Reduced vaccination and the risk of measles and other childhood infections post-Ebola

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The Ebola epidemic in West Africa has caused substantial morbidity and mortality. The outbreak has also disrupted health care services, including childhood vaccinations, creating a second public health crisis. We project that after 6 to 18 months of disruptions, a large connected cluster of children unvaccinated for measles will accumulate across Guinea, Liberia, and Sierra Leone. This pool of susceptibility increases the expected size of a regional measles outbreak from 127,000 to 227,000 cases after 18 months, resulting in 2000 to 16,000 additional deaths (comparable to the numbers of Ebola deaths reported thus far). There is a clear path to avoiding outbreaks of childhood vaccine-preventable diseases once the threat of Ebola begins to recede: an aggressive regional vaccination campaign aimed at age groups left unprotected because of health care disruptions.

The current Ebola crisis in West Africa is one of the worst public health disasters in recent memory, having caused more than 21,000 cases and 8400 deaths as of January 2015 and raising the specter of a broader international crisis (1). However, there are signs of hope. Evidence shows that the number of cases is declining in Liberia (2), and sustained transmission has been confined to Guinea, Liberia, and Sierra Leone, despite several transnational introductions including recent transmission in Mali. Stopping Ebola would be a triumph for the global health community and the public health agencies of the affected countries. But even after the last Ebola case recovers, the disruptions of local health systems caused by the outbreak could lead to a second infectious disease crisis that could kill as many as, if not more than, the original outbreak.

Through the combination of the World Health Organization (WHO) Expanded Programme on Immunization (EPI) and periodic supplemental immunization campaigns, annual childhood deaths from vaccine-preventable diseases have dropped from an estimated 500,000 in 2000 to 400,000 in 2010 (9). Measles is emblematic of this success; globally, estimated annual measles mortality has decreased from 499,000 to 102,000 since 2000 (4–5). The Ebola-affected countries have been an important part of this achievement: The three countries reported nearly 93,685 cases of measles in the decade between 1994 and 2003 (despite Sierra Leone not reporting in 4 years), and only 6937 between 2004 and 2013 (in both periods it is likely that only a fraction of measles cases were reported to the WHO) (6). Despite this success, measles susceptibility has been growing in all three countries in recent years, and each had planned a measles vaccination campaign prior to the Ebola outbreak.
experience of routine immunization, supplemental immunization activities (SIAs), and natural infection [using techniques from Simons et al. (5) and data reported to the WHO (6)]. The expected size of any regional post-disruption measles outbreak was then calculated using a phenomenological model of the previously observed relationship between population susceptibility and the percentage of susceptibles infected in an outbreak (i.e., the attack rate) in the region. Finally, we estimated the number of resulting deaths by applying estimates of the case fatality ratio (CFR) for outbreak settings to the overall attack rates (15). Full methodological details are available in the supplement.

We estimate that at the start of the Ebola crisis, there were 778,000 [95% credible interval (CrI): 715,000 to 915,000] unvaccinated children in the three countries (Fig. 1A). These children reside in a large contiguous cluster that crosses national boundaries. With every month of health care disruptions, we estimate that the number of children between 9 months and 5 years of age who are not vaccinated against measles increases by an average of 19,514 (assuming a 75% reduction in routine vaccination rates nationally), reaching 964,346 (95% CrI: 862,682 to 1,068,833) after 6 months (Fig. 1B), 1,068,833 (95% CrI: 914,108 to 1,288,857) after 12 months (Fig. 1C), and 1,129,026 (95% CrI: 934,926 to 1,409,052) after 18 months (Fig. 1D). The results of variations in the spatial distribution and magnitude of disruptions in vaccination are shown in the supplement. This growing cluster of measles susceptibility abuts non-Ebola-affected countries (e.g., Cote d’Ivoire) and regional cross-border migration is frequent (16, 17), thus placing their populations at risk (Fig. 1D).

This increase in unvaccinated children occurs on top of an already growing pool of measles susceptibility in the three countries (Fig. 2) resulting from years of suboptimal routine vaccination (6). After 18 months of disruptions, a large cohort of susceptible children will have entered the population. This growth in susceptibility increases the risk and projected size of regional measles outbreaks. If vaccination had continued at pre-Ebola rates, a generalized measles outbreak would have caused 126,868 (plausible range: 84,833 to 181,769) cases. However, the projected outbreak size increases to 227,484 (153,458 to 321,702) cases after 18 months of disruptions, resulting in a projected 5209 (1757 to 16,173) additional deaths from measles (15). Measles mortality could be at the high end of this range because of the limited health care services and increased prevalence of malnutrition and vitamin A deficiency associated with the Ebola outbreak (18).

The uncertain and rapidly changing Ebola situation in West Africa limits data availability and necessitates numerous analytic assumptions. Our assumption of a 75% reduction in routine vaccination rates is consistent with surveys of health care providers (19), and the qualitative assessment of those who have been involved in the response; however, as there is no reliable information on current vaccination rates, we have considered reductions of 25%, 50%, and 100% in sensitivity analyses. An unusual age distribution of measles cases, poor- or high-quality medical care, and other factors may lead to CFRs that are higher or lower than the range used here, although our estimates are based on a comprehensive assessment of measles CFRs in outbreaks (15). There may be preexisting pockets of susceptibility in older individuals not detected by our analysis for a variety of reasons (e.g., overreporting of vaccination); hence, campaign planning should not be solely based on the effects of the Ebola epidemic. The choice to project no further than 24 months into the future, and to focus on 18 months as the primary analysis, is necessarily somewhat arbitrary; however, it is unlikely that the region will remain measles-free if disruptions continue much beyond 2 years, and there is some evidence that the Ebola situation is beginning to improve (2).

Measles vaccine is just one of several childhood vaccines for which distribution may be limited by the Ebola outbreak. Similar reductions in the rate of vaccination would increase the number of children not receiving a pentavalent vaccine, Bacillus Calmette-Guérin (BCG), and oral polio vaccine (OPV) by about 600,000 to 700,000. These setbacks have the potential to erode the substantial gains in the control of these diseases over recent decades, and a large population of children susceptible to poliovirus infection could threaten the Global Polio Eradication Initiative, should wild poliovirus be reintroduced.

Epidemics of measles are often an early result of interruptions in the delivery of public health services. However, childhood infections are not the only, or even the worst, potential health consequences of disruptions in the health care system. Malaria is the biggest infectious killer in sub-Saharan Africa, and lack of vector control interventions and proper diagnosis and treatment can increase malaria morbidity and mortality [these concerns have prompted Médecins Sans Frontières to conduct mass drug administration of antimalarial drugs in some areas (20)]. Provision of care to individuals with chronic infections, such as HIV and tuberculosis, is negatively affected by the Ebola outbreak. Noninfectious causes of death increase substantially when medical care is not available (e.g., if maternal mortality rates rose to year 2000 levels, there would be an additional 4454 deaths for each year of health care disruptions).

However, childhood vaccine-preventable diseases are an area where there is a clear, relatively inexpensive, and one-time intervention that could erase the impact of Ebola-related health care disruptions. Coordinated campaigns across the three Ebola-affected countries (and possibly neighboring countries) targeting those children who likely missed critical routine vaccinations during the Ebola epidemic with measles and polio vaccines, and potentially other life-saving childhood vaccines, could thwart a second public health disaster and avoid nearly 12,000 deaths from measles alone. Such a campaign should not only target those age groups likely missed during the Ebola crisis (children from birth to an age equal to the length of health care disruptions plus 1 year of age; see Fig. 2), but also those groups where measles susceptibility was already suspected to be
on the rise. Hence, at the very least, a campaign should target children 6 months to 5 years of age (typical of the age range targeted by follow-up SIAs), perhaps extending the lower age range to those filing a request for helpful discussion in preparation of the manuscript. Downloaded from http://science.sciencemag.org/ on July 2, 2015

**REFERENCES AND NOTES**

22. ICF International, Demographic and Health Surveys (various); http://disprogram.org/data/.

**ACKNOWLEDGMENTS**

Supported by Bill & Melinda Gates Foundation grant OPP1094703 and U.S. Department of Homeland Security Science & Technology Directorate contract HSHQDC-12-C-00058 (B.T.G., C.J.E.M.); the RAPIDD program of the Department of Homeland Security Science & Technology Directorate and the NIH Fogarty International Center (C.J.E.M., B.T.G., A.J.T.); National Institute of Allergy and Infectious Diseases (NAID) grant R01 AI089674 and Bill & Melinda Gates Foundation grants OPP1096472 and 1032550 (A.J.T.). We thank M. Hanson for helping to organize the assessment of the impact of Ebola on measles vaccination and for motivating this work, and W. Hao for helpful discussion in preparation of the manuscript.

Demographic and Health Surveys data are made freely available to those filing a request (22). WorldPop project demographic data may be obtained from www.worldpop.org.uk. Data on measles incidence, routine vaccination coverage, and SIAs are available at www.who.int/immunization/monitoring/surveillance/data/en/. Ebola incidence data were extracted from publicly available situation reports (23–25).

**SUPPLEMENTARY MATERIALS**

www.sciencemag.org/content/347/6227/1240/suppl/DC1
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Science 347 (6227), 1240-1242.
DOI: 10.1126/science.aaa3438

Vaccinate children despite Ebola
During the medical emergency caused by the Ebola virus outbreak in West Africa, routine childhood vaccination programs have been suspended. If vaccination is not resumed soon, there could be even more deaths. Measles is highly infectious, and outbreaks are a sign of health care systems in trouble. Using mathematical modelling, Takahashi et al. estimate that about a million children across Liberia, Sierra Leone, and Guinea are vulnerable to measles. Aggressive public health programs are vital for this region to minimize harm, not only from measles but also from polio, malaria, tuberculosis, and other childhood infections.

Science, this issue p. 1240