WaSH Policy Research Digest

ISSUE #9, SEPTEMBER 2018: CHOLERA CONTROL

Detailed Review of a Recent Publication: Governments can achieve cholera control through a well-targeted and coordinated combination of universal WaSH access and vaccination

Lessler, J., Moore, S.M., Luquero, F.J., McKay, H.S., Grais, R., Henkens, M., Mengel, M., Dunoyer, J., M'bangombe, M., Lee, E.C., Djingarey, M.H. (2018). Mapping the burden of cholera in sub-Saharan Africa and implications for control: an analysis of data across geographical scales. *The Lancet, 391(10133),* 1908-1915. doi: 10.1016/S0140-6736(17)33050-7.

Cholera still occurs throughout sub-Saharan Africa, where it is endemic in some countries, and strikes in sporadic and deadly epidemics in others. In a paper published in March 2018, Lessler et al. present the findings from an analysis that allowed them to estimate the number of people in sub-Saharan Africa living in areas of high cholera incidence, defined as more than one case per thousand people per year. The authors were also able to estimate the reduction in cholera incidence that could be achieved by targeting these areas with prevention and control through two interventions: vaccination using Oral Cholera Vaccine (OCV) and providing access to water, sanitation and hygiene (WaSH). While a new generation of effective cholera vaccines is now available, the authors acknowledge that "access to safe water, appropriate sanitation and hygiene remains the foundation of sustained cholera control". Finding the most effective and appropriate mix of these two interventions is a policy challenge for decision makers.

Key Policy and Programmatic Takeaways

- Cholera remains a persistent health problem in sub-Saharan Africa and requires an integrated and well-planned response
- Cholera can only be controlled in a sustained manner over the long term by achieving universal access to water, sanitation and hygiene (WaSH), in households and beyond, particularly health care facilities and schools
- Oral Cholera Vaccine (OCV) is a useful measure to curb transmission in the short term, but is limited by the availability of the vaccine, the amount of time the protection lasts and low efficacy in children under 5
- Detailed mapping of cholera incidence can help in targeting high-risk areas, but must be supplemented by local investigations of cholera epidemiology and mapping of WaSH coverage
- Policy makers must determine the best mix of interventions, working across government to coordinate

Analyzing the geographical distribution of cholera risk in sub-Saharan Africa showed that more than 200 million people are living in areas with at least some cholera incidence. However, the analysis showed that most cholera incidence is concentrated disproportionately in a small number of districts; less than 5% of the total, home to 87 million people. National data may hide subnational epidemiological patterns; Nigeria, for instance, has had consistently low cholera incidence, but the eastern part of the country has large populations with high rates of epidemic cholera. This variation highlights the

The WaSH Policy Research Digest is issued by The Water Institute at UNC—problem solvers focused on the sustainable management of water for health and human development—and comprises a review of a recent article or report, and a short literature review on a WaSH topic. It provides objective, concise and timely information to advise WaSH policy development. To subscribe, please go to waterinstitute.unc.edu/wash-policy-research-digest. Questions or comments about this publication? Please contact us at waterinstitute@unc.edu.

importance of spatial targeting in cholera control, but also the need to both update maps over time and to supplement them with local investigations of cholera epidemiology and WaSH coverage when planning local control strategies.

The authors acknowledge that the people living in districts in sub-Saharan Africa with high incidence of cholera would be best helped by improvements to local water and sanitation infrastructure—what the authors term the "ultimate solution to global cholera"—which would ensure sustained cholera elimination and also provide broad benefits beyond cholera. Fast-tracking of water and sanitation improvements in areas with high cholera risk is also consistent with an emphasis on eliminating inequalities, given the fact that cholera is more likely to be found among the poorest and most disadvantaged (Borroto and Martinez-Piedra, 2000).

The value of oral cholera vaccines is, according to the authors, that they can "curb transmission in the short term, preventing death and disease while crucial improvements to infrastructure are made". The authors suggest that vaccination remains an important tool to prevent and control the spread of cholera during the many years that it will take to fully realize universal coverage of water and sanitation. They estimate that targeting high-risk districts with an integrated campaign of both WaSH and OCV could eliminate 50% of reported cholera by covering less than 4% of the population.

However, while the new cholera vaccines have shown some success, they do not provide long-term protection. They are also limited by their availability. Although supplies are increasing, at the time the article was written in May 2018 the number of doses available was still too low for large, generalized vaccination campaigns. Only about 17 million doses were produced in 2017. The estimates the authors prepared show the limitations of relying exclusively on vaccination. Assuming that OCVs would provide protection to 72% of those vaccinated aged over one year for three years after vaccination, they show that vaccinating all eligible individuals in the high risk populations would require 168.3 million doses of vaccine. This is substantially more vaccine than has been produced since the establishment of a global stockpile in 2013.

Regardless of which mix of interventions is used, it is clear that a well-planned and integrated approach is important. This is advocated by the Global Task Force on Cholera Control (an alliance of partners including WHO, UNICEF, the Bill and Melinda Gates Foundation, the CDC, and others) in the recently-released "Ending Cholera: A Global Roadmap to 2030" (GTFCC, 2017). This approach will require collaboration across ministries involving, at a very minimum, the ministries responsible for WaSH and for health (which are sometimes, but not always, also responsible for hygiene and sanitation). Coordination of health and infrastructure interventions—taking into account variations in both timing and geographical scale—is also required. For instance, while vaccination programs can be implemented on a population basis, WaSH interventions, especially water supply systems, are carried out at the scale of towns or villages. This has implications for geographical targeting, and the authors state that "finer scale maps supplemented by detailed analysis of the local situation" would be helpful.

Innovation is also required; a weakness of the paper is that the authors ignore interim WaSH solutions that can be implemented rapidly and don't require infrastructure, such as sustained household water treatment and safe storage of water supplies. Behaviour change interventions, such as the promotion of handwashing with soap at key times, can also be highly effective in limiting disease transmission.

Review prepared by Clarissa Brocklehurst, Adjunct Professor, Department of Environmental Sciences and Engineering, The Water Institute at the University of North Carolina at Chapel Hill

Literature Review: The role of WaSH in preventing cholera

The literature on the role of WaSH in the spread of cholera dates to the middle of the 19th century, when John Snow conducted his "Grand Experiment". In his seminal work "On the Mode of Communication of Cholera" (Snow, 1855), Snow documented the fact that the population of several areas within South London took their drinking water from one of two companies, and

that frequently neighbours within the same street were supplied by different companies. He further showed that during the 1849 cholera epidemic, both companies took their water from the same polluted part of the river Thames, but that by the 1853 epidemic one company had moved its source to a much less polluted part of the river. During the 1849 epidemic the infection rates were similar between customers of the two companies, but by 1853 the attack rate was much lower in people drinking water from the less polluted source. Cholera was thus established as the archetypal waterborne disease.

Outbreaks of cholera associated with contaminated water continue to this day. For example a recent outbreak in Western Uganda was caused by the consumption of faecally contaminated water (Kwesiga et al., 2018), as was an outbreak in India (Uthappa et al., 2015).

Despite the widespread acceptance of drinking water as a major exposure pathway for cholera, and continuing reports of outbreaks linked to contaminated water supplies, the role and value of WaSH interventions in the prevention and management of outbreaks and epidemics remain unclear. In part, this uncertainty follows a systematic review by Taylor et al. (2015) that concluded that the evidence base supporting WaSH interventions for the control of cholera was actually quite poor. Although some took this to mean that WaSH interventions were not effective in the control of cholera, the authors of the systematic review actually concluded that the lack of evidence was in large part due to inadequate study designs.

There are many observational studies reported in the literature that provide compelling evidence that inadequate drinking water, sanitation or hygiene have important impacts on cholera risk. Taken together as a whole, observational evidence provides compelling evidence of the importance all the WaSH related transmission pathways as risk factors for cholera. For example, in a particularly well-conducted study in a Kenyan refugee camp (Shultz et al., 2009) it was found that where three or more households were sharing the same latrine the risk of cholera more than doubled. This same study found that those families that stored their water in sealed or covered containers were only half as likely to develop cholera. In a case control study in Vietnam (Nguyen et al., 2017), risk of cholera was increased in those people who drank iced tea, did not always boil their drinking water or whose primary source of drinking water was located close to a toilet. Handwashing (Zohura et al., 2016), latrines (Grandesso et al., 2014) and water storage (Bhunia and Ghosh, 2011), have all been shown to be associated with cholera infections.

However, one has to be cautious about attributing overly simplistic explanations of the links between WaSH and cholera. Tickner and Gouveia-Vigeant (2005) argue that, though it is often believed that the major cholera epidemic that hit Peru in 1991 was caused by concerns about disinfection by-products, which led a reduction in chlorination, there was in fact no decision to stop chlorination and the epidemic was instead "caused by a much more complex set of circumstances, including poor sanitation conditions, poor separation of water and waste streams, and inadequate water treatment and distribution systems".

One of the potentially more important changes in thinking about cholera in the past few years has been the documentation of cholera "hotspots". In papers by Ali et al. (2017) and Lessler et al. (2018) (reviewed in detail in this Digest), both sets of authors showed that there are well-defined locations where cholera is far more prevalent than surrounding areas. Such hotspots may be important in the broader epidemiology of the disease as they act as loci where disease prevalence is multiplied, enabling further spread into surrounding areas. The explanation for the presence of these hotspots is not yet clear, but one plausible explanation is that they occur in areas where water, sanitation and hygiene are particularly poor. This may not represent failure of a single easily measured WaSH modality but complex interactions between several WaSH modalities, as documented by Tickner and Gouveia-Vigeant in 2005.

Although a vaccine does exist for cholera, it is essential not to become complacent. A meta-analysis of several studies by Bi et al. (2017) has shown that the cholera vaccine is far from ideal; the authors found that vaccine efficacy after two doses is only 58% and protection declines rapidly after just two

years. Furthermore, the efficacy of the vaccine is particularly low (30%) in children under five years old. Reliance on a vaccine alone is unlikely to prevent major epidemics of cholera. Instead, targeting improvement in provision of WaSH services in cholera hotspots is a potentially more effective strategy for the prevention of the spread of the disease. There is a need to better understand the factors behind the distribution of cholera hotspots and the value of improvements across all WaSH domains.

Literature review prepared by Paul Hunter, based on the work of Natalia Jones, Iain Lake, Maha Bouzid and Roger Few, all of University of East Anglia

References

Ali, M., Gupta, S.S., Arora, N., Khasnobis, P., Venkatesh, S., Sur, D., Nair, G.B., Sack, D.A., Ganguly, N.K. (2017). Identification of burden hotspots and risk factors for cholera in India: An observational study. *PloS One, 12(8)*, e0183100. doi: 10.1371/journal.pone.0183100.

Bhunia, R., Ghosh, S. (2011). Waterborne cholera outbreak following Cyclone Aila in Sundarban area of West Bengal, India, 2009. *Transactions of the Royal Society of Tropical Medicine & Hygiene, 105*, 214-219. doi: 10.1016/j.trstmh.2010.12.008.

Bi, Q., Ferreras, E., Pezzoli, L., Legros, D., Ivers, L.C., Date, K., Qadri, F., Digilio, L., Sack, D.A., Ali, M., Lessler, J. (2017). Protection against cholera from killed whole-cell oral cholera vaccines: a systematic review and meta-analysis. *The Lancet Infectious Diseases, 17(10)*, 1080-1088. doi: 10.1016/S1473-3099(17)30359-6.

Borroto, R. J., Martinez-Piedra, R. (2000). Geographical patterns of cholera in Mexico, 1991–1996. *International Journal of Epidemiology, 29 (4)*, 764–772. doi: 10.1093/ije/29.4.764.

Global Task Force on Cholera Control. (2017). *Ending Cholera: A Global Roadmap to 2030*. World Health Organization. Retrieved September 6, 2018 from http://www.who.int/cholera/publications/global-roadmap-summary.pdf.

Grandesso, F., Allan, M., Jean-Simon, P. S. J., Boncy, J., Blake, A., Pierre, R., Alberti, K. P., Munger, A., Elder, G., Olson, D., Porten, K., Luquero, F. J. (2014). Risk factors for cholera transmission in Haiti during inter-peak periods: Insights to improve current control strategies from two case-control studies. *Epidemiology and Infection, 142*, 1625-1635. doi: 10.1017/S0950268813002562.

Kwesiga, B., Pande, G., Ario, A.R., Tumwesigye, N.M., Matovu, J.K., Zhu, B.P. (2018). A prolonged, community-wide cholera outbreak associated with drinking water contaminated by sewage in Kasese District, western Uganda. *BMC Public Health, 18(1)*, 30. doi: 10.1186/s12889-017-4589-9.

Lessler, J., Moore, S.M., Luquero, F.J., McKay, H.S., Grais, R., Henkens, M., Mengel, M., Dunoyer, J., M'bangombe, M., Lee, E.C., Djingarey, M.H. (2018). Mapping the burden of cholera in sub-Saharan Africa and implications for control: an analysis of data across geographical scales. *The Lancet, 391(10133)*, 1908-1915. doi: 10.1016/S0140-6736(17)33050-7.

Nguyen, T.V., Pham, Q.D., Do, Q.K., Diep, T.T., Phan, H.C., Ho, T.V., Do, H.T., Phan, L.T., Tran, H.N. (2017). Cholera returns to southern Vietnam in an outbreak associated with consuming unsafe water through iced tea: A matched case-control study. *PLoS Neglected Tropical Diseases, 11(4)*, e0005490. doi: 10.1371/journal.pntd.0005490.

Shultz, A., Omollo, J.O., Burke, H., Qassim, M., Ochieng, J.B., Weinberg, M., Feikin, D.R., Breiman, R.F. (2009). Cholera outbreak in Kenyan refugee camp: risk factors for illness and importance of sanitation. *The American Journal of Tropical Medicine and Hygiene, 80(4)*, 640-645.

Snow, J. (1855). *On the Mode of Communication of Cholera*. John Churchill, London. 162.

Taylor, D.L., Kahawita, T.M., Cairncross, S., Ensink, J.H. (2015). The impact of water, sanitation and hygiene interventions to control cholera: a systematic review. *PLoS One, 10(8)*, e0135676. doi: 10.1371/journal.pone.0135676.

Tickner, J., Gouveia Vigeant, T. (2005). The 1991 cholera epidemic in Peru: Not a case of precaution gone awry. *Risk Analysis: An International Journal, 25(3)*, 495-502. doi: 10.1111/j.1539-6924.2005.00617.x.

Uthappa, C.K., Allam, R.R., Nalini, C., Gunti, D., Udaragudi, P.R., Tadi, G.P., Murhekar, M.V. (2015). An outbreak of cholera in Medipally village, Andhra Pradesh, India, 2013. *Journal of Health, Population and Nutrition, 33(1)*, 7. doi: 10.1186/s41043-015-0021-1.

Zohura, F., Bhuyian, S. I., Monira, S., Begum, F., Biswas, S. K., Parvin, T., Sack, D., Sack, R. B., Leontsini, E., Saif-Ur-Rahman, K. M., Rashid, M. U., Sharmin, R., Zhang, X., Alam, M., George, C. M. (2016). Observed Handwashing with Soap Practices Among Cholera Patients and Accompanying Household Members in a Hospital Setting (CHoBI7 Trial). *American Journal of Tropical Medicine & Hygiene, 95*, 1314-1318. doi: 10.4269/ajtmh.16-0379.