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# *Inside the Landmark PROSpect Trial*

In this collaborative podcast between Pediatrica Intensiva and OPENPediatrics, recorded in Melbourne, Australia, at the World Congress of the World Federation of Pediatric Intensive and Critical Care Societies (WFPICCS), Drs. Martha A.Q. Curley and Ira Cheifetz join Dr. Karen Choong and Dr. Traci Wolbrink to discuss the results of the PROSpect trial, a landmark international study evaluating prone positioning and high-frequency oscillatory ventilation in children with moderate to severe pediatric acute respiratory distress syndrome (PARDS). The speakers review the trial's adaptive design, key findings, and implications for clinical practice. They also share lessons learned from conducting a large-scale global trial during the COVID-19 pandemic, highlighting the importance of collaboration, research infrastructure, clinician engagement, and mentorship. The conversation underscores the importance of rigorous evidence generation to improve outcomes for critically ill children and guide future pediatric critical care research.

**SPEAKERS:**

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**Initial publication:**

November 24, 2026

***Sarah Marcley*** *00:03*
*This special podcast series from WFPICCS 2026 is a collaborative production of OPENPediatrics and Pediatric Intensiva, bringing together a global community of pediatric critical care clinicians, educators, and researchers to share perspectives from around the world.*

***Karen Choong*** *00:24*
*Karen Choong, I'm a pediatric intensivist from McMaster Children's Hospital in Hamilton, Ontario. Good morning, everybody. I'm at the 13th World Congress of the World Federation of Intensive and Pediatric Critical Care, held here in Melbourne, and I have two guests here with me today, Dr. Ira Cheifetz and Professor Martha Curley, along with Traci Wolbrink, and we just heard a plenary session where Martha presented on the results of the PROSpect trial, which is extremely exciting, a landmark clinical trial in pediatric critical care. And we're delighted to have the both of you here today to talk to us about your results.*

***Martha Curley*** *01:02*
*Thank you.*

***Ira Cheifetz*** *01:03*
*Thank you.*

***Karen Choong*** *01:04*
*Martha Curley. I hold the [Ruth M.] Colket Chair in Pediatric Nursing Science at Children's Hospital Philadelphia, and I'm a professor at the University of Pennsylvania School of Nursing.*

***Ira Cheifetz*** *01:15*
*Hi, Dr. Ira Cheifetz. I'm a pediatric intensivist at Rainbow Babies and Children's Hospital in Cleveland. I'm also the division chief for cardiac critical care, as well as a professor of pediatrics at Case Western Reserve University.*

***Traci Wolbrink*** *01:29*
*I'm Traci Wolbrink. I'm a pediatric intensivist at Boston Children's Hospital and co-director of OPENPediatrics.*

***Karen Choong*** *01:35*
*I'll just jump into asking the first question. Could you give us Martha a brief summary on what the PROSpect trial looked at? So PROSpect was a clinical trial that investigated prone versus supine positioning, and also high-frequency oscillatory ventilation and conventional mechanical ventilation. It*

*was a two-by-two factorial response adaptive trial, and what was really exciting to me about this trial is that it was conducted across the world, and so it was really exciting to come to this meeting on yesterday and present the results of the trial. You know, in total, we had 75 participating PICUs across the world, and I think when we ended the trial, Ira, it was around 43 sites that participated, but fundamentally we were comparing prone versus supine positioning, and we were comparing high-frequency oscillatory ventilation to conventional mechanical ventilation in kids with moderate to severe PARDS. Ira, can you summarize the results of the PROSpect trial for us.*

***Ira Cheifetz*** *02:48*
*Yes. So the the big picture summary is that neither high frequency oscillatory ventilation nor prone positioning improve ventilator free days in patients with moderate to severe pediatric ARDS, and thus the conclusion of the study is that neither of these therapies, oscillation or prone positioning, is recommended as a first-line therapy for PARDS.*

***Karen Choong*** *03:12*
*Can I ask you both, did these results surprise you, and if so, why?*

***Martha Curley*** *03:18*
*Well, I guess when we, when the DSMB [Data and Safety Monitoring Board] revealed to us the results in December, I did expect different results. We asked the question, and it was interesting that it was a response adaptive trial. So we had equal randomization, you know, in the first 300 patients, and then after that, we would enroll patients in the superior, you know, parts of the trial and away from non you know those arms that were not performing well, and so I really thought one of the at least one of the interventions because they're so core you know to pediatric practice and especially going through the pandemic and you know based on the Guérin study, you know, everyone was proning everyone, and so first, you know, myself, I conducted the first prone trial 20 years ago, and we closed for futility after 100 subjects. But that study was contaminated because we only enrolled kids with moderate disease. You know, a really mild disease ends up enrolling kids a little bit sicker, but we mandated the use of oscillation in kids when they hit an OI [Oxygenation Index] of 15. So that kind of contaminated Prone 1. So with Prone 2 the PROSpect trial, I really anticipated if there was going to be a signal, we'd find it given the design and the rigor of the study, and it just was not there. And then maybe Ira, you can comment on the ventilation piece of this.*

***Ira Cheifetz*** *04:55*
*Yes, from the prone positioning, actually, I agree with all of Martha's comments. I was a little surprised. I thought we would see a prone signal. Not sure the strength or the details, but I thought we'd see something: more proning or oscillation. Honestly, I'm not surprised. If you think back and look back through all the ventilatory studies ever done, no study's ever shown in pediatric critical care that any mode is superior than any other mode at improving outcomes. I think that's what we showed: the oscillator is not superior, and it's a mode of ventilation.*

***Karen Choong*** *05:27*
*Given what we know on the physiologic rationale for prone positioning and the adult data, why do you think, or what do you think, the explanation is for not finding superiority with prone positioning? I mean, fundamentally, the chest wall is different, you know, in kids as you know compared to adults. The rationale behind doing this study in kids was that you know kids are not just smaller proportions you*

*know than adults. There's a difference in chest size, the difference between the ratio of the heart and the chest in it by itself. There's a difference in compliance of the chest wall, so it may be that there would be differences, and that's why we did it. You know, we said, okay, so maybe there's differences. We're still arguing from a physiological perspective. You know, what's the cut score here? Is it age one? Is it age two? Is it age eight? So we're doing you know, a post hoc analysis now to probe the data a little bit more to better understand why. But fundamentally, the chest wall of a infant and child is not the same as an adult or a geriatric person. You know, it's much more flexible. It's much more pliable. You know, so maybe that has something to do with it, but we'll be able to tell because those of the people who participated in PROSpect always said, "Why are you collecting all of this data?" And we have so much data that we're going to be able to probe that a little bit more. You know, currently we're going to, even though it's 20 years ago data, we're going to pull all that data together where we can, and then hopefully figure out exactly why we're seeing these differences, because it's shocking. I mean, anyone who takes care of a critically ill kid knows that if you put him prone, you're going to see beautiful improvement in oxygenation in most of the patients most of the time, but sometimes you don't, and it's never translated to improve outcomes. So that's what we're finding here. It's just you could do this cosmetically; it looks good. You could still do it as a rescue maneuver. If somebody in front of you is just not responding to now conventional mechanical ventilation, you can place them prone as you're getting the ECMO circuit up and going, and you can certainly continue to prone kids for comfort. A lot of kids like to be on their bellies, and we certainly turn kids prone to you know for skincare issues. So we do that, but you're definitely not going to give them the sedation they need to keep them prone anymore, and you know, as we reported yesterday, we did have one serious adverse event in a patient who was randomized to prone and CMV [Conventional Mechanical Ventilation], and sadly, you know, that was a patient who self-extubated in the prone position, could not be reintubated, and eventually died a neurological death, so it's not a benign intervention. You know, it shouldn't be considered a benign intervention. And we certainly will turn kids prone if they're little, and it's easy to do, but certainly not in kids who have you know high BMIs or the big adolescents, so we're going to probe that data a little bit more.*

***Ira Cheifetz*** *08:51*
*The most common question I received after the presentation was, "Is there a subset of patients in whom proning might be beneficial?" And the answer is, Martha said, "That's the post hoc analysis." So there may be a signal there, but across the population studied, there was no benefit.*

***Karen Choong*** *09:08*
*Yeah, but I also we controlled for the world. You know, we controlled for age. We controlled for direct versus indirect lung injury. So, kind of no, there isn't even a you know an age signal here. But we'll [...].*

***Ira Cheifetz*** *09:24*
*Because there may be a weight or size signal, and we don't know that.*

***Martha Curley*** *09:27*
*Or recruitability, you know, kids who are recruitable or not. But certainly, few children were not removed from the prone arm. You know, once they were randomized to prone, they got prone, they stayed prone, and we really had high compliance, like over 80% compliance for that arm of the trial.*

***Karen Choong*** *09:50*

*It was such a well-conducted, rigorously methodologically sound trial, and that was a question that I had for you: Is this the definitive answer for proning, albeit you have more post hoc data to analyze. In the current era of ultrasound-guided management, are there other subpopulations that you might not be able to get data on from your post hoc analysis? Because we're trying to treat physiology, but now we have more tools to identify the physiology that we're treating.*

***Ira Cheifetz*** *10:25*
*Right, of course, there may be variables that we don't know. The study was designed now what nine years ago. A lot has changed in nine years. But to answer the first part of your question, I don't foresee anyone else in pediatric critical care repeating a prone or oscillation study. The study was well designed, well controlled, international, and we saw some of the many of the challenges to recruit patients, enroll patients, and I think these answers, at least with the data we have today, are going to be definitive for some time in the future.*

***Martha Curley*** *11:03*
*You're always going to have the naysayers of any trial, because those patients weren't my patients. I mean, you're always going to have that, but I can honestly say, given the adaptive design, you know, of this trial, we gave every potential for if there was signal, we would have we would have found the signal, and it simply was not there.*

***Ira Cheifetz*** *11:27*
*And it's generalizable results. And the study was done across five continents, with a nice distribution of patients, both North American and across the globe,*

***Traci Wolbrink*** *11:39*
*And with a variety of conditions. Right? What were your exclusion criteria and inclusion criteria? Are there any patients that you think that these results are not relevant for.*

***Ira Cheifetz*** *11:48*
*Early in the study, we did revise our inclusion-exclusion criteria to make it as much as we could real life. The patients who were largely excluded were those patients that most clinicians would feel or should not be prone, or those patients who are deemed potentially at higher risk of oscillation, but but these were you know real world exclusions after the first iteration that we learned real quickly that we needed to be real world.*

***Martha Curley*** *12:19*
*And it's also you know the oxygenation criteria. We also learned during this trial. I mean, we have PARDS criteria, and it's like one point in time, but you know our kids don't read our protocols, and they're all over the they vacillate around the parameters, the oxygenation parameters. So we had kids who, once they were identified as having PARDS and research candidates, with a little bit of help, they did well, and so they would drop out because they no longer met oxygenation criteria. And we certainly didn't want to enroll kids who really didn't meet criteria, you know, for the study. Kids who absolutely had, you know, moderate to severe PARDS. And so, you know, we're going to also write a paper on rapid improvers, like who are the kids that rapidly improved, you know, from this, and we certainly had a lot of exclusions of kids who are hypoxemic but not PARDS, and kids who could not be oscillated or proned, or the big cohort as well is the kids with cerebral hypertension, you know, that come in just*

*should not have been managed. You know on our blood gas criteria, so they could not be enrolled. So with any clinical trial, you apply the results of the trial. You know to the population from which it was drawn, and so you have to look at the inclusion exclusion. And as you're looking at a patient in front of you, you know, will the PROSpect study, you know, results apply to this patient that's sitting in front of me? And there's lots of nuances as well.*

***Ira Cheifetz*** *13:56*
*The other thing we're going to learn from this is those patients who who failed the protocol, who were not successful in adequately oxygenating and ventilating. When we did get into rescue, now the rescue approach was not controlled. It was at the completion of our protocol, but as Martha said, we collected a tremendous amount of data, and now I think many of the investigators who questioned all the data and why it was needed, we will have hopefully some more, I don't want to say answers, but insight into some rescue therapies and at this point, we've not even begun to look at those data, so I can't comment further. But there's more to come.*

***Martha Curley*** *14:32*
*But that's on the on the list of things to write before February of 27 when we lose all of our funding. Yes, but yeah, it's going to be interesting to see when you failed. You know, where did you go and what happened? You know, so the transition points and whether or not another mode captured the patient better or whatever, but kids either failed within the first day of going on protocol or they failed like you know three and a half days later. So we had early failures, late failures, according to you know clinicians' use of the parameters, but you know it's going to be interesting to see how they land. But it's also, you know, somebody chatted about the 10% mortality rate. Our mortality rate was 10%. Prone 1 was 8%. So there's also this phenomena when you're in a trial, people are paying attention to you. You are people are right on top of you know things that need to be changed. So I don't think our you know if you look at our population that were enrolled into this study, 10% mortality is you know real. I mean, we excluded kids who had like the BMTs that could not be salvaged. So, some of those high-risk, high-mortality kids were not part of this trial.*

***Karen Choong*** *15:55*
*This is a landmark trial, as I've mentioned before, for so many reasons: adaptive, real-world, international. You did it during COVID. How did you succeed?*

***Ira Cheifetz*** *16:11*
*Yeah, COVID was clearly a challenge, and as Martha said in her plenary presentation, it was COVID ugly. It went through a couple of years where enrollment was limited, and some places actually stopped. But I think the key of success here was the persistence, the drive, the focus of everyone involved in the study. Largely Martha, who who led us through this whole process, but really everyone involved stayed focused on the scientific mission, realized that there would be hurdles. Of course, at the time we didn't know how long that would be, and how long of you know challenge, how long of a challenge period would be. But with persistence, when we came out of that, we did see enrollment not only continue but quickly escalate.*

***Martha Curley*** *17:00*

*And it was this kind of you know the social distancing that happened. So it wasn't even like you know the research personnel not being able to get in there and screen and enroll. I mean, all the resources were being pushed to COVID. In fact, Ira, we wrote a paper on COVID specifically. We did an ancillary to PROSpect to look at COVID because that got the research people to stay on site and they got them screening. So we found a way around COVID. I want to also mention we had an interprofessional team. Natalie Napolitano, who was a respiratory therapist, she was a project manager, you know, for PROSpect. And we had issues with the oscillator because we had to figure out a way to scavenge gasses off the oscillator because if there wasn't any scavenging, then everything was going into the environment, and it was you know putting personnel at risk. So Natalie came up with a scavenging system that we implemented until you know the company could develop a closed circuit. So not only were we dealing with personnel issues, we were dealing with equipment issues. We were dealing with you know not being able to launch or you know maintain, and then the recovery part was really difficult because of social distancing. The whole, I was like, I know what is this? If you want to eliminate something, study something, and that's how I felt.*

***Ira Cheifetz*** *18:30*
*Well, especially coming out of COVID, with you know all the social distancing and the drop in RSV, influenza, that that upslope that I talked about, there was a lag after COVID until life got back to at least some sense of normalcy.*

***Traci Wolbrink*** *18:43*
*You know, we've heard a lot about the results. We've heard about these limitations, and I'm curious, you know, some really cool lessons that you've learned that you might apply to additional trials. Like, what was the, you know, key success in terms of the methodology, or things that you think went really well that you could adapt to next, you know, the next questions that we want to answer as part of community.*

***Ira Cheifetz*** *19:03*
*I mean, two things immediately come to mind. The first is designing a study with the input of true frontline clinicians. A primary endpoint of ventilator-free days being two or more came from the clinical world, asking clinicians, reviewing the protocol with clinicians, and not you know, yes, researchers are important, but frontline clinical people in the trenches. Who are going to be doing this study, and we did see, you know, if we look at our enrollment, the highest enrolling sites were those who really were clinically based units focused on the clinical care of patients, and then the other lesson learned and alluded to it a little bit earlier was international, international in terms of perspectives, breadth of patient population, but also real world enrollment of the hemispheres, the differences in viral seasons, also not only north and south, but also east and west. There were periods of time that it was Southeast Asia that was leading enrollment when they were in a viral season that was out of sync with North and South America and Australia, so both in terms of real world input, involvement, patient population, but then straightforward enrollment differences.*

***Martha Curley*** *20:19*
*It's interesting too. It's almost like an Energizer Bunny. How do you keep everybody engaged over the long haul, especially if they're not seeing the patients, they're screening every day, and it's like where's the patients or whatever. But then I think halfway through the trial, we we always figured out when to have conference calls, and we'd have morning calls, late in the evening conference calls, and you know*

*middle of day conference calls, and we would rotate who's leading these calls. But then we went into a team structure, and it was by geography, okay, and it was really longitudinal geography, you know. So straight down the world, you know, time zones, you know, who could come together, and the team leaders were the site investigators themselves. I mean, we would attend and kind of like these are the issues, and can we talk about these issues? But they led the meetings. It was incentivized. So, at every 25 patients enrolled, you know, the team that was a high enrolling team would get a prize. I mean, it was really working off, you know, people engaging, and it was really wonderful to watch, you know, people who had only who never met each other coming together and trying to figure out, well, gee, your consent rates are here and mine are here. Can you tell me, like, how do you do that? And so the cross-unit learning that was happening, and it was all driven by the site investigators who were absolutely, you know, phenomenal. You know, yeah.*

***Ira Cheifetz*** *21:56*
*The camaraderie amongst the various sites was really amazing. Being willing to share lessons learned, discuss hurdles within regions and across regions of the world, you also learn who are the night people and who are the morning people as you have to work through what 50 different time zones or whatever it was.*

***Traci Wolbrink*** *22:17*
*That's amazing, and you know, just think thinking about enrolling this many sites from across the world. How did you even begin? You know, with all the different, you know, IRB [Institutional Review Board] issues and you know enrolling any major lessons there? Things that you've learned?*

***Martha Curley*** *22:33*
*Well, you need definitely you know the team that we had at Penn with Amy Cassidy, who was the project manager for the great you know great deal of the study, worked hard to work locally with you know the local IRBs because we were a central IRB in the United States because that's what that's what we have to do. So Penn was the center you know the central IRB, but then every single other IRB was national. So we were dealing with England and we were dealing with Australia, and there were leads in those countries, but then those individuals had to shed their skin locally. So we had all of that, and it was really interesting as well, the consent issues. United States, there's you know no way we didn't even try to do a delayed consent because it was considered to be a high risk study, but Simon Erickson in Australia, you know, he moved the deferred consent into Australia. Same thing happened up in up in Canada. Reinout tried to do it in the UK, but they said absolutely not, and then definitely not in any of the Asian or the South American, you know, countries. So we had to deal with differences of consent depending upon local, you know, traditions. And then people we dealt with a lot of novice teams who had never worked on an international trial before. So the contracting, the data use agreements, the material transfer agreements, because we also have a bio repository associated with this study that we built to provide samples for the future for PARDS. So we had to deal with all of that as well, and every single country had their own thing. But I have to say. You know the Australians and the you know our investigators from Bangkok found a way to bring the bloods in, and then we had to be careful because it became so cost prohibitive to transfer the samples. So anything that had to clear through customs was enormously expensive. So then we had to figure out how much money we had and whether or not we could really do it. But you know, if you know one PICU, you know one PICU, and it's all different. You know, so you just have to meet people where they are and help them be successful. And I honestly, we enrolled a site in South America late in the game, and we knew we were*

*getting to the end. Okay, it was like, and we said you might not want to participate. Oh, we really want to participate, and it was wonderful. We had a conference call. There were like 20 people in the room. They were really engaged, and so you know we just found these pockets of excellence. You know, of sites who really wanted to learn how to do this, and you know, and it was fun working with them.*

***Ira Cheifetz*** *25:33*
*Absolutely, and to build on that, the other part is the differences in different regions of the world of just research structures. Of some areas have plentiful research assistants. Some most of the consulting enrolling are done by the attending physician. In the U.S. there's a lot of trainees. Other parts of the world, they're they're less trainees. It's more again attending based, and respiratory therapy and physiotherapy support varies greatly. So very different systems in various regions of the world. But what's really wonderful about this is, regardless of the systems, enrollment was worldwide, and centers were very successful, and they found local ways, individual ways to use their team, their local expertise and resources to enroll and and complete the study.*

***Karen Choong*** *26:19*
*I think this is a success story for PROSpect that can cannot be understated. You brought together an international community because they believed in the importance of the research question in the first place. You brought together clinicians that were not researchers and wanted to be involved because they wanted to learn, and you made that happen through your leadership and enabling them to lead amongst their own regions themselves, doing things that they were not used to doing, but how could they afford it? How did you afford it? How how did people conducting research is expensive? How did each of these sites, how did the international sites get onboarded? Was it something that they volunteered to do?*

***Martha Curley*** *27:05*
*I mean, that's the some of it is the ugly part of research, you know. We've had we did have sites who did a cost benefit analysis, and because they could not make a profit, they would not participate, which was kind of like, okay, that's wild. But you know, but that's what it is. I mean, you never when you participate in research, it's not because you're going to make money. Maybe it would if you were doing a drug study or something like that. But for clinical research, you know, the screening, 24 screening, the date, you know, sitting with parents who it might take hours, you know, to talk to a parent about whether or not they want to enroll, you know, their child who's suddenly critically ill into a study. It's it takes a lot of time just to do that, and then a lot of time for the research associates to come in and you know make things happen. Getting the patient on protocol, it was definitely like interprofessional. The nurses had to be on board. The respiratory therapists, you know, the local physician staff. So all of those people had to do this. And you, you know, we compensated people on a per patient enrolled status. So if you didn't enroll, you didn't get compensated. So all that work, you weren't, it was uncompensated work, and some, you know, some systems just could not tolerate that. But I do believe, you know, what they learned. They learned how to do research. They learned how to screen effectively in their unit. They learned how to consent. They learned how to read a protocol, get somebody on a protocol. You know, the case report forms and the DCC [Data Coordinating Center] was phenomenal, you know, centered up in Boston. All the data cleaning just because your data are in doesn't mean that it's done. I mean, it's all the queries going back and forth that have to, you know, have to be answered. But I have to say, there's the site engagement. There were sites who were so enthusiastic that they would the nurses would just stay over on their own time, you know, uncompensated time because they wanted to get the*

*patient into the study, and they had talked to the family about the study and they wanted to get the patient in the correct position or on the you know, correct ventilator mode, and they were just so engaged. So it's almost like a you know, it's an exciting. That's the exciting piece of it. And then even the randomization part, like, how's this kid gonna randomize? You know, and if you're looking at a very large patient in front of you and it's prone, it's like, okay, I guess we have to do that. So it was really the local, you know, the local engagement. People, when they were engaged, would find any way they could to get a patient into the trial. They would find a way. So it's really this salient thing that seldom gets described. But you know, you're either on board or you're not.*

***Ira Cheifetz*** *30:07*
*And the centers that were on board, you can just see the the fulfillment, the sense of just personal and team satisfaction to be able to enroll the patients and try to answer these scientific questions. Going back to one of your questions earlier, Karen, about surprises. One of the things that did surprise me is you know continuing with this you know international discussion is how international we became. When we started, we had concepts of having some European sites, Australia, New Zealand sites, and some limited sites in Asia. And we were approached, Martha said, by centers in South America and throughout the Middle East, wanting to be part of the study. And they were approaching us, and some of those sites became very successful, very engaged sites, and so I think one of the surprises is truly how international we became.*

***Karen Choong*** *30:55*
*And now you'll be primed for your next adaptive trial with the eager, interested international sites moving forward, that now you've taught how to do research.*

***Traci Wolbrink*** *31:05*
*Can I can I build on that? I'm curious what the educational structure was for training many of these novice researchers who haven't done studies like this before. What went into training and sort of getting them up to speed for you know to follow the protocols to enroll their patients?*

***Martha Curley*** *31:25*
*Well, the you know we handled that in the clinical coordinating center. The whole thing ran on a website. The website is still open, so you can see it's kind of locked down. But the educational section of the website was huge. So we had big PowerPoint presentations. We had little ones. We had just-in-time training. We had, you know, specific training for therapists, for nurses, for physicians, for the ventilation strategies. So, and then we had a whole bunch of materials that could be used at the bedside. So, some people, when they participated, we'd say, "Okay, get go into the website, look to see what's there, and then we will help you design a process that you could use locally, because everyone trains differently within their unit successfully. So we gave them enough, you know, materials from which they could then put their own logos on it. They could, you know, make it their own, and then we did require that there was training. So there was a pretest, posttest. People had to do training. You know, some people take it more serious than you know than others. And one of our protocol deviations was if the clinician at the bedside was untrained, and we monitored the extent to which you know that happened, and so we considered that a protocol deviation because we didn't want people touching these patients who didn't know anything about you know the protocols. In addition to that, we implemented walk rounds, and so every single day, if a patient was on trial, the investigator had to connect, you know, with the team, answer questions, and then, you know, help them better understand*

*or interpret the protocol. And we had, you know, I mean, thousands of days of people doing rounds, but then it also identified deficiencies if there was any problems or misinterpretations of the protocol early, rather than you know three days later. So*

***Ira Cheifetz*** *33:33*
*The other thing we did to build on all that training was that every center for their first three enrolled cases, we would have a debrief, and that debrief included Martha, Martin, or myself, plus a member of the clinical coordinating site as well as the data coordinating site, and we discussed each of their first three cases in detail in a interactive, scripted, but also informal discussion. That we made sure that we reviewed all the salient points, but also had time for open discussion of questions, concerns, hurdles, and what we found, having done a lot of these debriefs, is the first one was quite lengthy, a lot of questions. The second a little less so. The third one was very brief, and then they were off and going. And the learning curve for the protocol was about just that three patients. And I think that time and effort and investment made a world of difference as we continued our enrollment.*

***Martha Curley*** *34:26*
*Yeah, and we cover the trial 24/7.*

***Ira Cheifetz*** *34:28*
*Yeah.*

***Martha Curley*** *34:28*
*So if anybody was stuck at a bedside and like it's not working, what's happening? You know, you know Natalie and Traci, and at one point, you know Laurie Lee would take calls 24/7. You know, so and if they couldn't answer the question, then we got we were*

***Ira Cheifetz*** *34:47*
*Texts and WhatsApps at all hours, but the investigators were very respectful. I mean, if it was a question that needed to be answered at that moment, one of us got a message. Others were obviously emails and discussions later. But it was that availability and that ongoing interaction and discussion, real time made a big difference for the patients.*

***Martha Curley*** *35:08*
*Our mantra was Enroll, enroll, enroll.*

***Ira Cheifetz*** *35:11*
*If in doubt, text or call.*

***Traci Wolbrink*** *35:15*
*Well, this is you know. Thank you for sharing all of these details because I think when you think about a clinical trial, you realize they're are a lot of work. But hearing all of the elements that you all did to prepare the sites, to get everybody together, to have these calls, to check in after all of their their data enrollments is absolutely incredible, and just I think gives people a really good sense of what it means to run a trial like this. So I appreciate all of the those insights.*

***Ira Cheifetz*** *35:42*

*The learning curve. I've done this for a long time. The learning curve was very steep. A lot of time, a lot of effort, a lot of hours. But I would do it all over again, not only for you know personal learning, but also the learning and the teaching of so many clinicians and researchers involved in PROSpect. Most importantly, the patients who were cared for in a very structured, protocolized manner, but now results that will make a difference to patients around the world.*

***Karen Choong*** *36:12*
*I think PROSpect has given us a lot. You've given us important information from the trial, which will change practice and answer a lot of questions for clinicians that we've had for decades. You've taught us a lot about research methodology. You've taught us a lot about community and reaching out within our community of pediatric critical care clinicians across the world, and how to engage in research and do it in a team manner, and the end learner at the same time. What's your takeaway message after the PROSpect trial, be it the clinical results, be it the the trial execution, be it our community. Now that we're at the World Congress, what's your takeaway message or messages for us?*

***Ira Cheifetz*** *37:00*
*Great question. I think my takeaway message and kind of the one point that that I'll always focus on is PROSpect started with a discussion at an international conference between Martha, Martin, and myself about prone positioning oscillation. Do we have answers? Do we know what do we need to know? And it was literally a clinical discussion amongst three colleagues, and with that discussion and the persistence, you can answer these questions by forming the right team, and that team goes really deep amongst the primary investigators, but also all the support people who are involved through the CCC [Clinical Coordinating Center] and DCC, and be persistent. Answer your question. Be very systematic and rigorous in your methodology, in your protocol. Stay focused on the path you've chosen. Keep your eye always on the end result, whatever that result is, but the end process, and be persistent. And you can take a clinical question from a simple discussion amongst colleagues, and lead to an international study that again will affect patient outcomes worldwide.*

***Martha Curley*** *38:14*
*I mean, I think you know, for me, it's about patients and families. You know, our patients deserve evidence, and we can't just rely on well, we think so, and maybe, and whatever, and we always straddle the big neonatal and the adult world. We can't just take you know what they find in their patient populations and to apply it to us. And it's also the passion. I mean, when we started to talk about this, we needed to get grant funding. It was a huge grant that went in twice before it was funded, but we had a lot of really good people at the table putting together, you know, the protocols. You know, Brian Kavanaugh. You know, God bless Brian Kavanaugh. He, you know, read the protocol, every single line of the protocol, gave feedback when we needed help. Brian was there, you know. Michael Matthey was there, so we learned from other people, you know. And it really was a community build of the protocol. We mock reviewed it at a PALISI meeting, sent it out for review. Thank goodness it was funded. But for me, it was you know. Our patients deserve evidence, and our families need to be able to help us figure out how best to, you know, provide the care that we do. And it does take a community, you know. It was an international community, and it was a wonderful process because, you know, as Ira mentioned earlier, you know the big, huge mega center ICUs that you say, oh, of course they're going to be participating. You know the payload were the people who just cared about research and cared about their the patients and families and wanted to participate in a process in which they contribute any way they could to the larger scientific, you know, network that we have, and so, you know, we can always*

*argue with people about data, and you know, especially when a patient's in front of you, should we do this or that? And it's like based on what, you know. And now we have answers, and so you do it for the answer, you know. You do it to provide better care, to me it's a sense of community as well. Made tons of friends through the process, and you know I'm happy that we've now got the answer to these questions. And now I'm going to Bali, so I'm happy. I'm going on vacation, but and excited. Another thing too is that the all the work and all of what people contributed it landed well. You know, it will be published in the Lancet. You know that made me happy because when people spend so much time and effort collectively to do this work. You want it to land well as a clinical trialist, I really wanted it to land well, and it did. And you know, so that speaks to again, you don't get yourself published in Lancet, you know, for something that is not scientifically rigorous, you know, that has high credibility, so I'm very proud of that.*

***Traci Wolbrink*** *41:30*
*And you know, Martha, Ira, you both have incredible careers and have been very successful in so many research projects and endeavors. I'm curious if you are thinking about a junior trainee, fellow, nurse, respiratory therapist, physio that is interested in research. Do you have a piece of advice for them as they think about getting started on their career?*

***Martha Curley*** *41:53*
*I say go for it because especially now it's it's difficult for the junior investigators to think about growing a program of research. You know, is there going to be funding to do this type of research? And should your first study be an RCT [Randomized Controlled Trial]? Because they're difficult to conduct. But unless you know participate in larger trials, you learn the method, then you can design trials because you've learned the method. And unless we do them, we'll never have anybody. We won't have futures. And yeah, I mean, we look at methodologies on pragmatic trials, you know, platform trials. It's still in the pursuit of questions, you know, and we're still going to need multiple methods to answer our research questions because not all our questions lend themselves to one method, you know, and it may be that you answer the question, but now it's implementation science. And in our PROSpect, it's de-implementation science. How are we going to get people to de-implement this as a routine therapy? So.*

***Ira Cheifetz*** *43:02*
*My take-home message is to to the trainee would be come up with a you know an idea that you're passionate about, something that's scientifically sound, something that's scientifically important, and be persistent. But as you do that, surround yourself with the right group of mentors, colleagues. And we've I think both Martha and I have really stressed this already. It's a team; takes a village. You can't do any of this in isolation, or even as a you know two or three something. This is a global team, but as you're getting started, find the right people, ask the right questions, stay focused, stay dedicated, and you can do it. But the key is the team.*

***Martha Curley*** *43:41*
*Yeah, and this really also for junior investigators, it's relationship building, because you need to find, I mean, David Wypij, Lisa Asaro. I mean, we grew up together. You know, we did multiple clinical trials together, and we learned together. And if it wasn't for the DCCs, you know, also doing their part in data, and also have to please remember Barry and Associates. We had Barry. We hired people with the expertise who helped us, you know, in pediatrics create an adaptive trial, you know. And so if it weren't for Barry, if it weren't for the NIH, if it weren't for the DCC, the CCC, I mean, none of this would have*

*happened. So you have to know and build a team. Like, and you don't have to know everything. You just have to put a team together with people with complementary expertise and be respectful of that expertise.*

***Karen Choong*** *44:43*
*Thank you, Ira, Martha, for coming in to talk to us today and tell us about PROSpect. Thank you for the trial that's so well done that will inform us to do better for our patients and families. Thank you for speaking to us today.*

***Ira Cheifetz*** *44:57*
*Thank you for having us. It's been pleasure.*

***Sarah Marcley*** *45:00*
*This has been a production of OPENPediatrics. You can find the resources and journal articles referenced in this podcast in the description. We have more podcasts like this one available everywhere you get your podcasts. Visit openpediatrics.org for more information.*

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