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TRANSCRIPT - GR 05 30 2025 **"Research Lecture: Global Health Research in Times of Uncertainty"** guest speaker Scott Heysell, MD from the University of Virginia

Internal Medicine Grand Rounds

- All right. Welcome, everyone. We are nearing the end of our medical grand rounds season for the current academic year, and I think really have a highlight ahead today is the end of our Kerry Marshall Thorner's scholars Day Slash Week. So we've had several events this week to celebrate research within the Department of Medicine specifically around our residents, fellows, grad students, undergrad students, med students, all manner of students and trainees. So we'll announce some awards from our poster session and oral session. Now, prior to Dr. Scott Heisel's lecture on Global Health Research in times of uncertainty. So I'll invite up our research associate program, director, Dr. Jeff Sterich, to help hand out awards
- 1st off publication awards on the far left over there. So we have. We're recognizing 3 publications from trainees within the department of Medicine with high impact factors. First, st by Farhan, Nas. Il. 33, protects from our current c difficile infection by restoration of humoral immunity in the Journal clinical investigation. So congratulations to but nice.
- I'm gonna our second publication award to Vikram Sabhapathy, St. 2 positive t regulatory cells and renal inflammation and fibrosis after ischemic kidney injury in Journal of American Society of Nephrology and our 3rd publication award, I don't see here, Dr. Sean Doherty precision Oncology and melanoma, changing practices published in the Journal of Nuclear Medicine for our poster award winners. So 5 presenters receiving poster awards. First, st Iblin Goggins pulsed ultrasound targeted to the spleen mitigates against kidney injury and permits kidney repair. Don't see Iblen here. Oliver Pelletier. Program. Cell death protein. One regulates metabolic activity of regulatory t cells. In ischemia induced Aki
- Dan Bailey from developing. We've got one here. Daniel Bailey, developing a probe-based bioconjugation methodology to capture and identify the bacterial targets of chemokine derived antimicrobial Peptides.
- Right? Poster.
- Yeah. Okay? Oh, you better. Yeah. Thank you.
- Great last 2 poster presentations of Bjt revendron coronary calcium score versus coronary stenosis for the prediction of Major cardiovascular and transplant related outcomes in lung transplant patients and last poster recipient Mary Mcgrath, rates of hepatitis B vaccination in patients listed for liver transplant room for improvement cheering from the back row of grand rounds, our oral presentation recipients, and I don't know that I saw either Walk-ins first.st Becky Brown characterizing Serocitis type. Gvhd. I don't see Becky here, but claps for Becky and our other oral presentation winner, Sarah Young, improved survival with Sglt 2 inhibitors and immune checkpoint inhibitors and metastatic solid tumors. So congrats to Sarah right? And then I'll invite up Dr. Rahul Sharma to help to recognize the shirt to Jew immunology award.

- Thank you very much, Dr. And the organizers, for giving me the opportunity to present this award. It's a distinct honor and pleasure for me to be able to hand over this award because Dr. Shartij you was my mentor, and I was his unfortunately, the last mentee, before he was untimely taken away by lung cancer.
- To give a brief introduction. Dr. Zhu. He was an immunologist by training, and he was recruited to Uva School of Medicine Department of Medicine in 2,002 from Boston University. So he did his bachelor's and master's in biochemistry from National Taiwan University before joining Harvard University for his Phd. And he worked with Baru bin Asaraf and who's a Nobel laureate? And then he also
- I'm forgetting here, trained with another major immunologist, and I'm right now I'm blanking out. I thought, this is going to be after the grand rounds.
- But I don't have my glasses good founder.
- So with Alfred Nissanoff, so Alfred Nisanoff and Baru Benasar are the people who are actually critical for determining the structure of antibodies and its relation with antibody function. So some of the things that you see in classic textbooks is the work on which Dr. Zhu worked with Dr. Borubin and Alfred Nissanoff. Afterwards he joined Harvard Medical College as a professor, as assistant professor, and rose all the way, all the rank, all the way to full professor, where his work continued to on T cells and B cells, and his fame is that he was the 1st person to show that the helper T cells, the CD 4 t. Cells can kill in a fast and fast like independent manner, a phenomenon known as Aicd or activation induced cell, that to those who would have come to my mis class and learned about that. So this is how immune system gets down regulated. But for me it was new to immunology, and he he invited me with open arms. I was just a molecule virus, and he gave me the freedom to work on autoimmune diseases.
- And then that's what he does to all his trainees, and he was always open to interact with people, and you would always find him in the hallways giving advice to people and giving away reagents and authorships on projects and work so very generous, and mentor so unfortunately, he was taken away untimely
- at very young age. In 2,006. He was diagnosed with lung cancer, but it was a 6 years long battle, but he kept working throughout those 6 years, and me and him we published over a dozen papers during that time, and he was working up until the last week of his passing away, doing experiments in the lab even through all those cycles of chemotherapy, irritation, therapy so very inspiring. So
- now with that, I would say that he was a very not only dedicated scientist, but a very loving father and grandfather. He was fortunate to see his grandkids before he was taken away.
- so I'm happy for him, and he was full of life, full of zest, so happy to be associated with him, and and very happy to be able to present this award.
- So so this year our voters on the churches, you immunology award. We had a tie between again, Vikram Sampathy and Hira Inuit. Okay, wow! That's even special. So
- Vikram Savapati is my mentee. Well, you weren't 1 of the judges. So yeah, I was not one of you get to help present, not judge. Yep, so so congrats to those 2 investigators. Right?
- I think we have late arrival of one of our oral presentation winners. So, Dr. Young, if you want to come down quickly and grab your award, and then we'll start our lecture.
- Seconda. Right?

- Okay. Well, thank you to all our presenters for the great projects. And now we'll transition into our lecture from Dr. Scott. Heisel.
- Take us through our Cme. Slides.
- Dr. Heisel's objectives.
- Yeah. Clicker is not working all right so we'll leave the mouse out here for you. Scott and Dr. Shaina Hassan will now introduce our speaker.
- All right. Well, good afternoon, everyone. It's my distinct pleasure to introduce our grand round speaker for today. Dr. Scott Heisel. So, as a Northwest native, Dr. Heisel obtained his medical degree at Oregon Health Sciences University, and went on to complete a master's of Public Health degree with a focus in epidemiology and biostatistics prior to attending Yale University for Residency training in internal medicine and chief Residency. Afterwards he completed his fellowship training in tropical, infectious diseases, and Tugela Ferry, South Africa followed by further infectious disease training. Here at Uva his field experience includes living and working in rural South Africa, Tanzania, Bangladesh and Siberia, focusing on reducing global health inequities related to HIV and tuberculosis outcomes his research group strives to carry forward innovations through implementation of clinical trials, including a focus on pharmacokinetics and pharmacodynamics and modifying host responses to mycobacterial diseases. He also supports partners worldwide in an effort to reduce tuberculosis, related deaths and correct factors that contribute to tuberculosis, including poverty, health system management, and chronic medical conditions, such as HIV and diabetes. We're very excited to have him join us today, so please join me in welcoming Dr. Heisel.
- All right. Well, thank you, Shana. Thanks so much to the chiefs for inviting me, Dr. And others. This is a real treat. I was once in the shoes of those that put a poster together for this week for scholars. Week recycled. Perhaps you know a few ideas from poster to poster to get it done just in the nick of time, and I'm also really grateful to be able to reflect a bit today on my research career path in a very uncertain time. But I'd like to sort of strike a balance between doom and hope, and and hopefully sort of chart a way forward for us together.
- I will also just acknowledge that. I'm really thankful that you're taking a part out of your day for this. There's a competing meeting at the School of Medicine to talk about the fate of research and how we're gonna make our way through it. And I know many of our faculty are there right now. Also grateful to colleagues from Uganda, Tanzania, South Africa, that are online and joining us by zoom. So.
- So I was asked to put the talk together. I came up with sort of this title a general title, Uncertain Times. And I think it is, is no longer uncertain. I think it's certainly frightening. I think it's it is certainly
- harmful and harming people around the world in the way that we have as a nation chose to address health and chose to politicize health. So, of course, Usaid has been completely gutted. And that's having direct negative health impact around the world.
- I'll talk a little bit about a new Nih policy to restrict foreign subcontracts. So we receive a grant at Uva as a prime institution, and then we have a separate subcontract, for instance, to our colleagues in Tanzania.
- There's now policies that will restrict that, and some of us believe that that might be a limitation to performing any further work abroad any further research work abroad. But don't just take it from me, take it from a Uva grad.

- Francis Collins, former director of the Nih. Led the Human Genome Project. He says, that particular decision that I just mentioned will have tragic consequences. Children in low income countries will lose their lives for research that doesn't get done research into Tb tuberculosis research into malaria.
- So with that, these are my learning objectives. I'm going to try to mention a bit of our own research, and how that sort of informed the way that we think about Tb. And particularly tuberculosis among populations where it's more common. I'm going to share some personal stories as we go along.
- But I want us to really reflect on the commonalities of what drives conditions like tuberculosis in places where it's more common and how that's shared with what's driving illness here in the Us.
- I'm going to talk about global health. But Charlottesville is on the globe. The Bronx is on the globe. Brownsville, Texas, is on the globe.
- So we're gonna try to again strike some balance of of hope here as we work through this nationalistic funding environment.
- So I'd like to start my personal story with my 1st real scientific mentor. This is Dr. Jerry Friedland, one of the Aids doctors, as you see here on the cover of Newsweek.
- We have Aids doctors with us here in this room, Brian Wispelway. We just celebrated the retirement of Greg Townsend. We have those types of physicians here at Uva, but Jerry was really the 1st person that I met in residency that inspired me to become a scientist.
- I thought scientists were those that pipetted in a lab, and I wasn't really sure what this was all about, and he started working in a place in rural South Africa that I'll mention and we had the opportunity to work with him there during Residency during Internal Medicine Residency, and then went on to live for a year afterwards, completing what was for the 1st time really research in the context of living with people, with with the diseases that we were, we were focused on.
- Jerry was the most and is just the most joyful person I can remember. You know we've talked about just how challenging it was to care for people that were dying from HIV and Aids when there was no treatment.
- He is the son of Jewish immigrants from Eastern Europe, and grew up working in New York City with his dad on Saturdays. His dad was a window washer, and he hated working on Saturdays with his dad because his dad would make him wash the bottom of the windows. Dad, get the tops, and the bottom is where all the drunks would would urinate overnight, so so he hated it.
- But he's hilarious, and I could. We were in the back of a vehicle like in rural umzula Natal, and we're like caught behind these 2 cows that are like squeezed in the back of this truck. And you know we're just had this really deep conversation, and he kind of like looks at me, and then looks at the cows, and it's like, can you imagine what those cows are thinking right now, like we? Our day started off so different? You know. How do we get here right now and then? Proceeded to like, you know. Think about the cows for 15 or 20 min so I got a chance to to go and live and work in Tegela Ferry, South Africa at a time when there was an extensively drug resistant tuberculosis outbreak that we were trying to figure out and control and I learned so much from the people that you see in this photo. So this was back. You you'll notice, like a few differences.
- And this is when I was still sort of working as a shampoo model. You'll also notice Dr. Tanya Thomas, my partner in crime. And you'll also notice this little one, too,

who was there strapped to my chest during the time that we were having our Id badges photographed.

- And so our 1st daughter was there, and our only daughter, I guess. But 1st child was there with us, and and so she taught us how to connect with community, and we became friends with all of those that we were living and working with at the time and the research questions that we had were born from those conversations, and I learned as much from Gogo Gogo's the older woman that you see in the bottom here about opportunistic infections than I did from a textbook.
- Here's a photo of of Jerry just a little bit ago. And now that little one there is standing next to me at age, 16 years old, with the rest of our family, Jerry's wife, Gail.
- So you know, when you think of HIV and Tb. And I even sort of prompted you with some of these images you might think of that man in the eighties wasting away. You might have a racialized impression of what HIV and aids is, and where that is in the world. And I bet if you close your eyes, you're probably going to think of something a little bit different than the rest of the story that I'd like to share.
- So I had an opportunity to work quite extensively in a part of the world where HIV is increasing like nowhere else in the world, and that's in the Russian Federation.
- So this story sort of begins in Irkutsk, Siberia. This is sometimes known as the Paris of Siberia. During the Bolshevik Revolution many were exiled. The poets, the theater folk were there and and started this vibrant community but I had the opportunity to travel with direction of my now current division, chief, Eric Haupt, who, you'll see seated in the middle. I'm there to his left, and we were there at the invitation of some colleagues to learn about tuberculosis and understand drug resistance patterns and we were also accompanied above Eric's shoulder to his right by Galina Lyles, a former pulmonary, critical care fellow, who, some of you might know. But she was a medical student at the time. It's remarkable that we were able to to travel with a medical student with the approval of the University of Virginia to Irkutsk, Siberia and the other person that I want to highlight is the older man above my shoulder. That's Harvey Sloan. And so Harvey was there to help to organize a medical education component of the trip on behalf of an Ngo. He is the former mayor of Louisville, Kentucky, a lifelong physician and politician.
- He ended up starting one of the 1st Federally qualified health centers in the country, and was a force for change within the Kentucky political environment to the point where he ran a very tight race and lost for Governor of Kentucky, and then subsequently ran and lost an even tighter race or Senator from that State, despite having the endorsement of his good friend Muhammad Ali, whom he actually ended up running like the final sort of mile to this huge parade, with Muhammad Ali at his side. If you can imagine that, and ended up losing to one guy by the name of Mitch Mcconnell can imagine how different things might have been. Had that election gone a different way. He Harvey and and and I and Galena ended up having our flight diverted on that 1st trip to where we were hundreds and hundreds of miles farther north in Siberia in the middle of winter, and couldn't land on the icy tarmac where we were supposed to, and were diverted to the point where we ended up having to take an overnight train. We got on the train, and Harvey, just like jumped into his bunk and was fast asleep like it was, you know, the easiest thing in the world for him not so much for Glena and I, and so I kept in touch with him a bit and got back in touch with him after finding this book. And so he writes about his life of public service, which is just fascinating. He hobnobs by names, drops like with the best of them, talks about his friend Hunter S. Thompson, who's always high all the

time. The Clintons. It's a fascinating read but he was a student at Yale and would hop on the train hop, and he would ride the boxcars. Usually in the summertime. Many of us have probably ridden the New Haven line from New York City to New Haven, and he, just, you know, every once in a while hop on the train and get out and about. But it's an inspiring life of service.

- This will be my 1st of a few different book recommendations that I'll make throughout this talk.
- But to return to Irkutsk. We were there to think about tuberculosis. This man also thinks about tuberculosis. He says, as he addressed the who ministerial conference on Tb. That the disease claims more lives than any other infectious disease. That's true but it occurs in prosperous countries with high living standards, so sort of read into what he's saying. There, he's talking about white Russia, white, healthy Russia and it's compounded by all these socioeconomic losses. But he doesn't mention in the entire speech he doesn't mention. HIV.
- Well. HIV is actually the primary driver of tuberculosis in many parts of the world, and certainly in the Russian Federation there's more HIV incidents increasing incidence in Russia than there is in any country in the world, and you can see it's not just some sort of artifact of detection. There is an increase in incidence, but there's also a dramatic increase in mortality. So HIV is found. But HIV is not being treated in the same way as we think of it as a manageable chronic disease. Now here in the Us.
- And just look in the place where we're working in Irkutsk in the eastern part of the country. This is a seroprevalence survey of people who inject drugs, and over 50% of those were found living with HIV.
- So this is a problem of commercial heroin initially moving into heterosexual populations and spreading, as HIV spreads from person to person through social networks. But we were also wondering about again, just why is this not sort of a global emergency? And of course, it's geopolitical. And someone like Putin might feel that it's not necessary to sort of highlight that part of his country.
- But there is no research, very little research being done at this top at the topic at the time. This is just an example of how we looked at this, where we were searching different databases in both Russian and English, and there was a remarkable lack of research focus.
- And what I'll argue is that we research what we can. And we research what we can talk about. And when we're limited in what we can talk about. We're not able to address those topics in the same way that we could otherwise. So it's not that people weren't doing research at all in the country. They were focused on different topics because of funding because of what they were able to talk about.
- And this just gives you an example. The blue lines are, I think these are end up, being sort of annual prevalence rates. The Epidata is pretty terrible from Russia, a severe underreporting, but what you're supposed to see here is that the publication difference is very different for certain regions. And so, if the red line is sort of publications versus HIV prevalence. You can see a place like Siberia or the Ural region.
- There's a huge amount of HIV increase and very little published about it, very little research being done about it. So there's this mismatch. And in a country like Lesotho you just have a huge amount of research relative to the scope of the problem compared to a wealthy country like Russia.

- So where should the die-ins be? Where should people be excited and protesting and moving research forward in a way that requires advocacy. Well, in Eastern Europe and the Russian Federation, certainly, but it wasn't happening this example here from one of the big meetings that we go to, and Tb. And HIV here in Cape Town, you know, they're shutting down the main streets advocating for certain aspects of care, research, related care, or research related funding invest in Tb research, right?
- And then this is the single person that I found in the largest HIV Oriented conference in that part of the world, and he says repression and discrimination are barriers to HIV care. That's what his cardboard sign says. He was the only person that we found that we would sort of consider sort of part of civil society in that type of meeting and we know what improves HIV outcomes. We know what improves outcomes for people with Tb, these are the words that are now harder to talk about. We know that we need to end equality inequality. We need to be able to say words like racism, and how that impacts the care that one receives, how that impacts the type of research that we're able to do that. We care for people that are transgender, and we also provide transgender care. But we care for people that are transgender. And so we know this. This is the type of thing that we can talk about. But it's what's being restricted and becoming more and more difficult to do in a nationalistic research environment.
- And so this is what happens in autocracy. This is what happens in Russia to create the problem that you saw that I've highlighted in Russia. So this was maybe 10 or so years ago. It was illegal to post information for anything really related to gay men with regard to their health. They've restricted access to treatment for men who have sex with men.
- Pre-exposure, prophylaxis, or prep, which we commonly give is is unavailable. And sure enough there's increases in the amount of HIV and significant decreases in the amount of people being treated for the condition. Can you imagine in the metropolitan Liberal City, that is St. Petersburg, that there's 10% of people with HIV that are being treated.
- It gets worse. So Russia seeks to ban the international LGBT movement as extremist. This past 436 to 0 in their equivalent of Congress.
- But it can't happen here, though. Right? I mean, it's not really gonna happen here. Or so we thought, and kind of convinced ourselves that it might not happen here.
- You know there's Winsome Sears looking looking on as Governor Youngkin seeks to root out even even the terminology that's being used there by the Ap. To root out critical race theory and then maybe just to repeat this with sorrow for this court, but more for the many millions of American women who have today lost a fundamental constitutional protection.
- We dissent.
- So your 3rd book, recommendation.
- Second, it can't happen here right? It can't happen here. Some of you probably read this. It's worth reading again. Oh, my gosh, it's written in 1935, by Sinclair Lewis, talking about a Populist who ends up becoming President to sort of compare to Adolf Hitler, who was in his rise to dominance at that time, and talks about what life would be like with an American dictator. Buzz windrup was the character's name. He was the champion of the forgotten man sounds very familiar, doesn't it?
- So yeah, it can happen here. Right? So it has already happened. Oh we could have predicted it right. But these are the 1st grants that were cut. This is from yeah, the

7th of April. This happens sort of right out of the gate, but it's HIV aids, grants that are being cut, you know, focused on equity and transgender care.

- And so these are the. These are the political targets. It's happening to us here.
- So the Department of Health has cut massively the amount of care that we can provide, the amount of research that we can provide in the public health space. Our Ryan White grant the grant that ends up providing most of our care for people here living with HIV in our clinic has taken a massive hit. And so there are people that have been fired over the last couple of weeks that I would never have thought would ever have the opportunity to opportunity to do it would never have, you know, had never been in that situation. And even think I mean, there's 1 person I'll just mention so Veronica Ross is her name. Many of you know Veronica but she's provided more
- HIV care and cured or cared or treated whatever we want to to define as a treatment success without ever writing a prescription. And and she was fired because of because of a lack of funding and a lack of a political will. And and to the point, to this point, a lack of our local health system to to step up and to fill in where we need to fill in.
- So what happened to return to to Siberia?
- Well, we were there to think about tuberculosis and drug resistant tuberculosis and what we found was that all of the deaths in those with this very significant form of tuberculosis were among people that were living with HIV, and why were they dying? They were dying because they were not on antiretroviral treatment.
- And so I've had the good fortune to work with Eric Haupt, too many of, you know, and is just a very effective leader, and he can distill a very complex problem into sort of you know what needs to be the next sort of singular action. What can we do to take a step forward, and that, I think, was to, you know, to try to find a way to focus on antiretroviral treatment. This was different than what we were tasked to do.
- But along the way, you know, we got to do things like traverse deep into the tundra to to see things like a woolly mammoth, with actual hair and sort of dried blood and and and there's just vast amounts of sort of tunneling under the tundra in part that happened during World War 2 and beyond in the Cold War, to sort of protect Mother Russia with grain stores, should that should that ever be needed
- But what we ended up focusing on was taking a form of research, clinical research, community-based participatory research and adapting it for the Russian context with funding from the Nih in the form of an R. 21 and later an Ro. One and this was led by Becca Dillingham, whom many of you know, former faculty member and director of the Center for Global Health Equity. Before I had the chance to take on the position along with her colleagues, Karen Ingersoll, Avelena Waldman, who, you see, pictured there.
- And so this is just a way to connect people to one another. People that are living with HIV, living with tuberculosis to one another, connect them to human-based care. There's a community message board function, and we use this quite successfully in our patients with HIV here in the Us. And this was an evidence-based, research-based way to suppress viral load to improve a treatment for people with HIV.
- When we adapted it to the context, we found, not only did it improve those with HIV, but actually led to to a combined composite outcome, improvement of death and viral suppression. So about about, as you know, as good as one can get to the

point where we felt like we couldn't even take it forward in a clinical trial, because it was already sort of providing what we had best hoped for.

- This is just an example of sort of how the process was developed. This is sort of the implementation or pre-implementation part of this, where this is the thoracic surgeon at the TV hospital, Alexey Soldniski, and he sort of became this champion of the app itself.
- And you can imagine, you know, one of our thoracic surgeons getting really excited about an HIV app and then going to the HIV center and like helping to train infectious disease clinicians with the app. But that's what was happening.
- And and so I would again would never have thought that that was possible.
- But there was a lot of this sort of implementation framework that went into this, and we ended up sort of piloting it in certain ways and then expanding it in the second iteration, really across the entire oblast. So across the entire province we termed the app most, which was bridge rather than links, which had sort of a carceral connotation for people living in Siberia, and a lot of the work published was completed by Jackie Hodges, whom many of you will remember is now a infectious disease faculty at Duke.
- So it looked a little bit like this. We had funding from the Elton John Aids Foundation. We were able to sort of work with mobile testing and linking people together. This is the type of thing that we should be doing in the Us. And it's now been cut through mostly Cdc funding. But we're not providing and will not continue to provide, HIV testing and linkage to care in the same way that we have been able to previously when we were forced to stop mostly from Covid and other geopolitical tensions. This was prior to Russia's invasion of Ukraine. We had really remarkable success beyond our expectations in terms of the number of people that were found living with HIV and linked to care. You can see just some of the remarkable numbers in terms of those injecting drugs as an example and about 2,000 people or more were using this this application. And then this is just a photo that I think is important to appreciate as well is that you know these are also the victims. You know we are. We are victims. And and so this is a part of Russia that has very little connection to Moscow, and certainly very little connection to to the political elite. And and these are the people that that are suffering from those decisions.
- And so so we think, we we don't have this, you know. We don't have the connection to Russia, as you might imagine when we left, it was working, and we think it was integrated into the electronic medical record to the point that that application is still still in use. But as part of the cuts to the Ryan White HIV program here in the Us. And the country that we live in in the city that we live in. Positive links has been cut, and so you can go to Russia and use most. But you can't use positive links here in our our setting.
- So I'm gonna try to just get a little more positive as we work through this. Just get a little bit more hopeful.
- So because people were on antiretrovirals, we could do other things. The standard of care in Russia now was something where we could move forward with other studies. And this was a large global health study focused on tuberculosis outcomes and trying to understand the amount of medicine someone needs in order to optimally kill their tuberculosis, and we did so by looking at concentrations of drugs in the blood and looking at the relative drug resistance of their tuberculosis isolate. And we did so in Russia, but we did also, in places like Uganda and Tanzania and Bangladesh.and in Uganda we found that people with Sepsis and HIV that were

coming into the hospital that were very sick, met the criteria for sepsis. They had very low concentrations of the tuberculosis medicines in their blood, so not only were they really sick but they also were not having sort of adequate killing from their from their Tb regiment.

- So this led to a really remarkable collaboration among colleagues from Uganda, from Tanzania and this is a study that Dr. Chris Moore and I had the opportunity to lead is now in its final year, with lots of help, as you can see, Conrad Mazura, Edwin Wawagia, looking about 18 years old.
- Stella Vagama, Bb. Said Megan Null works with us here in the division, spends most of her time living in Tanzania. Mark Conaway from public health sciences is our statistician. And again, you know, Dr.
- Tanya Thomas. So what we had hypothesized was that because we found that many people didn't have the proper concentrations of Tb. Medicines in their blood, we also noted that it takes a long time to ultimately diagnose someone with Tb. And we were finding a fair amount of Tb. In those people with HIV and sepsis.
- And so we wanted to know if you gave someone Tb, treatment in the same way that we give Ceftriaxone for a bacterial infection, someone with sepsis. We give empiric antibiotics when someone comes in, it would be malpractice not to give someone antibiotics the moment that they hit the door with sepsis. If you're concerned about an infection.
- So we'd randomized the 2 groups. One got immediate treatment, the other got a high dose treatment, and that was a factorial design where we're able to look at those outcomes.
- And what we found is that the majority of people with HIV and Sepsis in Uganda and Tanzania had tuberculosis as their primary pathogen over half had. Mtb, so here in the Us. We often don't even find a pathogen, for sepsis is the minority of people that we find when we look for it here. Not only were we able to find a large number of pathogens, Tb. Was the most common and these data that you see here again, mostly just to focus on the amount of Tb that you can see in the large red column. These data were put together by Eva Otopolova, who, you also probably remember as a pulmonary critical care fellow, mentored by Jeff Stirk, a really exciting immunologic approach to sort of her career, is now an assistant professor at Tulane.
- But what we found sort of hot off the press is that among those people with Tb. Ultimately diagnosed with Tb. If you got anti-tb treatment immediately, you had a statistically significant improvement in your 28 day mortality.
- So this is just as exciting as it gets. This is, you know, as will be submitted to a a high impact publication, as as we like to say.
- But there was so much tuberculosis right? We found so much. Tb, there. And of course, I mean, this is what I think about everything is tuberculosis.
- So this is my next book, Recommendation. So this is John Green's Take on the World of Tb. Many of you might know John Green, one of his books.
- It has sold like 50 million copies, so he is a young adult author. Primarily, he is also a wildly popular youtuber. He and his brother have this Youtube sort of thing going called Vlog Brothers, and they're just fascinating, and they they are just unafraid to kind of, you know, interrogate these topics, and so he has thought about tuberculosis, in part because he has aligned himself with partners in health and had the opportunity to meet a young person by the name of Henry, who looked and acted a lot like his own son on a trip to Sierra Leone and chose to then think about

tuberculosis because Henry was suffering from Xdr. Tb. Or extensively drug resistant Tb. The same type of Tb. That I 1st encountered during my time living in South Africa and working with Jerry Friedland and others.

- And so he sort of takes this approach where you know all of our development in health here in the Us. Had some sort of connection to Tb. And we should know that history in order to understand how to move forward. But ultimately he does a job better than anything else. I've read recently to really center how this is happening. Our problem with a curable disease that we've known how to cure for many, many years is because we devalue certain human life in ways that lead to disease. And this is not like a new concept. But it's just a fascinating read. He'll tell you about a guy who you know, went to get his Tb. Treated at a sanatorium in Missouri. Around the turn of the century everyone was wearing coonskin caps, and it was like hot. And then he ended up, wanting to have something a little bit more stylish, but also protect from the sun, and so created this sort of felt cap with this really large brim went back to New York City and started selling this this hat and that guy's name was John Stetson, and so, you know, became this Stetson cowboy hat that we think of you know, just happened to exist on the Wild West somewhere. So I really really recommend it.
- But he talks about Henry and Henry was a young kid, and Tb. Is different in children as it is in adults, and certainly the treatment is different. There is very altered physiology. Some of our drugs for metabolizing medicines like Isoniazid, are not even mature. We don't have this enzymatic maturation until a few years of age, and so part of that same study that I mentioned, that involved colleagues from Russia and Tanzania, Uganda. We were able to look at childhood Tb. In children, where we noticed that outcomes were worse. And so the myth, in my opinion. But the mantra is that in the Tb. World, if you'd have a child that's diagnosed with Tb. As long as you get them on Tb. Medicines they do fine, and we didn't
- find that in Hydem where people in this room work, and we found that there was a lot of morbidity and mortality in childhood. Tb. And we also found that there wasn't adequate drug exposure, and despite even increased in dosages of medicines new who recommendations for children with Tb. We found that they weren't achieving adequate exposures.
- And then what was most fascinating is that we found that they were carrying other enteropathogens e coli salmonella shigella the same pathogens that lead to malnutrition, undernutrition, which is the most common driver of tb those same pathogens that led to the undernutrition related. Tb. Were then making their Tb. Harder to treat driving down the concentrations of their medicines, likely through a mechanism of enteropathy. And we have other data to sort of support that
- So this was a big finding, and we went ahead and have started a clinical trial to increase drug dosages based on a urinary assay that you can see here is represented by a receiver operating curve, showing that you can check urine concentrations of Tb. Medicines, and that's pretty equivalent to their serum concentrations.
- And we're going to increase medicines in some children early on. We're going to wait a few weeks and then increase them. So all children have the opportunity for that increase in drug dosage. But we're really going to interrogate the stool and the gut and figure out. Is this replicable? Are there mechanisms in the microbiome that would explain what we found?

- But I also mentioned this. Nih funded r. 0 1. it's up for renewal annually. It's early on, and it's 5 year, Grant, but it would come up for renewal, for instance, in November. And so we're about to start enrollment.
- And it's possible, if you read the letter of policy change, that this might not be renewed because of the foreign subcontract and foreign work. And so now there's moral dilemma in starting a clinical trial where we're exposing children to different dosages of medicines, where we may not be able to complete the trial and they're signing a consent form that says they're participating in this research because there'll be an outcome at the end that will benefit their community people with. Tb so that's that's what we're dealing with.
- And there's not a lot of ways to kind of see through this. There's a couple, and I'll and I'll mention.
- So one is, there's other forms of research. There's other forms of research community, and there's a long history of getting things done here in our institution. And so that same community that I mentioned in Haidm Tanzania was 1st interacted with in a meaningful scientific way with Eric Haup's research. This was done in the context of a malnutrition and enteric diseases focused. Grant, led by this guy, Dick Grant all across the world, and and Dick is the founding director of the center for Global Health Equity. And we have a lot of excited people thinking about global health and thinking about global health research. And so I'm invigorated by people that are you know, despite the climate excited to make this their career. So I think we need to remember that I think we need to focus on that. I love this picture of Dick. He's just like intellectually so inspiring. There is. There is almost no one I can think of that has as much intellectual curiosity. He's just interrogating poor Dr Justin mutter here after a great talk, but he's also incredibly generous. And so Dick and Nancy Grant have given money in order to fund research to bridge people. You know, people that are taking on a new idea and moving it in a different direction in global health equity. And so I have the privilege to bestow this generosity.
- Levi Bonk is a professor from global studies and anthropologist thinking about migrant health and health disparities on the Mexican border. You all know Chris Moore, who will tell us a lot about what's happening in emerging infectious diseases in Uganda and Michaela Dube, empowering Bolivian youth with autism, spectrum disorder.
- So this is this is the good part about what we do now? and I'll you know also, then mention my last book, Recommendation. So Levi wrote this book just as he was transitioning to faculty here called border hacker. So before he became an academic, he had a Fulbright to go to Mexico to think about the migrant health, or not even so much health. Just sort of you know. What was the migrant sort of crisis that was being described? What was it really like from an anthropologic perspective? And he meets a guy by the name of Alex, who was originally born in Guatemala, but he didn't know that grew up in New York City, and was trying to make his way back after being deported.
- Levi joins this migrant caravan, and I will leave it at that, because
- I learned so much about migrant health. I thought that I knew, and I did not know. I learned what it's like to, you know, someone to sit and sort of seek asylum, and what that asylum interview is like, and, as you can tell, I sort of understand a lot as I connect through through narrative. But
- But you got to read Border Hacker. Maybe of all the books I've mentioned, that's the one that I'd like you to think about. So I'll kind of wind down a bit. But this is one of

my favorite photos. These are colleagues that many of you in this room know, but a place in Tanzania on Kibangoto. Infectious Disease Hospital at the base of Kilimanjaro. This is a tree where we often sit outside, get a little food and think about what to do next with regard to research. And this particular photo happens to include colleagues from Uganda from Russia, from Bangladesh and I just also, wanna you know, we're listening to Museveni. Justine. Here. Who's speaking? I just want you even to kind of orient us to. You know the circle, the directionality of information, exchange of knowledge exchange?

- And we still, it's still hard, because you know, so much of the funding is is here in this us that we live in. But you know. So we still think of somehow, the problem solving has a directionality to it. And you know, we we can be the ones to sort of help problems that are more common elsewhere in the world in that unidirectional way. And that was not the case in these types of conversations that I've had.
- And so one thing that we've benefited from again from Nih funding is to be able to train our colleagues in a way that they are now positioned to compete for Nih grants of their own.
- So this is training grants for postdoctoral scientists that are poised to sort of have their 1st big breakthrough in research make their 1st big discovery or new research grant, but also research administrative training. And so there's now a pre award post award compliance office at Key Bongoto, the hospital that it showed you right nearby that tree that we can contact, and I can ask for the pre-award person, and an innocent Petro will be able to, you know, point me in the right direction in terms of how to sort of negotiate this new Grant submission process.
- And so, you know, it's been met with a fair amount of success. And this is just another kind of celebration, because we have to celebrate the good things. So this is Tanya here, with our longtime colleague, Stella Mpagama, and Blandina Mbaga, both of whom were trained with Eric Howe. But Stella and I have thought about almost every single tuberculosis, you know topic over the last 10 years that we've put pen to paper with. It's really been in conversation with her, and I love this photo from about 2010, with tea and hard boiled eggs, you know. I think you can get a lot done if you gotta got a couple of hard boiled eggs to keep you going.
- And so one of the things that Stella and her colleagues have focused on is what happens after someone has Tb disease. This is like long covid. Now, so what happens with the disability that incurs after someone is cured from Tb.
- We found that pulmonary rehabilitation, for instance, led by Tb. Survivors, can improve post-tb disability. This was also co-developed and analyzed by Edu Meadows. A current infectious disease fellow whom I know many of, you know.
- And so this is the trial that was just submitted, a new r. 0 1 to use nutrition, intensive nutrition, intervention, and pulmonary rehabilitation to improve outcomes.
- And this was submitted by Kibongoto.
- They're the prime institution, maybe, as a way to work around this subcontract issue. But just to to really say, you know, we're not the. They're the leaders. We're the helpers. We're not the leaders on this one and maybe that's and we benefit. We really have benefited from this, you know. Maybe this is how we we make it through. With this this type of arrangement.
- So a couple of reflections, and I'll conclude so. I think you've heard it, you know, through this this, you know few minutes that we've spent together, but I believe that health is a human right. Many other countries do. This is not a new concept.

- And the fact that we can't pass legislation to reflect that value we suffer from poor health here in the Us the system is working like it's supposed to work, you know. If not, everyone gets healthcare, because not everyone can pay for. You know what you need. That's just like just how it works. So the system is working as it as it is designed right now but it contributes to poor global health. And so when we devalue health here it can be used. It's harder to, you know, to collectively become angry about a poor global health outcome when we don't value it in the same way that we do here in the Us. It's collectively harder to become angry about not having research funding for a global health problem when we don't value health here in the same way, in the Us.
- There is a huge amount of work to be done globally right. And I think you've sort of seen that summarized here. But there is going to be a flood of research needs 3 years from now, 5 years from now, there's going to be an entire science about how to clean this up, an entire science, about how to correct what we now need to correct, and we are positioned. I mean, it will fall back to academia to do this type of work, and so we need to be ready for that and we need to remain energized to be able to do that.
- I had a really good friend. Just text me this this week. And she said you know there's they've cut a lot of branches, but the roots should remain strong. Let's hope they hold for some. You know, some regrowth, and that's what I'm holding on to I'm gonna carry that around for a little bit.
- However, it's hard to pivot, and we've heard this word like, well, you know, we can just pivot a little bit, and it's really hard to do. We've invested in a huge amount of time. And so you know, most of us as experienced researchers would say, Yeah, it's hard to pivot if you're advising someone, if you are seeking out a research career, I would say you have to have a foot in the Us. And it is really hard to say that. And
- I think we're in a very different world. But our pipeline is at risk, that is, it takes a year or so of someone that is unable to apply for a research grant in global health as an example, or HIV, or you name it. The pipeline is at risk. So we need to support our junior scientists in a different way than we're supporting them now.
- And so I think we have to stay in the game. It has to be new investment, real investment from, for instance, our endowment. We have a piece of that that's been described of what we could do to support researchers, and it's just not going to be enough if that's all that's being offered. So there needs to be a bigger plan in terms of how to use funds that we already have and and from a philanthropic standpoint. I think we need to not be building buildings at the moment, or, you know, investing in other sorts of of things, and we might just need to be funding actual research projects and shift to do that for a period of time.
- And we are incredibly dependent upon our philanthropic partners, and we're grateful for that. But I think we need to kind of shift and guide them in a different way. We need to elect and support local leaders. And I mean hospital leaders as well in in our community, because they will help guide us through these difficult times. We might need to remove the interim tags from from a few people in, in my humble opinion they may not, they may not want it. All right. So the last minute your book recommendations for the summer. You're on a train.
- You're in a coffee shop, you know. Someone's judging your read here. So you know, you gotta gotta look like you know something you're going to a family

reunion. You got to impress the Gen. Z. Folk in the crowd. How about read a John Green book?

- And you want to read it before the movie comes out. Because there is there is a movie coming out about work alright. Thank you so much.
- Good thing thinking a lot about it, especially these last few weeks. That's pretty not just local, but national. It's everything you said is true. We need to.
- Yeah, I've been thinking even more we need because we're we used to call ourselves a profession.
- That meant we were in it together, we were.
- And then I was always thinking it was a bit of an unethical thing to organize concerningly. It's sadly just been about money. My son's up to toss contracts and money, but we need to organize individually. A single lecture is not good to do it. It is to doing, and and I think walk and get it together. The ama is worthless. Have you heard anything with Rfk doing?
- Yeah, yeah.
- And I I don't know about other societies. I would say the same thing about the Infectious Disease society of America. Idsa.
- There's some advocacy. But the problem is is that you know, this is device. It's intentionally divisive. So the strategy intentionally divides. You know universities, for instance. Oh, I'm so glad we're not Harvard, you know. It's kind of what a lot of us are thinking right at this moment. Glad I'm not, Hopkins that, you know. Got, you know. However, many millions billions of dollars of Usaid cut. But yeah, I think that there needs to be a collective move for organization. So
- I'm not sure exactly what that next step is. But we're there. I think we're we're already there. So we're we're past the point of being demure past the point of some of our professional application.
- I'm there.
- Thanks, Brent.
- Alright. Thank you so much.