Hi, and welcome to the Princeton Pulse Podcast. I'm Heather Howard, Professor at Princeton University and former New Jersey Commissioner of Health and Senior Services. On campus and beyond, I've dedicated my career to advancing public health. That's why I'm excited to host this podcast and shine a light on the valuable connections between health research and policy.

Our show brings together scholars, policymakers, and other leaders to discuss today's most pressing health policy issues, domestically and globally. We highlight novel research at Princeton, along with partnerships aimed at improving public health and reducing health disparities. I hope you'll listen in as we put our fingers on the pulse and examine the power and possibilities of evidence-informed health policy.

Today's episode highlights a potential win in the fight against cervical cancer, one that comes from a place that you might not expect. Rwanda, a low-income country could become the first country in the world to eradicate the disease. According to the World Health Organization, cervical cancer is the fourth most common cancer among women globally, although it places a disproportionate burden on the global South. About 90% of new cases and deaths occur in low and middle-income countries because of barriers to protected vaccines, screenings, and early treatment. But Rwanda is hoping to beat the odds. The country boasts a remarkably ambitious vaccination program for the human papilloma virus or HPV, which causes cervical cancer and is piloting a screen and treat program to ensure earlier intervention. In fact, this small African country is doing a better job than most wealthy countries. How is this possible? And what can we learn from their efforts?

Here with me today to discuss are Professor Cristina Stefan, director of the Institute of Global Health Equity Research, and Alyssa Sharkey, a lecturer at Princeton University, whose research interests include global health equity and immunization. Christina, Alyssa, welcome to the show.

This is so great. I'm so glad you could join me for this really, really interesting topic. Cristina, can I start with you? Can you just tell us a little bit about your role at the University of Global Health Equity in Rwanda?
Cristina Stefan 02:32
Yes, sure. So I'm leading the Institute of Global Health Equity Research, which is part of the University of Global Health Equity, based in Rwanda. We are part of a larger family, PIH, which stands for Partners in Health. As background, I'm a professor in global health and medicine. And I joined this institute only about a year ago. We are talking about a very young university. The University of Global Health Equity is only seven years old, and the institute's only three years old. But I was really excited about joining the institute because we have embarked on becoming Africa's leading institute of global health equity research. We would like to be recognized worldwide for our innovative approach, for our impact, for our inclusivity and togetherness. And if I could perhaps just summarize the institute for those who do not know about it, I will define our institute because there are plenty of institutes in the entire world. What is different about our institute of global health is basically the approach or the angle on which we approach different things. And this is based on equity. So if I could define it in a few words, I would say that the institute is defined by research, by innovation, by impact, and perhaps most importantly by equity.

Heather Howard 04:16
Great, thank you and a perfect set-up for this conversation. Alyssa, can you tell us a little bit about your background, especially your work at UNICEF, and work on vaccinations?

Alyssa Sharkey 04:24
Yes, thanks. And thanks so much for having us, Heather. It's exciting to be here. So for the last 13 years or so I have worked for and with UNICEF in different capacities. I was in their New York office headquarters office and then I moved to the South Asia regional office, and then back to the New York headquarters office. And I was a senior health specialist in my last role there, working primarily to support UNICEF’s efforts globally to improve immunization equity. I also led a team and worked in a team that focused on implementation research, which is basically research to try to make programs work better. Well, as you can see, this is exactly why you're the right people to have this conversation with. Alyssa, can we jump in and talk about cervical cancer and what we know about the global burden of the disease. Cervical cancer is a very important problem worldwide. The latest estimates are that over 300,000 women each year die from cervical cancer. About 90% of those deaths are in low- and middle-income countries. But even here in the United States, the CDC estimates that about 4,000 women will die this year from cervical cancer. So it's a huge problem. It's actually the fourth most common cancer among women globally. But it's actually the leading cause of cancer in those countries, low- and middle-income countries that are supported by Gavi, the Vaccine Alliance. In these settings, women often don't have access to cancer screening, which means they're unlikely to be diagnosed until it's too late. And then access to treatment is lacking. Cervical cancer is something that can be cured if it's diagnosed at an early stage and treated properly. It's a huge problem. And something that I think, globally, we're really starting to think more about, and the importance of eliminating it.

Heather Howard 06:43
Cristina, do those numbers bear out in Rwanda? Can you talk about the burden there?

Cristina Stefan 06:48
Yes, sure. It is indeed reported that there were more than 300,000 deaths, according to the last report, in 2020. It is also estimated that there were 600,000 new cases. But the truth is that we don't know. And why I'm saying that is because in order to be able to give these numbers, you need to have cancer registries. And cancer registries are not available, or are not really comprehensive, in Africa, in general. So out of 54 African countries, I think, at the moment, there are only three or four which are really recognized as having a cancer registry. I'm mentioning this because we are talking about numbers, which are just estimations. From my personal point of view, as a clinician, I think the number is actually much, much, much larger. Cervical cancer is the most common cancer among Rwandan women, according to our registry. It's not a perfect registry, but it is a registry that still collects those cases. It is also the second leading cancer in Rwanda. And again, I'm going to give an estimation that there were more than 1,000 new cases and about 900 deaths in 2020. But every single time I talk about that, I would say we shouldn't really think about the numbers, because behind the numbers are real women. Behind the numbers are mothers and grandmothers and sisters. So the numbers are used, of course, from the statistic point of view, but I think we should really see the much bigger picture.

Heather Howard 08:55
The bad news is that we're probably undercounting the burden, and you've brought home how important it is to think about the human impact. But the good news is that it's treatable and actually preventable. Can you talk about the HPV vaccine and why that's so important? That'll help set us up for our discussion about those vaccine efforts.

Cristina Stefan 09:17
The HPV vaccine helps protect against cancers which are caused by HPV, the human papilloma virus, and prevent HPV-related infections, including cervical cancer, but not only cervical cancer. There are some mouth and throat cancers and also some anal and genital area cancers that also contribute to the burden of cancer in general. By getting vaccinated against HPV, individuals -- because we are not talking only about women, but men and women -- can be protected from these cancers. We also encourage vaccination for males, for boys. Individuals in general not only reduce the risks of developing cervical cancer, but also increase the opportunity for herd immunity, which, again, helps protect those who are not eligible for vaccination or cannot access the vaccine. And again, like other vaccines, the HPV vaccine is a very cost effective strategy to prevent HPV infection and, of course, associated health risks. It has been shown with evidence-based medicine and evidence-based research that it will be an extremely useful tool to reduce health care costs, and also economic burden.

Heather Howard 10:56
Alyssa, you've been involved in many vaccination campaigns. It sounds like the HPV vaccine is a tremendous breakthrough. But how is it different? How we get the word out and how we make sure people get vaccinated is a different challenge, right?

Alyssa Sharkey 11:15
It's quite a different challenge. As you probably know, most immunization programs reach either women during their pregnancies -- in their second and third trimesters, or they're intended to reach infants, young children. So that would be during either post-natal care visits or well-child visits. These are well established opportunities where both women and children are coming in to facilities for care for these
things and other things. But the target population for the HPV vaccine is different. It's intended to reach girls and, as Christina says, boys as well, but between the ages of nine and 14. The idea is to reach them prior to their sexual debut, before their first exposure to the human papilloma virus infection. So that makes it very different. And because the target population is different, that means that there needs to be a different platform or multiple platforms through which the vaccination services are provided. The timing is quite different as well. So it creates some challenges in countries that may have constraints within their health systems overall.

Heather Howard 12:45
Cristina, let's turn to you. Can you tell us about Rwanda's initiative to eliminate cervical cancer?

Cristina Stefan 12:54
I think the initiative taken by the government in Rwanda has been one of the most successful initiatives. I think it is well known that Rwanda now tries to compete with Australia in becoming the first country in the world to eliminate cervical cancer as a public health problem. What has been extremely successful in Rwanda was the vaccination campaign. First and foremost, the country initiated the national vaccination program against HPV, the human papilloma virus. This resulted in, I think, more than 200,000 girls vaccinated with all three doses of HPV. That was a program which started about 10 years ago through school vaccination program. So what they have achieved was actually a percentage, extremely high, I think between 93 to 96%. The HPV vaccination was extremely successful because it was integrated into the immunization program. In other words, free vaccine was offered to all eligible girls because obviously we have a certain period of time when we propose to vaccinate the girls, and also to all the other health facilities and any other health care services, such as the reproductive health services. I need to mention that tremendous progress has been made. In terms of vaccination, initially the program included three doses of HPV, now it has been reduced to only two doses of HPV. There are also studies that show that one might consider only a once-off vaccination with HPV because it will still be extremely efficient in preventing cervical cancer.

Heather Howard 15:15
It's exciting to hear about the successes. What are some of the challenges that you've seen? And how is this program funded?

Cristina Stefan 15:23
In terms of key challenges to this initiative... like many other countries, they were related to resource challenges. Keep in mind, cervical cancer is extremely important, but there are so many other competing priorities. And there was a degree of fear that the cervical cancer prevention efforts might detract scarce resources from other cost-effective interventions, such as, for example, child health interventions, maternal health, other NCDs. There was also the fear that introducing this HPV vaccination would compromise the health system in Rwanda, given its resource requirements, so the cost and the investment. Another challenge was related to training health care workforces because you need people to be trained and to be able to deliver cervical cancer prevention and control services at different levels of health care. And then, of course, infrastructure development, such as dedicated, established cervical cancer treatment centers and different laboratories where you could test for HPV. For the cost of logistics, in terms of funding, mobilization of the resources, especially supplies, initially
we had funding from Merck. Then it was obviously the discussion about long-term sustainability. The cost of the HPV vaccine program is co-financed by the Rwandan government and also by Gavi, the global vaccine alliance, which played an essential role.

Heather Howard 17:25
Thanks. Allysa, I heard four challenges. There’s the resource challenges, concerns that it might detract from other public health efforts, the health care workforce, and then broader infrastructure challenges. Do you see those in other countries? How are you seeing the HPV vaccine rollout in other countries? Are those consistent challenges?

Alyssa Sharkey 17:47
I think those are common challenges in low- and middle-income countries. And one thing that is important to note is how the COVID pandemic has added to the strains that the health systems in many countries are dealing with. There were certainly service and supply chain disruptions, resource diversion overall to the response efforts for COVID. These were things that actually limited immunization service access and availability broadly. And we saw that at the global level. In fact, we saw estimates of the global coverage for childhood immunization go from 86% in 2019, which was the global high and an extraordinary feat. But that went down to an estimated 81% of the world’s children. These are huge, huge impacts on the health of children. So I think these challenges that Cristina has mentioned are really important in a lot of countries. It’s been particularly challenging in the last few years. But in spite of that, the estimates are that, at the end of 2022, there were actually 100 to 125 countries that have introduced HPV vaccine into their national immunization programs for girls. And even about 47 countries have introduced it for boys. That’s really exciting. A lot is happening. The approaches that different countries are taking are quite different. Most are trying to reach children through schools. I think that’s an especially important mechanism when you have most girls in school. But some countries are also doing outreach to communities, or working through local leaders doing campaigns, communication strategies. There are a whole range of approaches that countries are using. But basically what we’re seeing is that each year more countries are introducing the HPV vaccine. That’s a very positive development.

Heather Howard 20:29
Cristina, Alyssa mentioned the COVID effect, how the pandemic has disrupted childhood vaccine campaigns across the world. Have you seen lower vaccination rates in Rwanda during the pandemic?

Cristina Stefan 20:42
Yes, of course. Rwanda is also part of the international environment, and everything that has been seen in other countries has been seen in Rwanda. We also had a decrease in vaccination. But the good news is that vaccination has picked up quite a lot. We are back on track with our vaccination efforts. If we talk about the WHO global initiative aimed at eliminating cervical cancer by 2030, with 90% of the population vaccinated by that time, we are very much on track in Rwanda. We have a much higher rate than 90%. So now, we’re really trying to put all our efforts into the second area of screenings. We would like to reach 70% in terms of screening. And then the third area, obviously, is related to treatment, which we’d like to see at 90%. We are trying to increase percentages in terms of screening and treatment as well.
Heather Howard 21:57
That's fabulous. I was going to ask you about that. Because while vaccines are a game changer for young women, what about women who are currently at risk? How do you pair that focus on the vaccine and prevention versus the early detection and treatment?

Cristina Stefan 22:16
When you talk about cervical cancer, you talk really in a very comprehensive way. So obviously, for the younger population, we will focus on vaccination and we are extremely successful. Now the focus is on how we reach the other group, those who are not really part of the vaccination, where the vaccine would definitely not impact the cervical cancer. All the efforts are now really to introduce the screening. We have a special population in Rwanda related to the HIV-positive women. We worked together with the community health workers to include those women and then to improve referrals for treatment, which takes place in the other centers.

Heather Howard 23:18
Alyssa, you've written about the gender and equity considerations that are unique to the HPV vaccine. Can you say more about how states should think about this?

Alyssa Sharkey 23:31
Yes, there are big equity considerations for all vaccines. We see, for example, issues reaching people who live in remote rural settings, or even urban poor settings that might be right next to a facility, but there are social barriers or other reasons that they're not accessing services. We see problems reaching people who live in conflict affected settings. There are really important challenges for reaching the most disadvantaged people. But gender also plays a role across all of these settings. We see, for example, that poor maternal education affects women's abilities to make decisions about when to take their children or themselves in for vaccinations or services. So those are the kinds of challenges that you might expect with HPV vaccination. Another one is misinformation and stigma about the vaccine. Is it safe, is it something that's going to have negative consequences in any way? But I think there are additional equity considerations and implications for HPV because it is typically delivered through schools. There are implications in places where children, and particularly girls, might not be in school. The latest estimates for UNICEF are that about 87% of children globally who are of primary school age are actually in primary school. But there are still an estimated 64 million children who are not in primary school. These rates are even lower for secondary school. Those are the target groups for this vaccine. There are lots of reasons that girls, in particular, might be absent from schools. For example, other obligations at home, long distances they have to travel through insecure routes, poor facilities for girls to manage menstruation. These are all gender-related implications of trying to reach girls in school. And then, of course, as you know, there were so many schools that were closed during the pandemic, which exacerbated those types of equity challenges. Maybe the last thing to say about the challenges with respect to HPV, in particular, is that adolescent health is a neglected area in a lot of countries. It's an under-resourced, fragmented, poorly coordinated, poorly funded area.

Heather Howard 26:42
Christina, do you want to anything you’ve talked about? Obviously, equity is a North Star for for you and the Institute, anything you would add about those equity challenges?

Cristina Stefan 26:54
Yeah, for sure. I mean, this is what this is our research that is really focusing on on on the equity issues. So I think that was really beautifully expressed by Alicia, you know, the equity issues, they still remain. The question is, how can we approach in perhaps in an innovative way, in a different way, have our voice heard and come up with solutions that we can really take equity at, at another level?

Heather Howard 27:25
So let's pull back. Cristina, sticking with you, what can other countries learn from Rwanda? You're actually here at Princeton for a conference on health equity in Africa. When people hear the story about the successes with Rwanda's efforts to eliminate cervical cancer, what do you tell them they should emulate?

Cristina Stefan 27:49
So perhaps, if we think back, what was really successful, what really worked? If we take a step back and assess what we have done well as a country, it is really all of us coming together. I need to mention that international collaboration played an important role. This would have not been possible without a strong political will, a really serious advocacy program. Also, by rolling out the HPV vaccination by targeting the social, the physical environment, we talked about the school based vaccination program. And something that may be specific to Rwanda would be utilizing the community health workers. Rwanda is a small country, about 12 or 13 million people, but there are so many community centers. It doesn't matter where you live in Rwanda; you will not need to walk further than an hour from your own home to get to a community health center. I would also say, if you think in terms of successful initiatives, something that was perhaps defining for the vaccinations campaign in Rwanda was the peer tracking. Peer tracking really was successfully implemented. For example, we will identify girls who have not completed the HPV vaccination series. And after vaccinating them, we ask them to help locate their peers and convince them that this is the way to do it. We were talking about three vaccinations. Now it will become easier with two vaccinations. I would recommend to other countries that they have a clear plan, and really understand what they want to do and how they want to do it. Also, Rwanda did a good job balancing the key health priorities, prioritizing, and allocating the resources properly. It is essential that people understand, and people learn. Again, the population in Rwanda didn't know about cervical cancer. There are many countries where cancer does not even exist in a language, so how do you explain the disease to someone when you cannot even translate the words. Conducting awareness campaigns and talking to people in the community made a big difference, along with strong coordination between public and private institutions for vaccination, screening, and treatment. And not only planning, but also monitoring and evaluating the implementation at every single step. This is why Rwanda, for example, has not only a national cancer control plan, but there's also cervical cancer plans and a very good program in terms of monitoring. So RBC, Rwanda Biomedical Center, has a dedicated center for NCD and one specifically for cervical cancer. We chose to use that determination and willingness to be successful in this initiative.

Heather Howard 32:16
Allysa, anything you'd add about what we can all learn from Rwanda's successes?

**Alyssa Sharkey** 32:22
Yes, just listening to Cristina talk about this comprehensive approach is super exciting. I think Rwanda has been quite unique, not just in its approach to this ambitious agenda to eliminate cervical cancer but more broadly. Rwanda really is a leader, globally, in trying to improve universal health coverage. As she says, there's political will. There's been planning. There are efforts to make sure that things are implemented. This is hugely exciting and important for us to learn from. The other thing is that Rwanda can really be held up for its strong focus on health equity. It's sort of the example where she's talking about the community, the work with communities and community health workers, that's a big part of making sure that everyone has has equal access. It's going to be the key not just to reaching high levels of vaccination, but to actually reaching everyone. That's the critical difference and approach that isn't always taken in other countries. So we have to figure out what Rwanda is doing, how they're doing it, perhaps using implementation research to really understand. Let's document what's working, what's not working, and why. And I think that's going to be hugely beneficial for other countries.

**Heather Howard** 34:01
So let's end by exploring that point. Cristina, you mentioned the importance of planning and monitoring. At the institute, how do you see your research in conversation with policymaking and informing policy and helping to strengthen the systems we've been talking about?

**Cristina Stefan** 34:25
Researchers at the Institute work very closely with the Rwanda Biomedical Center, under the Ministry of Health, with everyone. Our last research, for example, tried to have new sites where we would conduct clinical trials for increasing screening for HIV positive women. So this is a discussion that we are having, and we are in partnership with the Vanderbilt Medical Center and with the Ministry of Health and obviously with a policymaker because the results of the research need to be translated into policies.

**Heather Howard** 35:09
Alyssa, you've been on both sides of that equation, as a policymaker and a researcher. How do you see those in conversation and improving all these efforts?

**Alyssa Sharkey** 35:16
These clinical trials, the hard work to really understand what's most effective, is critical. But also, I think, as I mentioned earlier, we need to understand how to actually implement -- how to roll these programs out, and understand what works, what doesn't, especially for the most disadvantaged populations. How do we reach them? One thing I would say, overall, is that the immunization field is fortunate to have pretty good data systems. These are routine administrative data within government systems, but most countries also have nice immunization household surveys to understand who's being reached, who's not. In addition to that, I think there is a need for more qualitative assessments as well to understand the barriers that different people are facing and why they exist. All of those types of information are really important. We do see a lot of investment being made in things like digital health technologies to improve information and data around immunization. But again, I think the research that can really help
us understand how to do this is something that’s often not done but is so critically important for policymakers. And they need to have that information in a timely manner so that it can be integrated into their programs and policies.

**Heather Howard 37:19**
Cristina, any final thoughts?

**Cristina Stefan 37:20**
Yes. So the question comes again, can we really eliminate cervical cancer? I believe that eliminating cervical cancer globally is within reach. The ability to eradicate cervical cancer is here. But what I would like to end the session with relates to statistics and an article I read recently about Australia possibly becoming the first country to eradicate cervical cancer, because the expected incidence is really low. With vaccination and access to screening, Australia is on track to really achieve this goal. However, I would end by with a rhetorical question perhaps, or with a question that we still need to have an answer. Could Rwanda be the first one, and not Australia, since we do see remarkable success in vaccination and are trying very hard to catch up on screening and treatment? Of course, I don’t have an answer yet. So I would suggest that you watch the space. Even if we’re not the first one in the world to eradicate, I believe it will be a tight race between us and Australia.

**Heather Howard 39:00**
That is a good point on which to end. I want to thank Cristina and Alyssa for a really thought-provoking conversation about Rwanda’s ambitious efforts to eliminate cervical cancer, and that race that we hope many, many will win. That was very exciting. So thank you. Thank you. Thank you.