we didn't concentrate much about blood tests. I was quite interested to hear, that some patients would prefer a blood test. Interestingly, I guess that was probably quite divisive, I suspect. But of course, there is increasing use of capillary blood tests, so finger prick blood tests to identify certain things. And, you know, who knows, I mean, I've briefly mentioned CRP, and I don't think it's going to be that useful, but there might be something better than CRP one day, which could be a home test kit, that would say actually, you are about to exacerbate, now you need antibiotics - seven days. So I was quite interested with blood blood tests part of that. But otherwise it was reasonably similar wasn't it.

[Researcher\_1] 1:45:05

Certainly, I think one thing that came up that we definitely haven't touched on here, but came up on the patient's was, obviously everyone wears their i-watch or you know, whatever it is their Garmin that measures their base heart rate every day, constantly, this continuous monitoring kind of idea. And quite a few of the patients mentioned that they'd noticed that their resting heart rate would increase sort of by one BPM for say, four or five days before they started getting symptoms of infection. I was wondering if then if any of you guys have heard of the patients sort of monitoring themselves in this way, or maybe coming to you with any sort of worries when they're at this stage, they've seen something come up.

CFG1\_3 1:45:47

So our centre as part as got a part of project brief, where the patients use a lot of digital health. So they've got a Fitbit issued to them, a home spirometry kit, themometer, SATs probe, and they input the data daily. And they're just Switching now to the artificial intelligence stage of it, where the algorithm will pick up when they need to contact their centre for help, whether they need to have a clinic review, or whatever that may be.

[Researcher\_1] 1:46:17

That's really interesting. What was the sort of response rate? Were the patients generally acceptable with filling in that form well enough, or not?

CFG1\_3 1:46:23

though it's because it's certainly still part of a study area. So there's been participants have have like volunteered, they'd been offered the opportunity to do it. And so that we've got a small cohort inside the centre, I can't remember how many participants so far. But all of them, the uptake has been quite positive. And again, it's the same similar to when we have the patient focus groups, it tends to be the ones that are more compliant with their treatments that tend to partake in this. But hopefully, in the future, it may well roll out to more patients.

[Researcher\_1] 1:46:56

Anyone else had any insights on this kind of front.

CFG1\_4 1:46:58

I mean, we've issued a lot of Fitbits through our online portal. And so Bluetooth connected spirometers, Bluetooth connected weighing scales, Bluetooth connected Fitbits, which feed into the portal, the big caveat is we don't really, and that's why it's great to hear the research that [CFG1\_3] is part of we're not part of that part of brief project, because we don't really know what to do with the Fitbit data. So it's interesting. So you always need to remain mindful of that. There is some work out there. We a few years ago published a little bit looking at the Association of some of these home monitoring devices and pulmonary exacerbations, its in one of the journals, so small sort of pilot study. But yeah, I mean, it's, yeah, I mean, if it does predict - great, it'd be brilliant, It'd be great to see what the research eventually shows, because I think it just is in tune with what everyone likes to do, you know, with wearing watches and devices and things.

[Researcher\_1] 1:47:52

Brilliant. I am aware now that we're in the last two minutes. Is there anyone who has any burning desire to tell us something about say, diagnosing CF infection or exacerbation that we haven't touched up on the interview? Is there anyone who came into this thinking, Oh, well, they're going to talk about that. So but it just hasn't came up? Is there anything burning that you really want to tell us? Or that you feel it's important to tell us about this area? No, no, no, no, no, sorry.

[Facilitator\_1] 1:48:23

I was just going to really quickly mention one thing that we maybe haven't touched on as much as we did in the patient focus group, we've kind of talked about positive and negative tests for detection or monitoring. But we've not kind of necessarily talked about establishing an infection load, or a bacterial load or something like that, that may offer some motivation to patients, when they're in a treatment plan to kind of keep going with it, if they can see those numbers potentially coming down, that might say might help them stick with treatment, that they're really finding quite arduous, exhausting, you know, and potentially even making them feel unwell. But if they could see those levels coming down, say might offer some sort of level of motivation. I just wonder whether anybody has any thoughts around that.

[Researcher\_1] 1:49:20

Reporting continuous results, like a colony forming units and so on.

CFG1\_4 1:49:28

I mean, it's interesting, they're sort of quantitative stuff is always interesting, particularly as loads of that had been done with inhaled antibiotic treatments. And it does come down quite nicely with inhaled antibiotic treatment. Often the problem has always been correlating it closely with sort of patient outcomes as such. But I see I know what you mean, [Facilitator\_1], I mean, it'd be nice. You know, it's quite a motivating thing if you're on the right track, and then that sort of feeds into what I was talking about, in terms of duration of treatment, because actually, if you have that, and you could correlate it with outcomes, then, you know, I'd like to think we were more accurately then treating the patient in terms of length of time. Because I do think we often over treat patients and with antibiotics.

CFG1\_6 1:50:14

I think the problem that we've seen in the laboratory is when you get some chronic Pseudomonas infection. And although they're pn treatment, your clutures look the same, from one week to the next, you don't actually get a reduction, not all of the time. So your patient is probably getting better. But the culture just looks the same as it was, you know, previously, you don't always get that reduction in actual numbers to kind of feed back to you. And then there's always the danger where you're kind of full of antibiotics, you're gonna get a low bacterial culture because of that. So it's been you're holding back bacteria in your culture, so I could give you a false impression of reduction in bacterial load, and it could just be the way the sample has been processed or handled so there's pros and cons to both as what what I'm seeing

[Researcher\_1] 1:51:03

Absolutely, there any final comments? Otherwise, I'll let y'all go. We're all happy. Well, thank you all for joining us. It's been a really fascinating focus group.

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