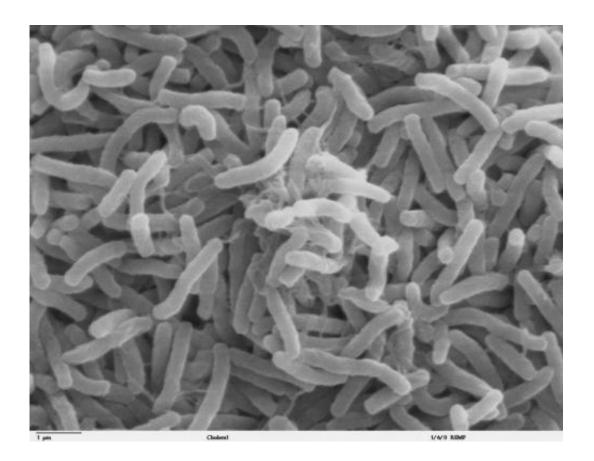


Less may be more in slowing cholera epidemics

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Scanning electron microscope image of Vibrio cholerae bacteria, which infect the digestive system. Credit: Ronald Taylor, Tom Kirn, Louisa Howard/Wikipedia

An oral cholera vaccine that is in short supply could treat more people and save more lives in crisis situations, if one dose were dispensed



instead of the recommended two, new Johns Hopkins Bloomberg School of Public Health research suggests.

More than 1.5 billion people around the world are at risk for <u>cholera</u>, a severe diarrheal illness caused by bacteria linked to poor water and sanitation. It is a major killer worldwide, causing an estimated two to three million cases and 100,000 deaths each year, primarily in developing nations.

A relatively new vaccine—internationally licensed by the World Health Organization (WHO) in 2011—is in short supply, with roughly two million doses kept in a WHO stockpile. Current protocol calls for two doses of the vaccine to be given at least two weeks apart. During recent outbreaks, including the one in Port-au-Prince following Haiti's devastating 2010 earthquake, the vaccine has not been in wide use—in part because there isn't enough of it. Roughly 120,000 people contracted cholera and more than 800 died from it in the months after the quake.

The Bloomberg School researchers set out to determine the best way to use this limited supply to make the biggest impact on health, and they published a report on their findings in *PLOS Medicine* on Aug. 25.

Using mathematical modeling, the researchers estimated that if vaccination had begun within a year of the earthquake, with enough vaccine to cover 50 percent of the population of Port-au-Prince with a single dose (1.05 million doses), the one-dose strategy would have prevented 78,317 cases of cholera and prevented 783 deaths. They found that two doses would have protected five percent fewer people. That's because the logistics of refrigerating the vaccine between doses and ensuring that people were found for their second dose two weeks after the first would cost money and valuable time that could have been spent vaccinating more people.



Little is known about the effectiveness of a single dose of the vaccine, and the researchers concede that giving one dose to more people may lead to less individual immunity. But a single dose could actually improve herd immunity, protecting more people in the long run.

"When vaccine supplies are limited, one dose of vaccine is at least as good as two and it makes things logistically easier and cheaper to deliver. And in an outbreak, it is important to get as much vaccine out there as quickly as you can," says study leader Justin Lessler, an assistant professor in the Department of Epidemiology at the Bloomberg School. "When we have a limited supply of vaccine, we need to make hard decisions. This research tells us that when responding to an outbreak, one dose may be the way to go."

An estimated five to 10 percent of people who develop the cholera infection in their intestines will have severe disease characterized by excessive diarrhea, vomiting and leg cramps. The rapid loss of body fluids leads to dehydration and shock and, without treatment, death can occur within hours. There is virtually no cholera in the United States as it tends to be transmitted by unclean water and poor sanitation practices. The key to eradicating cholera, the researchers say, is upgrading water and sanitation. The vaccine is supposed to be a stopgap measure, they say, until sustainable infrastructure improvements can be implemented.

Along with Haiti, the researchers also used their models to analyze a 2008-2009 cholera epidemic in Zimbabwe, which resulted in 98,351 reported cases and 4,288 deaths. If vaccination had begun four months after the first reported case, with enough vaccine to cover 50 percent of the population with one dose (6.7 million doses), a single-dose vaccination campaign would likely have averted an estimated 70,854 cases and nearly 3,000 deaths. That means administering one dose would have averted 16 percent more cholera cases and deaths than a two-dose campaign, according to the model.



The findings were similar when looking at a 2013 outbreak in Guinea. A two-dose campaign took place in two rural areas but not in the capital, Conakry. If a timely campaign had been done there starting two months after the first case was reported, the researchers found, a one-dose campaign covering 50 percent of the population (828,000 doses) would likely have averted an estimated 2,826 cases and 51 deaths. The model predicts that 21 percent fewer cases and deaths would have been reported with a one-dose campaign than if a two-dose campaign had been conducted.

"Either of these scenarios would have been a huge improvement over what really happened, but our model shows that less is often more," says study co-author Andrew S. Azman, a research associate at the Bloomberg School. "Because of the herd immunity that occurs when more people are vaccinated, it appears people are safer getting one dose of <u>cholera vaccine</u> instead of two because their neighbors would also be protected if there are doses available to more people. One dose with more indirect protection means people are less likely to be exposed to the disease."

In Juba, the capital of South Sudan, there is currently a <u>cholera outbreak</u> underway and there are about 250,000 doses of <u>vaccine</u> available. Officials there have chosen to test the one-dose strategy in order to reach more people more quickly. Azman, Lessler and other co-authors from Médecins Sans Frontières of the current study will be investigating the Juba experience to see how this mathematical research is translated in the real world.

More information: "The Impact of a One-Dose versus Two-Dose Oral Cholera Vaccine Regimen in Outbreak Settings: A Modeling Study," *PLOS Medicine*, 2015. journals.plos.org/plosmedicine journal.pmed.1001867



Provided by Johns Hopkins University Bloomberg School of Public Health

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