Progress and Remaining Gaps in Estimating the Global Disease Burden of Influenza

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Today, I'm talking with Dr. Joseph Bresee, the Associate Director for Global Heath at the CDC. We'll be talking about the surveillance of influenza. Welcome, Dr. Bresee.

[Joseph Bresee] Thanks for having me.

[Sarah Gregory] Your study is about the progress and gaps estimating the global burden of influenza. Tell us about the different kinds of flu and how they affect people. For instance, regular seasonal flu epidemics and then pandemics.

[Joseph Bresee] That's a great question. So, seasonal flu—epidemic flu—and pandemic flu are sort of like two faces of the same thing. And to understand those, think about the viruses. Flu viruses are a family of related viruses. Some of the viruses have evolved over time to cause disease in humans and spread between humans, while others have adapted to infect other animals, like ducks or pigs. Human flu viruses cause seasonal flu epidemics. In the U.S., flu epidemics occur in the winter and we vaccinate against those flu viruses that occur in the winter. Influenza pandemics, on the other hand, are caused by non–human viruses, like swine viruses or duck viruses. They gain the ability, through mutation, to infect and cause disease in humans, and then spread between humans. Because humans don't have immunity against these non–human viruses, pandemics can spread very quickly and cause a lot of severe disease very quickly. In 2009, which is the last pandemic we had, the virus spread globally, after it emerged in Mexico, within about a few weeks. So, while we experience seasonal epidemics of influenza every single year, pandemics are fortunately pretty uncommon. Only four have happened in the last hundred years or so.

[Sarah Gregory] Okay, I think you sort of touched on it already, but how big a problem is the flu in the world?

[Joseph Bresee] So, flu is one of the leading causes of respiratory disease and, in fact, death from respiratory disease, all over the world. Let me give you some numbers—five to 15 percent of everybody in the world is infected with flu every year. And so that counts for hundreds of millions of cases of flu each year. We just did a study that CDC led, that included about 80 countries, that looked at how many deaths occurred. And so, of those hundreds of millions of cases, between 290 and 650 thousand deaths occur each and every year from flu, and tens of millions of people are hospitalized. So, flu is really a huge cause of death, of disease, of hospitalizations, and of just daily disease, staying home from work and missing school, every year in the world.

[Sarah Gregory] Okay, so why is it important to have data on the flu?

[Joseph Bresee] Well, we need data on how important flu is to make wise investments on how to prevent or control it. So this means knowing which groups are most impacted, where it causes the most deaths. The problem is, of course, flu is, in many ways, an invisible disease or a hidden disease. Most people who get the flu don't get tested. Even if you do go to a doctor, and you do get tested, you often show up several days later, when you're no longer positive. Because of that,

the results of these flu testing, flu becomes a sort of drastically undercounted or underappreciated disease. So, studies that are specifically designed to measure the burden of flu in a community, or a country, or a region, are really critical to understanding the importance of flu, and then using those data to understand whether you should invest in a vaccination program or an antiviral program to reduce that burden.

[Sarah Gregory] Okay, you just said something I've never heard before. If you wait too long and you're tested, you don't show up positive?

[Joseph Bresee] Yeah. Flu causes disease in two ways. Think about it. Primary infection—you get a virus in your nose, it replicates, it divides, and it moves down into your lungs, and you get pneumonia from flu. And that usually happens fairly quickly, you get sick. Sometimes, though, and maybe more often than not, flu will cause an infection, you'll have underlying heart disease, or underlying lung disease, or diabetes, or some other disease altogether, and flu will make that worse. And so, when you get to the hospital, it's not because of the respiratory infection, it's because you have chronic obstructive pulmonary disease complications or a heart attack or a stroke that was, that was instigated by the flu. So when those people show up, four to five to seven days after initially getting the flu, you no longer have the virus, but you still have the disease that the virus triggers.

[Sarah Gregory] And then, so how do vaccines and antivirals play into stopping or treating flu?

[Joseph Bresee] So, vaccines remain the single best way to prevent influenza and is found in most places and in most groups to be a cost-effective way to do so. Vaccines reduce influenza cases as well as preventing complications. They also have the added benefit in healthy young people of preventing lost days of work or missed school days, which helps economically, as well. Antiviral medications, on the other hand, are used for treatment, so once you get sick, you take antiviral medications. They're really effective in reducing the length of illness and reducing complications, as well. The big problem with both these things are, unfortunately, both antivirals and influenza vaccines are underused in low- and middle-income countries, where they're needed most, and this results in a lot of missed opportunities for prevention.

[Sarah Gregory] Who collects data on influenza outbreaks and how do they do it?

[Joseph Bresee] Well, every country, or almost every country, around the world conducts surveillance for influenza. And using the surveillance data, they test for the viruses, they look at people with disease, they can determine when influenza epidemics are occurring. For decades now, really since the 1960s or 50s, the World Health Organization has worked to coordinate all these countries. And so, the countries, as they collect data, can share the data with other countries and with the World Health Organization that allows the world to understand what's happening in country X or Y, but also if there's a signal that maybe a new virus emerging, like a pandemic virus, or a new outbreak that needs a response. CDC works with WHO to do this. We fund a part of WHO's program to do this. We also support more than 60 national governments around the world to develop the ability to detect and respond to influenza epidemics or pandemics, and to share those data with the global community. We're now working with many of the countries we've worked with for the last 15 years on this surveillance capacity, to transform that capacity into vaccination programs.

[Sarah Gregory] So, this is maybe slightly different than what we're talking about, but I know that CDC is involved in deciding which seasonal flu is which or gonna to happen?

[Joseph Bresee] We do help with that. We're a World Health Organization collaborating center, and what that means, there are four of these centers around the world, we're one of them. And those groups get together, we get together with the other three laboratories, in Geneva usually, twice a year, to decide what goes in the vaccines each year.

[Sarah Gregory] What are some of the major gaps in the collection of good data?

[Joseph Bresee] I think there are two big ones. And while there are a lot more data now than there were five to 10 years ago because of all these initiatives, I think we still have too few data, from low-income countries, especially. And we have too few data on the severe outcomes, or complications, of flu. And severe outcomes are really important because that's what drives policy makers, decision makers, ministry of finance to invest in flu prevention. If you know their hospitalizations, their deaths, that's a much more compelling case to invest money in prevention. And finally, I guess, the third thing maybe, a lot of countries, especially middle-income countries who are sort of thinking about whether to invest in flu vaccination or stockpiles of antivirals, need to know about the cost of flu, and we don't have much data in those countries on that.

[Sarah Gregory] And so is there something being done about these gaps?

[Joseph Bresee] Fortunately, there's lots being done, actually. CDC, among a bunch of other international partners, are continuing to work with countries to build the capacity for estimating the disease burden and for developing these influenza prevention programs. World Health Organization, through an international collaborative program called the Pandemic Influenza Preparedness Framework, are supporting the lowest income countries to collect these data. We're really fortunate in the influenza world, I would say, to have exceedingly good collaborations on influenza prevention and control worldwide, led by colleagues at WHO. But it's a really big job and it'll take a lot of years and a lot of resources to both build it and maintain it. And we're always mindful, with the constant threat of a pandemic or the next epidemic, that it really is urgent that it work.

[Sarah Gregory] Your article discusses large disparities between different countries. How do high-income countries address flu differently than low- and middle-income countries?

[Joseph Bresee] Well first, as you can imagine, high-income countries have long had good data on the burden of flu in those countries. And they've used that to justify an investment in influenza vaccination programs or antiviral treatment programs. Both of those have reduced the burden of influenza in those countries. The problem is, of course, these tools—vaccines and antivirals—are really drastically underused in low- and middle-income countries, both because the costs of the disease, but also just because there's a historic lack of disease burden data that's limited the ability of those decision makers in those countries to make a compelling case for investing in flu prevention. We're finding this changing as more data are collected and countries are becoming more aware of the impact of influenza in their countries. They're starting to develop these policies. The best example is the country of Laos in Southeast Asia. A couple of years ago, they initiated an annual influenza vaccination program targeting their high-risk groups in the country—the first low-, low-middle income country to do so. And it was on the heels of about 10 years of working with CDC, both to estimate the disease burden, the cost, the cost-

effectiveness of the vaccine, to sort of line up the evidence. And given that evidence, they invested in vaccination program, despite being a low-income country. I think as we start to think about how we engage countries, what data they need to make decisions, Laos is a great example for the roadmap to do that.

[Sarah Gregory] I guess along the same lines as you were already saying, what is the bottom line reason for this disparity?

[Joseph Bresee] I think what we found is, clearly, that low-income countries or people living in low-income countries or tropical countries, have higher risk of severe influenza disease and death from flu. We know that. It's probably due to a bunch of reasons. One of the reasons is they have less ready access to care when they get sick. And so, they can have the same illness, but if they show up five days later with pneumonia versus showing up on day two where that pneumonia could have been prevented, they're in worse shape. Another reason is they have fewer vaccines or antivirals to treat them, and so because of that, they have more disease. And finally, among the other myriad of causes probably, some of the countries have higher fractions of the population with diseases that cause more, that lead to more severe flu disease, like HIV infection. So, I think that there's a myriad of these causes that come together in these countries, that sometimes they have two or three greater risks of death from flu than, say, the United States.

[Sarah Gregory] Your article is about progress, as well as gaps, so that's good news. In the last decade, data collection from low- and middle-income countries has improved. So, how has this happened and what do these findings reveal?

[Joseph Bresee] Well, it's happened because both countries and international organizations have committed themselves to the work. We all realize that influenza is a global disease and a global threat, and that reducing the threat to any one country requires all countries to work together. The first step to do that, clearly, is by understanding how much disease is occurring, who's it occurring in, and where is it occurring. We found that, not surprisingly, the burden of influenza is greatest in Africa and South Asia, and among older adults and very young children, the very groups that we target for vaccination in many countries. For many years, strangely enough, up until very recently, flu was thought to be a disease of rich countries. And now we're finding, as data are collected in low-income and middle-income countries, it's just not true.

[Sarah Gregory] Why would they think it was a disease of rich countries?

[Joseph Bresee] 'Cause no one ever looked in low-income countries. Low-income countries have traditionally had very poor surveillance, had other priorities to worry about. And so, we didn't do much with flu research or flu surveillance in those countries, up until about 10 or 12 years ago. And as the data are building now, we're realizing not only is flu everywhere in the world, but if you're a kid or an adult in a low-income country, your risk of dying of flu is much greater than, say, the United States or France.

[Sarah Gregory] So, I guess that kinda goes back to the disparity issue?

[Joseph Bresee] Exactly.

[Sarah Gregory] Yeah. Are there plans or recommendations for going forward? And what do you see as the greatest needs?

[Joseph Bresee] Well, it's clearly not enough to know about flu and its impact each and every year, although that's vital—we need to do something about it! And so, in the coming years, CDC and a bunch of other global partners are beginning to invest more and more in growing influenza vaccination programs, so not only do we learn about flu through surveillance, but we actually do something about flu to reduce it. The vaccination programs, we feel strongly, will both reduce the illness globally, but also make us safer from the next pandemic, 'cause vaccines you're going to need to use during a pandemic are the very same vaccines and processes and systems you use during seasonal flu. So you practice every year for seasonal flu, so you're ready to produce vaccine and use vaccine quickly and timely and efficiently during a pandemic. The other need, of course, in all of this, is more effective vaccines for flu, and vaccines you can give less often, that are more amenable to giving a low-income country. These are being worked on really actively right now, and I think we look forward to a future with even better tools to reduce influenza disease and deaths.

[Sarah Gregory] I've heard that if you get enough seasonal flu vaccines, that eventually you kind of have a basic resistance to flu. Is this true?

[Joseph Bresee] It's not, actually. It's a good, it's. . .it's a myth, though, and it's a myth that a lot of people think about and use as an excuse not to get vaccinated every year. I think one of the key features, or bugs, in flu, so to speak, is that it mutates really fast and continuously. And so what happens is, as the viruses circulate all over the world year-round, they continue to mutate, and they mutate in ways that evade the human immune system. So, the virus that we saw this year, we've developed a lot of antibodies to, as a population. Those antibodies are now pushing this virus antigenically, their proteins on the surface, to a different place. And so, when they show up next year, the year after, they'll look different and our immune system won't recognize it as well.

[Sarah Gregory] Well, that's too bad. So, tell us about your job at CDC and how you're involved in this research.

[Joseph Bresee] Well, at CDC I'm an epidemiologist and a pediatrician, and have worked on flu and other infectious diseases for about 25 years now. I'm really lucky to be here, I think, and we have a great team, dedicated, smart people that are really committed to reducing the threat of flu, both here and overseas. I am proud to work at CDC, frankly. That CDC is just sort of this agency that enables work to be done, and is fundamentally driven by making sure that we can use our resources and energies to protect the health of the public. For this particular project, I've been fortunate to chair a World Health Organization committee for the last five years that has tried to be a mechanism or an engine to catalyze some of this work.

[Sarah Gregory] Thank you so much, Dr. Bresee. Listeners can read the article, Progress and Remaining Gaps in Estimating the Global Disease Burden of Influenza, online at cdc.gov/eid.

I'm Sarah Gregory for Emerging Infectious Diseases.

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.