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Hi. My name is Tapfumanei Mashe. I'm from Zimbabwe. Today, I'm going to walk you through a presentation entitled the Power of Genomic Surveillance, and I will share a Zimbabwe story about how we have used gene surveillance to respond to outbreaks.

So just to introduce the topic, so today I'm going to focus on cholera and typhoid outbreaks. So, as you know, that's-- cholera is traced back into the 19th century, and it was first picked in India. And the current pandemic, which is circulating is the seventh pandemic, which arrived in Africa in 1971. And, of note, Zimbabwe first recorded a cholera outbreak in 1972, at a squatter camp [informal shantytown].

Then, for typhoid, Zimbabwe recorded the first typhoid outbreak in 2009, around December. Then, in 2010, there was a resurgence of typhoid in two suburbs, Tafara and Mabvuku, of Harare.

So, for the cholera outbreak, what happened was, in from 1972, we have been recording outbreaks of cholera annually But, of note, is the 2008-2018 outbreaks, which I'm just going to share with you. So the 2008 outbreak was one of the biggest outbreaks which was recorded, and it had a case fatality, a high case fatality, or it caused deaths of a lot of people. And the most affected areas were at Budiriro and Glen View which are in Harare. So this 2008 was a main outbreak. It caused about more than 98,000 cases and around 4.2 deaths.

So this outbreak, the response to this outbreak was, as you know, cholera is managed by oral rehydration, but also ciprofloxacin was used as one of the mitigation responses to this outbreak. So, after the 2008-2009 outbreak, then another outbreak was reported, though the cases were not that high. In this last, it wasn't, in 2010 and 2011 outbreak, which was also recorded in Harare. Then, in all these outbreaks, in terms of resistance, the strains were susceptible to ciprofloxacin. So the main drug of choice or the main drug for management of this outbreak was ciprofloxacin.

Then, in 2018 we had another outbreak, now, which has killed a lot of people. And this is the 2018-2019 outbreak which happened around September. But, of note, in March of the same year, there was another outbreak of cholera which happened, and the strain then was also susceptible to ciprofloxacin. But, all of the sudden, now, this new outbreak which happened from September, the strain was resistant to so many antibiotics.

As you can see, when we now did a sequencing-- I'm also going to share the plasmid that we picked-- so that's when we found that genomic surveillance is very, very important in outbreak response. So we had to do phenotypic testing of the organisms in for that ciprofloxacin was not working. Tetracycline was also not working, which is also another option for cholera management, doxycycline, but all these antibiotics were not working.

And of surprise was also the third generation super-strength doses antibiotics are not used to treat or to manage cholera. But what we picked was this strain was also ESPO-positive. And, because of this, a highly resistant strain circulating in 2018, we had to do a genomic surveillance on which to do a genomic sequencing of these chains to see what was the main cause of this resistance.

So I am also going to share the plasmid that we picked. Of surprise, we picked a plasmid which was-- which had extra 16 resistance genes. Though I have showed some of the genes that we picked from the plasmid here, but I'm also going to show the plasmid. So this plasmid had extra 14 resistant genes, and the management of this outbreak and what you end up doing, though we were pushing issues to do with water and sanitation, but the solution to this outbreak was the use of vaccine.

So what we did to manage the outbreak was oral rehydration, as always. Then, for the antibiotics, what we ended up using was azithromycin, which is the last drug of choice when it comes to cholera management. Though we tried to improve issues to do with WASH, waste management, but the ultimate solution was the introduction of vaccination as a mitigation measure. And 1.5 million people were vaccinated from the 17 affected suburbs.

So I'm just going to show you the plasmid that we picked from these strains. So this was the plasmid, and these are some of the resistant genes that we picked. And from the history of this plasmid, it's a plasmid that is usually associated with cholera, but this one had additional 14 resistant genes. So that's when we found that, this gene, it picked the plasmid in the environment.

So I'm going to share with you the typhoid outbreak in Zimbabwe, how we managed. So, in Zimbabwe, I'm just going to give you a brief of the typhoid outbreaks in Zimbabwe. So typhoid was first picked in 2009, as I've said before, in Mabvuku. But, from there, we have been monitoring the strains, and what we found was that, in 2008 and 2010, 2011, and 2012, these strains were so susceptible to ciprofloxacin as the main drug of choice for typhoid management.

Then it turned in 2014. That's when we first picked our first resistant strain. And this strain we picked it in Budiriro, the same area which we had recorded the 2008 outbreak of cholera, is actually as mentioned before that for the management of that outbreak of cholera we are using ciprofloxacin. Maybe there was a selective pressure, and that's where we also first picked our first ciprofloxacin-resistant strain of typhoid.

So, from 2014, we saw an increase in the resistance or increased number of strains that were resistant to ciprofloxacin, from 4.6% to around 21%. And, in 2017, there was just a slight increase of just 1%, but to our surprise, in 2018, when we also had that cholera outbreak, we also had a cholera-- we also had a ciprofloxacin-resistant outbreak of typhoid in one of the suburbs called Kuwadzana, And, of note, this outbreak, it also managed to spread to another suburb which is about 300 kilometres away from Harare.

And yet, the strains with the 100% of resistance to ciprofloxacin, so that the drug of choice changed from ciprofloxacin to ceftriaxone and also azithromycin. But to manage this outbreak, we had also to introduce a vaccination. So, yes, we also managed to push issues to do with WASH, waste management, but the measure that we ended up resorting to was vaccination of people in the nine affected suburbs of Harare, and around more than 318,000 people were vaccinated between the age of 6 to 12 months.

So what we have learned of this outbreak was that it's important to do genomic surveillance to check what is really causing resistance. So for the outbreak, what we picked was it was due to a plasmid. And then, also, for this one, we have seen that it was-- there was a combination of two things, a mutation of the chromosome and also a plasmid-mediated resistance, the ciprofloxacin resistance, which was also caused by QNRS gene. So because of all these results that we got from sequencing, we thought a vaccination was going to be the best remedy as we are going to-- as we managed the issues to do with WASH and the provision of clean water there.

So, overall, what we got from these outbreaks was it is very, very important to promote genomic surveillance both to help you to understand why there is resistance, what is the main type of this resistance, and how best you can give or how best you can improve or how best we can use evidence-based mitigation measures other than just to use methods that you are not very sure of.

So I would like to thank you for listening. I would also like to share my gratitude.