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For many years, South Africa has had the largest HIV epidemic in the world, due in large part to the lack of action during the administration of former president and AIDS denialist, Thabo Mbeki, who served from 1999 to 2008. Now, with new leadership and more accessible treatment, Dr. Ingrid Katz and her colleagues are trying to make up for lost time with the Treatment Ambassador Program. Their goal is to get people to start and stay on treatment, reduce transmission, and end the epidemic. Dr. Ingrid Katz is the Associate Faculty Director for Harvard's Global Health Institute and an assistant professor of medicine at Harvard Medical School. Dr. Katz, thank you for coming back. Welcome.

Thank you for having me.

So your work focuses on HIV/AIDS treatment in South Africa and Kenya, and the last time you were here you had just started enrolling participants in a pilot study of the Treatment Ambassador Program. Could you tell us what the goal of this study is?

Yeah, absolutely. Just to back up a little bit and frame the situation in South Africa, so South Africa still continues to have the largest HIV epidemic in the world, with over 7 million people now living with HIV. South Africa itself, as a country, and certainly global investors have done a lot to stem the tide in that. And there are now roughly about 3 and 1/2, 3.8 million people on treatment, which is a phenomenal outcome if you think about where South Africa was when they first started getting treatment in around 2004.

So just to stop you there.

Yeah.

Where were they in 2004? Could you give us a little bit of a perspective on how great that change has been? Yeah, absolutely. So, South Africa, as we all know, was under a system of apartheid until 1994, when Nelson Mandela assumed office and apartheid ended. At that time, there was a lot of political upheaval and a lot of social chaos. And unfortunately, what ensued after Mandela left office was Mbeki taking over, who was a devout AIDS denialist. And as the HIV epidemic exploded, that unfortunately created a Venn diagram of bad things to happen-- the overlap of an AIDS denialist running the country with the explosion of the AIDS epidemic. And South Africa quickly became the country with the largest HIV epidemic in the world. And because the government at that time was not interested in promoting treatment for people living with HIV, even though we had effective treatment in this country since 1996, it was really running unabated in South Africa.

There were efforts done, certainly multi-nationally, and then people within country, liked the Treatment Action Campaign activists, scientists, researchers, clinicians, who absolutely wanted to get people on treatment and did everything they could. And there was certainly a small stream of treatment coming into the country, but nowhere near where it needed to be to really stem the tide of the epidemic. So in 2003, George W. Bush announced the PEPFAR program, which has been monumental for HIV treatment globally. And that brought treatment to South Africa in 2004. During that time, Mbeki was still in charge, and so what essentially had to happen is that vertical programs needed to run separately from the Department of Health to provide treatment for people living with HIV-- so essentially creating two systems, one for people not living with HIV and one for people who needed treatment.

And again, all the people who were leading in the country on this issue were poised and ready to ramp up treatment. But it was a really a parallel program for many years, and really until Mbeki stepped down and Zuma took over. At that time, there was a lot more interest in bringing these treatment programs into the public health system and public clinics. So over time, as PEPFAR managed to de-escalate and pass a lot of the costs over to the South African government, they were also able to incorporate treatment programs into the government programs. But there was a huge time loss. And in any situation, any epidemic-- and we know this right now from the measles epidemic-- once you fall behind, you're permanently playing catch up until you can get over the hump of decreasing incidence.

So now that Zuma-- because Zuma came in power and was more receptive to getting treatment to people, South Africa still has a large epidemic, but it's better than it had been. And you said 3.8 to 3.9 million people are on treatment out of 7 million?

Yeah.

OK, so your goal is to get even more people on treatment.

Right.

And so with the Treatment Ambassador Program, how are you hoping to do that?

Right. So, we still have in South Africa about 40% of the population living with HIV not in care. And why is that? We know since September of 2016, treatment has been freely and widely available to all people living with HIV in South Africa. So it is no longer a question of access or cost, per se, of the medication. Of course, there are costs that people incur when they have to get transport to a clinic or maybe lose a day of work. So why is there still such a large number of people who are not on treatment? And really, that's where we have to focus. And I think a lot of the discussion that we think about now relates to the fact that this group, this 40%, is going to be very different from the 60%. Because the 60% who are on treatment were waiting for access. They wanted to be on treatment. They needed to be on treatment. So they had access to treatment and were able to get on. And this 40% may just face additional barriers that we need to be addressing more creatively.

So a lot of us in this community have started to think more broadly about what are called differentiated care models-- so really looking at different key populations and trying to understand what their barriers are to treatment, so that we can design more effective programs. And the Treatment Ambassador Program was really a step forward in that direction. And I would say on the continuum of decision making, our target population for the treatment ambassador program where people who were highly-marginalized, who had either never entered a treatment program, or had been in treatment previously, but had been out of care-- for us, a median of about two years. So people who were really not tapped into the health care system.

We spoke the last time you were here a little bit about the study, and you were in the pre-pilot phase when we spoke last. Maybe you could just remind the listeners, sort of in a nutshell, what the study looked like, what the study design was.

Yeah, absolutely. What we know from a lot of the qualitative work that we've done in South Africa, and certainly also quantitative studies, is that people face barriers to treatment for many reasons, often quite complex. But certainly, some of the key reasons are deep stigma that people face when living with HIV, a lack of ability to disclose, and a lack of social supports. And again, the lack of social supports are particularly relevant in South Africa, because apartheid essentially ripped the fabric of that society apart. And so as the society is continuing to stitch itself back together, that is still an area where people face deep challenges. So our goal with the Treatment Ambassador Program was to use all of the research that we've done to date trying to understand why people may face these challenges and design a program using peers who would be trained in something called motivational interviewing, which is essentially a psychological technique to help engage people in their own awareness of their decision making.

So it promotes behavior change within the individual. And unlike Cognitive Behavioral Therapy, where you really need an advanced degree to be able to do that work, motivational interviewing is something that you can train lay populations to do. And our goal always with our work is the ability to close that no-do gap of implementation science and really think about ways that this can be disseminated in the community. So we knew that whoever was going to be doing this and delivering our intervention could not be someone who had to have three PhDs and 20 years of training. It needed to be somebody who could be available readily in the community. And the peer aspect was really critical, because we knew from our qualitative work that the sense of social isolation that people feel when they have a new HIV diagnosis was what often led them to make decisions that may be more harmful for their health.

So we hired people who were living with HIV and very open about that and were in treatment, but may have struggled themselves in the past. So they were people who our participants really related to. And we train them in this technique of motivational interviewing, and we also had a manual that they used that had a lot of detailed content. And really, this was supposed to be a menu-based intervention. So for our participants, they had the choice. We had a lot of different options for them. They met with a treatment ambassador for over eight weeks-- one-on-one sessions-- to address whatever barriers were important to them.

So if it was stigma, they would focus on stigma. If it was challenges with disclosure, then they would focus on that. And it was set up in such a way that if the participants said, you know, I have someone in my life I'd like to disclose, but I'm feeling uncertain. They could bring that person into that room and have that discourse with them with the treatment ambassador there as a support person. Because our goal ultimately when we finish the intervention is for that person to feel like they could enter treatment and have support people in their lives. Because obviously, the treatment ambassador wasn't going to be walking with them hand-in-hand for the rest of their life. And of course, again, with the motivational interviewing, we were really trying to tap into that intrinsic motivation, which is a very different paradigm from what a lot of the people there are living with. A lot of the medical system is quite paternalistic, in the sense that it's kind of directives from on high. And I think our goal here was really to empower our participants to be making choices that were healthy for them.

So the intervention that you've already done was part of the pre-pilot, so now you're--

We're actually done with the pilot now.

You're done with the pilot, OK.

Yeah, and we have some data. So it's really interesting. And again, the type of grant we got is a pilot intervention through NIH that allows you to really get into the weeds of the work. Any funder now is careful about spending a large amount of money on things if it isn't going to work. And I think one of the things that we, as researchers, need to be really cognizant of is if we're designing interventions, and we want to take them to scale, we have to be certain that they're effective in the communities that we're targeting before we ramp it up. I think sometimes it's easy to kind of get ahead of ourselves. And this was a case where we had some interesting and somewhat discrepant findings that we're still teasing apart a little bit.

So in our initial study, what we were looking at primarily was acceptability and feasibility. That's a goal with the pilot study. And we can absolutely say that we met the threshold for that. We had a randomization schema, where half of our participants were basically in a control arm, and the other half were receiving this intervention. And amazingly, we lost two people initially, but the rest of the group stayed with us for the full eight weeks, plus followed them out for six months to do survey information. And this is really a group that has not been engaged in care. We didn't recruit from clinics. We did this in the community. So just to be able to know we could engage so deeply with participants over a series of weeks was a very promising sign, and I think really spoke to how effective these treatment ambassadors were. And all of the qualitative work we did on the back end really affirmed that. People really felt connected to this person. And I think this is something we've been thinking about a lot in terms of scalability, as to whether there's some way to incorporate technology, mobile phones or something, that can still give people enough of that connection without it having to be kind of a face-to-face human. And I'm not sure yet. I think that's more work we need to understand.

But it was clear from exit interviews, people really felt deeply connected to this person. So that's great. Our early data to look at efficacy-- and again, it was hard, because we were certainly not powered to look at efficacy, but we always want to see if there is some increase in uptake. There did seem to be a slight uptick in treatment initiation at the three-month mark in our intervention arm as compared to our control arm. But again, it wasn't significant, because these numbers were so small. Interestingly, now we just got to the one year mark where we recruited people, and now we're looking back. So our team in South Africa actually went back and reached out to everyone who was in the study and looking back through the data to see in terms of-- we have access to national registry clinic data to see what's happened. And there, we see a marked difference. So the people in the intervention arm were looking at about between 25% and 30% uptake of treatment in that arm, as opposed to in the control arm, which is more like an 8% to 10%. So again, both arms, there was over time some engagement in care, but the intervention arm seemed to definitely perform better-- probably significantly so, but we're still analyzing those data.

I don't know if I missed it, but the control and the treatment arm, what was the difference between-- The treatment arm got the treatment ambassador--

Right, control is just status quo. We were doing surveys with them, so there was some interaction with our research team. But we didn't try to change behavior.

Interview them and find out what their-- why they weren't seeking treatment, and--

Yeah, we asked a lot of questions. I mean a lot of our work is really driven by socio-behavioral factors, right. So we did a lot of questions around mental health, stigma. So we were trying to assess if there were changes, either secular changes over time, or changes that the intervention maybe was promoting. And we're still going through those data as well to see if there's any kind of long term change in depression or any of these other factors in the population who started treatment.

OK.

So that was it with the control arm.

Yeah, so the control is just sort of like if we don't do anything, but we keep talking to you, and finding out how you're doing.

Right.

And still, even then, 8% of people you found sought treatment.

Yeah.

I mean even if just something as simple as talking to somebody, finding out how they're feeling, could--

Right.

Yeah, that's interesting.

Yeah, and again, that's absolutely right, and part of the reason why we did this as a randomized trial. Because you want to try to control for a situation where someone just is having engagement with a research team that may change behavior. So we wanted to kind of compare apples to apples.

So this was an NIH funded study, and you've also had NIH funding to study young adults, newly diagnosed with HIV, using an intervention called Standing Tall. Could you tell us more about that? And I think that's something that just started last year. Is that right?

Yeah, absolutely right. We're just finishing our first year of the study, and I'm super excited about it. So again, the theme is trying to really target these key populations. The first intervention we did was with a group of people who were really disenfranchised from care. In South Africa, another really important population is young people. So we know from national data that young people are actually testing at pretty high rates. And South Africa has done tremendous work to ramp up testing. But there's a huge drop-off between testing and treatment initiation, with a really strong focus in young people. And these are people-- I'm talking about people who are newly diagnosed. I'm not talking about people who acquire HIV perinatally.

This is a group that I think a lot of people believe may be driving the epidemic in some ways. Because they're young, they're sexually active, they're otherwise healthy, and they may be acquiring HIV in their teens, early 20s. So we really wanted to look at this population and see if we could come up with a more creative solution. Because it was clear the drop off was happening between testing and starting treatment. And that says, essentially, that people understand their status, but they're not able to engage in care.

And the treatment that's available can reduce transmission. It can eliminate the possibility of transmission.

Exactly. It essentially eliminates the risk of transmission. So there's multiple reasons to get on treatment. Of course, it's lifesaving. And now we have lots of data to show the sooner you get on treatment, the better for your health. But also, it essentially eliminates transmission to any partners. So there's lots of good reasons to get people on treatment. I mean people really see treatment as a mode of prevention in many ways. So our focus here was, again, on young people, so a slightly different group from our Treatment Ambassador Program. And a lot of the work that colleagues of mine have done and certainly some of our early work speak to the fact that the current situation in clinics is very challenging for young people. There are not adolescent specialists the way there are in the United States. It's kind of pediatric care or adult care. And usually, young people transition to adult-level care in their early teens. So that's a very vulnerable time for young people.

And then, of course, there's factors related to adolescent development and the developing prefrontal cortex that is still not in place for many young people that can leave them particularly vulnerable. Clinics in the public sector are hugely overburdened and very crowded. And so, when a lot of us are thinking about these differentiated care models, we're also trying to think about ways to decant some of these very overburdened clinics. Because those clinics really should be reserved for people who are quite sick, and not for people who are otherwise healthy and just need some level of care-- so treatment, some social support. So we decided for Standing Tall that we would develop a model of treatment outside of a clinic setting. So now we're in the pre-pilot phase for that, which is really our iterative phase of development. We call it our field-testing phase, where we get a lot of input from participants.

So we recruit a small group of young people to participate in this with us, and we walk through the intervention with them. And in each step of the way, we ask for feedback. So it's a really great, formative time to test everything out, and see what's working, and see what's not working. And this is based, again, on qualitative work we've done up to this point. So Standing Tall is developed in conjunction with the Desmond Tutu HIV Foundation. Linda-Gail Bekker is the site PI, and she's world-renowned for her expertise in young people living with HIV and HIV prevention. And so, using their expertise and understanding of the community of young people in kind of the Cape Town metro area, we decided that we will build a program where we both recruit people who are newly diagnosed in a community and then offer them treatment in what are called treatment clubs. And this is built largely on models that were piloted by Medecins Sans Frontieres who also works in the Cape Town metro area in a township called Khayelitsha, where they have offered treatment clubs for a while, both for medication adherence, and now they're starting to offer it for treatment initiation as well.

Adherence clubs are huge in Cape Town. So these are really for people who have been in care, have done well, and now they're kind of getting this reward. And they're saying, you don't have to come to this overcrowded clinic anymore. You can go to this nice, little meeting hall. You'll get your meds. You can check in with counselors. The nurse can draw your labs if needed. And then once a year or twice a year, you come back to the clinic just to get kind of a more systematic check-in. So that's great for people who are doing well. And it certainly helps with that decanting of busy clinics. The problem is for people who are struggling to initiate, it doesn't really help them in that way. Because this is kind of for the people who've been with the program.

So we thought, you know what, why don't we just move up the needle here and see what we can do. Let's push the envelope a little bit. And again, MSF really leads in this area. So we are developing these treatment initiation clubs, where young people can come in after they're tested. They can sit with some peers. We will have a counselor there. Again, we'll have some content that we're developing right now around counseling young people who are newly diagnosed, and we'll offer them treatment on-site. This is outside the box at this point. There are no randomized studies that have ever been done to look at this. And again, Medecins Sans Frontieres tends to be more programmatic in focus, so they haven't necessarily done published research on this. But we're closely partnering with them. I think they've been really great leaders here. So that's why we're up to.

And so for this study, what are you-- how similar is it to the Treatment Ambassador Program, in terms of design. Do you have a control arm that's looking at-- are you doing control and treatment, the same kind of thing?

Yep, same thing in that sense. I mean, again, we'll be having our research team connected to young people who are newly diagnosed and putting into place all the things that are standard of care in country in terms of providing lists and access to clinics that would provide treatment for young people. And then we'll be following them out over time, both populations, to look at all of those other socio-behavioral factors, like depression and stigma, to understand what is happening. Because certainly it is a traumatic event for people to be diagnosed, particularly when they're young and otherwise healthy. So we're going to be wanting to follow that out over time, no matter what.

So talking about the pre-pilot and pilot phase, and you spoke about how important the pre-pilot phase is to gather data and test things. Is there anything that you learned in either study from the pre-pilot phase that you incorporate into the pilot that was striking, that you thought, oh, wow, I'm really glad we did this. Because this turned out to be really important.

Yeah, so I am now not even sure how people can come up with an intervention without doing the pre-pilot phase. Because, again, our interventions are human-focused. These are not drug trials. These are trials that really look at behavior change. So in order to really engage with people that we're trying to help, we need to understand how they feel about what we're doing. So the pre-pilot to me is critical, particularly in this early phase of intervention development. Because, again, it's very iterative. It's feedback-heavy. We are mostly there to listen. We have done a year of qualitative work before each of these studies. So we understand our population, but again, I think it's risky to put something out there without having some real-time feedback.

So our goal in this pre-pilot phase, as it was with Treatment Ambassador Program, is to start this, run it for a very small group of people, maybe 10 to 15 max, and then throughout, after every session, we'll be asking them questions. We'll be trying to understand what we can do better, so that when we actually test it to really look at all of these other measures we want to understand, we will have had what we hope is the most participant-informed intervention we can get. And I think, especially as someone from America who's working in South Africa, even though I work very closely with my South African colleagues, I think there's a real risk for any of us who do research in low-resource settings of invoking a certain kind of paternalistic or neo-colonialist attitude. I hope that all of us are very conscious not to do that. But I think, again, one of the things that we want to be really mindful of is we're working for-- I think of my employers as my participants. So I am paid to work for them, and so my goal is to make sure that these interventions meet their needs and not mine or anyone else.

Dr. Katz, thank you very much for coming in. It was great to have this conversation with you.

Thanks so much for having me.

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Next time on *Think Research*.

The SO/GI data collection gap makes it really difficult to, one, estimate the number of LGBTQ or sexual and gender minorities in the population, and it also hinders the ability of the health care and research communities to assess and address the needs of LGBTQ people.

Our community-engaged series continues with Harry Reyes and his work on improving electronic health records to address LGBTQ health disparities.

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