Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I’m Bob Barrett. An estimated 700 million people worldwide are living with chronic kidney disease and the number of these individuals who progress to kidney failure is increasing. In many cases, the transition from chronic disease to kidney failure comes as a surprise. Roughly half of the patients who proceed to kidney failure are admitted to the hospital for emergency unplanned dialysis. A number of predictive models have been developed to identify patients at risk for progressing to kidney failure, providing an opportunity to discuss available therapeutic options, establish a management plan and ease the transition to kidney failure.

Unfortunately, these models do not account for updated clinical laboratory values which limits their accuracy. They also predict kidney failure occurring two or more years in the future but cannot inform risk on a shorter timescale, limiting their ability to identify patients with more immediate need of kidney replacement options.

A new article appearing in the October 2023 issue of *Clinical Chemistry* evaluates whether machine learning can improve the prediction of kidney failure risk, reducing morbidity and mortality and improving quality of life. In this podcast, we are pleased to welcome the article’s lead and senior authors. Martin Klamrowski is a PhD student in biomedical engineering at the University of Ottawa in Ontario, Canada and his research focuses on building predictive models for advanced chronic kidney disease.

Dr. Greg Hundemer is a kidney specialist and clinical researcher at the Ottawa Hospital and his research interests involve improving care for patients living with chronic kidney disease. So, Dr. Hundemer, let’s start with you. How did you come up with this research question?

Greg Hundemer: I’m a nephrologist so I deal mostly with patients with kidney disease and I specifically work in a clinic that is called a multi-
care kidney clinic but it’s designed really for patients with advanced chronic kidney disease who are approaching kidney failure where they’ll need dialysis or kidney transplant or something like that for them to survive.

Really, the challenge with this population is that despite our best efforts, about 50% of these patients start dialysis in an unplanned fashion, meaning they start dialysis in kind of a crash scenario, or they go to the emergency room and have to be rushed on dialysis and it’s not -- one, it’s not a great experience for the patient but it’s also actually associated with high rates of morbidity and mortality. So when you start dialysis like that, you’re more prone to heart disease, infections, death, and a number of other adverse complications. Really, the way we like to start patients on dialysis is to kind of do it in a smooth, planned fashion where you prepare them ahead of time, they kind of know what they’re getting into. They start as an outpatient in the ambulatory setting and you do see that patients do a lot better in terms of quality of life and long-term outcomes when they can start dialysis in kind of a smooth or planned fashion rather than this crash start.

So really this research kind of came off of how can we better improve getting more of our patients to start dialysis in this way rather than crashing onto dialysis because 50% seems way too high to be acceptable and I think we can have a lot of room as a nephrology community to improve that. And so I hope this sort of research helps improve these outcomes for this patient population.

Bob Barrett: Was there a knowledge gap that this study kind of fills in?

Greg Hundemer: Yeah. So where I think this study fits in in terms of a knowledge gap is because like I said, about 50% of patients with advanced chronic kidney disease start dialysis in an unplanned fashion. I think we need a way to better predict which patients in our population are those that are likely to imminently have kidney failure and need to be prepared for dialysis. Currently, this 50% unplanned starts occurs even with patients who are followed longitudinally by kidney specialists so clearly, there’s something we’re missing clinically where we’re not identifying the right patients, or at least not identifying them early enough to actually kind of take the steps needed to prepare them for dialysis.

So doing things like creating a fistula, we’re teaching them about the different options that are available to them once their kidneys reach kind of a critical threshold where they need some additional support. So I think by identifying way to better predict which of these patients are likely to progress quickly and have kidney failure in the short term, we are better able to kind of educate them and prepare them
accordingly. So that’s really where the knowledge gap I’m hoping this research will fill.

Bob Barrett: Okay, let’s bring our PhD student in here, Martin Klamrowski. Martin, let’s talk about machine learning and how it can improve upon existing kidney failure prediction models.

Martin Klamrowski: So I can start with the definition that might be a bit of a mouthful. Machine learning, roughly speaking, is the statistical estimation of functions. You know, at the lowest extreme of this definition, you could do this in your head, you can take an average of some numbers and make this somewhat pedantic point that you in effect done machine learning in your head and you’d be correct, at least in your epistemology.

The thing is that this definition is not wholly useful to distinguish traditional stats from machine learning because, you know, this definition goes for simple linear regressions you can fit in your head and it goes for Cox regression models that currently represent the gold standard in kidney failure prediction, to random forest, to even the large language models that are kind of dominating the conversation around AI right now. So yes, the definition would be along the lines of approximation of functions. But more typically, when we’re invoking the term machine learning, we’re only doing so with the application of algorithms that go beyond pure optimization and they actually do learning, and it’s important to distinguish these two points because they’re not exactly the same thing.

And I should also add, you know, you often hear people throw scale components in stat definitions, and so the real differentiator between traditional stats and machine learning can likely be considered along the lines or along the axis of scale and complexity to your problem. So bringing back to the question, basically, when we throw a machine learning algorithm at a problem, we’re coming in with the hypothesis that there within the data, there lies some complexity, some intricate interaction or dependency between the elements that characterize our samples. That simpler models like the Cox regression would just not be able to account for.

So that’s one of the things we’re leveraging in the study and I think the second would be how we can improve on kidney failure prediction models. The second would be more lab data. Existing kidney failure prediction models, they don’t account for more recent follow-up data and I think our study shows that this appears to be wholly suitable for predicting at the longer timeframes. One thing our study shows is that if you want to predict at shorter timeframes and more dynamically, you need to be looking at dynamic lab data, and
I think that’s where a major advantage for machine learning may lie.

More generally, I think the question will be, what kind of models do you want to leverage the ever-growing laboratory data stream, growing in count and in dimensionality and I think our study provides some clear indicators for that.

Bob Barrett: Okay. Well then, what are the next steps in this research?

Greg Hundemer: In terms of the next steps, I mean, Martin has done really great work here with local data in Ottawa. So we’ve mostly dealt with a large cohort of patients that we’ve seen here locally in Ottawa and a few other centers around Ontario, Canada. But really, what we want to do is make this prediction model that Martin has created more generalizable to different populations. So our next step is to kind of broaden it and study it in larger populations. So we’re looking at taking it to the provincial level or we deal with all of Ontario, which is about 14 or 15 million individuals. And so we’re looking at this kind of broader population and eventually, we want to study it in different provinces in Canada and then move it to the United States and other places around the world where we can see how well does this machine learning prediction model work in other geographical locations and with different patient populations.

And I think even beyond that, once we kind of have it shown that it’s accurate in predicting kind of short-term kidney failure and short-term dialysis needs, we eventually want to kind of incorporate it into clinical practice and really test it there. So we want to work it into most hospital systems that use electronic medical records and we want to be able to integrate it within kind of the normal workflow for kidney disease clinics and kidney disease patients where clinicians and patients actually get kind of the output of this model of like, what are the risks? What are your short-term risks for having kidney failure in X timeframe? And that’s really going to help both patients and providers kind of realize the situation and know how to address it to hopefully prevent some of these kind of crash dialysis starts which we know are such a bad outcome for patients.

Bob Barrett: Okay, well finally, looking at these findings, how might they impact clinical care?

Greg Hundemer: Yeah. So I think if we can show in other settings that if this model continues to perform as well as we’re seeing right now, we’re hoping, like I said, we could integrate it to within workflow for kidney disease clinics where it’s in the electronic medical records, easily accessible by patients and providers. And ultimately, if say, you get a patient that prediction model marks as very high risk for needing -- having kidney failure
and needing dialysis in the next six months or so, the clinician then has time to act on that, where they can actually prepare the patient for dialysis, put a fistula in, teach them about kidney transplant, kind of show them these other options, and I hope that we can have seen major strides in this kind of 50% of patients starting -- crashing onto dialysis in this unplanned fashion that we know has a number of poor outcomes.

If we can lower that number even by 10, 20%, that makes a huge difference for patients because that’s a much reduced morbidity, reduced mortality, better quality of life, and even beyond just kind of the impact to the patient, you got to think of how this impacts our healthcare system as a whole.

Because when patients are starting dialysis in the hospital or crashing to the emergency room and they have all these adverse effects from that, that’s a huge burden on the healthcare system. That costs a lot to different healthcare systems and if we can reduce the rates of unplanned dialysis with prediction models like this, I think we will actually see a huge cost savings in terms of the financial burden of unplanned dialysis. So that’s my hope is we can both improve patient outcomes and also reduce healthcare costs with this model.

Bob Barrett: That was Dr. Greg Hundemer and Martin Klamrowski from the Ottawa Hospital in Ottawa, Ontario, Canada. They published a study describing the use of machine learning to predict kidney failure in the October 2023 issue of *Clinical Chemistry* and they were our guests in this podcast on that topic. I’m Bob Barrett. Thanks for listening.