Melanie Cole (Host): Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole and joining me today is Dr. David Fischer. He's an assistant professor of neurology at the Hospital of the University of Pennsylvania, and he's here to highlight the RECOVER Program for Disorders of Consciousness at Penn Medicine.

Dr. Fischer, it is a pleasure to have you join us today. Neuroprognostication involves the evaluation of disorders of consciousness after acute brain injury to assess a patient's level of consciousness and chances for meaningful neurologic recovery. You wrote recently, that a conventional neuroprognostication for disorders of consciousness is variable, frequently fails to meet the standards of current guidelines, and prone to error.

Can you explain why this is the case, given the frequency of stroke, trauma, and other disorders of consciousness that occur in this country?

Dr David Fischer: Sure, Melanie. Thanks for the question and thank you for having me. I think, you know, in order to understand kind of the scope of the problem, I think it's helpful to imagine yourself in the shoes of someone whose loved one is comatose from an acute brain injury.

You know, when we're talking about acute brain injuries, we're talking about things like hypoxic ischemic brain injury after a cardiac arrest, traumatic brain injury, stroke, brain bleeds. And what all of these have in common is they tend to occur suddenly, and without any kind of warning. You have to imagine a scenario where in the matter of just a few moments, someone can go from feeling reasonably healthy to being completely comatose and rushed to the hospital. And so, as a family member this can be extremely scary and overwhelming.

Now layer on top of that, the fact that soon after these patients get to the hospital, clinicians are often approaching these family members and asking questions like - should we be continuing aggressive, life support, or should we be stopping life support and allowing these patients to die?

And you can imagine that for families that are already overwhelmed and scared, this is an enormous question that can make people feel even that much more overwhelmed. Now, if you're a family member who's tasked with making this decision about whether to continue or stop life support, what you'd probably want to know is, well, what are the chances

that my loved one will wake up again and have a meaningful neurologic recovery?

Now, the kicker to this whole problem is that the truth of the matter is that families often don't get great guidance about this. This is something that we've encountered clinically and has also kind of been borne out in the literature that clinicians, and specifically neurologists, are highly variable in the guidance we give to families and oftentimes just not accurate in terms of predicting whether a patient will wake up again.

What that means is that families oftentimes don't get the support that they need in making these decisions, and may be getting wrong guidance sometimes, which might be leading to avoidable morbidity and mortality. Now, if you think about why this is the case, why are we not providing the best possible guidance to families?

I think the answer is that it's complicated, but I think it ultimately boils down to the fact that the traditional clinical infrastructure for making neuroprognostication decisions just really isn't optimized for the problem. And I'm not just talking about Penn. I'm talking about much more broadly in the medical and scientific community. Doctors just aren't put in the best positions to make these decisions well.

And I mean a few things by that. One is that neuroprognostication is one of often many competing responsibilities that neurologists have. So general neurologists may simply not be aware of some of the advances in research and clinical guidelines that have occurred in the subspecialized field of neuroprognostication in the last few decades, may not be translating some of those new tools into clinical practice. Another big problem is that there's a lot of different clinicians, all of whom have very unique and valuable insights into what recovery entails. Beyond neurologists, we're talking about physical medicine and rehabilitation specialists.

We're talking about palliative care specialists. We're talking about physical and occupational therapists, but oftentimes all of these different disciplines aren't communicating all that well. And the last kind of structural problem, and I think the biggest one, is that a lot of the neurologists who make these decisions in the ICU or hospital setting, tend to spend all of their time in the ICU or hospital setting, and don't tend to see what these recoveries look like outside of the hospital. Which means that a lot of the neurologists and clinicians who are guiding

families about what recovery is likely to look like, often haven't seen those recoveries and can't provide any kind of first-hand experience about that.

So ultimately, what all of this results in is families who are scared and overwhelmed, who oftentimes aren't getting the guidance or support they need in making one of the biggest decisions of their lives about continuing or stopping life support for their loved ones.

Host: Thank you so much, Dr. Fischer. That was an informative answer, and as you're telling us about the limitations for clinical care research and education, which is what you were really discussing right there, can you tell us the current guidelines and what's happening at the moment to limit those clinical practice research and education initiatives in neuroprognostication?

Dr David Fischer: Absolutely. So, there have been a lot of advances in the last few decades. Neuroprognostication looks very different now than it did even just 10 years ago. The guidelines in essence right now acknowledge the fact that no single tool is really perfect for predicting a patient's capacity to wake up and have a meaningful recovery.

And therefore, the guidelines often recommend taking a multimodal approach and using multiple tests to try to anticipate a patient's likelihood of recovery. What we see is that contrary to that, a lot of literature has shown that many clinicians don't take a multimodal approach, often have one or two tests that they prefer to get.

And so because each of these tests are alone relatively inaccurate, that's one source of problems. Another recent inclusion in clinical guidelines are some of these new tools that have only been developed in the last several years. For example, neuroimaging has been used for quite a while in the process of neuroprognostication, to look at brain structure and to try to anticipate recovery based on that. But there have been developments that now allow us to measure brain function as well as structure. And some of those functional MRI scans can give us more detail about a patient's current level of consciousness and capacity to recover consciousness.

However, what we're seeing is that a lot of these tools have not been translated into patient care even after they've been endorsed by these guidelines.

Host: Well, tell us a little bit more then about the program at Penn Medicine and its blueprint for longitudinal care in the practice of neuroprognostication, tell us a little bit about some of the things that it's really trying to address here, Dr. Fischer.

Dr David Fischer: In order to address a lot of the problems that I just described in terms of traditional neuroprognostication, I've come up with this program called the RECOVER program, which is an acronym for Recovery of Consciousness via Evidence-based Medicine and Research. And the objective of the program is to provide comprehensive, specialized, and longitudinal care to patients with disorders of consciousness resulting from acute brain injury.

And the way that we try to accomplish that is by providing integration across all of these previously fragmented dimensions of care. So, the way it works is, as follows. If there's a patient at the Hospital of the University of Pennsylvania who's not waking up after their severe brain injury and neuroprognostication becomes a question, we will see them as part of a specialized and interdisciplinary consult service.

In addition to having a neurologist such as myself, we also have physical medicine and rehabilitation doctors, a palliative care specialist, physical and occupational therapists, and we all see these patients in parallel to provide our own unique care. And when we see these patients, we collect prognostic data in a more systematic and guideline-based way, collecting not only conventional tools, but also trying hard to translate some of these advanced technologies into clinical practice, like functional MRI.

And after we collect all of this data, we then meet on a weekly basis as an interdisciplinary team to discuss patients, and to try to come up with a more comprehensive approach to prognostication. So that we can guide families, not just about likelihood of neurologic recovery, but also what are the resources that are going to be necessary in order to support that recovery, so that families can really go into this decision as informed as possible.

We then take more responsibility for guiding families through this decision, throughout the course of their hospitalization, meeting several times often to help give families the support and guidance that they need. And if patients ultimately survive beyond hospital discharge, we provide longitudinal care and support, to patients and their families.

And the idea is that by providing this interdisciplinary integration, this integration across the acute and chronic settings, we can provide support to the patients and families that they need. And get the feedback that we need in order to make these decisions more accurately in the future.

Beyond the hope of improving clinical care here and now, we also have an eye towards improving the future of neuroprognostication care. We do that in part through education, neurology trainees, physical medicine and rehabilitation trainees are incorporated throughout every step of this program so that they can learn these practices and prevent, potentially perpetuate them wherever they go to ultimately practice. And we also do research. So, big problem with neuroprognostication has been that we have been very slow to translate what we know into clinical practice. But another problem, is that there is just a limitation to what we know. And so, more research is going to ultimately be necessary in order to provide better and more accurate guidance to families.

And so we're trying to push that research forward. Patients and families who pass through this program are given the opportunity to participate in that research, where we study things like how neuroprognostication is done, how we might be able to do it better. We are in the process of trying to develop even better tools for predicting consciousness recovery and return of neurologic function.

And we're also trying to understand more basically, you know, what is going wrong with the brain during a disorder of consciousness? And is there an opportunity to intervene potentially with novel therapies, to help patients wake up after their brain injury?

Host: What an exciting program. And Dr. Fischer, are there any technologies that you'd like to share with other providers that you feel have changed the landscape with what you're doing at Penn Medicine? Are there any specific neuroimaging techniques or anything, that you employ to aid in this diagnosis and eventual initiative?

Dr David Fischer: Absolutely. And there's all sorts of new technologies that are currently in development. One of the technologies that we, are most focused on translating into clinical care and pushing forward is functional magnetic resonance imaging, or fMRI. And as opposed to conventional MRI, which measures just structural integrity of the brain, functional MRI actually measures brain activity in order to tell us more

about a patient's level of consciousness and capacity for future consciousness recovery.

To give you more detail that, we use functional MRI in essentially three ways. When patients are in the MRI scanner, we will actually ask them to imagine moving their hands. And it turns out that a subset of patients who look completely unresponsive, who don't move their hands if you ask them to, do show evidence of brain activity that tells you that they're trying to move their hands.

And this phenomenon has been termed covert consciousness, and it's something that we are interested in looking for in any of our patients who pass through the program. We also deliver other types of stimuli while patients in the scanner, we play language and see if language centers of the brain become appropriately activated.

And we also look at how well the brain is functioning at rest. And so, we're taking a much more comprehensive approach to understanding what kind of brain activity a patient has, and whether or not that brain activity can predict future recovery.

Host: This is so interesting Dr. Fischer, what great work you're doing. Before we wrap up, I'd like you to speak about the patients and their families. You touched on it earlier. And while you're telling us that, you can explain a little bit about the target for this program, but how you're all working together for that multidisciplinary approach for patients and their families and these target providers all working together to help the patient.

Dr David Fischer: I think at the end of the day, this program has lots of different goals, but I think the most important thing ultimately is that, patients and their families get the support they need when making potentially one of the biggest decisions of their life. Regarding whether to continue or stop life support for their loved one with brain injury.

And that's ultimately our most important goal. And we try to do that by working as an interdisciplinary team, providing a more holistic and comprehensive approach, to patient care to provide the best possible guidance we can, to their families. Right now, the main patient population that we are taking care of are the patients with brain injury at the Hospital of the University of Pennsylvania. But we acknowledge that this is a problem that affects many more hospitals than that. And so, our

hope is that eventually this program will allow us to provide evaluations to patients who are at other hospitals, or patients who have left other hospitals and need outpatient evaluation, so that we can try to provide this guidance to other families as well.

Host: Thank you so much, Dr. Fischer, for joining us today. And to refer your patient to Dr. Fischer at Penn Medicine, please call our 24/7 provider only line at 877- 937- PENN. Or you can submit your referral via our secure online referral form by visiting our website at pennmedicine.org/referyourpatient.

That concludes this episode from the specialists at Penn Medicine. I'm Melanie Cole. Thanks so much for joining us today.