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John Williams: Hi everyone. [I'm John Williams](#), Professor of Pediatrics and Chief of the Division of Pediatric Infections Diseases here at the Children's Hospital of Pittsburgh.

Stephanie Dewar: And I'm [Stephanie Dewar](#), Vice Chair of Clinical Affairs and Program Director of the Pediatric Residency Training Program, and welcome to That's Pediatrics from UPMC Children's Hospital of Pittsburgh. Joining us today, we have [Dr. Tim Shope](#) who is a Professor of Pediatrics here at Children's. He has an interesting past history in that he was previously with the US Navy for quite some period of time where he mentored and trained countless pediatricians who are now stationed throughout the world. Dr. Shope joined us here at Children's in 2011 and his primary interest is diagnosis and management of common pediatric infections, such as [otitis media](#), or ear infections, sinusitis, urinary tract infections, and he's here to talk to us today about an interesting tool called [UTICalc](#), so welcome Dr. Shope. It's so nice to have you.

Dr. Tim Shope: Thanks a lot. It's great to be here.

Stephanie Dewar: So I'm just very curious, Dr. Shope, how you actually became interested and what kind of made you curious about developing this tool for UTICalc.

Dr. Tim Shope: This was my colleague, Nader Shaikh's idea originally, and he's the first author on the JAMA Pediatrics publication that came out in June of this year.

Dr. Tim Shope: It seems kind of simple, the classic case of a child that comes in in the first two years of life with a fever, a high fever, and no other signs of infection that maybe you have to think about a urinary tract infection, but oftentimes, it's not so straightforward. Let's say the child has a cold at the same time. Race matters, Caucasian versus non-Caucasian and a child's prior history may matter. There are a lot of variables that we have to consider when we're looking at a child, and because they're younger, under 24 months, they can't spontaneously void, so we have to oftentimes do a catheterization which is a relatively invasive test. It's uncomfortable. It's traumatic for the parents, so we'd like to not have to do this test on people who are very unlikely to have a urinary tract infection, and then also considering the number of variables, it's hard for, I think clinicians to be able to balance five important variables that may be going in different directions in their mind, so we wanted to improve on what the AAP, American Academy of Pediatrics already has. It has very similar variables to what ended up in our UTICalc, but it's in a paper that's not necessarily readily available and we wanted to create it in a user-friendly fashion.

Dr. Tim Shope: We kind of used the BiliTool that I think many of us are familiar with for estimating a child's risk of developing significant jaundice in the newborn period. That's very highly used, very user friendly, and we wanted to develop something like that.

Stephanie Dewar: So you were looking at making sort of an app type availability for this tool for the physician in their primary care office or emergency department?

Dr. Tim Shope: Exactly, yes.

Stephanie Dewar: And how would that differ from what people's current practice is today?

Dr. Tim Shope: So we don't know exactly what the current practice is today. We know that the AAP has a guideline for managing urinary tract infections in children under 24 months of age, and that's published, and we know from many prior studies that people don't always adopt guidelines very well. I've actually looked at the practice here in our emergency department to see how compliant our doctors are in managing urinary tract infections and they actually test much less than the AAP recommends. This study is not yet published. It's been rejected several times.

John Williams: Rejected by journals or rejected by our doctors?

Dr. Tim Shope: Rejected by journals, but we know, say, in our emergency department, about one-third of children that comes in with fever are tested, and for example, at CHildren's Hospital of Philadelphia, about two-thirds of them are tested, so it's likely that there are significant variations in practice, and we don't know how adherent people really are to the guidelines, or even if the guidelines are perfect. There may be better ways of determining who needs to be tested.

John Williams: Can I ask you a question, Dr. Shope? Sort of the big picture question of this because you make it sound like this is relatively common in primary care practice and in the emergency department, or the ED. How many of these kids really have urinary tract infections?

Dr. Tim Shope: So we determine that based on studies in which children are generally seen in emergency departments. Their clinicians make decisions about who to test and who don't. Each of the studies that have looked at that have tested a variable number of these children. None tested every child, but the studies show around 5% to 7% of children presenting with fever have a urinary tract infection.

John Williams: So it's common enough that it's really not great for the doctor treating the patient to say, "Well, you probably don't have one." They really should have more information is what you're saying.

Dr. Tim Shope: Yeah, they would be right. 93% of them don't have a urinary tract infection. The concern is for parents that have had kids with UTIs, they're pretty significant.

Children can be quite uncomfortable with these and there's a risk of scarring to the kidneys, and so that may or may not have longterm effects, but it's significant enough that we want to diagnose it early enough and treat it with antibiotics, and treating earlier with antibiotics reduces the risk of scarring.

Stephanie Dewar: And so you mentioned earlier that this is an age group, specifically under the age of two with fever who may have other symptoms. I'm wondering if we just can't reassure ourselves that perhaps they'll get a course of antibiotics anyway without actually diagnosing a urinary tract infection. What would be the importance of knowing that it's actually the urinary tract that's infected.

Dr. Tim Shope: That's a good question, and actually there's some British studies that have looked at children that present with fever in outpatient offices and the clinician made their initial diagnosis and treatment, but then they came behind them and actually tested those children for urinary tract infection, and it was a large proportion of children who were diagnosed with something else like an ear infection actually had urinary tract infection. It might have been one-third, maybe 50%. It was quite impressive so we know that this probably occurs, that children are misdiagnosed and treated with antibiotics. Obviously, the antibiotics you would use for an ear infection are different than what you would use for a urinary tract infection so the concern is that there may be resistant organisms or organisms that are not susceptible to the antibiotic that they were placed on.

John Williams: Okay. So I hear you saying how important it is to identify these. Can you talk a little bit about the UTICalc, and sort of how you developed it, and how it works?

Dr. Tim Shope: Sure.

John Williams: It sounds like a pretty significant advance.

Dr. Tim Shope: Okay. So it's on the web. Actually, I can't remember the exact URL but if you Google Pit UTICalc, you will find it and it has five prompts, and so you complete the child's age, the height of the temperature, the race, whether the child is an uncircumcised male or female, or a circumcised male, and whether there's another source of fever, and that would include something obvious like a rash, croup, bronchiolitis, pneumonia, but it could also include the common cold, which in fact, does reduce the risk of UTI, so you plug in all these variables, and you get a probability of UTI. It may come out 7% and then we had to use a threshold for which treatment would generally be recommended, and there's not a lot of research on that, but we used 2% or 3% as the cutoff where we recommend that you consider treatment. We're just trying to assist the clinicians in what they do. So... I'm sorry. Recommend that you do testing. It's a two-step process so then the testing occurs, and that can be either a urine dipstick in an outpatient office, or a urinalysis, which includes a dipstick by a machine, and then also can include microscopic analysis, and so depending on

what test the clinician does, they fill in. Then there's a second screen, and you fill in those results and get your post-test probability of UTI.

Dr. Tim Shope: And that's kind of important because actually, some of the clinical factors actually still matter in determining the likelihood of a UTI, so for example, if you have a child who has a temperature of 40 degrees centigrade, is Caucasian, is a girl, and is under 12 months of age, and has no other source of fever, she has a probability of UTI of around 25%. But let's say the leukocyte x-rays was only trace and the nitrite was negative. Then you're sort of in a quandary. That test doesn't look very positive, but based on the clinical factors, that child probably still has about a 15% chance of a UTI and would meet the criteria for treating empirically while you're waiting for the culture to come back.

John Williams: But one more question on that. If I understand you right, this, the UTICalc can also be used in some cases to decide that you don't need to do the catheterization, to put the baby through this uncomfortable procedure.

Dr. Tim Shope: Yeah, exactly, and compared to the AAP guideline, when we modeled the UTICalc versus a separate validation database different than the one from which it was derived, we reduced the children who needed to be tested by 10% and picked up a few additional children. Hopefully, we'll develop better biomarkers, indicators of inflammation that we can add to the UTICalc in the future that might even reduce that more potentially.

Stephanie Dewar: So that's really interesting science and simple technology. It sounds like to help minimize unnecessary testing and also target those children who might be at higher risk. I wonder if it would be okay if we change gears a little bit on this.

Dr. Tim Shope: Absolutely.

Stephanie Dewar: I'm very curious how you got from what you did in your career in the US Navy to what you're now doing here at Children's and what kind of motivated that change and your interest now.

Dr. Tim Shope: Yeah, well, so the Navy was real great for me. They offered me a fellowship where I learned research and teaching, what's called an Academic General Pediatrics Fellowship and I used that as a residency director and kind of in a leadership management position in the last part of my career, but what I never really had a chance to do was use all the research training that I got. It's hard to do research in the military because you could be deployed after receiving a grant or you could have one of your partners deployed, and then you have to see all their patients, so that was real frustrating. You never really had anything predictable, so I was looking around as I was retiring, and I always admired the work that was done here in the Division of General Pediatrics.

Dr. Tim Shope: I come from a family history of infectious disease researchers and always considered infectious diseases to be very interesting to me, and so I've read

much of the work of Ellen Wald, and Jack Paradise, and Alejandro Hoberman, and so I jumped at the opportunity. One of my colleagues from fellowship, Deborah Bogen, she and I overlapped and we talked at a conference. She said, "Hey, you need to talk to Alejandro," so I did, and the division had just received a number of large grants, and he said, "Just come and help us. We have more work than we can do with the number of people that we have here," and I said, "Well, what about writing grants? I haven't been doing that since my fellowship. Will I be able to support myself?" He said, "Don't worry. We have so much work. We'll worry about that later," and here we are seven years later. We've got a new round of grants that have been funded supporting all our work and we're working on... I counted before coming over here 11 new projects that are a combination of NIH and government-funded work versus industry-sponsored work. These are the things, the irons that we have in the fire for our next wave, so that's where we are right now.

John Williams: Well, that's a really interesting progression. I wonder if you could talk about... because I know that you still do a lot of clinical care of patients, and this is something that in academic medical centers like ours, most people tend to do a lot of clinical care and a little research, or a lot of research and a little clinical care. Yet, I think if I remember right, you do about half and half.

Dr. Tim Shope: Yeah, that's correct. It isn't common. We work as a team, our clinical trials unit. There's six of us. Three are full-time researchers and three are about half-time clinical. I think it's important. I'm glad I can stay connected clinically because that's where all these research findings that we have really impact what general pediatricians do in the office every day. That's what drew me to this place. That's where the good ideas come from. Sometimes I have to stand up and say, "This is a good theoretical idea but it's not going to work well in the clinical setting," and I'm sort of representing the clinicians in that respect, so we work really well together as a team. Every grant, we all work on parts of it but we have the big hitters, Alejandro, Nader Shaikh, and Judy Martin are usually the PIs on our projects.

Stephanie Dewar: I'm wondering, is there anything new and innovative that we could expect as far as infectious diseases in childcare settings or in school-based situations that you're aware of or working on?

Dr. Tim Shope: So as you know, that's something that I've worked on over the years, developing proper exclusion criteria and return-to-care criteria for children in childcare and schools, and I've worked with the AAP on that, on a book called Managing Infectious Diseases in Childcare and Schools, and we're actually doing the fifth edition of that. No earth-shattering changes. One thing that's been really great is that the current editors at The Redbook, which are the... infectious disease bible, I guess we could call it... have worked really closely with us to make sure that what we're recommending and what they recommend in the Redbook are in lockstep, and so that's been really exciting. We make all these policies. They're pretty well out there in most childcare centers as far as implementation.

That's the difficult part because states invent their own rules and they're not always evidence based, and it's a real challenge. I've been working in Pennsylvania for the past four years trying to have the state government change their policies because it leads to a lot of unnecessary exclusion, and then that leads to parents losing work, and lost wages, and a lot of issues that really affect children in our office. Oftentimes, a child has pink eye. They have to see a doctor when this is a condition that'll resolve in most cases on its own, so it's a long, lifetime battle to try to solve that. No earth-shattering news on that front.

John Williams: Well, as a parent of four children who when they were young were all in daycare, I would like you to keep fighting that fight because as pediatricians, we know how common these respiratory viruses are, and the children had them yesterday, and they'll still have them in two days, and yet, the daycare will say, "Oh, no. They have to be out for 24 hours," as if there's a magic period there.

Dr. Tim Shope: Yeah, yeah. Actually, there is some exciting work that I've been collaborating with Andy Hashikawa who's a pediatric emergency department physician in Ann Arbor at University of Michigan, and he has submitted a grant proposal. Hopefully, it'll be funded but I've been a consultant on that where he's actually filming children in childcare settings and noting what they touch the most, put in their mouth the most, and then basing cleaning, sanitizing, and disinfecting recommendations based on what they actually touch the most and what's the most highly-contaminated areas, so this'll be a randomized trial if it gets funded where people, a team comes in and cleans up at the end of the day, and at various intensities, and that would be extremely exciting because it would add a lot of evidence to something that hasn't been studied very well previously.

John Williams: I think it's going to be pretty gross at a daycare. That's my prediction.

Dr. Tim Shope: Yeah, it's a cesspool but, hey, a lot of us don't realize that we are covered by bacteria that vastly outnumber us, and in some ways it's actually a good thing being exposed to all those antigens, viruses, bacteria. As we interact with those, we develop our immune system and there's some good research that shows that that actually reduces the risk of allergic diseases like asthma later in life.

Stephanie Dewar: That is really simple but interesting innovations to look at people's environments, especially daycare centers, which as you described as cesspools, which is a word that I also common use with families that it's a cesspool of microbes for better or for worse. It's just an interesting place to exist.

Dr. Tim Shope: Right. It's all part of this hygiene theory, and children that grow up with pets in their home in the first year of life, or grow up on farms, they're exposed to all these antigens. It seems gross because we can't see them, and I think the average person in the way public is sort of turned off by this, but it's a really important way that our bodies interact with the environment, and I think overall healthy, but we want to still get exposed to those antigens, not the super bad ones, and develop our immune system in a healthy way. Immunizations we've

developed against the really bad diseases, but common cold viruses, for example, maybe they're there for a good reason.

Stephanie Dewar: So I'm wondering. You're a person who's lived and worked in other places. I'm just wondering is there, aside from the excitement about the research here in Pittsburgh, is there anything unique about the community or the way that we live and care for our Children's, or is it a good place to be for research because it's nice and generalizable to the United States?

Dr. Tim Shope: I think Pittsburgh is a bit homogenous. Our clinic population is a good melting pot but we don't have a lot of immigrant families in Pittsburgh. I know it's something that the city is actively working on, and in terms of ability to participate in research and do research, our clinic population is fantastic. People consent to research studies at a very high rate, I think because we have such a longstanding track record, and there's trust in the community and what we do. We take really good care of our kids that are... all of our children but especially those that are participating in research studies, and they get a little extra attention, I think, when they're in a research study, so it's a fantastic place. We often try to collaborate with other sites, and it's frustrating because other sites cannot enroll at the same rates that we do for a variety of reasons. We have a really good established team and support staff with our research nurses, and research assistants, and things like that.

John Williams: I just want to ask one quick final question, Dr. Shope. You mentioned you're from a family of infectious disease researchers, so the first person to grow influenza virus from a human and prove that flu is caused by a virus was a Shope. Relative of yours?

Dr. Tim Shope: Yes, that is my grandfather.

John Williams: Oh, my God.

Dr. Tim Shope: Richard E. Shope.

John Williams: I already thought you were cool. Richard Shope. Now you're like 50 times more cool.

Stephanie Dewar: Wow. That's Pittsburgh, right? Everybody knows somebody.

John Williams: There you go.

Stephanie Dewar: Well, thank you so much for joining us today. This has been really illuminating for me personally, and I think is going to be very beneficial for those who join us on the podcast.

Dr. Tim Shope: Great. I've enjoyed it very much. Thanks for inviting me.

