Behind the Breakthrough Podcast - University Health Network

Season 5 - Dr. Mamatha Bhat

Transcript

BTB

Hello and welcome to another edition of Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christian Coté . And joining us on the podcast today Dr. Mamatha Bhat, a clinician with UHN's Ajmera Transplant Center and award winning scientist at the Toronto General Hospital Research Institute. Dr. Bhat is pioneering the first translational research program worldwide dedicated to improving the outcomes for liver patients after transplant. Dr. Mamatha Bhat welcome to Behind the Breakthrough.

DR. MAMATHA BHAT

Thank you so much, Christian, I really appreciate the opportunity to discuss my research with you today.

BTB

We're looking forward to doing a deep dive with you. Let's start big picture. What's the scope and scale of liver disease in Canada today?

DR. MAMATHA BHAT

Over 3 million Canadians actually have chronic liver disease and a significant number pass away over 5000 individuals pass away on an annual basis due to end stage liver disease and its complications. So the scope is quite huge, and in fact, continues to grow. So although Hepatitis C is now curable, we do have this new epidemic of fatty liver disease as well as alcoholic liver disease that are increasing, especially on the heels of the pandemic as well as diabetes and obesity that are growing in our population.

BTB

Okay, so for those patients, where transplant is the only treatment option left, what's the prognosis for them?

DR. MAMATHA BHAT

As a clinician, scientist, and hepatologist, I take care of patients who are evaluated for liver transplantation. And I take them through that process and look after them in the long term after

transplant. So the nice thing about liver transplantation is that overall, one year survival rates have dramatically improved in the last 30 years. But if we look at survival beyond a year after transplant, unfortunately, those outcomes have not substantially improved in the last 30 years. And they continue to be compromised by complications such as an increased risk of cancer, as well as an increased risk of heart disease, cardiovascular events that compromise their long term survival.

BTB

Okay, so what do we know about why these complications occur post transplant for liver patients?

DR. MAMATHA BHAT

Some of it is the existing comorbidities or the existing issues that they came in to transplant with. So many people come into transplant with diabetes with chronic kidney disease, and they may have been exposed to say smoking or other issues that will have an impact in terms of their longer term survival. But then, once they have received a transplant, they are on anti rejection medication or immunosuppression. Now, immunosuppression certainly is critical to protecting the graft or protecting this new liver from being rejected. But at the same time, there are certain side effects that are associated with the long term use of immunosuppression. Now this is true in any condition for which you require immunosuppression. But the reality is that you're inhibiting the immune system's capacity to recognize abnormal cells, whether it's infection, or cancer cells that are starting to develop, the immune system is less able to recognize those abnormal cells.

DR. MAMATHA BHAT

Therefore, transplant recipients in general have a higher risk of infection, as well as cancer because they are unable to recognize those abnormal cells as effectively. The other thing is that these immunosuppressants have an impact on insulin production by the pancreas. And there is as well some weight gain that may occur over time, that also increases insulin resistance. So patients who have received a liver transplant and transplant in general have a higher risk of diabetes, as well as the associated heart disease risk over time. So we know based on the literature that liver transplant recipients have a two to three times higher risk of heart attacks over a 10 year period, as compared to the general population. So these are complications that we know are compromising the long term survival of our patients. But we don't really have optimal measures to address these complications and say, improve those long term outcomes.

BTB

What I'm wondering then is with all this depth of knowledge of these complications, they're well known. What's your take on, why these long term survival rates have remained stagnant for so long?

DR. MAMATHA BHAT

Well, I think some of it also has to do with the indications for transplant. So traditionally, Hepatitis C was the number one indication for transplant. And about five years ago, this condition became curable.

BTB

Right.

DR. MAMATHA BHAT

And so this has led to a decrease in the importance of graft failure or liver transplant graft failure in our patients and the ascendance of cancer and heart disease as important causes of long term survival compromise.

BTB

So they were overshadows essentially…

DR. MAMATHA BHAT

Yes.

BTB

By Hepatitis C until Hepatitis C was…

DR. MAMATHA BHAT

Correct. Correct.

BTB

I see, okay,

DR. MAMATHA BHAT

So now actually, we've looked at our patients at UHN and in fact, cancer and heart disease are on the ascendance, whereas graft failure previously was the most important reason for mortality in the long term after transplant.

BTB

So that brings us to one of the primary research focus of your lab, you set out to test if you could predict in advance and you tell me if I have this right, you set out to predict in advance those complications that

result in poor long term outcomes for liver transplant patients. And to do that, you took a very novel approach using artificial intelligence. Talk to us first about how did you land on that approach?

DR. MAMATHA BHAT

Yeah, so as I was completing my research training, so I received a CIHR fellowship to pursue my research training, there was emerging evidence and emerging publications on the use of artificial intelligence for diagnosis of diabetic retinopathy, and diagnosis of skin cancer lesions. And I was really impressed by the potential for artificial intelligence in the clinical area that I worked in. So as I launched my independent research program, I started reaching out to computer scientists in the Toronto ecosystem, to see if anyone was interested in collaborating to apply those tools to my area of interest.

DR. MAMATHA BHAT

Now in liver disease and liver transplantation, on a daily basis, we look at the complexity of data and the patterns in the data to make individualized predictions or personalized predictions for our patients. We do this on a day to day basis, subconsciously. So I was interested in seeing whether say, artificial intelligence, could really further examine that complexity and provide us with some insight into personalized predictions for our patients, and really simulate the expert clinician in making such predictions, and maybe even go a step beyond by considering all the historical changes in data over time.

BTB

Tell us like who did you end up partnering with? Because he's quite well known my understanding is.

DR. MAMATHA BHAT

Yeah, so I partnered with actually a few different computer scientists across the University of Toronto ecosystems. So Bo Wang certainly is an important collaborator, who was co senior author on this particular publication. I also reached out to Anna Goldenberg, who is a well known computer scientist around the same time and really was very enthusiastic in collaborating on papers that we ended up publishing in Lancet Digital Health. So I think it was really the clinical questions that I saw in my practice, and say, even discussions with patients that then inspired me to pursue some of these questions that I think have great potential in clinical practice.

BTB

And great, I think, inspiration for maybe paving the way for further use of artificial intelligence. I love that. Okay, so in 2021, you published a paper that you were just referring to that's been called a potential paradigm change for liver transplant patients. First of all, walk us through the study, how did it work?

DR. MAMATHA BHAT

In the study, we used the scientific registry of transplant recipients, which is the US database of liver transplant recipients. Actually, it's a transplant registry for all solid organ transplant recipients in the US. And it's actually a goldmine in terms of the amount of data that's there. So we used that as our training set. We trained on a large number of patients, actually over 65,000 liver transplant recipients who had long term follow up data. And we then tested our algorithm, so we validated our algorithm using our data at UHN on over 4000 liver transplant recipients. We evaluated various deep machine learning algorithms. So deep machine learning algorithms refers to accounting for longitudinal changes in data over time, as well as say the interrelationships that exist on a large number of variables. So we had over 160 variables that we were accounting for, as well as their longitudinal changes over time to then inform personalized predictions.

DR. MAMATHA BHAT

We trained these different deep machine learning models. And we found that there was a certain model that worked most effectively and most accurately to predict one year and five year survival from a given time point in a patient's trajectory. And then, from there, we determined what were the main features or the main variables that were predictors of outcome. And from then on, we can actually determine what are the personalized or individual patients predictors of outcome. So say for a given patient, you can then envision giving them a one year and a five year outlook from a given visit. And tell them well, these are the predictors of this outcome.

DR. MAMATHA BHAT

So say, for example, you talk about cardiovascular mortality or cardiovascular events. This is your risk over the next five years of a heart event, a cardiovascular event. And these are the factors that you could modify in your health to optimize those outcomes. And this is what I could work on as your physician to improve your health and potentially change that trajectory that we are anticipating.

BTB

So there's like a direct impact as a result of this research to your practice in clinic. And I just want to let everyone know out there, we'll be posting Dr. Bhat's 2021 paper on our webpage for Dr. Bhat's episode. I'm just trying to how reliable then, in terms of the algorithm, is there a way of predicting that measure of accuracy?

DR. MAMATHA BHAT

Yes, the area under the curve, which is what we use to determine how this algorithm works, overall, how effective and accurate this algorithm is overall. So the AUC was around point eight zero, on average for overall survival, and then survival, compromised by cancer, cardiovascular disease, infection, and graft failure. So we looked at those five different outcomes. And we can predict that for each individual patient coming forward.

BTB

Has anyone done this before with such a high rate of reliability in terms of predicting liver transplant patient outcomes?

DR. MAMATHA BHAT

Actually not, not using the same approach particularly and what people have done in transplant in general, is mainly retrospective studies and population level studies. Now, with this particular approach, we have this ability to individualize the predictions, which is not something people have done in the past. So you can do this, like say, with a logistic regression model, with just say three or four parameters, you can assign a certain number of points or weighting to each of those parameters to generate a prediction. But the beauty of our approach is that you can consider a large number of variables and take into account the interrelationships among those variables and the patterns over time.

DR. MAMATHA BHAT

And then that is actually what we intuitively would do in our practice. So it really is more reflective of the reality of clinical practice and clinical prediction. The fact that you have all this data out there and a machine learning algorithm can really kind of bring it all together and synthesize it to provide it individualized prediction is really novel in transplant medicine.

BTB

What was the reaction of the medical science community then to your study when it was published?

DR. MAMATHA BHAT

I think what reflects the impact of the publication is the fact that it was published in a high impact journal. So Lancet Digital Health is a very high impact journal, first of all, and I now have a series of three papers actually published in Lancet Digital Health. Each of those papers proposed either novel methodology that was designed for the specific clinical questions, so we didn't necessarily use off the shelf machine learning tools, we actually didn't, we created and fine tuned existing methods to the specific clinical question.

DR. MAMATHA BHAT

And this was only possible because of ongoing crosstalk and ongoing discussions with my computer science collaborators such as Bo Wang, Anna Goldenberg, who really had also that ability to create new methods based on the clinical question and the nuances of the clinical question. What I find in the literature in general is that many people will use off the shelf machine learning tools that may not perform very well. And then in the end may not transfer very well to new environments. So the novelty in this series of studies is really the ability to create new methods that are going to perform very well, for that specific clinical question.

BTB

I'm curious Mamatha of the fact that these were purpose built tools specifically for your research, does that get in the way of being able to scale these programs to be able to use this particular program, you know, in clinics around the world?

DR. MAMATHA BHAT

So that's an excellent question. And in fact, that's something that we are wanting to prospectively study, we are now deploying these machine learning tools. So the paper with Bo Wang additionally, a more recent paper on graph fibrosis, where we developed a machine learning tool to predict graft failure and fibrosis, we've created the data engineering infrastructure to prospectively validate these tools in our liver transplant program. Now, what ideally we would do is then also evaluate the performance of these algorithms across various centers, not only in Canada, but also worldwide.

DR. MAMATHA BHAT

And I think what we will find is that the algorithm performs somewhat differently across different institutions. And what we will then do is identify what are the factors that are causing compromised performance in certain settings, and how we can fine tune the algorithm accordingly, based on that knowledge to optimize performance in those newer settings.

BTB

And I'm curious on the business side or commercialization side, because you are again, creating these programs purpose built for your research, is it important to perhaps be patenting these programs, so that in terms of commercial ownership, it's with you people at UHN?

DR. MAMATHA BHAT

I have been working closely with our commercialization at UHN to discuss the potential for patenting, as well as wider scale deployment. And certainly these are ongoing discussions. As I was publishing these papers, to be honest, I was very interested in the academic side of things, and I hadn't really planned for the commercialization aspect. But certainly, it's something that I've been encouraged to look into. And this is something that I think will help us scale this up at a broader level.

BTB

The reason I ask is because it's not like you're taught commercialization and the business side of medicine and healthcare research. Would you have any advice for younger people in this regard?

DR. MAMATHA BHAT

Yes, I think it's important to consider that aspect as one starts submitting papers to publication. If this is a discovery, or an invention that could have broader impact, it's important to consider that before

starting to disseminate your work more broadly. And that's something that I've learned along the way, and certainly something that I consider these days when I submit papers for publication.

BTB

I'm curious about your reaction to the results of the first paper in 2021, just personally?

DR. MAMATHA BHAT

I think as a clinician, what I found very exciting was that ability to personalize the care of an individual. It's not something that I'd seen previously within my own field in hepatology, so in liver disease and liver transplantation, and I found that to be very exciting. So the ability to actually say to an individual patient, this is what you could do to change your future to change the trajectory of your health over the coming years. So I found that potential to be very exciting for my field of research.

BTB

And in terms of the clinician and impact. I'm curious, what do you envision as being the potential of how to apply these programs?

DR. MAMATHA BHAT

I think in liver disease and liver transplantation, this is an area of research where there's a lot of this complexity and pattern recognition happening. So when we look at blood test results, we are looking at patterns to say, well, this person most likely has rejection or this person most likely has fatty liver disease as the cause for their liver enzyme elevation. So we're constantly looking at patterns. And I think that having machine learning tools that can simulate those predictions, simulate those diagnostic and therapeutic response predictions is going to be very helpful from a clinical practice perspective. Now, I would say that these algorithms should not substitute the decision making of the expert clinician. They should be used as co-pilots in that decision making process.

BTB

I was going to ask you about that because a lot of people are concerned about AI and the fact that, you know, does it become the doctor, but that's not really the case. It's a tool that you can harness to help you become more proactive, obviously, in terms of Preventive Medicine in the clinic,

DR. MAMATHA BHAT

Yes. And I think what it can do is actually bring something up that you may not have thought of, for example, all of us are very busy in our clinical practice. And so we may not realize that there has been this gradual decline in someone's kidney function over time, and that we should be proactively changing someone's immunosuppression, or someone's management in general, by virtue of that

gradual decline. So if we don't do that at this point, then that person could ultimately end up needing dialysis.

DR. MAMATHA BHAT

So what can we do to change that trajectory? Well, this machine learning algorithm could help us identify this as a problem. And tell us well, these are things you could do to change that trajectory. And I was also going to add that our prospective evaluation will include these changes in management that occur, and we are going to feed that data back to the algorithm so that the algorithm can learn, become more robust, and it learns from what those changes have caused, in terms of outcome.

BTB

So I'll put you on the spot, do you have a prediction for how then this might help liver patients after transplant in terms of long term survival?

DR. MAMATHA BHAT

Right now, we have actually determined that the life expectancy of liver transplant recipients is 20 years less than the Canadian average life expectancy. Anything we can do to improve on that and ultimately, transform transplant into a cure would be a huge step forward, I think. So the ability to personalize the care of patients using these algorithms is really promising. And I think that over the coming years, there are developments in say cardio metabolic disease, including the dramatic uptake of GLP-1 receptor agonists, SGLT2 inhibitors, these are all therapies in the diabetes sphere, there are newer treatments in the cancer sphere. So what this sort of prediction will do is help us understand where our therapy should be going as well.

BTB

In your clinical practice, have you translated the findings from these research papers into practice yet?

DR. MAMATHA BHAT

Yes, we have developed the data engineering infrastructure with the close collaboration of Mike Brudno, who's the chief data scientist for UHN. And so his team has a lot of expertise in the development of the data engineering infrastructure to facilitate deployment of machine learning tools. Now, what's unique about our tool is that it integrates clinical and laboratory data over time. And this is somewhat unique and different to the other machine learning tools that are currently in deployment, which use more imaging data.

DR. MAMATHA BHAT

And so I think it'll be very interesting for us to see how this can impact outcomes both short term as well as long term. The other thing I should say is that we do have patient partners engaged in our work. And so our patient partners are actually critical to informing how best to develop the dashboard and present

these predictions in a way that is clear to patients. But it's also presented in an empathic way. So we want it to be presented in a way that will then empower patients in their own care.

BTB

Let's touch on another 2021 study of yours where you found women are at a disadvantage and are more likely to die waiting for a liver transplant than men. Why is that?

DR. MAMATHA BHAT

Our current prioritization system takes into account four laboratory tests so four blood tests, and those are the INR which is representative of the clotting function. The bilirubin, which is a byproduct of red blood cell breakdown, but is conjugated or produced by the liver, creatinine and sodium. So those four blood tests have been shown to reflect the severity of liver disease in an individual. This particular scoring system was developed based on a hepatitis C heavy population. So it was developed actually back in 2002. And it subsequently underwent some refinement some years later. And this is the particular scoring system that we've been using in Canada in Ontario since November 2012.

DR. MAMATHA BHAT

So what we have realized over the years based on the US and Canadian experience is that this particular scoring system, unfortunately disadvantages certain subgroups of people because it doesn't reflect the severity of liver dysfunction of women as well as those with biliary diseases such as primary sclerosing cholangitis, or primary biliary cholangitis. The reason for women being disadvantaged is many fold. So the creatinine and the sodium, so the creatinine represents kidney function, but it also correlates with muscle mass. And so women on average will have lesser muscle mass than males. And so the creatine intends to under represent the severity of liver dysfunction in women.

BTB

So it's not an accurate measure in terms of liver disease within women?

DR. MAMATHA BHAT

Correct? Yeah. So what happens is actually in progressive liver disease, the kidneys go along with the liver. So the problem is that there's under perfusion or the blood supply to the kidneys is compromised. And over time, there is this worsening kidney function that occurs in conjunction with the progressive liver disease. And so the creatinine is one reason.

DR. MAMATHA BHAT

The other thing is that women tend to be shorter stature and of smaller body frame than males. And many of the deceased donor organs, most of the deceased donor organ offers come from male deceased donors as opposed to female deceased donors, because of the causes of death. Stroke, and maybe motor vehicle accidents, suicides. So these were all unfortunately, the causes of death in

deceased donors and most deceased donor organs will tend to come from males as opposed to female. So in order to say match the size of that organ to the female recipient, the donor has to be of similar body frame to the female recipient.

BTB

What's been the reaction to this paper?

DR. MAMATHA BHAT

Our paper actually showed that women had a lesser chance of attracting a deceased donor organ offer. And the fact that our program, our liver transplant program offers living donor liver transplantation, as a path to transplantation, have resulted in equity on the waitlist. So it resulted in this ability for women in our program to have equal access to transplant as compared to men with decompensated liver disease or end stage liver disease. Now, I think this is not the ideal because ideally, we would want to refine the prioritization system to be more equitable to women, as well as those with PSC or primary sclerosing cholangitis as well as primary ability cholangitis.

DR. MAMATHA BHAT

And actually, that is something we are currently working on through a CIHR funded study, we have developed, deep machine learning method to account for such disadvantage. So all the factors that lead to that disadvantage, and optimize that prioritization on the waitlist for women, as well as those subgroups that are currently disadvantaged.

BTB

I guess there's an educational component perhaps that could be triggered by your findings in terms of awareness for organ donation and in terms of signing your card?

DR. MAMATHA BHAT

Yes, certainly. So when I discussed this paper a few years ago, when it came out, certainly there was a lot of talk about how we needed to, as a community, increase awareness of organ donation. This was work that I disseminated through channels such as the Canadian Liver Foundation, and the Canadian Donation and Transplant Research Program, with whom I've worked closely. And this did certainly create awareness that we need to do better in terms of organ donation. As well, this served as an impetus for this current work, which I think will help make prioritization more equitable across patient subgroups.

BTB

Your lab has been called the first translational research program worldwide dedicated to improving post liver transplant Outcomes. What's the genesis of that mission that you created for you and your team?

DR. MAMATHA BHAT

I've actually been very interested overall in certain indications for transplant, including fatty liver disease, as well as liver cancer as indications for transplant. And what I observed in my clinical practice, and my interactions with patients really served as the genesis for this program, because I saw this as an area of research where there wasn't that much work going on. And I felt that my interdisciplinary background would be well suited to generating new knowledge that could improve such outcomes.

DR. MAMATHA BHAT

So, in terms of my research background, I have a PhD in bioinformatics and molecular biology. So I had a background both in the wet lab as well as in bioinformatics. So the analysis of omics data pathway analysis. So that kind of interdisciplinary expertise was actually what served as the inspiration for my program. And then I brought together the machine learning angle to kind of bring all of this together.

BTB

You're listening to Behind the Breakthrough, the podcast all about groundbreaking medical research, and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christine Coté . And today we're speaking with Dr. Mamatha Bhat award winning scientist at the Toronto General Hospital Research Institute. Dr. Bhat is pioneering research to improve the outcomes for liver transplant patients. Mamatha, you were born and raised in Montreal, you've talked in the past about growing up loving science, especially biology. And yet, for a while there, I understand you were leaning towards a creative passion, playing violin and dancing What or who was it that finally steered you into medicine?

DR. MAMATHA BHAT

I think you know, it was a series of experiences over time and mentorship over time. In high school, I was always very interested in biology as a subject, as well as mathematics. So I think that's part of the inspiration for the use of AI in my work. And then over time, I had mentors along the way. So in high school, as well as in CEGEP, which is pre University in Quebec, I had inspiring mentors in the area of biology, that really inspired my passion towards medicine and heading towards that career pathway. I also had volunteer experiences during those times, so interacting with physicians as mentors, as well as interacting with patients, having discussions with patients and I thought that pursuing a career as a physician would allow me to both create new knowledge and also care for individuals with various conditions.

DR. MAMATHA BHAT

Now in terms of liver disease and liver transplant, that particular interest came up during my internal medicine training, when I met patients with end stage liver disease who underwent transplant and I was really impressed by the dramatic transformation, people who were at death's door, going through the process of transplant and coming out of this, within a few hours, their skin color had returned to normal and they were away, and were able to live, ultimately, normal lives within a few months after that transplant. So I saw that trajectory that really was so impressive. And I had mentors in that field at McGill University, which is where I did my medical training, who really inspired me towards that path.

DR. MAMATHA BHAT

The other thing is hepatology, as I mentioned, there's so much complexity in the biochemistry, it's our metabolic factory. So the liver is our metabolic factory, it performs over 500 functions. So it's a very fascinating organ. And it's an organ that has no machine that is able to replace its critical functions. There is dialysis for people with end stage kidney disease, there are machines that can keep people alive if they have end stage lung disease or heart disease. But there is nothing out there that can replace the critical functions of the liver. This is the one organ that is so complex that its complexity cannot be replicated by a machine.

DR. MAMATHA BHAT

So I just found that very fascinating that this is our metabolic factory that is able to perform so many complex functions, yet it is somewhat under appreciated. You know, you only realize its importance when it breaks down. And so for me, it was really amazing to see how transplant could address that problem, address that presentation at death's door, and really help people enjoy a second life. That miraculous transformation was really something that was impressive to me as a trainee.

BTB

You've mentioned along your career path, the critical role that mentors have played for you, you now run a very robust lab. You have fellows and people you're mentoring, how do you take what they taught you and how do you then now translate that into your mentorship style?

DR. MAMATHA BHAT

It's interesting, I run a highly interdisciplinary program. So as I mentioned, I come from an interdisciplinary background. And so I have recruited and taken on students with interdisciplinary expertise so I have members on my team who are computer science trainees, I have clinical trainees, people who have this bioinformatics and wet lab expertise. And what I do is try to recognize what are the unique skill sets of trainees and bring them together so that they can generate new knowledge. And I use my clinical experience to inspire those research questions. And I think that's really the highlight of my program. It's highly interdisciplinary and recognizing complementary skill sets so that you can generate new knowledge. So that's how I try to inspire my trainees.

BTB

Now, as a clinician, you see patients, you see their need for improved treatments for cures? How do you reconcile that urgency of their need with the fact that science takes time?

DR. MAMATHA BHAT

You're absolutely right. Science does take time. And I think that as a clinician scientist, we have this unique ability to recognize what are the clinically important problems. And we can take inspiration from our experience with patients. So say, when I'm on the liver transplant ward, I also will reflect on what might be clinically impactful questions that I can then bring back to my research team. And as I said, you know, I've had discussions with patients on a few occasions where they bring a question up, that then triggers a research idea in my mind, that could then be brought to the clinic. So in terms of research, coming to the clinical setting, I think, if we're working with data that already exists, it is easy to take lessons and generate new knowledge from that data, and develop algorithms on that basis. So that's been a basis for my research program.

DR. MAMATHA BHAT

But if one is looking to generate new data, such as omics data from samples, you know, liver samples or blood samples, then that is certainly something that is going to take time. So I think for the most impact, certainly science takes time, you know, if you want to have the greatest impact on patient care, and patient outcomes, this is not something that you can do overnight, it certainly takes a lot of persistence, and also reflection on what might be the most clinically impactful questions to work on and to focus on.

BTB

I'm curious, do you ever feel pressure in your work?

DR. MAMATHA BHAT

Yeah, I would say in the clinical work, certainly, I'm working with patients who have end stage liver disease, and certainly there are patients who pass away unfortunately, on the waitlist. So 20% of patients on the waitlist pass away, unfortunately. And so we want to advocate and try our best for our patients. But there are certain things beyond our control, including the availability of organ offers. So I think that is certainly pressure on the clinical side.

DR. MAMATHA BHAT

On the research side, I think generating that new knowledge requires that one, apply for grants, and bring together papers to publish new results. And certainly that is its own pressure. But I would say that overall, I enjoy the diversity of practice that I have both clinical and research, and the ability to mentor trainees in that work. So overall, I would say, you know, although there are certain pressures to this work, I'm very satisfied and very happy with the team that I've built and that ability to create new knowledge that will help patient care and patient outcomes.

BTB
There's a Nobel Prize winner named Dr. Elizabeth Blackburn, who was asked about the virtues of successful scientists, what does it take? And she said, resilience, persistence, as well as being opportunistic and creative. Does that resonate with you at all?

DR. MAMATHA BHAT

Absolutely, it resonates with me. So I would say, one has to be nimble and willing to incorporate new tools and new techniques into one's work to address specific questions. So this is something that I've adopted as a philosophy in my work as I mentioned. I've often reached out to potential collaborators with complementary skill sets or skill sets that are completely different from my own. Because I felt that that would enrich the ability to answer interesting questions. I think one has to be very reflective and creative and nimble, to adapt to new changes.

DR. MAMATHA BHAT

So this AI that has now become a critical element of my research program. It's actually what I I'm known for now beyond UHN. I brought that into my research program as I was just launching it. And that was at a time when people were very skeptical. So in my field, when I said that I was planning to use such tools in my program, there was a great deal of skepticism. Because people weren't aware of AI, say around four years ago, there was a lot of skepticism. But nowadays, there is so much more awareness and interest in incorporating such tools. And many people are looking to incorporate machine learning tools into their program. So I recognized that this was an area that had a lot of potential in my particular field. But I started that at a time when people were not as aware, and were actually skeptical. So I think maybe one message is recognizing newer tools, and also pursuing incorporation of such tools, even if there is maybe a reluctance of the larger community to embrace them at that time. So that's one thing.

DR. MAMATHA BHAT

The other thing in terms of persistence and resilience, I would absolutely agree, I think, as a scientist, one needs to be very persistent and motivated. So to continue working on research, even when there are negative results, or even when your grant gets rejected, you should always go back to the drawing board and see what it is you can improve about your research, what are changes that one could make in order to make this research project work. And if it's something that will not work, then recognizing that and putting that aside. The other thing for me anyways, I felt like working on different questions of interest within my field, and really inspired by the clinical applications and questions was also critical in helping me progress this research program.

BTB

In terms of disseminating your work, and putting it out there, there's a constant challenge I see for scientists in terms of how to amplify your work in a way that's accessible, so that it reaches the widest

possible audience, not just preaching to academia, what would be your guidance to young scientists in that regard?

DR. MAMATHA BHAT

I think it's very important to read broadly about the field, or the area of research that you're working on. So not just focusing on the minutiae of maybe a certain protein, or a certain pathway, and its role within the disease, but looking at the disease or the condition more broadly. So understanding where your work would actually fit into the larger scheme of things is very important. And that can only be possible with a broader awareness. Now, how do you make this accessible to the general population? We often use scientific terms when describing our work. And I think it's important for trainees even to acquire that skill of being able to present your work within a few sentences. So say even someone from the general population asks about the research that you're doing. You present it in verbiage that is accessible, and I think that's the way that people will understand the importance of research, and the importance of that research in helping people fulfill their optimal health.

BTB

Yeah, advancing outcomes in the clinic.

DR. MAMATHA BHAT

Yes.

BTB

Right away.

DR. MAMATHA BHAT

Yeah.

BTB

Or down the road. Exactly.

DR. MAMATHA BHAT

Yeah. And I think actually, at a broader level, if people in society understand the importance of this-

BTB

Exactly.

DR. MAMATHA BHAT

…research, then you know, the federal government may increase investment in research accordingly. So I think you need advocates. At the societal level, you need patient advocates as well. So I'd encourage trainees to also engage with patient partners if they can through different society. So like, say, in my field, it's the Canadian Liver foundation or the Canadian Donation Transplant Research Program, that are the associations or foundations that can help you connect with patients and understand what is the clinical inspiration for their work, so that they can also understand how to broadly disseminate their knowledge.

BTB

There's a leadership expert we like to quote here on the show named Simon Sinek who has a great line where he says people don't buy what you do, they buy why you do it. Why do you do what you do?

DR. MAMATHA BHAT

That's a complicated question. I would say, you know, because there are different factors that inspire me in doing what I do. Certainly, as I mentioned, my clinical experience and interactions with patients certainly inspires what I do. Working with trainees and discussing interesting ideas certainly inspires the research that I do as well, and we often will discuss the most recent machine learning papers or the development of new methods to address specific clinical questions. And I think that's very exciting, you know, that ability to generate that new knowledge, I find very inspiring. I think those were the main reasons for why I do what I do, you know, the ability to ultimately improve patient care, and outcomes is a critical element of my program.

BTB

So what's next for you and your lab? What should we look out for?

DR. MAMATHA BHAT

I'm very interested in integrating omics data with clinical and laboratory data for personalized predictions. And certainly, we have projects in this regard that are in the pipeline. And I think that's really the way that we can drive progress in medicine by using all the different pieces of data that are available or generated to personalize predictions and outcomes for that individual patient in front of you.

BTB

Dr. Mamatha Bhat award winning scientist at the Toronto General Hospital Research Institute. Thanks so much for sharing your pioneering work and continued success.

DR. MAMATHA BHAT

Thank you so much, Christian, it was really a pleasure to speak with you today.

BTB

For more on Dr. Bhat’s research, go to our website, www.behindthebreakthrough.ca or uhn.ca. And click on the drop down under UHN news. And let us know what you think we crave feedback. That's a wrap for this edition of Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at the University Health Network in Toronto, Canada's largest research and teaching hospital. I'm your host, Christian Coté . Thanks for listening