CoReCCT Site Webinar-20240606_130428-Meeting Recording

June 6, 2024, 12:04PM

55m 22s

Guck, Jonathan started transcription

Paul Dark 0:36

First slide, let's get more specific to today. The first thing is to say is that I'm part of a much broader team. Some of the faces and names in terms of leading some of the trials and the methodology around the trials are present here today and also mentioned on this slide. Behind those people are a huge array of senior managers and support staff, particularly at Warwick Clinical Trials Unit, but also various parts of our trials ecosystem that are here supporting this trial. So, I also would acknowledge and thank them as well. Next slide please Johnny.

So the background is pretty straightforward. You will know this better than me that we have a huge number of adults each year receiving ventilation on invasive ventilation on ICU. But we know that while those interventions that we provide can be life saving, that our patients often experience fairly negative physical and psychological social impacts thereafter. We know from patients that they're keen that we progress more research in this space. And indeed, funders are very keen to support our most critical patients, given the cost both to patients and services that we provide. So, we need to do more research to improve the offer of our care and at the same time, we want to do things much more efficiently in the way we conduct trials. Next slide, please Johnny.

So hence the origin of what we have named the CoReCCT Consortium or Confederation, which is the Confederation of Respiratory Critical Care Trials for short and you can see the logo down in the bottom and CoReCCT is a brand new concept in respiratory critical care research which aims to offer long term efficiency gains through the harmonisation of trial processes, data collection, patient follow up, so patients have much more streamlined follow up processes. And critically important in the NHS around site set up, to provide the kind of efficiencies we're looking for to get trials up and running as soon as possible and for patients to be offered research.

In the first instance, we're bringing together 4 clinical trials and we're going to call those domains. You may be familiar with domains in platform trials through pandemic in critical care. This is not designed as a platform, it's a confederation of individual trials but we coined the domains name, and we'll refer to that as we as progress through this webinar today. The critical thing is that these domains exist along NHS patient care pathways for acute respiratory failure. Next slide please Johnny.

So I want to think of a sort of a prototypic patient pathway and you'll hear from the individual domains that there is some flexibility around this. But if one thinks of a patient on a ward, on an acute care ward, developing respiratory failure and maybe considered suitable for intubation, risk of intubation, then the first of our domains is operational there and called the Awake Prone and we're going to hear a lot more about that later on.

But if the patient subsequently does need intubation and fails, that intervention requires admission to ICU, the process of intubation and the device that is used is the subject of the PROTECT Airways trial, which is a trial that aims to minimise the risk of hospital acquired infection in those patients. And you'll hear more about that later on. And then finally, we have two exciting ventilatory modalities, mechanisms to support patients and to help wean patients that you're going to hear about as well. So you can see from left to right as the patient moves from the ward into ICU and intubation and then exposed to mechanical ventilation. Next slide please, Johnny.

So what does this mean for sites in the first instance? Well, if we consider research staff, then we hope to set up so you are interested in hopefully offering patients one, at least one to two, of the Confederation trials. Clearly would be fabulous if you considered offering all four, but the notion here is to try and get you to think about at least two of the trial interventions.

We set up the Confederation to help you seamlessly enrol patients into one more, one or more of the trials where appropriate and we've got various overarching CRFs and a unified database that's going to help you do that. And so, there'll be a lot of drop down mechanisms at randomization that allows you to see the appropriate bits of the CRF and then the CRF will be obscured if you're not doing that relevant

information, so there's no duplication of data collection across the trials, which is critically important. In terms of your R&D departments, we've talked about the importance of efficiency. They're very time pressed and resource poor actually. And so we're trying to develop a system where we've got a single site agreement for the four trials ready to minimise burden. And that sites can set up to recruit one or more confederation trials using our consolidated site agreement approach. Next slide please.

So what does it mean to participants? And this is, you know, the research that we're offering our patients critically important that there is benefits for them, not just the research process itself and the interventions. But I think critically important is the follow up period that we're going to unify follow up so patients are not exposed to multiple questions, multiple CRFs, that we have a unification of follow up that once they've been enrolled into trials. We've got an overarching master protocol to complement the separate domains you'll be familiar with master protocols.
in ICU over the pandemic. We're going to use a similar approach here that overarches all four trials and obviously there will be specific domain related protocols as well. With CoReCCT patients are given the opportunity to access more or one or more of the treatment arms. And remember these are all non-drug trials. So they're all non-CTIMP trials along their care pathway, providing with the opportunity to achieve the best healthcare outcomes. So the notion of embracing randomised care rather than random care. And all of this whilst minimising burden to patients and research staff by streamlining trial operations. Next slide please Johnny.

So this is a great slide this from Warwick, putting the whole concept together with the four domains running horizontally from left to right and then the PICOs across the top. I'm sure we'll be able to share this slide set with you. I'm not going to go through this in detail now, but you can see how the whole thing works together and you can start to see about the scale of ambition here when one looks at the sample sizes to make sure that we're confident of success or otherwise in the results of the trial. Next slide please, Johnny.

So where are we? We've been thinking about this for some time. Each of the four individual trials have been funded and contracts have been commenced. So the ethics process for the CoReCCT confederation has already been presented to an appropriate Ethics Committee, and that is largely favourable. There's some minor

things to address but patients and the ethics committee were delighted to receive this approach and think it is it is an excellent way to be considering researching in a setting. So that's happened in April. We are planning over the early to mid to summer period to open the Awake Prone and the RELEASE ventilation trials. They were funded quite early in this process and so they're a little bit more advanced planning so that is the plan for July and August. Leading on from that, around late August, September, there will be a substantial amendment within the ethics framework to propose PROTECT Airways and UK NAVA another ventilation trial to the Ethics Committee and they are primed, ready to receive that. So, a lot of seamless approaches here which is really excellent, and we hope that both of those trials will commence recruiting in the autumn. So that's where we're up to. Next slide please Johnny.

So I am going to introduce Keith, who is leading the Awake Prone trial. I'm really looking forward to hearing from the leaders of each of these trials and learn more about their trials. Over to you Keith. Thank you.

Couper, Keith 10:55

Thank you Paul and thank you everyone for joining today. It's fantastic to see so many people here who are interested in CoReCCT. So, I'm the chief investigator of Awake Prone and it's my pleasure today to talk about it. So, if we can go to the next slide.

So I guess just to give you 30 seconds of context of this. So, we know that proning patients with moderate to severe ARDs who are invasively ventilated reduces mortality. We also saw that during the COVID pandemic many of us started to try to prone patients prior to intubation and hoping that that was effective. And what we subsequently found from randomised control trials, that if you've got COVID-19 and you're not intubated and you are proned, then you have a reduced risk of needing tracheal intubation. So Awake Prone is essentially trying to extend that and test that in a non-COVID cohort because we don't, you know, we know from the pandemic very much that patients with COVID behave very differently to all our other patients with respiratory failure. So, our populations for Awake Prone is hospitalised adults with acute hypoxaemic respiratory failure and we've defined that as saturations of less than 94% or equal to 94%, on 40% or more supplemental oxygen. Patients can't

have their primary cause of their respiratory failure being COVID-19 and they need to be suitable for intubation if they deteriorate. And what we're comparing is five days of awake prone positioning with standard care, with a primary outcome of intubation. Recruiting quite a lot of people, but this is a really exciting intervention because potentially we can reduce the number of people that need intubation and this, you know we see a lot of these people in our hospital wards with this kind of respiratory failure, and it's incredibly attractive intervention if it was to be effective and potentially very implementable throughout the NHS, but also throughout the world.
So next slide, Johnny.

So one really important thing about Awake Prone is that we want it to be implemented in all acute hospital settings that care for patients with acute hypoxaemic respiratory failure. So acute medical units, acute wards, critical care units, respiratory support units are all prime settings for Awake Prone. We know and very much appreciate that different hospitals are set up differently and it may be that in some hospitals it'll be possible to deliver the trial in some settings but not others. That's absolutely fine. We'd still absolutely love to have you on board and to take part in awake prone. So, you know we would like to, I guess part of our question is, can we reduce critical care admissions? But we are including patients on critical care, but also all these other settings and the idea is we make this applicable to all our patients with acute hypoxaemic respiratory failure through including as many as possible across these different settings but recognising the differences in hospitals.
So next slide, Johnny.

So just a quick summary of our eligibility criteria. You have to be in hospital, you have to be an adult. You need to have acute hypoxaemic respiratory failure and you need to be suitable for intubation if you were to deteriorate. And within that hospitalised cohort, as I said, you can be in any setting where it's safe to deliver the intervention.

Exclusion criteria: You can't have COVID-19 as the primary cause of your respiratory failure, because I think we're pretty confident now that in those patients awake prone positioning is the right intervention. The next exclusion is, if you've got acute pulmonary odeoma due entirely to cardiac cause. Very different patient groups, so

not suitable for this trial, but a relatively small number of the patients. Patients need to be willing to attempt to awake prone positioning. So that's part of our eligibility is just to ask the patient if they're willing. It's not to say that it's necessarily going to work perfectly in every patient, but they need to be willing to at least attempt it. And there can't be any contraindication. So, things like spinal fractures, very large abdominal wounds are not going to be appropriate for the trial. Again, very small population. And, if you've been intubated before or during that current hospital admission other than for a procedure or operation, again you wouldn't be eligible for awake prone. So next slide.

So, I've just seen a question pop up, we'll do that at the end probably rather than go through them now.

So, intervention wise, it's awake prone positioning for five days or up to five days. We obviously stop earlier if the patient recovers, if they're intubated or a few other reasons or if the patient wants to stop. We're aiming for a target of over eight hours or more per day. We know the duration of awake prone positioning is likely to be associated with how effective it is. We know that not every patient is going to tolerate that. That's absolutely fine. What we're asking you to do is just to target that duration as much as possible. It can be one long period or multiple shorter periods, and if they can't tolerate a full awake prone positioning, so fully on their front, then they could go to a three-quarter prone position and that's an option if they can't tolerate that, that full awake prone position.
So next slide, Johnny.

And the control group is essentially no awake prone positioning. So generally, these patients will be sat up in bed in a sort of semi-recumbent position. And I think that next slide is our last slide just to cover Awake Prone.

So, the other things that we often get asked about and the key thing here is Awake Prone is intended to be a highly pragmatic generalizable trial. So all treatment decisions apart from awake proning or not awake proning are at the discretion of clinical team. So, the saturation target you're aiming at, what blood gases you want to do, whether you're going to use non-invasive respiratory support or not, any drug treatments, entirely at the discretion of clinical team. Equally, the decision to intubate

the patient is not protocolised and is entirely decided by the clinical team, in collaboration with the patient, and that's really about the trial trying to be as pragmatic as it possibly can.

So, obviously Awake Prone is about trying to prevent intubation. But for those patients that are intubated, there's obviously then the opportunity to go in to Protect Airways. And I think we're going to move on to Protect Airways now, which is introduced by Gareth.

Gareth Kitchen 17:41
Thanks very much, Keith. Yeah. My name's Gareth Kitchen. I'm a consultant anaesthetist in Manchester with Paul and I'm the Chief Investigator for PROTECT Airways, guided by Paul Dark as Co chief investigator.

So we are investigating in a new type of endotracheal tube or advanced airway protection device that is CE marked and available in the NHS but doesn't have that body of evidence yet as to whether it's better than the standard of care. So, we're after all comers really, anybody that's going to be intubated in ICU over18 years of age and they're likely to be ventilated for 24 hours.

So the intervention is this Venner PneuX tube, which I'll go through in detail on one of the subsequent slides and the comparator is the standard of care in your institution. So that's either an endotracheal tube with subglottic suction if you use it or a standard of standard endotracheal tube if that's what you use.

And now the outcome is going to be duration of mechanical ventilation. So, from intubation to liberation of ventilation and that's another, as with all these trials, pragmatic outcome, and we think that the mechanism of action will be reduction in ventilator associated pneumonia. But we're going to be measuring the time from intubation to extubation.

Our sample size is 2194 patients, obviously half in each group, and it's a UK multicentre open label pragmatic, individually randomised trial.
Next slide please.

So again, we're going to work with individual units as to where this is going to take

place. We imagine the majority of recruitment will happen in critical care units, but if you are a unit that intubates a lot of patients in A&E or in medical wards or even in operating theatres, we're open to randomization if you think an intubated patient on intensive care is going to be intubated for 24 hours or more.
Next slide please.

So in detail, again, it's simple. You know our inclusion criteria. 18 years or older, need for mechanical ventilation and likely to be remain ventilated for at least 24 hours after randomization.
Next slide please.

And our exclusion criteria, again very minimal. If you were expecting to withdraw treatment within the next 24 hours or if there's a tracheostomy present at screening, we wouldn't include those patients.
Next slide please.

And so, here's the device. You know, it's familiar. It looks like a standard endotracheal tube. It's actually the tube from the intubating LMA for the anaesthetists among you and it has certain features. So, the cuff, as you will see, you can't see it there. It's a silicon tube, a silicon cuff that inflates by expansion rather than a plastic bag expanding at the end of the tube. It therefore doesn't get the microchannels. And it reduces the amount of micro aspiration that might be occurring. It's inflated and maintained to be inflated with the tracheal seal monitor to an electronic device that maintains the pressure that's connected to the blue port there. And it has three subglottic ports attached to that beige coloured suction tube there.
Next slide please.

So the control as I mentioned at the beginning, it's the standard of care within your institution. So, as you can see in this picture, a standard endotracheal tube or a tube with subglottic suction is equally fine.

And lastly, just talking about the consent process, because this decision might need to be made in a particularly quick manner, we're generally going to go with the deferred consent model prior to randomisation. But if we do think there's time we can discuss with consultees and even the participant if they're conscious prior to

randomization.
Thanks very much. We'll take questions at the end.

Camporota Luigi 21:48
Well, good afternoon. My name is Luigi Camporota. I'm one of the investigators of the RELEASE trial together with Danny McAuley and Louise Rose. If I could have the next one Johnny please.

RELEASE is about a study essentially. If we follow the CoReCCT investigators plan as all, patient has been intubated and is in the early hours post the intubation. And these patients are normally receiving invasive mechanical ventilation and they have moderate to severe hypoxaemic respiratory failure. What does that mean? It means that a PF ratio less than 20kPa regardless of the chest X-ray. So we look at gas exchange oxygenation criterion alone. Well, the intervention of this trial is early airway pressure release ventilation. Early means that we want to have it as a primary modality of ventilation rather than as a rescue mode of ventilation for patients failing conventional ventilation. So, this is a head-to-head comparison: earlier APRV versus the standard land protective ventilation (the one that you normally use for patients in this category). But at that point, we would be very keen not to have APRV in this comparative group. Just have a good separation of interventions. And the outcome is going to be duration of invasive mechanical ventilation from the time of randomisation. And then there is a health economics cost utility at six months. We aim with your help to recruit 710 patients in total and you can see the study design is a pragmatic study but is randomised controlled with that health economics embedded. Thank you, Johnny. The next one please.

OK, so who could participate in the trial. So clearly all of you who see these patients, patients with acute respiratory failure, which is I assume will be most of you, if not all of you, and have clinical equipoise for airway pressure release ventilation. And I think the third point is quite important because given the evidence available for airway pressure release ventilation it will be quite important that everyone has the agreement to essentially maintain the trial allocation for patients, so either stay on airway pressure release ventilation unless there's some stopping criteria or maintain a conventional ventilation without minimal crossover. Next please.

So again, this is the population in terms of the inclusion criteria we would like adults or with age of at least 18 years of age who will receive invasive mechanical ventilation. We talked about the severity of acute hypoxemia respiratory failure mainly based on PF ratio less than 20 kilo pascal and a PEEP that is greater than five, which is essentially as the standard definition and most patients if not all patients at this stage will have at least a PEEP of five. And they are expected to receive or require invasive mechanical ventilation for at least 48 hours.
Thank you, Johnny.
So these are the exclusion criteria. Now what you will see, you will see two boxes, the one on the left, these are sort of absolute exclusion criteria in a way that if a patient receives received invasive mechanical ventilation for more than 60 hours. And this is the idea of having a deliver an earlier airway pressure release ventilation. Or if the patient receives invasive mechanical ventilation for reasons other than a parenchymal lung disease, such as an airway disease like asthma or COPD or a vascular disease like pulmonary emboli or a neuromuscular disease. In this case, there is no biological rationale while why airway pressure release ventilation should have any effect in addition to the conventional ventilation, so we would be absolutely excluding those patients.

There are some temporary exclusion criteria you will see on the right hand side, for example patients with shock. They might not be able to accept or be randomised to airway pressure release ventilation, but clearly there can be reconsidered once the shock is resolved and the patient is more stable. The same thing for severe hypercapnic respiratory acidosis whether a patient has got pneumothorax but has not been drained. Patients with traumatic brain injury or clearly patients who you decide will not be suitable for continuing organ support. And the one at the bottom is clearly patients who have more chronic lung disease with respiratory failure, which is chronic and normally require oxygen at home prior to admission to intensive care. Next one please.

So this is just a schematic of looking at the idea. So, this is a patient with lungs that have been with a condition causing severe respiratory moderate to severe respiratory failure. So usually parenchymal infiltrates. And the on the left hand side you can see the control the comparator which is the normal ventilation that we use in in clinical practise, so unprotected ventilation. You normally set a plateau pressure or peak

pressure. You normally set a tidal volume. Peep is highly variable based on sometimes five or two or sometimes local practise, but the key thing conventional ventilation tend to have a relatively shorter inspiratory time compared to the expiratory time. So the idea is that with lung protective ventilation that we use normally we aim for a lower stretch of the lung. Whereas on the right side this is the intervention, the airway pressure release ventilation, where we still maintain a certain plateau pressure or inspiratory pressure. But now the breath is delivered over a longer respiratory time to facilitate gradual recruitment and stabilisation of the lung. But at the same time a shorter respiratory time to prevent collapse.
And we provide that in a very personalised way and I'll show you in a second how to do it and there will be plenty of training and material so we can become really confident in setting this modality of ventilation. But the idea is that through this airway pressure release ventilation, we make the lung more homogeneous and homogeneity is really key for lung protection. And that's the purpose, the biological rationale for delivering airway pressure release ventilation. So if we can go next, please Johnny.

So the so and again this is a, is an intervention that can be nurse led. All the all the team will be trained and there will be some package available for each individual site. It will be protocolised, so we will protocolise ways of transitioning from conventional ventilation to APRV if the patient gets randomised to receive APRV and then we'll guide you through how to optimise and titrate airway pressure release ventilation. And then finally, to wean airway pressure release ventilation in a way that the patient continues to receive that intervention without crossing over to the other side. And then some troubleshooting will find out some common issues that normally faced during transition of APRV, and we'll find out how to how to circumvent them and maintain the patient on the intervention.
And if we go next please.

Yes. So this is a typical screenshot or what airway pressure release will look like and what you will see is a very it's a, it's a longer inspiratory time and a quite short expiratory time, which will look truncated like that because the expiratory time is very short. And if we go on next please Johnny.

Essentially, what the way we.

Set the expiratory time which would be part of the training is by a next please again, sorry, a couple of animations. That is a way of finding out the peak expiratory flow by just freezing the screen. And then essentially measuring the ending expiratory flow, which is the flow at the time of reinflation into inspiration. And then what we would like to have is an end expiratory flow that is 75% of the peak and we can titrate the Plow which, sorry, the Tlow, which is the expiratory time until we get that perfect tration and next please.

So again, control is a standard conventional ventilation. Whatever you do in your unit, but no APRV and that's the key having maximum separation between the two groups. Next, please again.

And so this is the enrolment process. You basically identify the potential participants, give the information, can get the consultee agreement, but also if not possible there will be a professional consultee, so there will be a clinician not involved in the care of the patient, but they can provide that initial agreement and then there will be the randomization in the two groups. And next please.

And that is all we've got to say for RELEASE for now. But there will be plenty more to come in the future. So thank you for your attention. And then Dan or Phil over to you.

HOPKINS, Phillip (KING'S COLLEGE HOSPITAL NHS FOUNDATION TRUST)
33:39
Well, thank you very much, Luigi. Good afternoon. Thanks for joining to all the sites. My name is Phil Hopkins. I am an ICU and anaesthetic consultant at King's College Hospital and I'm ably assisted by my co-Chief Investigator Dan Hadfield, who's a senior academic nurse at KCLH, a massive thank you to my CoReCCT Co investigators for allowing us to complete the patient pathway really, as Paul mentioned with a trial aimed at improving ventilatory weaning.
So a little bit of context around this research around weaning for example using pressure support is very limited, surprisingly limited.
But we think that UK NAVA and related research is important for four main reasons. We want to get patients off ventilators quicker and improve their outcomes. We want to improve the experience patients have when they're ventilated.

We want doctors, nurses and physiotherapists looking after the patients to have a better time of doing that and we want to help teams save money.
So NAVA is a pragmatic open label randomised control trial comparing NAVA technology with conventional ventilation and again as you would expect, it has standard outcome measures and you can see the sample size there of 900.
NAVA technology involves 2 simple interventions that might reduce the time patients spend on ventilators and improve their comfort. It has NAVA monitoring, which allows doctors, nurses and physiotherapists to see if a patient has intact neural drive and understand what ICU interventions like sedation boluses do to that drive, and also be able to see asynchrony or dyssynchrony on the ventilator, when compared when looking at a patient in any mode of ventilation, whether it's SIMV, PRVC or pressure control.
NAVA Technology itself has improved a lot over the last couple of years and is now much simpler and easier to use and although we will be focusing on sites that have Getinge of ventilators, we are happy to speak to other sites for which we will have a separate involvement pathway.
So we're looking at patients who are expected to be ventilated for more than 4 to 8 hours. So if you're randomising today, we'd expect them still to be ventilated at the at the end of the weekend. Adult patients. And we're looking for patients who are at clinical risk for difficult or prolonged weaning from invasive ventilation. And there'll be a simple definition and guide within our protocol in relation to this. But they’re our main inclusion criteria and we tried very hard to make our trial as easy and as pragmatic as we can to include and provided the patient is at risk of prolonged weaning for either an acute critical illness problem like pneumonia or ARDS or a chronic health issue like heart failure or COPD or obesity, you can include those patients. The exclusions are fairly obvious and related to this requiring the insertion of a nasogastric tube or an orogastric tube and involve things like severe damage to the spinal cord or brain stem, then the presence of some kind of contraindication to an oesophageal device and obviously the patient receiving end of life care.
The intervention, as I've already mentioned, involves placing a nasogastric tube or an orogastric tube. The NG tube itself is a bit easier to insert than a standard NG tube, and we're hoping that because the intervention is very familiar to ICU teams, that it will be an attractive one. The improvements to NAVA mode, also NAVA tech monitoring and mode in the last couple of years, should also help as well and make the intervention much less problematic than it has historically been.

And we'll be asking the teams during the intervention to be doing these two aspects of NAVA technology, NAVA monitoring and NAVA mode, and we're hoping that the data we ask and research teams, nurses, PIs to collect will be very, very simple and very, very obvious and hopefully really useful to normal bedside nurses and doctors who are trying to look after these patients.
The control arm is just standard care. Obviously in the control patients you can't put a NAVA catheter in, but otherwise we would just expect good standard ventilatory weaning and airway practise.
So we will be expecting both arms to have daily sedation holds and daily assessment for liberation from invasive ventilation. But at the end of the day, that's exactly what we know that all sites do with intensive care patients anyway.
And the enrolment process is again pragmatic and it also involves the potential for deferred consent because we want people to go to place nasogastric tubes as part of the initial resuscitation procedures. And then a very standard consent process following that.
Just to finish off, just to highlight a couple of important things, as I say, we've tried to make the the placement of the nasogastric NAVA catheter within the protocol very straightforward. NAVA technology is now much easier to use than historically it has been. We hope that it's a research question that people think is reasonable to ask and we obviously provide the NAVA catheters and any NAVA modules that sites might need free. In addition to providing appropriate training, focused training for any sites as and when they need it. We hope this makes the trial attractive. Thank you very much.

Guck, Jonathan 40:39
Great thanks to all the speakers for presenting there. I hope the callers on the line, found that a useful introduction to CoReCCT as a whole, but also each of the four trials that are participating, I can see we've had several questions in the chat, most of which have been answered already, but if any more springs in mind, please feel free either to raise those in the chat now or verbally. We can see a couple coming through there. So we'll just give everyone on the line a chance to have a look at those before we respond.

PD

Paul Dark 41:01
Yeah.

Guck, Jonathan 41:15

So Mel, thanks very much for your your query there around accruals and I think this is a very key question really for our sites, while we're setting up CoReCCT in a you know uniform approach, it is worth highlighting that any recruit you have will count as a single accrual or so if you recruit a patient first to say Awake Prone that is an accrual, if they later are recruited to a subsequent trial, let's say PROTECT Airways, that will be a second accrual there. So you would receive 2 accruals for that same participant even though. For their multiple trials. Hopefully that resolves that query.
Oh, thanks, Keith. I can see you've put a response in there just going down.
So we've got a query there from Donna around the NAVA technology.
So, Daniel, Phil, I'm not sure if you're able to step in there.

HOPKINS, Phillip (KING'S COLLEGE HOSPITAL NHS FOUNDATION TRUST) 42:13

I'm I can I can. I cannot. Essentially, the the NAVA technology.
Has improved because the engineering of the novel catheter is now better. For example, you can leave them in the patients longer.
And the fall back mode in NAVA is more straightforward now, so you remain in NAVA rather than flipping backwards and forwards between pressure support and NAVA, so that the mode is more more robust.
Aspect. Obviously I've spent a lot of time.
Testing the technology and I must say, once you get over a short learning curve, it now does seem to be much, much improved.
But you know we will be providing the part of this is to provide training as it is with the other trial other three trials and to make sure that teams are really comfortable and feel really supported when they're taking part in the in in this trial.

Guck, Jonathan 43:13

Thanks, Phil. Thanks Donna as well. Any other questions that spring to mind?
Hopefully you can see from our timelines we are progressing quite rapidly at the moment with set up for all four trials, so Awake Prone and RELEASE are hoping to start recruitment soon. Keen of course to engage with as many sites as we can for those two trials. But also of course the NAVA and PROTECT Airways who are coming

on board later. Thank you, Lucy. I can see their question around Getinge ventilators. Will these be supplied as part of the trial?

Paul Dark 43:37
OK.

HOPKINS, Phillip (KING'S COLLEGE HOSPITAL NHS FOUNDATION TRUST) 43:45
I I I can answer that if you like, we'll we'll be having a twin track approach to the NAVA technology.
So that we'll have our main pilot sites will obviously already have the Getinge Servo platform.
And but they will receive the catheters free and module additional modules if they need it. But we we've thought very carefully about this and we want to if there are any sites who are interested in exploring.
Using NAVA technology when they don't currently have the.
Platform, Getinge are providing the support to the trial are clearly are open to that idea, but obviously we'd want to spend a bit more time with those sites and give them a bit more set up time, but it's not a it's not a barrier to inclusion.


Guck, Jonathan 44:34
First question we have is around the database, so we have a bespoke databases in set up at the moment at Warwick. So if if any callers on the line participate in other Warwick managed trials, the database itself should look quite familiar to you. There will be one trial database at CoReCCT level where patients are recruited and data is entered wherever possible that streamlined. So there'll be a core data set if patients are recruited to multiple trials to avoid duplication.
And any of the trial specific aspects will be captured there as well. So things around the specific interventions will be captured there as well. So hopefully that helps that query. The next question there is around the consent process.
Again we we try to streamline our consent process as much as possible. So there will be separate approaches for consent for each trial. So if a patient is eligible for multiple trials at that point in time, there will be a consent for that particular trial to consider with the patient or their relative, whether it's appropriate for them to take part and to resolve any questions they have. Our consent forms have been unified so,

so the consent items on the form should be very familiar if a patient takes part in multiple trials, hopefully that means the consent items themselves are already familiar with them, and that just eases the process somewhat. And of course, yeah, we're we are aware there is a potential for risk of overwhelming patients and their relatives wherever multiple trial approaches are made so it is a key concern of ours and we want to address that as much as we can.

In terms of the Scottish approval process, so at the moment we've had our initial ethics application go into a Welsh REC, but we are liaising with the Scottish REC as well to to ensure our consent process is a fit for purpose across all the devolved nations.

So just a look at our queries now as the centre, can we pick which arms of the study we'd participate in? Yeah, very good question there, Chloe. So sites are free to choose to take part in however many trials you wish. If you only want to take part in one trial, that's fine. This will work as if a traditional trial was in in place at your site. Ideally, we'd like our site to take part in multiple trials and that's where we see the most benefits to be gained. To be honest, those efficiency benefits will come on board with the more trials you you participate in. So if you want to take up part in four trials, brilliant. This should work very well at your centre.
If a smaller number of trials suits you, no problem at all.
And our following question, so yes, there is a singular IRAS and REC submission. So at the moment that has been submitted for our CoReCCT master protocol Awake Prone and RELEASE, our two earlier trials. We will submit an amendment to add NAVA and PROTECT Airways later on. So there will be 1 IRAS ID covering the four trials and the CoReCCT master protocol.

Equally, we are keen to be as flexible as we can from a site perspective, so we've been liaising with R&D managers across the UK. Most managers feel that we can set CoReCCT as one study. If you wish to take part in additional domains later, brilliant we can add those on as amendments locally, so hopefully that approach is suitable for most sites.
And a question here around delivering a training package. Yeah, absolutely. I can. We we foresee that there are challenges associated with this. So we as trial teams are offering bespoke training packages for each of the trials, NAVA and RELEASE in

particular will have intensive training to support the nurse led interventions there. And we can provide some more details of that after the call because you know we're absolutely on board with you there. We need to make sure your teams at site are well trained in this. And is there additional support other than cost per patient. So yeah, we can provide financial details after the call and provide provide you with more details on the training packages we'll provide as well.

Joy Dearden 48:50
Good afternoon.

Guck, Jonathan 48:56
I'll just perhaps open up the call at that point just to see if any of the RELEASE and NAVA teams would like to add any additional info around the nurse led package we we are setting up.

Camporota Luigi 49:11
No, Johnny, just to say that there will be. We're working now on on several things about the training for just for the delivery and also for something about consent for the patient, just to make it easier and reduce the workload of the for the investigators and people are sort of trying to get participants so will be will be in touch with more details shortly.

Guck, Jonathan 49:44
Thank you, Luigi.
Do you have minimum recruitment targets for setup? Again, brilliant question there. I think we're keen to take a pragmatic approach here and we will discuss recruitment targets with individual individual sites. I think as always we're keen to take on board a range of sites depending on your size, your recruitment capability, so we can more than happy to discuss this with you guys as well.

Daniel Hadfield 50:21
Come in and say about the training that it's obviously a big benefit that we're developing training materials.
Together collaboratively and that we're sharing our resources so that if you're participating in more than one trial, then the the people that you're interacting with

will know about those materials and that should be a big help. Like Luigi, we're putting together our training material at the moment and think we'll all have our own website.
And different ways to access the training material. And I think we'd all be happy, certainly we'd be happy to come along to your local meetings to discuss anything in more detail should you want us to. If you want us to present your research meetings that might be useful.

Guck, Jonathan 51:19
Thank you, Darren. Query there around the associate PI scheme. Yes, absolutely. We're keen to apply for the NIHR's associate PI scheme for each of the individual trials.
This should mean that we could, if your site is participating in all four trials, that could mean 4 associate PIs at your site. So we hope this is a very attractive opportunity to support your PIs, you know, broaden the input across the board, but also act as a training and development opportunity as well.

Paul Dark 52:18
Johnny, would you like me to do a short summ up? I see there's a few more questions coming in there, aren't there?

Guck, Jonathan 52:26
I think, yeah, given given timelines that would be great. Paul, any final questions, please feel free to keep adding those to the chat and we'll get back to you either during the meeting or shortly after. But I'll hand over to to Paul now. Thank you.

Paul Dark 52:32
We'll get back to you.
Yeah, Johnny. Thank you. And I really want to thank you all for joining today. Questions are fantastic. Thanks for listening to each of the main leads and thank you for Warwick and Johnny for setting all of this up. Look, it has been recorded and it is shareable. So we'll do that in terms of the interventions, these have been separately judged as fundable and critically important in the pathway. And they've been judged by the NIHR separately. And so this is really important.
The confederation approach is a new venture for the UK, so you can see yourselves

as all being trail blazers in this proposition to create a community to do these kind of respiratory trials. And I think the future ambition, if this works out and the NIHR and the RDN are watching this very closely is how we can build confederation communities like this to progress patient pathway trials in the future so.
It could be in the future that there are other interventions brought into this confederation, but that is speculative at the moment, but a really exciting opportunity for the future. So thank you so much for joining us today and I'll just send you back to Johnny, to summarise. Thank you.

Guck, Jonathan 53:59
Thank you, Paul. Yeah, just to echo, thanks so much for your time. We really appreciate the time out of your day to to attend this talk. Hopefully we've given you a very good summary of what we're doing here. If you are interested in finding out more, please do get in touch. I'll pop our ICU e-mail address in the chat here and yeah, fire off any interest or questions to us and yeah, hopefully we can progress site set up some of these centres very soon.
Yeah, as I say, thanks so much for your time and we'll leave it there. Take care all.

MP **Mel Penacerrada** 54:29
Yeah, all the very best. Thank you very much for your time. I.

GO **Grainne O'Connor** 54:32
Bye bye. Thank you.

Guck, Jonathan stopped transcription