Season 2 Episode 2 – CONVINCE

Guest: Peter Blankestijn, MD, Krister Cromm, MD & Sandip Mitra, MD

Peter Kotanko
Welcome to the Renal Research Institutes Frontiers in Kidney Medicine and Biology, where we share knowledge and advances in kidney research with the world. This episode discusses the CONVINCE study, a prospective randomized multicenter clinical trial designed to study high-volume hemodiafiltration versus High-flux hemodialysis treatment. The study assessed morbidity, all-cause mortality, and patient-reported outcomes. My guests for this episode are Professor Dr. Peter Blankestijn from the Department of Nephrology at the University Medical Center, Utrecht, Krister Cromm, expert director, patient experience clinical research at Fresenius Medical Care, and Dr. Sandip Mitra, Consultant Nephrologist and Honorary Lecturer, University of Manchester. They are here to discuss with me—this landmark study. Welcome, and thank you for joining us today.

Sandip Mitra
Thank you.

Peter Blankestijn
Thank you.

Peter Kotanko
Like many others, I was deeply impressed by the results of the CONVINCE trial. And I mean, everyone who reads this paper may read it from a slightly different angle. The first question I would have been, can you summarize in a few sentences?

What do each of you think is the most important outcome of this study? Maybe Peter, if you want to start.

Peter Blankestijn
This study, for the first time, shows that when high-volume hemodiafiltration is consistently delivered to patients, it reduces the risk of mortality. So, there was an improvement in the quality of treatment of end-stage kidney disease patients, and indeed, we as a group were very excited when we heard about these results.

Krister Cromm
I find that this is a fantastic outcome. What I see so striking about CONVINCE is that it already started with an excellent first step: developing patient-reported outcomes within the CONVINCE

trial. So, even though we did not truly co-develop the questions with the patients, we did have authentic, meaningful interactions with patients through qualitative interviews.

Krister Cromm
We found out about topics worth investigating for patients that we've spent from fatigue, recovery after dialysis, different symptoms during dialysis treatments, and between that were not part of the conversations between doctors and patients. And that is how we got the conversations and the interest going from the patient's bottom up.

And I think that is the truly amazing part about CONVINCE that we were able actually to convince patients to participate and say, look, we want to share our experience here, and that will allow later generations also to truly change the way a patient so everybody in kidney care deal with the problems and develop new maybe treatment paradigms, different ideas of how to approach dialysis care.

And, of course, hemodiafiltration is a great example because we all believed in it, and we all knew that if we were able to deliver, you know, consistently high convective volumes, we would be able to show differences from the patient's perspective. And this is something that we will later present, you know, after the mortality differences that have sparked this huge amount of interest in the study.

Sandip Mitra
I have practiced nephrology for many years and have a program that can offer a tube to patients; CONVINCE is a landmark trial in incenter thrice weekly hemodialysis. There are several reasons for this. There is a survival benefit in patients with high-dose hemodiafiltration as defined by the CONVINCE study itself. Most importantly, it is consistently delivered compared to the standard of care.

High flux hemodialysis. So, it is still delivered as a 23% reduction in all-cause mortality, particularly benefiting patients with AV fistula, high flow rates, and a relatively low comorbid burden. The second important outcome for me as a practicing nephrologist in dialysis is a huge lesson in that a high dose can be achieved consistently over a period when the dialysis conditions and the patient characteristics are favorable, and this dose appears to make a difference.

And it matters for our patients. You know, there are other factors in outcome measures that I haven't seen quite published yet from the CONVINCE program. I'm presuming it's coming, such as patients, quality of life matters, the patient-improved outcomes, etc. So, does it make

patients feel better? It is an important question, and it matters for our patients. But that, I presume, is part of ongoing sort of studies.

And so I'm going, and before I finish, I guess one other outcome that matters to me is that it has delivered one of the best hemodialysis trials, which I believe is the reason why you have secured such a high-impact publication, a remarkable achievement by the investigating team under very difficult circumstances, a very good balance between the two arms of randomization, very high retention rates in dialysis, the improvement and of course delivered during the COVID pandemic.

So, the trial is unique in many ways. Those are important lessons for us as clinicians and researchers practicing and trying to answer various questions in dialysis. And how to deliver good care.

Peter Kotanko
Peter, Krister, and Sandip thank you so much for what is the most important aspect to you. Now, there is something that one cannot read in the paper, and this is the history of this study. How did CONVINCE come to fruition? I mean, was this a meeting? Can you say maybe we spend a minute or two on the history of comments?

Because I think this is certainly very interesting. How did the two of you learn from each other? How was the consortium formed? I mean, I mean, no one would wake up in the morning and say, oh, let's do a study on the high volume HGF, so if you can shine some light on that.

Peter Blankestijn
The concept of hemodiafiltration, of course, has already existed for decades. And it's only about 15 years ago, or maybe a little more, that the regulatory authorities accepted this online production of fluids. And that created the possibility to address whether it matters and the concept of hemodiafiltration versus standard hemodialysis.

Indeed, four trials tried to address that question, all done in Europe, but none of the trials were allowed to conclude. We did an individual participant meta-analysis of all the data from these four trials. When doing that, there was a clear suggestion of a benefit for hemodiafiltration compared to standard hemodialysis, especially when the high volume was administered, and these 23 liters are not a result of long scientific discussions.

It was simply the lower end of the highest tertial in this meta. So that's the end of the story concerning this number of 23 liters. So basically, when we did this meta-analysis six or seven years ago, and the result was there, there's a clear suggestion, but there are some methodological issues. So, the world was divided into believers and nonbelievers.

And then suddenly, the European Commission came up with this call, which they named comparing the efficacy of existing therapies or something like that. And then I thought, well, this is the golden opportunity to submit the idea of doing a trial and, again, comparing the two therapies that now have hemodiafiltration with consistently delivered high dosages. This

consortium exists because we tried earlier in the European grant system to obtain money for a trial.

So basically, the group already more or less existed. And yeah, we submitted this idea, awarded with grant money from Brussels.

Krister Cromm
I had quite a different route into CONVINCE, I have to say. So, it started far away for me, not even in Europe. I was in Hong Kong at that time, and I was researching the resilience resources of dialysis patients. So, I looked at hope and optimism and self-efficacy, things that, you know, influenced the quality of life of dialysis patients.

And my research interest was how, you know, these aspects interact with different parts of quality of life. Right. Does it interact with physical functioning? Are there more mental aspects involved? What about fatigue, depression, anxiety? That all are very important for dialysis patients, you know, achieving a holistic good outcome, you know, from the perspective of the user of dialysis therapy.

At that time, I met Professor Bernard Canaud in Asia Pacific, and we talked about the quality of life in dialysis and then stayed in touch. And I knew there had been an original grant application in 2014 that had been unsuccessful. Also, the European Commission wasn't quite sure how this would benefit the individual citizens directly to ensure a better playing field and better outcomes in health care across the member states for the patients.

And that's how the conversation started again on patient-reported outcomes. And when we applied again, I had the opportunity to meet Peter, and we discussed how this could be measured, right? How could this be turned into a turning point for the trial or beyond that, maybe even for nephrology? So we had high hopes.

And that's why I said we should use electronic patient-reported outcomes. We should change the granularity. We shouldn't just, you know, ask patients thousands of questions and pieces of paper that, you know, nothing will be changed from the patient's perspective because they won’t see how all these questions relate to an outcome. That's how we started the conversation, and that's how we also brought Mathias Rosa, Professor Rosa from Seriti, into one consortium. We had long discussions about what the right methodology would be.

You know, what we still needed to develop and what questions we needed to ask. We also decided to use a system that could later be used for computer adaptive testing so that patients

only asked questions that were relevant to them personally. And that would reduce the number of questions to be asked because, you know, the questions wouldn't repeat.

And that's how we all started with selecting patient-reported outcome measurement and information system for this study and adapted. We started embarking on this journey together, and apparently, we convinced the European Commission that this was the right way forward and excited everybody. And here we are.

Peter Kotanko
What I like about this history is that it's the collaboration between very different disciplines to identify the intersection and integrate something more than the sum of the two parts. While you were talking, Krister, I was just wondering about this whole concept of PROMs in HD F RCT. Did everyone embrace this from time zero, or were discussions? I think this is because this is such a novel aspect, and not all nephrologists may have known that methodology.

And so, I'm just curious here.

Krister Cromm
I can recall that we had a heated discussion, and that was great because we engaged in true scientific debate, you know, across the borders of different disciplines and, you know, looking at the advantages and disadvantages. There were many voices that maybe we can't even deliver on, right? It might fail if people do not fill in the surveys online.

There could be all sorts of things that could go wrong. But yes, I mean, it was worth taking a risk. And I think it wasn't only cross-sectional but across disciplines that we really had, I think, different age groups involved in the trial with people with very different experiences, different countries, different mentalities that made this worthwhile.

Also, I think we all got closer to each other, understood each other's perspectives and experiences, and respected that we could contribute something.

Peter Kotanko
Peter, what was your thought when you heard for the first time about this?

Peter Blankestijn
We designed the study all the years ago, six years or maybe even close to seven years ago. At that time, patients reported outcomes were very new. You had the SONG initiative, maybe as well, but it only started early, shortly before. And so, the whole thinking about patient-reported outcomes and quality of life taken into consideration was very new at the time.

Peter Blankestijn
The moment we decided to go for this grant application, we had a discussion; it must be a good old-fashioned trial with good old-fashioned clinical endpoints, all-cause mortality at the time. We indeed discussed it well; let's make it innovative somehow, and then the reported outcome was a logical choice. And at that time, I did not know anything about patient-reported outcomes.

From the beginning, I felt this could be the diamond on our cake because it was a real innovation and innovative development on a large scale. And that was the nice thing about this European grant system. We could apply this on a large scale and do all these developments Krister mentioned because money, time, and people were willing to do that.

So, in due time, it became even more interesting to me as a physician, and I was even more convinced that this is nice what we are doing and important for the field.

Peter Kotanko
I think that especially the inclusion of PROMs will have a long-lasting impact. This trial may be one of those model trials that will be replicated in the kidney field repeatedly, at least in terms of design and inclusion of PROMs. I mean, this is just my humble opinion. But I think that also, in this respect, this trial sets itself apart from many other trials, from all other trials that have been extensive RCT studies conducted in the kidney field.

Krister Cromm
What I can say is that I am very grateful to Peter for taking that leap of faith towards something not so well known because the easier route would have been to lay the focus more on the health and economic part and to look for an established patient-reported outcome questionnaire rather than saying, okay, we turn this upside down. We start with what exactly is important.

What types of patient-reported outcomes are important and that he forged this understanding within the consortium that we should not see it as a risk but as a true opportunity to turn things around. I think that is making a difference. And I can only agree with Peter that this will serve as a role model, in a way, for future studies.

Peter Kotanko
Peter and Krister, you're so intimately knowledgeable of the trial. What do you think of the main limitations of the trial? I mean, everyone can read the discussion section. I think you spelled out

some of the limitations, but are there others that you would think are relevant for our audience to be aware of?

Peter Blankestijn
An often-heard comment is the whole discussion about generalizability. Thus, whether these results apply to every patient is a logical question. The answer is probably no, or it is difficult to say a strong yes because in such a clinical trial and the way we designed it and the way we defined inclusion criteria, it was inevitable that there was some selection.

The main issue in the list of inclusion criteria that resulted in some selection is the likelihood of achieving the 23 liters, a clinical judgment by the dialysis staff. Secondly, the willingness and the ability to fill out or to participate in patient-reported outcome assessments. This inevitably resulted in somewhat better or less diseased patients within the end-stage kidney disease population, and some people find that a limitation.

I very much disagree. I think this is not a limitation, but this is a strong point of the study because, by this selection, we could find a group within the end-stage kidney disease patients that experience the benefits of this treatment. So, does this apply to all patients? The answer is no. The study indicates that the specific type of patient is those without clinically apparent cardiovascular disease or diabetes and those with an AV fistula, which was 80% of the population.

So, that is not such a CONVICE finding. I think so, but it all had relatively good patient. But by finding that, it's great to know that relatively good patients benefit from this treatment. And that is nice.

Peter Kotanko
Thank you. Peter, Krister, what do you think?

Krister Cromm
I think that the picture is complex. And the reason why I say this is because I visited most of the centers. As I've spoken with many of the patients, I know that at least within the Fresenius clinics, hemodiafiltration was quite common in many centers. So it wasn't the case that we, you know, would only recruit those patients with the best chances of success in the trial.

And at the same time, we, of course, see that patients have done remarkably well. And the story could be related to a lot of aspects. Right? It could be related to the care. We also know that patients who are regularly asked for their well-being usually do a lot better because there is more of a loop between the care team, the doctors, the nurses, and the patients themselves to find, you know, the best possible outcomes for the patients.

And I wouldn't be surprised if this has also happened within CONVINCE that we have had relatively, you know, the average population of patients, groups of people. And they were treated very well. And, you know, people have found solutions for those patients. So that gives a lot of hope from convince. And I think the only regret I have is that we could not bring in more patients and more countries into this trial.

And we tried very, very hard. Peter, we both recall writing letters to the ministries in different countries, especially Poland, asking them to participate. And it was quite difficult because we weren't sure if patients were, you know, being reimbursed for their treatment if they participated in this trial. And I can only hope that within that rather complex framework of the European Union, we can convince people to participate in those trials because this trial has shown that patients benefit.

So, I hope that you know, in future trials like this, I mean, this could serve as an inspiration for, you know, regulators to allow this trial to take place. And we now have, you know, surveys for patients in eight different European languages. And I would certainly hope we could add many more languages inside Europe and outside to use this trial to help this interaction between petitioners and kidney patients.

Peter Kotanko
So these are certainly very, very important points. Now, Sandip, you have been a coauthor of a paper that appeared, I think, 11 days after the publication of the original trial in Nephrology Dialysis Transplantation, and it had the title hemodiafiltration for all. Are we convinced? I'm very interested. Sandip, what would be your primary concerns about CONVINCE?

Sandip Mitra
Thank you, Peter. I think Peter Blankenstijn and Krister have already been alluding to some of the scientific questions that have been delved into and that happen within any RCT. Many questions arise, sometimes more than answers that these trials have delivered. So, what would you like to see a trial delivered in such a practical way?

Is it delivering the outcome measure? The main concern, as Peter and Krister were saying, is that the patients that have benefited from the therapy had a relatively low comorbid burden, which is diabetes and cardiovascular disease, and obviously, over more older patients than the younger ones. Those very early on in dialysis, within two years. And other than that, it means that it benefits less.

A lot of patients are excluded from dialysis. I'm pleased to hear the description that Krister has given in terms of how the selection process went. That's not quite detailed in the paper and was generally a discussion point in such meetings as to how the recruitment happened. Was there any unconscious bias in delivering these to secure patients? So, it's reassuring to hear that it was efforts made by the units to achieve those converted volumes.

However, looking at the patient population that benefited, it excludes many patients in dialysis. But that is quite intriguing because, hypothetically, the cardiovascular benefit has been the hypothesis driving many hemodiafiltration trials in the past and more recently. We've always felt that people with high disease burden and cardiovascular disease are likely to have benefited particularly from this therapy.

And so it sort of challenges the biological plausibility that in the nephrology community that we've been posing, and of course, the cardiovascular deaths weren't as different as the infection cause of deaths. Again, this challenges our assumption that the mechanistically understood how these therapies work. Perhaps we must rethink how inflammation, infection, and cardiovascular outcomes are interlinked.

But certainly, the study seemed to challenge some of these hypotheses and made us, you know, question or pose questions around these outcome measures. One of the things Krister again points to is the care that was delivered to these patients. So, there's a natural bias in providing high-volume HDF; you must pay greater attention to dialysis prescriptions.

And that itself, combined with very high fistular rates, creates a scenario that is not quite the norm in dialysis units. Can I create an 82% fistula rate in my dialysis centers? It is not the norm, essentially. That was a major issue regarding how we can deliver benefits more inclusively to all our patients with a technique that will offer benefits; of course, the issue around case mix or the ethnicities are largely a Caucasian population, of course, recruited into this patient into the study. My dialysis center population is a different mix of patients. So how do we study these therapies or dialysis techniques to be more inclusive, to study the patients, thus, perhaps for future trials, that would be great attention to inclusivity? We have already heard about how languages, translation, etc., can be incorporated in this trial.

So, there are those two issues to consider from this trial. And then, of course, the other factor that has perhaps again raised a question is that it wasn't quite the high blood flow rate. Still, it was particularly the use of a fistula, as both are very well matched in high blood flow rates, but the prevalence of fistular rates was high.

That could mean two things. One is that it is impossible to give such a benefit with catheters or graphs. Still, the catheter patient has a disadvantage by being much lower in number and therefore not achieving this. The critical sort of quantum is required to show the benefits. Or is it that even in these patients with the required care, one can achieve better outcomes?

So, there is perhaps some disparity here in access and how we offer access to these patients a lot around the hemodiafiltration technique and the care. I would love to see some practice pattern data in the paper or a subsequent paper. We can learn a lot about the practice patterns in these units to see how the study was delivered.

Peter Kotanko
Thank you, Sandip, for these important comments. I mean, scientists are very much like the fact that trials challenge pervasive hypotheses. And I was particularly interested to see that HDF, for whatever reasons we can speculate here and in agreement with previous data, may have a substantial beneficial impact on infectious outcomes and on inflammation.

And I mean, we don't know the answer to that. That's just an observation. But it's an important hypothesis to explore further, and any thoughts around that.

Peter Blankestijn
I think our priory hypothesis was indeed, as Sandip correctly mentioned, a beneficial effect, probably mainly on the cardiovascular mortality part. However, I believe it is essential to realize that the hazard ratios are all in the same direction, in the direction of the benefit of hemodiafiltration, and it happened to be significant for infection and not for cardiovascular disease.

And in our earlier meta-analysis, it was just the other way around. So, I think the overall conclusion could be that cardiovascular and infection could have a beneficial effect in both fields. Indeed, one other limitation you might have of this study is that we cannot say anything about the mechanism. I think that is indeed the case, most likely, at least in this my interpretation, that there is not one mechanism, but there are multiple mechanisms that could be of significance.

And which mechanism is more important than another mechanism? I do not know. But that could also be a strong point of hemodiafiltration being a general and generic nonselective type of intervention, which is different from, let's say, a pharmacological intervention. We would probably agree that many of the pharmacological trials in end-stage kidney disease patients failed to show benefit because maybe they only target one mechanism, and that is perhaps the good thing about hemodiafiltration, that it potentially affects multiple mechanisms.

Peter Blankestijn
So overall, I think that in terms of mechanism, which, of course, is from a scientific point of view, it is a fascinating discussion, but it will remain a discussion with much speculation. At least, that's my opinion.

Sandip Mitra
And I believe that's perhaps the reason for the setting of the trial results. It's impossible to collect biological samples of such disparate biomarkers and unique toxins, etc., but that was the nature of the setting we were undertaking. The trial was being undertaken. But it does seem like the question as an open question remains as to the biology being delivered.

Do you believe Peter, it is due to the urine inspection of the clearance profile of these techniques compared to more conventional dialysis techniques?

Peter Blankestijn
It seems logical to think that the enhanced clearance of uremic toxins or certain groups of uremic toxins could be relevant. That could be at least part of this discussion of mechanism. But to what degree have whether this is 30% of the explanation of the outcome or 50% or whatever percentage? I think that is impossible to say.

Sandip Mitra
The other thing that intrigued me was that given the uremic burden concept and the enhanced clearance of this technique, the patient group that seemed to benefit most were the ones who were very early on in dialysis. Within the first two years of dialysis. I know we didn't have detailed data on residual renal function, but that seemed to be something concrete as to how we would have envisaged a better blood purification treatment, too. Do you have any thoughts on how that could have resulted in that outcome? Do you have any idea of the patient groups that were in the trial in the first couple of years of dialysis?

Peter Blankestijn
Of course, I agree, Sandip, with you. And I think may I quote Miquel Botha, the methodologist of that trial, and he always tells me that as a clinician, you always look with a microscope at all these numbers. But this detailed analysis should be interpreted as explorative. Full stop, explorative.

And that's all. So you try to do, let's say, tune down the enthusiasm or the relevance of such analyses.

Peter Kotanko
Thank you both for this excellent discussion. I'm wondering in your mind, and this is a question for all three of you. I mean, what will the future look like? Will there be a pre-convince era of kidney dialytic Kidney replacement therapy and a post-CONVINCE era? What do you think are the next steps, and maybe Krister, would you mind starting?

Krister Cromm
There is this type of schism with CONVINCE, and it's not quite as visible yet because I believe it showed in a trial that it is possible to use electronic patient-reported outcomes regularly and that they should be included in regular assessments. And I think there will also be many more opportunities for predictions.

So, start discussions with patients. If you are going down a specific road, you will be able to achieve something, or you may be able to do a tradeoff. There will be these discussions, and I don't think this has been the norm in nephrology because there was not the data available for it so that people could speak with confidence about what potential outcomes are possible and refocus that.

So, in that sense, I believe there's much room for future research with a different focus and a lot more partnering with the individuals concerned. And that will lead to a different way of organizing health care. At least, this would be my hope for this trial.

Peter Kotanko
Thank you, Krister. Sandip. What's your view here?

Sandip Mitra
I think it's put a spotlight on the fact that trying to focus on the technique and the practice of dialysis could deliver better outcomes. And there's a set of quite a landmark study in that setting, unlike many negative dialysis trials we have experienced. But as we discussed, dialysis is a one-size-fits-all therapy in daily practice. It is pretty much homogenized in dialysis units. And here is a study that shows benefit in showing benefit in a in a in a in a in a group of patients, particularly. So, to transform practice, we need to add momentum to this through a few unmet needs. One of them is perhaps the power of additive drugs. You know, we've seen some real momentum in nephrology producing three or four RCT SGL inhibitors that are transforming the landscape, and there is quite a galvanizing effect of active trials with similar benefits.

In this regard, hemodiafiltration is in a sweet spot because there is an ongoing trend in the UK called HDRD, similar in design, almost done at the same time with a slightly longer follow-up period. Still, aiming to achieve the high target volume rather than restricting patients to do not

achieve the target volume, therefore wider net cast and more inclusive in terms of patients who are recruited into the trial on the HDF high volume target group, I think that might give us a bit of more answers to the generalizability question.

I'm glad the study has completed recruitment in the follow-up phase, but it will be reported in 2025. So we've got to wait for those data to come through. So, that might be a good addition to the evidence that we must draw conclusions because we need to strive to find consensus and guidelines on practice. The care domains that are required to deliver good outcomes will be important.

The second element is the implementation of the service always lagged behind the evidence in a big way, and dialysis, particularly, there are not just believers and nonbelievers. Some units practice HDF, and other units that do not operate HDF. And for these two different categories of centers, there are two different challenges. The ones who are practicing HDF can deliver high-dosage HDF, and that's because of the greater engagement of clinicians and nurses in the patient groups that we've talked about.

And that is an implementation of all stages from the clinical and the practicing teams. The units that haven't got HDF offerings now have different challenges, perhaps greater ones because the cost of setting up hemodialysis and treatment and water quality assurance is important. There's quite a significant upheaval regarding how they practice dialysis, some units reused, etc. So, the wider practice of HDF limited by units that do not currently offer HDF is given. We need to address some of those challenges.

Cost would be a barrier to it. Regulatory concerns, safety issues, all these things need to be delivered. I think that that will be a major, major challenge. Of course, there are also issues around environmental constraints where water is a scarce resource. Does it provide some of these effects? So, for those units, major questions must be answered and delivered to address those unmet needs.

But I think the other, as I said, I started by saying, is that one big sort of take-home message is that the dialysis community can deliver large trials. And remember, the DOPPS gives us our first indications of the high dose of HDF after HD itself. And maybe we need to, you know, submit these grants and look for funding opportunities to do these large trials collaboratively, be more inclusive so that we can deliver some positive results and try and start improving outcomes.

So, there are these two sorts of challenges here. You need personalized treatments within a dialysis unit and then break the mold of a one-size-fits-all treatment. Based on some of the findings of the studies. And then how do you overcome some of these limitation challenges

beyond the scientific audience, which is more around the payers, the health systems, and the disease burden?

Peter Kotanko
Thank you. I very much agree with the points you just mentioned, Sandip. This one-size-fits-all concept is probably incorrect because it doesn't work like that in many aspects of medicine. A one-size-fits-all. And, of course, dialysis is organized like that. So, of course, I agree with you, but maybe that is incorrect.

Peter Blankestijn
So there is a great need for better prediction of effects, and that's one of the ambitions we have to go deeper into the dataset and try to find out if we can predict in more detail how What subgroup of patients benefit, especially, and maybe also on the other end of the spectrum to what subpopulation, it doesn't matter or it has no additive value as compared to hemodialysis.

You may know that we have done such an analysis in this trial of the meta-analysis dataset of the four earlier trials, and that generated some nice results. It's quite identical, as we have found now. So, the somewhat younger patients, the non-diabetics, and patients without cardiovascular disease benefit, especially in the analysis we did in the four previous trials.

A second issue, I think, is whether there is a pre-CONVINCE era and a post-CONVINCE era. I think the answer is yes. And, of course, I'm not unbiased enough to address such a question. One aspect is also the fact that we succeeded in doing such a trial in this type of consortium, which is also quite special.

I happened to be the chairperson of this group, but it was fun to do, and I think it was great that we could work with these three big dialysis providers who delivered most patients to the trial and came up with these results. So, it is possible to do significant trials in dialysis.

And I think that that is a major, that's a message of major significance concerning. Yeah, who to, what to do tomorrow. So that's an often-asked question, at least I have been contacted by many of my colleagues, and you say, well, okay, this is very interesting, but we do not, we’re not in hemodiafiltration what you advise me to do.

Indeed, I think Sandip correctly mentioned that your infrastructure and dialysis unit cannot deliver this high-quality water. Yeah. Then there is the need for a big investment. You need a significant investment if your dialysis machines are not sufficiently equipped to do that. And there's also a learning curve concerning the dialysis stuff.

So, indeed, if you only do hemodialysis, so you start from scratch, there is quite a bit of investment. That is correct. But once you have made these investments, and that's more or less of a one-time investment, then price differences are limited. My guess is. And this environmental aspect, yeah, when we started the trial, that was not on the agenda, but Sandip is, of course, I very much agree with you that the whole environmental impacts of hemodialysis in general and a few more hemodiafiltration in particular of course is considerable.

So that is a task, I think, for the industries and fields to find solutions to reduce substantially, dramatically, considerably. You choose the words you think are most appropriate concerning reducing the environmental impact of standard hemodialysis and hemodiafiltration. And I think that is a topic for tomorrow and the coming years.

Peter Kotanko
I fully agree with what you are saying. I mean, there are major challenges ahead of us. To me, the CONVICE trial was a big sign of hope, hope on multiple levels. First, we as a nephrology community can come together and pull this off with support, in this case, from the European Union, academia, and dialysis providers.

Peter Kotanko
This is to me; this gives me a lot of hope for the future. It also gives me hope that we have a positive trial, right? So, this is another important aspect. And, of course, hypotheses are challenged. I mean that the entire history of science exists of challenged hypotheses, and that's good. But at least we know now in summer 2023 where we stand on, and of course, I'm eager to learn what the next steps will be, both in Europe, in Asia, and here, of course, in the United States.

Peter Kotanko
I want to thank all three of you. This has been a wonderful conversation, and I look forward to continuing the exchange of thoughts.

Peter Blankestijn
Thank you. Thank you.

Sandip Mitra
Thank you.

Krister Cromm
Thank you very much.

Peter Kotanko

Thank you for joining the Renal Research Institute for this Frontiers in Kidney Medicine and Biology episode. We invite you to engage with us on our social media channels. We look forward to seeing you again soon for the next Frontiers in Kidney Medicine and Biology episode.