References

- 1. Renehan A, Gilbert D. Anal cancer: different epidemiological and clinical definitions. *Int J Epidemiol* 2017;46:2091–92.
- Islami F, Ferlay J, Lortet-Tieulent J *et al.* International trends in anal cancer incidence rates. *Int J Epidemiol* 2016;46:924–38.

Integration of water, sanitation and
hygiene intervention delivery atInternational Journal of Epidemiology, 2017, 2093–2094
doi: 10.1093/ije/dyx025Advance Access Publication Date: 27 February 2017



hygiene intervention delivery at Advance Access Publication Date: 27 Februar health facilities with a reactive ring vaccination programme to reduce cholera

Christine Marie George* and David A Sack

Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

*Corresponding author. Department of International Health, Program in Global Disease Epidemiology and Control, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Room E5535, Baltimore, MD 21205, USA. E-mail: cgeorg19@jhu.edu

Globally there are estimated to be 2.8 million cholera cases annually, resulting in 95 000 deaths.¹ Ali and colleagues recently reported results on the spatiotemporal risk for cholera and estimated overall and indirect cholera vaccine effectiveness of a ring vaccination programme, by analysing data from an oral cholera vaccine (OCV) trial in Kolkata, India.² Cohorts in close proximity to a cholera case had a 5-11 times higher risk of cholera during the 1-month period after the onset of case illness when compared with cohorts not exposed to a case. High OCV coverage for populations within 25 m of a cholera case resulted in an overall and indirect vaccine efficacies of 91% and 93%, respectively, during this 1-month high-risk period when compared with lowvaccine coverage areas. These promising findings show the high level of protection that could potentially be achieved if a reactive ring vaccination programme was conducted around identified cholera cases. This is of particular importance given the limited supply of OCV globally.

Consistent with this study, previous studies have found household contacts of cholera patients to have a 130–150 times higher risk of developing a cholera infection than the general population during the 1-week period after onset of illness in the index patient.^{1,3–5} This high risk is likely due to a shared contaminated environmental source or secondary transmission from infected household members.^{3,4} Most recently Debes and colleagues expanded on these previous studies by investigating the risk for cholera for all those living in close proximity to an index case in rural Matlab, Bangladesh. The authors reported that those living within 50 m of an index case were at a 20 times higher risk of cholera during the 1-week period after the onset of case illness compared with those living near controls.⁶

The protective immunity conferred by OCV takes several days to develop. Therefore the 1-week period when those living in close proximity to a cholera case are at highest risk of cholera is the time when little or no vaccine protection would be conferred by a ring vaccination programme. In an effort to develop a targeted intervention for this high-risk population during the 1-week period when they are most susceptible, the Cholera-Hospital-Intervention-for-7-Days (CHoBI7) was developed.⁷ Chobi mean picture in Bangla, for the pictorial modules provided as part of this intervention. This intensive handwashing with soap and water treatment intervention is delivered by a promoter to cholera patients and their accompanying household contacts at the time of admission to a health facility, and is reinforced through home visits. CHoBI7's pictorial modules emphasize the importance of water treatment with chlorine and handwashing with soap during the 1-week high-risk period for cholera after onset of patient illness. In Bangladesh, this intervention included the distribution of chlorine tablets, soapy water made of water and detergent powder (a lowcost alternative to bar soap), a handwashing station, and a drinking water vessel with lid and tap.

The recent randomized controlled trial of the CHoBI7 intervention in Dhaka, Bangladesh, found that delivery of this targeted water, sanitation and hygiene (WASH) intervention resulted in a significant reduction in symptomatic cholera among household contacts of cholera patients during the 1-week high-risk period after onset of case illness.⁷ Furthermore, delivery of this 1-week intervention resulted in

sustained handwashing with soap and improved water quality in cholera patient households up to 12 months following the intervention.⁸ This result was consistent with findings from Deb and colleagues, who found that delivery of narrow-neck drinking water vessels and chlorine to cholera patient households in slums in Kolkata, India led to significant reductions in cholera infections among household contacts.⁹ The high efficacy of these interventions is likely attributed to the WASH interventions reducing the spread of cholera within patient households from infected individuals and from contaminated drinking water.

Given the limited supply of OCV globally and the delay in in achieving vaccine protection conferred by a ring vaccination programme, a more comprehensive targeted package of interventions, beyond vaccine alone, is needed. Integration of an intensive WASH programme targeting cholera patients treated at health facilities and their household contacts with an OCV ring vaccination programme for those living in close proximity to the cholera case presents a promising approach for limiting cholera transmission and reducing the number of cholera infections. This intervention would provide protection against cholera for a high-risk population when they are most susceptible and would deliver OCV to a cholera hotspot where overall vaccine efficacy is likely high.

An intervention combining this type of targeted WASH intervention along with a targeted OCV campaign would require cholera patients to be quickly identified at health facilities, OCV to be readily available, and rapid response teams to be ready to intervene. This means a plan needs to be in place before cholera outbreaks occur. We recommend that cholera-endemic countries determine the feasibility of integrating this approach into their cholera control plans.

References

- Ali M, Nelson AR, Lopez AL, Sack DA. Updated global burden of cholera in endemic countries. *PLoS Negl Trop Dis* 2015; 9:e0003832.
- 2. Ali M, Debes AK, Luquero FJ *et al.* Potential for controlling cholera using a ring vaccination strategy: re-analysis of data from a cluster-randomized clinical trial. *PLoS Med* 2016;**13**:e1002120.
- Spira W, Khan MU, Saeed Y, Sattar M. Microbiological surveillance of intra-neighbourhood El Tor cholera transmission in rural Bangaldesh. *Bull World Health Organ* 1980;58:731.
- Hughes JM, Boyce JM, Levine RJ *et al.* Epidemiology of eltor cholera in rural Bangladesh: importance of surface water in transmission. *Bull World Health Organ* 1982;60:395.
- Weil AA, Khan AI, Chowdhury F *et al.* Clinical outcomes in household contacts of patients with cholera in Bangladesh. *Clin Infect Dis* 2009;49:1473–79.
- Debes AK, Ali M, Azman AS, Yunus M, Sack DA. Cholera cases cluster in time and space in Matlab, Bangladesh: implications for targeted preventive interventions. *Int J Epidemiol* 2016, Oct 27. pii: dyw267. [Epub ahead of print.]
- George CM, Monira S, Sack DA *et al.*, Randomized controlled trial of hospital-based hygiene and water treatment intervention (CHoBI7) to reduce cholera. *Emerg Infect Dis* 2016;22:233–41.
- George CM, Jung DS, Saif-Ur-Rahman KM *et al.* Sustained Uptake of a Hospital-Based Handwashing with Soap and Water Treatment Intervention (Cholera-Hospital-Based Intervention for 7 Days [CHoBI7]): A Randomized Controlled Trial. *Am J Trop Med Hyg* 2016;94:428–36.
- Deb B, Sircar B, Sengupta P *et al*. Studies on interventions to prevent eltor cholera transmission in urban slums. *Bull World Health Organ* 1986;64:127.

A note on the use of Egger regression in Mendelian randomization studies

International Journal of Epidemiology, 2017, 2094–2097 doi: 10.1093/ije/dyx191 Advance Access Publication Date: 12 September 2017



Eric AW Slob,^{1,2*} Patrick JF Groenen,^{1,3} A Roy Thurik^{1,2,4} and Cornelius A Rietveld^{1,2}

¹Erasmus University Rotterdam Institute for Behavior and Biology, ²Department of Applied Economics, ³Econometric Institute, Erasmus School of Economics, Rotterdam, The Netherlands and ⁴Montpellier Business School, Montpellier, France

*Corresponding author. Department of Applied Economics, Erasmus School of Economics, Erasmus University Rotterdam, Burgemeester Oudlaan 50, 3062 PA, Rotterdam, The Netherlands. E-mail: e.a.w.slob@ese.eur.nl.

A large number of epidemiological studies use genetic variants as instrumental variables to infer causal relationships.^{1,2} For a genetic variant to be a valid instrument in these so-called Mendelian randomization (MR) studies,