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Supplement to December 2017

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Global Health Security Supplement to December 2017

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Alana Mermin-Bunnell (b. 2001), *28,616*, 2017. Watercolor and pen on paper, 16 in × 20 in/40.64 cm × 50.8 cm. Digital image courtesy of the artist/private collection, Atlanta, Georgia, USA

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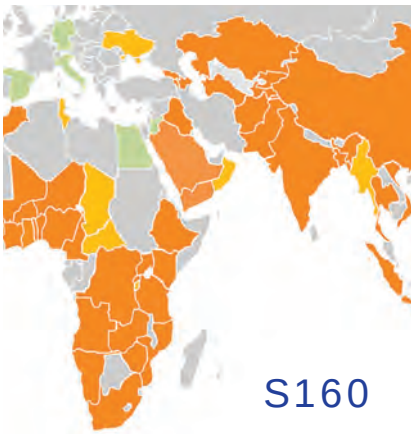

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Progress and Opportunities for Strengthening Global Health Security

Frederick J. Angulo, Cynthia H. Cassell, Jordan W. Tappero, Rebecca E. Bunnell

In today's interconnected world, an infectious disease outbreak that is not rapidly detected and controlled at its source can become a costly global health threat, both in lives lost and economic turmoil (*1*,*2*). Every year, thousands of outbreaks occur worldwide, many of which involve pathogens with pandemic potential. Since 2009, the World Health Organization (WHO) has declared public health emergencies of international concern for outbreaks of influenza A(H1N1) in 2009, Ebola in West Africa in 2014, and Zika in the Americas in 2015 (*2*). In 2007, the International Health Regulations 2005 (IHR 2005) entered into force, and all 196 state parties were legally bound to implement the core capacity required under the regulations. However, in 2014, almost two thirds of member states reported not being in compliance (*3*). To accelerate progress toward IHR 2005 compliance, the Global Health Security Agenda (GHSA) was launched by 29 countries, WHO, the Food and Agriculture Organization of the United Nations, and the World Organisation for Animal Health in 2014 and now includes >60 nations (*4*).

Also in 2014, the US government provided $6 billion in emergency funding to end the Ebola epidemic in West Africa and to begin the implementation of GHSA as an initial 5-year initiative. The Centers for Disease Control and Prevention (CDC) received $1.8 billion of these funds to contain Ebola in West Africa; these efforts included assistance for countries at risk for introduction of Ebola and support for work with partners to enhance global health security through GHSA implementation. As the need for action to rapidly control outbreaks and epidemics is increasingly recognized, it is useful to take stock of accomplishments and persisting gaps in global health security.

This special supplement of *Emerging Infectious Diseases* on global health security presents an inventory of key efforts by CDC, in collaboration with many partners, to foster health security worldwide, especially by strengthening national public health core capacities. This supplement begins with several summary articles and then provides specific examples of global health security improvements in articles organized by sections entitled Prevent, Detect, and Respond.

Tappero et al. (*4*) and Fitzmaurice et al. (*5*) summarize selected CDC contributions to enhancing global health security from 1980 through 2017 and describe how expanded efforts under GHSA have been built on a framework created by the long history of CDC for capacity building efforts in selected partner countries. Another keynote article in the supplement describes how, after the 2014–2016 West Africa Ebola outbreak, Liberia, Sierra Leone, and Guinea have made substantial progress toward IHR 2005 implementation (*6*). To ensure credibility in the international effort to strengthen public health capacities for IHR 2005 compliance, WHO has developed and implemented the WHO Joint External Evaluation (JEE) tool (*7*). The JEE process is a vital independent global health security monitoring tool that through October 2017 has been implemented in 58 countries and is documenting both the advances toward, and gaps remaining, in national capacities for prevention, detection and control of public health threats (*5*,*7*).

Prevent

Preventing the emergence and spread of infectious disease threats requires prevention and control of antimicrobial resistance, zoonotic diseases, vaccine-preventable diseases (VPDs), and their potential spread across international borders. Global efforts aimed at building national capacities for IHR 2005 compliance are complemented by targeted disease and country-specific efforts. For example, the Enhanced Gonococcal Antimicrobial Surveillance Program aims to inform country-specific treatment guidelines and enhance prevention and control efforts (*8*), and the President's Malaria Initiative's collaboration with the Antimalarial Resistance Monitoring in Africa Network supports the early detection of *Plasmodium falciparum* resistance to facilitate appropriate interventions (*9*).

Zoonoses prevention and control programs use a One Health approach with multisectoral collaboration between human and animal health. Several countries have

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conducted One Health prioritization exercises to identify their major zoonotic diseases (*10*), a critical step in efforts to control endemic zoonotic diseases (*11*). Ethiopia, the Democratic Republic of the Congo, and Georgia are all developing successful integrated zoonotic prevention and control programs (*12*).

Maintaining high population-wide vaccine coverage is a crucial prevention activity, particularly for VPD health security threats. For example, the failure to sustain high vaccine coverage led to a nationwide measles epidemic in Mongolia, a country previously verified as measles-free (*13*). VPD strategies include data improvement teams, which visit district health facilities and can result in improved vaccine administration data through evaluations and training efforts (*14*). Another approach for VPD is the Latin American Pertussis Project, a collaboration among 6 countries to address pertussis, a poorly controlled VPD in the region (*15*). Finally for antimicrobial resistance, zoonotic diseases, VPDs, and other public health threats, border health efforts aimed at preventing spread of communicable diseases across international boundaries are essential and have been used successfully (*16,17*).

Detect

Global health security relies on all countries having ≥3 capacities: 1) an adequate national public health laboratory capacity to safely transport and accurately evaluate biologic specimens with appropriate diagnostic testing methods, 2) a sustained and timely public health surveillance system, and 3) a trained competent workforce to conduct essential outbreak investigations. Although rapid laboratory confirmation of public health threats is a complex endeavor, requiring long-term technical assistance and major resources, many countries are advancing key components. For example, Ghana conducted a national public health laboratory system assessment in support of the Second Year of Life initiative for sustaining adequate vaccine coverage through 24 months of age and for monitoring GHSA-sponsored public health laboratory enhancement efforts (*18*). South Korea is enhancing its public health laboratory to meet the standards of the US Laboratory Response Network, which will facilitate the ability of this country to rapidly determine the etiology of most public emergencies (*19*).

Surveillance is the cornerstone for rapidly detecting public health threats. The WHO Early Warning Alert and Response Network is a major tool for conducting public health surveillance in humanitarian emergencies, including in refugee and displaced person camps (*20*). Other vital global health security assets are CDC regional Global Disease Detection centers in 10 countries that have provided novel public health surveillance and informatics contributions alongside laboratory research since 2001 (*21*). Other disease- and country-specific efforts have also informed best practices, including enhancing anthrax surveillance programs in anthrax-endemic countries (*22*) and use of alternative surveillance approaches, such as burial permit reviews, to describe cholera mortality rates in Tanzania during a 2016 epidemic (*23*).

Rapid detection of public health emergencies also requires an adequate public health workforce, particularly trained field epidemiologists, who can conduct timely and appropriate field investigations. The CDC international 2-year Field Epidemiology Training Program (FETP) began 35 years ago and has established 65 FETP programs in 90 countries, with >3,900 graduates of the 2-year field epidemiologist training (*24*). To meet the global health need for more trained field epidemiologists, particularly at the district level, training has been expanded in many countries to include a 3-month FETP-Frontline program (*25*). In 2014–2016, a total of 24 new FETP-Frontline programs were initiated with >1,860 participants (*4*).

Respond

Efficiently responding to public health emergencies is essential for preventing further disease spread and controlling outbreaks at their source. Outbreak responses worldwide have demonstrated the need for a structured incident management system, which is a critical component for a highly functional and efficient Emergency Operation Center. Many countries, particularly GHSA partner countries, have enhanced their emergency response capacity by establishing emergency operation centers with a strong incident management system foundation (*26,27*). Complex humanitarian emergencies frequently involve the most difficult settings, including fragile states and areas of conflict, and recent case studies illustrate the difficulty of supporting a sustained response in such settings (*28*). After the 2014–2016 West Africa Ebola epidemic, CDC established the Global Rapid Response Team (GRRT) to ensure a ready force of trained responders. In the first 16 months, GRRT members deployed 291 times to 35 countries (*29*). Medical countermeasures, which are medical interventions aimed at controlling public health emergencies, can be essential for rapid response and containment and include using vaccination during outbreaks of cholera, typhoid, yellow fever, and Ebola virus disease (*30*).

Conclusions

Global health security relies on IHR 2005 compliance by all countries and, as such, remains an unfinished journey (*31*). Although much has been accomplished through the first years of GHSA implementation, JEEs around the world highlight numerous prevent, detect, and respond capabilities that still need strengthening. Also lacking is an evidence base of the most effective, timely, and cost-effective approaches to building national capacities for IHR 2005

compliance. As countries and partners continue their work to build health security capabilities, there will be useful opportunities to evaluate different implementation strategies and to document the impact of newly acquired capacities. Continuing this work and thereby sustaining this momentum toward IHR 2005 compliance is critical for protecting Americans and other persons worldwide.

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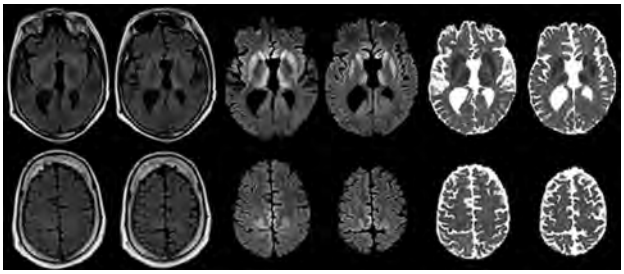

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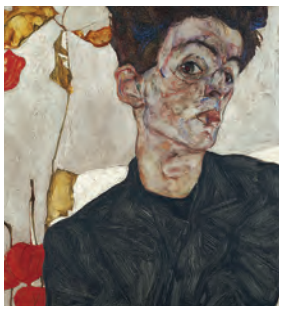
- Control of Foot-and-Mouth Disease during 2010–2011 Epidemic, South Korea
- Novel Serotype of Bluetongue Virus, Western North America



EMERGING INFECTIOUS DISEASES https://wwwnc.cdc.gov/eid/articles/issue/19/4/table-of-contents

US Centers for Disease Control and Prevention and Its Partners' Contributions to Global Health Security

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To achieve compliance with the revised World Health Organization International Health Regulations (IHR 2005), countries must be able to rapidly prevent, detect, and respond to public health threats. Most nations, however, remain unprepared to manage and control complex health emergencies, whether due to natural disasters, emerging infectious disease outbreaks, or the inadvertent or intentional release of highly pathogenic organisms. The US Centers for Disease Control and Prevention (CDC) works with countries and partners to build and strengthen global health security preparedness so they can quickly respond to public health crises. This report highlights selected CDC global health protection platform accomplishments that help mitigate global health threats and build core, cross-cutting capacity to identify and contain disease outbreaks at their source. CDC contributions support country efforts to achieve IHR 2005 compliance, contribute to the international framework for countering infectious disease crises, and enhance health security for Americans and populations around the world.

To contain health threats and ensure global health security, all countries must rapidly detect and respond to public health emergencies and, when overwhelmed, call upon global deployment capacity. This need is clearly evident, as the world is more susceptible to infectious disease threats due to increased international travel and trade, spread of newly emerging or reemerging microbes, and inadvertent release of dangerous pathogens from laboratories or bioterrorism acts.

Following the 2002–2003 severe acute respiratory syndrome (SARS) coronavirus outbreak, which demonstrated how rapidly a pathogen could spread to 26 countries (*1*), the World Health Organization (WHO) in 2005 adopted the revised International Health Regulations (IHR 2005), a legally binding international treaty. In June 2007, all 196 WHO member states committed to reaching IHR 2005 compliance by 2012 (*2*). The 2009 pandemic of influenza A(H1N1) resulted in the first declaration of a public health emergency of international concern under IHR 2005 (*3*) and provided new evidence that the world was ill prepared for a global health crisis. Numerous threats followed H1N1, including cholera in post-earthquake Haiti in 2010 (*4*); Middle East respiratory syndrome coronavirus in Saudi Arabia in 2012 (*5*) and its exportation to the Middle East, Europe, Asia, and the United States; West Africa Ebola virus disease in 2014 (*6*); chikungunya virus in 2013 and Zika virus in 2015 in the Americas (*7*); and yellow fever virus reemergence in Africa, China, and Brazil in 2015 (*8*). Despite these serious threats, only 33% of WHO member states had self-reported IHR 2005 compliance by December 2014 (*9*).

Building and maintaining global preparedness for pandemic threats and IHR 2005 compliance requires coordination and technical expertise across multiple stakeholders. To protect Americans and the global community from health threats, the US Centers for Disease Control and Prevention (CDC) has established a global health protection platform that works with ministries of health (MOHs); other partners (e.g., host country partners, WHO, nongovernmental organizations, and academic institutions); CDC country offices; and agency programs, including those dealing with influenza, emerging zoonotic diseases, HIV, malaria, and polio (*10*). CDC has also worked on building cross-cutting core capacities to ensure protection from these specific diseases and unpredictable new health threats through initiatives such as the Field Epidemiology Training Program (FETP) and the Global Disease Detection (GDD) network (*11*,*12*). This report highlights selected CDC global health protection platform accomplishments, enhanced through the

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Global Health Security Agenda (GHSA), that strengthen emergency mitigation and capacity-building partnerships dedicated to containing threats at their sources.

Emergency Mitigation of Global Health Threats

Ending the West Africa Ebola Outbreak

The unprecedented 2014–2016 West Africa Ebola epidemic devastated Guinea, Liberia, and Sierra Leone, 3 of the world's poorest nations (*13*). These countries accounted for >99% of reported cases (28,652) and deaths (11,325) from Ebola virus infections (*6*). Ending the epidemic required enormous efforts from affected countries and collaborations with international partners, including CDC (*6*). CDC supported >3,500 staff deployments, engaging in epidemiologic fieldwork, laboratory testing, risk-reduction communications, improvements in infection control, and research on risk factors for transmission, viral persistence, and an Ebola vaccine (Table 1).

In December 2014, the US Congress authorized $1.2 billion in emergency funding for CDC to end the Ebola epidemic and accelerate GHSA implementation in partnering countries (Figure 1) (*14*). In early 2015, these funds made it possible for CDC to augment its response with new CDC country offices in Guinea, Liberia, and Sierra Leone, which enhanced response activities to end the epidemic. These countries are now implementing GHSA to build national resilience and preparedness capability (Table 1; Figure 1). Key examples of this work's impact are the efficient identification and control of the past 7 Ebola virus clusters (*17*) during 2015–2016 and the rapid response to a cluster of deaths from *Neisseria meningitidis* infection in Liberia in 2017 (*18*). These countries are demonstrating that they are now better prepared to prevent, detect, and respond to serious disease threats (Table 2).

Global Rapid Response Team

The 2014–2016 West Africa Ebola epidemic was the largest emergency response in CDC's history (*6*). The identification, training, and deployments of >3,500 CDC staff taxed agency human resource systems and challenged response continuity in the early months. To ensure sustained readiness for the next health emergency, CDC now trains and rosters a Global Rapid Response Team of >400 experts with a broad range of technical and language skills, poised to deploy on short notice and remain in the field for up to 6 months (Table 1).

During September 2015–June 2017, these responders were mobilized >420 times and contributed >14,000 cumulative person-days to emergency response in the field, in Atlanta's Emergency Operations Center (EOC), or both (Table 1). During this period, the Global Rapid Response Team responded to 13 emergencies in 25 countries, including Zika virus in the Americas (217 mobilizations, 9,494 person-days, 15 countries and territories, and EOC); yellow fever in Angola and the Democratic Republic of the Congo (20 mobilizations and 1,097 person-days); Hurricane Matthew in Haiti (59 mobilizations and 1,235 person-days); and, most recently, Ebola virus in the Democratic Republic of the Congo.

Rapid Humanitarian Responses

Humanitarian crises resulting from natural disasters (e.g., earthquakes, tsunamis, floods, and droughts); armed conflict; or civil strife routinely lead to large-scale population displacements. Whether migrating outside their countries as refugees or internally displaced in their homelands, disrupted populations routinely experience increased illness and death from respiratory and diarrheal pathogens associated with overcrowding; disrupted health services (e.g., childhood immunizations, treatment for HIV and tuberculosis); and lost access to food, clean water, and sanitation (*19,20*). For >50 years, CDC has provided technical support to WHO, United Nations agency partners, and others to define the public health aspects of such complex humanitarian emergencies and establish disease surveillance and interventions to mitigate the health consequences of displacement (*21–24*).

The number of persons affected by complex emergencies has increased over the past decade. In 2016 alone, >125 million persons needed humanitarian assistance (*25*). During 2007–2016, CDC responded to >20 crises that each affected ≥10,000 people, each with a crude mortality rate of ≥1/10,000 persons/day (e.g., the 2010 earthquake in Haiti, the Horn of Africa drought and famine of 2011–2014, and the Syrian crisis since 2012). During 2011–2016, CDC deployed staff for >380 missions in >40 countries to apply public health principles and epidemiologic science to mitigate the health impacts of complex emergencies (Table 1). For the crisis in Syria, CDC deployed staff who worked with nongovernmental organizations and the United Nations Children's Fund to establish and train staff to conduct surveillance, measles vaccination campaigns, and nutritional surveys. In response to the 2011–2012 Horn of Africa famine, CDC worked with partners to implement morbidity and mortality surveillance systems in 3 countries (Table 1).

Public Health Emergency Management Program

The terrorist attacks of September 11, 2001, intentional use of anthrax spores as a biologic agent during that same year, and increasing numbers of outbreaks and complex humanitarian responses prompted CDC to develop a US-based public health emergency management (PHEM) program (*26*). CDC initially implemented its incident management system (IMS) and activated its EOC in response to SARS

Table 1. Selected US CDC global health protection platform accomplishments*

Global health protection accomplishments	Number	Timeframe
Emergency mitigation of global health threats		
Ending the West Africa Ebola outbreak		
CDC staff deployments overall, domestic and international	>3,500	2014–2016
Departing passengers in the 3 affected countries screened for Ebola virus disease	>339,000	2014–2016
Vaccinations of health workers in Ebola trial	>8,000	2015
Days of continuous operation of high-throughput laboratory capacity in Sierra Leone; >23,000 specimens tested	421	2014–2015
US healthcare workers trained in Anniston, AL, to work in West Africa	>600	2015
GRRT		
CDC-trained GRRT experts prepared to deploy on short notice to a public health emergency	>400	2017 (Jun)
GRRT mobilizations (>14,000 cumulative person-days), supporting responses to global health emergencies including Zika, yellow fever, cholera, measles, polio, and Ebola	>420	2015–2017 (Jun)
Rapid humanitarian responses		
Staff deployments in response to public health humanitarian emergencies in >40 countries	>380	2011–2016
Staff deployments to 6 countries in response to Syria crisis	85	2012–2016
Countries with morbidity/mortality surveillance systems implemented in response to Horn of Africa famine	3	2011–2012
PHEM program		
Fellows from 28 countries trained through CDC PHEM fellowship	69	2013–2017 (Jun)
Countries that have received CDC emergency management technical assistance and training	56	2013–2016
Countries that participated in a real and/or simulated response with CDC technical assistance	19	2013–2016
Global Disease Detection Operations Center		
Serious public health threats assessed	>1,500	2007–2016
Countries where serious outbreaks were investigated/contained, where CDC provided technical assistance	>190	2007–2016
Unique diseases tracked globally	>170	2007–2016
Outbreaks monitored and reported in >130 countries for ≈40 different diseases	≈300	2016
GDD activities		
GDD regional centers	10	2006–2016
New diagnostic tests established in national or regional laboratories	>380	2006–2016
New strains/pathogens detected and/or discovered (new to the world, new to country or region, or new modes of transmission likely because of increased ability to detect through newly introduced laboratory tests) in which GDD assisted in detection and identification	79	2006–2016
Outbreaks responded to by GDD center that provided epidemiology and/or laboratory assistance	2,051	2006–2016
Outbreak investigations in which laboratory support was provided	1,363	2006–2016
Participants who received public health trainings conducted at national and/or regional level on topics, including epidemiology, laboratory, all-hazards preparedness, and risk communication	115,566	2006–2016
Capacity-building partnerships to contain threats at the source		
GHSA implementation		
GHSA countries: 17 Phase I countries, 14 Phase II countries, and CARICOM†	>31	2015–2017 (Mar)
Phase I countries with enhanced surveillance systems for zoonotic diseases	13	2015–2017 (Mar)
Countries that detected dangerous pathogens using new equipment and capabilities	16	2015–2017 (Mar)
Phase I countries supported in development of Emergency Operations Centers	16	2015–2017 (Mar)
Joint External Evaluation		
GHSA assessments conducted before tool finalization	6	2016
Evaluations completed	52	2016–2017 (Jul)
Public health workforce development		
Countries with CDC-supported FETPs	65	1980–2016
Graduates of FETPs-Advanced	>3,900	1982–2016
Outbreaks investigated by FETP-Advanced trainees	>3,300	2005–2016
New FETPs-Frontline started	24	2014–2016
Participants in FETPs-Frontline	>1,860	2015–2016
Global vaccine-preventable disease activities		
STOP program volunteers trained in surveillance principles to detect and respond to cases of polio and other vaccine-preventable diseases	2,010	1998–2017 (Jul)
Countries with volunteers deployed for the STOP program	77	1998–2016
Countries supported by CDC to build national STOP programs	4	1998–2016
NPHIs		
Members of International Association of National Public Health Institutes and supported by CDC	>100	2016
Countries receiving NPHI development support from CDC	>20	2016
Persons across the globe served by NPHIs	5 billion	2016

*CARICOM, Caribbean Community; CDC, Centers for Disease Control and Prevention; FETP, field epidemiology training program; GDD, Global Disease Detection; GHSA, Global Health Security Agenda; GRRT, Global Rapid Response Team; NPHI, National Public Health Institute; PHEM, public health emergency management; STOP, Stop Transmission of Polio.

†CARICOM is an organization of 15 Caribbean nations and dependencies. In 2015, the US government committed to accelerating GHSA implementation with 31 countries and CARICOM (Figure 1). In 17 Phase I, 14 Phase II, and CARICOM nations (Figure 1), CDC provides technical assistance to support country capacity assessments, the development of 5-year GHSA road maps, and annual GHSA implementation plans. In the Phase I countries, CDC also provides financial support for implementation of the GHSA action packages (Table 2) (*14–16*).

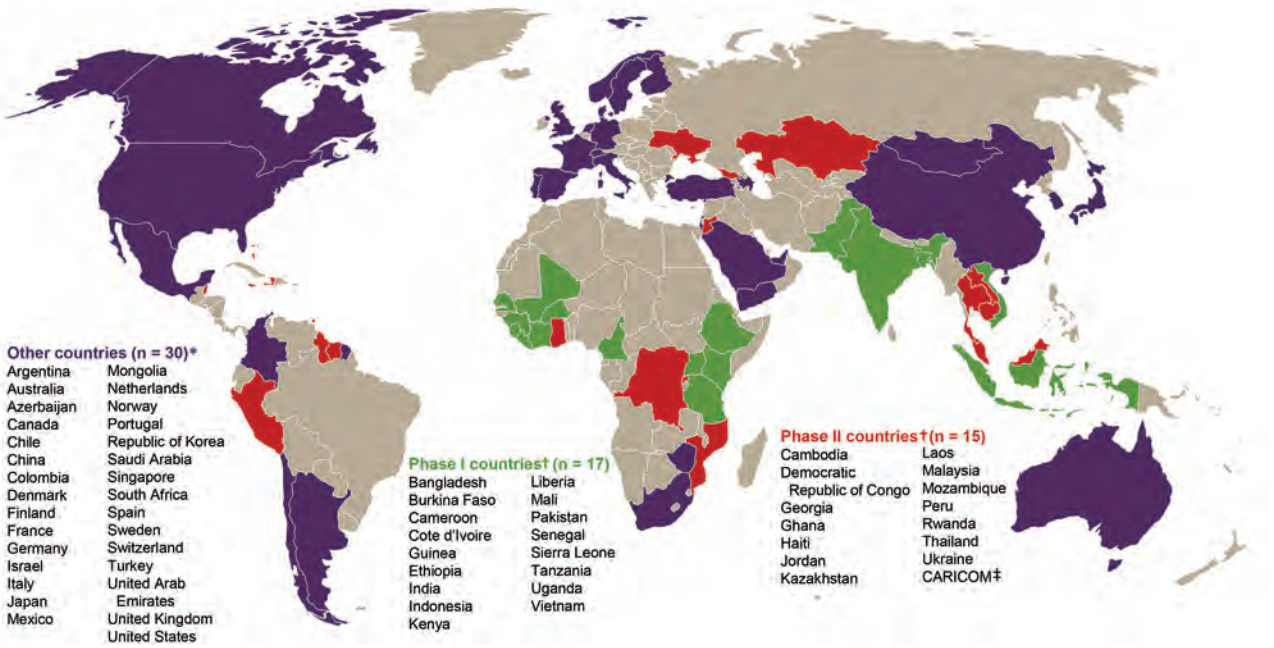

Figure 1. Global Health Security Agenda (GHSA) member countries as of July 25, 2017 (https://www.ghsagenda.org/members). *GHSA member countries that are not directly supported by the US government. †US government–supported GHSA member countries. CDC provides technical assistance to support country capacity assessments, the development of 5-year GHSA road maps, and annual GHSA implementation plans in Phase I, Phase II, and CARICOM nations. In the Phase I countries, CDC also provides financial support for implementation of the GHSA Action Packages. ‡CARICOM is an organization of 15 island nations. CARICOM, Caribbean Community; GHSA, Global Health Security Agenda.

outbreaks in 2002–2003. During 2001–2016, CDC has responded to 62 public health emergency events; on 244 other occasions, components of PHEM were used to support responses not requiring full EOC activation. In 2009, the PHEM program began assisting MOHs with strengthening their emergency preparedness through IMS trainings, EOCs, and emergency response plan development.

In 2013, in response to increasing global requests for more sustained emergency management training out of CDC's EOC, CDC established its PHEM Fellowship Program. Also in 2013, CDC received accreditation from the Emergency Management Accreditation Program (*27*). CDC is now a recognized world leader in PHEM, providing technical assistance to GHSA and other countries (Figure 1).

Global Disease Detection Operations Center

CDC established the Global Disease Detection Operations Center (GDDOC) in early 2007 to identify and monitor health threats to the American public and global community. Using event-based surveillance for early alerting and situation awareness, a team of analysts routinely monitor numerous information sources (e.g., Internet, traditional and social media) for disease events using keywords in >50 languages, and validate accuracy with MOHs, WHO, Food and Agricultural Organization of the United Nations, World Organisation for Animal Health, and other partners. GDDOC monitors 30–40 public health threats daily, tracking situations that could develop into public health emergencies of international concern (*28*). During 2007–2016, GDDOC conducted event-based surveillance and disseminated information on >1,500 outbreaks occurring in >190 countries (Table 1).

GDDOC outbreak response support has included staff deployments and the provision of personal protective equipment, laboratory diagnostic test equipment, reagents, and supplies. GDDOC deploys CDC staff directly to the host country and through the WHO-hosted Global Outbreak Alert and Response Network. Emergency funding from the US Congress in 2014 for Ebola and GHSA made it possible to dramatically augment bilateral and Global Outbreak Alert and Response Network deployments for the West Africa Ebola epidemic. During 2016–2017, GHSA support substantively enhanced GDDOC's capacity to conduct event-based surveillance.

Global Disease Detection Regional Centers

Following the 2002–2003 SARS outbreak, in 2004, the US Congress authorized funding for CDC to establish a regional Global Disease Detection (GDD) Program. Currently, CDC works with MOHs in 10 countries (Table 1; Figure 2) to host GDD Centers in a network supporting >90

Table 2. Global Health Security Agenda's prevent, detect, and respond framework against infectious disease threats and its 11 measurable action packages (*14,15*)

Steps and actions
Prevent: systems, policies, and procedures to mitigate avoidable outbreaks
Surveillance to guide slowing of antimicrobial resistance
National biosecurity system
Policies and practices that reduce the risk of zoonotic disease transmission
Immunization of 90% of children ≤1 year of age with >1 dose of measles vaccine
Detect: a national surveillance and laboratory system capable of reliable testing for >5 of 10 core tests relevant to the country's epidemiologic profile on specimens from disease clusters in >80% of districts
Standardized surveillance for 3 core syndromes
Regional and national interoperable electronic reporting systems
Timely reporting to World Health Organization (WHO), World Organisation for Animal Health (OIE), and Food and Agriculture Organization of the United Nations (FAO)
Multidisciplinary public health workforce with ≥1 epidemiologist per 200,000 population
Respond: a national public health Emergency Operations Center capable of activating an emergency response in <2 hours
Trained rapid response teams
Linkages between public health and law enforcement for suspected biologic attacks
National framework to engage international partners during a public health emergency

countries. GDD Centers develop public health capacity by conducting epidemiology-, informatics-, and laboratory-based activities and scientific research. GDD Centers characterize public health threats through surveillance, applied research, and pathogen detection and discovery. During 2006–2016, GDD Centers conducted surveillance for key infectious diseases and syndromes; established >380 new diagnostic tests in national or local laboratories in 59 countries; assisted in the discovery and/or detection of 79 strains or pathogens new to the world, country, or region; responded to 2,051 requests for disease outbreak assistance; and trained 115,566 professionals at the national and regional level on public health topics (Table 1). Increasingly, GDD Centers are leading applied research and surveillance efforts to identify the most effective and efficient capacity-building activities that ensure health security.

Capacity-Building Partnerships to Contain Threats at the Source

Global Health Security Agenda Implementation

With growing recognition that infectious disease outbreaks can become pandemics, resulting in considerable loss of life and economic cost, GHSA was launched in February 2014 by 29 countries, WHO, the Food and Agricultural Organization of the United Nations, and the World Organisation for Animal Health to rapidly identify and mitigate infectious disease threats at their source (*15*). Now, >60 nations are GHSA member countries (Figure 1). The group of 7 industrialized democracies (G7), South Korea, Canada, Nordic countries, and a growing list of private partners have pledged financial support for GHSA implementation in up to 76 countries (Figure 1).

In 2015, the US government committed to accelerating GHSA implementation with 31 countries and the Caribbean Community, an organization of 15 island nations (Figure 1). The United States is investing >$1 billion to advance GHSA's prevent, detect, and respond framework against infectious disease threats through implementation of 11 measurable action packages (Table 2) (*14–16*). In 17 Phase I countries, 14 Phase II countries, and the Caribbean Community (Figure 1; Table 1), CDC supports country capacity assessments, 5-year roadmaps, and annual GHSA implementation plan development. In addition, in Phase I countries, CDC provides financial support for implementation of these action packages; substantial progress was achieved in the first year (*16*). To reduce the risk of emergent zoonotic infections, 13 countries have expanded surveillance systems in humans, wildlife, and animals to foster prevention (Table 1). Ten countries have expanded surveillance systems to include more vaccine-preventable diseases (VPDs), which should strengthen national vaccine delivery systems, including the capacity for emergency vaccination to mitigate an outbreak. For example, community-level monitoring can accelerate targeted immunization, halving the number of vaccine-preventable meningococcal disease cases in West Africa outbreaks (*29,30*).

To enable disease detection and response efforts, a strong national reference laboratory system requires a tiered laboratory network, including capable central reference laboratories linked to regional and peripheral laboratories with appropriate testing capacities at each level; systems for timely and safe transport of samples and return of results; and procedures that assess and ensure quality. GHSA resources have supported enhanced training for laboratory technicians in 17 Phase I countries, and 16 countries have detected dangerous pathogens using new equipment (Table 1). All 17 Phase I countries have established or expanded the training of field-based epidemiologists, thereby greatly enhancing the number of staff that can detect and effectively respond to health threats at the subjurisdictional level.

A national IMS with coordination of response through EOCs is essential for mitigating public health threats. Sixteen Phase I countries have established or strengthened their national EOCs to manage and monitor health events in real time; of these, 11 have activated their EOCs for simulated and/or real emergency responses.

Joint External Evaluation

With so few countries meeting their IHR 2005 commitments through 2014, a validated monitoring program to

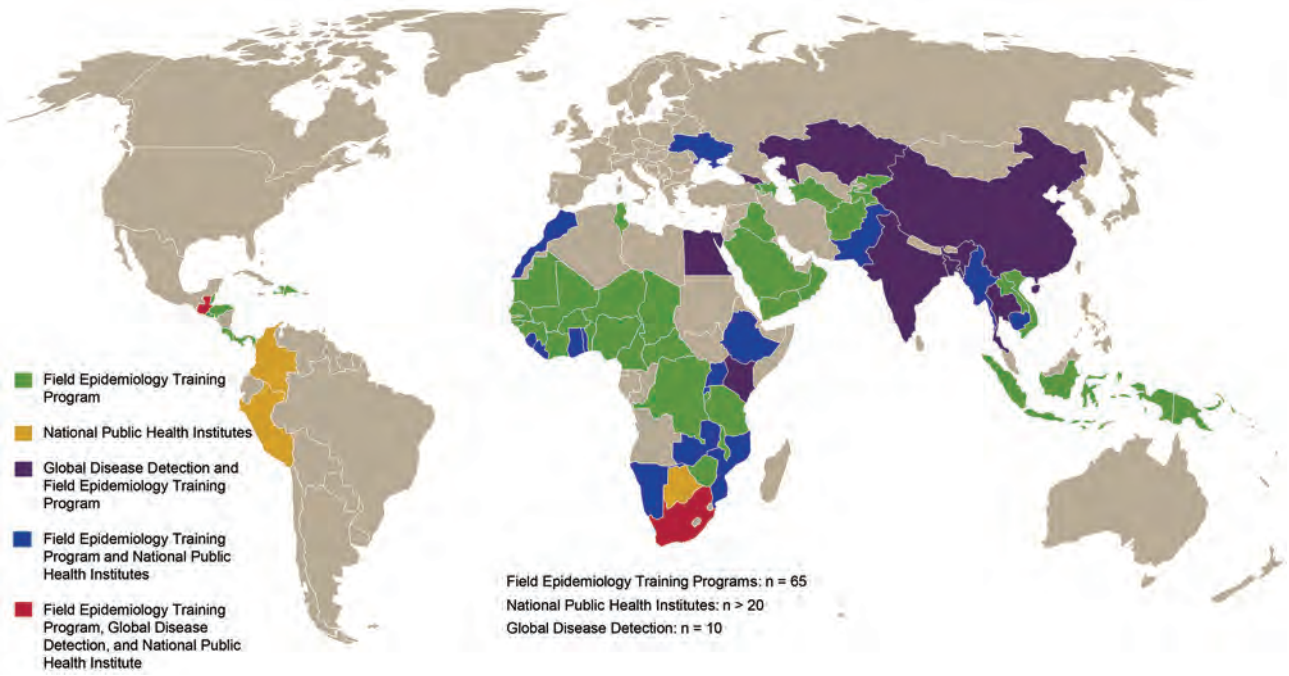

Figure 2. Selected programs that enhance US Centers for Disease Control and Prevention (CDC) global health protection platform. This map does not include CDC international influenza, malaria, HIV/AIDS, and immunization programs.

measure and facilitate progress toward compliance was needed. With CDC support, external and independent GHSA assessments were piloted throughout 2015 in 6 countries to establish a baseline for targeting implementation (Table 1; Figure 3). In February 2016, WHO, working with CDC and GHSA partner countries, adopted the Joint External Evaluation (JEE) tool to harmonize independent monitoring for both GHSA targets and IHR 2005 compliance efforts across all 19 IHR core preparedness capacities (*31*). JEEs are designed to establish a baseline measurement for a country's capacity, inform national policy setting, target resources, track progress, and highlight priority areas for improvement.

By mid-July 2017, 52 JEE country assessments were complete, and 27 JEE reports were publicly posted. An additional 25 countries are scheduled for a JEE through 2018 (Table 1; Figure 3).

Public Health Workforce Development

A well-trained and retained public health workforce is a cornerstone for achieving IHR compliance. CDC is helping develop a global workforce through the FETP-Advanced, modeled after CDC's 2-year Epidemic Intelligence Service (*11*). Since FETP's inception outside North America in 1980, CDC has supported FETPs-Advanced in 65 countries and graduated >3,900 advanced field epidemiologists (Table 1; Figure 2); of these graduates, up to 80% continue to serve in public health programs in their home countries (*12*). In GHSA Phase I countries, >1,600 persons have completed FETP training. In 2001, CDC started an FETP-Intermediate of 6–9 months' duration to address district-level public health surveillance and outbreak response gaps in 13 countries. Through 2016, >700 disease detectives had completed intermediate training. During 2005–2016, FETP-Advanced graduates conducted >3,300 outbreak investigations (Table 1). In response to the West Africa Ebola epidemic, FETP prioritized the expansion of FETP-Frontline programs, providing a 3-month training for district surveillance officers to improve local disease detection and response. During 2014–2016, CDC supported 24 new FETP-Frontline programs, mentoring >1,860 participants (Table 1).

International Influenza and Respiratory Diseases

Since the 1980s, CDC has supported influenza surveillance and laboratory capacity globally. As of June 2017, CDC supports influenza activities in 79 countries, assisting MOHs and other laboratory partners in the Global Influenza Surveillance and Response Network in the early detection of potential pandemic threats and provides the world with access to new influenza strains to enable the development of effective seasonal influenza vaccines and vaccines against novel influenza strains that have pandemic potential (e.g., the H7N9 avian strain currently circulating in China) (*32*). With GHSA support, the online International Reagent Resource portal (https://www.internationalreagentresource.org/) has provided reagents to national

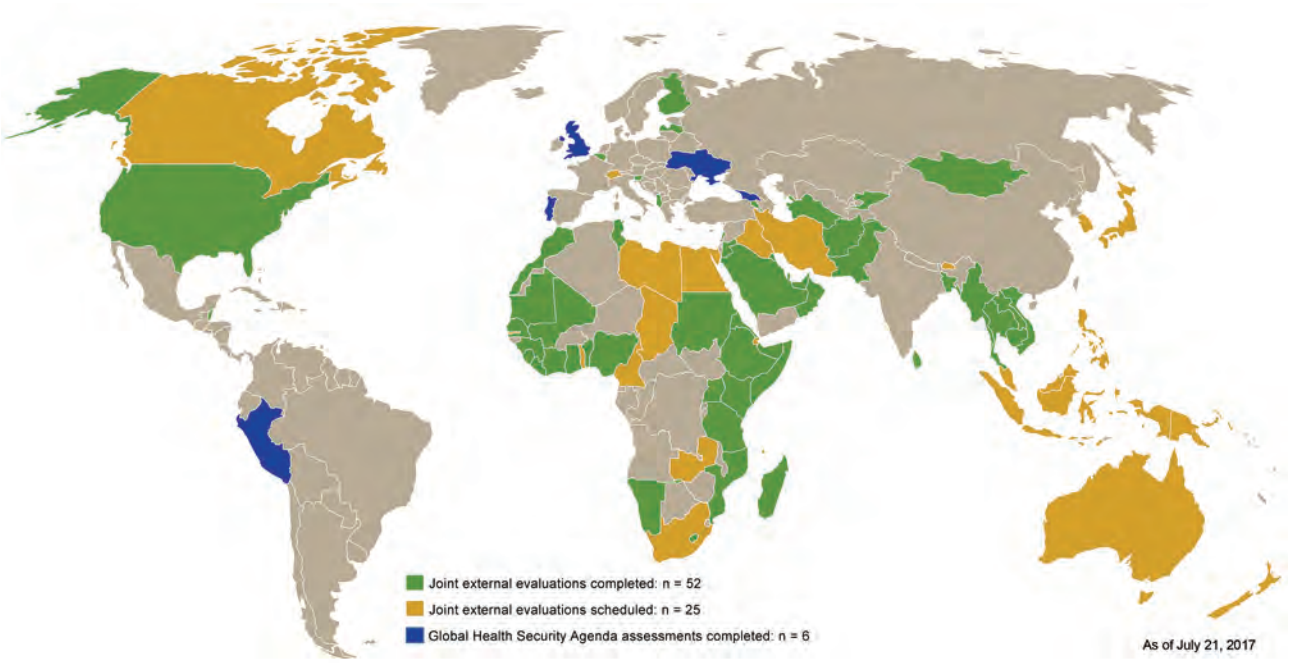

Figure 3. Country progress with independent Global Health Security Agenda and Joint External Evaluation assessments through 2018.

influenza laboratories and other respiratory disease laboratories worldwide.

CDC has supported global laboratory networks for polio, measles, and rubella for several decades, providing diagnostic testing, technical support, training, and reference laboratory services. Since 2001, CDC has worked with MOHs, WHO, and the Meningitis Vaccine Project, funded by the Bill and Melinda Gates Foundation, to develop and administer meningococcal vaccines to millions of persons living in the Africa meningitis belt and leads the MenAfriNet Consortium to enhance surveillance to monitor the effectiveness of vaccines and emergence of new meningococcal strains (*33*).

GHSA supports MOHs to conduct surveillance for severe respiratory diseases and other illness clusters. To support this effort, laboratories are provided with test kits and reagents, packaging and shipping protocols, and training in advanced molecular testing methods, allowing detection of multiple pathogens simultaneously.

International Emerging and Zoonotic Diseases

Most known, new, or emerging infectious disease threats are zoonotic in origin (*34*,*35*). Zoonoses are responsible for an estimated >2 billion human illnesses and 2 million human deaths annually (*36*). Under GHSA, many countries are undertaking efforts to identify and prioritize zoonotic diseases of greatest national concern through a One Health approach (i.e., linking human, environmental, and animal health) (*37*). This approach helps a country focus limited resources for surveillance, laboratory capacity building, outbreak response, and prevention and control efforts and helps to enhance communication, collaboration, and engagement across critical sectors of government. With technical assistance from experts on zoonotic and emerging infectious diseases, many countries have initiated surveillance to establish etiologies of acute febrile illness. These efforts have begun to increase countries' capacity to collect sterile specimens; prepare, store, and ship specimens; and collect and report data to clinicians and surveillance systems. Acute febrile illness surveillance has contributed to countries' understanding of etiologies and pathogen-specific disease burden and can inform clinical algorithms and care and treatment of patients with acute febrile illness. GHSA implementation has demonstrated that enhancing disease-specific capacity improves national public health capacity building overall. Coordinated efforts between cholera experts and emergency management to prevent, detect, and respond to cholera in Cameroon have led to increasing timeliness of EOC activation for other outbreaks. Preventing zoonotic or emerging infectious diseases is one of the critical tenets of GHSA. CDC infection, prevention, and control experts are supporting efforts to build infection control and antimicrobial drug resistance capacity in 10 GHSA Phase I countries. During the West Africa Ebola epidemic, widespread gaps in infection, prevention, and control systems and resources led to outbreak amplification (*38*). Today, these national policies and practice guidelines are in the Ebola-affected countries to help support sustainability of these efforts.

Global VPD Activities

Country capacity to conduct high-quality VPD surveillance is critical to increase coverage to prevent, detect, and respond to VPD outbreaks. CDC has supported global laboratory networks for polio, measles, and rubella for several decades, providing diagnostic testing, technical support, training, and reference laboratory services. An effective multidisciplinary workforce, including epidemiologists, laboratorians, and data managers, is needed to collect, analyze, and report VPD surveillance data that are accurate, timely, and useful for decision making.

Since 1998, CDC has provided technical and financial support to develop VPD surveillance capacity in low- and middle-income countries through the Stop Transmission of Polio (STOP) program of the Global Polio Eradication Initiative (*39*). Through July 2017, a total of 2,010 STOP volunteers have been trained in surveillance principles to detect and respond to polio and other VPDs. These volunteers have deployed in 48 teams for 3–6-month assignments to 77 countries (Table 1) (*39*). STOP volunteers have played a crucial role in enhancing country capacity to respond to outbreaks of other priority infectious diseases, contributing to CDC's global health protection platform. CDC also has supported 4 countries at high risk for polio to build their own national STOP programs (Table 1) (*40–42*). VPD surveillance also helps build countries' public health systems. For example, in Nigeria in 2014, the polio EOC quickly converted to respond to Ebola (*43*).

National Public Health Institutes

National governments are responsible for keeping their citizens healthy and addressing public health challenges. To that end, many countries have established national public health institutes (NPHIs) to carry out essential public health functions, including outbreak detection and response (*44*,*45*), and facilitate progress toward IHR 2005 compliance. CDC is the US government's NPHI and is 1 of >100 members representing 88 countries in the International Association of National Public Health Institutes (IANPHI) (Table 1). With IANPHI, CDC directly supports >20 IANPHI countries in establishing or strengthening their own NPHIs (Figure 2) through developing strategic plans aligned with public health priorities, determining necessary policy changes, creating sustainability plans, and providing technical assistance (Table 1).

Public Health Implications and Future Directions

Outbreaks, regional epidemics, and pandemics are costly (*46–50*). During February–July 2003, SARS spread across 4 continents, infected 8,100 persons, killed 774 persons, and cost the global economy $40 billion (*46*). In the first year of the 2009 influenza H1N1 pandemic, >575,400 persons succumbed worldwide (*47*). A severe influenza pandemic could cost as much as 4.9% of the world's gross domestic product (*48*). In 2015, the West Africa Ebola epidemic cost Guinea, Liberia, and Sierra Leone about $2.2 billion (*49*).

Because of the recognized need to achieve IHR 2005 compliance worldwide to ensure health security, increasing number of countries that have made GHSA commitments, and early progress achieved with GHSA implementation, the world is becoming better prepared to respond to threats. CDC is helping advance health security through its global health protection platform. More work is needed and momentum in GHSA implementation needs to be sustained so Americans and citizens around the world will have enhanced protection from newly emerging infectious diseases and other health threats.

Members of the Global Health Science Group: Elizabeth Bell, Andrew T. Boyd, Shelly Bratton, Daniel J. Brencic, Susan T. Cookson, Arthur G. Fitzmaurice, Olga Henao, Donna Jones, Stephanie Lambert, Barbara Marston, Meredith Lee Pinto, and Cyrus G. Shahpar.

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Dr. Tappero is the senior advisor for global health with CDC's Center for Global Health (CGH). He provides strategic scientific and programmatic contributions to CGH's work across four divisions (Division of Global Health Protection, Division of Global HIV/AIDS and Tuberculosis, Division of Parasitic Diseases and Malaria, and Global Immunization Division), implementing public health programs in >60 CDC country offices with multinational organizations, nongovernmental organizations, philanthropies, and other domestic and global partners.

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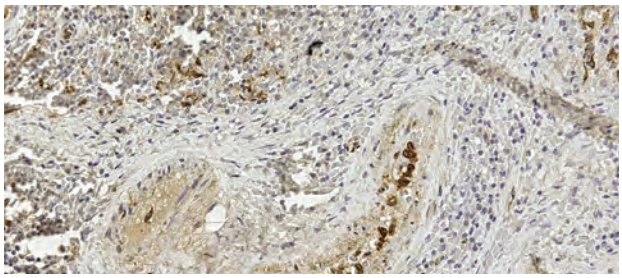
- A Framework for Modeling Emerging Diseases to Inform Management
- Epidemiology of Hospitalizations Associated with Invasive Candidiasis, United States, 2002–2012
- Epidemiology of Human Anthrax in China, 1955–2014
- Mathematical Modeling of Programmatic Requirements for Yaws Eradication
- Estimated Incidence of Antimicrobial Drug–Resistant Nontyphoidal Salmonella Infections, United States, 2004–2012



- Oral Cholera Vaccine Coverage during an Outbreak and Humanitarian Crisis, Iraq, 2015
- Modeling Tool for Decision Support during Early Anthrax Event
- Analysis of Anthrax Immune Globulin Intravenous with Antimicrobial Treatment in Injection Drug Users, Scotland, 2009–2010

- Sequelae and Other Conditions in Ebola Virus Disease Survivors, Sierra Leone, 2015
- Cost-Effectiveness of Increasing Access to Contraception during the Zika Virus Outbreak, Puerto Rico, 2016
- Host-Associated Absence of Human Puumala Virus Infections in Northern and Eastern Germany
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Contributions of the US Centers for Disease Control and Prevention in Implementing the Global Health Security Agenda in 17 Partner Countries

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The Global Health Security Agenda (GHSA), a partnership of nations, international organizations, and civil society, was launched in 2014 with a mission to build countries' capacities to respond to infectious disease threats and to foster global compliance with the International Health Regulations (IHR 2005). The US Centers for Disease Control and Prevention (CDC) assists partner nations to improve IHR 2005 capacities and achieve GHSA targets. To assess progress through these CDC-supported efforts, we analyzed country activity reports dating from April 2015 through March 2017. Our analysis shows that CDC helped 17 Phase I countries achieve 675 major GHSA accomplishments, particularly in the cross-cutting areas of public health surveillance, laboratory systems, workforce development, and emergency response management. CDC's engagement has been critical to these accomplishments, but sustained support is needed until countries attain IHR 2005 capacities, thereby fostering national and regional health protection and ensuring a world safer and more secure from global health threats.

Recent infectious disease outbreaks have demonstrated that a local threat can rapidly become a global crisis that jeopardizes the health, economy, and safety of persons everywhere. Severe outbreaks and regional epidemics, including severe acute respiratory syndrome, Middle East respiratory syndrome, Ebola virus disease (EVD), Zika virus, and novel influenza viruses, have highlighted the importance of countries developing core capacities to contain public health threats, as outlined in the International Health Regulations (IHR 2005) (*1–3*). As of 2014, fewer than a third of 196 countries reported achieving IHR 2005 capacities (*4*). The Global Health Security Agenda (GHSA), a partnership of nations, international organizations, and civil society, was launched in 2014 with the mission to build countries' capacities to respond to infectious disease threats, thereby progressing toward IHR 2005 compliance (*5*). Global health security relies on all countries building IHR 2005 capacities to rapidly detect and control public health threats at their sources.

GHSA is built on 3 pillars: 1) prevent avoidable epidemics; 2) detect threats early; and 3) respond rapidly and effectively. To date, 61 countries have joined GHSA, including approximately a dozen countries partnering with low- and middle-income countries to assist in their GHSA work. In 2014, the United States committed to working with 31 partner countries and the Caribbean community to meet targets associated with each of 11 technical areas (termed Action Packages) that align with GHSA's 3 pillars (*6*). Through GHSA, the United States has committed technical and fiscal support to a subset of 17 countries termed Phase I and technical assistance with work plan development in Phase II countries. Exceeding this commitment, the US Centers for Disease Control and Prevention (CDC) works to strengthen global health security capacities in approximately 3 dozen countries, including Phase I and Phase II countries, as well as Ebola preparedness countries, which surround those countries affected by the recent EVD outbreak (Figure). CDC works across all 11 GHSA technical areas, with a special emphasis on 4 that serve as a platform for public health emergencies and health security: surveillance, laboratory systems, workforce development, and emergency response management. CDC staff stationed in partner countries, with support from CDC headquarters–based subject matter experts and funded partners, provide direct technical assistance to partnering government counterparts (*7–9*). CDC's goal is to help countries achieve

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[1]Members of this group are listed at the end of this article.

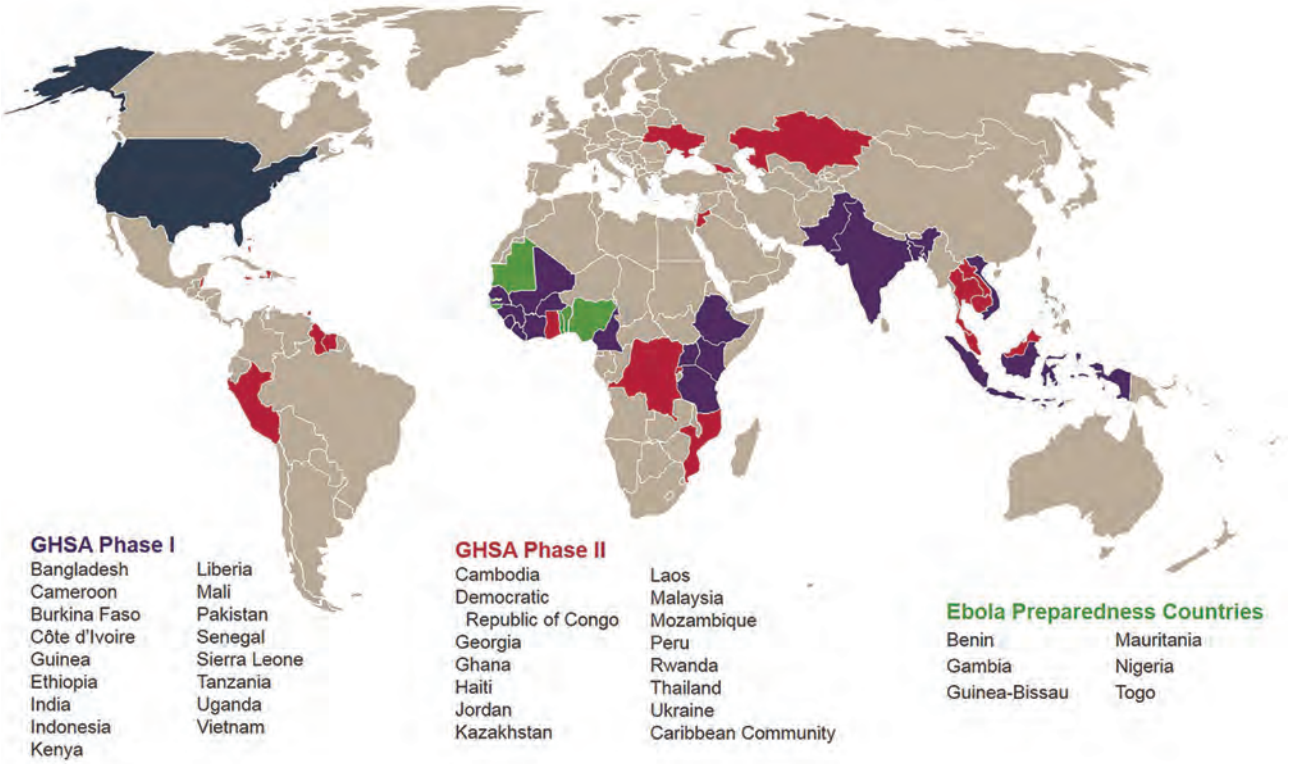

Figure. GHSA countries supported by the US Centers for Disease Control and Prevention. GHSA, Global Health Security Agenda.

GHSA and IHR 2005 targets by strengthening sustainable systems and capacities to respond to health threats locally, thereby preventing the spread of disease and protecting persons in the United States and around the world from outbreaks and other public health threats. Descriptions of CDC's early GHSA work with counterparts in Uganda and Vietnam have been published (*10*,*11*), but substantial progress has been made across all Phase I countries. Here we document the major GHSA accomplishments that these 17 countries achieved with CDC support during April 2015–March 2017. These successes are now informing ongoing program implementation in these and other countries.

Methods

In January 2015, CDC technical staff commenced working with ministries of health (MOHs) and other partner country counterparts to assess baseline capacities related to 11 GHSA technical areas. By June 2015, annual country work plans had been developed, detailing activities through which CDC would assist countries in achieving their first-year objectives in each technical area. The level and nature of CDC support varied across activities depending on technical assistance needs, inputs from other collaborators, and host country and donor financing. CDC staff reported on activity progress on a quarterly basis. Reports indicated the status (i.e., completed, on track, delayed, or canceled) and described progress toward completion of each work plan activity. Reporting information was provided to CDC headquarters–based evaluators 4 times: December 2015, April–May 2016, July–August 2016, and October–November 2016. Results were used to improve and update work plans.

Trained CDC evaluators analyzed quarterly reporting data by technical area, objectives within technical areas, and activities within objectives. In May 2016, CDC evaluators analyzed reporting information for completed activities across all 17 Phase I countries and grouped results into the following categories: 1) real-time surveillance and reporting; 2) national laboratory system and biosafety/biosecurity; 3) workforce development; and 4) emergency management and Emergency Operations Centers (EOCs). This organizational framework reduced the likelihood of missing information because of misclassification, such as if different countries reported related activities in similar, but different, technical areas. For example, national laboratory system and biosafety/biosecurity activities were batched for analyses to ensure all relevant laboratory activities were analyzed together. Activities in other technical areas were analyzed in November 2016.

A CDC evaluator analyzed the completed activity descriptions, objective descriptions, and activity progress data across all Phase I countries for each of the 4

categories. A second CDC evaluator reviewed and validated the first evaluator's analyses; discrepancies were discussed and resolved by a CDC subject matter expert familiar with GHSA technical areas and overseeing all analyses for consistency. Completed activities were summarized by using common terminology for similar major accomplishments achieved by countries with CDC support. (Data on accomplishments achieved by <6 countries are available but not shown here.) Evaluators provided CDC headquarters and field staff with lists of countries that had achieved each major accomplishment, so they could add a country that had not been identified through reporting data analyses or remove a country from an accomplishment category if appropriate. CDC field staff worked with MOHs in some countries to confirm that the revised language accurately reflected country progress.

In November 2016, this process was repeated for completed activities in all 11 technical areas, resulting in a final list that integrated all accomplishments organized into 4 categories (Tables 1–4). In April 2017, CDC field staff in all 17 countries confirmed that the partner country had achieved these major accomplishments with CDC assistance during April 2015–March 2017. CDC evaluators determined the number and proportion of countries that achieved each accomplishment with CDC support.

Results

Overall, our analysis found that CDC supported 675 accomplishments across all 11 GHSA technical areas in 17 Phase I countries. These accomplishments reflect achievements in ≥6 countries (Tables 1–4). Eleven countries each achieved ≥40 of these accomplishments, and each of the 17 countries achieved ≥18.

Disease and Syndromic Surveillance

Surveillance Systems

With CDC's technical assistance, 16 countries established real-time surveillance systems and mechanisms for detecting potential public health events at the national or subnational level. Surveillance systems were improved for zoonotic diseases (13 countries), vaccine-preventable diseases (10 countries), and antimicrobial resistance (7 countries). Thirteen countries met GHSA targets for real-time surveillance of ≥3 syndromes indicative of potential public health emergencies (e.g., severe acute respiratory syndrome, acute flaccid paralysis, acute hemorrhagic fever, acute watery diarrhea with dehydration, and jaundice with fever). In 11 countries, CDC helped countries expand and enhance previously established indicator-based surveillance systems to capture potential threats from larger geographic areas and improve timeliness. CDC supported community immunizations in response to surveillance data on vaccine-preventable diseases in 13 countries (Table 1).

Surveillance Strategic Planning

CDC identified national policies, legal authorities, and gaps in conducting public health surveillance in each of the 17 Phase I countries. In 13 countries, CDC worked with MOHs to determine the appropriate level of subnational jurisdictions (e.g., districts) for reporting surveillance information to the national MOH. Plans and procedures for multisectoral surveillance were developed with ministries of health, agriculture, and defense in 7 countries and with port health services for national points of entry in 8 countries (Table 1).

CDC assisted 12 countries in documenting gaps in surveillance data collection, analysis, and interpretation capabilities; 8 of these countries developed plans for improving interoperability of disparate surveillance systems to better integrate available data from different sources. Eleven countries conducted specialized assessments for immunization surveillance and 9 for antimicrobial resistance (e.g., drug-resistant *Mycobacterium tuberculosis*) surveillance (Table 1).

National Laboratory System

Laboratory Confirmation of Outbreaks

CDC trained laboratory technicians in all 17 Phase I countries and provided 16 countries with new laboratory diagnostics to confirm potential outbreaks identified by surveillance systems, focusing on priority pathogens (e.g., influenza virus, poliovirus, HIV, *M. tuberculosis, Salmonella enterica* serovar Typhi, *Plasmodium* spp., and *Vibrio cholerae*). CDC worked with 9 countries to assess diagnostic capabilities for priority pathogens and 10 countries for antimicrobial resistance. CDC assisted 9 countries in establishing new systems for transporting specimen samples to national reference laboratories (Table 2).

Biosafety and Biosecurity

CDC provided technical assistance to 6 countries to inventory dangerous pathogens and develop plans to manage them in their national laboratory systems. CDC helped 15 countries train technical and administrative staff on biosafety and biosecurity. Eight countries identified staff in the ministries of health, agriculture, and defense responsible for inspecting and certifying laboratories for biosafety and biosecurity compliance (Table 2).

Workforce Development

Field Epidemiology Training Programs

All 17 Phase I countries now participate in basic-level frontline (3-month training), intermediate (6- to 9-month

training), or advanced (2-year training) Field Epidemiology Training Programs (FETPs) (*13–15*) (Table 3). These field-based, CDC-supported programs train members of a nation's health workforce to become disease detectives at national and subnational levels. Since April 2015, CDC has established 14 new frontline and 2 new FETPs-Advanced in Phase I countries. Trainees from all countries investigated real or potential outbreaks as part of their training. Numbers of trainees per country ranged from 24 to 622; nearly half of trainees were frontline surveillance officers (*16*).

Table 1. Key CDC-supported accomplishments toward achieving GHSA targets related to real-time surveillance in 17 Phase I countries, 2015–2017*

GHSA targets and CDC-supported accomplishments	Related JEE indicators (*12*)	No. countries
Strengthened foundational indicator- and event-based surveillance systems that are able to detect events of significance for public health, animal health, and health security		
Surveillance systems		
Established systems and mechanisms at national or subnational levels for detecting public health events from a variety of sources	D.2.1	16
Improved timeliness or geographic coverage of routine public health threat reporting	D.2.2, D.3.2	11
Expanded surveillance systems for ≥3 syndromes indicative of potential public health emergencies (e.g., severe acute respiratory syndrome, acute flaccid paralysis, acute hemorrhagic fever, acute watery diarrhea with dehydration, jaundice with fever)	D.2.4	13
Expanded surveillance systems for zoonotic diseases to include additional pathogens or broader geographic coverage	P.4.1, D.2.1	13
Expanded surveillance systems to include additional pathogens that cause vaccine-preventable diseases	D.2.1	10
Conducted community immunizations in response to vaccine-preventable disease surveillance information	P.7.1, D.2.3	13
Expanded surveillance systems for antimicrobial resistance to include additional pathogens or broader geographic coverage	P.3.2, D.2.1	7
Strategic planning and assessment		
Developed plans to improve the flow and timing of surveillance information and reporting	D.2.2, D.2.3, D.3.1, D.3.2	10
Assessed immunization surveillance, case management, and reporting systems	D.2.2	11
Assessed antimicrobial resistance and drug-resistant tuberculosis surveillance and reporting capacity	P.3.2, D.3.2	9
Training		
Participated in ≥1 level of FETPs	D.4.1	17
Integrated FETP trainees into core public health surveillance functions	D.2.3	15
Improved communication and collaboration across sectors and between subnational, national, and international levels of authority regarding surveillance of events of public health significance		
Strategic planning and assessment		
Identified national policies, legal authorities, and gaps for the conduct of public health surveillance	P.1.1, P.1.2, D.2.1, D.2.2, D.2.4	17
Identified subnational units responsible for indicator- and event-based surveillance	D.2.1	13
Documented national priority public health threats or completed risk assessment	D.2.3, R.1.2	9
Multisectoral coordination		
Developed plans to implement a joint system for surveillance with defined roles, responsibilities, operational processes, and procedures for priority diseases with ministries of health, agriculture, and defense	D.2.1, D.2.2, P.2.1, P.4.1	7
Developed plans and procedures for surveillance capacity for port health services at points of entry	R.3.1, D.2.1, PoE.1	8
Training		
Trained community members to detect and report potential health threats	D.2.1, D.3.2	14
Improved country and regional capacity to analyze and link data from and between strengthened, real-time surveillance systems, including interoperable, interconnected electronic reporting systems		
Strategic planning and assessment		
Assessed reporting systems for development of the national surveillance plan	D.2.2, D.3.1, D.3.2	10
Documented gaps in surveillance data collection, analysis, and interpretation capabilities	D.2.3	12
Developed plan for interoperable information systems supporting indicator- or event-based surveillance and data exchange and integration for priority diseases	D.2.1, D.2.2	8
Training		
Developed training curriculum for health systems personnel in surveillance methods and data use	D.2.1, D.2.2, D.2.3, D.2.4	16
Trained surveillance staff to ensure best practices according to International Health Regulations standards	D.2.1, D.2.2, D.2.3, D.2.4, D.4.1	9

*Countries: Bangladesh, Burkina Faso, Cameroon, Côte d'Ivoire, Ethiopia, Guinea, India, Indonesia, Kenya, Liberia, Mali, Pakistan, Senegal, Sierra Leone, Tanzania, Uganda, and Vietnam. CDC, US Centers for Disease Control and Prevention; FETP, Field Epidemiology Training Program; GHSA, Global Health Security Agenda; JEE, Joint External Evaluation tool.

Additional Training

Other CDC-supported training activities addressed additional GHSA targets. In 14 countries, CDC worked with MOHs to train community leaders in event-based surveillance. In 16 countries, CDC helped develop training curricula for surveillance and data analysis methods in English or the predominant national language (i.e., French or Vietnamese). In 7 countries, CDC provided trainings and developed infection prevention and control programs for healthcare facilities to combat antimicrobial resistance. In 13 countries, CDC led multidisciplinary and multisectoral public health trainings, including One Health trainings for preventing zoonotic disease spillover from animals to humans (Table 3).

Workforce Strategic Planning

CDC supported 16 countries in strategic planning related to the national public and animal health workforce. CDC assisted 6 of these countries in creating national multisectoral workforce development strategic plans based on assessments of existing public health training programs, educational systems, and gaps in the national public health workforce (Table 3).

Emergency Management and Response

EOCs

CDC worked with all 17 Phase I countries to improve public health emergency management capacities, such as by establishing EOCs and training EOC staff in incident management in 15 countries. Twenty-nine staff from 14 countries' MOHs, national public health institutes, and other national and international organizations completed CDC's Public Health Emergency Management Fellowship program (*17*). CDC helped 15 countries develop EOC policies and protocols, and 11 countries activated the EOC for an exercise or real public health emergency response (Table 4).

Multisectoral Coordination

CDC provided assistance to 14 countries to complete public health risk assessments and document national priority public health threats. Nine countries established One Health mechanisms for joint response across human, animal, and environmental health sectors to prevent or limit animal-to-human spillover of zoonotic diseases (*18*). CDC worked

Table 2. Key CDC-supported accomplishments toward achieving GHSA targets related to national laboratory systems in 17 Phase I countries, 2015–2017*

GHSA targets and CDC-supported accomplishments	Related JEE indicators (*12*)	No. countries
Real-time biosurveillance with a national laboratory system		
Strategic planning and assessment		
Identified national policies, legal authorities, and gaps for the conduct of a national public health laboratory system	P.1.1, P.1.2, D.1.2, D.1.3, D.1.4	17
Operationalized national plan of action with internationally accepted best practices for priority diseases	D.1.1, D.1.2, D.1.3, D.1.4	11
Developed tier-specific testing strategies for priority diseases at designated laboratories	D.1.3	10
Specimen referral system		
Established functional system for specimen transport to reference laboratories within the appropriate timeframe of collection	D.1.2	9
Conducted investigations or training exercises to confirm functionality of specimen referral systems	D.1.2	8
Training		
Trained laboratory technicians	D.1.1, D.1.3	17
Effective modern point-of-care and laboratory-based diagnostics		
Strategic planning and assessment		
Assessed diagnostics, data quality, and staff performance	D.1.1, D.1.3, D.1.4	9
Assessed antimicrobial resistance and drug-resistant tuberculosis laboratory capacity	P.3.1	10
Diagnostics		
Acquired new diagnostic equipment and capabilities (e.g., specimen test kits) to detect priority pathogens (e.g., influenza virus, poliovirus, HIV, *Mycobacterium tuberculosis*, *Salmonella enterica* serovar Typhi, *Plasmodium* sp., *Vibrio cholerae*)	D.1.1, D.1.3	16
Whole-of-government national biosafety and biosecurity system is in place, ensuring that especially dangerous pathogens are identified, held, secured, and monitored in a minimal number of facilities according to best practices; biologic risk management training and educational outreach are conducted to promote a shared culture of responsibility, reduce dual-use risks, mitigate biologic proliferation and deliberate use threats, and ensure safe transfer of biologic agents; and country-specific biosafety and biosecurity legislation, laboratory licensing, and pathogen control measures are in place as appropriate		
Biosafety and biosecurity		
Trained staff on biosafety and biosecurity	P.6.2	15
Identified staff in ministries of health, agriculture, and defense responsible for inspection or certification of laboratories for compliance with biosafety and biosecurity requirements	P.6.1	8
Inventoried dangerous pathogens and developed a plan to manage them	P.6.1	6

*Countries: Bangladesh, Burkina Faso, Cameroon, Côte d'Ivoire, Ethiopia, Guinea, India, Indonesia, Kenya, Liberia, Mali, Pakistan, Senegal, Sierra Leone, Tanzania, Uganda, and Vietnam. CDC, US Centers for Disease Control and Prevention; GHSA, Global Health Security Agenda; JEE, Joint External Evaluation tool.

with 13 countries to assess baseline capacities of agencies to respond to biologic threats across public health, animal health, law enforcement, and other sectors. CDC initiated activities to strengthen response coordination across multiple sectors in 12 countries and identified points of contact for multisectoral information-sharing in 10 countries (Table 4).

Discussion

During April 2015–March 2017, CDC supported 17 Phase I countries in achieving 675 accomplishments in 11 GHSA technical areas. Although GHSA is still in early stages of implementation, CDC's support to countries has helped improve their capabilities, especially in the cross-cutting areas of public health surveillance, national laboratory systems, workforce development, and emergency response management. Accomplishments in these technical areas have also contributed to the countries' progress in the other GHSA technical areas and IHR 2005 core capacities.

Robust surveillance networks linked with laboratory testing can enable early detection of public health threats before they escalate into outbreaks and threaten communities, nations, and the world. CDC's efforts to build country capacity to detect potential outbreaks focused on increasing the numbers of diseases captured by surveillance and reporting systems, expanding these systems to include additional subnational jurisdictions and community-level surveillance, and strengthening processes to improve the timeliness and efficiency of communication across all levels.

CDC worked with health, agriculture, defense, and other ministries to broaden the types of pathogens and syndromes that can be detected by improved surveillance systems. As a result of CDC's GHSA work, countries that previously had systems to monitor a limited range of potential public health threats are now better able to detect animal-to-human disease spillover, healthcare-associated infections, and other potential outbreaks by monitoring more diseases and syndromes systematically and frequently. Early detection of public health threats can lead to timely interventions to prevent escalation into major outbreaks (*19–21*). Phase I countries have already used improved surveillance data to inform prevention efforts. For example, increased surveillance of vaccine-preventable diseases resulted in community immunizations to prevent further

Table 3. Key CDC-supported accomplishments toward achieving GHSA targets related to workforce development in 17 Phase I countries, 2015–2017*

GHSA targets and CDC-supported accomplishments	Related JEE indicators (*12*)	No. countries
Workforce including physicians, veterinarians, biostatisticians, laboratory scientists, farming and livestock professionals, and field epidemiologists who can systematically cooperate to meet relevant International Health Regulations and performance of veterinary services core competencies		
Strategic planning and assessment		
Created national, multisectoral workforce development strategic plan	D.4.3	6
Assessed country's public health training programs, education system, and workforce gaps	D.4.1, D.4.3	15
Assessed country's current status of One Health workforce	P.4.2, D.4.1	8
Identified needs for core public health emergency management staff	R.2.1, D.4.1, R.1.1	15
Assessed laboratory staff performance	D.1.4	9
Identified staff in ministries of health, agriculture, and defense responsible for inspection or certification of laboratories for compliance with biosafety and biosecurity requirements	P.6.1	8
FETP		
Conducted 3-month FETP-Frontline	D.4.2	15
Conducted FETP-Intermediate or Advanced (6 months–2 years)	D.4.2	11
Participated in FETP-Intermediate or Advanced run by another country	D.4.2	6
Provided FETP to ≥1 staff member from ≥50% of subnational jurisdictions	D.4.1, D.4.2	6
Integrated FETP trainees into core public health functions	D.4.1, D.2.3	15
Other training		
Conducted public health multidisciplinary (e.g., One Health) trainings	P.4.2	13
Trained laboratory technicians	D.1.1, D.1.3	17
Trained staff on biosafety and biosecurity	P.6.2	15
Developed infection prevention and control training programs, including antimicrobial resistance prevention	P.3.3	7
Trained community members to detect and report potential health threats	D.2.1, D.3.2	14
Developed training curriculum for health systems personnel in surveillance methods and data use	D.2.1, D.2.2, D.2.3, D.2.4	16
Trained surveillance staff to ensure best practices according to International Health Regulations standards	D.4.1, D.2.1, D.2.2, D.2.3, D.2.4	9
Activated EOC for an exercise or real emergency response	R.2.3, R.3.1	11
Trained EOC staff in public health emergency management (basic level)	R.2.1, D.4.1	14
Committed to train EOC staff through CDC's Public Health Emergency Management Fellowship	R.2.1, D.4.1	16
Recruited key staff for public health emergency management	R.2.1, D.4.1	13

*Countries: Bangladesh, Burkina Faso, Cameroon, Côte d'Ivoire, Ethiopia, Guinea, India, Indonesia, Kenya, Liberia, Mali, Pakistan, Senegal, Sierra Leone, Tanzania, Uganda, and Vietnam. CDC, US Centers for Disease Control and Prevention; EOC, Emergency Operations Center; FETP, Field Epidemiology Training Program; GHSA, Global Health Security Agenda; JEE, Joint External Evaluation tool.

spread of measles and other diseases in 13 countries, including Guinea, Indonesia, and Liberia, where vaccination coverages are low. Furthermore, CDC worked with Phase I countries to incorporate hands-on experience investigating potential outbreaks into FETPs.

Surveillance capacity-building efforts also focused on expanding geographic coverage. Public health surveillance and laboratory capacity have typically been concentrated in urban centers, limiting countries' abilities to detect outbreaks in rural areas (*20*,*22*). CDC assisted Phase I countries with establishing integrated surveillance systems that share data across healthcare facilities, subnational jurisdictions (e.g., districts), and MOHs. CDC helped countries train surveillance officers throughout multiple levels of countries' health systems. In addition to training field epidemiologists through FETPs, CDC helped countries enlist the help of community leaders in detecting threats early by training them on community-based disease surveillance and reporting to complement healthcare facility surveillance. Community-level disease monitoring has been shown to influence intervention efforts and reduce the incidence of disease and prevalence of premature death. For example, community health workers in West Africa used surveillance data to target immunizations and reduce the number of cases of vaccine-preventable meningococcal disease by half (*23*,*24*). These efforts aim to prevent outbreaks at the source before spreading rapidly within large cities or to other countries.

National laboratory systems are integral for assessing public health threats and targeting outbreak response efforts. Laboratory testing of specimen samples is necessary to confirm suspected public health threats identified through disease and syndromic surveillance (*25*). Timely confirmation of public health threats relies upon laboratory systems that link central reference laboratories with peripheral laboratories, securely and rapidly transport specimens from patients to laboratories, and efficiently report accurate test results from laboratories to patients and MOHs (*26*). CDC's assistance has been vital to providing countries with diagnostic capabilities and establishing specimen transport systems to decrease the time from specimen collection to testing at a certified national public health laboratory. This work is necessary to confirm public health threats so response efforts can be directed appropriately. CDC's training of laboratory technicians will empower countries to confirm potential outbreaks of a broader set of pathogens more accurately and expediently.

Table 4. Key CDC-supported accomplishments toward achieving GHSA targets related to emergency management in 17 Phase I countries, 2015–2017*

GHSA targets and CDC-supported accomplishments	Related JEE indicators (*12*)	No. countries
Public health EOC functioning according to minimum common standards		
Strategic planning and assessment		
Identified national policies, legal authorities, and gaps for the conduct of public health emergency response	P.1.1, P.1.2, R.1.1, R.1.2, R.2.1, R.2.2, R.2.4	17
Assessed baseline of national public health emergency management capacities	R.1.2, R.2.1	14
Documented national priority public health threats or completed risk assessment	D.2.3, R.1.2	9
EOC facility		
Obtained buy-in from country leadership for permanent EOC facility and associated program	R.2.1, R.2.2	15
Identified facility location or funding mechanisms for EOC	R.2.2	16
Developed EOC policies, plans, protocols, or standard operating procedures	R.2.2, R.2.4	15
Multisectoral coordination		
Operationalized multisectoral One Health mechanisms to limit animal-to-human spillover of zoonotic diseases	P.4.3, P.2.1	9
Initiated activities to strengthen response coordination (e.g., through MOUs) across public health, animal health, law enforcement, and other sectors	R.3.1, R.1.1, P.2.1, P.4.3, PoE.2	12
Identified points of contact and informal process for communication and information-sharing across public health, animal health, law enforcement, and other sectors	R.3.1, P.4.3, P.2.1, PoE.2	13
Improved logistics planning to deploy staff, medicines, and supplies during a public health emergency	R.4.1, R.4.2, R.1.1, PoE.1	10
Trained EOC staff capable of activating a coordinated emergency response within 120 minutes of the identification of a public health emergency		
Strategic planning and assessment		
Identified needs for core public health emergency management staff	R.2.1, D.4.1, R.1.1	15
Assessed baseline capacity of partnering agencies for response to a biologic threat	P.2.1, R.3.1	12
Training		
Activated EOC for an exercise or real emergency response	R.2.3, R.3.1	11
Trained EOC staff in public health emergency management (basic level)	R.2.1, D.4.1	14
Committed to train EOC staff through CDC's Public Health Emergency Management Fellowship	R.2.1, D.4.1	16
Recruited key staff for public health emergency management	R.2.1, D.4.1	13

*Countries: Bangladesh, Burkina Faso, Cameroon, Côte d'Ivoire, Ethiopia, Guinea, India, Indonesia, Kenya, Liberia, Mali, Pakistan, Senegal, Sierra Leone, Tanzania, Uganda, and Vietnam. CDC, US Centers for Disease Control and Prevention; EOC, Emergency Operations Center; GHSA, Global Health Security Agenda; JEE, Joint External Evaluation tool; MOU, memo of understanding.

CDC worked with other US government entities and partner countries' ministries of health, agriculture, and defense to address potential biosecurity threats, such as by ensuring that countries keep inventories and management plans for dangerous pathogens stored in laboratories. Countries applied CDC's expertise to ensure proper laboratory management and biosafety certification, which are imperative for ensuring the integrity of the national laboratory system. This work is critical for preventing national and international public health emergencies by preventing potential biosecurity threats.

Trained field epidemiologists, laboratory technicians, and emergency responders are crucial for detecting and responding to public health threats early and effectively, and EOCs with incident management systems are essential for response coordination (*27*). In July 2014, when the major EVD outbreak was worsening in West Africa, CDC-trained disease detectives performed contact tracing on 894 contacts of EVD case-patients in Lagos, Nigeria (*27*); only 11 deaths in Nigeria resulted from this EVD outbreak, although models estimated thousands of deaths would have occurred without timely investigation and emergency management (*19*). This example illustrates the potential impact of GHSA implementation. Training disease detectives and developing effective incident management can mean the difference between small outbreaks that are quickly and effectively controlled and larger outbreaks with substantial global health implications. CDC established new FETPs in 16 Phase I countries to rapidly train disease detectives. CDC worked with Phase I countries to establish EOCs and train emergency response staff. A component of the training involved activating the EOC for exercises or real public health emergencies. These activations incorporated a multisectoral approach to bring together public health, animal health, border security, and other sectors. These efforts strengthen capacities and test countries' abilities to respond to public health threats effectively and rapidly.

The accomplishments we describe have enhanced global health security, but GHSA relies on strong partnerships to sustain capacity-building efforts. CDC's work has strengthened collaborations among countries, US government agencies, and international governments and organizations. While emphasizing a multisectoral approach for building GHSA capabilities, CDC uniquely provides direct technical assistance to MOHs, developing their expertise so they can sustain GHSA accomplishments. CDC worked with multiple partners, including national ministries of health, agriculture, and defense, to establish mechanisms for cross-sectoral communication and collaboration that are essential for outbreak prevention, detection, and response that did not exist before GHSA. CDC's technical assistance complemented efforts by other nations and US government entities, including the US Agency for International Development, the Defense Threat Reduction Agency, and the US Department of Agriculture. Notably, the relatively small US investment in GHSA led to additional investments from other donor nations. For example, South Korea committed $100 million to build global health security capabilities in 13 countries (*28*).

In addition to technical assistance, CDC contributed to the development of the Joint External Evaluation (JEE) tool, an independent, transparent evaluation that employs 48 indicators to measure progress toward GHSA and IHR 2005 targets (*12*). A benefit of the JEE is its potential for standardizing metrics and streamlining CDC's technical assistance across multiple countries. CDC worked with the World Health Organization and other partners to develop a library of achievements needed to advance from one level of capacity to higher levels (*29*). Most of the accomplishments we describe (Tables 1–4) are among the milestones in the library, with related JEE indicators associated with each. This work demonstrates the feasibility and effectiveness of these activities in the field. The milestones library, together with JEE scores, helps CDC standardize and streamline technical assistance to complement activities planned by other partners. Although the administrative efforts required to undergo the JEE delayed CDC's activities in some countries, the JEE process has now been operationalized, and countries have built their evaluation capacities by completing these baseline assessments. As of September 2017, a total of 58 countries, including 14 Phase I countries, completed the JEE with CDC support, identifying countries' IHR 2005 capabilities and the explicit gaps in need of prioritization.

Our report has a few limitations. First, this report is not comprehensive of all CDC's GHSA achievements. It focuses on CDC-supported accomplishments in 17 countries, excluding CDC's GHSA achievements beyond Phase I countries, including in Ebola preparedness countries where CDC prioritized GHSA work to build detection and preparedness capabilities to prevent cross-border spillover of EVD and other disease threats. Also, in initial analyses, evaluators determined that some accomplishments had been achieved by <6 Phase I countries and thus omitted these from the list provided to CDC field staff for validation; however, ≥6 countries might have achieved some of these by March 2017. Furthermore, CDC field staff validated accomplishments subjectively based on their interpretations of standardized language, potentially resulting in underreporting or overreporting. Despite these limitations, this report describes substantial accomplishments in 17 countries that resulted directly from the technical assistance provided by CDC. These achievements align with GHSA targets, suggesting that CDC has helped these countries move closer to attaining IHR 2005 core capacities, thus creating a safer world.

In conclusion, GHSA was launched with a goal of making the world safer from infectious disease threats by improving countries' IHR 2005 core capacities (*4*). CDC's efforts have been critical as part of a long-term process of building and sustaining global health security capacity in countries with less-developed public health systems. Initial accomplishments have laid the groundwork for further GHSA advancement in these 17 countries, and lessons learned might improve the efficiency of GHSA implementation in additional countries. Ongoing GHSA implementation offers an alternative to the cycle of panic and neglect that describes the current response to pandemic threats (*30*). The initial successes we describe demonstrate that strategic appropriation of technical and financial resources can accelerate progress toward GHSA targets and global achievement of IHR 2005 core capacities. CDC's continuing work with partner countries ensures sustainability and further progress rather than regression. Furthermore, investments in global health security have been shown to have positive health, security, and economic impacts (*31*,*32*). These improvements in international capacity to rapidly detect, respond to, and control infectious disease outbreaks and other public health threats at their sources translate into enhanced global health security, because fewer public health threats can spread throughout a country and reach other nations, including the United States.

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Ebola Response Impact on Public Health Programs, West Africa, 2014–2017

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Events such as the 2014–2015 West Africa epidemic of Ebola virus disease highlight the importance of the capacity to detect and respond to public health threats. We describe capacity-building efforts during and after the Ebola epidemic in Liberia, Sierra Leone, and Guinea and public health progress that was made as a result of the Ebola response in 4 key areas: emergency response, laboratory capacity, surveillance, and workforce development. We further highlight ways in which capacity-building efforts such as those used in West Africa can be accelerated after a public health crisis to improve preparedness for future events.

The Ebola epidemic that was first recognized in 2014 and ravaged the West Africa countries of Liberia, Sierra Leone, and Guinea was a stark illustration of the risks that emerging pathogens and epidemic-prone diseases pose to local and global health security in settings that had limited public health capacity. More than 28,000 Ebola cases were reported from the 3 countries during the epidemic, and >11,000 persons died (*1*). These countries are among the least developed in the world (*2*), and their weak infrastructures and underfunded health systems were further compromised by the epidemic. During the initial months of the Ebola epidemic, limited capacity to rapidly identify suspected cases, confirm diagnoses, and implement preventive measures contributed to widespread transmission (*3*). By the time control was achieved, there had been widespread, devastating impacts on those infected and their families, as well as on the nations' healthcare systems and economies (*4*) and population health (*5*). Control of the outbreak required substantial effort from host country governments and populations and crucial resources and inputs from multilateral and bilateral partners, nongovernmental organizations (NGOs), and individual persons from outside the 3 countries. In usual circumstances, establishing public health systems and capacities to detect, prevent, and respond to urgent global health threats requires long-term planning and investment (*6*). However, the swift and massive response to this epidemic established methods and resources that are transferable to responses to other health threats, affording an unparalleled opportunity for more rapid expansion of emergency response capacities than would usually be possible in such settings.

We describe public health progress that was made as a result of the Ebola response in 4 key areas: emergency response, laboratory capacity, surveillance, and workforce development. We then reflect on the challenges and opportunities of supporting this progress immediately after the large public health response.

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Emergency Response

Although response coordination was challenging, especially during the initial phase, establishment of incident management systems (IMS) for the Ebola response facilitated coordination of multiple partners that contributed to control of the main outbreak. In Liberia, the Ministry of Health (MOH) established a national IMS in July 2014, with support from the US Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and other partners. Management of daily activities through Emergency Operations Centers (EOs) improved coordination of response efforts at national and county levels (*7*). During the response, the physical location for the national EOC moved from a temporary location to a new permanent infrastructure on the campus of the MOH. In Sierra Leone, outbreak response was coordinated primarily through national and district Ebola response centers supported by civilian and military personnel and resources from the United Kingdom. During the response, new infrastructure

was created to increase coordination capacity, emergency response coordination plans were developed, and designated staff were trained. In Guinea, the IMS was coordinated through a Guinea-led National Coordination Cell with support from WHO, CDC, and the Public Health Agency of Canada. An EOC was established, and staff received basic training in emergency management that facilitated coordination efforts.

The appearance of Ebola clusters after continuous transmission was controlled provided evidence that Ebola virus could persist in survivors of Ebola virus disease (EVD) and could be sexually transmitted to others, initiating new chains of transmission (*8*–*10*). Therefore, it was essential to maintain capacity to rapidly recognize and respond to Ebola cases. The first well-characterized case of transmission related to viral persistence occurred in Liberia, ≈1 month after the epidemic had first been controlled and before Liberia had met the WHO criteria to be declared free of Ebola transmission (*8*,*9*). At that point, the response structure and resources remained in place. The diagnosis was rapidly confirmed, the response was robust, and there was no evidence of secondary transmission.

Additional clusters (2 in Liberia, 3 in Sierra Leone, and 1 that began in Guinea and spread to Liberia) occurred after interruption of transmission in each country (Figure). The responses to these additional clusters were also robust; in most instances, transmission was limited to 0 or 1 generation (*11*). In Sierra Leone, responses to 2 clusters were coordinated through the same structures used to respond to the main epidemic. The responsibility for emergency response coordination was transferred to the Ministry of Health and Sanitation on January 1, 2016. The agency's abilities were immediately tested by the recognition of an EVD case, likely related to transmission from an EVD survivor, on January 14, 2016 (*12*). The Ministry of Health and Sanitation stood up its emergency response structure and led a complex control effort that required coordination across 5 districts (*13*). The response led to identification of 131 contacts and implementation of enhanced community surveillance in 1 district for 2 months after the end of contact monitoring. The cluster was limited to 1 generation; disease occurred only in the index case-patient and a single high-risk contact.

The final cluster of Ebola during the epidemic was recognized in March 2016 (*10*) and occurred under conditions that were similar to the initial situation in the main epidemic; cases were first diagnosed in southeastern Guinea, and a person with a history of high-risk contact fled across the border to Liberia, where Ebola was confirmed in a patient at a hospital in the capital, Monrovia. Responses were led by host country government IMSs and supported by a range of international partners. Although

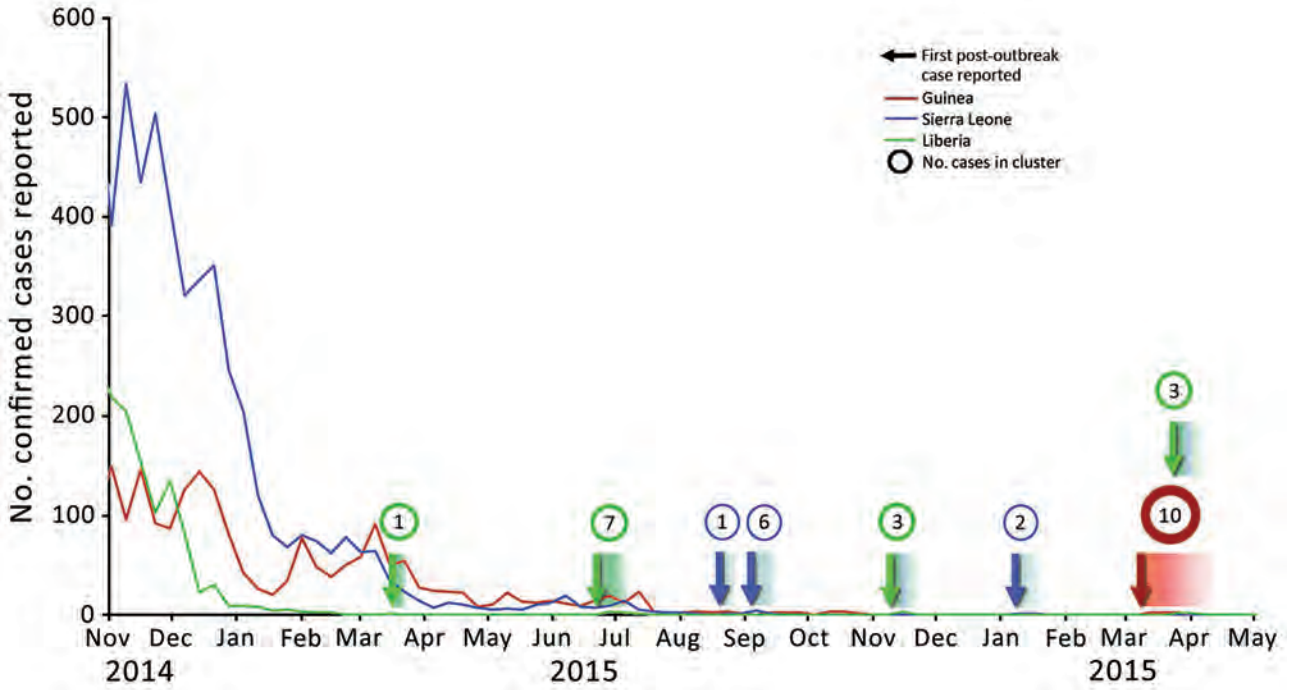

Figure. Ebola virus disease clusters after interruption of the 2014–2015 Ebola outbreak in Liberia (green), Sierra Leone (blue), and Guinea (red). Lines reflect total weekly case numbers during the primary outbreak. Arrows indicate the first reported case in each postoutbreak cluster; color indicates the country where the cluster was first recognized (the March 2016 cluster began in Guinea, but spread to Liberia), and gradients indicate timespan of cluster. Circle sizes are proportional to cluster size, and the total number of confirmed and probable cases in each cluster is shown in the circles.

the cluster in Guinea was not identified until there had already been 3 generations of viral transmission, and initial contact identification efforts were delayed by community resistance, the response was effective, containing spread to 2 additional generations. In Liberia, transmission was limited to 1 generation, affecting only immediate family members of the index case-patient. These outcomes were vastly different than that for the initial introduction of Ebola in West Africa.

IMSs have proven beneficial for response efforts beyond those for which they were originally established. The effective control of the Ebola outbreak in Nigeria after travel of an infected person from Monrovia to Lagos in July 2014 was facilitated by the use of an established polio IMS (*14*). Likewise, IMSs established for the Ebola response have provided a structure for organization of other response efforts. In Liberia, increases in the number of measles and Lassa fever cases led to the activation of the IMS on March 14, 2016; the IMS coordinated case investigations, contact tracing, diagnostic evaluation, case management, and prevention efforts. In Sierra Leone, the IMS was activated for an outbreak of measles, which was successfully controlled after a vaccination campaign, and for investigation of cases of acute flaccid paralysis. In Guinea, the EOC established during the Ebola response was integrated into the newly formed Agence National de Sécurité Sanitaire (ANSS) and is responsible for managing epidemics in Guinea; the EOC is managed by a dedicated team of 5 ANSS staff members assisted by CDC, Public Health Agency of Canada, and NGO partners. The EOC has been activated to coordinate investigations and responses to yellow fever and measles outbreaks and provides strong support to the surveillance unit of the ANSS by coordinating meetings and information sharing, producing situational reports, and providing logistic support.

Expansion of Laboratory Capacity

At the beginning of the Ebola epidemic in West Africa, diagnosis relied on complex tests, primarily reverse transcription PCR (RT-PCR), conducted in carefully controlled settings. Capacity to conduct these tests in Liberia, Sierra Leone, and Guinea was limited, and the initial diagnosis was confirmed by testing of samples sent to an international reference laboratory. During the outbreak, most samples were tested by international teams in field laboratories (*15*). However, over the course of the outbreak, capacity to conduct RT-PCR was established or expanded in national laboratories in each country, and capacity for new technologies was developed, including the use of the GeneXpert platform (Cepheid, Sunnyvale, CA, USA) for PCR and rapid diagnostic tests (RDTs) based on lateral flow assays. These new tests became critical for confirmation of cases later in the outbreak and for ruling out disease and supporting Ebola surveillance. For example, hospital staff performed testing that identified the first case in Liberia during the final outbreak in early 2016 (*16*). In Guinea, Ebola RDTs were used to expand testing capacity to a broader patient population than would have otherwise been tested and to screen for infection status among the deceased to allow families to proceed rapidly with burial. OraQuick Ebola Rapid Antigen Tests (OraSure Technologies, Inc., Bethlehem, PA, USA) were piloted at 15 sites in Forécariah Prefecture in October 2015 by the Guinea MOH and Red Cross staff (*17*) and eventually used to test >4,000 febrile patients and >3,000 deceased patients. Although there appears to be potential for a useful role for Ebola RDTs, progress has been limited for availability, liscensing, and development of guidelines for use of these tests, and the role of postoutbreak Ebola-specific RDTs has diminished. As of late 2017, Liberia, Sierra Leone, and Guinea maintain national and sometimes regional capacity to conduct EVD testing.

In all 3 of these countries, the expansion of Ebola diagnostic capacity extended beyond the ability to diagnose acute infection. Serologic testing contributed to the understanding of disease transmission (*18*), and programs were established that supported testing of semen and other body fluids for Ebola virus RNA (*19*). Local determination of viral sequences also provided key information to inform control efforts; for example, a laboratory established in Sierra Leone in April 2015, staffed by locally trained scientists, conducted rapid sequencing of full Ebola RNA genome sequences and informed the investigation of subsequent Ebola clusters (*13*,*20*).

Expanding Ebola diagnostic capacity improved capacity for diagnosis of other diseases of public health importance, and there has been substantial progress in developing or updating laboratory strategic plans, establishing and improving sample transport networks, and safely storing biologic specimens. In Liberia, diagnostic capacity has been established or reestablished for all identified priority reportable diseases (Table 1), and a nationwide sample transport system has transported >50,000 laboratory specimens from >302 sites across all 15 counties since April 2015. In Sierra Leone, focused collaborative efforts have improved the infrastructure at the national reference laboratory and supported broad training in quality management; progress in establishing systems for sample transport has been limited. In Guinea, much of the laboratory equipment and infrastructure used for Ebola RT-PCR diagnosis by international partners, including a field laboratory established by the US Defense Threat Reduction Agency, have been donated to the MOH. Multiple partners are assisting the MOH to expand diagnostic capacity on these platforms to other diseases of epidemic potential.

Table 1. Timeframe for establishment or reestablishment of capacity to test for key notifiable diseases in Liberia after 2014–2015 Ebola outbreak and response*

IDSR priority disease	Q1 2016	Q2 2016	Q3 2016	Q4 2016	Q1 2017
Acute flaccid paralysis	Sent to WHO/regional laboratory outside Liberia for testing				
Acute watery diarrhea (cholera)	†	†	‡	§	§
Acute bloody diarrhea (shigella)	†	†	‡	§	§
Human rabies	Sent to WHO/regional Laboratory outside Liberia for testing				
Lassa fever	†	†	‡	§	§
Measles	‡	§	§	§	§
Meningitis	†	†	†	‡	§
Neonatal tetanus	Not applicable; diagnoses based on clinical symptoms				
Viral hemorrhagic fever (including Ebola virus disease)	§	§	§	§	§
Yellow fever	‡	§	§	§	§

*IDSR, Integrated Disease Surveillance and Response framework; Q, quarter, WHO, World Health Organization.
†Capacity was not available during the specified quarter.
‡Capacity was partially established.
§Established laboratory capacity.

Improved Surveillance

Before the Ebola epidemic, sentinel and event-based disease surveillance systems were generally limited in all 3 affected countries; these were further disrupted by the epidemic. However, the Ebola response and health system recovery efforts in these countries have led to improved surveillance for EVD and other epidemic-prone diseases. Event-based surveillance in Liberia is implemented as part of a broad system for Integrated Disease Surveillance and Response (IDSR), which documents 14 priority diseases and conditions. A 5-year IDSR strategic plan is in place and surveillance officers at national and subnational levels have undergone training based on updated IDSR technical guidelines (*21*). Through the Community Event-Based Surveillance system (https://www.globalcommunities.org/liberia), events in the community are reported to a surveillance focal person at the closest health facility, then to the district and county surveillance officers, and reported weekly to the MOH Disease Prevention and Control unit at the national level. Timeliness and completeness of reporting were high before the Ebola outbreak, fell during the outbreak, and currently average >99%. Efforts are ongoing to improve the quality of both the reported data and the response to reports of notifiable diseases and to implement an electronic early warning system to further improve alert notification and response.

Since the Ebola outbreak in Sierra Leone, IDSR-based surveillance has been implemented nationwide. Although IDSR had been technically adopted by Sierra Leone, its implementation had been incomplete before the Ebola outbreak. Improvements in the quality of data collation, analysis, and presentation by central public health authorities have been supported through training, mentorship, and supportive supervision that has included comprehensive data quality audits. The system now monitors 28 priority diseases, conditions, and events. Surveillance data are reported electronically in all 13 districts by using a mobile electronic Integrated Disease Surveillance and Response system (eIDSR) that is compliant with the DHIS2 data management system (https://www.dhis2.org/); this system resulted in 94% of health facilities reporting to their districts in 2016 (Table 2).

In August 2015, Guinea's MOH created and validated the Surveillance of Epidemic-Prone Diseases plan. In February 2016, IDSR training was conducted for national trainers, who then trained other surveillance system staff. Also in early 2016, Guinea established a novel program to monitor for Ebola resurgence. Ebola survivors were engaged in active surveillance for Ebola-like illness among their contacts and in their communities (Surveillance Active en Ceinture SA-Ceint [*22*]). During the final months of the Ebola epidemic, the MOH also launched community-based surveillance for epidemic-potential diseases in priority prefectures, which supported reporting of key community-level alerts to the local health facility. A DHIS2-based eIDSR reporting system was established for collection of monthly surveillance data in all 38 prefectures of Guinea; the eIDSR system is being expanded in 2017 to include the weekly and immediate surveillance reporting, including case-based surveillance for priority diseases.

Expansion of Human Capacity

Building public health capacity within the staff of governments is expected to have long-term, broad impacts (*6*). Although it is difficult to precisely measure the effect of a capable public health workforce, quality public health responses are highly dependent on the availability of well-trained staff. When Ebola spread to Nigeria, trained epidemiologists rapidly mounted extensive and successful contact identification and monitoring activities and kept Ebola from spreading broadly, likely preventing a catastrophic outcome (*23*). Thus, a major priority in building public health capacity is to support training in surveillance and epidemic response.

In each of the countries most affected by the Ebola epidemic, the response offered an opportunity to identify persons who have capacity to conduct public health activi-

Table 2. Improvements in the timeliness and completeness of routine district surveillance reporting after 2014–2015 Ebola outbreak and response, Sierra Leone, 2015–2016*

	November 8–4, 2015			May 29–June 4, 2016		
Health district	No. district HFs	No. (%) HFs reported to district	Timeliness	No. district HFs	No. (%) HFs reported to district	Timeliness
Kambia	68	30 (44†)	T‡	69	67 (97)	T‡
Port Loko	106	0 (0†)	NR†	111	102 (92)	T‡
Bombali	104	0 (0†)	NR†	113	111 (98)	T‡
Koinadugu	72	24 (33†)	T‡	72	63 (88)	T‡
Tonkolili	103	0 (0†)	NR†	107	96 (90)	T‡
Kono	86	80 (93)	T‡	91	91 (100)	T‡
Kenema	123	26 (21†)	T‡	123	(120 98)	T‡
Kailahun	86	16 (18†)	T‡	86	85 (99)	T‡
Bombali	121	38 (31†)	T‡	128	128 (100)	T‡
Moyamba	100	95 (95)	T‡	101	101 (100)	T‡
Bonthe	55	54 (98)	T‡	55	50 (91)	T‡
Pujehun	77	0 (0†)	NR†	77	47 (61§)	T‡
Western Area	114	65 (57§)	L§	120	118 (98)	T‡
Overall	1,215	428 35	NC	1,253	1,179 (94)	NC

*Timeliness indicates timing of districts reporting to national level. During 2015, 35% of HFs in Sierra Leone reported Ebola cases to their respective districts. During 2016, 94% of health facilities reported to their districts, and all districts reported at the national level. Data source: CDC Sierra Leone Country Office analysis of Sierra Leone Ministry of Health data. HF, health facility; L, late; NR, no report; NC, not calculated; T, on time.
†Level of completeness <50%; performance did not meet minimum standard.
‡Level of completeness >50% and <80%; performance met minimum standard, but did not meet target.
§Level of completeness >80%; performance met target.

ties. Many persons engaged as surveillance officers during the response demonstrated interest in and aptitude for these activities and have since chosen to pursue training and careers in public health.

Training in field epidemiology is among the top priorities related to expanding public health capacity. Frontline Field Epidemiology Training Programs (FETPs) have been established in all 3 of the countries most affected by the Ebola epidemic. The FETP-Frontline program provides 3 months of on-the-job training and supervision for surveillance officers working within the MOH (*24*). In Liberia, the FETP-Frontline was launched in August 2015; by early 2017, more than 120 surveillance officers in Liberia had completed training, and there are now trained staff in all 15 counties and each of Liberia's 90 districts. Sierra Leone established a FETP-Frontline program in June 2016 that has now graduated >35 trainees from the national response structure, including all districts. By early 2017, FETP participants had conducted >50 case investigations for acute flaccid paralysis, rabies, maternal deaths, cholera, measles, yellow fever, meningitis, neonatal tetanus, and unexplained deaths, as well as investigations of outbreaks of Lassa fever and rubella. In Guinea, the FETP was launched in December 2016 by the training of 8 MOH staff who will mentor their peers. A cohort of 25 MOH staff began the training program in January 2017; 80 staff are expected to graduate by mid-2018.

FETP-Intermediate, a 9-month program to train supervisory surveillance officers and strengthen their field epidemiology, data analysis, and public health skills (*24*), was launched in Liberia in April 2017 and in Sierra Leone in mid-2017 and will launch in Guinea in early 2018. This training will equip surveillance officers with knowledge and skills to supervise staff and provide leadership during outbreak responses.

Workforce development has included a broad range of other training activities. In Liberia, Sierra Leone, and Guinea, focused training and mentoring on infection prevention and control (IPC) principles and practices was provided at health facilities in the area of an Ebola cluster by using an approach termed ring-IPC (*25*), and thousands of healthcare workers have been trained in IPC principles. Sierra Leone has initiated workforce capacity building in preservice and in-service training programs in laboratory, epidemiology, infection prevention and control, program management, and emergency management. In Guinea, laboratory training has included diagnosis of EVD, meningitis, cholera, and shigellosis, as well as sample transport, biosafety/biosecurity, quality management systems, and molecular biology. A critical element of workforce development has been to support training of managers responsible for public health programs.

Effects of the Ebola Response on General Public Health Capacity

The resources committed to the Ebola response and post-Ebola recovery have facilitated improvements in the public health systems in West Africa. Beyond resources, there are several other critical requirements for effective expansion of public health capacity. In a 2008 practice note (*26*), the United Nations Development Programme highlighted the essential nature of the "demand side" of the capacity-building equation: the requirement that host countries value and support the need to invest in the identified capabilities. Throughout the epidemic, there were examples of

uncertainty within national governments and the affected populations about whether the Ebola threat was real (*27*) but also evidence of growing appreciation of the need for and the ability to successfully implement control measures. The governments of the affected countries have expressed broad appreciation for the support provided by international partners (*28*).

Effective capacity building also requires trust of those offering support (*26*). Partnerships should be established and expanded transparently and must be based on understanding and mutual responsibility. Development of this type of partnership usually takes years. However, the Ebola epidemic juxtaposed external responders with those from the host country under conditions that demanded close and effective working relationships that could not function without mutual trust and respect. Maintaining effective relationships built during the crisis has likely accelerated progress during postepidemic recovery. Successful, locally led responses to new clusters of Ebola and to conditions such as measles and acute flaccid paralysis demonstrate the potential for a crisis such as the Ebola epidemic to lead to improvements in local capacity that can have long-lasting benefits, improving health security for the affected nations and the world.

Since the development of the Joint External Evaluation (JEE) tool (*29*), progress toward compliance with 2005 International Health Regulations (*30*) can now be assessed systematically. Liberia and Sierra Leone were among the 25 countries that completed initial JEEs by the end of 2016 (*29*); a JEE was completed in Guinea in April 2017. Progress was evaluated by comparison with previously conducted self-assessments; all 3 countries achieved acceptable levels of compliance in several areas assessed by the JEE and clear progress in others. The JEE is not meant to be used to compare countries; however, the performance measures in the Ebola-affected countries were consistent with those achieved by several countries that had higher development indexes.

There are serious risks to the progress that has been achieved in the region. All 3 Ebola-affected countries continue to receive crucial ongoing support from international donors and technical partners. However, although the US government maintains a high priority for supporting global health security activities (*31*), critical funding to support critical activities, such as surveillance, laboratory capacity, and workforce development, was provided through a one-time emergency appropriation (*32*). It will likely not be possible for the US government and its partners to maintain the staffing in West Africa that was established in the wake of the outbreak. Neither is it certain that resources for capacity building from other donors will be sustained. Although surveillance systems currently continue to provide timely data on critical disease threats, it may not be possible to maintain community-based activities that were established during or after the Ebola outbreak. The gains made in laboratory capacity are especially fragile; laboratories in all 3 countries continue to rely on support from partners for equipment maintenance and replacement, reagents, and ongoing training. Local laboratory capacities and sample transport function remain suboptimal, and there is persistent need for international partners to provide reference laboratory testing, as was the case for the May 2017 outbreak of meningococcal meningitis in Liberia (*33*).

Clearly, it is ideal to build public health capacity before the occurrence of a public health threat. However, there are lessons from the post-Ebola capacity-building efforts to strengthen global health security. Donors and organizations that support an emergency response should be reassured that resources committed to a response—if appropriately coordinated and targeted—can have an impact beyond the response itself. When possible, continuing support into the postepidemic period could both optimize readiness for possible resurgence of the initial threat and contribute to broad and rapid progress toward health security goals.

Conclusions

Global health security relies on the ability of all countries to prevent, rapidly detect, and respond to public health threats at their source. The West Africa Ebola epidemic highlighted the importance of strong public health systems and the need for local public health systems that include ongoing surveillance, a well-trained workforce, laboratory capacity, and emergency response capabilities. In settings with limited public health capacity or in which the magnitude of a health threat overwhelms local capacity and requires international support, response efforts provide a unique opportunity for strengthening public health systems and can serve as a further catalyst to accelerate progress toward global health security goals.

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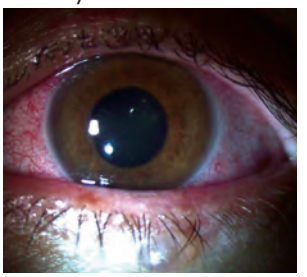
- Ebola and Its Control in Liberia, 2014–2015
- Epidemiology of Epidemic Ebola Virus Disease in Conakry and Surrounding Prefectures, Guinea, 2014–2015
- Hospital Preparations for Viral Hemorrhagic Fever Patients and Experience Gained from the Admission of an Ebola Patient
- Trematode Fluke *Procerovum varium* as Cause of Ocular Inflammation in Children, South India
- Association between Landscape Factors and Spatial Patterns of *Plasmodium knowlesi* Infections in Sabah, Malaysia



- Feasibility of Xpert Ebola Assay in Médecins Sans Frontières Ebola Program, Guinea
- Prognostic Indicators for Ebola Patient Survival
- Invasive Group A *Streptococcus* Infection among Children, Rural Kenya

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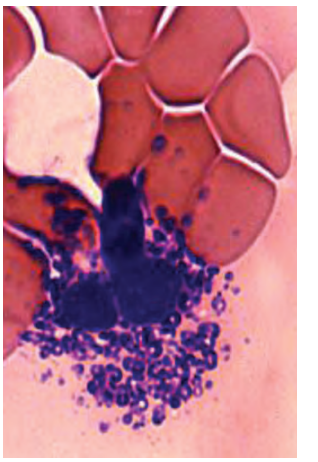

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Joint External Evaluation—Development and Scale-Up of Global Multisectoral Health Capacity Evaluation Process

Elizabeth Bell, Jordan W. Tappero, Kashef Ijaz, Maureen Bartee, Jose Fernandez, Hannah Burris, Karen Sliter, Simo Nikkari, Stella Chunong, Guenael Rodier, Hamid Jafari, and the CDC JEE Team and WHO Geneva JEE Secretariat[1]

The Joint External Evaluation (JEE), a consolidation of the World Health Organization (WHO) International Health Regulations 2005 (IHR 2005) Monitoring and Evaluation Framework and the Global Health Security Agenda country assessment tool, is an objective, voluntary, independent peer-to-peer multisectoral assessment of a country's health security preparedness and response capacity across 19 IHR technical areas. WHO approved the standardized JEE tool in February 2016. The JEE process is wholly transparent; countries request a JEE and are encouraged to make its findings public. Donors (e.g., member states, public and private partners, and other public health institutions) can support countries in addressing identified JEE gaps, and implementing country-led national action plans for health security. Through July 2017, 52 JEEs were completed, and 25 more countries were scheduled across WHO's 6 regions. JEEs facilitate progress toward IHR 2005 implementation, thereby building trust and mutual accountability among countries to detect and respond to public health threats.

In consideration of the growth in international travel and trade, the emergence and reemergence of international disease threats, and other public health risks, in 1995 the 48th World Health Assembly called for a substantial revision of the International Health Regulations (IHR). The 2003 severe acute respiratory syndrome (SARS) outbreak led to the rapid spread of the SARS coronavirus across 4 continents, resulting in 8,098 cases and 774 deaths (*1*). The failure to contain SARS at its source gave new momentum to amending the IHR, resulting in adoption of the revised IHR in May 2005 (IHR 2005) that went into effect in June 2007 with the stated goal that all member states self-report annually on their progress toward complying and that all member states would fully achieve compliance within 5 years (i.e., by mid-year 2012) (*2*,*3*). IHR 2005 is a legally binding instrument among all 196 World Health Organization (WHO) member states. Despite two 2-year extensions (2012 and 2014), by 2016, only one third of member states self-reported having attained IHR 2005 compliance (*4*). In addition, although 195 of the states reported their compliance status at least once during the annual reporting period during 2010–2016, most member states failed to report annually on their progress toward compliance.

As a consequence, in November 2014, the IHR Review Committee on Second Extension for establishing national public health capacities and on IHR 2005 implementation recommended strengthening the self-assessment system, implementing in-depth reviews of events, and developing options "to move from self-evaluations to approaches that combine self-evaluation, peer review and voluntary external evaluation involving a combination of domestic and independent experts" (*5*). Following these recommendations, WHO developed an IHR 2005 monitoring and evaluation framework comprising 4 components: annual reporting, Joint External Evaluation (JEE), after-action review, and simulation exercise (*6*).

Global Health Security Agenda (GHSA) and Independent External Country Assessments

The GHSA was launched in February 2014 at the US Department of Health and Human Services. It comprised representatives of 26 nations, WHO, the Food and Agriculture

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[1]Additional members who contributed data are listed at the end of this article.

Organization of the United Nations (FAO), and the World Organisation for Animal Health (OIE) to prevent, detect, and respond to serious infectious disease threats with the capacity for rapid spread and to galvanize national efforts toward IHR 2005 compliance to prevent such diseases (*7*).

At the first GHSA Ministerial Meeting, hosted by the White House in September 2014, the GHSA Executive Steering Committee called for development of a comprehensive, independently administered monitoring and evaluation framework for GHSA. A GHSA evaluation tool would be used to establish a national baseline for GHSA capacities across the agenda's 11 technical areas (also known as Action Packages) and to monitor progress of GHSA implementation over time. Six GHSA member nations (Republic of Georgia, Peru, Portugal, Uganda, United Kingdom, and Ukraine) volunteered to pilot the tool in their countries and to make the findings publicly available on the GHSA website (https://www.ghsagenda.org/). The US Centers for Disease Control and Prevention (CDC) led the development of the GHSA monitoring and evaluation tool, working closely with Finland (the chair of the 2015 GHSA Executive Steering Committee), and a few subject matter experts (SMEs) from Georgia, Peru, Tanzania, Uganda, and the United Kingdom serving with ≥1 of GHSA's 11 technical area working groups. The GHSA tool development also was informed by several existing monitoring and evaluation frameworks: the WHO IHR Annual Reporting Tool; OIE tool for the Evaluation of Performance of Veterinary Services; CDC's Public Health Emergency Preparedness Performance Measures; Global Immunization Index; International Atomic Energy Agency Safety Assessment; and the WHO Ebola Virus Preparedness Checklist. WHO participated as an observer on several of the first 6 GHSA monitoring and evaluation assessments.

WHO Joint External Evaluation Tool

In March 2015, as Ebola virus disease (EVD) threatened to spread from Guinea, Liberia, and Sierra Leone to other West Africa countries and beyond, WHO regional offices conducted Ebola assessment missions to independently assess the capacities of the countries to prevent, detect, and respond to a potential importation of EVD. The findings of the assessments highlighted gaps in the IHR 2005 core capacities for these countries in detecting, notifying, and responding to EVD that the annual self-reporting monitoring tool did not identify. Although the annual reporting tool serves a different purpose from the disease-specific checklist used during these EVD preparedness assessments, the results were a proxy measure of the capacity of the country to manage a specific outbreak. For example, in the Eastern Mediterranean Regional Office (EMRO), public health contingencies for points of entry were self-reported to be available in 84% of the countries assessed, but the Ebola assessment mission found that only 30% of countries had such contingency plans. Similarly, all countries assessed by data from the annual reporting self-reported the existence of IHR multisectoral committees, but the mission found multisectoral committees in only 25% of these countries. This finding provided evidence that the self-reporting of IHR capacities might not accurately reflect the actual capacities in some countries (*8*,*9*).

During 2015, external and independent GHSA assessments were completed in the 6 countries by rostered SMEs from WHO as observers and GHSA partnering countries; results were made publicly available at the GHSA website. Lessons learned from these 6 GHSA pilot assessments informed revisions and the adoption of a final GHSA monitoring and evaluation tool, with results displayed in a tricolor (i.e., red, no capacity; yellow, limited capacity; green, full capacity) framework organized by technical area.

In January 2016, WHO convened a meeting with CDC and other GHSA partners in Cairo to integrate and standardize the existing IHR monitoring and evaluation tool with the GHSA external assessment tool. In February 2016, the WHO Secretariat and partners approved the consolidated voluntary JEE tool as part of the IHR Monitoring and Evaluation Framework (IHRMEF) across 19 core preparedness and response capacities for infectious disease, chemical, radiologic, and nuclear threats (*10*) (Table).

JEE Process

Countries volunteer for JEEs by submitting a written request to WHO through their WHO representative or

Table. JEE tool technical areas*

Element and technical areas
Prevention
1. National legislation, policy, and financing
2. IHR 2005 coordination, communication, and advocacy
3. Antimicrobial resistance in zoonotic disease
4. Food safety
5. Biosafety and biosecurity
6. Immunization
Detection
8. National laboratory system
9. Real-time surveillance
10. Reporting
11. Workforce development
Response
12. Preparedness
13. Emergency Operations Centers
14. Linking public health and security authorities
15. Medical countermeasures and personnel deployment
16. Risk communication
Other hazards
17. Points of entry
18. Chemical events
19. Radiation emergencies

*The JEE tool incorporates all elements of the IHR 2005 (*2*) and the Global Health Security Agenda (https://www.ghsagenda.org/) assessment tool to evaluate a country's capacity to prevent, detect, and respond to public health risks across 19 technical areas. JEE, Joint External Evaluation; IHR 2005, International Health Regulations 2005.

through the regional IHR coordinator at their WHO regional office. The JEE process is part of a continuum to strengthen countries' ability to prevent, detect, and respond to health emergencies (Figures 1, 2), which includes a self-assessment and external evaluation, simulation exercises, after-action reviews when an actual event occurs, and development of a national action plan and implementation. The requesting countries use the JEE tool to conduct a self-assessment involving all relevant sectors (including food and agriculture, animal health, and security sector). The countries then share the findings with the JEE Secretariat or with the WHO regional office, which assemble an external assessment team of international experts led by WHO and non-WHO experts. The results of the JEE self-assessment are shared with the external assessment team in advance of their week-long independent assessment. The external assessment team comprises ≈8–12 internationally recognized experts from multiple sectors. The mission typically lasts 1 week and comprises an internal briefing; meetings and consultations; field visits; and a final briefing to the primary JEE sector-relevant ministries, partners, civil society, and others. The external assessment team reviews the JEE self-assessment with the host country through 19 facilitated, multisectoral discussions between host country experts and the external assessment team. The JEE process brings together a multisectoral approach (e.g., animal and human health, food and agriculture, and security and law enforcement), enabling engagement and cooperation, often for the first time, of these disparate but health-related country experts and policy makers. Strengths, vulnerabilities, scores, and 3–5 priority actions for each of the 19 technical areas are jointly developed based on the standards in the JEE tool.

At the completion of the assessment, the JEE team presents its findings, along with recommended priority actions and capacity scores, to the leaders of the line ministries and policy makers in the country. A final report is developed, shared with the country, and posted publicly. The country is expected to use the JEE report and other relevant assessments to develop a national action plan for health security or update an existing national action plan with associated costs so that compliance gaps can be addressed through domestic resources in collaboration with donors, partners, multilateral agencies (e.g., GHSA partnering countries, WHO, OIE, and FAO), and the public–private sector through technical assistance, funding support, or both (*11*).

Completed JEEs

By the close of the 70th World Health Assembly meeting (May 22–31, 2017) in Geneva, 41 countries had completed a JEE; 11 additional countries completed a JEE as of July 19, 2017. A total of 27 JEE reports (with the remaining under development) were posted on the WHO website (Figure 3) (https://extranet.who.int/spp/) as well as at the GHSA website (*12*). As of July 19, 2017, a total of 52 countries had completed a JEE, and an additional 25 countries are scheduled to complete a JEE by the end of 2017. In addition, the 6 GHSA countries that had previously completed an external GHSA pilot assessment of their capacities across the 11 GHSA action packages have now developed plans to complement their GHSA evaluation with a full JEE to complete the external assessment across all 19 IHR 2005 core capacities.

Use of JEE Findings

The Strategic Partnership Portal, developed and hosted by WHO, is a member state–mandated information-sharing Web

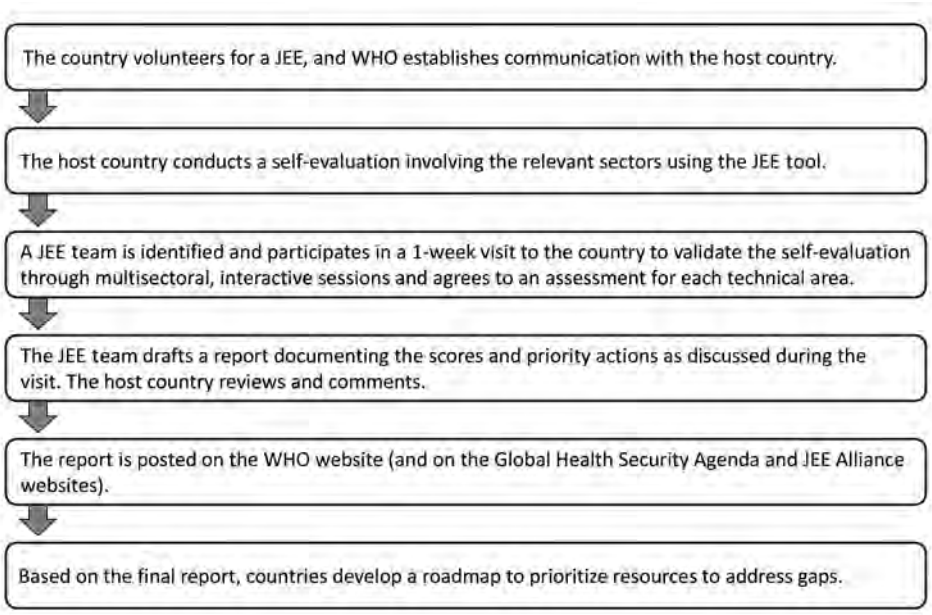

Figure 1. JEE process. Each JEE follows a standardized process that aligns with the principles of transparency, multisectoral engagement, and public reporting of the International Health Regulations 2005 (*2*) and the Global Health Security Agenda (https://www.ghsagenda.org/). JEE, Joint External Evaluation; WHO, World Health Organization.

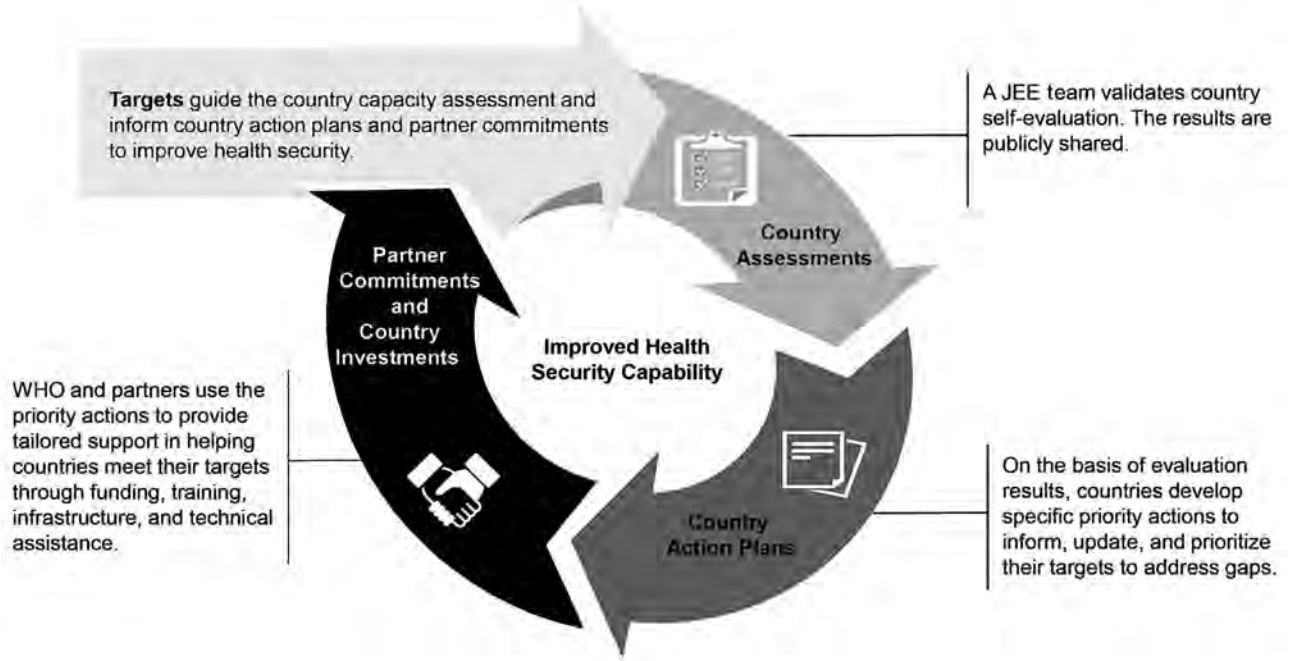

Figure 2. JEE continuum iterative process to identify and fill gaps in addressing requirements for each indicator under 19 technical areas. Each JEE follows a standardized process that aligns with the principles of transparency, multisectoral engagement, and public reporting of the International Health Regulations 2005 (*2*) and the Global Health Security Agenda (https://www.ghsagenda.org/). The process to improve health security capacity requires continuous evaluation of capabilities and (re)alignment of resources. JEE, Joint External Evaluation; WHO, World Health Organization.

portal designed to enhance communication between countries, donors, partners, and WHO to better inform financial and technical support provided to countries. It is intended to monitor and map all contributions (e.g., financial, technical, in-kind, and in-service) from donors and partners to facilitate alignment of in-country efforts to address gaps and priorities and to reveal possibilities for future collaboration. The Strategic Partnership Portal is a 1-stop portal to facilitate sharing of information about current and future activities and investments to enable a more coherent, transparent, coordinated approach and more informed resource allocation decisions (*12*).

Standardization and Quality Assurance of JEEs

In July 2016, WHO convened a JEE working group comprising members from WHO, CDC, the US Department of Agriculture, and the Government of Finland. The group examined lessons learned and best practices from the first 10 JEEs to ensure the standardization of the JEE implementation process and maintain high-quality evaluations and results, while rapidly scaling up JEE missions to meet countries' demands.

Rostering SMEs

The Government of Finland, with the WHO Secretariat, led development of a consolidated global roster of SMEs, working with all 6 WHO regional offices, the Global Outbreak Alert and Response Network Secretariat, and the IHR rosters of experts, as well as the GHS country steering committee, to identify appropriate and highly qualified SMEs to support the JEE missions. The Government of Finland, the Government of Germany, CDC, FAO, and OIE provided substantial technical support through their technical experts, as well as financial support for travel and logistics. JEE mission team leads were selected primarily from Finland, CDC, US Department of Agriculture, OIE, FAO, and WHO and initially comprised technical staff who were engaged in the JEE tool development. Currently, the consolidated JEE list of experts comprises ≈400 technical experts from government agencies, multilateral organizations, and academic institutions worldwide (https://extranet.who.int/spp/list-of-experts) (*12*).

Staffing JEE Country Teams

The JEE working group developed principles for composing the independent experts' country teams to ensure that teams have appropriate professional experience; gender and geographic representation balance; organizational diversity; and a mixture of new and experienced JEE participants for a transparent, objective, and credible outcome. WHO developed standard operating procedures for rostering JEE country teams to ensure standardized methods to guide the formation of the external country teams' composition.

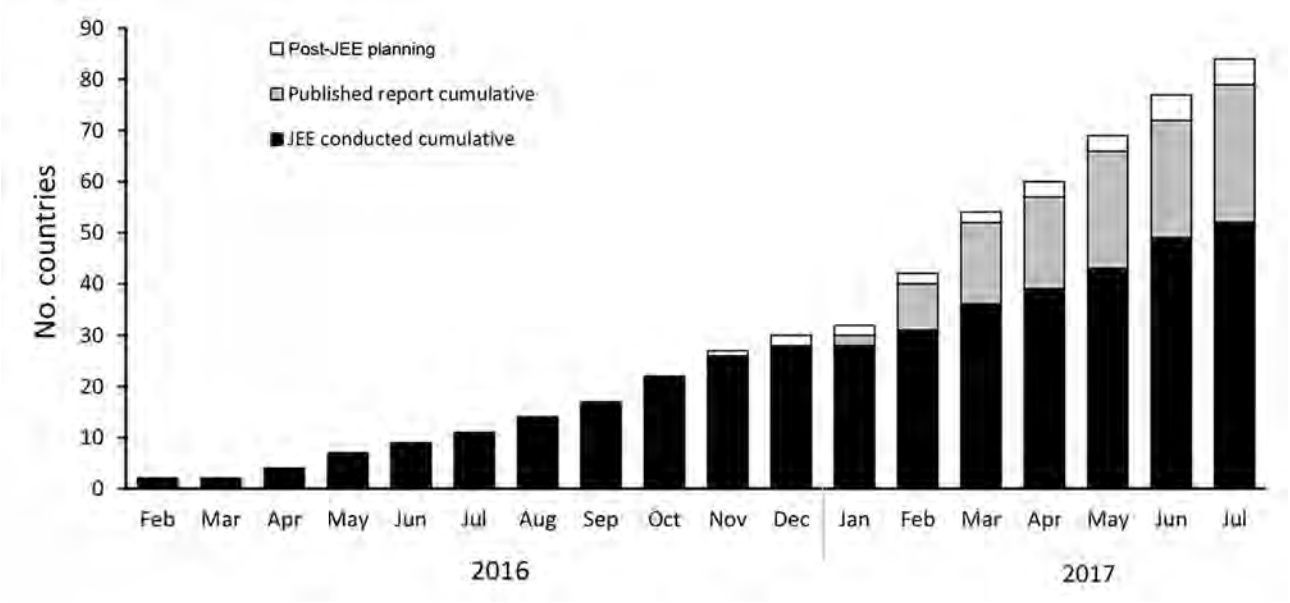

Figure 3. JEE scale-up over time. Each JEE follows a standardized process that aligns with the principles of transparency, multisectoral engagement, and public reporting of the International Health Regulations 2005 (*2*) and the Global Health Security Agenda (https://www.ghsagenda.org/). JEE, Joint External Evaluation.

Team Lead Training

After the initial JEEs were conducted and the working group reviewed lessons learned at the July 2016 meeting, it became evident that a strong team lead was an important contributor to a successful mission with a timely and accurate report with 3–5 specific priority actions for each of the 19 technical areas. The JEE working group developed a participatory team lead training, piloted at the WHO regional office in Brazzaville, Congo, during October 18–20, 2016; a total of 17 team leads from various key partners were trained. WHO reviewed and refined the training design and materials, and the second team lead training occurred in Lyon, France, during January 31–February 1, 2017; an additional 23 team leads were trained. Team leads who have been trained in facilitation, a common approach to applying the JEE tool, and development of final scoring enhances the standardization of results across country missions and comparability over time.

External Evaluation Team Member Orientation

Another component of strengthening and standardizing the JEE missions and results is to ensure the external evaluation team members have a common understanding of the JEE process, mission requirements, and familiarity with the tool itself. With assistance from CDC and working group partners, WHO developed an online orientation to better prepare external evaluation team members (i.e., SMEs), enabling them to review the self-guided materials before participating on a country mission. The JEE team online orientation is available for rostered SMEs on the WHO online learning site (https://extranet.who.int/hslp/training/enrol/index.php?id=116).

Country Self-Assessment Support

A strong and thorough country self-assessment is critical to obtaining high-quality JEE results. The external team reviews and validates the country's self-assessment using the JEE tool and an incomplete, superficial, or less-than-timely country self-assessment can make it difficult for the external evaluation team to accurately assess, or appropriately recognize, a country's health systems' capacities if documentation and confirming evidence is lacking. The WHO EMRO piloted a JEE orientation workshop to support participating countries that provided training in the JEE tool and process, an approach that has proven highly successful (*13*). A key factor in maintaining high-quality evaluations was developing country orientation materials and providing on-site support for the self-assessment process by conducting an orientation workshop in each country. The WHO Secretariat developed guidance and materials based on the EMRO model to provide support and assistance to countries in implementing their self-assessment, an essential element in high-quality, timely self-assessments.

JEE Tool Interpretation Guidance

As the number of JEEs grew and an increasing number of team leads and SMEs used the tool in real-world settings, ensuring that teams interpreted the tool consistently

became important. In addition to the in-person team lead training and online SME orientation, WHO, with input from the JEE working group, developed a separate guidance tool to clarify areas and language that caused confusion or commonly elicited questions. Feedback on the tool and its use was solicited from JEE team members, technical experts, and the regional offices engaged in implementing the JEE. Most feedback received was incorporated into the Tool Interpretation Guide, scoring recommendations, guiding discussion questions, and expanding the glossary to ensure consistency in tool use and to maintain the tool's integrity and the validity of already conducted JEEs and the ability to measure future progress in these countries. However, certain elements of the tool might need to be modified to resolve outstanding concerns discussed during the April 19–21, 2017, WHO consultation on the JEE tool. For example, 2 indicators on finance (1 on routine financing and 1 on emergency financing) will be added to the JEE's National Legislation, Policy, and Finance technical area. In addition, referencing and linking with other technical areas will be improved, including scoring issues related with human and animal health technical areas.

Discussion

The completion of 52 JEEs and the planning of 25 additional JEEs provide evidence for growing support and interest by WHO member states to volunteer for the JEEs. However, there are also technical limitations related to the JEE tool and the need for advocacy and communication of the JEE process to countries. WHO has obtained systematic feedback from participants on JEE teams related to the tool's technical limitations and challenges associated with interpretation and scoring related to overlapping technical areas. WHO convened a consultation during April 19–21, 2017, involving relevant multisectoral partners and agency representatives, including member state partners who have undergone JEEs, to obtain recommendations to address these limitations and challenges.

WHO headquarters and regional offices and organizations, such as CDC, have developed communication materials that can be shared with countries potentially interested in volunteering for JEEs to provide them with information about advantages associated with JEEs and transparency of the reports. This transparent and collaborative approach has helped with strengthening existing collaborations and in establishing possible new collaborations and technical partnerships with potential public and private partners and donors willing to provide technical or financial assistance to address the gaps identified through JEEs. This well-coordinated implementation style also has been instrumental in establishing a "twinning process" between 2 countries, whereby 1 country establishes a technical partnership with another to provide assistance.

Sustaining the momentum for conducting and periodically repeating JEEs is critical to the success of the IHRMEF. To ensure coordination, management, and sustainability for the JEE process, WHO has established the JEE Secretariat at WHO headquarters in Geneva. Some member states and private partners and donors have provided the funding resources. Also, in support of the work of the WHO JEE Secretariat and ensuring the process continues, GHSA has created entities to support and accelerate the IHR 2005 implementation. These entities include the Alliance for Country Assessments for Global Health Security and IHR Implementation and an Alliance Advisory Group. The Alliance for Country Assessments for Global Health Security and IHR Implementation (https://www.jee-alliance.org/) is an open partnership platform for facilitating multisectoral collaboration on health security capacity building and IHR implementation. The Alliance Advisory Group is drawn from Alliance members: 12 countries (2 from each WHO region); 4 nongovernment organizations and foundations; and 4 multilateral organizations. The Alliance Advisory Group members for the first 2-year term are the countries of Australia, Bangladesh, Cambodia, Finland, Georgia, Indonesia, Pakistan, Peru, Saudi Arabia, Senegal, Uganda, and the United States; the Bill and Melinda Gates Foundation; the Elisabeth R. Griffin Foundation (Chair of the GHSA NGO Consortium); the No More Epidemics Campaign; and the Training Programs in Epidemiology and Public Health Interventions Network. WHO, OIE, FAO, and the World Bank are permanent members.

Global health security relies on all countries working together in the spirit of transparency and mutual accountability to develop and maintain the core capacities required under the IHR 2005 implementation. Achieving implementation entails all member states having the capacity to prevent and to rapidly detect, verify, notify, and respond effectively to all public health threats while limiting the international spread of disease and its effect on travel and trade. Measuring progress toward implementation is therefore critical for efforts aimed at enhancing global health security. Completing a JEE demonstrates a country's commitment to developing capacities required under the IHR 2005 and supports countries in establishing an objective baseline assessment of their public health capacities; identifies strengths and limitations within their health systems; and enables prioritizing opportunities for capacity development in disease prevention, detection, and response across all sectors, including all 19 technical areas and all hazards. The comprehensive, all-hazard assessment of capacities can inform a country's roadmap/action plan, guide allocation of national resources, and engage current and prospective donors and partners to effectively target resources and technical assistance. Although JEEs provide an objective and transparent assessment, the effect of the JEEs

depends on rapid development of a country-owned and country-led post-JEE national action plan for health security and its implementation to address the gaps by the country itself, as well as through support from donors and public and private partners. Member states are encouraged to conduct annual self-assessments using the JEE tool and are expected to conduct the JEE once every 4–5 years. Countries are encouraged to use the other voluntary components of IHRMEF (i.e., after-action review and simulation exercises) to provide qualitative assessment of IHR functionality and performance to validate plans, develop and practice staff competencies, and ascertain whether gaps identified during an actual public health event or tabletop exercise are addressed. Collectively, the IHRMEF can help measure progress and realign country plans as needed and report progress on implementation as part of annual reporting (*14*,*15*). Countries and partners need to commit to working together to implement national plans of action expediently and effectively to ensure impactful progress in addressing gaps and deficiencies. The JEE is a valuable mechanism to facilitate and measure progress toward IHR 2005 implementation and thereby enhance global health security.

Additional members who contributed data: CDC/US Department of Health and Human Services JEE Team: Avery Avrakotos, Benjamin Dahl, Emily Dodd, Jacob Eckles, Richard Garfield, Michael Mahar, Hermence Matsotsa, Leah Moriarty, Christopher Murrill, Michelle Noonan-Smith, Alexandra Smith, Daniel Stowell; WHO Geneva JEE Secretariat: Nirmal Kandel, Nathalie Roberts, Adrienne M. Rashford, Raj Sreedharan.

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Synergies between Communicable and Noncommunicable Disease Programs to Enhance Global Health Security

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Noncommunicable diseases are the leading cause of death and disability worldwide. Initiatives that advance the prevention and control of noncommunicable diseases support the goals of global health security in several ways. First, in addressing health needs that typically require long-term care, these programs can strengthen health delivery and health monitoring systems, which can serve as necessary platforms for emergency preparedness in low-resource environments. Second, by improving population health, the programs might help to reduce susceptibility to infectious outbreaks. Finally, in aiming to reduce the economic burden associated with premature illness and death from noncommunicable diseases, these initiatives contribute to the objectives of international development, thereby helping to improve overall country capacity for emergency response.

The first cohort of infants with Zika virus–related birth defects was reported in 2015 in Brazil, where >4,000 cases of infant microcephaly were documented by the end of that year (*1*). Brazil's Zika outbreak was a recent occurrence, but the country's baseline preparedness for public health disruptions has had a relatively long history. The foundation for the emergency response to the 2015 epidemic can be traced back to 1988, when Brazil introduced a health services system for the provision of primary and prenatal care (*2*). As the spread of Zika intensified in 2015, this system provided the infrastructure for recognizing and handling the epidemic relatively quickly. No Zika transmission occurred during the 2016 Summer Olympics in Brazil, despite increased international travel to and from the country at that time. The relatively quick detection of Zika enabled by Brazil's primary health network and health surveillance system may have increased the ability to control the epidemic at the source, ultimately enhancing global health security.

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Brazil's experience with Zika has illustrated the interplay between 2 key factors that determine the strength of global health security: 1) country capacity for rapid response to emerging contagions (emergency preparedness), and 2) the strength of ongoing activities to support the underlying population health (health infrastructure). In this example, the interconnectedness between these 2 factors was highlighted by the contribution of the existing primary care infrastructure to the success of the Zika emergency response. Brazil's public health system, ordinarily set up for routine care rather than emergent outbreak containment, enabled the documentation of new cases of the not-yet-identified infection, and an existing surveillance platform, the Notifiable Diseases Information System, facilitated identification of the epidemic by tracking confirmed Zika cases and their birth defect consequences (*1*). These preexisting structures, which typically address common health needs such as maternal and noncommunicable disease (NCD) care, might have been instrumental in ensuring a timely response to Zika, potentially helping to reduce the risk of cross-border spread of the virus. By contrast, such structures were not present during the 2014 outbreak of Ebola in West Africa, where the virus affected multiple countries and threatened to spread to other continents before being contained at high financial and human cost.

Role of NCD Prevention and Control in Global Health Security

NCDs, represented primarily by cardiovascular disease, cancer, chronic respiratory disease, and diabetes, have overtaken communicable diseases as the leading sources of premature death and disability in low- and middle-income countries (LMICs) (*3*). During 1990–2010, low-income countries experienced a 42% increase in NCD-related death and disability while sustaining a 14% decline in communicable disease burden (*4*).

As NCDs become the leading disease category in developing countries, the provision of NCD-related services

increasingly forms the backbone of health delivery systems, helping to build up infrastructures that would be essential for containing infectious disease emergencies. This fact means that it is no longer fitting to consider global health security from the perspective of infectious disease alone. NCD initiatives—programs that support the prevention and control of NCDs—are essential for global health security in several ways. First, in addressing health needs that typically require long-term chronic care, these programs support the development of stable health delivery and health monitoring systems, which can serve as necessary platforms for emergency preparedness in low-resource environments. Second, by improving the baseline level of population health, the programs might help to reduce susceptibility to infectious outbreaks. Finally, in aiming to reduce economic pressures associated with premature illness and death from NCDs in LMICs, these initiatives contribute to the goals of international development, thereby helping to improve overall country capacity for emergency response.

NCD Initiatives as a Means for Improving Health System Capacity

As demonstrated by Brazil's experience with Zika, a health delivery system that ordinarily addresses NCDs can be a first line of defense when a communicable disease emergency occurs. Integration between initiatives to reduce NCDs and communicable diseases has been recognized as essential for efficient distribution and use of health resources, both human and financial (*5*), and can provide a sustainable foundation for emergency preparedness (*6*). Specifically, in the context of developing countries, a health infrastructure built around routine and/or long-term NCD services can provide crucial support for emergency response efforts in terms of population outreach, routes for emergency resource allocation, or procurement and distribution of medications and other medical supplies. Such an infrastructure ensures ongoing presence of public health workers in regions susceptible to outbreaks, thus helping to speed up access to vulnerable populations in the event of a health security emergency. Information platforms for NCD monitoring and surveillance can also enable detection and response to sequelae of infectious diseases, including developmental, cardiac, neurologic, or pulmonary complications. For example, most patients in Central and South America with chronic Chagas disease, caused by the parasite *Trypanosoma cruzi*, show development of a dilated cardiomyopathy that can be tracked along with other noninfectious causes to determine spikes in transmission.

NCD Initiatives as a Means for Reducing Susceptibility to Spread of Infections

The presence of clinical links between NCDs and communicable diseases implies that the optimal path to communicable disease control may require consideration of NCDs. The proliferation of NCD risk factors associated with current demographic trends in longevity and urbanization can raise a population's baseline susceptibility to infection-related health security risks. The detrimental effect of uncontrolled NCDs and NCD risk factors on health security concerns can be illustrated by the examples of diabetes and tobacco use. Diabetes has been shown to increase the severity of endemic diseases such as tuberculosis, melioidosis, dengue, and malaria (*7–9*). Diabetes also interferes with tuberculosis treatment, threatening the progress of global tuberculosis control in countries with high rates of both illnesses, such as China and India (*10*,*11*).

Tobacco smoking, besides playing a primary role in all leading NCDs, is a notable risk factor for the acquisition and accelerated progression of variety of infectious diseases, including influenza, tuberculosis, pneumonia, sexually transmitted diseases, and hospital-acquired infections (*12–15*). Tobacco use is also among the factors facilitating the convergence of infectious and chronic illnesses in LMICs and compounds the role of other factors, such as urbanization and displacement, in worsening health outcomes. Urbanization in China and India, in particular, has resulted in large groups of rural migrants who are increasingly affected by lifestyle-associated chronic conditions such as diabetes and hypertension while also experiencing added exposure to communicable diseases associated with overcrowding, notably tuberculosis (*13*,*16*). In these examples, focusing on infectious conditions alone without also addressing NCD factors may undermine the principal intent of global efforts to strengthen population health security. Benefits to integration of services across communicable diseases and NCDs have already been shown in the context of treatment for HIV alongside several other chronic conditions (*17*,*18*).

NCD Initiatives as a Means for Strengthening Economic and Social Outcomes

The economic burden of unaddressed NCDs in developing countries can impair global health security efforts by adding strain on developing economies. More than 80% of NCD-related deaths now occur in LMICs, and NCDs are no longer considered diseases of the developed world (*19*). Because NCD-associated illness in developing countries is more likely to occur prematurely (in persons <70 years of age), illness can be a substantial impediment to human and economic development (*20*,*21*). Reduction in premature NCD deaths in LMICs has been identified as a main goal in the United Nations Agenda for Sustainable Development (*22*). The World Economic Forum estimates that future NCD growth trends could cost the global economy US $47 trillion in cumulative losses through 2030 (*23*). Investment in efforts to reduce NCD-related productivity losses can indirectly reinforce global health security efforts by relieving

socioeconomic pressures in some populations and reducing incentives for cross-border migration.

Despite the surge of premature deaths from NCDs in LMICs, resources committed for NCDs in LMICs remain relatively limited (*24*,*25*). Only 1.5% of the development assistance for health distributed to developing countries in 2013 was for NCDs, even as NCDs account for more than half of the all-cause death and disability burden in these countries (*26*,*27*). Fortunately, several cost-effective solutions can make a difference for NCD control in low-resource settings. One option is the standardization of hypertension treatment, recently outlined by the Global Hearts Initiative (*28*), which can simplify and thus enable the broad adoption of treatment protocols for preventing and reducing cardiovascular disease (CVD). CVD, the largest contributor to NCD death and disability in LMICs, may also be addressed in a low-cost manner by exploring the use of generic versions of fixed-dose combination medications, also known as polypills (*4*). Existing laboratory investments can be leveraged relatively easily across both NCD and infectious disease testing, and disease surveillance programs can incorporate NCD monitoring elements. These strategies for NCD control can prove valuable in supporting the goals of health emergency preparedness efforts by strengthening population outreach, patterns for medical resource allocation, and baseline population health.

Centers for Disease Control and Prevention Initiatives for NCD Prevention and Control

The Global NCDs, Injury, and Environmental Health program with the US Centers for Disease Control and Prevention (CDC) advances a 3-pronged approach to prevention and control by strengthening surveillance, expanding the evidence base, and enhancing workforce capacity (Table 1). The program objectives support the UN Sustainable Development Goals (*29*) and the Global NCD Monitoring Framework (*30*) through supporting training and technical exchange with countries for health promotion activities; using public health data to research innovative, culturally appropriate solutions and improve policy decisions; and supporting the implementation of cost-effective interventions to reduce risk factors such as tobacco use, harmful use of alcohol, unhealthy diets, and physical inactivity. The following programs are some examples of activities that share the long-term goal of contributing to NCD burden reduction in LMICs.

Standardized Hypertension Management

The Standardized Hypertension Treatment and Prevention project promotes the use of the following evidence-based tools and practices: 1) standardized treatment protocols, 2) team-based care, 3) access to a core set of medications, 4) registries for patient monitoring, 5) patient empowerment, 6) community engagement, 7) policy interventions, and 8)

Table 1. US Centers for Disease Control and Prevention approaches to NCD, injury, and environmental health control and prevention*

Strategy/activity domain	Goal	Activities	Programs
Strengthening surveillance	Strengthen country and partner capacity for surveillance and monitoring and evaluation systems	• Support surveillance systems through surveys • Use technology to improve data collection, analysis, and reporting • Develop data analysis, dissemination, and visualization tools to track progress toward global NCD targets and evaluate policy impact • Strengthen civil registration, vital statistics, and cause of death and disease registries to inform public health and medical decisions	• Cancer registries • Bloomberg Data for Health Initiative • Global School Health Surveillance • Road traffic injury • Tobacco control • Violence against children
Expanding the evidence base	Scale up interventions to improve health outcomes	• Generate scientific evidence by developing, implementing, and scaling up interventions to accelerate impact for priority risk factors or disease outcomes	• Cervical cancer • Diabetes • Economics of NCD risk factors • Environmental health • Global Hearts Initiative • Maternal mortality • Malnutrition • Shandong Ministry of Health Action on Salt Reduction and Hypertension
Enhancing workforce capacity	Strengthen national public health capacity, infrastructure, and workforce	• Develop training modules • Provide quality training, technical exchange, and mentorship • Utilize web-based training tools • Support mini-grants for relevant projects • Encourage networking	• Field Epidemiology Training Program • NCD short course for program managers

*NCD, noncommunicable disease.

sodium reduction counseling. This project is being piloted in 2 countries. In Barbados, the focus is to improve patient care in 2 publicly funded clinics; in Malawi, the project is designed to enhance 2 HIV clinics funded by the US President's Emergency Plan for AIDS Relief.

Global Hearts Initiative

To support governments in strengthening CVD prevention and control, the World Health Organization (WHO), CDC, and other partners launched the Global Hearts Initiative to promote a set of evidence-based interventions that, when used together, can have a major impact on improving global heart health. These interventions include prevention approaches for tobacco control and standardized protocols for CVD management at the primary healthcare level (*31*).

Prevention and Control of Tobacco Use

The CDC Global Tobacco Control program works with in-country and global partners to monitor the global tobacco epidemic through surveillance systems aimed to assess tobacco use among adults and adolescents to promote tobacco control efforts. CDC provides technical assistance and training packages on tools for standardized surveillance of tobacco use across multiple countries.

Field Epidemiology Training Programs

Field Epidemiology Training Programs (FETPs) are country-owned programs that strengthen national capacity in epidemiology, surveillance, and outbreak response, including those related to NCDs. Through dedicated curriculum and mentorship, FETP has helped develop expertise within ministries of health in chronic disease surveillance and response, including cardiovascular disease, toxicology, nutrition, tobacco, cancer, injury, and maternal and child health/birth defects. Initial surveillance efforts to first detect and then confirm a causal link between Zika infection and Guillain-Barré syndrome and microcephaly through cohort and case-control studies were led by FETP residents and graduates in Brazil and Colombia. In other locations, FETP residents have led investigations into risk factors for virus-related cancers (e.g., human papillomavirus, hepatitis B virus); current practices related to cervical cancer screening; and the interplay between chronic and infectious disease, such as smoking and tuberculosis. FETP work in nutrition has assisted in emergency famine response, preventing infectious disease outbreaks in displaced persons camps.

Bloomberg Data for Health Initiative

The goals of this program are to assess the feasibility, quality, and validity of nationally representative mobile phone surveys; implement NCD mobile phone surveys in 10 countries and support face-to-face WHO STEPwise Approach to Surveillance Surveys in 6 overlapping countries; and compare findings from the 2 data collection methods. These surveys will be implemented by participating countries and ministries of health in collaboration with relevant ministries of information and technology, national statistical offices, and telecommunication operators. A course to improve the use of locally available data, entitled Data to Policy, is providing skills in economic evaluation, burden measurement, and impact modeling to develop policy briefs covering both infectious (e.g., avian influenza, antimicrobial resistance, malaria control) and noninfectious (e.g., colon cancer, tobacco, nutrition) topics.

Cancer Registries

CDC is working with the International Agency for Research on Cancer of the WHO and other partners to establish 6 regional support centers (hubs) that provide training and assistance to cancer registries around the world. CDC supports these centers in Asia and sub-Saharan Africa and is working with partners to develop a regional hub in the Caribbean. Because little is known about the costs of setting up cancer registries in LMICs, CDC has piloted a cost assessment tool in many of its partner countries. The tool estimates the resources required to operate and improve cancer registries, including funding for the registries, how much it costs to register a cancer case, and factors that affect the efficiency of cancer registries (*32*). The goal is to create accessible information that would help public health leaders to make appropriate decisions on adding registries to their national cancer plans and improve existing cancer registries all over the world (*33*).

Sodium Reduction and Hypertension

In an innovative partnership, the CDC is working with China's National Health and Family Planning Commission and the Shandong provincial government on the Shandong Ministry of Health Action on Salt Reduction and Hypertension (SMASH) project (*34*). The aim of SMASH was to reduce daily salt intake from condiments from 12.5 g/day in 2011 to 10 g/day in 2015 and to improve hypertension control within the province. Approaches to reducing sodium intake include changes to food labeling, distribution of scaled spoons for home cooking and preparation, and reforming food industry practices, all of which are being broadly adopted. SMASH also works with restaurants to develop sodium standards for Shandong cuisine, conducts chef training to develop lower-salt menus, tracks salt usage, conducts chef contests for new recipes, and develops communication materials and activities for consumers.

Micronutrient Malnutrition

Since 2000, the International Micronutrient Malnutrition Prevention and Control Program works with global partners to eliminate vitamin and mineral deficiencies among

vulnerable populations throughout the world. This program supports monitoring for micronutrient deficiencies and supports efforts by governments, food industries, and civic organizations to implement interventions, such as food fortification and supplementation. CDC recommends the use of micronutrient powders—sachets of vitamins and minerals that can be mixed into food (home fortification)—to reduce micronutrient deficiencies among children ≥6 months of age.

Partnerships of NCD Programs and Global Health Security Agenda Activities

The Global Health Security Agenda (GHSA) (https://www.ghsagenda.org/) is an international effort to prioritize action for global health security. It aims to support the goals of the 2005 International Health Regulations, which strives to increase country capacity for addressing health threats including but not limited to those of infectious origin (35). Integration of NCD-related activities into broader disease-control engagements may allow for economies of scale with respect to overall health outcomes. CDC's Global NCDs, Injury and Environmental Health programs reach ≈40 countries, with potential to address both infectious and noninfectious diseases by linking activities in surveillance, evidence generation, capacity strengthening and partnerships with current GHSA Action Packages (36). These programs are organized under 3 broad categories for disease control: prevent, detect, and respond (Table 2).

The relevance of current NCD-related activities to GHSA goals can be illustrated by the potential contributions of ongoing programs such as the Global Hearts Initiative, FETP, and Data for Health. Global Hearts can serve GHSA objectives of threat detection by establishing a mechanism for real-time surveillance and medical workforce development and can support avenues for emergency response by strengthening medication supply chains. Alternative survey methods, such as the mobile phone–based Data for Health initiative, can provide insight into the possibility of using innovative approaches to disease surveillance and detection, especially in low-resource environments where traditional surveillance methods might be too slow or expensive. FETPs can enhance local detection capabilities by training district, regional, and national medical and surveillance personnel in recognizing and preventing emerging threats to health security alongside noncommunicable conditions.

Conclusions

Incorporating NCD control strategies alongside and within ongoing GHSA efforts for infectious disease control in LMICs can offer a long-term path for a resilient health infrastructure that can respond well both in normal times and during health emergencies. Specific GHSA goals in developing countries can be strengthened by investment in NCD programs like Global Hearts, which can bolster pathways for population outreach, and FETP, which can produce cadres of public health workers.

The growing epidemiologic and infrastructural overlap between NCDs and infectious diseases has motivated increased consideration of NCDs as a component of global health security. Most recently, global resources for NCD prevention and care have increased (*24*) alongside growing recognition that investment in the prevention and control of chronic conditions can improve the capacity to respond to both acute public health crises and long-term health events. To the advantage of NCD control efforts, common NCD

Table 2. Opportunities to incorporate NCD activities within GHSA action packages*

GHSA category	GHSA Action Package	NCD-related activities in support of GHSA goals
Prevent	Immunization	• Human papillomavirus vaccination • Hepatitis B virus vaccination
Detect	National Laboratory System	• Assist laboratories in integrating essential NCD testing into current systems • Train laboratory staff on essential NCD testing
	Real-Time Surveillance	• Integrate NCD indicators into current surveillance systems • Support adoption of EMR • Train staff on EMR use and NCD indicator data entry • Implement monitoring aspects from Hearts Technical Package • Implement Data for Health • Support cancer registries • Support tobacco use surveillance • Enhance birth defects surveillance for Zika virus
	Workforce Development	• Expand NCD training via country-level Field Epidemiology Training Programs • Cross-train local public health staff on NCD basics to link to current efforts, depending on local needs and capacity • Implement workforce training aspects from Hearts Technical Package
Respond	Medical Countermeasures and Personnel Deployment	• Incorporate NCD treatment into public health emergency responses, as appropriate (e.g., natural disasters, refugee crisis, migration)

*EMR, electronic medical records; GHSA, Global Health Security Agenda; NCD, noncommunicable disease.

challenges in developing countries can be met at relatively modest cost in several ways, from population-level approaches for the prevention of known NCD risk factors like tobacco use to patient-level approaches for low-cost treatment of highly prevalent but treatable conditions like hypertension (*4*,*37*). The synergies between communicable and noncommunicable disease control offer broad implications for developing countries, where building up clinical, laboratory, and regulatory capacity for handling both NCD and emerging disease threats in LMICs can go a long way in improving health security locally and, by extension, worldwide.

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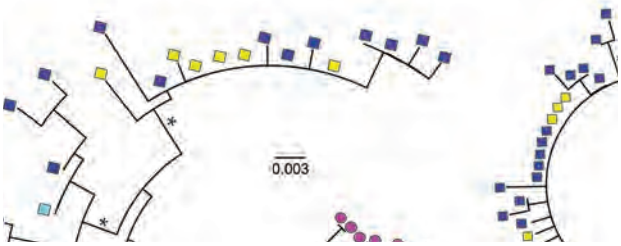
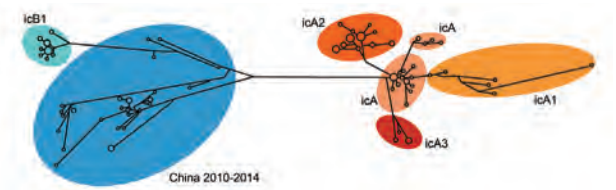
April 2017: **Emerging Viruses**

- Biologic Evidence Required for Zika Disease Enhancements by Dengue Antibodies Neurologic Complications of Influenza B Virus Infection in Adults, Romania
- Implementation and Initial Analysis of a Laboratory-Based Weekly Biosurveillance System, Provence-Alpes-Côte d'Azur, France
- Transmission of Hepatitis A Virus through Combined Liver–Small Intestine–Pancreas Transplantation
- Influence of Referral Pathway on Ebola Virus Disease Case-Fatality Rate and Effect of Survival Selection Bias
- *Plasmodium malariae* Prevalence and *csp* Gene Diversity, Kenya, 2014 and 2015
- Presence and Persistence of Zika Virus RNA in Semen, United Kingdom, 2016
- Three Divergent Subpopulations of the Malaria Parasite *Plasmodium knowlesi*
- Variation in *Aedes aegypti* Mosquito Competence for Zika Virus Transmission
- Outbreaks among Wild Birds and Domestic Poultry Caused by Reassorted Influenza A(H5N8) Clade 2.3.4.4 Viruses, Germany, 2016





- Highly Pathogenic Avian Influenza A(H5N8) Virus in Wild Migratory Birds, Qinghai Lake, China
- Design Strategies for Efficient Arbovirus Surveillance
- Typhus Group Rickettsiosis, Texas, 2003–2013
- Detection and Molecular Characterization of Zoonotic Poxviruses Circulating in the Amazon Region of Colombia, 2014
- Reassortment of Influenza A Viruses in Wild Birds in Alaska before H5 Clade 2.3.4.4 Outbreaks Incidence and Characteristics of Scarlet Fever, South Korea, 2008–2015
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- Molecular Identification of *Spirometra erinaceieuropaei* in Cases of Human Sparganosis, Hong Kong
- Zika Virus Seroprevalence, French Polynesia, 2014–2015
- Persistent Arthralgia Associated with Chikungunya Virus Outbreak, US Virgin Islands, December 2014–February 2016
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EMERGING INFECTIOUS DISEASES https://wwwnc.cdc.gov/eid/articles/issue/23/4/table-of-contents

Surveillance for Antimicrobial Drug–Resistant *Neisseria gonorrhoeae* through the Enhanced Gonococcal Antimicrobial Surveillance Program

Emily J. Weston, Teodora Wi, John Papp

Monitoring trends in antimicrobial drug–resistant *Neisseria gonorrhoeae* is a critical public health and global health security activity because the number of antimicrobial drugs available to treat gonorrhea effectively is rapidly diminishing. Current global surveillance methods for antimicrobial drug–resistant *N. gonorrhoeae* have many limitations, especially in countries with the greatest burden of disease. The Enhanced Gonococcal Antimicrobial Surveillance Program is a collaboration between the World Health Organization and the Centers for Disease Control and Prevention. The program aims to monitor trends in antimicrobial drug susceptibilities in *N. gonorrhoeae* by using standardized sampling and laboratory protocols; to improve the quality, comparability, and timeliness of gonococcal antimicrobial drug resistance data across multiple countries; and to assess resistance patterns in key populations at highest risk for antimicrobial drug–resistant gonorrhea so country-specific treatment guidelines can be informed.

Bacterial infections can cause disease ranging in severity from mild to life-threatening, and resistance to antibiotics may hamper treatment. *Neisseria gonorrhoeae* is a common, worldwide sexually transmitted infection (STI) that can lead to severe reproductive sequelae, such as pelvic inflammatory disease, infertility, ectopic pregnancy, and epididymitis. If left untreated or improperly treated, gonococcal infections can become disseminated and cause sepsis (*1*,*2*). In addition, infection may also facilitate HIV transmission (*3*).

Emerging Antimicrobial Drug–Resistant *N. gonorrhoeae*

N. gonorrhoeae has adapted to treatment through all mechanisms of antimicrobial resistance (AMR). Antimicrobial drug–resistant *N. gonorrhoeae* has outpaced novel treatment options; the third-generation cephalosporin ceftriaxone is among the most recent drugs currently being prescribed for treatment against gonorrhea. Gonococcal resistance to penicillin and tetracycline was first reported in Asia during the 1970s; resistance became widespread in multiple regions of the world during the early 1980s. High levels of resistance to quinolones (e.g., ciprofloxacin) developed by the mid-2000s; the US Centers for Disease Control and Prevention (CDC) removed these drugs from recommended treatment regimens for gonorrhea in 2007 (*4*). Public health agencies in most countries and the World Health Organization (WHO) recommend treating gonorrhea with ceftriaxone in combination with azithromycin in an attempt to slow simultaneous emergence of AMR to 2 unrelated compounds (*5*–*9*). However, recent reports suggest that this combination is becoming less effective in treating gonorrhea (*10*,*11*).

An estimated 357 million new STIs were reported among adults 15–49 years of age in 2012; 78 million of those new cases were attributed to gonorrhea (*12*). For 2012, the global incidence rate of gonorrhea among men was 24 cases/1,000 (regional range 13–41 cases/1,000); among women, the incidence rate was 19 cases/1,000 (WHO regional range 8–37 cases/1,000). Among men, estimates for the incidence rate were highest in the Western Pacific Region and second highest in the Southeast Asia Region. Among women, estimates of incidence rate were also found to be the highest in the Western Pacific Region but were documented next highest in the African Region.

Adding to global burden estimates, many countries, especially those that are resource poor, have been unable to readily implement or improve laboratory diagnostics for gonorrhea; therefore, syndromic surveillance is often used. Among male patients, WHO recommends monitoring trends in urethral discharge as an indicator of an incident gonococcal infection (*13*). However, syndromic surveillance is limited in the ability to assess the

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occurrence of gonorrhea because the data are difficult to interpret; other organisms, such as *Chlamydia trachomatis*, may cause urethritis; and some symptomatic men may not seek care. Further, inconsistencies in reporting among countries may lead to difficulties in comparing estimates (*13,14*). As with all communicable diseases, critical infrastructure for accurate epidemiologic practices and laboratory testing for *N. gonorrhoeae* should be in place for high-quality surveillance, and the ultimate goal should be to reduce the incidence of gonococcal infections. Incorporating surveillance with both epidemiologic practices and laboratory testing to replace syndromic surveillance further prepares against the threat of antimicrobial drug–resistant gonorrhea and is imperative in enhancing global health security.

Global Surveillance Activities for Antimicrobial Drug–Resistant *N. gonorrhoeae*

CDC's Gonococcal Isolate Surveillance Program (GISP), a surveillance system established in 1986 to monitor trends of antimicrobial susceptibilities of *N. gonorrhoeae* in the United States, has been instrumental in documenting AMR patterns of gonorrhea and the spread of resistance among different drug classes. Laboratory and epidemiologic data collected through GISP are analyzed to estimate the proportion of isolates with resistance or decreased susceptibility in key populations; findings are disseminated annually (*15*). In 2014, for example, data from GISP demonstrated increases in the prevalence of reduced susceptibility to azithromycin and to cefixime. Data from GISP were used to modify and inform US sexually transmitted disease treatment guidelines (*6*).

The Gonococcal Resistance to Antimicrobial Surveillance Programme (GRASP) in the United Kingdom and the Australian Gonococcal Surveillance Program (AGSP) have also established country-specific surveillance systems to monitor trends in susceptibility to antimicrobial drugs for treatment of gonorrhea. Member states of the European Union participate in the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP). Though the methodologies of each surveillance system differ, all 3 surveillance programs analyze and disseminate susceptibility trend data similar to GISP (*16–18*). Data from each of these countries have also been used to inform local treatment guidelines (*7–9*).

On a more global scale, the WHO Gonococcal Antimicrobial Surveillance Program (GASP), which is not related to the Euro-GASP surveillance, has been collecting gonococcal antimicrobial susceptibility data since 1992. GASP is a worldwide laboratory network that is coordinated by focal points and regional coordinating centers. Each designated regional focal point, in partnership with its WHO regional office, collates susceptibility data submitted by participating countries. These susceptibility data have provided evidence to inform national, regional, and global treatment guidelines.

There are many challenges in the current GASP framework. The cumulative number of countries reporting AMR data for any antibiotic increased from 56 in 2009 to 77 in 2014. However, the number of countries reporting susceptibility data for ≥1 antibiotic each year shows a declining trend, from 56 countries in 2009 to 52 countries in 2014. In 2014, the WHO European Region (n = 24 countries) accounted for most reports in GASP; only 2 countries in Africa and 1 country in the Eastern Mediterranean Region provided data to GASP. The lack of reports from some regions reflects the financial and laboratory constraints of countries in resource-poor settings to implement GASP. In addition, a recent WHO survey from 108 countries showed that only 46% had conducted AMR testing for gonorrhea during the past 5 years (*13*). The AMR data for gonorrhea from GASP may be reported from differing countries from year to year, making interpretation of trends difficult (*13*).

Globally, some countries have suboptimal surveillance systems and laboratory diagnostics because of limited epidemiologic and laboratory capacity and lack of political will and funding (*4*). Very often, countries rely on syndromic management of STIs, which limits their collection of isolates for susceptibility monitoring. This results in a vicious cycle of limited laboratory capacity to conduct antimicrobial susceptibility testing (AST); thus, sample sizes for AMR surveillance are limited. As a result, some isolates obtained in GASP are not systematically collected but are convenience samples, making it difficult to generalize findings.

In a different setting, many resource-rich organizations have used nucleic acid amplification tests (NAATs) for diagnosis of gonorrhea, which has also limited the collection of cultures for AST. NAATs in particular can detect nonviable gonococci, have high sensitivity compared to other diagnostic methods (especially for rectal and oropharyngeal specimens), can be self-collected, can detect multiple pathogens in 1 test, and can provide results rapidly (*4*). As a result, some countries in the GASP network have not collected a minimum sample size of 100 isolates of urethral discharge as recommended by WHO to confidently detect a 5% resistance, the typical cutoff point used to inform revision of treatment recommendations (*19,20*). These small sample sizes ultimately do not support comparison of data across countries and regions (*13*) and assessment of trends over time. There are also issues related to quality of laboratory testing. Variation in AST methods and limited capacity of laboratory methodologies for specimen collection, culture testing, AMR testing, and quality assurance procedures (*4,13*) can result in data that are invalid and incomparable across countries. In addition, AST results are reported as MICs, which are the lowest antimicrobial concentrations

that inhibit growth of a microorganism. As MICs increase, organisms can grow at higher antimicrobial concentrations that provide an early warning or alert of impending resistance (*15*). GASP has noted that countries frequently batch test isolates, which possibly leads to delayed reporting. Such practices may compromise global preparedness for emerging resistance if any of these isolates are found to have critical MICs many months after being collected.

Finally, many countries participating in GASP do not routinely obtain demographic, behavioral, or clinical data with the isolates, so it is not possible to identify and understand epidemiologic factors or known behavioral risk factors associated with resistance. Global surveillance for gonococcal AMR should be strengthened, especially in the most disease-burdened countries, where the greatest need for AMR monitoring is essential. Because of the impending spread of resistant extended-spectrum cephalosporins, monitoring AMR is essential to inform treatment guidelines and policy, as well as interventions for gonococcal infections. As part of a collaborative effort between WHO and CDC, sentinel countries are being strategically selected to enhance the GASP program. Selected countries will link valid and comparable laboratory data to epidemiologic data to establish mechanisms for early warning of emergence of antibacterial drug resistance to inform national and global treatment guidelines and policies.

Enhanced Gonorrhea Antimicrobial Surveillance Project Implementation

A 2013 CDC report categorized antimicrobial drug–resistant gonorrhea as an urgent threat that required immediate and aggressive action (*21*). Data in that report were primarily from GISP (*15*). The contents of the report helped spur the National Strategy to Combat Antibiotic Resistant Bacteria (CARB). A basic tenet of CARB is to improve international collaboration and capacities for AMR prevention, surveillance, control, and antibiotic research and development. To enhance this global response, CDC was encouraged to collaborate with countries to strengthen antibiotic stewardship and help ensure that laboratories around the world could identify and report resistant bacteria (*22*). Recognizing the need to establish a robust sentinel surveillance program for emerging drug-resistant *N. gonorrhoeae*, and reflecting on the known successes of GISP (as well as evidence from other country surveillance systems) and the call to enhance global health security, WHO and CDC developed the Enhanced Gonococcal Antimicrobial Surveillance Program (EGASP) in late 2015.

The primary objective of EGASP is to monitor trends in antimicrobial susceptibilities in *N. gonorrhoeae* by using standardized sampling and laboratory protocols at selected sentinel sites and reference laboratories. A second objective of EGASP is to improve the quality, comparability, and timeliness of gonococcal antimicrobial resistance data across multiple countries. Further, EGASP aims to assess resistance patterns in key populations at highest risk for antimicrobial drug–resistant gonorrhea to eventually inform treatment guidelines and other policy measures.

Prior to implementation, EGASP coordinators make an assessment site visit. Selection of countries for EGASP implementation is based on *N. gonorrhoeae* morbidity, ease of access to healthcare providers, competent laboratory services, government engagement, and a partner in the country (such as a WHO or CDC country office) that will help champion the project when technical advisors are not in the country. Although a minimum threshold of *N. gonorrhoeae* morbidity has not been established because of limited available data, countries that have been able to document a high rate of identified gonorrhea cases are prioritized for this surveillance activity.

Urethral specimens are collected from patients at selected clinics who had symptoms suggestive of gonorrhea (i.e., urethritis, dysuria); a Gram stain test is done, and a culture is sent to a participatory laboratory for processing. Before the patient leaves the clinic, antibiotics are prescribed on the basis of the results of the confirmed Gram stain. Treatment is provided on the basis of local treatment guidelines for gonococcal or nongonococcal urethritis; treatment is provided for both gonorrhea and chlamydia infections.

Bacterial identification testing is performed on any culture isolates; those confirmed to be *N. gonorrhoeae* are tested for susceptibility to specific antimicrobial drugs currently recommended to treat gonorrhea by using Etest (bioMérieux, Durham, NC, USA). Etest was selected for MIC determination in EGASP because it is comparable to agar dilution but available at a lower cost and enables the calculation of trends of drug susceptibility data over time (*4*). AST results for ceftriaxone, cefixime, and azithromycin are recorded at each EGASP surveillance site for analysis. The EGASP country may additionally select other antimicrobial agents for assessment depending on local interests. Because of the considerable quality assurance and control methods that are required with the use of Etest, laboratory personnel are required to complete a CDC training program and pass 2 annual quality assurance proficiency tests administered by CDC.

Behavioral and clinical data, such as demographics, prior antibiotic use, sexual behavior history, and treatment, are collected on a case abstraction form for each person enrolled in EGASP. Persons who have a positive *N. gonorrhoeae* culture are enrolled into EGASP and their isolates are submitted for AST. EGASP continuously enrolls symptomatic persons with confirmed *N. gonorrhoeae*. A coordinator is assigned at each sentinel site and is responsible for data collection (including the review of the abstraction forms to ensure that all questions have been reviewed

before a person leaves the clinic); appropriate gonococcal isolate collection; confirming that all isolates are sent to the designated reference laboratory; and ensuring that all surveillance and laboratory personnel are adhering to the clinical, laboratory, and data standard operating procedures. Data from the sentinel sites and laboratories are later merged and sent to the Ministry of Public Health or equivalent, and monthly progress reports are sent to WHO and CDC for quality assurance and technical assistance review.

The first EGASP site was implemented in late 2015 in Bangkok, Thailand, where 2 sentinel sites and 2 reference laboratories were selected. In addition to WHO and CDC, partners include the Thai Ministry of Public Health (MOPH) and CDC's Thailand Ministry of Public Health–US Centers for Disease Control Collaboration (TUC); CDC staff are from the Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. One sentinel surveillance site in Thailand, Bangrak Hospital, is the largest STI center in Bangkok and has several clinics on campus; currently, 2 clinics contribute specimens for EGASP. Silom Community Clinic at the Hospital for Tropical Medicine, a CDC partner that has been involved in community HIV trials, is the second sentinel surveillance site in Thailand.

EGASP Thailand currently collects specimens from all symptomatic male patients with urethritis. Both laboratories passed their first 2 external quality assessments. Their own internal quality control assessment of surveillance found several items that led to updated standard operating procedure instructions and development of a surveillance training course. Analysis of EGASP data from the first year of surveillance is currently under way; description of the cases and the antimicrobial susceptibility distribution tables will be published in a WHO/CDC report in 2017. To date, however, ≈1,100 male patients who had urethritis have been enrolled in Thailand EGASP; samples from 54% of male patients were confirmed as culture-positive for gonorrhea. AST was performed on 590 isolates; all of these also have a respective chart abstraction showing clinical and epidemiologic data.

In fall 2016, WHO and CDC completed an initial assessment EGASP visit to a Western Pacific Region country to determine if surveillance could be initiated in this region. According to current plans, EGASP surveillance will be established in 1 Western Pacific Region country by the end of calendar year 2017. The vision for EGASP is to include at least 10 sentinel-enhanced countries through all 6 WHO regions. WHO and CDC plan to implement EGASP surveillance in a country after appropriate assessments (i.e., review of *N. gonorrhoeae* morbidity, ease of access to healthcare providers, competent laboratory services, government engagement, and an in-country WHO or CDC partner) have been made. Depending on global AMR funds, the plan is to implement EGASP surveillance for the next 4–6 years. Afterward, WHO and CDC hope that participating countries will serve as examples for other countries, and the 2 agencies will share a generic EGASP protocol and standard operating procedures with interested countries. WHO and CDC plan to release annual reports of results from EGASP surveillance.

In addition, unlike GASP, where country-specific data are currently reported directly to regional focal points, the reporting of EGASP surveillance data is being implemented into WHO's Global Antimicrobial Surveillance Systems (GLASS) to ensure sustainability and country ownership. The WHO Antimicrobial Secretariat coordinates GLASS; this division is responsible for strengthening AMR surveillance of bacteria, viruses, and fungi; *N. gonorrhoeae* is 1 of 9 priority bacterial infections that are being monitored. GLASS is being launched to support a standardized approach to the collection, analysis, and sharing of AMR data on a global level; countries will enter EGASP data into the GLASS system, and the surveillance data will be submitted directly to WHO and CDC (*23*). In addition, while it is envisioned that GASP will soon report country-specific data through GLASS, at this time, WHO plans to commence with EGASP in this system first.

Conclusions

Consistent and systematic surveillance for antimicrobial drug–resistant gonorrhea is essential to assess if, when, and how resistance is spreading globally and to inform national and global action to control and mitigate AMR in gonorrhea. Globally, it is a critical time in which the capacity for both culture and AST need to be strengthened and implemented where absent. Building sustainable surveillance systems is the key to understanding trends; having the knowledge of global patterns and trend data puts all stakeholders in a better position to understand threat levels and to prepare action and response plans. Although EGASP is still in its infancy, its goals are the implementation of strong epidemiologic and laboratory capacities and the ability for WHO and CDC to provide technical assistance to many countries. This surveillance program is designed to enable each country to assess resistance patterns in key populations at highest risk for antimicrobial drug–resistant gonorrhea, and enables countries to use these data to inform their own treatment guidelines. In addition, EGASP contributes to the global picture for standardized surveillance, as it will assist us in understanding global and regional trends for antimicrobial drug–resistant gonorrhea and will facilitate targeted response to global health threats. This international preparedness plan of implementing strong surveillance to detect resistant gonorrhea replicates other efforts currently being undertaken

at CDC and WHO and serves as a lesson learned from the 2014–2015 West Africa Ebola response as a way to enhance overall global health security.

Establishing surveillance systems to monitor the emergence and spread of antimicrobial drug–resistant *N. gonorrhoeae* supports the development of evidence-based, regional treatment recommendations rather than the current approach that is based on a few systematic surveillance systems. This process would support the evaluation of treatment recommendations and, in some cases, may permit for more treatment options if antimicrobial susceptibility patterns differ globally. EGASP will build capacity in countries to conduct robust surveillance by facilitating the collection of relevant epidemiologic data associated with accurate laboratory results; this is a model that could be applied to other infectious agents. This clearly serves the global health security community as an early warning for antimicrobial drug–resistant *N. gonorrhoeae* and supports improved clinical activities.

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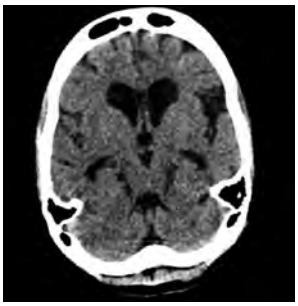
- Multiorgan WU Polyomavirus Infection in Bone Marrow Transplant Recipient



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- Falling *Plasmodium knowlesi* Malaria Death Rate among Adults despite Rising Incidence, Sabah, Malaysia, 2010–2014
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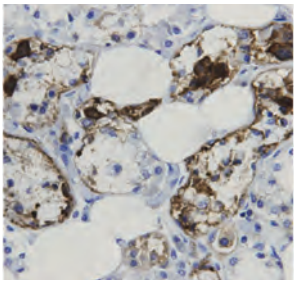

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Capacity Development through the US President's Malaria Initiative–Supported Antimalarial Resistance Monitoring in Africa Network

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Antimalarial drug resistance is an evolving global health security threat to malaria control. Early detection of *Plasmodium falciparum* resistance through therapeutic efficacy studies and associated genetic analyses may facilitate timely implementation of intervention strategies. The US President's Malaria Initiative–supported Antimalarial Resistance Monitoring in Africa Network has assisted numerous laboratories in partner countries in acquiring the knowledge and capability to independently monitor for molecular markers of antimalarial drug resistance.

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"One finger does not kill a louse." — Kikuyu proverb

Substantial recent progress has been made in malaria control, particularly in sub-Saharan Africa. During the past 5 years, malaria mortality rates have declined 31% in the region, an achievement attributable to many factors (*1*). From 2010 to 2015, the proportion of at-risk persons sleeping under an insecticide-treated net in Africa increased from 30% to 53%, the proportion of febrile children evaluated with a malaria diagnostic test at a public facility increased from 29% to 51%, and the proportion of pregnant women receiving 3 doses of preventive antimalarial treatment increased 5-fold. Another development is the growing availability of oral artemisinin-based combination therapies (ACTs), which rely on an artemisinin plus a longer-acting partner drug from another class to treat uncomplicated malaria (*2*). ACTs, which are quick-acting, inexpensive, and generally well tolerated, have been critical in treating millions of cases of uncomplicated malaria each year, reducing risk of progression to severe disease and death. The widespread availability and use of ACTs has been recognized as a main contributor to the decline in cases in Africa (*3*).

However, recent studies from Southeast Asia have identified the emergence and spread of *Plasmodium falciparum* parasites that are less susceptible to both artemisinin and the partner drug component of ACTs (*4*,*5*). International malaria control efforts experienced a similar setback in the 1950s, when chloroquine resistance first surfaced on the Thailand–Cambodia border and spread to Africa within 2 decades (*6*), and again in the 1970s with the rise and spread of *P. falciparum* parasite populations resistant to sulfadoxine/pyrimethamine (*7*). Fortunately, genetic markers of resistance to antimalarial drugs, including those for

artemisinins (*8*) and partner drugs (*9*), are now used more easily to rapidly detect and track the spread of potentially resistant parasites.

The growing threat of antimalarial drug resistance is a major concern of the global health community. The US President's Malaria Initiative (PMI), established in 2005 to support countries in scaling up malaria prevention and control efforts, now covers 19 countries in Africa plus the Greater Mekong subregion. PMI has helped provide nearly 400 million ACT treatment courses since its inception (*10*). During 2005–2015, the Global Fund to Fight AIDS, TB, and Malaria supplied an additional 582 million treatments (*11*). Losing these medications to drug resistance would not only jeopardize the progress achieved in reducing malaria infections in recent years but also threaten global health security by putting millions of additional persons at risk for death from malaria.

To monitor whether a country's recommended ACTs remain efficacious, therapeutic efficacy studies (TESs) should be conducted at least every 2 years. TESs use a standard World Health Organization (WHO) protocol (*12*) to enroll uncomplicated malaria patients, who are given a quality-controlled ACT and monitored over 4–6 weeks for parasite clearance or the reappearance of parasites matching the infecting strain. Pending confirmation, therapeutic efficacy rates falling below 90% indicate an ACT may no longer be optimal for a given region or country. The US Agency for International Development's support of a broad network of TES sites in the Greater Mekong subregion, begun in 2006, was instrumental in identifying suboptimal efficacy rates in the region. Subsequent PMI support for countries to conduct TESs in the Greater Mekong subregion and across sub-Saharan Africa continues to provide crucial data on the clinical efficacy of ACTs.

In addition to monitoring therapeutic outcomes in a TES, WHO also recommends testing the collected samples for genetic markers of antimalarial drug resistance to provide insight into the molecular underpinnings of treatment failure. Recently, WHO listed specific polymorphisms in the propeller domain of the *kelch 13* (*K13*) gene that could be used to identify suspected artemisinin-resistant parasites (*13*). Even though investigating for the presence of *K13* and other genetic mutations is an important complement to the primary outcome of TESs, it often falls outside a routine TES's scope and budget and is often beyond a country's capability.

To address this shortcoming, the PMI-supported Antimalarial Resistance Monitoring in Africa (PARMA) Network was created in 2015 with 2 primary objectives: 1) to assist PMI countries in testing samples from TESs for genetic markers associated with antimalarial drug resistance; and 2) to support training and capacity building of African collaborators who possess sufficient infrastructure in laboratory (e.g., real-time PCR, thermocyclers, gel electrophoresis) and bioinformatics (e.g., computer with sufficient memory and processing power) to incorporate these assays in future studies. By using dried blood spot samples collected during a standard TES, PMI's support of additional testing through PARMA requires no extra blood draw or inconvenience to patients. After TES completion, samples are brought to the Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA) Malaria Branch (Division of Parasitic Diseases and Malaria, Center for Global Health) by a laboratory-based trainee from the participating country partner. At CDC, trainees participate in 4–6 weeks of molecular laboratory training to process their countries' recently collected TES samples, with the goal of generating antimalarial drug resistance marker data. Under the tutelage of CDC personnel, trainees learn molecular methods of testing for resistance markers to artemisinins and other drugs used in the treatment and prevention of malaria (Table). These methods may include DNA isolation, photo-induced electron transfer PCR (*14*), TaqMan-based real-time PCR (e.g., for *mdr1* gene copy number), Sanger sequencing, and PCR techniques that distinguish whether a recurrent infection matches the initial parasite (recrudescence) or is a new one (reinfection) (*15*). In addition to receiving instruction and training in the laboratory, trainees receive training in bioinformatics analysis and guidance on interpreting their findings, which they are encouraged to share with global monitoring entities such as WHO and the Worldwide Antimalarial Resistance Network. Depending on time, appropriateness, and interest level, other molecular (e.g., *hrp2* gene deletion associated with false-negative malaria rapid diagnostic test results) and nonmolecular (e.g., serology) training may be offered to strengthen laboratory capacity

Table. Antimalarial drug resistance genes that may be analyzed by the President's Malaria Initiative–supported Antimalarial Resistance Monitoring in Africa Network*

Gene	Chromosome	Type of mutation	Antimalarial drug(s) associated with resistance
pfcrt	7	Polymorphism	Amodiaquine, chloroquine
pfmdr1	5	Polymorphism Change in copy number	Amodiaquine, chloroquine, lumefantrine, quinine Mefloquine
pfdhfr	4	Polymorphism	Pyrimethamine
pfdhps	8	Polymorphism	Sulfadoxine
Propeller domain of *kelch*	13	Polymorphism	Artemisinin derivatives (e.g., artesunate)
plasmepsin 2 and *3*	14	Change in copy number	Piperaquine

*Markers are selected based on the needs and priorities of each country's malaria control program. This list will be expanded as additional molecular markers are identified.

in support of malaria control and elimination programs. While at CDC, trainees interact with epidemiologists and public health professionals who provide advice on integrating the newly acquired knowledge and skills to benefit their country's national malaria control program.

Much as in the medical adage "see one, do one, teach one," PMI envisions its support of training at CDC as the first step in the knowledge transfer process. The PARMA Network's experience with its first partner, the Department of Parasitology of Université Cheikh Anta Diop de Dakar in Senegal, illustrates how these training visits foster proficiency and self-sufficiency. After completing 6 weeks of molecular training at CDC in 2015, 2 trainees from Senegal returned to their laboratory and, a few months later, were visited by a CDC Malaria Branch representative who supported the successful implementation of molecular testing methods in the Université Cheikh Anta Diop de Dakar's malaria laboratory. In early 2016, the Senegal laboratory used high-resolution melting and Sanger sequencing methods to determine the presence of antimalarial drug resistance molecular markers, including *K13*, on samples from TESs in their own country. Rounding out the process in August 2016, Université Cheikh Anta Diop de Dakar and CDC partnered in teaching a 1-week regional training session, Advanced Molecular Detection Tools and Analysis for Malaria, at the university. Laboratory workers from the PMI countries Mali, Senegal, and Zimbabwe and the non-PMI country Morocco attended using their own funding.

Following on Senegal's success, additional PMI countries are now participating in the PARMA Network and have sent samples, trainees, or both to CDC (Figure). Countries already possessing results include Angola, Guinea, Kenya, Malawi, Mali, Tanzania, and Zambia. Other countries, including Benin, Ethiopia, and Rwanda, will participate in the network with their next TES. The ultimate goal is to enable institutions in Africa to independently offer molecular monitoring, diagnostic training, and associated support to other countries. Building capacity through this type of regional partnership will harmonize testing and quality assurance protocols among African countries. A sustainable model allows countries to enhance ongoing TESs by independently identifying antimalarial drug resistance markers in the local parasite population. Furthermore, with its current 34 sites spanning 11 countries, the expanding PARMA network provides an opportunity for investigators to collaborate in analyzing trends in malaria data over time and

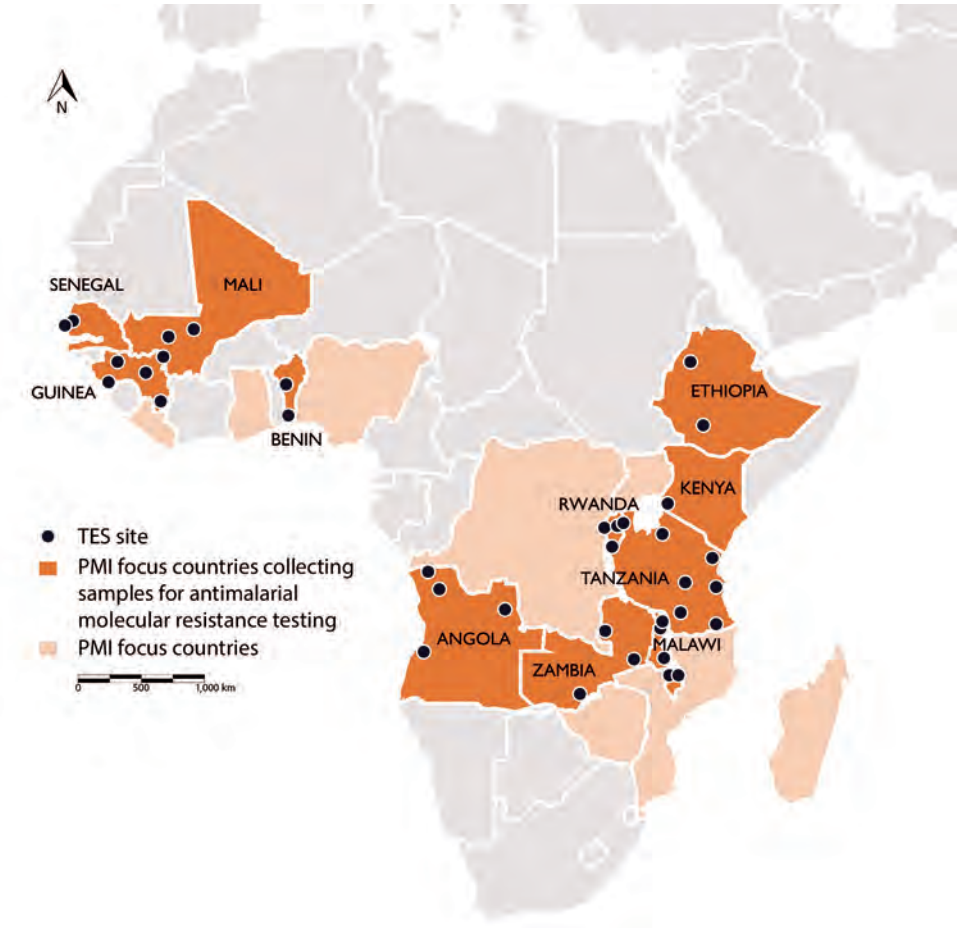

Figure. US President's Malaria Initiative (PMI)–supported therapeutic efficacy study (TES) sites, where samples were collected to test for molecular markers of antimalarial drug resistance, 2015–2017.

space. Capabilities acquired, connections forged, and lessons learned through this laboratory network can be used to combat other infections of importance to global health security, ranging from viral hemorrhagic fever to pandemic influenza to emerging arboviral disease.

Improving molecular surveillance capability in Africa could preserve antimalarial drug efficacy on the continent. Molecular surveillance can complement conventional TES methods and serve as an early warning system to trigger and direct follow-up investigations in areas of suspected resistance. Accelerating the confirmation of resistance and assisting countries in identifying appropriate actions are consistent with the aim to prevent, detect, and respond to human disease threats in the name of global health security. Whether that entails targeted interventions (e.g., heightened case surveillance, intensive indoor residual spraying of insecticide); switching to 1 of the other 5 WHO-approved ACTs; or developing a new option remains to be determined. Several innovative compounds show promise (*16*), including those possessing substantial differences from existing antimalarial drugs in their class and those with completely novel mechanisms of action; ongoing studies continue to produce safety and efficacy data. Available strategies include adding a third drug to the current 2-drug approach of treating uncomplicated malaria (triple therapy) (*17*), exploring the safety and efficacy of sequential administration of different ACTs, and extending the treatment duration of existing therapies (*18*). Regardless of the strategy chosen, surveillance programs such as PARMA and the PMI-supported TES network will be instrumental in keeping malaria control in Africa a step ahead of the parasite.

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Prioritizing Zoonoses for Global Health Capacity Building—Themes from One Health Zoonotic Disease Workshops in 7 Countries, 2014–2016

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Zoonotic diseases represent critical threats to global health security. Effective mitigation of the impact of endemic and emerging zoonotic diseases of public health importance requires multisectoral collaboration and interdisciplinary partnerships. The US Centers for Disease Control and Prevention created the One Health Zoonotic Disease Prioritization Tool to help countries identify zoonotic diseases of greatest national concern using input from representatives of human health, agriculture, environment, and wildlife sectors. We review 7 One Health Zoonotic Disease Prioritization Tool workshops conducted during 2014–2016, highlighting workshop outcomes, lessons learned, and shared themes from countries implementing this process. We also describe the tool's ability to help countries focus One Health capacity-building efforts to appropriately prevent, detect, and respond to zoonotic disease threats.

Emerging and endemic zoonotic diseases pose a threat not only to the health of animals and humans but also to global health security. An estimated 60% of known infectious diseases and up to 75% of new or emerging infectious diseases are zoonotic in origin (*1*,*2*). Globally, infectious diseases account for 15.8% of all deaths and 43.7% of deaths in low-resource countries (*3*,*4*). It is estimated that zoonoses are responsible for 2.5 billion cases of human illness and 2.7 million human deaths worldwide each year (*5*). Emerging zoonoses are responsible for some of the most high profile and devastating epidemics (*6*–*8*); however, endemic zoonoses (*9*,*10*) may actually pose a more insidious and chronic threat to both human and animal health. As one comparison, the 2014 Ebola epidemic was responsible for 11,316 deaths and $2.2 billion in economic losses (*11*), whereas each year rabies accounts for ≈59,000 human deaths and roughly $8.6 billion in economic losses worldwide (*12*). The global impacts of emerging and endemic zoonoses on both human and animal populations make fostering collaboration between human and animal health sectors using a multisectoral, One Health approach a critical step toward improving animal and human health.

Early detection of zoonotic pathogens through enhanced laboratory capacity and surveillance at the animal–human interface is a crucial step toward controlling and preventing zoonoses (*13*–*20*) and a core capacity for implementation of the World Health Organization International Health Regulations 2005 (IHR 2005) and the Global Health Security Agenda (GHSA; https://www.ghsagenda.org/) (*21*). Rapidly detecting, responding to, and controlling public health emergencies at their source, including those caused by outbreaks of zoonotic diseases, is essential for global health security. However, in low-resource settings, capacity-building efforts should be initially focused on a few key diseases (*22*). Disease prioritization enables effective capacity building and resource allocation to increase surveillance, guide research, and improve preparedness and response protocols, further advancing global health security and the international health regulations (*23*–*25*).

To address this prioritization need, the US Centers for Disease Control and Prevention (CDC) developed the One Health Zoonotic Disease Prioritization (OHZDP) tool (*22*,*26*) as a multisectoral approach to rank a country's zoonotic diseases using an objective, semiquantitative method. The OHZDP tool enables a country or region to bring together representatives from human, animal, and environmental health sectors to prioritize the endemic and emerging zoonoses of greatest national concern that should be jointly addressed by human, animal, and environmental health ministries using country- or region-specific criteria. Zoonotic diseases can be prioritized even in the absence of reliable prevalence data by using alternative measures for disease burden so that outcomes are provided in a timely manner, enabling country representatives to give immediate

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feedback, develop action plans, and capitalize on collaborations built during the prioritization process.

During 2014–2016, CDC implemented 7 OHZDP workshops. We summarize overarching themes identified from these workshops and highlight successes and lessons learned to best support additional countries in prioritizing zoonotic diseases by using this tool.

Methods

CDC conducted OHZDP workshops using methods previously described (*22*,*26*). CDC maintains a pool of trained OHZDP workshop facilitators to conduct workshops and to train in-country facilitators to promote country ownership of the prioritization process and to leave the capacity to conduct future prioritization workshops in each country. We interviewed workshop facilitators, reviewed data from workshop materials maintained as part of our routine monitoring and evaluation activities, and reviewed available publications for information on alternate methods and outcomes. Variables collected are number and type of workshop participants by sector (voting members and observers), disease assessment criteria selected during the workshop and the resulting zoonoses rankings, and outcomes or planned next steps for multisectoral capacity building activities. Where appropriate, data for certain variables (e.g., disease ranking criteria) were standardized and combined into larger categories to look for overarching themes. Data were analyzed using Microsoft Excel (Microsoft, Redmond, WA, USA).

Results

During 2014–2016, at countries' request, CDC conducted OHZDP workshops in Thailand, Kenya (*27*), Ethiopia (*28*), Azerbaijan, Cameroon, South Africa, and the Democratic Republic of the Congo. All countries prioritized diseases on a national level; 4 (57.1%) workshops were specifically conducted to advance GHSA implementation in the country, but all countries had a goal to strengthen multisectoral collaboration and focus laboratory, surveillance, and prevention efforts. All workshops took place over a 2-day period, with an additional 1–2 days for training local facilitators, when requested.

All workshops used standard methods as previously described (*22*,*26*) for conducting the preworkshop activities and the in-country facilitated group work. Two countries (Kenya and Thailand) diverged from the standard methods by including more than the recommended number of voting members. Kenya placed voting members into 5 groups, then used group discussion and consensus to assign weights to the individual criteria (*27*). Thailand held 2 separate, concurrent workshops that produced 2 different outcomes; these outcomes were then combined at a separate meeting held 1 month later to develop a final list of criteria by discussion and consensus. Members were then grouped by their agencies and voted on the ranking or weight applied to each criterion before conducting a final ranking of the diseases.

Facilitators and Participants

Fourteen CDC-trained OHZDP workshop facilitators were used for the 7 workshops and represented interdisciplinary backgrounds with expertise in zoonoses. A total of 21 in-country facilitators were trained at 5 of the 7 workshops, with an average of 4 (range 2–6) facilitators per workshop. In-country facilitators represented ministries of health (n = 8), agriculture (n = 5), environment (n = 1), and wildlife (n = 1); research institutes (n = 2); CDC in-country staff (n = 2); and other partners (n = 2). Field Epidemiology Training Program graduates were a resource for in-country facilitators in 2 workshops. Postworkshop debrief meetings and CDC facilitator interviews revealed specific lessons. For example, facilitators who held high-level positions were not available for the entire workshop because of competing priorities. In addition, it was deemed important that in-country facilitators be seen as unbiased during the facilitation process.

A total of 107 voting members participated in the 7 workshops (range 5–33), and multiple sectors were represented (Table 1). The average number of voting members per workshop was 15, but excluding 2 outlier workshops

Table 1. Sectors represented by voting members, voting members per workshop, and percentage of voting members by sector for One Health Zoonotic Disease Prioritization workshops in 7 countries, 2014–2016*

Sector and no. workshops where present	Median no. voting members/workshop (IQR)	% Total for all workshops (range)
Public health, n = 7	5 (3–6)	35.5 (16.7–50.0)
Animal health, n = 7	5 (2.5–6.5)	30.8 (16.7–50.0)
Wildlife, n = 2	5.5 (3.75–7.25)	10.3 (0–40.1)
Research institution, n = 3	3 (2–5)	10.3 (0–25.0)
Environmental health, n = 3	1 (1–2)	4.7 (0–25.0)
Local universities, n = 3	1 (1–2)	4.7 (0–25)
International partners,† n = 2	1.5 (1.25–1.75)	2.8 (0–8.3)
One Health coordinating mechanism, n = 1	1 (1–1)	0.9 (0–8.3)

*The total number of voting members for all workshops was 107. Countries: Thailand, Kenya, Ethiopia, Azerbaijan, Cameroon, South Africa, Democratic Republic of the Congo. IQR, interquartile range.

†International partners were the Food and Agriculture Organization of the United Nations, International Livestock Research Institute, and the World Health Organization.

that grouped voting members (Kenya, n = 33; and Thailand, n = 22), the average was 10 (range 5–11).

Six of workshops included observers from partner organizations or ministries. The number of observers averaged 10 (range 1–26) per workshop. Observers typically included in-country representatives from ministry partners, universities and research institutes, the World Health Organization, the Food and Agriculture Organization of the United Nations, Defense Threat Reduction Agency, the US Agency for International Development and its implementing partners, and CDC.

Zoonotic Disease Lists

All countries provided an initial list of zoonotic diseases from the relevant ministries to the OHZDP core planning team. Many of these lists were initially created by referencing the countries' human and animal health sector reportable disease lists. The presence of a reportable disease list did not reflect the surveillance capacity, and this variable, if selected, was assessed on-site by in-country subject matter experts. The core planning team conducted an extensive country and regionally specific literature review on the disease list. Voting members reviewed and approved the disease list on the first day of the workshop for use in the prioritization process.

Each list, on average, included 37 (range 25–43) diseases or syndromes. Zoonoses on these lists were classified as 41.4% (range 27.8%–51.3%) bacterial, 37.7% (range 28.0%–44.4%) viral, 18.3% (range 13.9%–25.0%) parasitic, 2% (range 0%–11.1%) fungal, and 0.8% (range 0%–4%) prion in nature. All lists included endemic and emerging zoonotic diseases relevant to the country or region.

All 7 initial country lists included the following bacterial zoonoses: anthrax, brucellosis, leptospirosis, plague, Q fever, salmonellosis, and zoonotic tuberculosis. All lists also included the following viral zoonoses: Crimean-Congo hemorrhagic fever; coronaviruses, including Middle East respiratory syndrome and severe acute respiratory syndrome; flaviviruses, including yellow fever and West Nile; hemorrhagic fever viruses, including Ebola and Marburg; rabies; and zoonotic influenza viruses. Six of the country lists included the following parasitic diseases: cysticercosis or taeniasis, echinococcosis, and toxoplasmosis.

Prioritization Criteria

Six of the 7 countries selected 5 disease-ranking criteria; 1 country selected 6 criteria. All selected criteria were categorized into 7 overarching topic areas; 4 of those topics were further broken down into 2–3 more specific subtopics (Table 2). All 7 countries ranked diseases on the basis of social, economic, or environmental impact. Six of 7 countries ranked zoonotic diseases on the basis of availability of proven interventions, epidemic or pandemic potential, and severity of disease in humans; 5 ranked zoonoses on the basis of documented presence of disease in the country or region.

When looking at the weighting, or level of importance, voting members assigned severity of disease in humans and epidemic/pandemic potential as the 2 criteria with the highest average weight. Next were documented presence of disease in the country or region, and economic, environmental, or social impact. Last, availability of proven interventions and all other remaining criteria categories were assigned the lowest weight. However, no single criterion stood out across all 7 workshops.

Table 2. Disease ranking criteria chosen by country during One Health Zoonotic Disease Prioritization workshops in 7 countries, 2014–2016*

Disease ranking criteria	No. countries	Average assigned weight† (range)
Economic, environmental, and/or social impact	7	0.193 (0.150–0.210)
Economic impact only	3	
Economic and/or social impact	2	
Economic, environmental, and/or social impact	2	
Availability of interventions (i.e., vaccines and/or medical treatment)	6	0.183 (0.160–0.200)
Epidemic/pandemic potential (and/or sustained transmission in humans)	6	0.202 (0.170–0.220)
Human-to-human transmission potential	5	
History of previous outbreaks	1	
Severity of disease in humans	6	0.206 (0.180–0.230)
Case-fatality rate	3	
Morbidity and/or mortality rate	3	
Presence of disease in country and/or region	5	0.200 (0.170–0.210)
Human and/or animal cases of illness reported in country and/or region‡	4	
Human or animal disease prevalence and distribution in country	1	
Laboratory capacity/diagnostic testing capacity	2	0.179 (0.160–0.198)
Existing multisectoral collaboration	2	0.183 (0.170–0.195)
Bioterrorism potential	1	0.194
Mode of transmission	1	NA

*Countries: Thailand, Kenya, Ethiopia, Azerbaijan, Cameroon, South Africa, Democratic Republic of the Congo. NA, not applicable.
†Thailand was excluded from this weighting analysis since the method used in this pilot workshop differed from the standard method adopted for all future workshops.
‡One country looked at human cases only; the other 3 looked at both human and animal cases.

Criteria Questions and Responses

Six of the 7 countries created 1 single or compound question for each selected criterion. One country created 2 separate questions for 4 of their 5 criteria, for a total of 9 questions. Voting members chose ordinal variables for all responses assigned to each criteria question. Seven (17.5%) questions had a binary response (yes/no), whereas most (82.5%) had ≥3 possible responses per criteria question. Regardless of the number of responses per question, all scores were normalized among criteria by using standard OHZDP tool methods (*22*).

A higher ordinal value (or score) was assigned to the responses for each question that correlated with a more severe, or negative, outcome. For example, a disease with a 50% case-fatality rate would receive a higher ordinal value than a disease with a 10% case-fatality rate. For questions that evaluated existing preventive measures, diagnostic capacity, and multisectoral collaboration, a higher ordinal score was given to responses indicating existing capacity or resources. For example, a zoonosis that could be diagnosed in the country would receive a higher score than one that could not.

Zoonotic Disease Ranking

As a result of the tool's ranking process in these 7 countries, 19 diseases or syndromes were ranked as prioritized diseases (Table 3). Of those, zoonotic influenza virus (n = 5), rabies (n = 5), brucellosis (n = 5), and anthrax (n = 4) were ranked by the most countries. Four of the 7 countries ranked a mix of endemic and emerging zoonoses; 2 ranked only endemic zoonoses (*27*,*28*), and 2 ranked only emerging zoonoses. Of the 4 countries that listed endemic and emerging diseases, on average, 76% (range 60%–83%) of the zoonoses on the final list were known to be endemic in the country. Six countries ranked viral, bacterial, and fungal zoonoses, and 2 countries also ranked parasitic diseases; 1 country ranked only viral diseases.

Final Prioritized List of Zoonotic Diseases

Four of the 7 counties used the original zoonoses produced by the OHZDP tool as their final prioritized list. Two countries agreed to adjust their lists to incorporate other zoonoses that the voting members felt should be in the top 5, and 1 country chose to adjust the order of the rankings to better reflect importance but retained the same zoonoses. Five countries chose a final list of 5 prioritized zoonoses, 1 country chose 6, and 1 country chose 3.

The most common zoonoses seen on the final prioritized lists remained the same as the original ranked list with the exception that rabies was selected in an additional country and brucellosis was removed in 1 country (Table 4). Five of the seven countries included both endemic and emerging zoonoses on their final prioritized lists; 69% (range 33%–83%) of these prioritized zoonoses were considered endemic to the country prioritizing the disease. Two countries prioritized only endemic zoonoses (*27*,*28*). All of the emerging zoonoses prioritized by each country were viruses. All voting members came to consensus on the final prioritized zoonoses list, modified or not. This final list was then endorsed and adopted by the participating ministries.

Outcomes

Six of 7 countries planned follow-up activities as part of the workshop. Twenty postworkshop action themes were

Table 3. Top zoonotic diseases prioritized by the One Health Zoonotic Disease Prioritization Tool for 7 countries, 2014–2016*

Zoonosis	No. countries listing disease, by rank order						Total no. countries
	1	2	3	4†	5‡	6	
Brucellosis (*Brucella abortus* and *B. melitensis*)		1	1§	4§			5§
Rabies	3		2				5
Zoonotic influenza			2		3		5
Anthrax	2	1	1				4
Hemorrhagic fevers (Ebola/Marburg)		1			2		3
Salmonellosis		1		2			3
Arbovirus infections (e.g., yellow fever and West Nile virus)			1			1	2
Crimean-Congo hemorrhagic fever	1			1			2
Echinococcosis		1					1
Hantavirus infection				1			1
Hendra virus infection					1		1
Leptospirosis				1			1
Monkeypox					1		1
Nipah virus infection		1					1
Q fever				1			1
Rift Valley fever					1		1
SARS					1		1
Trypanosomiasis		1					1
Zoonotic tuberculosis (*Mycobacterium bovis*)	1						1

*Countries: Thailand, Kenya, Ethiopia, Azerbaijan, Cameroon, South Africa, Democratic Republic of the Congo. SARS, severe acute respiratory syndrome.
†One country had 4 diseases that shared the no. 4 ranking place.
‡One country had 4 diseases that shared the no. 5 ranking place.
§One country had both *B. abortus* and *B. melitensis* on its ranked list.

Table 4. Final combined prioritized list of zoonoses by the One Health Zoonotic Disease Prioritization Tool for 7 countries, 2014–2016*

Zoonosis	No. countries listing disease, by rank order						Total no. countries
	1	2	3	4	5	6	
Rabies	4		2				6
Zoonotic influenza			3		2		5
Anthrax	2	2					4
Brucellosis (*Brucella abortus and B. melitensis*)		1	2†*	2†*			4†*
Hemorrhagic fevers (Ebola/Marburg)		2		1			3
Salmonellosis		1		1			2
Zoonotic tuberculosis (*Mycobacterium bovis*)	1				1		2
Arbovirus infections (e.g., yellow fever and West Nile virus)						1	1
Crimean-Congo hemorrhagic fever				1			1
Echinococcosis					1		1
Leptospirosis				1			1
Monkeypox					1		1
Rift Valley fever					1		1
Trypanosomiasis		1					1

*Countries: Thailand, Kenya, Ethiopia, Azerbaijan, Cameroon, South Africa, Democratic Republic of the Congo.
†One country had both *B. abortus* and *B. melitensis* ranked separately on the final prioritized list.

identified (Table 5). All 6 countries sought to ensure that the final prioritized list and any after-action items were approved by all participating ministries. Developing or updating and approving some type of national One Health strategy, guiding principles, or workplan was also universally identified as a desired outcome of this prioritization process. Four of the 6 countries indicated plans to use this list to establish recurring meetings, a multisectoral One Health working group or coordinating mechanisms, or both; 1 country that did not list this as an outcome already has a One Health coordination mechanism in place. The remaining action areas focused on various aspects of capacity building (Table 5).

Kenya, which did not plan postworkshop activities, had previously created a One Health strategic plan in 2012 (*29*). The plan included many of the same capacity-building activities stated by other countries, and prevention and control activities were already under way for 4 of the 5 prioritized zoonoses. Kenya's prioritized list validated existing activities and enabled the Zoonotic Disease Unit, the One Health coordinating mechanism for Kenya, to garner further support from the Government of Kenya to continue these efforts.

Discussion

During 2014–2016, CDC successfully carried out 7 OHZDP workshops in Thailand, Kenya (*27*), Ethiopia (*28*), Azerbaijan, Cameroon, South Africa, and the Democratic Republic of the Congo. Several other tools and methods have been applied to prioritize zoonotic diseases (*30–36*), but the OHZDP process is unique in that it enables country-led decisions using a multisectoral approach to prioritize both emerging and endemic zoonotic diseases while strengthening One Health collaborations and developing action plans to build capacity for the prioritized zoonoses. In addition, the OHZDP tool can meet the needs of those working in areas where quantitative data on zoonoses are lacking. Last, the OHZDP process provides outcomes in a timely manner so that participants may give immediate feedback and capitalize on One Health collaborations built during the prioritization process.

We have found key successes and lessons learned through the review of these workshops. First, successful outcomes are dependent on trust, transparency, equal representation, and consensus from all relevant sectors participating in the prioritization process and approving the final prioritized list of zoonoses. The CDC-trained OHZDP workshop facilitators not only conduct workshops but also train in-country facilitators to promote country ownership of the process and to build in-country capacity to conduct future workshops. Trained facilitators ensure that the prioritization process is standardized and conducted effectively. We found that using an interdisciplinary team of trained facilitators who remained neutral, unbiased, and did not focus on their specific sector, affiliation, or area of expertise enabled voting members' voices to be heard and recognized. Our review found that most voting members were from the human (35.5%) and animal (30.8%) health sectors, but additional sectors were represented where available, ensuring the multisector nature of this process.

To accommodate a larger number of voting participants, methods were modified in 2 workshops. However, because these methods have not been rigorously tested, it is still advised that future workshops maintain the recommended number of participants (8 to 12) to enable more focused discussion during and timely results from the 2-day workshop.

Funding partner advocacy and support of the process and future activities is a potential benefit of observer participation. However, care is needed to ensure that the number of observers in their role as advisors and participants during discussions do not overwhelm or influence the process. Keeping to the recommended 10–15 total

Table 5. Categorized action item themes from One Health Zoonotic Disease Prioritization Workshops for 6 countries, 2014–2016*

Action item themes	Total no. workshops
Obtain ministry approval of prioritized list and activities	6
Obtain ministry support of a new or updated national plan	6
Develop a national One Health strategy, guiding principles, or work plan	5
Identify funding and technical assistance	4
Create a One Health coordinating mechanism	3
Improve data sharing across sectors	3
Establish recurring meetings	3
Develop disease-specific subcommittees	3
Strengthen the One Health workforce	3
Improve community outreach/communication	3
Improve surveillance	2
Perform a One Health capacity gap analysis	2
Link activities back to GHSA/IHR 2005	2
Improve reporting	2
Conduct research studies	2
Improve or develop laboratory capacity	1
Improve prevention and control	1
Improve outbreak response	1
Evaluate One Health impact	1
Perform the prioritization on local level	1

*Countries: Thailand, Ethiopia, Azerbaijan, Cameroon, South Africa, Democratic Republic of the Congo. Kenya was excluded because it had a plan already in place before the prioritization workshop that it continued to support. GHSA, Global Health Security Agency; IHR 2005, International Health Regulations 2005.

observers (*26*) is needed so that voting members can focus on the workshop process. We recommend having an overview summary at the end of the workshop that is open to a larger group of higher level in-country representatives and other partners to share the workshop outcomes in a timely way.

The OHZDP tool was designed to accommodate diversity in location (i.e., globally) and scale (i.e., local, national, regional) into the prioritization process so participants can select criteria relevant to their needs. We found that most countries were interested in selecting criteria that targeted zoonoses known to be present in country with the following attributions: high illness and death rates in humans; pandemic potential; availability of proven interventions; and economy, environment, or societal impact. Most prioritized zoonoses were endemic diseases, illustrating that countries wanted to first focus their limited resources on diseases for which they could successfully implement enhanced diagnostic capacity, surveillance, and proven interventions.

Common priority action items identified in these workshops are highly relevant to advancing global health security, including improving data sharing between ministries, improving communication to the public, strengthening the One Health workforce, developing disease-specific subcommittees, and increasing general surveillance and outbreak response capacity. Such activities will enhance the capacity of countries to rapidly detect, respond to, and contain public health emergencies, including outbreaks of zoonotic diseases, at their source and thereby ensure global health security. Most countries with identified priority action items planned to use this list to solicit or engage funding partners, which highlights countries taking ownership of the prioritization process, and recognizing and advocating for support around their country-specific priorities. Six countries made sure that the prioritized list and any after-action items were approved by all participating ministries and that a national One Health strategy or multisectoral coordination mechanism was established if it had not been already. By forming or hosting these prioritization workshops with a ministerial One Health coordinating committee, these after-action plans are more readily taken up.

Four of the 7 countries conducted this activity to meet Joint External Evaluation and GHSA zoonotic disease prioritization and collaboration goals. The next step is that these countries then build these plans into their existing activities. These countries are supported by global health partners to help meet these goals.

As part of the continual improvement process for the OHZDP tool, we are employing postworkshop evaluations, in addition to continuing the postworkshop debriefs and facilitator interviews to ensure that these workshop continue to have successful outcomes. Moving forward, lessons learned from OHZDP workshops conducted during 2014–2016 will be applied to standardize and enhance the prioritization process in the future.

All 7 prioritizations were conducted during or in the wake of the 2014 West Africa Ebola outbreak (*11*). This event likely influenced the outcome for 1 country that prioritized Ebola despite the disease not being endemic or a likely risk in the country or region. Periodically repeating this prioritization process could help eliminate bias from current events, as well as aid in reevaluating if currently prioritized diseases still pose a public health threat, if sufficient capacity has been built, and if newly emerging diseases or other zoonoses need to be considered.

In summary, the GHSA uses a One Health multisectoral approach to strengthen the capacity at the global and national levels to prevent, detect, and respond to human and animal infectious disease threats, whether naturally occurring or accidentally or deliberately spread, that threaten global health security. Both endemic and emerging zoonotic diseases are recognized as being critical for global health security and related efforts. The OHZDP tool aids the GHSA mission by helping countries and regions prioritize their zoonotic diseases of greatest national concern and focusing GHSA capacity-building efforts on improving laboratory capacity, surveillance, outbreak response, and prevention activities on a few key zoonoses at

first. The OHZDP process also supports progress toward the Joint External Evaluation, specifically for the zoonotic disease indicators, on having national laboratory, surveillance, and joint outbreak response plans and strategies in place for priority endemic/emerging zoonotic diseases with evidence of a multisectoral, coordinated approach. A multisectoral zoonotic disease prioritization with equal engagement from all sectors active in zoonotic disease work is one of the most cost-effective ways a country, especially one with limited resources, can begin using a One Health approach to prevent, detect, and respond to public health threats. By building these capacities and strengthening One Health partnerships for prioritized diseases, a country will not only more effectively address existing diseases but also have the systems in place to be better prepared to detect and respond to new and emerging diseases that may occur and become a threat to global health security.

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EID Podcast:
Musings on Sketches, Artists, and Mosquito Nets

James Abbott McNeill Whistler was born in Lowell, Massachusetts, on July 11, 1834. When he was 9 years of age, his family moved to St. Petersburg, Russia, and there he studied drawing at the Imperial Academy of Science.

In ***Man at Table beneath Mosquito Net***, Whistler himself might be the subject of this black ink drawing, part of a collection of such drawings from 1854 to 1855. Whistler captures the continued struggle of humans versus biting and stinging insects, including those that transmit vector-borne pathogens, from an intimate perspective.

Despite the mosquitoes teeming around him, the man is able to sketch intently and without worry, sheltered by the confines of his personal impenetrable veil. The flurry of cross-hatched, finely scrawled lines in these ephemera could be seen to mimic a mosquito's flight path but this was simply a common technique that Whistler used in his sketches.

James Abbott McNeill Whistler (1834–1903) ***Man at Table beneath Mosquito Net***, 1854–55.

Mosquito nets, particularly bed nets or sleeping nets, have, in some shape and form, been used for thousands of years. Herodotus described how people living in marshes in ancient Egypt fished with nets during the day then slept under the same nets to repel insects. Today, pyrethroid-treated mosquito nets are used extensively in malaria-endemic countries in Africa, yielding life-saving returns for little cost.

The World Health Organization reported that in 2012, 207 million cases of malaria occurred, causing an estimated 627,000 deaths, mostly in children under 5 years of age. Today, another aspiring young artist working under his or her mosquito net may be sketching formative works that will someday inspire conversation and comment, and be a prelude of greater things to come, as did Whistler's ***Man at Table beneath Mosquito Net***.

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EMERGING INFECTIOUS DISEASES

Zoonotic Disease Programs for Enhancing Global Health Security

Ermias D. Belay, James C. Kile, Aron J. Hall, Casey Barton-Behravesh, Michele B. Parsons, Stephanie Salyer, Henry Walke

Most infectious diseases that recently emerged in humans originated in animals. Besides close contact between animals and humans, other factors probably contribute to the cross-species transmission of infectious diseases. It is critical to establish effective mechanisms for coordination and collaboration between the animal, human, and environmental health sectors before new threats emerge by bringing the different sectors together to tackle endemic zoonotic diseases of greatest concern. Such multisectoral partnerships should begin by identifying priority zoonotic diseases for national engagement with equal input from the different sectors. Improvements in surveillance and data sharing for prioritized zoonotic diseases and enhancements of laboratory testing and joint outbreak response capacities in the human and animal health sectors will create and strengthen the mechanisms necessary to effectively detect and respond to emerging health threats, and thereby enhance global health security.

Zoonotic disease pathogens such as rabies virus have been causing outbreaks in humans for thousands of years (*1*). In fact, most infectious diseases in humans originate in animals, and the frequency of such transmissions has been increasing over time (*2*,*3*). Taylor et al. identified that 75% of emerging infectious organisms pathogenic to humans are zoonotic in origin (*3*). Recently emerged zoonotic diseases include globally devastating diseases such as Ebola virus disease, Middle East respiratory syndrome, highly pathogenic avian influenza, severe acute respiratory syndrome, and bovine spongiform encephalopathy (*2*–*4*). These and other zoonotic diseases affect many countries, result in high morbidity and mortality rates in humans and animals, cause disruptions of regional and global trade, and strain national and global public health resources (*5*). Newly emerging health threats are associated with substantial economic costs, including direct and indirect impacts on the healthcare system, costs associated with the actual response, and overall disruption of economic activity.

The World Bank estimated that 6 major zoonotic disease epidemics during 1997–2009 resulted in an economic loss of ≥$80 billion (*5*). Experiences from most recent outbreaks indicate that detecting and effectively responding to emerging epidemics require a multisectoral approach. In 2010, recognizing the need for multidisciplinary collaboration to address health threats at the human–animal–ecosystem interface, the World Health Organization (WHO), Food and Agriculture Organization (FAO), and World Organisation for Animal Health (OIE) formalized their collaboration and identified 3 priority areas of work together, 2 of which are zoonotic diseases (rabies and zoonotic influenza) (*6*). Endemic zoonotic diseases have the dual impact of causing illness and death in humans and animals as well as substantial economic loss in resource-poor societies where livestock farming is a major engine of economic growth at the household and national levels. Fortunately, proven control and prevention strategies exist for many zoonotic diseases that are most prevalent in affected communities (e.g., rabies, anthrax, brucellosis) (*7*).

To better prevent, detect, and respond to global infectious disease threats, the US government and other partners developed the Global Health Security Agenda (GHSA) with initial implementation in 17 phase 1 countries in Africa and Asia (*8*,*9*). GHSA is intended to make progress in the implementation of WHO International Health Regulations, the OIE Veterinary Services Pathway, and other similar frameworks for achieving an adequate level of preparedness to tackle emerging health threats in animals and humans. To build the necessary infrastructure and human capital, the US government and global partners allocated funds to advance GHSA across 11 action packages that included zoonotic diseases. In this paper, we describe specific steps to prevent, detect, and respond to endemic zoonotic diseases and how to leverage them to detect and effectively respond to emerging and reemerging zoonotic health threats, and thereby enhance global health security. Some of the steps have been implemented in several GHSA phase 1 countries.

Approaches for One Health Zoonotic Disease Program Implementation

Mitigating the impact of endemic and emerging zoonotic diseases of public health importance requires multisectoral collaboration and interdisciplinary partnerships.

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Collaborations across sectors relevant to zoonotic diseases, particularly among human and animal (domestic and wildlife) health disciplines, are essential for quantifying the burden of zoonotic diseases, detecting and responding to endemic and emerging zoonotic pathogens, prioritizing the diseases of greatest public health concern, and effectively launching appropriate prevention, detection, and response strategies (Table). Multisectoral approaches under a One Health umbrella are more expedient and effective, and lead to efficient utilization of limited resources (*4*,*5*).

Prioritization of Zoonotic Diseases

Developing strategies to prevent, detect, and respond to zoonotic diseases is challenging in resource-poor settings where there are other competing public health priorities. In addition, effective mitigation of their impact requires multisectoral collaborations and interdisciplinary partnerships that may take time to establish. Therefore, having all relevant sectors jointly identify zoonotic diseases of greatest concern is an essential first step for many countries. Multisectoral partnerships are easier to create if participants from multiple sectors, including human, animal (domestic and wildlife), and environmental health develop a prioritized list of zoonotic diseases to work on together and commit to sharing public- and animal-health resources. Engagement of different sectors early in the process facilitates collaboration during program implementation and ensures program ownership. In addition, systems developed to address the prioritized diseases can be leveraged to tackle other zoonotic infections and emerging health threats.

To help identify high-priority zoonotic diseases for multisectoral engagement, the One Health office at the Centers for Disease Control and Prevention (CDC) developed the One Health Zoonotic Disease Prioritization tool, a semiquantitative tool for prioritization with equal input from represented sectors, irrespective of whether reliable surveillance data are available (*10*). The tool is designed to bring together a multidisciplinary team of professionals from human, animal, and environmental health agencies and other relevant sectors with a common goal of developing country-specific criteria for ranking zoonotic diseases of greatest national concern. The tool has been used to select zoonotic diseases for further programmatic activity in multiple countries in the implementation of the zoonotic disease action package of GHSA (*11*,*12*). Typically, the prioritization is performed by trained facilitators during a workshop with voting members from multiple ministries covering human, animal, and environmental health and from multinational organizations (e.g, FAO, WHO, OIE), academic institutions, and other partners working in the area of zoonotic diseases (e.g., CDC, US Agency for International Development). The country's government ministries should select participants. In countries that have conducted prioritization workshops, CDC provided training to in-country workshop facilitators to promote country

Table. Implementation of zoonotic disease program activities using the One Health approach of cross-sectoral collaboration

Activity	Methods/mechanisms	Benefits
Prioritization of zoonotic disease	Semiquantitative tool Workshop consisting of multisectoral teams	One Health multisectoral collaboration promotion and strengthening Efficient use or resources
Assessment of zoonotic disease burden	Measurement of cases of illness Hospitalizations Disability Quality-adjusted life years Economic cost Deaths	Assistance in identifying priorities
Zoonotic disease surveillance	Evidence-based surveillance Indicator-based surveillance Syndromic surveillance Mechanisms for data sharing and dissemination	Early identification of outbreaks Opportunity for preemptive action Evaluation of prevention, detection, and response programs
Joint human and animal outbreak response	Joint training of human and animal health workforce Cross-sector emergency management systems Joint risk assessments	Early detection and prompt control of zoonotic disease outbreaks
Development of laboratory systems in public health and veterinary sectors	Improved specimen collection, storage, and transportation National and regional laboratory capacity development Laboratory quality and safety management	Identification of disease etiologies Assistance in risk mapping of priority zoonotic diseases Surge capacity during emergencies Support for surveillance and outbreak response
Implementation of prevention and control strategies	Vaccination of animals and humans as needed Community and human and animal healthcare provider education Culling of animals (e.g., highly pathogenic avian influenza)	Protection of human and animal health Strengthening of vaccination infrastructure Education of communities to assist in emergency response

ownership of the process. Minimizing the role of external facilitators helps to retain objectivity in the process and allow decision making by the host country representatives.

Assessing Burden of Zoonotic Diseases

Accurately estimating the burden of zoonotic diseases is a critical step in both identifying public- and animal-health priorities and assessing the impact of prevention and control strategies, including potential economic effects on the food supply, such as with avian and swine influenza viruses. Metrics for human zoonotic disease burden may include numbers of cases of illness, hospitalizations, deaths, disability, or quality adjusted life years, and economic impacts such as healthcare-associated costs and lost productivity. Some of these metrics can also be used to assess animal health burden. In countries where zoonotic disease data may not be readily available, the burden of different zoonotic diseases could be better ascertained by conducting studies in selected regions. Such studies may focus on zoonotic diseases selected in the prioritization process or diseases that are deemed more prevalent on the basis of limited epidemiologic or clinical data. Estimation of disease burden should involve studies in humans and affected or implicated animal species. Conducting ecologic and wildlife studies may be necessary to define risk to humans from selected zoonotic pathogens in animal reservoirs or arthropod vectors. Investigators should consider using existing databases or laboratory specimens, such as banked sera collected as part of HIV indicator surveys, to quantify the potential risks to humans of some zoonotic diseases.

Zoonotic Disease Surveillance in Animals and Humans

A rapid and effective response to endemic and emerging zoonotic diseases relies heavily on a timely and efficient surveillance and reporting system (*13*). Surveillance in animals and humans is critical for early identification and possible prediction of future outbreaks, allowing for preemptive action. Components of effective surveillance include establishing event-based and indicator-based surveillance, and adequate laboratory capacity in both public health and animal health laboratory systems. Training epidemiologists and establishment of effective laboratory systems are critical for a successful zoonotic disease surveillance program.

An effective surveillance system may require the following: standard case definitions for priority zoonotic diseases under surveillance, based on existing guidance from global human and animal health organizations such as WHO, CDC, OIE, and FAO; evaluation of existing national surveillance systems to determine their timeliness, effectiveness, and usefulness; new or refined surveillance and reporting systems and linkages to share data between public health and animal health agencies and other relevant sectors (*14*); evaluation of potential electronic disease reporting mechanisms, including the use of smartphone technologies; establishment of surveillance data dissemination platforms (which may include regular reports and publications) to provide awareness and feedback to human and animal health agencies and other stakeholders; evaluation of available diagnostic tests and appropriate testing capabilities in central and regional public health and animal health laboratories; and establishment of a national emergency management system, such as an Emergency Operations Center, to assist in coordinated zoonotic disease surveillance, response to zoonotic disease outbreaks, and prevention and control efforts across relevant sectors.

Laboratory Systems

Timely, accurate, and reliable laboratory tests are critical for building outbreak response capacities, identify etiologies of disease, and to monitor endemic and emerging zoonotic diseases in humans, domestic and food animals, and wildlife. Well-functioning and separate national public health and animal health laboratory systems are essential to identify etiologic agents so that appropriate prevention, detection, and response strategies can be implemented. Laboratories should be an integral part of the public health infrastructure with a system for rapid testing of prioritized samples and timely sharing of results. Successful and sustainable laboratory systems require strategic interagency planning across sectors and building on existing capacities in country to standardize laboratory methods, prioritize laboratory resources, and develop information sharing channels (*15*). A requirement for ensuring testing quality is commitment from the top levels of management to provide the necessary resources to sustain the functional roles of the laboratory in an environment that supports quality and safety. The roles and responsibilities of all human and animal laboratory staff need to be defined, documented, and communicated, and written policies and procedures should be available and understood. In addition, all laboratory staff should be trained on these policies and procedures to ensure they are executed in a consistent and reliable manner. Accurate and reliable test results depend on having a sample that has been collected, stored, and transported correctly; sample requirements vary by the disease and suspected pathogen. Laboratories should be designed to optimize workflow, support the quality of testing, and protect the safety of laboratory staff and the community. Regularly conducted proficiency testing helps to monitor the quality and performance of the laboratory.

Critical human and animal laboratory systems that countries need to establish or expand include central and regional laboratory capacity; specimen referral systems for rapid, safe, and reliable specimen transport; laboratory training programs that promote workforce development and retention; and affordable, flexible laboratory

accreditation schemes to ensure lab quality (*16*). Opportunities for mentored relationships with reference laboratories or private partnerships should be encouraged (*16*). Laboratories may assist in determining disease burden and characterization of human, animal, and ecologic drivers of disease spillover from animals to humans to optimize models for predicting disease emergence (e.g., risk mapping).

Outbreak Response Using One Health Approach

A successful zoonotic disease outbreak response requires 1) the ability to detect the outbreak using established surveillance systems including event-based reporting; 2) adequate laboratory capability to confirm the outbreak etiology; 3) a workforce trained to respond and perform descriptive and analytical epidemiology for animal and human diseases; 4) the ability to implement appropriate control and prevention measures; and 5) an outbreak and emergency management system in place to coordinate multisectoral response activities at the national to subnational levels. Involvement of all relevant stakeholders is crucial, including those in human, animal, and environmental health sectors. Outbreak response activities are best supported by an overarching operations framework that clearly identifies the roles and responsibilities of key institutions and officials for all relevant sectors and provides direction for coordination of activities at the local and national levels. Countries should establish functional cross-sector coordination and communication pathways before an outbreak occurs. Multisectoral collaboration is easier during an emergency if agencies had already been collaborating in a joint priority setting and actively working together to address prioritized zoonotic diseases.

Early detection of an impending human outbreak may in some instances be achieved through detection of an increase in disease in animal populations, such as livestock and wildlife populations. Detection of an outbreak or an increase in case count of a zoonotic disease by the wildlife, livestock, or public health agency should trigger enhanced surveillance by the other agencies. This detection can only occur if there is effective communication between the different sectors. Outbreak response protocols or national strategies should be developed for priority zoonotic diseases that specifically address coordination of activities, data sharing (including how to integrate animal, human, and environmental health information), trigger points or threshold for action, and roles and responsibilities of each stakeholder. Establishing joint training opportunities for animal and human health workers will facilitate information sharing and enhance collaboration for effective prevention, detection, and response programs. When possible, joint simulation exercises can be conducted to demonstrate proficiency of a response and adequate interagency and multisectoral collaboration.

Prevention and Control of Zoonotic Diseases

The prevention and control strategies of zoonotic diseases will vary by disease and availability of proven interventions (Figure). Some of the zoonotic diseases most prevalent in resource-limited areas are vaccine preventable (e.g., rabies, brucellosis, anthrax). Therefore, implementation of routine immunization programs may be needed for disease prevention. Depending on the disease, this may be primarily human vaccination or vaccination of livestock or other domestic animals. For some diseases, such as highly pathogenic avian influenza, prevention and control may involve large-scale culling and effective biosecurity programs. For diseases such as anthrax and rabies, preemptive vaccination of animals will prevent outbreaks in the animal population while at the same time protecting humans. In others

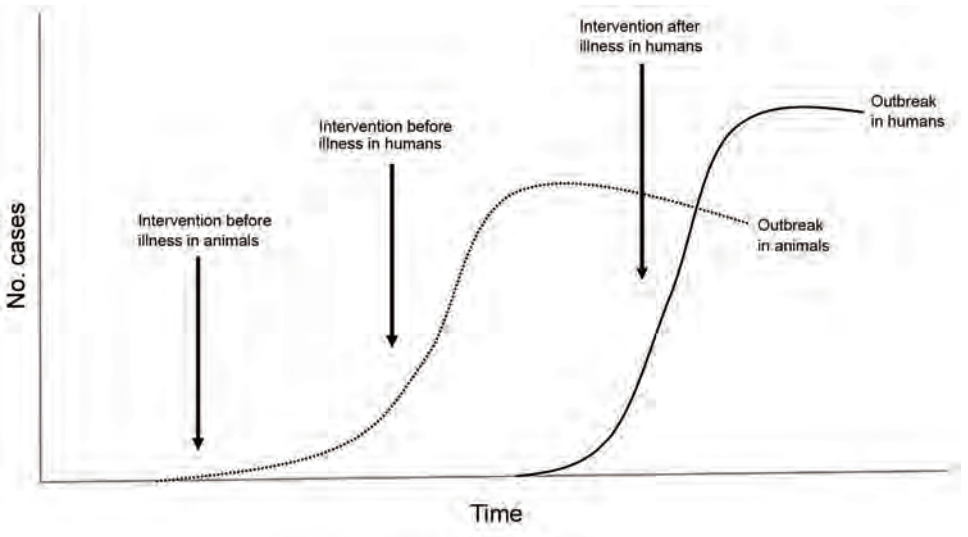

Figure. Opportunities for intervention to prevent and control endemic and emerging zoonotic diseases.

(e.g., Rift Valley fever), disease outbreaks in animals may be the first signal to start implementation of prevention programs such as ring vaccination of animals. Waiting until an outbreak is detected in humans can be costly to the lives of animals and humans and can strain limited public health resources.

Effective human and animal disease surveillance systems are critical for early detection and response, for planning prevention and control programs, and to evaluate the effectiveness of control and prevention strategies. Timely and effective communication and collaboration between human and animal health agencies are essential to develop disease prevention and control strategies involving both human and animal populations. As part of an effective response, countries should consider developing and evaluating communication strategies to educate human and animal healthcare providers and the general population on zoonotic disease transmission and prevention. Community education programs may include safe farming and biosecurity measures, animal slaughtering practices, understanding animal contact and exposure risks, and use of personal prevention measures to avoid or reduce exposure to vectorborne and other zoonotic diseases. Livestock and poultry are key sources of food and livelihood, and important economically for trade; prevention strategies that target zoonotic diseases associated with food animals must be compatible with the needs of the communities that are economically dependent on those animals.

Communicating effectively regarding prevention strategies will also enhance engagement in future outbreak control efforts because the communities will better understand the reasons behind any intervention. Similarly, a well-informed population can serve as an early alert system, notifying appropriate authorities about possible cases of disease in humans or animals. For zoonotic diseases with potential domestic and food animal reservoirs, important strategies in disease control can include animal vaccination, vector control, test and treat, or cull programs, and effective biosecurity measures. The development and implementation of cost-effectiveness and cost-benefit models to evaluate and refine disease prevention and control methods and programs will ensure effective use of resources; evaluations may include the negative effects culling has on societal well-being and livelihood of farmers.

Conclusions

Effective zoonotic disease prevention, detection, and response requires close collaboration, including well-defined roles and responsibilities among the animal, human, and environment health sectors. Such collaborations can help reduce illness and deaths in animals and humans and minimize their social and economic impact at the household and national levels. In most countries, animal health and human health decision makers are located within different ministries. Establishing multisectoral One Health partnerships across agencies and with interdisciplinary personnel at the national, subnational, and local levels (including government departments responsible for health, agriculture, veterinary services, environment, and laboratories) can strengthen zoonotic disease detection and response activities. These structures must be in place before an outbreak, epidemic, or pandemic occurs to have an effective, coordinated public- and animal-health response. Countries that lack a well-functioning coordination mechanism could fail to rapidly detect and effectively respond to emerging health threats, which could spread to other countries and threaten global health security.

Countries should consider convening regular cross-sectoral meetings to build multisectoral and interdisciplinary relationships, encourage transparency, and combine efforts across agencies. Developing mutually agreed-upon standard operating procedures is essential. Identifying designated points of contact ensures improved coordination across sectors, allowing for quicker collaborative response to zoonotic disease outbreaks. Additional benefits of establishing a formal, multisectoral coordination mechanism include identifying high-priority research areas and developing training opportunities for interdisciplinary outbreak response teams. Multisectoral collaborations should also be established at subnational levels. Identifying One Health focal points at the local, district, and regional levels is critical and the list of these designated contacts should be shared among sectors. These approaches will enhance cross-sectoral utilization of limited resources while leveraging each sector's capabilities for improved prevention, detection, and response of zoonotic diseases.

In some countries, formal, national collaborative One Health coordinating mechanisms were established to facilitate multisectoral engagement. Examples include the Zoonotic Disease Unit in Kenya, the Zoonotic Disease Secretariat in Cameroon, and the Guidelines for Coordinated Prevention and Control of Zoonotic Diseases in Vietnam (*17*). Creation of such mechanisms with dedicated financial and human resources will facilitate outbreak detection and response, prevention and control of high-priority endemic zoonotic diseases, and early detection and response to emerging health threats. They also allow countries to develop shared visions to maximize impact and build in measurements for success, and help design an overall plan for sustainability of cross-sectoral collaborations.

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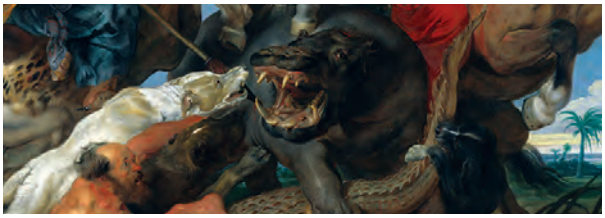
- Acute Encephalitis Syndrome and Scrub Typhus in India
- Hematophagous Endeavors, Fact and Fancy
- Processes Underlying Rabies Virus Incursions across US–Canada Border as Revealed by Whole-Genome Phylogeography



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- Opiate Injection–Associated Skin, Soft Tissue, and Vascular Infections, England, UK, 1997–2016

- Risk for Death among Children with Pneumonia, Afghanistan
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Frameworks for Preventing, Detecting, and Controlling Zoonotic Diseases

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Preventing zoonotic diseases requires coordinated actions by government authorities responsible for human and animal health. Constructing the frameworks needed to foster intersectoral collaboration can be approached in many ways. We highlight 3 examples of approaches to implement zoonotic disease prevention and control programs. The first, rabies control in Ethiopia, was implemented using an umbrella approach: a comprehensive program designed for accelerated impact. The second, a monkeypox program in Democratic Republic of the Congo, was implemented in a stepwise manner, whereby incremental improvements and activities were incorporated into the program. The third approach, a pathogen discovery program, applied in the country of Georgia, was designed to characterize and understand the ecology, epidemiology, and pathogenesis of a new zoonotic pathogen. No one approach is superior, but various factors should be taken into account during design, planning, and implementation.

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Rapid detection, response, and control of public health emergencies, including outbreaks of zoonotic diseases, can prevent the international spread of diseases and ensure global health security. In 2014, the Global Health Security Agenda (GHSA; http://www.ghsa.org) was launched to help countries achieve their World Health Organization International Health Regulations (2005) (*1*) obligations of establishing a framework for rapidly detecting, responding to, and controlling infectious disease threats. As of June 2017, a total of 59 countries agreed to contribute to the public health capacity-building efforts of the GHSA. These efforts focus primarily on 11 action packages; specific goals and objectives include preventing zoonotic diseases.

The prevention and control of zoonotic diseases impose a unique, often heavy burden on public health services, particularly in resource-limited settings. Because zoonotic diseases can deeply affect animals and humans, for many zoonotic infections, medical and veterinary health agencies have a large stake in disease surveillance and control activities. Collaboration between agencies is pivotal but takes time, requiring dedicated planning and well-exercised coordination of activities. Achieving this level of collaboration can be daunting in many real-world situations where resource disparities, differences in institutional culture and priorities, disparate legal authorizations, and many other factors can impede development of the formal structures needed to ensure effective implementation of disease prevention and control programs. Field observations and anecdotal reports suggest ongoing risks to human health, to the preservation of wildlife, and, in many cases, to livestock production—the last of which can compound human hardships by negatively affecting livelihoods—in the absence of formal structures that enable intersectoral collaboration.

One-sided disease prevention (enacted either by the human or animal health sector), although well-intentioned, often is inefficient at curtailing the spread of zoonotic infections. For example, in developing countries where canine rabies is still endemic, a rabies prevention program focused primarily on preventing human deaths by increasing access

to vaccines for postexposure prophylaxis (PEP), with little or no simultaneous investment in vaccination of dogs, will undoubtedly save lives but is not as cost-effective as investing in mass canine vaccination aimed at eliminating disease from the primary reservoir (*2*). In the absence of efforts to eliminate the source of the virus in dogs, the high costs associated with procurement, distribution, and administration of PEP will persist. Engaging animal and human public health sectors in the implementation of a comprehensive, multisectoral, rabies prevention and control program has a greater and more rapid impact on humans than does using a stand-alone PEP program (*2*). A comprehensive rabies prevention and control program should focus not only on the stockpiling of human rabies vaccine for PEP but also on dog population control, mass canine rabies vaccination, community education, laboratory diagnostic testing, and establishment of joint animal–human rabies surveillance and response systems (*3*,*4*).

Successfully enacting simple measures to promote coordination and multisectoral reporting of suspected disease outbreaks can significantly increase the likelihood of successful disease prevention and control program implementation in resource-limited settings. Jointly training community health workers to build local networks between and among animal and human health providers can empower and enable them to investigate and enact control measures in the context of suspected zoonotic disease outbreaks. A veterinary worker trained to recognize syndromes suggestive of zoonotic disease in humans and given the necessary skills and tools to alert public and animal health authorities on suspected cases can be integral to outbreak detection.

In many circumstances, a precondition for the successful integrated control of zoonotic diseases is the generation of a list of joint zoonotic disease priorities (*5*). Joint multisectoral disease prioritization is important for several reasons. First, a zoonosis of paramount concern to the agricultural or wildlife sector might be of lesser concern to practitioners of human health and vice versa. This lack of awareness between different sectors on how differing disease prevention and control activity affects one another and the overall disease burden reduces buy-in and motivation for allocating resources toward disease prevention and control by the lesser-affected sector. As an example, parapoxvirus infections can confer substantial rates of illness and death on juvenile goats, sheep, and cattle, but human infections are generally mild and self-limited (*6*). In the absence of a specific or new threat, public health authorities might be reluctant to contribute scarce surveillance and laboratory diagnostic resources to building coordinated detection and response capabilities around this infection. The discussion and deliberation of a One Health prioritization process can build consensus and commitment among diverse stakeholders for subsequent implementation activities. On the other hand, decision-makers in animal and human health sectors generally agree on rabies—which exacts a serious toll on humans, companion animals, and livestock alike—as a joint priority. The process of formal prioritization has the additional benefit of encouraging joint review of surveillance systems and data and other health-associated statistics in a deliberative process across ministries. Strengthening surveillance systems, laboratory diagnostic techniques, and response procedures can be applied to other zoonotic diseases with minimal additional investment.

Many possible models of joint program implementation strategies can be aimed at preventing and controlling zoonotic diseases. We highlight 3 distinct approaches that can be considered not only on the basis of resource availability (e.g., human and financial resources) but also on the nature of the disease (Figure 1). The first, rabies in Ethiopia (a Phase 1 GHSA country), illustrates the institution of a comprehensive or "umbrella" approach program for rabies prevention and control, which, although resource intensive, may have

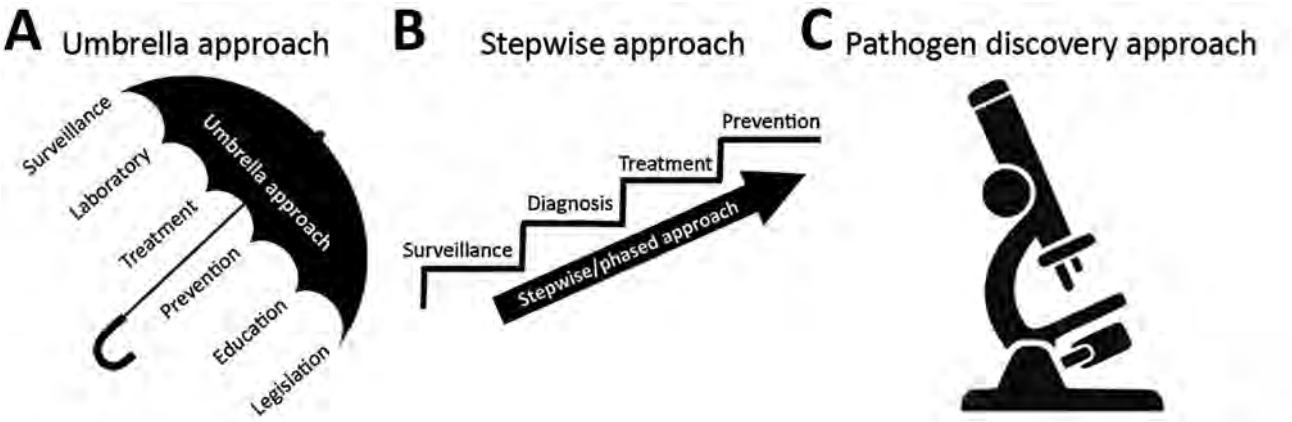

Figure 1. Three program approaches for implementing integrated zoonotic disease detection, prevention, and control programs. A) Comprehensive (umbrella) approach, designed to accelerate collaboration and impact. B) Phased (stepwise) approach in which each step builds on prior developed program areas and capacities. C) Pathogen discovery approach, based on the necessity of early intersectoral collaboration to generate knowledge in the context of discovering an emerging zoonotic pathogen, which can subsequently take an umbrella or stepwise approach for program implementation.

a more rapid and transformative effect on disease incidence. The second, monkeypox in the Democratic Republic of the Congo (DRC; a Phase 2 GHSA country), highlights a phased program or stepwise approach to building disease prevention and control capacity based on establishment of a robust foundation of surveillance, followed by augmentation of technical capacities during research activities. The final example is Akhmeta virus in the country of Georgia (a Phase 2 GHSA country). Akhmeta virus, first identified in 2013, causes a zoonosis thought to be derived from wildlife (*7*). The disease first came to light during a cattle-associated outbreak of cutaneous lesions among herders in Georgia. This example demonstrates a pathogen discovery approach that focuses on how discovery of a new zoonosis can stimulate innovation and the motivation for capacity development at the intersection of human, domestic animal, livestock, and wildlife health.

Approaches to Implementing Zoonotic Disease Prevention and Control Programs

Ethiopia—A Comprehensive (Umbrella) Approach

An example of the use of a comprehensive (umbrella) approach to program implementation is the Rabies Prevention and Control Program implemented in 2015 in Ethiopia. The program involves collaboration and partnership between the Ethiopian Public Health Institute, the Ministry of Livestock and Fisheries, Addis Ababa Urban Agriculture Bureau, and the US Centers for Disease Control and Prevention (CDC) directed toward priority zoonotic diseases identified by the Ethiopian government in September 2015. At the conclusion of the Ethiopia joint zoonotic diseases prioritization workshop, rabies was identified as the priority disease (*8*).

Canine rabies is endemic to Ethiopia; an estimated 105 dog bites/100,000 humans occur per year, and >1.7 deaths/100,000 persons are reported every year (*9*). A prominent element of the GHSA Zoonotic Diseases Prevention and Control Program is a pilot rabies prevention and control program in selected zones in 3 regions and the capital city, Addis Ababa. The rabies program, designed using an umbrella approach, has the potential to impact ≈10.6 million persons. The program was designed to ensure that the basic principles necessary to successfully control canine rabies could be enacted simultaneously in a coordinated manner.

In Ethiopia, the rabies prevention and control program incorporates laboratory-based surveillance; sustained canine mass vaccination programs; increased access to modern cell culture–based human rabies vaccines for PEP; and efforts around education, legislation, and government support. Simultaneous launch of a comprehensive suite of program components is challenging in resource-limited settings. Often for rabies, when resources are limited, vaccines for humans and animal-bite surveillance programs receive the highest priority for funding. Evidence-based program implementation has repeatedly demonstrated that eliminating rabies in dogs is the most cost-effective method to prevent and control the disease (*4*). Although several effective strategies exist for eliminating canine rabies, many countries lack the resources to implement such strategies effectively. The Ethiopia GHSA rabies program benefits from strategic investment of government engagement and intensive technical consultation and assistance, mainly possible because of the large amount of financial resources earmarked toward these efforts. Without such resources, an umbrella approach to program implementation might not have been feasible. International partner resources have supported supplemental staffing of surveillance officers, underwriting training and technical workshops, and procurement of laboratory equipment and consumable supplies. The cross-cutting, comprehensive nature of this program, incorporating elements from 9 of the 11 GHSA action packages (Table 1), is anticipated not only to save lives with long-term, cost-saving implications but also to serve as a platform for prevention and control of other zoonoses.

DRC—A Stepwise Approach

An example of the use of a stepwise approach for zoonotic disease program implementation is the monkeypox detection and prevention program in the Tshuapa Province of DRC, where human disease is endemic. The program began by establishing a strong public health laboratory–based surveillance system, which was used to then gradually introduce additional activities, such as research and applied public health (veterinary and human). Many questions remain about monkeypox virus, including the extent and nature of human-to-human transmission (e.g., whether specific high-risk behaviors are linked to transmission), the precise zoonotic reservoir(s) of the virus, and ecologic determinants of disease incidence (*10*). Evidence

Table. Capacity-building program areas included in zoonotic disease programs in 3 countries*

	GHSA Action Package										
	Prevent				Detect				Respond		
GHSA country†	AMR	Zoonotic diseases	Biosafety, biosecurity	Immunization	Lab	Surveillance	Reporting	Workforce	EOC	PH law	Medical counter
Ethiopia		√	√	√	√	√	√	√	√	√	
DRC		√	√	√	√	√		√			√
Georgia		√	√		√	√		√			

*AMR, antimicrobial resistance; DRC, Democratic Republic of the Congo; EOC, Emergency Operations Center, GHSA, Global Health Security Agenda; PH, public health.
†Ethiopia, GHSA Phase 1; DRC, GHSA Phase 2; Georgia, GHSA Phase 2.

suggests that waning vaccine-based immunity conferred by smallpox vaccination might contribute to the increased disease incidence in rural DRC (*11*).

In 2010, CDC partnered with the Kinshasa School of Public Health and the DRC Ministry of Health to strengthen laboratory-based surveillance for monkeypox in the Tshuapa Province. The program provided appropriate specimen collection kits and monkeypox-specific data collection tools; 2 training sessions for ≈60 local animal and human health workers, which emphasized a One Health approach to disease detection and response; the hiring of local staff to periodically reinforce surveillance principles at local public health offices at regular intervals; and diagnostic testing support at the national laboratory (*12*). These efforts increased the number and type of appropriate diagnostic specimens for monkeypox diagnosis submitted to the laboratory for testing (16-fold), the number of cases that were formally investigated (30-fold), and the proportion of laboratory-confirmed monkeypox cases (2.5-fold).

Ministry of Health officials attributed a more rapid recognition and response to the Ebola virus disease outbreak in Lokolia, Tshuapa, in 2014 to the cross-cutting nature and application of the training and surveillance activities provided by the monkeypox program, including reinforcement of key surveillance principles. Persons who had received training under this program ultimately held key leadership roles in the Ebola outbreak response. In addition, because of the multisectoral relationships established through the monkeypox program, Ministry of Agriculture authorities together with the Ministry of Health co-instituted and supported a temporary ban on the sale of animal carcasses suspected to be integral to the transmission of disease until bushmeat consumption could be ruled out as a vehicle for ongoing virus transmission.

The enhancement and reinforcement of a strong surveillance system for monkeypox has resulted in establishment of a foundation on which additional research activities can be added in a stepwise manner. The outcomes and effects have included development of a mechanism to identify geographic locations for longitudinal biologic sampling of wildlife to investigate suspected sylvatic animal species that could be reservoirs for monkeypox virus. Partners from the University of Kinshasa continue to be instrumental in helping design studies, conduct field work, and train young and motivated scientists in DRC. Together with ecologic research activities, epidemiologic research and response activities have been conducted to assess the extent and nature of human-to-human transmission, risk factors for zoonotic introduction of disease in communities, and the extent to which smallpox vaccination might or might not provide long-term protection against disease acquisition >30 years after routine childhood vaccination (*13*,*14*). A partnership with a Congolese educational entity (International Conservation and Education Fund) has proved particularly fruitful by providing evidence-based, locally vetted recommendations for disease prevention, including risks from exposure to wildlife, for tens of thousands of community members.

Overall, these and additional program and research efforts among multiple intersectoral partners greatly increased the capacity to detect and respond to monkeypox disease. Simultaneously, these efforts enabled the gain of critical pieces of scientific knowledge that can be used to protect human lives and develop more efficient evidence-based program implementation options.

Georgia—An Approach for New Disease Detection Programs

When an emerging zoonotic pathogen is detected, scientists can begin to study its epidemiology, ecology, and pathology using knowledge about closely related organisms as a starting point. Research and surveillance can be initiated simultaneously while in-country partners begin to learn and identify techniques related to sample collection, processing, and diagnostics and build information exchange systems among ministries to facilitate surveillance and response. As part of a joint research and capacity-building program, a coalition of intragovernment partners designed and implemented a research and surveillance program in Georgia using a One Health approach that focused on the new orthopoxvirus, Akhmeta virus, discovered in 2013 (*7*). After this discovery, CDC collaborated with partners at the National Center for Disease Control and Public Health (NCDC) and the National Food Agency in Georgia to initiate a response that focused on examining and collecting data on the epidemiology and characteristics of this virus while simultaneously building laboratory capacity to detect infections in humans and animals through ELISA, PCR, and sequencing diagnostic methods. Coordinated between CDC and the Ministries of Health and Agriculture, the work seeks to expand surveillance for orthopoxviruses while building a knowledge base through epidemiologic, ecologic, molecular, and immunologic research. Partners at NCDC, National Food Agency, and the Laboratory of the Ministry of Agriculture and CDC lead these efforts.

A major ecologic research effort also was initiated through this program to investigate the geographic distribution and seasonal dynamics of Akhmeta virus in potential small mammal reservoirs. At least 700 samples from small mammals have been collected from multiple locations. In addition, studies are under way to establish the burden of disease and identify possible risk factors for human and livestock infections. Samples from humans suspected to have orthopoxvirus infection are sent to NCDC for diagnostic evaluation and positive samples are characterized locally by nucleic acid sequencing and viral isolation.

Although still in its early phases, this collaboration, centered around detecting and investigating a newly identified zoonosis, already has resulted in the discovery of additional

instances of human orthopoxvirus infection in Georgia, a greater understanding of other prominent etiologies for cutaneous lesions, isolation of orthopoxvirus from terrestrial rodents, and enhanced collaboration around surveillance and response between the human and veterinary public health sectors. Each innovation has fostered intersectoral collaboration and capacity building across multiple technical areas.

Conclusions

GHSA is a global initiative that aims to accelerate the progress of participating countries toward achieving their International Health Regulations (2005) obligations of rapidly detecting, responding to, and controlling public health emergencies to enhance global health security. Minimizing the threat posed by zoonotic diseases is one goal of GHSA. The conceptual framework of One Health provides a model on which to build programs to successfully detect, prevent, and control zoonotic diseases (*15*). All 3 suggested approaches for zoonotic disease prevention and control program implementation underscore the importance of strong multisectoral collaboration, engagement, and commitment, essential principles of the One Health framework. Success can be achieved in many ways with any these approaches. A successful program can be designed to be overarching, involving the redesign of entire surveillance and/or laboratory systems to maximize interconnectedness, or it can be constructed to suit a specific context. Programs can focus on known gaps in prevention and control of a particular disease or consider the availability of resources to dictate selection of a specific approach. Optimal approaches will share a foundation of mutual interest across sectors and support a platform for coordinated actions. In the most streamlined form, basic program requirements should comprise surveillance and response activities (human and animal); laboratory diagnostic capacity; data analysis; reporting structures; and the determination of thresholds, triggers, or both that can signal the need for additional action. Recognition of disease in animals may signal the start of an outbreak in humans. Early detection of illness in livestock, companion animals, or wildlife (as was seen in the examples described in Ethiopia, DRC, and Georgia) can alert public health authorities that actions are needed to stem burgeoning risks to humans. Early detection is particularly important where humans heavily depend on livestock production or bushmeat and where peridomestic or domestic animals are prominent.

Establishing systems at the national level with subsequent replication and tiered proliferation to regional and subregional levels (i.e., decentralization) requires constant refinement and modification consistent with local capacities and needs. For a comprehensive program implementation, as described for rabies in Ethiopia, piloting the broad-based integrated system at several distinct locations was determined to be the key first step so that system gaps or inconsistencies could be addressed and costs estimated before nationwide implementation. In DRC, the program for monkeypox detection and control was built step-by-step on a platform of surveillance, with next steps determined by needs and gaps identified through evaluation of data and surveillance performance. Technical capacities were augmented through ongoing program enhancements and research activities. In Georgia, gaps in scientific knowledge about an emerging pathogen drove the initiation of integrated human, livestock, and wildlife disease surveillance and enhancement of laboratory and research capacity.

The lessons learned through the design and implementation of these programs are continuously derived from persons working at different levels of all contributing institutions. Most significantly, the work should focus on eliminating solely vertical program elements (i.e., those with few or no points of intersection across partner agencies) (Figure 2). Programs should instead work toward integration with existing programs and health systems (both human and animal) when feasible, with points of intersection at all operational levels. Second, continued reinforcement of the key principles and expected effect of the program from the highest levels of participating entities to the lowest is not only conducive to program success but also vital for ongoing material (e.g., financial) and personnel support.

Finally, an indispensable element of GHSA zoonotic disease prevention programs is training of the future workforce. Not just in the animal health sector, where

Figure 2. Three program approaches for implementing integrated zoonotic disease detection, prevention, and control programs. A) Comprehensive (umbrella) approach, Ethiopia. Photo credit: Ohio State University. B) Phased (stepwise) approach, Democratic Republic of the Congo. Photo credit: US Centers for Disease Control and Prevention. C) Pathogen discovery approach, country of Georgia. Photo credit: US Centers for Disease Control and Prevention.

sizable gaps are evident, but also training must be performed to ensure that human public health workers appreciate and know about the importance of veterinary medicine and animal health in controlling zoonotic diseases and that young, university-based scientists have the training and experience necessary to address questions and problems posed by endemic and emerging zoonotic diseases. The training of future public and animal health professionals is a huge component of all 3 programs described in this report.

Achieving the end goal of an effective, fully integrated program for preventing and controlling zoonotic diseases has many possible approaches. The 3 described here differ in their disease-specific context, but all were equally affected by the situation, the resource base, and the initial technical capabilities of the GHSA partner country in which the program was created. The suggested approaches for zoonotic disease program implementation have limitations. Scientific evidence is scant to support 1 approach over another. There is a need for increased zoonotic disease program evaluation and subsequent publication of empirically based recommendations for program design and implementation based on the identified strengths and weaknesses of various approaches. In the interim, national governments and partners can use the approaches we suggest as a guide during the program design phase when they consider suitable approaches for their specific context and settings.

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Use of a Diagonal Approach to Health System Strengthening and Measles Elimination after a Large Nationwide Outbreak in Mongolia

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Measles is a highly transmissible infectious disease that causes serious illness and death worldwide. Efforts to eliminate measles through achieving high immunization coverage, well-performing surveillance systems, and rapid and effective outbreak response mechanisms while strategically engaging and strengthening health systems have been termed a diagonal approach. In March 2015, a large nationwide measles epidemic occurred in Mongolia, 1 year after verification of measles elimination in this country. A multidisciplinary team conducted an outbreak investigation that included a broad health system assessment, organized around the Global Health Security Agenda framework of Prevent-Detect-Respond, to provide recommendations for evidence-based interventions to interrupt the epidemic and strengthen the overall health system to prevent future outbreaks of measles and other epidemic-prone infectious threats. This investigation demonstrated the value of evaluating elements of the broader health system in investigating measles outbreaks and the need for using a diagonal approach to achieving sustainable measles elimination.

Measles, a highly transmissible infectious disease that causes serious illness and death worldwide, is often referred to as a public health "canary in the coalmine" because it can be used as both a signal of weak health systems and a driver for strategies and policies to strengthen health systems (*1*). When programmatic weaknesses in immunization systems occur, measles is frequently the first vaccine-preventable disease (VPD) detected (*2–5*). Moreover, because of the high transmissibility of measles virus, the recognizable clinical presentation of nearly all cases in high-incidence settings, the high efficacy of the vaccine for prevention, and lifelong immunity after vaccination or acute infection, measles epidemiology generally reflects population susceptibility and indicates vulnerable communities, areas with lack of response capacity, and weaknesses in the health system (*6,7*). Measles elimination, therefore, becomes a useful vehicle to achieve broad strengthening of the overall health system (*8*). The "canary in the coalmine" approach to measles elimination efforts takes advantage of vertical strategies that focus on using surveillance data for action and to identify areas missed by vaccination, and of horizontal strategies that build systems and health services to sustain the gains and achieve broader objectives. The combination of these approaches has been described as a diagonal approach (*9*).

The Global Vaccine Action Plan (GVAP), approved by the World Health Assembly in 2012, set targets for vaccination coverage and a goal to achieve measles and rubella elimination in 5 of the 6 World Health Organization (WHO) regions by 2020 (*10*). In 2012, the Measles & Rubella Initiative partners launched the Global Measles and Rubella Strategic Plan 2012–2020 with targets aligned to the GVAP (*11*). Measles-driven policies and elimination strategies can provide opportunities for improving immunization service delivery performance, as well as strengthening health systems to help achieve the United Nations Sustainable Development Goals and Universal Health Coverage (*8,9,12*). The Global Health Security Agenda (GHSA) is a partnership between governments, multilateral organizations, and civil society launched in 2014 to promote global health security against infectious disease threats and drive full implementation of the WHO International Health Regulations (IHR 2005) (*13*), organized within a framework of Prevent-Detect-Respond (*14*). Recognizing that immunization is a key requirement to advancing global health security (*12*), the framework includes monitoring of measles vaccination

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coverage as a GHSA performance indicator, dovetailing with ongoing efforts to increase vaccination coverage and achieve measles elimination (*11*,*15*).

Mongolia, a WHO member state in the Western Pacific Region (WPR), participates in the GHSA (*16*) and has received support to strengthen IHR 2005 capabilities and response capacity for public health events of international concern. In 2009, Mongolia established an Early Warning, Alert, and Response Network (EWARN) (*17*) to supplement existing disease-specific, case-based surveillance systems by collecting syndromic event-based data from public primary health facilities. With GHSA support, a national public health Emergency Operations Center (EOC) and corresponding Incident Management System (IMS) were established in 2015 to coordinate response activities, particularly during outbreaks. In addition, satellite emergency response hubs termed Emergency Operations Points (EOPs) were established at national public health agencies.

In March 2014, the WHO WPR Verification Commission for Measles Elimination verified that measles elimination, which is defined as no measles case reported for 36 months in a country meeting required program performance indicators (*18*), had been achieved in Mongolia. However, in March 2015, multiple laboratory-confirmed measles cases were detected in the capital city, Ulaanbaatar; by June 5, 2015, a total of 11,181 suspected cases had been reported nationwide from all 21 provinces (*19*). The government of Mongolia requested that WHO and the US Centers for Disease Control and Prevention, in collaboration with the Ministry of Health and Sports (MOHS), conduct an outbreak investigation to assess factors contributing to ongoing transmission and provide recommendations for outbreak response and elimination strategies. In addition to identifying risk factors for transmission and evaluating the response vaccination activities and strategies, we used the measles outbreak as an opportunity to conduct a broader evaluation of the health system and emergency response strategies, following the GHSA framework, to prevent future outbreaks in Mongolia. Because nosocomial transmission of measles virus was identified early in the investigation as being a possible contributor to the outbreak, we conducted an assessment of infection prevention and control (IPC) practices in select healthcare facilities (HCFs). We also reviewed surveillance data, standard operating procedures (SOPs), and practices, and evaluated national emergency preparedness activities and response processes during the outbreak.

Methods

Outbreak Investigation

To better describe the epidemiology of healthcare-associated measles and to identify and recommend prevention measures, we reviewed data from case-based surveillance for March 1, 2015–June 26, 2016. Confirmed cases were either laboratory confirmed by positive test result for measles-specific IgM ELISA or PCR or clinically confirmed by meeting criteria of rash plus fever and $\geq$1 of the following: cough, coryza, or conjunctivitis. We also reviewed National Center for Communicable Diseases (NCCD) measles surveillance data for cases with onset during December 1, 2015–June 27, 2016, during which period-specific healthcare exposures were collected for case-patients. We defined healthcare-associated cases as laboratory-confirmed measles virus infection in a patient who was a healthcare worker (HCW) or who was hospitalized (non-HCW) during the 7–21 days (measles incubation period) preceding onset of signs or symptoms and who had an epidemiologic link to a hospitalized case-patient or lacked a known community source.

Assessment of IPC Policies and Practices (Prevent)

We assessed IPC practices at 3 hospitals in Ulaanbaatar with a large number of reported outbreak cases in surveillance data: 2 national referral tertiary care hospitals (1 of which was NCCD, the national HCF for infectious diseases) and 1 district hospital. We also assessed 1 primary care facility. At the 4 selected HCFs, we conducted structured interviews of facility staff and directly observed IPC practices and compliance with MOHS guidance and recommendations from previously published IPC documents (*20*–*25*). We reviewed MOHS occupational health policy, MOHS bulletins to HCFs, and HCF occupational health policies to evaluate vaccination and furlough policies.

Assessment of Surveillance (Detect)

We reviewed policies, SOPs, and protocols, conducted key informant interviews, and analyzed data for January 1, 2014–June 27, 2016. We used this information to assess national laboratory-supported measles case-based surveillance and EWARN surveillance for fever and rash syndrome.

Assessment of Emergency Preparedness and Outbreak Response (Respond)

We conducted interviews with key stakeholders at national and subnational levels of the emergency response system and reviewed EOC, EOP, and IMS SOPs. We identified and mapped roles, responsibilities, and mechanisms and verified them with stakeholders. After the investigation, we held a consultative training workshop with MOHS, NCCD, and Mongolia Field Epidemiology Training Program (FETP) staff to formulate specific recommendations on the basis of evidence from the investigation findings.

Findings and Recommendations

Outbreak Investigation

Of 33,947 confirmed case-patients with rash onset during March 1, 2015–June 27, 2016, a total of 14,407 (42%) were hospitalized and 2,222 (7%) reported visiting an HCF during the incubation period before rash onset, particularly during the initial phase of each of the 2 waves of intense transmission in 2015 and 2016, when ≈25% of cases had HCF exposure (Figure 1). During December 1, 2015–June 27, 2016, we identified 603 total healthcare-associated measles cases. Of these, 55 (9%) occurred in HCWs; 220 (36%) occurred in infants ≥9 months of age who were eligible for routine measles vaccination; and 448 (74%) occurred in infants ≥6 months of age who were therefore eligible for postexposure or outbreak response measles vaccination.

Prevent: IPC Assessment

Some IPC policies were available, but lack of corresponding infrastructure limited proper infection control to prevent measles virus transmission in hospitals. For example, we found inconsistent implementation of appropriate procedures for isolation or cohorting of confirmed measles cases; in addition, no negative pressure isolation rooms existed in any of the HCFs visited, and only 1 airborne isolation room existed in the country.

Policies and SOPs for measles contact tracing and postexposure prophylaxis (PEP) in HCFs existed; however, these recommendations were generally not practiced during the outbreak. The National Standard on Measles Surveillance Guidelines from 2003 recommended routine contact tracing of measles cases and, where appropriate, administration of measles-containing vaccine (MCV) or immunoglobulin as PEP (*26*). However, we found that contact tracing efforts in HCFs became quickly overwhelmed by the increasing case counts, primarily because of limited financial and human resources. Specific guidance for measles PEP in HCFs was not provided during the outbreak, and MCV and immunoglobulin supplies were not made available for PEP.

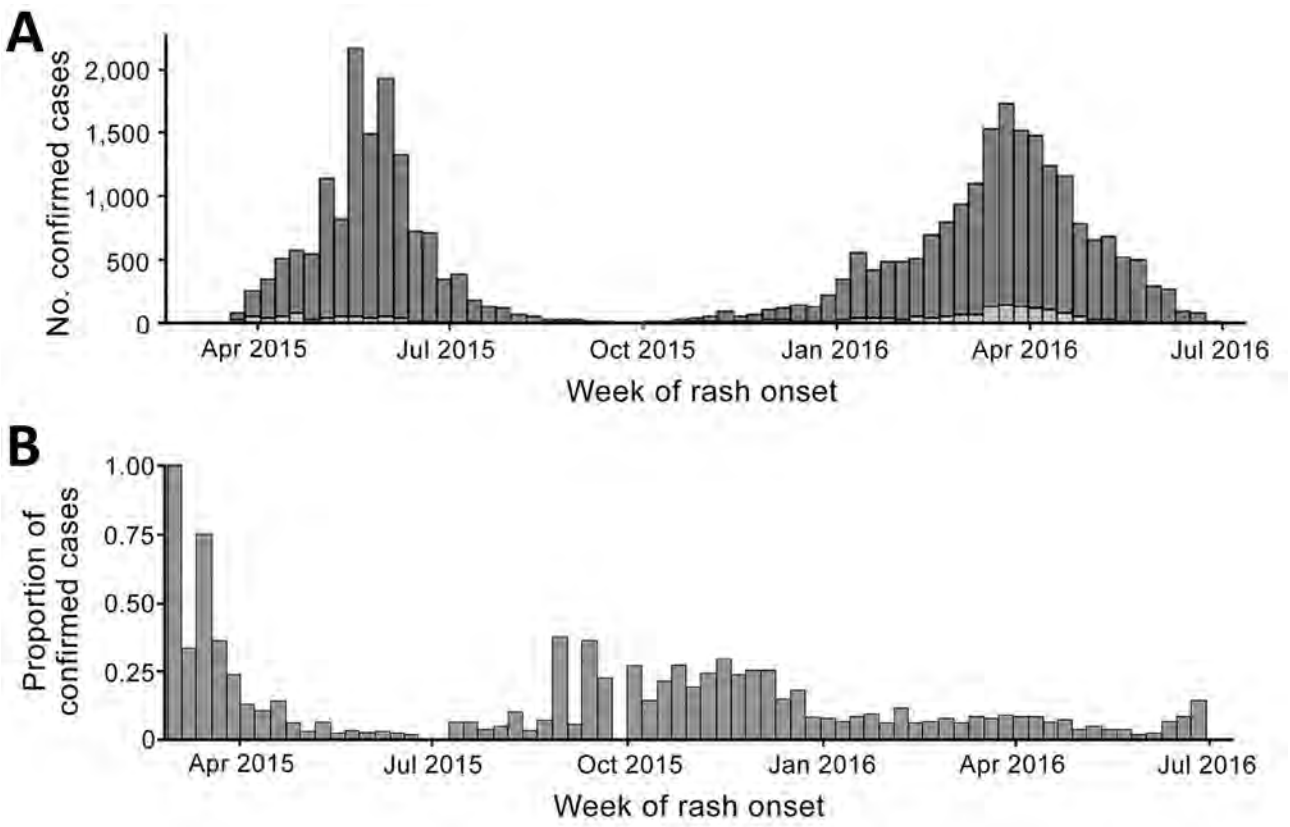

Figure 1. Confirmed measles cases in Mongolia, March 1, 2015–Jun 27, 2016. A) Confirmed cases by epidemiologic week of rash onset and reported exposure to a healthcare facility during the 7–21 days (measles incubation period) before rash onset. B) Proportion of confirmed case-patients by epidemiologic week of rash onset and reported exposure to a healthcare facility during the measles incubation period. Light gray indicates healthcare exposure during incubation period; dark gray indicates no exposure or unknown. Cases were confirmed by laboratory results (positive IgM ELISA or PCR) or clinical criteria (rash plus fever and ≥1 of the following: cough, coryza, or conjunctivitis).

Occupational health safeguards to prevent measles generally were not present. Proof of measles vaccination was not a mandatory condition of employment in HCFs; records of measles immunity status were not routinely kept at HCFs. Although MCV was reportedly offered to HCWs during the outbreak, we found inconsistent provision of the vaccine for HCWs, and records of staff vaccination during the outbreak were not available to review. Nonimmune HCWs were not furloughed or temporarily reassigned from patient care activities after measles exposure, unless and until febrile rash illness developed. In addition, HCWs who were furloughed did not receive a salary during the furlough period. Therefore, HCWs likely worked providing care to patients during the highly contagious period that begins 4 days before rash onset and lasts until 4 days after rash onset.

Detect: Disease Surveillance Assessment

According to surveillance protocols, cases detected by EWARN meeting the syndromic case definition of fever with maculopapular rash are investigated and also reported through the measles case-based surveillance system, using an individual case investigation form and collecting a specimen for laboratory testing for case confirmation. Surveillance protocols did not distinguish between appropriate procedures for routine surveillance and enhancements to surveillance that are needed during outbreaks and did not include parameters on when to scale back specimen collection or how to perform epidemiologic linkage for case confirmation.

Cases from epidemiologic and laboratory surveillance databases were not linked by using the standard practice of assigning unique identifiers to each case and specimen. More than 14,000 specimens were collected and tested during this outbreak, overwhelming the national reference laboratory and leading to delays in case confirmation. Epidemiologic linkage was not performed uniformly or according to the WHO WPR recommended case classification algorithm (*27*). Trends in EWARN and case-based surveillance were not routinely compared, and compatible cases detected by EWARN were not consistently reported and investigated through the case-based system. EWARN data indicated an initial increase in fever and rash cases beginning in epidemiologic week 17 of 2014. However, we found discrepancies between EWARN and case-based data in 2014, with much lower sensitivity in the case-based system, possibly leading to delayed detection of initial cases as many suspected cases were not investigated and tested. The first confirmed cases were detected in epidemiologic week 9 of 2015, in Ulaanbaatar and in Umnogovi Province, bordering China.

Respond: Emergency Preparedness and Outbreak Response Assessment

The IMS SOPs and staffing needs for the national EOC and HCF EOPs were still under development at the time of the outbreak, which limited the coordination capacity of the IMS during the outbreak. The EOC was not staffed until May 2016, as the outbreak was winding down, and even once staffed, it was never activated. Relationships between and roles of the EOC and EOPs were not clearly delineated. There was limited preallocation of resources and funding to the EOC and EOPs in the event of a public health emergency, delaying and constraining response activities. The response lead, termed the Event Manager in Mongolia, did not have the authority to release funds or resources without substantial review by supervisors, also delaying response activities. Frequent reassessments and/or risk assessments of the outbreak and response activities to ensure that needs matched the available resources were not performed. Finally, no national outbreak preparedness and response plan existed that identified the basic needs for measles outbreaks (i.e., vaccination, airborne precautions, laboratory support) or SOPs outlining airborne disease outbreak response activities.

The NCCD EOP was formally activated in December 2015 to lead the measles outbreak response. The NCCD EOP used a draft IMS proposal, and although the draft covered basic sections required in a public health emergency response (logistics and finance sections), the structure (Figure 2, panel A) did not mirror standard IMS structure as recommended by WHO (*28*). In addition, critical organizational subdivisions required for a successful measles outbreak response were not delineated in the structure, such as the inclusion of operations teams to support epidemiologic investigation (case investigation and contact tracing) and IPC activities (Figure 2, panel B).

Response demands exceeded the capacity of available NCCD EOP staff and resources, especially at the outbreak peak. No staff roster or surge capacity were available to mobilize staff from other national agencies that had applicable skill sets (e.g., epidemiologists, intensivists, logisticians, laboratorians, FETP) to address this deficit.

Selected Recommendations

As a result of our investigation, we developed several recommendations. These recommendations addressed the gaps in policy, practice, and infrastructure identified as likely contributing causes of the outbreak and sustained virus transmission.

Prevent

Recommendations for long-term systems strengthening included improving physical building infrastructure necessary for proper IPC of measles and other contagious respiratory diseases. In the short term, measles contact tracing and PEP in HCFs should be implemented according to existing national guidelines. MCV and immunoglobulin for

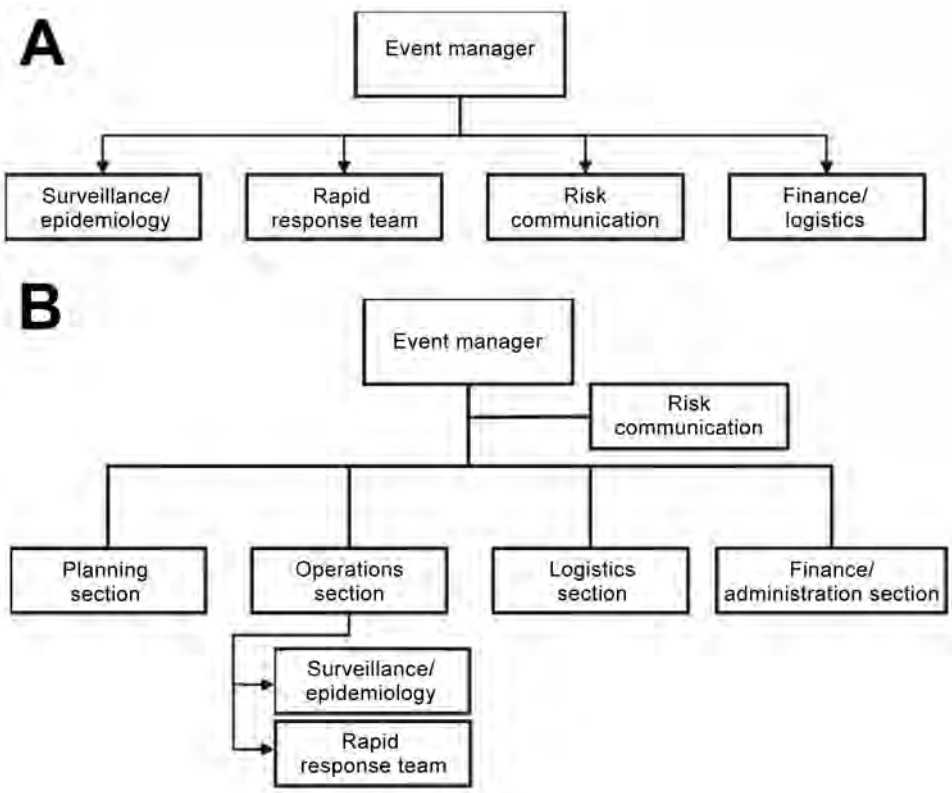

Figure 2. Flowcharts for organization of the Incident Management System in Mongolia during (A) and after (B) the 2015–2016 measles outbreak. Restructuring of the system after the outbreak was designed to better align with World Health Organization recommendations (*28*). Note that this figure does not represent a complete Incident Management System, only a restructuring of the existing system.

PEP should be stockpiled and mechanisms developed for rapid mobilization and delivery once a measles outbreak is confirmed. To limit healthcare-acquired transmission during measles outbreaks, only staff who have 2 documented MCV doses or evidence of immunity through serologic testing should be allowed to interact with patients (*29*). HCFs should maintain records of staff measles immunity status, proactively identify staff without immunity, and provide MCV. HCWs should be encouraged to remain at home when they feel ill and should not suffer financial losses for doing so.

Detect

A comprehensive surveillance review should be conducted to identify gaps in surveillance performance and improve data flow to decision makers for prompt, effective action. One of our key recommendations was to establish coordination mechanisms to align EWARN and case-based VPD surveillance systems so that cases are adequately and promptly investigated and so that trends in one surveillance system trigger enhanced surveillance mechanisms in the other surveillance system. In addition, we recommended improved linkage between epidemiologic investigation and laboratory testing, appropriate use of a unique identifier variable, and case classification including epidemiologic linkage for case confirmation.

Respond

We recommended that a national outbreak preparedness and response plan for measles and other airborne infectious diseases be established and agreed upon by all relevant stakeholders. Emergency response SOPs should be finalized as an urgent preparedness activity to map out the organizational structure per WHO recommendations, define the interaction of the EOC and EOPs, delineate procedures for activation and deactivation, define roles and responsibilities of positions in the IMS structure, and outline data flow and communication mechanisms with national and subnational staff and partner agencies (*28*). Emergency response SOPs should incorporate lessons learned from previous outbreaks and should be distributed to all stakeholders at each level of the public health system, including primary health clinics. The IMS could be strengthened by mapping out further subdivisions that are required for an effective outbreak response for airborne diseases (Figure 2, panel B). The EOC and EOPs should implement training for staff members regarding their specific roles in emergency response and run periodic exercises, using a mock measles outbreak scenario, to test the SOPs and emergency response capacity and coordination with relevant public health stakeholders outside of the EOC and EOPs. Systems breakdowns identified through these activities should lead to the refinement of emergency preparedness and response guidelines and other relevant SOPs, such as those for IPC and surveillance.

Conclusions

Until measles is eradicated worldwide, the risk for measles virus importations and subsequent outbreaks will remain in countries such as Mongolia that have achieved measles elimination. Prevention of large measles outbreaks that may occur after virus importations can be achieved by implementing measles elimination strategies, maintaining high 2-dose measles vaccination coverage, and developing robust capacity for rapid response. Measles outbreaks in postelimination settings can provide valuable lessons on how to prevent and overcome hurdles on the road to eradication and can reveal weaknesses in health systems that might undermine control efforts for other infectious diseases.

Preventing and controlling measles outbreaks require established policies and procedures that pay special attention to specific settings where measles virus introduction and sustained transmission may occur. For example, HCFs can serve as amplification points for outbreaks of measles and other infectious diseases (*30–33*). Given the universal challenges of efforts to quickly identify cases of infectious diseases and appropriately triage patients in busy HCFs, vaccination of all HCWs and use of PEP should be prioritized because these methods are likely the most effective strategies to prevent and reduce healthcare-associated measles.

Rapid detection and response to measles outbreaks is essential for elimination efforts and can prevent infections and reduce the number of deaths (*34,35*). The IHR 2005 and GHSA frameworks outline guidance on surveillance system strengthening to ensure countries have the capacity to detect and respond to outbreaks of VPDs such as measles, as well as new and emerging pathogens (*13,36*). As a part of this guidance, syndromic surveillance systems such as EWARN should be used to provide sensitive signals of major public health events but must be linked to systems for immediate case investigation, confirmation, and coordinated response activities, ideally through an incident management system or its equivalent. EWARN should be tightly linked with case-based surveillance through routine data sharing. Case-based surveillance is a key requirement for achieving measles and rubella elimination and provides the added benefit of being a standard against which signals from parallel syndromic surveillance systems such as EWARN can be checked and calibrated.

Achieving successful control of measles outbreaks requires a multifaceted strategy involving surveillance, laboratory capacity, contact tracing, vaccination, and hospital IPC measures; thus, maintaining a capacity for coordination of activities is critical for an effective, cohesive outbreak response (*37*). During measles outbreaks, the speed and completeness of response measures are critical and dictate the extent of measles transmission and burden of disease (*38*). Delaying or poorly implementing response efforts such as contact tracing and targeted vaccination can lead to an exponential increase in additional exposures, infectious cases, hospitalizations, and substantial geographic spread, which can quickly overwhelm existing healthcare infrastructure, leading to further amplification of the outbreak. Examining overall national emergency response capacity is essential not only to evaluate how the country will react to another measles outbreak but also to identify gaps that are applicable to other potential epidemic-prone diseases. Our multidisciplinary assessment resulted in specific, actionable recommendations for strengthening the structure and effectiveness of emergency response planning, which, if properly implemented, will have a wide-reaching effect on the reduction of illness and death during public health emergencies.

The broad health systems assessment we conducted, following the Prevent-Detect-Respond framework of the GHSA, is an example of one tactical element of a comprehensive diagonal approach to link measles elimination with immunization program and health system strengthening. Other proposed tactical elements included reaching the chronically unreached by using measles risk assessments and campaigns to identify and target underserved populations and geographies; introducing routine use of a second dose of measles vaccine to create new opportunities to receive vaccines and other child health interventions in the second year of life and beyond; and advocating for measles elimination to support institutions, policies, and practices needed to sustain high-quality immunization programs (*9*). The diagonal approach has successfully leveraged activities aimed at specific disease elimination or eradication efforts to strengthen health systems and overall immunization service delivery performance. For example, in several settings, including South Korea, Sri Lanka, the United States, and some provinces in China, school entry vaccination check laws have had a broad effect on overall coverage and equity of immunizations (*39–44*). Similarly, strengthening laboratory-supported surveillance systems and outbreak response capacity (including local epidemiologic capacity through FETP programs) to achieve elimination enables improved capacity to monitor surveillance performance and to detect other VPDs, such as yellow fever, Japanese encephalitis, and emerging diseases such as Ebola and Zika. For example, the existing polio eradication infrastructure in West Africa was a critical platform that was leveraged to enable rapid case detection, investigation, confirmation, and contact tracing as part of the Ebola outbreak response during 2014–2015 (*45*). In addition, established case-based surveillance systems for measles or dengue have been used to detect cases of Zika in settings where that disease is an emerging epidemic (*46*).

When measles outbreaks occur because of gaps in the confluence of multiple sectors of health systems that include immunization, IPC, surveillance, and emergency response, the GHSA framework provides useful tools to leverage outbreak investigations to strengthen the overall health system and prevent future outbreaks of measles and other infectious disease threats. In this way, GHSA investments to Prevent-Detect-Respond reduce rates of illness and death. Even relatively small measles outbreaks can have substantial cost implications (*7*); investments in measles vaccination in low- and middle-income countries yield a positive economic return on investment of 27–67 times the cost (*47*). By using the substantial multilateral investments by countries and donors to global health partnerships including GHSA, GVAP, and the Measles & Rubella Initiative to strategically strengthen health systems with a diagonal approach to measles elimination, this positive return on investment could become exponentially higher.

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Enhancing Workforce Capacity to Improve Vaccination Data Quality, Uganda

Kirsten Ward, Kevin Mugenyi, Amalia Benke, Henry Luzze, Carol Kyozira, Ampeire Immaculate, Patricia Tanifum, Annet Kisakye, Peter Bloland, Adam MacNeil

In Uganda, vaccine dose administration data are often not available or are of insufficient quality to optimally plan, monitor, and evaluate program performance. A collaboration of partners aimed to address these key issues by deploying data improvement teams (DITs) to improve data collection, management, analysis, and use in district health offices and health facilities. During November 2014–September 2016, DITs visited all districts and 89% of health facilities in Uganda. DITs identified gaps in awareness and processes, assessed accuracy of data, and provided on-the-job training to strengthen systems and improve healthcare workers' knowledge and skills in data quality. Inaccurate data were observed primarily at the health facility level. Improvements in data management and collection practices were observed, although routine follow-up and accountability will be needed to sustain change. The DIT strategy offers a useful approach to enhancing the quality of health data.

Optimal immunization coverage against vaccine-preventable diseases (VPDs) is essential for achieving and maintaining global health security. Obtaining such coverage relies on high-quality immunization data, which are a prerequisite for good decision making; effective and efficient public health action, monitoring, and evaluation; and improved population immunity against VPDs (*1–3*). Enhanced demand for vaccination data and scrutiny of their quality are evident in strategic guidance documents for the Global Polio Eradication Initiative (GPEI) (*4*), the Global Vaccine Action Plan (*5*), and the recently introduced data quality requirements for financial support from Gavi, the Vaccine Alliance (*6*). Availability and quality of vaccination data are often inadequate to inform policy, effective management, and monitoring of vaccination programs (*3,7,8*).

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In 2013, Uganda conducted a national data quality self-assessment (DQS) (*9*) (Ministry of Health, Uganda, unpub. data) and found that the quality of administrative vaccination data was suboptimal, particularly at the subnational level, which was likely contributing to inflation of administrative coverage data (*10*). Reasons for poor data quality included inaccurate vaccine dose administration data generated at the health facility, deficiencies in healthcare worker knowledge and skills, scarcity of standard recording and reporting tools, and inadequate implementation of recommended practices for data management collection, analysis, and use. Many of these issues had been previously identified in Uganda and elsewhere (*8,10–12*). To guide implementation of recommendations from the DQS, the technical working group for the Ugandan National Expanded Program on Immunization (UNEPI) developed the National Data Quality Improvement Plan. This plan laid out how, and at what level, the recommendations would be addressed, recognizing limited published evidence regarding effectiveness of specific approaches to strengthen immunization data quality (*3,12,13*). Given the importance of an effective workforce, a central component of the Data Quality Improvement Plan was to enhance the capacity of existing healthcare workers to manage, analyze, and use vaccination data. The chosen approach was guided by growing evidence supporting on-the-job training of healthcare workers that includes feedback and follow-up (*14*), which had previously been used successfully in Uganda (*15,16*). This article describes the initial implementation (November 2014–September 2016) and outcomes of Uganda's national strategy to improve administrative vaccination data quality, defined by the dimensions of management; collection; data produced (accuracy, timeliness, completeness); analysis; and use (*17*).

Methods

Preparation for the Data Improvement Team Strategy

The data improvement team (DIT) strategy was developed and managed by a national DIT strategy management group, which included UNEPI, the Resource Center (the

responsible entity for managing health information) of the Uganda Ministry of Health, World Health Organization (WHO) Uganda, the US Centers for Disease Control and Prevention (CDC), the African Field Epidemiology Network (AFENET), UNICEF, and Gavi. Implementation was funded jointly by Gavi Health Systems Strengthening Grant 1, WHO, UNICEF, and CDC and led by a national coordinator from AFENET, with technical assistance from CDC.

The strategy aimed to strengthen the immunization information system and quality of the resultant data at the district and health facility levels through practical classroom training, deployments involving rapid data quality and organizational assessments, and on-the-job training (Figure 1). The number of DIT members required for each district was determined on the basis of ability to reach all health facilities that provided immunization services in that district (range 6–117) within 5 to 6 working days, spending 2 to 3 hours at each. A district-level DIT included an average of 4 district staff members (with additional members in high-population areas) and 1 Makerere University School of Public Health (MakSPH) student. Districts were asked to identify staff to form a DIT, which included the district biostatistician, district Expanded Programme on Immunization (EPI) and surveillance focal persons, and a health records assistant. MakSPH staff and the national DIT coordinator led recruitment of students.

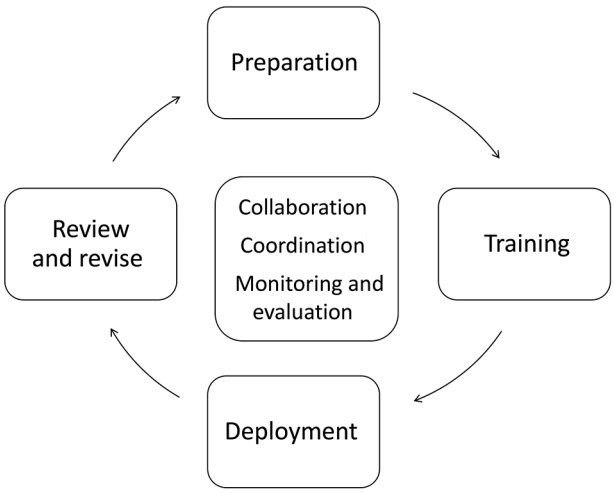

Figure 1. Overview of processes and key activities of the Uganda data improvement team (DIT) strategy to improve vaccination data quality. At the center are elements that are ongoing throughout implementation of the 4 main activities: financial, technical, and logistical collaboration between Expanded Program on Immunization partners, coordination provided by a DIT strategy management group and the DIT national coordinator, and routine monitoring and evaluation. Preparation includes discussing and developing budget, designing the approach to implementation and materials for training and monitoring and evaluation, training supervisors, grouping districts into regions, and identifying DIT members. For training, grouped by region, DIT members from several districts attend a 3-day training led by staff from the Ministry of Health Expanded Program on Immunization and the DIT strategy national coordinator. This training included a combination of technical lectures, practical case studies (80% of all sessions), and a practice visit to a health facility (half-day). Deployment core activities include district and health facility organizational assessment and a rapid data quality improvement questionnaire to identify strengths and gaps in resources and systems for immunization data management, collection, analysis, and use. Results inform recommendations developed by the DIT members who provide on-the-job training of staff to strengthen action on recommendations. DIT members debrief leadership (region, district, health facility) on findings and recommendations, and harness support to implement recommendations. Finally, national DIT strategy management groups review activities and results at several time points (Figure 2); based on evidence from implementation and current national priorities, the strategic and operational approaches are revised, then reimplemented.

The DIT strategy was designed to be implemented in a phased approach by region (Figure 2); several district-level DITs were trained together, then deployed in their respective districts. All official government districts in Uganda as of November 2014 were divided into 17 DIT operational regions to ensure that the number of attendees at regional training was logistically manageable and there was close geographic proximity between districts in each region.

Training

Before implementation, a 5-day orientation to the strategy and Uganda's immunization information systems was provided to national staff, who self-selected to support delivery of the regional-level training and to conduct supportive supervision of DIT activities. The 3-day regional training aimed to build selected DIT members' knowledge and skills in data management and quality, which were applicable during the DIT deployment and their regular duties thereafter (Figure 1).

Deployment

In the week after each regional training, DIT members were deployed to their home districts for 5 to 6 days to work at the district office and visit health facilities (Figure 1). Working in pairs, DIT members identified problems, proposed solutions, developed recommendations, and enhanced staff capacity through on-the-job training on locally identified problems (e.g., how to create an immunization monitoring chart) (Figure 2). DITs initially prioritized health facilities with outlying (high or low) coverage for the third dose of the diphtheria/tetanus/pertussis/*Haemophilus influenzae* type B/hepatitis B vaccine (Penta3), negative dropout rates, or inadequate completeness or timeliness of Health Management Information System (HMIS) monthly reports (*18*). Staff from the Ministry of Health and national EPI program partner organizations provided supportive supervision to DIT activities

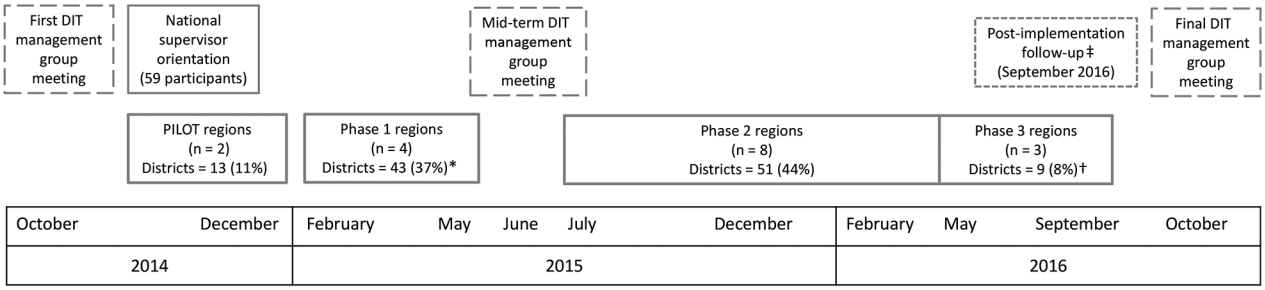

Figure 2. Implementation timeline for the DIT strategy to improve vaccination data quality, Uganda, 2014–2016. Systematic comparison of the number of doses of vaccine recorded on the paper-based monthly HMIS report and the electronic HMIS data was conducted only in the first 48% (n = 56) of districts where the DIT strategy was implemented. *Design of training curriculum changed to enhance delivery through case-study–based and practical sessions. Additional content was added in the following areas: monitoring and evaluation activities for the DIT strategy, supportive supervision, and development of specific, measurable, achievable, realistic and time-bound recommendations. †Mobile application introduced for DIT members to report results from organizational assessment and data quality improvement questionnaire. ‡Postimplementation review conducted in sample of districts and health facilities. DIT, data improvement team; HMIS, Health Management Information System

in some districts, assisting coordination and implementation of activities, conveying national-level support for the DIT strategy to district leadership, and enhancing their own awareness of ground-level operations.

Monitoring and Evaluation

A participatory and utilization-focused (*19,20*) approach was taken to routine monitoring and evaluation of processes, outputs, and short-term outcomes. Training was evaluated through a self-administered survey focused on quality of the training experience; a pretest and posttest measured participants' acquisition of knowledge and level of preparedness to implement DIT activities. DITs conducted an organizational assessment at the district and health facility levels to inform their work and to gather baseline information on key indicators (*21*). Organizational assessments contained a mix of closed and open questions covering dimensions of, and factors affecting, vaccination data quality. Results of organizational assessments were reported to the DIT national coordinator either through a reporting template in Excel (Microsoft, Redmond, WA, USA) (106 districts, 1 Kampala division) or by using an open data kit–based mobile application linked to a cloud-based database (5 districts, 4 Kampala divisions).

At the health facility, DITs also used a data quality improvement (DQI) questionnaire to review practices for data management, collection, accuracy, analysis, and use (Table 1). The primary purpose of this questionnaire was to identify gaps that would inform recommendations and on-the-job training. For purposes of analysis for monitoring and evaluation, DQI questionnaires from health facilities were sampled from 107 of the 116 districts (92%) for which these data were not reported through the mobile application. The sample included all hospitals and every second health facility selected from an alphabetized list, until the sample size reached 50% of all health facilities in the district. In an additional 7 districts, DQI reports from all visited health facilities were entered in the mobile application. Descriptions of the DIT activities, outputs, and recommendations were presented in a written report for each district health management team. Line-listed results from organizational assessments and DQI questionnaires were aggregated nationally and quantitative data were descriptively analyzed in SAS version 9.3 (*22*) and Tableau version 9.3.1 (*23*). The sign test was used to assess the statistical significance of the direction of difference between sources of vaccine dose administration data and was performed in R version 1.5.1 (*24*).

After DITs had been deployed to all districts, a review of DIT implementation was undertaken to gather feedback about the approach and understand extent of action on recommendations through a rapid organizational-level survey in a sample of districts and health facilities. Four regions were selected from the 17 DIT operational regions; 2 or 3 districts were selected from each region, and within each of these, 4 health facilities were selected, totaling 11 districts and 44 health facilities. If a selected site could not be visited, it was replaced with the next one of the same type on an alphabetized list of health facilities in the district. Selection was purposeful to gain insights across a range of characteristics, including geographic location, implementation of national supervision, Reaching Every District categories (*25*), and level (type) of health facility (*26*). Eight data collectors (4 AFENET/CDC staff and 4 MakSPH students) completed a 1-day training, then worked in pairs to visit the selected sites to conduct the survey through group interviews with district and health facility staff. Resultant data were descriptively analyzed in Epi Info software (*27*).

Table 1. Reach and key observations in district and health facilities from the first phase of the data improvement team strategy to improve vaccination data quality in Uganda*

Data quality domain	Description	Districts, no. (%)	Health facilities, no. (%)
DIT strategy reach	District and health subdistrict staff trained	454 (NC)	NC
	District and health subdistrict staff deployed as DIT members	441 (NC)	NC
	Districts reached	116 (100)*	NA
	Districts where harmonization of monthly report and DHIS2 data conducted	48 (56)*	NA
	Health facilities (that provided immunization services) reached	NC	3,443 (89)†
Knowledge and practices			
Collection	Process for incorporating late HMIS monthly reports (HMIS105) into the DHIS2	98 (84)‡	NC
	Known (documented) target population <1 y of age	NC	1,797 (53)§
	Demonstrated use of immunization data recording and reporting tool		
	Child register	NC	2,713 (78)§
	Tally sheet	NC	2,847 (84)§
	HMIS monthly report forms	NC	3,086 (91)§
	Vaccine control books	NC	1,980 (58)§
Analysis	Monthly immunization coverage for Penta3 charted on a monitoring chart	NC	1,099 (32)§
	Monitoring chart of immunization coverage for Penta3 displayed	NC	1,153 (34)§
Use	Demonstrated use of immunization data to inform action	79 (68)‡	1,503 (44)¶
Management	Old copies of immunization data are archived in an organized and easy-to-locate manner		
	Child register	NC	2,367 (70)§
	Tally sheet	NC	2,239 (66)§
	HMIS monthly report forms	87 (75)‡	2,455 (72)§
	External factors		
Collection + analysis + use	Inability to access the DHIS2 in ≥1 month in the 3 months before DIT visit	56 (48)‡	NC
Management + collection + analysis + use	Presence of specific roles# responsible for immunization data management and reporting	107 (92)‡	1,399 (41)¶
Collection	Blank copies of immunization data collection tools available at time of DIT visit		
	Child register	NC	1704 (50)§
	Tally sheet	NC	2,459 (72)§
	HMIS monthly report forms	NC	1,706 (50)§
	Vaccine control books	NC	1,806 (53)§

*A total of 112 districts plus the 5 Kampala divisions each were considered a separate district for DIT strategy operational purposes. Total DIT strategy operational districts = 116. Data from Ugandan Ministry of Health, November 2014. DHIS, District Health Information System; DIT, data improvement team; HMIS, Health Management Information System; NA, not applicable; NC, not calculated; Penta3, diphtheria/tetanus/pertussis/*Haemophilus influenzae* type b/hepatitis B vaccine, third dose.
†Of 3,856 health facilities that provide immunization services, identified by the DITs at time of visit.
‡Of 116 DIT strategy districts where the DIT district checklist was completed during deployment.
§Of 3,392 health facilities where the data quality improvement tool was completed by DITs.
¶Of 3,443 health facilities where the health facility checklist was completed by DITs.
#At district, these roles included an HMIS focal person or biostatistician. At health facility, roles included health records assistant or health information assistant.

The proportion of health facilities in a district submitting monthly HMIS reports on time to the district (timeliness) and the proportion of expected reports received by the district (completeness) are routinely calculated in the national electronic HMIS (*12,18*). In districts for which these data were available for the 3 months and after the DIT visit (n = 104) and for the second 3-month period after the DIT visit (n = 95), timeliness and completeness, by month and district, were extracted from the electronic HMIS. Median timeliness and completeness were calculated per district across each 3-month period, then compared between periods to identify change.

Review and Revision

The national DIT strategy management group held periodic meetings (Figure 2) to review results from monitoring and evaluation and the budget, as well as to solicit feedback from all stakeholders. These meetings, in conjunction with national priorities, informed any adjustment of DIT activities and implementation plan.

Results

Training and Deployment

During November 2014–September 2016, all 112 districts and 5 divisions of Kampala (total 116 DIT operational districts) in Uganda sent staff to DIT regional training and deployed district-level DITs. Seventeen regional trainings, covering 2–14 districts per training, attended by 451 district and health subdistrict staff and 35 MakSPH students (some attended multiple trainings [range 1–9]). In response to participant and stakeholder feedback, the training format was altered to enhance the balance between the practical and didactic sessions (Figure 2). After training, 83%

(355/429) of district staff demonstrated improved knowledge on posttest compared with pretest scores, and more participants felt "fully prepared" to conduct DIT activities (14% pretest, 82% posttest).

In total, 476 DIT members (including 35 MakSPH students) were deployed and reached 89% of health facilities that provided immunization services (Table 1). Health facilities not visited (n = 413) were predominantly health center IIs (HCIIs; n = 332, 80%), which offer a limited number of services, serve smaller catchment areas, and are often geographically remote. Initially, DITs reviewed paper copies of monthly HMIS reports from health facilities submitted to the district office and compared doses reported for all antigens with those recorded in the electronic HMIS for the 12 months before the DIT visit (Table 1). Time spent on this activity reduced the time available to reach all priority health facilities by an average of 8 hours per district. Because early results showed high congruence between these 2 data sources (Figure 3, panel D), this activity ceased after the midterm review meeting, enabling DITs additional time to conduct organizational and DQI assessments and develop recommendations for improvement (average 1.2 hours per health facility) and to implement on-the-job training (average 1.5 hours per health facility).

Through the organizational assessment, DQI questionnaire, and discussions with staff, DITs identified a combination of external factors, often specific to the site visited, that affected vaccination data collection, management, analysis, and use. Commonly identified challenges included poorly motivated, new, untrained, or absent staff; unavailability of materials for recording and reporting

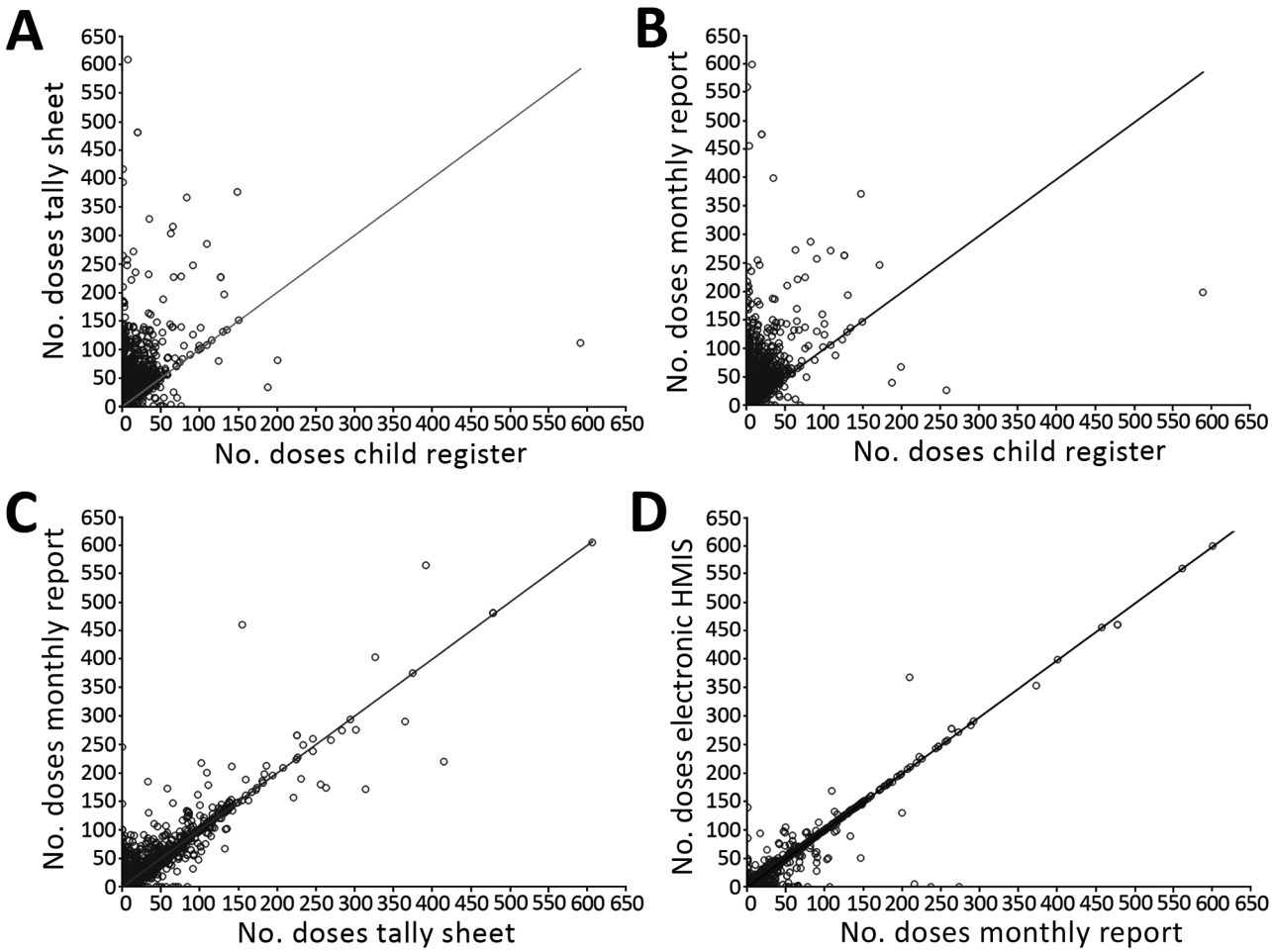

Figure 3. Comparison of the number of doses of Penta3 recorded on different vaccine dose recording and reporting tools, Uganda. A) Doses recorded on tally sheet compared with immunization register (n = 1,664 health facilities); B) doses recorded on monthly report compared with immunization register (n = 1,686 health facilities); C) doses recorded on monthly report compared with tally sheet (n = 1,713 health facilities); D) doses recorded on the HMIS compared with monthly report (n = 1,661 health facilities; 3 outliers not shown [total no. doses >650]). p<0.001 for all comparisons. Data from sample of 2015 DQI tools; 1,667 (83%) sampled from 107 districts and 343 (17%) from a census of 7 districts. Data were missing from 2 districts. HMIS, Health Management Information System; Penta3, diphtheria/tetanus/pertussis/*Haemophilus influenzae* type b/hepatitis B vaccine, third dose.

data; competing priorities on staff time due to integration of services; inadequate supportive supervision for data quality; limited transport, technological, and financial resources; variable understanding and commitment by political or organizational leaders; and competition with other public health initiatives for human, financial, and material resources.

In Uganda, doses of vaccines administered are recorded on 4 tools: tally sheet, child register, and monthly report (at health facility) and the electronic HMIS (entered at district level using data from health facilities' monthly report). We found variable congruence between monthly totals of vaccine doses across these 4 sources for any given month (Figure 3). On average, the number of administered doses aggregated on the monthly report was higher than that recorded individually on the tally sheet (Figure 3, panel C), which was higher than that recorded on the child register (Figure 3, panel A). This finding suggests that vaccine administration is overreported by the health facility and that use of the child register is low compared with other sources of vaccine dose administration data (Figure 3, panels A, B). We found stronger agreement between the number of doses on the paper HMIS monthly report and those in the electronic HMIS (Figure 3, panel D), highlighting infrequent transcription error or loss of data from district to national level. There was individual variation in the discordance by health facility, with no clear pattern by district or health facility type. Similar patterns in data congruence were also seen for single-dose measles vaccine offered to older children (data not shown).

Postimplementation Follow-Up

The postimplementation follow-up survey found that DITs had visited all sampled districts (n = 11) and 77% (34/44) of sampled health facilities. Recommendations provided by DITs addressed all dimensions of data quality; however, the extent of implementation varied (Table 2). Recommendations for each district most frequently related to improving systems for archiving, checking data on monthly HMIS reports, and charting coverage data. At the district level, recommendations relating to data management and collection were more fully implemented than those related to analysis and use (Table 2). Recommendations for health facilities most commonly focused on improving recording and reporting of data, analysis, and archiving. Recommendations related to management and collection were more completely implemented than those related to analysis. No health facility reported taking action on recommendations to improve data use (Table 2). Reasons for inaction across all recommendations included insufficient availability of required materials (standard data collection/reporting tools, archiving space); inadequate human resource capacity (new staff, untrained staff, low motivation); and a management structure that limited staff awareness of, and roles in, immunization data collection, management, analysis, and use.

During the follow-up survey, district staff frequently reported that participation in the DIT activities catalyzed improvements in existing, or development of new, systems and processes, such as supportive supervision about vaccination data quality. Health facility staff felt that the visit by the DITs was a catalyst for provision of updated recording and reporting tools and helped them develop systems to

Table 2. Key themes from DIT recommendations to improve vaccination data quality and extent of implementation of these at follow-up in select districts and health facilities in Uganda*

Theme of recommendations	Districts, no. (%), n = 11				Health facilities, no. (%), n = 34			
	Completely implemented	Partially implemented	Not at all implemented	Unable to determine	Completely implemented	Partially implemented	Not at all implemented	Unable to determine
Analysis and use of EPI data, including monitoring charts	2 (22)	1 (11)	6 (67)	0	8 (32)	9 (66)	8 (32)	0
Archiving of data	3 (38)	3 (38)	1 (12)	1 (12)	11 (61)	5 (28)	2 (11)	0
Meetings to review results	0	0	1 (50)	1 (50)	†	†	†	†
Recording and reporting of data	1 (20)	1 (20)	2 (40)	1 (20)	16 (49)	6 (18)	7 (21)	4 (12)
Systems for review/checking of reported data	3 (43)	0	3 (43)	1 (14)	2 (40)	2 (40)	1 (20)	0
Use of immunization data for decision making	1 (50)	1 (50)	0	0	0	0	5 (100)	0
Improve accuracy and knowledge of catchment area population	†	†	†	†	1 (50)	0	1 (50)	0

*District and health facilities visited during postimplementation follow-up that showed evidence of visit from DIT. DIT, data improvement team; EPI, Expanded Programme on Immunization.
†Theme not identified at this level.

Table 3. Extent of self-reported changes catalyzed by the DIT visit to improve vaccination data quality in select districts and health facilities in Uganda*

Area of change	No. (%) districts reporting change, n = 11	No. (%) health facilities reporting change, n = 34
Supportive supervision visits include review and follow-up on quality of vaccination data	9 (82)	†
Routine checking of accuracy of data entered into the DHIS2	8 (73)	†
Checking completeness and accuracy of monthly report data before acceptance	8 (73)	†
Analysis and use of data	6 (55)	†
Archiving of data	6 (55)	†
Changes in supply of recording and reporting tools	†	18 (53)
Checking monthly report data with primary data source	†	18 (53)
Improved practice in recording data on tally sheets and child register	†	50 (17)
Analysis and use of immunization data	†	47 (16)

*District and health facilities visited during postimplementation follow-up that showed evidence of visit from DIT. DHIS, District Health Information System; DIT, data improvement team.
†Change in this area not reported at this level.

enhance completeness and accuracy of data reported on the monthly HMIS report (Table 3).

Timeliness and completeness of HMIS monthly reporting (from health facility to district) averages >90% nationally (*28*). This high performance limits the opportunity for and measurement of change; however, there was some improvement. Comparing 3 months before and after DIT implementation, 15% (15/104) of districts showed improvement in completeness, 6% (10/104) decreased completeness, and the remainder no change. From the initial 3 months to the second 3 months post-DIT implementation, completeness improved in 25% (24/95) of districts, decreased in 10% (9/95), and showed no change in the remainder. More districts showed improvement in timeliness of monthly HMIS reporting. Comparing 3 months before DIT implementation to 3 months after, 38% (40/104) improved, 20% (21/104) decreased, and the remainder showed no change in timeliness. From the first to second 3-month periods after implementation, 27% (26/95) of districts showed improvement, 50% (47/95) decreased, and the remainder showed no change.

Discussion

EPI partners in Uganda took a collaborative approach to developing, funding, and implementing a strategy to address recommendations from Uganda's most recent DQS. Over 23 months, 351 district staff and 35 MakPSH students were trained and 479 DIT members were deployed, in phases, to all districts and 89% of health facilities that provide immunization services in Uganda. Rapid assessments of organizational-level immunization information systems and accuracy of resultant data identified gaps in skills and systems for data management, collection, analysis, and use. Assessments indicated that the child register was underused, and the tally sheet was used as the primary data recording tool, with greater variation in the difference between these primary data sources than for data aggregated at the district and national levels. Timeliness and completeness of HMIS monthly reports from health facilities was high at baseline; although some districts showed improvement, there was volatility in these changes. Recommendations for improvement and changes made by district and health facilities related predominantly to strengthening systems and processes, with those related to management and collection more completely implemented than those related to analysis and use.

DITs identified that poor data quality stemmed largely from inaccurate and incomplete recording and reporting of vaccine dose administration data at the health facility and poorly implemented processes for data management, collection, analysis, and use. These problems likely contributed to overreporting of administrative data, as identified in the 2013 Uganda DQS (*10*). If data are improperly recorded at, or inaccurately reported from, the health facility to the district level, these data will remain inaccurate in the national HMIS (*18*). Although data are prone to errors such as incorrect entry, incompleteness, or late reporting, accurate recording and reporting of vaccine doses administered from the initial point at which they are generated is critical to improving the quality and utility of data at all levels of the health system (*29*). The relationship between data quality and use could be considered cyclical, in that improving accuracy could improve confidence in the data, which would help drive demand and use, further driving data quality. At a service delivery level, if data are not used to monitor performance, opportunities can be missed to identify issues as they arise, such as problems with dropouts, changes in target population, or underserved areas, all of which can lead to underimmunized children and can leave the population vulnerable to outbreaks of epidemic-prone VPDs, which threatens global health security (*30*).

Improving data accuracy in a situation of overreporting may result in lower immunization coverage estimates (*7*). Despite implying poorer program performance, increased accuracy would enhance the utility of the data for informing immunization program implementation, including identification of underimmunized or nonimmunized populations that may have been masked by overreporting.

Underrecording of individual-level vaccination status in the child register inhibits the ability of healthcare workers to identify and follow up with inadequately immunized children, both routinely to maximize coverage and during VPD outbreaks. Underrecording also reduces the utility of the child register as a secondary data source to verify caretakers' recall when home-based vaccination records are not available (*31*). Home-based records enable health facility staff to routinely verify individual vaccination status and are critical to the success of periodic independent coverage surveys, which are valuable to verify administrative vaccination data. However, discordance between sources of data on vaccination coverage and inherent limitations in many sources of vaccination data make it difficult to determine true immunization coverage.

Some components of the DIT strategy are not typical of other approaches to national data quality improvement initiatives and could be applicable to other countries and other health data. First, the strategy was facilitated through a hybrid funding commitment across multiple organizations, which allowed it to be implemented nationally. Second, the combination of site-specific problem identification followed by immediate, on-the-job training was found to be a useful approach to strengthening healthcare workers' awareness, knowledge, and skills. A similar package of interventions has been seen to improve the quality of supportive supervision for immunization in Georgia (*13*). Systematic literature reviews highlight the effectiveness of multifaceted approaches, which include audit, feedback, and supportive supervision, in building health workforce capacity (*14,32*). The capacity to understand the gaps and challenges faced and to tailor improvement strategies accordingly appears fundamental to improving immunization coverage (*33*). Third, involvement of existing national and district staff helped build sustainability. Finally, MakSPH students, many of whom were redeployed several times, developed their own knowledge and skills, which they felt enhanced their future job prospects. They also brought an external eye that enhanced problem detection, accountability, and external motivation of DITs and health facility staff.

There are limitations to individual methods used for monitoring and evaluation of the DIT strategy, although in combination they facilitated a better understanding about implementation and short-term change (*34*). DIT members and data collectors were trained in the use of data collection instruments, standard question prompts were included, and data validation was built into the mobile application. Systematic sampling of DQI tools for analysis reduced some systematic error and improved internal validity of these data. The magnitude of difference between sources of vaccination data was influenced by variation in month of assessment and number of doses reported, which was, in turn, a function of health facility type. Administrative data on timeliness and completeness of reported vaccination data are likely limited in specificity and internal validity. Feasibility influenced purposive selection of sites for the postimplementation follow-up, which was also open to researcher bias, although use of selection criteria helped reduce this (*35*). Different data collection methods were used for routine monitoring and postimplementation follow-up, which did not allow for extensive quantitative comparison between resultant data. Unless directly attributed through individual report, observed changes could not be credited solely to the DIT strategy.

Implementation of the first phase of the DIT strategy catalyzed stronger administrative vaccination data in Uganda. Informed by these experiences and results, a second round of DIT visits to all districts, targeting all health facilities, is being implemented. Planned modifications include follow-up to further determine extent of implementation of recommendations at all sites and degree of short-term change, as well as regular regional-level meetings of districts to improve accountability and drive action on recommendations. Assessment of vaccination data congruence will continue to focus on the health facility, although assessment of this across the immunization information system should be undertaken periodically to rule out any systematic data entry error or loss of data. The DIT strategy and observed changes have the potential to benefit data from other health initiatives, particularly those reported through the HMIS. Other countries looking to address vaccination data quality issues should consider a similar approach, using existing staff, on-the-job training, mechanisms for routine follow-up, and collaborative resource mobilization. Efforts should focus on identifying site-specific issues and building local workforce knowledge, skills, and awareness, as well as strengthening systems, to enhance availability, quality, and use of vaccination data.

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Expanding Pertussis Epidemiology in 6 Latin America Countries through the Latin American Pertussis Project

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The Latin American Pertussis Project (LAPP), established in 2009, is a collaboration between the Centers for Disease Control and Prevention, Pan American Health Organization, Sabin Vaccine Institute, and the ministries of health of 6 countries in Latin America. The project goal is to expand understanding of pertussis epidemiology in Latin America to inform strategies for control and prevention. Here we describe LAPP structure and activities. After an initial surveillance evaluation, LAPP activities are tailored to individual country needs. LAPP activities align with Global Health Security Agenda priorities and have focused on expanding laboratory diagnostic capacity, implementing a laboratory quality control and quality assurance program, and providing epidemiologic support to strengthen reporting of pertussis surveillance data. Lessons learned include that ongoing mentoring is key to the successful adoption of new technologies and that sustainability of laboratory diagnostics requires a regional commitment to procure reagents and related supplies.

Pertussis, also known as whooping cough, is one of the most poorly controlled vaccine-preventable diseases in the world. The bacterium *Bordetella pertussis* causes the disease, which is endemic worldwide and associated with cyclical increases every 2–5 years (*1*). The disease is typically more severe and associated with more complications in and deaths of infants <1 year of age, particularly those <6 months of age (*1*,*2*). Despite the widespread availability of pertussis vaccines and high vaccination coverage rates, pertussis continues to be a leading cause of death among children (*2*). A recent study modeling pertussis incidence and death estimated that in 2014, there were 24.1 million cases and 160,700 deaths worldwide among children <5 years of age (*3*). Although these findings emphasize the importance of pertussis as a cause of childhood deaths, the estimates are limited by lack of reliable surveillance data and diagnostic capacity (*4*).

The number of pertussis cases reported in the Americas region overall had declined from the early 1980s until the early 2000s, but several countries, including the United States and some countries in Latin America, observed increases in pertussis cases, and outbreaks of pertussis, during that period (*5*–*8*). Given the transmissibility of pertussis and global interconnectivity, such outbreaks can represent a public health threat. Since 2002, many Latin America countries have reported increases in the number of pertussis cases, including Argentina, Brazil, Chile, Colombia, Panama, and Mexico (*5*–*7*,*9*–*13*). However, estimation of the effects of pertussis in Latin America is complicated by the lack of published data on pertussis deaths, country-specific differences in case definitions, and variability of diagnostic tests available (*6*,*9*). In addition, reported pertussis incidence and case fatality rates vary widely among countries in Latin America, despite similar vaccination schedules and coverage (*6*). This difference may be caused partly by areas of suboptimal vaccination coverage within countries, as well as differences in case management, surveillance infrastructure, and case identification by healthcare providers (*8*,*9*,*14*,*15*). The recent increase of reported pertussis and the varied incidence among Latin America countries highlight the need to reinforce surveillance reporting and diagnostic capacity across the region (*5*,*7*,*8*).

Worldwide, diagnosis of pertussis is challenging because the symptoms may resemble those of other respiratory diseases, and the accuracy of available laboratory diagnostics depends on both the timing (Figure 1) and quality of specimen collection (*16*,*17*). Diagnostics recommended by the World Health Organization (WHO) include culture and PCR of nasopharyngeal specimens and serologic testing (*16*–*19*). Direct fluorescent antibody assay is not

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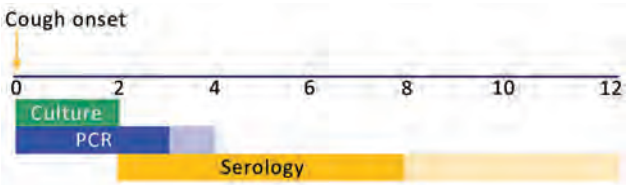

Figure 1. Optimal timing for diagnostic testing for pertussis, in weeks. Dark colors indicate optimal timing window; lighter colors indicate that tests may provide accurate results during these periods.

recommended because it has low sensitivity and specificity for *B. pertussis* (*16*,*17*,*20*); however, it is used in some parts of Latin America (*6*). Because no single pertussis diagnostic assay is optimal for detection of infection at all stages of disease, a complementary testing strategy (i.e., a combination of culture, PCR, and serologic testing) may maximize the surveillance system's potential for case confirmation (*16*,*17*). However, multiple diagnostics for pertussis are not used or widely available in Latin America, in part because of lack of technical training and limited access to reagents and supplies.

Strong epidemiologic and laboratory surveillance are crucial to rapidly identifying and controlling pertussis outbreaks and assessing the effects of disease control measures, as well as to monitor changes in pertussis epidemiology and the evolution of the organism (*21*). Throughout the nations of Latin America, reporting pertussis is mandatory, and surveillance systems adhere to WHO surveillance recommendations; however, the countries may have differing case definition criteria (*6*,*22*). Surveillance programs in Latin America face similar barriers to those reported in other regions (*23*), including lack of awareness of the disease, lack of a regional standard case definition, and limited laboratory capacity (*5*,*6*,*8*,*9*). Pertussis reporting in the region tends to focus on cases among hospitalized infants or young children, and cases are often confirmed by clinical criteria only; these factors may lead to underestimation or overestimation of disease prevalence (*6*,*8*,*24*).

In 2009, the Pan American Health Organization (PAHO) Technical Advisory Group on Vaccine Preventable Diseases identified a need for improved epidemiologic information for pertussis to inform vaccination policies and surveillance recommendations (*25*). In this context, the Latin American Pertussis Project (LAPP) was established in 2009 to expand the understanding of pertussis epidemiology in the region by strengthening both laboratory diagnostic capacity and epidemiologic surveillance in selected countries.

LAPP

LAPP is a collaborative effort between the Centers for Disease Control and Prevention (CDC), PAHO, the Sabin Vaccine Institute (Sabin), and ministries of health (MOHs) of participating countries in Latin America. CDC provides technical support of epidemiology and laboratory diagnostics to partners; PAHO provides expertise on immunizations and coordination with the MOHs; and Sabin provides overall funding and project management, as well as logistical support and feedback for project activities. In each country, the MOH committed national-level public health personnel, including staff from both the pertussis surveillance department and the national reference laboratory (NRL), to participate in LAPP activities.

The project's specific objectives are to expand laboratory capacity for identification of *B. pertussis*, strengthen laboratory-based pertussis surveillance, and standardize and improve pertussis reporting within each country. To achieve these objectives, the LAPP strategy includes an initial in-country assessment of the pertussis surveillance system and laboratory capacity. Based on country-specific findings, each country receives on-site laboratory and epidemiologic training, guidance, and technical assistance, and participates in a laboratory quality control and quality assurance (QC/QA) program. The model used to strengthen surveillance focuses on mentoring and ongoing communication with laboratory and surveillance country staff on each specified activity (Figure 2).

LAPP goals are consistent with the objectives set by the Global Health Security Agenda (GHSA), which was launched in 2014, to strengthen global and national capacity to respond to infectious disease threats (*26*,*27*). LAPP activities support GHSA goals by improving national reference laboratory diagnostic capacity and strengthening national MOH surveillance and reporting through training and ongoing mentoring (*26*,*27*). Many LAPP country partners are also GHSA members.

Countries were selected for inclusion in LAPP on the basis of reported pertussis disease burden, potential for integrating and sustaining new laboratory capacities, and country-level requests to PAHO and CDC for technical support. LAPP began in 2009 with 3 participating countries, Argentina, Mexico, and Panama, and expanded to include Chile and Colombia in 2013 and Brazil in 2015. Budget restrictions limited extension of LAPP beyond these 6 countries.

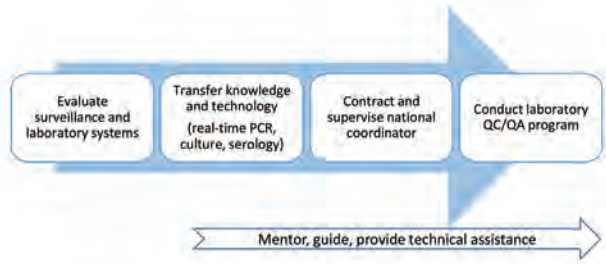

Figure 2. Latin American Pertussis Project model to strengthen pertussis surveillance, currently in use in 6 countries in Latin America. QC/QA, quality control and quality assurance.

Initial LAPP Surveillance Evaluation

In all participating countries, a 1- to 2-week in-country evaluation of the national surveillance system is conducted by a LAPP technical team comprising epidemiology and laboratory staff from CDC, the PAHO regional advisor for immunization, and, in many countries, the in-country PAHO representative (Table). In each country, the LAPP technical team works directly with the central-level MOH personnel from both the NRL and pertussis surveillance programs. Procedures from CDC's Updated Guidelines for Evaluating Public Health Surveillance Systems and a standardized laboratory questionnaire are used to evaluate the pertussis surveillance system (*28*). Activities include interviews of key stakeholders and review of data sources at national, state, and local levels. To provide an overview of national pertussis surveillance function, each MOH selects ≥3 sites to visit; these sites are representative of different levels of surveillance reporting and performance within the country and may include hospitals and health facilities in addition to local and regional health departments.

The LAPP technical team meets with national, regional, and local officials who share information on pertussis surveillance system organization and reporting, pertussis vaccination schedule and coverage, outbreak investigation data, laboratory diagnostic capacity and network organization, and data management. Semistructured interviews are conducted to identify system strengths, weaknesses, and areas where LAPP assistance could reinforce surveillance.

To evaluate laboratory capacity for detecting *B. pertussis*, the LAPP technical team visits the NRL and regional laboratories to comprehend workflow and assess availability of appropriate equipment and space for testing and results analysis. The team uses a structured questionnaire to obtain information about laboratory procedures, specimen collection and transportation, diagnostic assay protocols, data entry and management, and biosafety.

At the conclusion of the in-country assessment, the LAPP technical team provides the MOH with a detailed written report that summarizes potential opportunities and challenges and recommends activities to strengthen pertussis surveillance. After the assessment, in collaboration with the MOH, the team develops a work plan that prioritizes activities in both laboratory diagnostics and epidemiology surveillance.

Expanding In-Country Laboratory Capacity for Identification of *B. pertussis*

Laboratory capacity for identification of *B. pertussis* is expanded through training in complementary pertussis diagnostics. Based on the in-country assessment and country interest, the LAPP technical team provides laboratory training for NRL staff in ≥2 pertussis diagnostics: nasopharyngeal culture, multitarget real-time PCR, or single-point anti–pertussis toxin IgG serology. The 1-week, in-country laboratory training course reviews pertussis diagnostics; natural history of disease; optimal testing schedules; and specimen collection, transport, processing, and storage. Training also provides hands-on practice using the 3 diagnostic tests, including assay documentation, reviewing QC/QA test criteria, troubleshooting, interpretation of results, and reporting. Training on pertussis culture focuses on appropriate sample collection and use of a biochemical testing algorithm to distinguish *Bordetella* species. Countries are trained in use of a multitarget, real-time PCR assay, which is known to be sensitive and specific, and enables identification of multiple *Bordetella* species that can cause pertussis-like disease (*29*). The serologic assay, developed by CDC in collaboration with the US Food and Drug Administration (FDA), is a highly specific, quantitative, single-point, and reference-calibrated ELISA that requires minimal reagent preparation and temperature control (*19*). Laboratory training details the advantages and limitations of each assay and emphasizes the importance of a comprehensive diagnostic program that encompasses the 3 complementary diagnostic tests. LAPP donates reagents and materials for the training and provides technical support to the NRL through email/telephone communication and in-country follow-up visits. On the basis of the individual situation of each country, LAPP may donate a real-time PCR instrument, a temporary supply of reagents, or both to ensure implementation of the new diagnostic tests. All 6 participating LAPP countries received laboratory training in pertussis culture and multitarget real-time PCR, and 5 received training on single-point IgG serologic assays. LAPP donated a real-time PCR instrument to the NRL in Argentina, Brazil, Colombia, and Panama.

Table. LAPP activities and participation for pertussis epidemiology in 6 countries in Latin America, with evaluation dates*

Country	Dates of surveillance evaluation	Laboratory diagnostics training†	Participate in LAPP QC/QA	Epidemiologic surveillance training	Epi Info training	Provider awareness training
Argentina	2009 Nov–Dec	Y	Y	Y	Y	N
Panama	2010 Jan	Y	Y	Y	Y	Y
Mexico	2010 Nov	Y	Y	Y	N	N
Chile	2013 Jan–Feb	Y	Y	N	N	N
Colombia	2013 July–Aug	Y	Y	N	Y	Y
Brazil	2015 May	Y	Y	N	Y	N

*LAPP, Latin America Pertussis Project; QC/QA, quality control and quality assurance.
†Training included culture and multitarget real-time PCR for all countries, and included serology for Argentina, Mexico, Chile, Colombia, and Brazil.

Strengthening Laboratory-Based Pertussis Surveillance

After the laboratory training, LAPP provides continued strengthening of pertussis laboratory surveillance through ongoing technical support for NRL staff in diagnostic testing, and assistance with implementation of a QC/QA program. The LAPP technical team provides mentoring of trained staff through quarterly teleconferences, 1–3 follow-up visits per country, and frequent correspondence regarding diagnostic issues as they arise (Figure 2). If requested, additional technical guidance on other methods, such as molecular typing, pulsed-field gel electrophoresis, and pertactin deficiency screening, are provided through sharing of standard operating procedures. In addition, LAPP encourages country partners to provide ongoing training on specimen collection and transport at the local level to support improved surveillance.

LAPP encourages the implementation of QC/QA measures, which are crucial to the reliability of laboratory results. LAPP supports NRLs with an annual QC/QA testing program by sending panels of blinded specimens for multitarget real-time PCR testing. Depending on the interest of each country, QC/QA panels can also be shared for pertussis culture and serology. Panel concordance with CDC results is assessed, results are shared with the country, and overall performance is shared with all partners. Currently, all 6 LAPP countries are participating in the multitarget real-time PCR QC/QA program; 1 country participates only in culture QC/QA and 1 only in serology QC/QA.

Standardizing and Improving Pertussis Reporting within Each Country

To better understand the true burden of pertussis disease in the region, LAPP works with national-level MOH staff to ensure and strengthen standardized case reporting procedures and regularly monitor and analyze surveillance data. Specific LAPP activities depend on the unique situation and interest of each country. Examples of these activities include review of case definitions, standardization of national reporting forms, and development of surveillance indicators. In many Latin America countries, surveillance coordinators are charged with oversight of multiple vaccine-preventable diseases, limiting their ability to focus on pertussis and strengthen associated surveillance activities. Therefore, to ensure improvements in surveillance data quality, LAPP may employ a national pertussis surveillance coordinator, who is co-managed by LAPP and the MOH. National pertussis coordinators were hired by LAPP in Argentina, Panama, and Brazil.

LAPP supports improvement of pertussis reporting by providing additional training as funding allows. Staff from Argentina, Mexico, and Panama participated in a 3-week training course on epidemiology, surveillance, and data analysis, which was held at CDC in November 2011. Surveillance coordinators receive ongoing epidemiology technical assistance through biweekly to quarterly teleconferences with the LAPP technical team and in-country training, as needed. For example, in Argentina, Brazil, Colombia, and Panama, LAPP provided in-country training on Epi Info (https://www.cdc.gov/epiinfo), a free and publicly available suite of epidemiology software tools provided by CDC, to facilitate data management and analysis for surveillance reporting. In response to a country's request for assistance amid increasing suspicion and detection of pertussis among medical and public health providers, LAPP developed and presented an in-country provider awareness training that reviewed pertussis epidemiology and clinical presentation, along with best practices for diagnosis, treatment, and laboratory diagnostics.

In an effort to understand differences in surveillance and reporting in each country, and to foster collaboration and communication in the region, LAPP hosts quarterly teleconferences to facilitate communication on topics of the participants' choosing. Initially, each participating country gives a presentation on its surveillance system, providing an opportunity for colleagues to discuss different approaches to disease identification and reporting. Examples of other teleconference topics include pertussis case definitions, laboratory testing and capacity, chemoprophylaxis recommendations, antimicrobial drug resistance, and infant immune response after maternal pertussis vaccination. These activities support GHSA priorities to improve disease detection by promoting communication between reference laboratories and surveillance staff, and among countries participating in LAPP.

As new prevention and control strategies are introduced, country emphasis may shift from strengthening surveillance activities to evaluating the effectiveness of specific vaccine policies or interventions. LAPP is able to adjust its role and act as a mentor for these special studies by providing feedback on study methods and data analyses (*30*,*31*). Many Latin America countries have recommended pertussis vaccination during pregnancy to decrease the risk for disease among infants (*6*,*9*), and LAPP has provided methodological support for country-specific studies to assess the impact of this strategy. For these special studies, the MOH and local sites participating in these activities are responsible for seeking in-country internal review board and ethics approvals.

LAPP Lessons Learned and Next Steps

During the initial 6 years of LAPP, several common themes have emerged, providing valuable lessons and influencing the program's planned next steps. Upon joining LAPP, all countries were committed to strengthening their pertussis culture techniques and expanding their pertussis laboratory

capacity to include functions such as multiple real-time PCR targets and serology. Although all NRLs have incorporated real-time PCR into their diagnostic assessment for pertussis, many partners faced challenges in securing funding to support these diagnostics or in finding local providers of reagents and supplies, even when adequate funding was available. LAPP faced similar challenges in sending donated equipment, reagents, and related supplies, because of the complicated importation processes that exist in many countries. National commitment is essential for sustainability of these new diagnostics, which will depend on identifying funding and providers for equipment, reagents, and related supplies.

Another lesson learned is that ongoing mentorship and communication are key components in the process of strengthening existing surveillance systems. Successful transfer of new laboratory diagnostic processes and assistance in standardizing disease reporting required continuous support and discussion among dedicated partners. Regular teleconferences, including the LAPP technical team and individual or multiple countries, provided the opportunity to troubleshoot issues such as diagnostic implementation or analysis of surveillance data. In addition, adding the position of surveillance coordinator to concentrate on pertussis surveillance facilitated the communication process between LAPP and MOH and among in-country laboratory and surveillance staff.

LAPP has promoted communication and collaboration between LAPP-associated countries through regularly scheduled teleconferences for both laboratory and surveillance staff. These teleconferences have served as a forum for sharing country experiences and lessons learned, as well as discussing topics of interest and proposed collaborations. Ongoing communication can lead to new opportunities; discussion among partners has led to requests for country-specific trainings. For example, Argentina, Brazil, Colombia, and Panama requested Epi Info training to facilitate analysis of their surveillance data. In addition, such communication and collaboration between countries could facilitate the ability to respond rapidly to outbreaks across country borders and harmonize the regional response.

Although LAPP has established itself operationally, further work remains. Known challenges should be addressed to sustain improvements in pertussis surveillance. Key among these will be assisting LAPP countries in identifying sources and funding for diagnostic reagents and other needed supplies. Equally necessary is demonstrating the effects of LAPP activities on pertussis surveillance at the country level. Evidence of success is essential for project sustainability and will encourage participating countries to continue to improve their pertussis surveillance programs. Evidence of success may lead to additional funding sources, which would allow LAPP to expand the partnership to other interested countries. Finally, LAPP could continue to provide technical mentorship for special studies as new regionally or globally relevant research questions arise.

LAPP supports strategies endorsed by multiple public health entities, such as the WHO Global Vaccine Action Plan (*32*), PAHO Regional Immunization Vision and Strategy (*33*,*34*), and GHSA. Specifically, LAPP activities that increase laboratory capacity to detect disease help inform immunization policy and support the GHSA goals to detect, characterize, and report potential outbreaks early. LAPP's focus on providing laboratory diagnostic and epidemiology training also aligns with the GHSA priority on training an effective biosurveillance workforce; the surveillance skills obtained through LAPP training may be transferable to other disease threats.

In conclusion, LAPP has developed a partnership between CDC, PAHO, Sabin, and the MOHs of 6 Latin America countries to strengthen national laboratory and surveillance capacity to more rapidly and accurately detect and monitor pertussis. Such efforts can contribute to more rapid control of pertussis outbreaks and thereby enhance global health security. Subsequent areas of emphasis include demonstrating the effect of LAPP activities at the country level; continuing to address the challenges partners face in sustaining these improvements; focusing efforts to expand laboratory-based surveillance for pertussis to other Latin American countries; and continuing to support special studies to answer relevant research questions.

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June 2016: **Respiratory Diseases**

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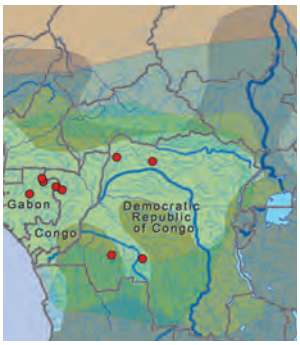
- Perspectives on West Africa Ebola Virus Disease Outbreak, 2013–2016



- Human Infection with Influenza A(H7N9) Virus during 3 Major Epidemic Waves, China, 2013–2015
- Integration of Genomic and Other Epidemiologic Data to Investigate and Control a Cross-Institutional Outbreak of *Streptococcus pyogenes*
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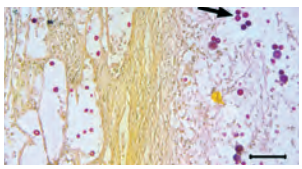

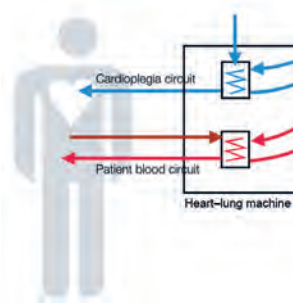

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- Experimental Infection and Response to Rechallenge of Alpacas with Middle East Respiratory Syndrome Coronavirus
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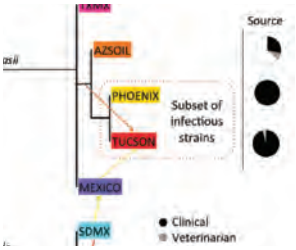

- Prospective Validation of Cessation of Contact Precautions for Extended-Spectrum β-Lactamase–Producing *Escherichia coli*
- Whole-Genome Analysis of *Cryptococcus gattii*, Southeastern United States

- Prevalence of Nontuberculous Mycobacterial Pulmonary Disease, Germany, 2009–2014

EMERGING INFECTIOUS DISEASES https://wwwnc.cdc.gov/eid/articles/issue/22/6/table-of-contents

CDC Activities for Improving Implementation of Human Papillomavirus Vaccination, Cervical Cancer Screening, and Surveillance Worldwide

Virginia Senkomago, Denise Duran, Anagha Loharikar, Terri B. Hyde, Lauri E. Markowitz, Elizabeth R. Unger, Mona Saraiya

Cervical cancer incidence and mortality rates are high, particularly in developing countries. Most cervical cancers can be prevented by human papillomavirus (HPV) vaccination, screening, and timely treatment. The US Centers for Disease Control and Prevention (CDC) provides global technical assistance for implementation and evaluation of HPV vaccination pilot projects and programs and laboratory-related HPV activities to assess HPV vaccines. CDC collaborates with global partners to develop global cervical cancer screening recommendations and manuals, implement screening, create standardized evaluation tools, and provide expertise to monitor outcomes. CDC also trains epidemiologists in cancer prevention through its Field Epidemiology Training Program and is working to improve cancer surveillance by supporting efforts of the World Health Organization in developing cancer registry hubs and assisting countries in estimating costs for developing population-based cancer registries. These activities contribute to the Global Health Security Agenda action packages to improve immunization, surveillance, and the public health workforce globally.

Cervical cancer is one of the most commonly diagnosed cancers and a leading cause of cancer death among women worldwide; in 2012, there were an estimated 528,000 new cases and 266,000 cervical cancer deaths globally (*1*). Nearly all cervical cancers are caused by persistent infection with oncogenic human papillomavirus (HPV) types, most commonly HPV-16 and HPV-18 (*2*,*3*). Progression from persistent HPV infection to invasive cervical cancer occurs over a long period (average 7–10 years), during which cervical precancers can be detected by screening and treatment initiated to prevent invasive cervical cancer (*4*). Cervical cancer incidence is remarkably lower in North America (6.6 cases/100,000 persons) and Western Europe (7.3 cases/100,000 persons), where cervical cancer screening and treatment programs have been implemented for several decades, than in sub-Saharan Africa (34.8 cases/100,000 persons) and Latin America and the Caribbean region (21.2 cases/100,000 persons), where cervical cancer screening programs are comparatively nascent or not yet developed (Figure) (*1*,*6*).

The discovery of the strong causal relationship between persistent infections with oncogenic HPV types and cervical cancer has led to development of HPV vaccines to prevent infection by oncogenic HPV types, and HPV tests that are being used to improve cervical cancer screening. Currently, 3 HPV vaccines have been developed: a bivalent vaccine that protects against HPV-16 and HPV-18; a quadrivalent vaccine that protects against HPV-16, HPV-18, and nononcogenic HPV types 6 and 11; and a 9-valent vaccine that protects against those in the quadrivalent vaccine and 5 additional oncogenic HPV types (HPV-31, -33, -45, -52, and -58).

The World Health Organization (WHO) now recommends 2 doses of HPV vaccination for girls 9–14 years of age in all countries where cervical cancer prevention is a public health priority and introduction is feasible and sustainable. WHO also recommends vaccination of multiple age cohorts (e.g., 9–14 years) in the first year of introduction, if feasible for the country. HPV vaccination has been introduced in 71 (37%) countries worldwide; however, most developing countries with higher cervical cancer incidence rates have not yet introduced HPV vaccination (*7*). CDC is working with various partners to assist in development of global HPV vaccination policies and guidelines, and provide technical assistance in implementation and evaluation of country HPV vaccination pilot projects or programs.

Five HPV tests have been approved by the US Food and Drug Administration for clinical applications in cervical cancer screening, and additional tests are available outside the United States. In 2013, WHO released new cervical

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cancer screening guidelines recommending the use of primary HPV testing as the preferred method in areas where effective cytologic (Papanicolaou [Pap]–based) screening programs did not already exist (*8*). CDC is working with various partners in development of cervical cancer screening guidelines and policies, and implementation and evaluation of cervical cancer screening activities.

Global cervical cancer prevention has been identified as a key actionable issue by the Council on Foreign Relations' taskforce report on the emerging global health crisis from noncommunicable diseases (NCDs). In its report, this taskforce explains that a US focus on global NCDs, including cervical cancer prevention, would leverage and ensure the effectiveness of US global health investments

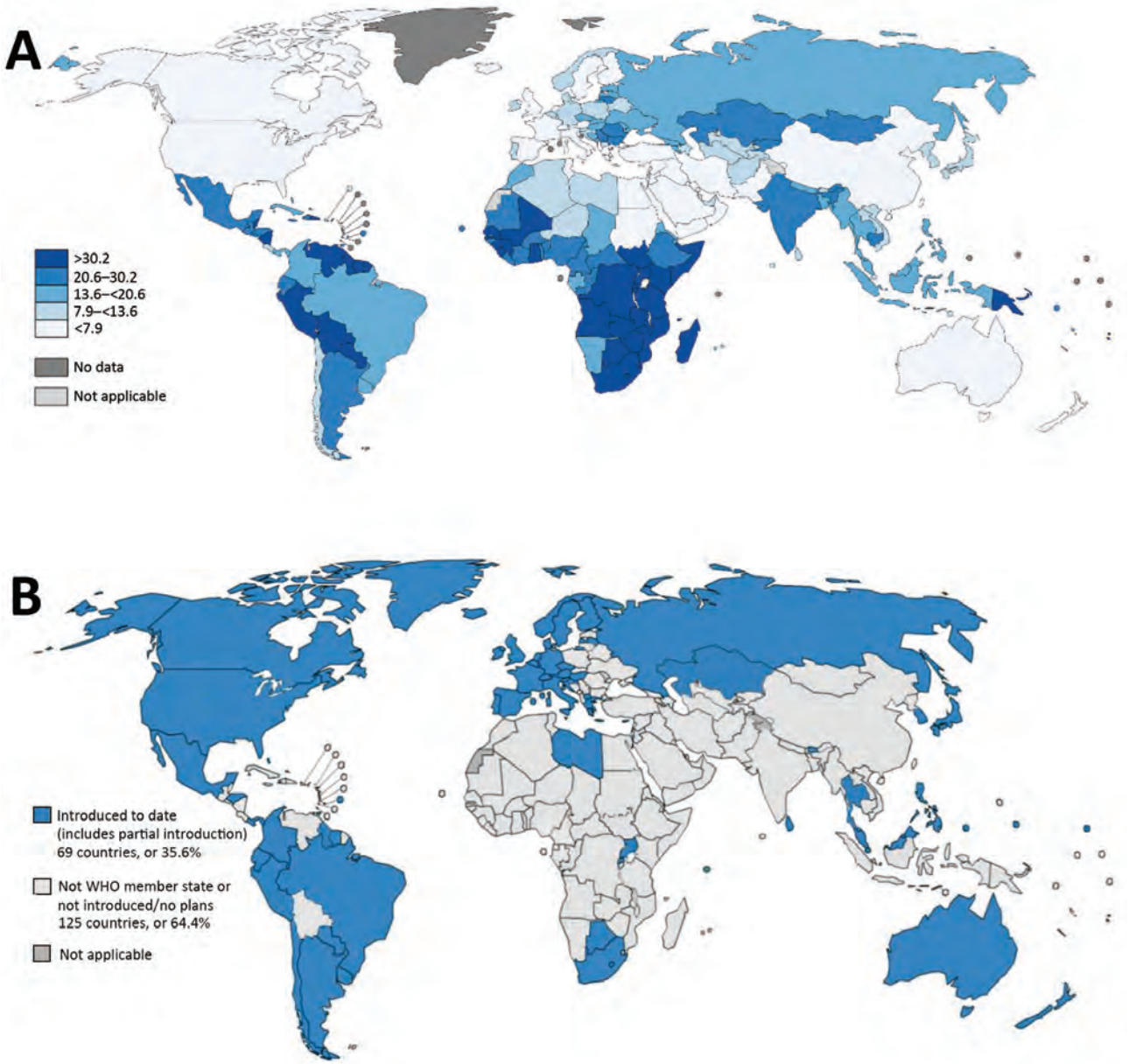

Figure. Worldwide cervical cancer incidence and human papillomavirus (HPV) vaccination status. A) Estimated cervical cancer incidence rates per 100,000 persons in 2012. Source: GLOBOCAN, 2012, WHO. B) Progress in HPV vaccine introduction in national immunization programs, 2016. Source: WHO, 2016. Many countries with high cervical cancer incidence rates (primarily countries in sub-Saharan Africa, Asia, and a few in Latin America) have not yet introduced HPV vaccination in their national immunization programs. Cervical cancer can also be prevented by screening and treatment for precancerous lesions; incidence and mortality rates in high-income countries have decreased largely because of effective screening programs. Data for cervical cancer screening coverage worldwide are limited; 2002 World Health Survey data showed that the proportion of women who had a Papanicolaou test in the previous 3 years greatly varied among countries; 11%–83% in industrialized countries, and 1%–73% in developing countries (*5*). WHO, World Health Organization.

that have been made in infectious disease prevention (*9*). As part of the CDC Strategic Framework for Global Immunization, during 2016–2020, the agency is committed to supporting introduction of HPV vaccine for cervical cancer prevention (*10*). Global activities of CDC in cervical cancer prevention described in this article, including providing technical assistance on HPV vaccination program introduction and laboratory assessment of HPV vaccines, training field epidemiologists, and improving cancer registration, also contribute to the Global Health Security Agenda (GHSA) action packages to improve immunization, surveillance, and workforce development. These efforts contribute to global health security by enhancing the workforce capacity of countries to rapidly detect, respond, and control public health emergencies, thereby preventing these emergencies from spreading to other countries.

Global HPV Vaccination Activities

Global HPV Vaccination Policies and Guidelines

Since 2005, CDC has provided technical support to WHO and its Strategic Advisory Group of Experts in the development and revision of HPV vaccine policies and guidelines. CDC participated in WHO technical work groups providing expertise for the development of the first WHO position paper and recommendations for HPV vaccination that were released in 2009 (*11*). CDC also assisted in the development of the 2010 WHO report focused on evaluating HPV vaccine coverage and providing guidance for HPV vaccine impact monitoring (*12*). In addition, CDC participated in a series of WHO meetings during 2013–2015 that were focused on revising guidelines for future HPV vaccine trials, including guidance on trial design and clinical endpoints for evaluation of new prophylactic HPV vaccines (*13*). As further data became available from vaccine trials, CDC provided ongoing consultation to WHO headquarters and the Pan American Health Organization (PAHO) when deliberations were under way for reduced-dose vaccination schedules and consideration of vaccination for boys. The Advisory Committee on Immunization Practices of CDC has provided ongoing opportunities for policy makers from other countries to attend and learn from US deliberations on vaccine policy.

Implementation of HPV Vaccination Globally

Technical Assistance on HPV Vaccine Introduction

Gavi, the Vaccine Alliance, is a public–private sector partnership that funds lower-income countries for new and underused vaccines to ensure equal access of vaccines to the poorest children. CDC is a core member of the Gavi HPV Global Leadership Team, composed of international immunization partners who provide guidance in the design, implementation, monitoring, and evaluation of Gavi support for HPV vaccine introduction. In 2012, Gavi introduced its program of financial support to eligible countries for HPV vaccine introduction. Because 9–13-year-old girls were a new immunization target population for these countries, the Gavi program required demonstration of the ability to deliver vaccine to this population through smaller-scale pilot projects. Gavi provided funding for vaccine procurement, as well as operational and technical assistance with new vaccine introduction (*14*).

After 5 years of learning and experience from ≈24 country pilot projects across multiple regions and continents, the program is transitioning to catalyzing countries to scale-up of HPV vaccinations nationally, marking the first addition to national immunization programs beyond early childhood (*15*). CDC has played a key role in this transition at the global level by contributing lessons learned in pilot projects and providing feedback on the new guidelines. Gavi financially supports the introduction of HPV vaccination among Gavi-eligible countries according to the new WHO Strategic Advisory Group of Experts guidelines. These guidelines recommend targeting multiple birth cohorts of girls 9–14 years of age in the first year of vaccine introduction, if feasible for the country, followed by single-birth cohorts, to ensure maximum vaccination coverage (*16*).

CDC continues to provide technical and field support to key countries to assist with decision-making on HPV vaccine introduction, applying for financial support, implementation planning, and evaluation of vaccine introduction and programs. CDC works closely with ministries of health, WHO regional and country offices, and other immunization partners to support countries in vaccine implementation planning, including interpreting lessons learned from pilot projects, ensuring equity and coverage in delivery of vaccine, reviewing communication strategies and social mobilization planning, emphasizing the need for monitoring, and assessing financial cost of vaccine introduction. In the past 2 years, CDC has provided technical assistance to Laos, Cambodia, the Solomon Islands, Nepal, Ethiopia, Liberia, Zimbabwe, and Sierra Leone in implementing and evaluating HPV vaccine pilot projects or scale-up planning for national vaccine introduction.

Technical Assistance on Laboratory-Related HPV Activities

CDC has provided technical assistance to WHO and countries on assessment of HPV vaccine quality, safety, and efficacy, and on standardization of HPV testing. HPV vaccine clinical trials rely on HPV testing, both HPV serologic testing and HPV nucleic acid detection, to establish a vaccination-naive population and document biological endpoints. WHO, with support from the Bill and Melinda

Gates Foundation, established the WHO HPV LabNet during 2006–2011 to assist in standardization of HPV testing. When LabNet was active, the CDC HPV Laboratory served as 1 of 2 Global Reference Laboratories. LabNet supported development of international standards for HPV DNA and HPV serologic analysis, developed proficiency testing for HPV DNA assays, and published an HPV laboratory manual, among other accomplishments. CDC has continued to support WHO initiatives related to HPV testing and HPV vaccine development through technical support in drafting the WHO technical report on the quality, safety, and efficacy of recombinant HPV virus–like particle vaccines that was released in 2015, as well in the 2 workshops held to explain the document to vaccine manufacturers and national regulatory agencies (*13*).

Evaluation and Implementation Research on Global HPV Vaccination

CDC has supported implementation research and evaluation activities before and after HPV vaccine introduction in various countries. CDC conducted implementation research in western Kenya to assess HPV knowledge, attitudes, and beliefs to assist development of communication messages (*17*). CDC has been a technical partner in facilitation and leadership of HPV pilot project evaluations to optimize program performance; CDC has participated in or facilitated postintroduction evaluations in Laos, Ethiopia, the Solomon Islands, Cambodia, and Nepal. These program evaluations help to clarify effectiveness of program delivery, community messaging, and overall system functioning. In addition, CDC has completed coverage assessments in pilot projects in Laos, Cambodia, and Liberia to evaluate age- and dose-specific vaccination coverage among the target population, as well as assessed equitable access and vaccine acceptability. CDC also has ongoing collaborations with global immunization partners to examine and summarize HPV vaccine introduction progress worldwide, including a summary of HPV vaccination in the Americas during 2006–2010 and a global summary of HPV vaccination introduction in 39 countries in 2012 (*18,19*). Last, CDC economists have completed cost evaluations of HPV pilot programs in Zimbabwe and Cambodia to estimate the financial impact of introduction of HPV vaccine and assist future scale-up planning.

Global Cervical Cancer Screening Activities

Global Cervical Cancer Screening Recommendations and Manuals

CDC has provided technical support and expertise in the development of global cervical cancer screening recommendations and manuals. CDC participated in the development of the second version of the WHO guidelines on cervical cancer screening and treatment, which provide resource- and HIV-stratified recommendations for implementing cervical cancer screening (*8*). WHO guidelines recommend the implementation of primary HPV screening in countries where Pap-based screening programs do not exist or are not effective. CDC partnered with PAHO in conducting policy dialogues to promote these WHO guidelines and HPV-based screening in Costa Rica, Guatemala, and El Salvador. CDC and PAHO/WHO also developed a manual to guide program managers in integrating HPV testing into cervical cancer screening programs (*20*). In addition, CDC worked collaboratively with the Union for International Cancer Control to develop a curriculum to educate nurses about HPV and cervical cancer. In many low- and middle-income countries with limited numbers of physicians, nurses play a key role in cervical cancer screening and treatment. Three workshops have been held in Central and South America to disseminate the curriculum.

Implementation of Cervical Cancer Screening Globally

CDC is an implementing agency of the US President's Emergency Plan for AIDS Relief (PEPFAR) and works with ministries of health to deliver sustainable HIV/AIDS prevention, care, and treatment. Given that cervical cancer incidence is higher among HIV-positive women, CDC has played a key role in convening a technical consultation on HIV and cervical cancer to support screening among HIV-positive women through the PEPFAR program. PEPFAR has provided support for cervical cancer screening in ≥250 clinics in 11 countries in Africa (*21*). PEPFAR cervical cancer screening has become part of a larger public–private partnership known as Pink Ribbon Red Ribbon (PRRR). CDC serves on the steering committee of PRRR, and on the ground, CDC offices in Tanzania, Zambia, Botswana, and Ethiopia collaborate with PRRR in implementation of screening and vaccine services.

For >20 years, CDC has been providing cervical cancer screening to low-income, uninsured, and underserved women in the United States through the National Breast and Cervical Cancer Early Detection Program. Known as one of the few organized screening programs in the United States, this program operates under a set of fundamental tenets that include providing screening and patient navigation services to women for appropriate follow-up and care; quality assurance, surveillance, and monitoring systems by using existing infrastructure help to monitor timeliness and quality of the screening services; and public education and outreach for providers and women to ensure that services are accessed. CDC shares its expertise in operating an organized cervical cancer screening program with other countries by providing technical assistance in the implementation and improve-

ment of cervical cancer screening. Since 2013, CDC has worked with the Thai Ministry of Public Health and the Thai National Cancer Institute to examine strategies to increase cervical cancer screening coverage. CDC and other international partners provided scientific expertise and training for a demonstration project examining the efficacy, feasibility, and cost-effectiveness of primary HPV testing for cervical cancer screening in 1 province in Thailand. The project found that primary HPV testing was feasible and more sensitive than routine Pap-based screening in detecting cervical precancers (*22*). CDC continues to work with the Thai National Cancer Institute in planning for the development of recommendations to expand primary HPV testing for cervical cancer screening in Thailand.

The National Breast and Cervical Cancer Early Detection Program of CDC has also been working with the US-Affiliated Pacific Islands, including freely associated states such as the Federated State of Micronesia, to examine resource-appropriate ways to increase cervical cancer screening coverage. Together with experts from the Office of Population Affairs (Title X), the American Congress of Obstetricians and Gynecologists Committee on Healthcare for Underserved Women, and the American Society for Colposcopy and Cervical Pathology, CDC has organized expert meetings to discuss the possible use of primary HPV testing or visual inspection with acid to increase screening coverage in the Pacific Islands. These methods might enable screening and treatment to take place in 1 or 2 visits with fewer resources than are needed by Pap-based screening. CDC continues to work with health professionals in the US-Affiliated Pacific Islands and with other health organizations in designing a demonstration project that will study the effectiveness of visual inspection with acid or HPV testing in increasing cervical cancer coverage in the region.

Evaluation of Cervical Cancer Screening Programs

CDC is a partner in the Improving Data for Decision Making in Global Cervical Cancer Program (IDCCP), a project led by the CDC Foundation and aimed at increasing the availability and quality of data for planning and decision-making to improve cervical cancer screening programs in low- and middle-income countries. The IDCCP toolkit was developed with funding from the Bill and Melinda Gates Foundation and offers standardized and globally endorsed guidance that can be adapted at the country level to support the collection of high-quality data for cervical cancer screening programs. WHO and the George W. Bush Institute are key partners in the development of the IDCCP toolkit (*23*,*24*).

The IDCCP tool kit includes 5 modules. The first module is the cervical cancer data systems assessment module that provides guidance on implementing data systems for cervical cancer prevention and treatment. The second is the population-based survey module that provides country stakeholders with standardized questions on cervical cancer screening and treatment that can be incorporated into existing population-based surveys. The third is the cervical cancer patient and program monitoring module that outlines a process for data collection, aggregation, analysis, and reporting for screening and treatment programs. The fourth is the facility-based surveys module that provides tools to gather and evaluate information on location and readiness of facilities to deliver cervical cancer screening and treatment services. The fifth is the comprehensive cervical cancer costing analysis module that enables health program planners to estimate and analyze program and service costs. CDC has been engaged in development and pilot testing of the modules; the modules are under review with partner organizations before final publication (*25*).

CDC also provides technical assistance to countries in analysis of national cervical cancer screening data. CDC collaborated with the Thailand Ministry of Public Health to analyze national cervical cancer screening data from its Behavior Risk Factor Surveillance Survey in 2010 (*26*). CDC also provided technical assistance in analyzing national cervical cancer screening data from China in 2010, conducted an environmental scan in Kenya to assess perceptions of barriers and benefits of cervical cancer screening, and is currently collaborating with the Public Health Foundation of India to assess national cervical cancer screening coverage (*27*,*28*).

Workforce Development for Global Cancer Prevention

Most cancer cases and deaths occur in low- and middle-income countries, where workforce capacity and resources for cancer prevention and control are limited. Few open-access materials are available to deliver cancer trainings in low-resource settings. To help address this gap, CDC has developed a cancer curriculum for Field Epidemiology Training Programs (FETPs), ministry of health staff, and public health personnel in low- and middle-income countries.

The FETP is a 2-year training in applied epidemiology modeled after the CDC Epidemic Intelligence Service program. The establishment of FETPs started in 1975, and CDC currently supports FETPs in 65 countries (*29*). FETP fellows are primarily trained to respond to public health emergencies from infectious diseases to collect, analyze, and interpret public health data and turn the results into action. In 2010, FETPs started focusing on training field epidemiologists in NCDs to address the growing burden of these diseases in low- and middle-income countries.

The CDC cancer curriculum will provide FETPs with applied cancer epidemiology training focused on cancer screening, registration, and comprehensive cancer control. CDC has held workshops to pilot test the curriculum at FETP meetings in Atlanta, India, Nigeria, and Morocco, and the curriculum modules are under review before final publication.

CDC also provides support and mentorship to FETPs in conducting applied research projects. Since 2016, CDC has supported 11 cancer-related FETP research projects, most of which focused on evaluation of programs or analysis of survey data on cervical cancer screening. Some examples of these FETP projects include an assessment of healthcare providers' knowledge of national guidance for cervical cancer screening in primary healthcare centers in Mexico; an evaluation of the referral mechanism in cervical cancer screening programs in India; and an evaluation of healthcare workers' knowledge, attitudes, and practices in cervical cancer screening programs in Thailand.

Improvement of Global Cancer Surveillance

WHO has developed a Global Monitoring Framework on Noncommunicable Diseases to track global progress in preventing and controlling NCDs. All governments have approved this framework, which includes monitoring 3 key indicators related to cervical cancer prevention: national coverage of cervical cancer screening, HPV vaccination, and cancer incidence. Thus, cervical cancer surveillance involves monitoring national screening and HPV vaccination coverage through national data systems and tracking cancer incidence with cancer registries. However, the number of low- and middle-income countries with available estimates of national cancer burden is limited; the percentage of the population covered by cancer registries is estimated to be 2% in Africa, 6% in Asia, and 25% in Latin America and the Caribbean (*30*).

CDC is a key partner in the Global Initiative for Cancer Registry Development that is being led by the WHO International Agency for Research on Cancer (IARC) to improve cancer registration worldwide (*31*). The Global Initiative for Cancer Registry Development aims to increase global capacity to collect high-quality population-based cancer registry data in >150 countries by developing regional hubs that can tailor training and support to countries in that region and also assist in advocacy for cancer registration. CDC provides support for the operation of cancer registry hubs in sub-Saharan Africa and Asia. In addition, CDC is also supporting the newly formed Caribbean cancer registry hub in collaboration with IARC, the US National Cancer Institute, the North American Association of Central Cancer Registries, and the Caribbean Public Health Agency.

CDC has developed a tool to estimate costs of operating population-based cancer registries and has partnered with WHO/IARC to pilot test this tool in several low and middle-income countries, including Kenya, Uganda, Colombia, India, and Barbados. From these pilot projects, CDC and partners found that the cost for cancer registration for a single cancer case varied from ≈$4 to $113, which translated to only a few cents per person when examined at the population level (*32*). CDC continues to work with several countries to evaluate drivers of costs for cancer registration and to work with additional countries in assessing costs of cancer registration.

Conclusions

The global burden of cervical cancer remains high, particularly in low- and middle-income countries. Research advances have identified HPV as the cause of nearly all cervical cancers, as well as some cancers of the vagina, vulva, penis, anus, and oropharynx. HPV is an emerging infectious threat; countries can reduce the burden of HPV-associated cancers, including cervical cancer, by implementing HPV vaccination. HPV tests are also a major component to improving cervical cancer screening. CDC provides technical assistance and collaborates with global partners on HPV vaccination and cervical cancer screening. Activities in global cervical cancer prevention build on and further leverage the global footprint of CDC preventing infectious diseases. These activities also relate to the GHSA action packages to improve immunization, surveillance, and public health workforce globally, which contribute to rapid detection, response, and containment of public health emergencies at their sources for enhanced global health security.

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US Federal Travel Restrictions for Persons with Higher-Risk Exposures to Communicable Diseases of Public Health Concern

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Published guidance recommends controlled movement for persons with higher-risk exposures (HREs) to communicable diseases of public health concern; US federal public health travel restrictions (PHTRs) might be implemented to enforce these measures. We describe persons eligible for and placed on PHTRs because of HREs during 2014–2016. There were 160 persons placed on PHTRs: 142 (89%) involved exposure to Ebola virus, 16 (10%) to Lassa fever virus, and 2 (1%) to Middle East respiratory syndrome coronavirus. Most (90%) HREs were related to an epidemic. No persons attempted to travel; all persons had PHTRs lifted after completion of a maximum disease-specific incubation period or a revised exposure risk classification. PHTR enforced controlled movement and removed risk for disease transmission among travelers who had contacts who refused to comply with public health recommendations. PHTRs are mechanisms to mitigate spread of communicable diseases and might be critical in enhancing health security during epidemics.

In August 2014, the World Health Organization declared the Ebola virus disease outbreak in West Africa a public health emergency of international concern. In response to this outbreak, the Centers for Disease Control and Prevention (CDC) published Interim U.S. Guidance for Monitoring and Movement of Persons with Potential Ebola Virus Exposure, known as the Monitoring and Movement Guidance (*1*). This guidance recommended controlled movement, which was defined as limitation of long-distance travel by commercial means, for persons with higher-risk exposures (HREs), which were defined as having had a high-risk exposure to Ebola virus on the basis of epidemiologic risk factors or close contact with a person with symptomatic Ebola for a prolonged period who was not using appropriate personal protective equipment (*1*,*2*). In addition, in March 2015, CDC published revised criteria for use of federal public health travel restrictions (PHTRs) in the Federal Register so that these tools could be used to prevent travel of persons exposed to a communicable disease of public health concern and to support enhanced public health response to communicable disease outbreaks (Table 1) (*3*).

CDC uses federal PHTRs to protect the traveling public by preventing commercial air travel or other means of international travel across US borders of persons with a communicable disease or at risk for development of a disease that poses a public health threat (*3*,*4*). Federal mechanisms used to implement travel restrictions include the public health do not board (DNB) and Public Health Lookout lists (*5*,*6*). The DNB tool was developed in 2007 to prevent persons who met criteria (Table 1) from boarding commercial flights of any duration that have departures to or from the United States (*5*,*6*). A Public Health Lookout list is issued to complement the DNB, notifying US Customs and Border Protection (CBP) officers who subsequently notify CDC when a person on PHTR attempts to enter the United States at any port of entry (i.e., seaport, airport, or land border) (*7*). Federal PHTRs are typically not applied to domestic travel on trains, buses, or ships because the mechanism for verifying travelers on these conveyances is different than that of the robust, existing system for commercial air travel and international travel across US borders.

Federal PHTR can be considered for any persons with a suspected or confirmed disease of public health interest or a HRE to a communicable disease that poses a public health threat should the person become symptomatic during travel (*5*). Before the Ebola virus disease outbreak in 2014, PHTRs had only been used for persons with suspected or confirmed infectious pulmonary tuberculosis (99%) or confirmed measles (*6*) and not for persons at risk for development of a disease of public health

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Table 1. Criteria for placement on and removal from federal public health travel restrictions, March 2015*

Criteria for placement	Criteria for removal
Be known or likely infectious with, or exposed to, a communicable disease that poses a public health threat AND meet 1 of the following 3 criteria 1) Be unaware of diagnosis, noncompliant with public health recommendations, or unable to be located OR 2) be at risk for traveling on a commercial flight, or internationally by any means OR 3) travel restrictions are warranted to respond effectively to a communicable disease outbreak or to enforce a federal or local public health order.	Proven noninfectiousness or no longer being at risk for becoming infectious (by documented laboratory confirmation, lapse of known period of infectiousness, or lapse of incubation period without development of symptoms)

*Criteria were obtained from the Centers for Disease Control and Prevention (*3*).

interest. Under the revised criteria for federal PHTRs, and in conjunction with the Monitoring and Movement Guidance in place during the 2014–2016 Ebola epidemic (*1*), persons with HRE to Ebola virus were eligible for federal PHTR (*3*).

In addition, persons with HREs to other communicable diseases that posed a public health threat were also eligible for DNB placement. Thus, CDC considered and applied PHTR to persons with HREs to Lassa fever virus and Middle East respiratory syndrome coronavirus (MERS-CoV). These contacts were monitored by occupational health or local or state health departments. Travel restrictions were not considered for contacts of 2 patients with cases of infection with MERS-CoV imported into the United States in 2014 (*8*). Guidance for use of controlled movement for an exposure to MERS-CoV, including use of federal PHTR, has been published (*9*). To illustrate how travel restrictions might protect the health of the traveling public and contribute to enhanced global health security, we describe persons with HREs to a communicable disease of public health interest who were eligible for and placed on PHTR during 2014–2016.

Methods

CDC maintains case records for persons for whom federal PHTRs are requested in its Quarantine Activity Reporting System, a secure, restricted-access database (*10*). Demographic, clinical, and exposure information is obtained from the requesting agency, typically a local or state health department, as well as evidence that the criteria for implementing and removing PHTR are met and the dates and times of major events leading to placement or removal of federal PHTR. We identified all persons placed on federal PHTRs because of HREs to any communicable disease of public health concern during a 3-year period (2014–2016); persons whose travel was restricted because of a confirmed or suspected communicable disease have been reported elsewhere (*6*,*7*) and were excluded from this analysis.

For all identified persons, we examined demographics including sex, age, and location at time of PHTR placement (i.e., within or outside the United States). We determined the circumstances of the exposure (high-risk or close contact) and the type of contact the person had with the case-patient with the communicable disease (i.e., healthcare, household, or community exposure). In addition, we described the circumstances under which persons were removed, either related to the disease-specific incubation periods or a revised exposure risk classification based on reassessment or a change in guidance, and the number of days spent under PHTR. This record review and analysis was determined by CDC to be Public Health Practice: Non-Research and therefore not subject to review by the CDC Institutional Review Board.

Results

In the 3-year cohort time frame, all restrictions for persons exposed to a communicable disease of public health concern were implemented during a 1-year period (August 2014–July 2015); a total of 164 persons were considered eligible for federal PHTR as a result of exposure to Ebola virus, Lassa fever virus, or MERS-CoV. Exposures to Ebola virus and MERS-CoV were related to an ongoing epidemic of those diseases. Of persons eligible, 160 (98%) were placed under PHTR: 142 (89%) persons were exposed to Ebola virus in the United States or West Africa, 16 (10%) were contacts of a confirmed case-patient with Lassa fever imported into the United States, and 2 (1%) were exposed to MERS-CoV during an outbreak in South Korea (Table 2). Four (3%) persons were not placed under PHTR because of imminent ending of the monitoring period for the patient or insufficient identifying information needed for placement on PHTR. Most (154, 96%) persons were located in the United States at the time of placement. Median age was 38 years (range 5 months–72 years); 49 (31%) were male, and 84 (52%) were female. Sex was not reported for 27 (17%) contacts.

Of those placed under PHTR, 136 (85%) were removed after completion of the incubation period (14 days for infection with MERS-CoV, 21 for Ebola and Lassa fever) on the basis of the last day of exposure and after

Table 2. Characteristics of persons placed on federal public health travel restrictions because of higher-risk exposure to a communicable disease or pathogen of public health concern, January 2014–December 2016*

Characteristic	Ebola	Lassa fever	MERS-CoV	Total
No. contacts identified	142	16	2	160
Median age, y (range)	38 (0–71)	39 (1–69)	51 (39–72)	38 (0–72)
Sex				
M	44	4	1	49 (31)
F	72	11	1	84 952)
Not reported	26	1	0	27 (17)
Location at time of placement				
United States	138	16	0	154 (96)
Outside continental United States	4	0	2	6 (4)

*Values are no. (%) persons except as indicated. MERS-CoV, Middle East respiratory syndrome coronavirus.

confirmation that they remained asymptomatic. Another 20 (13%) were removed because of a revised exposure risk classification after a change in guidance, and 4 (2%) were removed because of a revised exposure risk classification based on reassessment. Ebola contacts were on PHTR for an average of 12 days, MERS-CoV contacts 9 days, and the Lassa fever contacts 13.5 days. None of the persons on PHTR attempted to travel into, out of, or within the United States.

Persons Exposed to Ebola in the United States

Most (128, 88%) persons eligible for PHTR for an Ebola exposure were exposed to 1 of 4 cases of Ebola virus disease identified in the United States: 2 imported cases and 2 locally acquired cases (*11–13*) (Table 3). During October 7–November 2014, a total of 124 (97%) contacts were placed on PHTR (Figure).

The state health department (SHD) of jurisdiction identified 53 contacts for the first Ebola case-patient, who had traveled from Liberia to the United States before becoming symptomatic. Controlled movement was indicated for all contacts, and 50 (94%) were subsequently placed on PHTR; 3 (6%) contacts were not placed on PHTR because their 21-day monitoring period was scheduled to end 1 day after they were identified as needing travel restrictions. Of the 50 contacts who were placed on PHTR, 49 (98%) were healthcare workers who were assessed as high-risk contacts because of an unidentified breach in infection control in the healthcare facility where the first case-patient was treated. One community contact was considered to have had close contact with the case-patient. This contact was placed on PHTR because the person had imminent travel plans but could not be located, and it was unknown whether the person was symptomatic. None of the 50 contacts showed development of symptoms of Ebola.

Two healthcare workers who provided care to the first case-patient became the second and third confirmed Ebola case-patients in the United States (*11*,*12*). Two SHDs identified 72 contacts who were eligible for PHTR because of their potential exposure to Ebola: 24 contacts of the second case-patient and 48 contacts of the third case-patient. A total of 71 (99%) persons were placed under PHTR; 1 person was not placed because of insufficient identifying information.

Of persons placed on PHTR, 37 (52%) were high-risk contacts and 34 (48%) were identified as having close contact. Among high-risk contacts, 31 (84%) were healthcare workers who had provided care to the second or third case-patients and 6 (16%) were community contacts. Of the 34 contacts initially identified as having close contact, 24 (71%) were removed from PHTR within 1 h after it was determined that their exposure risk classification had changed. Of these 24 contacts, 4 were reclassified after further epidemiologic assessment, and 20 were reclassified after revision of the risk classification guidelines (*14*). Of the contacts for the second and third case-patients who remained on PHTR for the duration of their incubation periods (47, 66%), none showed development of symptoms of Ebola.

Table 3. Types of contacts, by risk level, identified for federal travel restrictions because of exposure to 4 case-patients given a diagnosis of Ebola in the United States, October 7–November 14, 2014*

	Case-patient 1		Case-patient 2		Case-patient 3		Case-patient 4		Total
Risk level	High risk	Close contact	High risk	Close contact	High risk	Close contact	High risk	Close contact	
No. contacts identified	52	1	24	0	14	34	3	0	128
Household contact	0	0	0	0	0	0	1	0	1
Healthcare exposure	51	0	23	0	8	0	0	0	82
Community contact†	1	1	1	0	6	34	2	0	45
Contacts placed on travel restrictions‡	49	1	24	0	13	34	3	0	124

*High risk was defined as being within ≈3 feet (1 m) of a person with symptomatic Ebola for a prolonged period while not using appropriate personal protective equipment.
†Includes 20 contacts with persons on airplanes.
‡Two healthcare workers and 1 community contact with an exposure to case-patient 1 were not placed on travel restrictions because their 21-d incubation periods were scheduled to end 1 day after they were to be placed under travel restrictions. One community contact exposed to case-patient 3 was not placed on travel restrictions because of insufficient biographical data needed for placement.

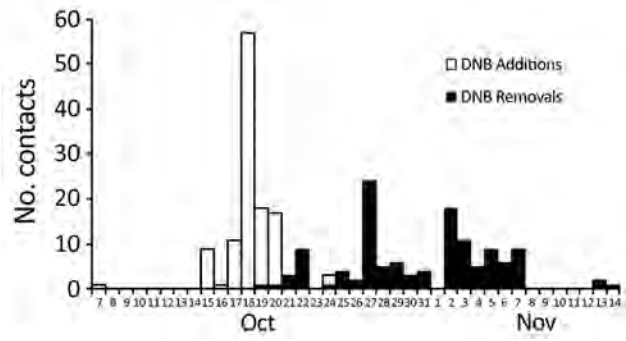

Figure. Timeline of federal public health travel restriction actions for 124 contacts of US case-patients with Ebola, October 7–November 14, 2014. DNB, do not board.

In October 2014, a fourth case of Ebola diagnosed in the United States was reported in a healthcare worker who had returned from West Africa (*13*); this case was not related to the other cases. The health department identified 3 high-risk contacts: 2 in the community and 1 in the household of the case-patient. All contacts were placed on PHTR and remained asymptomatic.

Persons Exposed to Ebola Outside the United States

Four contacts located outside the United States were identified and placed under PHTR because of exposures to Ebola cases in West Africa. Two contacts were household contacts of a deceased patient with Ebola in West Africa; the contacts had confirmed commercial travel scheduled to the United States during their 21-day incubation periods. Both contacts were removed from PHTR immediately after their incubation period, and we confirmed that neither contact became symptomatic. In addition, 2 HRE contacts were reported to CDC by foreign ministries of health (MOHs) and placed under PHTR because they reportedly had planned commercial air travel before completing the monitoring period. None of these contacts attempted to travel to the United States while on PHTR.

During December 2014–April 2015, a total of 14 persons were identified as having had a high-risk exposure to Ebola while working in and around an Ebola treatment center in West Africa that reported unsafe infection control practices. Upon their return to the United States by chartered flight, these persons were subjected to controlled movement and placed under PHTR. These persons were monitored by state public health officials and all remained asymptomatic.

Persons Exposed to Lassa Fever or MERS-CoV

CDC used federal PHTR during May–July 2015 for high-risk contacts of a person exposed to an imported case of Lassa fever and persons exposed during an international outbreak of infection with MERS-CoV. In May 2015, a person who had traveled from West Africa was confirmed to have Lassa fever, and 16 persons were identified as being high-risk contacts: 6 (37%) household contacts, 7 (44%) community contacts, and 3 (19%) healthcare providers. These persons were closely monitored by the SHD and removed from PHTR after completing their incubation periods. In July 2015, in response to the MERS-CoV disease outbreak in South Korea, CDC identified 2 contacts with confirmed commercial air travel involving the United States; both contacts were considered community contacts of patients infected with MERS-CoV and were placed on PHTR. One person was identified in a US territory, monitored until completion of the incubation period, and removed from PHTR. The second person was placed under quarantine in South Korea until completing the incubation period, at which time this person was removed from PHTR and able to travel back to the United States.

Discussion

CDC recommended controlled movement for persons with HRE to these high-consequence diseases because of the risk for a person becoming symptomatic and exposing others during commercial travel; federal travel restriction tools were used to support recommendations outlined in published movement and monitoring guidance and in the Federal Register (*1*,*3*,*9*). These PHTRs aligned with recommendations of the International Health Regulations 2005 in response to specific public health risks, as well as with the World Health Organization Emergency Committee guidelines regarding travel restrictions for persons with Ebola and contacts (*15*,*16*). No person in this cohort attempted commercial air travel while under PHTR, suggesting that the use of federal travel restriction tools might reinforce the need for adhering to public health recommendations.

Federal PHTR reduced the risk for disease transmission among the traveling public even if any of the restricted persons chose not to comply with public health recommendations and had attempted commercial air travel. Most persons with HREs were located in the United States and under direct active monitoring along with community-level movement restrictions imposed by state authorities. All public health actions regarding travel restrictions were coordinated between state/local authorities and CDC.

Federal PHTR provided support and assurance for SHDs, especially during the 2014–2016 Ebola epidemic, when SHDs were monitoring several thousand persons with various risk classifications for symptoms, in addition to those persons with HREs who were placed on PHTR (*17*). Because most persons in the data cohort were located in the United States, their exposure risk assessments were completed by SHDs, who made the request for PHTR for those persons with HREs. Foreign MOHs or CDC assessed

the risk for persons abroad who were planning to travel. Exposure risk classifications were developed with CDC subject matter experts and aligned with published disease-specific movement and monitoring guidance (*2*). CDC continues to evaluate travel restriction criteria as it relates to persons with HREs and disease-specific exposure risk classifications and might refine them as needed during future outbreaks.

Consistent communication and strong collaboration with partners was critical for successfully implementing travel restrictions. The nature and volume of persons placed on PHTR in compressed timeframes during the Ebola outbreak was unprecedented and required close collaboration between local, state, federal, and international partners, as well as the travel industry. SHDs or foreign MOHs were responsible for obtaining biographical data for contacts, determining date of exposure and exposure risk level, and then requesting PHTR placement if a contact was placed under controlled movement. SHDs and MOHs worked with CDC to track dates for removal from PHTR on the basis of incubation periods of contacts to ensure PHTR were removed as soon as the incubation period of the person had been completed. CDC worked closely with the US Department of Homeland Security, using standard processes of internal and external approvals (*6,18*), to promptly implement and remove PHTR for a large number of persons over a short timeframe.

CDC notified all US-based persons of their placement on and removal from PHTRs; notifications to contacts outside the United States were provided to in-country public health officials who then informed the persons. All persons were compliant with public health recommendations for controlled movement, and none contested their travel restrictions. States assisted persons on PHTRs who were housed at locations near a healthcare facility during their incubation periods. US Department of State assistance was made available to those US citizens placed under PHTRs while located overseas.

In addition, CDC worked closely with the airline industry to minimize the burden for those persons who had travel planned during their incubation period and issued formal requests for airline change fee waivers. The established relationship between CDC and the airline industry was critical to the successful waiver of change fees for persons. US-based airlines generally do not have established criteria for denying boarding for ill passengers and follow CDC recommendations for restricting travel of persons as it protects the health of other passengers traveling on their aircraft.

Challenges in implementing and removing PHTRs for this data cohort were related to the large number of urgent requests for PHTRs over short periods during outbreaks. Implementing and removing PHTRs are detailed administrative processes requiring extensive resources to coordinate an all-hours response to a large number of urgent requests for PHTRs. After the Ebola outbreak, CDC trained surge staff in administrative process for implementing and removing PHTRs as a means to supplement personnel resources during future outbreaks that generate a high volume of urgent requests for PHTRs.

Under the revised criteria for federal PHTRs (*3*), and in conjunction with disease-specific Monitoring and Movement Guidance, such as that published for Ebola virus and MERS-CoV (*1,9*), PHTRs are valuable tools for state and local officials, as well as foreign MOHs, during outbreaks of communicable diseases of public health concern. PHTRs reinforce recommended controlled movement of persons with HREs to communicable diseases, even if these persons refuse to comply with public health monitoring and recommendations to postpone commercial travel. PHTRs can enhance global health security by providing a mechanism to mitigate international importation, transmission, and spread of highly communicable diseases during epidemics of high consequence or emerging infectious diseases.

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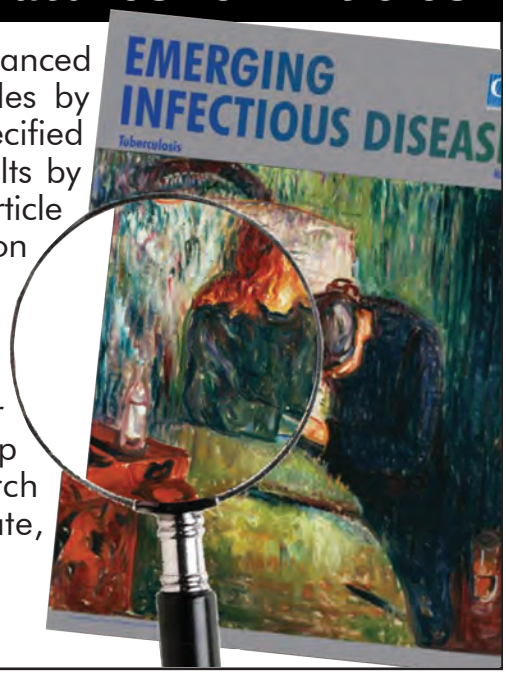

Responding to Communicable Diseases in Internationally Mobile Populations at Points of Entry and along Porous Borders, Nigeria, Benin, and Togo

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Recent multinational disease outbreaks demonstrate the risk of disease spreading globally before public health systems can respond to an event. To ensure global health security, countries need robust multisectoral systems to rapidly detect and respond to domestic or imported communicable diseases. The US Centers for Disease Control and Prevention International Border Team works with the governments of Nigeria, Togo, and Benin, along with Pro-Health International and the Abidjan-Lagos Corridor Organization, to build sustainable International Health Regulations capacities at points of entry (POEs) and along border regions. Together, we strengthen comprehensive national and regional border health systems by developing public health emergency response plans for POEs, conducting qualitative assessments of public health preparedness and response capacities at ground crossings, integrating internationally mobile populations into national health surveillance systems, and formalizing cross-border public health coordination. Achieving comprehensive national and regional border health capacity, which advances overall global health security, necessitates multisectoral dedication to the aforementioned components.

The consequences of insufficient national and regional public health capacities at points of entry (POEs), such as established airports, seaports, or ground crossings, in border regions and among internationally mobile populations became apparent during the 2014–2016 West Africa Ebola epidemic. Within weeks of the first Ebola case in a remote area of Guinea, the epidemic had inconspicuously spread across land borders to Liberia and Sierra Leone (*1*,*2*). A limited number of cases spread over land to Senegal and Mali and through air travel to Nigeria, Spain, and the United States (*3*–*5*). Throughout the almost 2-year epidemic, common local and long-distance international human movement between highly connected communities increased the geographic impact of disease.

National public health systems are designed to detect communicable diseases among established communities and healthcare infrastructure and to respond to minimize their domestic spread. Economic, linguistic, familial, health-seeking, and other factors influence the complexity of cross-border networks. The associated formal and informal international movement challenges national systems' capacities to detect public health events among these mobile populations (*6*,*7*). Border health strategies minimizing the risk of importation and exportation of disease through POEs, as well as across porous land borders, are not a common feature of national surveillance systems.

In 2005, all World Health Organization (WHO) signatory member states renewed their commitment to addressing the elevated health risks of our increasingly interconnected world by adopting the revised International Health Regulations 2005 (IHR 2005) (*8*). These regulations define legally binding requirements to mitigate the international spread of disease, including required public health capacities at POEs and detection and response collaboration between neighboring and regional countries. Under the IHR 2005, member states are responsible for designating the airports, seaports, and, where justified for public health reasons, ground crossings that must meet POE core capacity requirements defined in the IHR Annex 1 (*8*). Many countries have not yet met IHR 2005 obligations for designated POEs, leaving them particularly

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vulnerable to possible importation or exportation of communicable diseases (*9*,*10*).

The US Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine (DGMQ), part of the National Center for Emerging and Zoonotic Infectious Diseases, oversees the achievement and maintenance of IHR 2005 core capacities at US POEs. Given this domestic experience, DGMQ began responding to requests for technical assistance from Guinea, Liberia, Sierra Leone, and other regional countries in August 2014 to initiate and strengthen border health measures, primarily exit screening at international airports (*11*). These measures helped Ebola-affected countries meet WHO recommendations, thereby enabling at least some commercial air carriers to continue servicing these countries and providing a vital channel for provision of supplies and response personnel (*12*).

As the number of Ebola cases declined, DGMQ evolved its strategy in the region from outbreak response to longer-term border health capacity building under the premise that effective border health strategies before and during a public health event can help reduce the risk of exporting or importing a communicable disease. Border health strategies could potentially obviate the need for unaffected countries to implement costly entry-screening measures for persons returning from affected countries, as many Western countries did during the Ebola epidemic (*12*,*13*). In this article, we describe a set of border health system strengthening strategies, along with successes and lessons learned from integrating those strategies through partnerships with Nigeria, Benin, and Togo. These countries are highlighted because of their contributions to enhanced global health security through their substantial progress with implementing a comprehensive border health approach.

Strategies

DGMQ created the International Border Team (IBT), which, with funding from the Global Health Security Agenda, established formal partnerships with 10 countries (Benin, Côte d'Ivoire, Ghana, Guinea, Guinea-Bissau, Liberia, Nigeria, Senegal, Sierra Leone, and Togo) to advance a comprehensive border health strategy (*14*). In this article, we describe in detail the development of each component in this strategy: 1) operational IHR 2005–compliant public health emergency response plans (PHERPs) and supporting standard operating procedures (SOPs) at nationally prioritized POEs; 2) plans for allocating resources to strengthen detection, notification, and referral procedures for prioritized geographic areas and POEs at highest risk for importation or exportation of a high-consequence communicable disease owing to population connectivity and international travel patterns; and 3) timely cross-border and regional public health data sharing, coordination, and collaboration to detect and respond to communicable disease.

Border Health Strategy 1—Developing POE-Specific PHERPs and SOPs

The IHR 2005 require designated POE to demonstrate capacity for "appropriate public health emergency response by establishing and maintaining a public health emergency contingency plan" (*8*). At many POEs, individual agencies often know appropriate procedures to take during a public health event, yet the procedures are not documented or shared. In the absence of an agreed-upon plan, stakeholders risk gaps or redundancies in communication, surveillance, and response efforts, consequently increasing the risk of an uncoordinated and delayed response. Public health response plans and SOPs are beneficial at IHR-designated POE, as well as at smaller, less-resourced POEs.

A POE PHERP with accompanying SOPs is a multiagency coordination plan that describes procedures to prevent the introduction and transmission of suspected communicable diseases through that POE during routine and response operations. Having the SOPs in writing—available, trained on, and exercised—ensures a timely and coordinated response with all involved sectors. In the airport context, public health, civil aviation, airport authorities, safety and security agencies, airlines, medical and ambulance services, police, and other agencies that have a role in implementing the PHERP are all critical participants in developing, finalizing, exercising, and operationalizing the plan.

The International Civil Aviation Organization (ICAO), the UN specialized agency that ensures that member states' civil aviation operations and regulations conform to global norms, has developed aviation sector guidelines in accordance with IHR 2005, including those for the development of public health emergency contingency plans at airports (*15*). When developing an airport plan, partners must reconcile ICAO guidance with multiple other global guidance documents as well as other key airport and country planning documents, such as the Aerodrome Emergency Plan, the National Civil Aviation Plan, and the National Public Health Plan. To facilitate the PHERP development process, IBT created a template document, consolidating the WHO Guide for Public Health Emergency Contingency Planning at Designated Points of Entry (*16*) and the ICAO Template for a National Aviation Public Health Emergency Preparedness Plan (*17*). IBT also documented the methodology to create a PHERP through a core planning team, and incorporated lessons learned from DGMQ's experience in developing communicable disease response plans in the United States. Partner countries have also applied the PHERP development process to seaports and ground crossings.

Border Health Strategy 2—Establishing Priorities for Capacity Building at Identified POE and Border Regions

Nations often have insufficient financial and personnel resources to build robust border health capacity at all POEs and along entire international borders. To address these challenges, nations can strengthen border health by allocating resources to select POEs and border areas, prioritized by public health risk of importation or exportation of communicable disease, among other considerations. IBT has developed a low-resource field method to gather information from national, subnational, and local stakeholders and community members to characterize population mobility patterns and strength of proximal and distant intercommunity connectivity. This method consists of key informant and focus group discussion guides that a facilitator uses in conjunction with maps of the relevant geographic areas to guide participants through describing the characteristics of those who move into, through, between, and out of identified areas with population movement and connectivity patterns that may increase the impact of a public health event. Nations can use the information, summarized in reports and on maps, to inform their understanding of areas, including POEs, at disproportionately higher public health risk of importation or exportation of communicable disease based on human movement (*18–20*).

The WHO IHR 2005 core capacities self-assessment tool enables nations to quantitatively measure current IHR capacities at POEs (*21*). However, the IHR self-assessment tool was developed to evaluate capacities at designated POEs, often international airports, with established infrastructure and resources, and is not as applicable to lower-resource POEs, such as many ground crossings, especially those that are far from urban centers. Further, although the IHR self-assessment tool reserves space to record comments for each question, tool implementation and results analysis focus on the quantitative results. In 2015, IBT developed the Border Health Capacity Discussion Guide (BHCDG) and piloted it in 5 West Africa countries (*22*). The BHCDG complements the IHR self-assessment tool by gathering qualitative information from national, subnational, and border area stakeholders on border health capacities, where infrastructure may not be robust. Nations can use the BHCDG alone or with the IHR self-assessment tool to better understand current capacities and develop an action plan to strengthen gaps in detection, notification, and referral procedures. Specifically, the guide facilitates the collection of qualitative information on the following:

- Communication capacity: communication systems, including identified points of contact for ground crossings, to report and receive notifications of public health events and communication efforts to inform travelers and neighboring communities on public health events or interventions
- Information and data systems: border characteristics, including additional, proximal, unofficial ground crossings, traveler volume, purpose of travel; surveillance systems that incorporate health assessments and responses to public health events at ground crossings; and plans and procedures for public health data sharing with cross-border and regional counterparts about events, such as outbreaks and case investigations
- Response and referral systems: public health and medical services available at and/or near ground crossings and coordination with referral health facilities and response plans and training describing how to prepare for, and respond to, public health events at ground crossings.

Border Health Strategy 3—Timely Cross-Border and Regional Public Health Collaboration

Effective and timely national health surveillance, coupled with communication and coordination with neighboring and regional countries, supports achieving the IHR principle to protect "all people of the world from the international spread of disease" (IHR 2005 Article 3.3 [*8*]). Through border health strategies 1 and 2, nations build public health capacities at designated and prioritized POEs and border areas to better detect and notify public health events among most international travelers. However, persons travel across porous borders outside a POE or may pass through a POE undetected by health screening measures for several reasons, including being asymptomatic while traveling. Border health strategy 3 addresses the development of cross-border relationships that support prompt communication and coordination between neighboring and regional countries to report and respond to communicable disease events with elevated risk of cross-border transmission.

Nations should incorporate all POE, regardless of infrastructure, into their national health surveillance systems as additional peripheral reporting units expected to follow standard, site-appropriate detecting and reporting practices (*23*). For example, after detecting an ill traveler, a POE official could record event information on a standardized surveillance report form and submit that form to the POE's referral facility or surveillance unit. Where POEs are not staffed, and along borders without identified POEs, nations can provide communities with additional education to empower them to report potential priority communicable diseases following standard procedures.

To support binational and multinational public health collaboration and coordination, nations can develop and disseminate clear national- and local-level plans that, among other objectives, define when and what public health event information to share across a border, and how to maintain coordination with cross-border counterparts.

Some of these collaborations exist informally, but without formalized documentation they may not be clearly defined, may be challenging to supervise, and may not reflect the most current policies and priorities. In addition to documenting domestic plans at the national and local levels, nations can work with neighbors to create integrated cross-border communication and response plans. Real-time data sharing and coordination across borders benefit from maintenance of multinational plans and procedures, along with routine communication to ensure that the plans reflect current priorities.

Successes and Lessons Learned

Border Health Strategy 1

Port Health Services of the Federal Ministry of Health in Nigeria, with implementation support from Pro-Health International (PHI) and technical guidance from IBT, began developing, operationalizing, and training staff on PHERPs at 2 international airports: Murtala Muhammed International Airport in Lagos, the 5th busiest airport in Africa, and Nnamdi Azikiwe International Airport in Abuja, the 13th busiest (Figure) (*23*). To develop these plans, Port Health Services, Federal Ministry of Health, airport authority, civil aviation, airlines, immigration, customs, and security partners actively participated in a series of PHERP and SOP development workshops facilitated by IBT and PHI.

During the introductory PHERP workshops, participants established multiagency core planning teams composed of 8 to 10 persons nominated based on their experience, knowledge, and ability to represent their agencies during the planning process. PHI and Port Health Services, with technical guidance from IBT, facilitated a series of core planning team meetings for Murtala Muhammed International Airport, resulting in a complete PHERP after 10 months. The approved plan now serves as one of the first IHR 2005–compliant PHERPs in West Africa.

The Nnamdi Azikiwe International Airport core planning team, established in March 2016, also finished its PHERP after 11 months of planning. In addition, the core planning team, IBT, and PHI are initiating a new training curriculum and exercise schedule. This training and exercise series is informed by best practices from US CDC quarantine stations and designed to enable responders to execute the PHERP. These tools and workshops can be adapted for use at other types of POE, such as seaports or ground crossings.

Border Health Strategy 2

In 2016, Togo and Benin, with implementation support from the Abidjan Lagos Corridor Organization (ALCO) and technical guidance from IBT, used IBT field methods to better understand population movement patterns and connectivity related to economic opportunities, healthcare seeking, and cultural festivals, among other

Figure. Points of entry within Nigeria, Benin, and Togo targeted for comprehensive border health capacity building through development of public health emergency response plans. Insets show location of enlarged area in West Africa and Africa.

factors, with a geographic focus along the international coastal highway—critical because of the high international traveler volume. These countries are working collaboratively, along with IBT and ALCO, to interpret and map the information about crucial points of interest and linguistic, tribal, and other factors associated with the populations that congregate or travel to or through these points. In addition, the countries are using the information to improve national and cross-border surveillance plans including, for example, strengthening preparedness for movement associated with annual celebrations attracting regional visitors. Further, Togo, Benin, and Nigeria are analyzing population mobility and retrospective cholera surveillance data to inform coordinated preparedness and response plans. The countries used this approach to strengthen cross-border coordination during a multinational Lassa fever outbreak in early 2017.

The Benin and Togo ministries of health used the BHCDG following its adoption, in consultation with WHO, ALCO, and IBT, at nationally prioritized ground crossings along the corridor (Kodjoviakopé and Sanvee Condji in Togo and Hillacondji and Kraké in Benin) and a binationally prioritized ground crossing on their shared border (Tohoun and Aplahoue) (Figure). The BHCDG findings gathered from local officials at the POE revealed details about a consistent lack of plans and procedures for responding to public health events, few or no formal mechanisms for collaboration or communication with the neighboring country during a health crisis, and lack of transport and referral mechanisms in place for ill travelers identified at the border. The ministries of health, with technical support from IBT, are implementing an action plan to address the identified areas for improvement using the BHCDG results.

In Nigeria, PHI facilitated BHCDG discussions with personnel at the Semé and Idiroko ground crossings with Benin, the busiest ground crossing in Nigeria. PHI, in collaboration with WHO and the Federal Ministry of Health, adapted the BHCDG to focus on border health human resources, the surveillance system, and binational and regional data sharing—areas not covered in depth by the IHR 2005 self-assessment tool. These discussions occurred 2 weeks after a baseline IHR self-assessment conducted by WHO and national authorities. PHI presented results from the BHCDG discussions to the IHR competent authority and the WHO, who are developing a POE-specific action plan to address gaps identified through the IHR self-assessment and BHCDG activity.

Border Health Strategy 3

Nigeria's surveillance system has identified border communities as key components and provides them with tailored training on how to detect and report public health event information. This training, implemented by PHI and the Nigeria Centre for Disease Control, led to improved relationships and communication between border area personnel, health facilities, Local Government Area (Nigeria's district-level administrative unit) surveillance and Port Health officials, and the national level.

The International Border Team and ALCO, with cosponsoring from the US Agency for International Development (USAID) Benin, facilitated 2 multinational meetings among Nigeria, Benin, Togo, Ghana, and Cote d'Ivoire (which participated in the second meeting only), to formalize cross-border and regional public health data sharing and coordination strategies. Participants included IHR 2005 national focal points, ministry of health legal representatives, national and local public health surveillance leads, national immigration representatives, local port health and quarantine representatives, national and local agricultural and animal health representatives, and the Field Epidemiology Training Program Benin resident advisor. Products from these successful meetings include a draft memorandum of understanding and 7 supporting SOPs and annexes covering the following topics: priority diseases for real-time cross-border reporting; minimum reporting requirements for a cross-border report of a communicable disease; national activities to support cross-border coordination across public health response activation phases; determination of whether a public health event meets criteria for a cross-border report of a communicable disease; determination of whether a public health event meets criteria for responding to a cross-border report of a communicable disease; communication structure for reporting a cross-border event; and communication structure for responding to a cross-border report of a public health event.

In addition to signing the final documents, follow-up steps include consolidating and disseminating cross-border contact information for public health officials working in border districts. Participants noted that they will use the final compendium of jointly produced documents as a training manual for officials working along the borders.

Discussion

Human mobility is inherently associated with the spread of infectious diseases (*20*,*24*). As transportation networks expand, the speed of travel increases, the volume of passengers and the goods they transport grows, and the potential for the spread of pathogens and their vectors from remote locations to distant countries increases. The Global Health Security Agenda was launched in 2014 to accelerate IHR 2005 implementation to advance global capacity to rapidly detect, respond to, and control public health emergences at their source (*14*). To be maximally effective, a comprehensive global health security agenda must incorporate POEs, border regions, and

internationally mobile populations. We have described a set of border health strategies that, when implemented together, are designed to advance national, binational, and regional border health systems. These advanced systems can contribute to improved early detection, effective communication, and timely and adequate response, thereby reducing the risk of international spread of communicable diseases without hindering the free movement of persons and goods.

Border health approaches, for the most part, can leverage tools and strategies in the existing public health and medical systems and infrastructure. The International Border Team's experience working with partners in Nigeria, Benin, and Togo demonstrates several successes with implementing low-resource methods to strengthen border health capacities. Perhaps the most noteworthy success across all border health strategies was the bringing together of partners to improve multinational and multisectoral collaborations and communication.

Having a written emergency response plan is a key IHR 2005 requirement. Almost complete PHERPs and priority SOPs have been developed for 2 of the highest-volume international airports in West Africa, with others at varying stages of development. Completion, operationalization, and exercising of the PHERPs will help countries meet several of their IHR requirements.

National leaders in each country, along with ALCO and PHI, expressed that the additional information provided by the BHCDG helped them develop a more complete understanding of existing border health capacities and added context to the quantitative results of the IHR 2005 self-assessment. BHCDG information also catalyzed expanding POE-focused capacity-building plans to encompass strengthening communication networks with neighboring countries. The countries plan on using the BHCDG at other priority ground crossings identified, in part, by using information on cross-border population mobility and connectivity.

The challenges experienced to date may be typical of any multisectoral, multinational partnership and were often overcome because of the value placed on the partnerships and in maintaining open dialogue. West Africa has many critical public health challenges; occasional delays in implementation of the comprehensive border health strategy are the result of partners having to respond to competing, higher-priority problems. Achieving consensus on plans and approvals to implement new strategies is time-consuming because of the number of stakeholders who must validate them. Finally, incompatible technology and processes, as well as different languages in neighboring countries, add complexity to information sharing.

Despite the challenges, for resource-limited countries with porous land borders and high cross-border mobility resulting from shared familial, cultural, linguistic, and economic ties, border health security, and therefore health security as a whole, is best achieved by implementing a comprehensive border health strategy involving relevant local, national, and regional sectors. The examples from Nigeria, Benin, and Togo demonstrate that development of a border health system can be successful by including PHERPs for POEs, prioritizing border areas through risk-based assessments using the BHCDG and population mobility mapping, and enhancing timely cross-border surveillance and coordination. Implementing these strategies will help to achieve global health security by supporting countries to prevent the spread of potential health threats across international borders.

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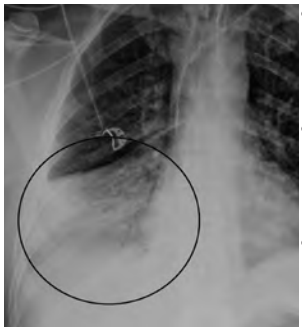

- Ebola in West Africa—CDC's Role in Epidemic Detection, Control, and Prevention
- Use of Internet Search Queries to Enhance Surveillance of Foodborne Illness
- Achievements in and Challenges of Tuberculosis Control in South Korea
- Ebola Virus Outbreak Investigation, Sierra Leone, September 28–November 11, 2014
- Neurologic Disorders in Immunocompetent Patients with Autochthonous Acute Hepatitis E
- Mycotic Infections Acquired outside Areas of Known Endemicity, United States
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https://wwwnc.cdc.gov/eid/content/21/11/contents.htm

EMERGING INFECTIOUS DISEASES

Assessment of National Public Health and Reference Laboratory, Accra, Ghana, within Framework of Global Health Security

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The Second Year of Life project of the Global Health Security Agenda aims to improve immunization systems and strengthen measles and rubella surveillance, including building laboratory capacity. A new laboratory assessment tool was developed by the Centers for Disease Control and Prevention to assess the national laboratory in Ghana to improve molecular surveillance for measles and rubella. Results for the tool showed that the laboratory is well organized, has a good capacity for handling specimens, has a good biosafety system, and is proficient for diagnosis of measles and rubella by serologic analysis. However, there was little knowledge about molecular biology and virology activities (i.e., virus isolation on tissue culture was not available). Recommendations included training of technical personnel for molecular techniques and advocacy for funding for laboratory equipment, reagents, and supplies.

The International Health Regulations (*1*) recommend that countries develop, strengthen, and maintain the capacity to detect, notify, and report major events resulting in public health risk and emergencies of international concern, such as infectious disease epidemics. The difficulties encountered in providing timely laboratory testing during the recent epidemic of Ebola in West Africa (*2*) highlighted that global health security relies on adequate public health laboratory capacity in all countries, including Ghana. The 2012–2020 Global Measles and Rubella Strategic Plan calls for effective case-based surveillance of measles and rubella with laboratory confirmation (*3*).

The World Health Organization (WHO) recommends that all countries implement virologic surveillance of measles and rubella to help identify sources of infection and verify elimination (*4*). The WHO Global Measles and Rubella Laboratory Network (GMRLN), established in 2000, has >700 laboratories serving 191 countries, providing diagnostic support for measles and rubella surveillance (*5*). As of 2015, only 48% of countries reporting laboratory-confirmed measles cases also reported measles virus genotypes, and only 10% of countries reporting laboratory-confirmed rubella cases also reported rubella virus genotypes (*6*).

To support the WHO/GMRLN recommendations for measles and rubella surveillance, including virologic surveillance, the Measles and Rubella Global Specialized Laboratory (GSL) (Division of Viral Diseases, National Center for Immunization and Respiratory Diseases) at the Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) supports laboratory capacity building in all WHO regions. The global reach of the GSL at CDC enabled partnering with the Global Health Security Agenda (GHSA), launched in 2014 and aimed at prevention, detection, and response to infectious disease outbreaks worldwide (*7*).

Laboratories play a critical role in the surveillance of measles and rubella, which requires high-quality testing. However, there is currently no tool to assess the capacity of a laboratory, especially for measles and rubella surveillance or to compare different laboratories within the GMRLN. In response to the need for a standardized capacity measurement tool, the CDC GSL developed the CDC International Measles and Rubella Laboratory Capacity Review tool. This tool was field tested at the National Public Health and Reference Laboratory (NPHRL) in Accra, Ghana, as part of the Second Year of Life Project, within the GHSA. This project aims to improve immunization systems and to strengthen disease surveillance for vaccine-preventable disease, including building laboratory capacity for surveillance of measles and rubella and supporting implementation of surveillance for congenital rubella syndrome.

In Ghana, the NPHRL, which is a GMRLN laboratory, currently performs testing to detect measles- or

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rubella-specific IgM. The capacity to conduct molecular testing is minimal. The objectives of the assessment of the capacity of NPHRL were to describe the status of the laboratory and determine the needs for equipment and training required to initiate molecular testing. We describe the new CDC International Measles and Rubella Laboratory Capacity Review tool and the results of the laboratory capacity assessment of the NPHRL.

The CDC International Measles and Rubella Laboratory Capacity Review tool was created in Excel (Microsoft, Redmond, WA, USA) by using the International Influenza laboratory capacity tool (*8*,*9*) as a model. The tool is organized into 8 sections. Each section is composed of a set of questions that guide the process of assessing laboratory capacity to help identify the strengths and challenges of the laboratory, including priority areas for strengthening: 1) general laboratory (39 questions), 2) specimen collection and reporting (32 questions), 3) virology laboratory (19 questions), 4) molecular biology (27 questions), 5) laboratory biosafety and safety (31 questions), 6) quality assurance/quality control (20 questions), 7) equipment (11 questions), and 8) training (36 questions). These questions aimed to identify the capacity of a laboratory to frequently respond to public health events, such as a measles and rubella outbreak, by accurately testing specimen and reporting data in a timely manner; identify safety and biosafety measure implementation in place; and professional development of laboratory staff. These questions also helped to collect information on the role of the laboratory in public health surveillance; and conditions of the facility, including the building, availability of electricity, water, and air conditioning.

Each question was assigned a point value of 1 or 0, except for multiple option questions, for which each option was assigned either a value of 0.25 or 0.5 to minimize total score difference between questions in the same section. Weighting of questions was not applied because the tool was used to capture areas of strength and weaknesses to enable the country to prioritize areas that need score, to be strengthened first on the basis of their public health objectives and available resources.

Assessment data were entered into an Excel-based file and scores were calculated. The points for each section were automatically summed and divided by the total number of points available in the section and converted into a percentage. The assessment of NPHRL was conducted during 5 days in March 2016 by 2 subject matter experts from CDC who had expertise in laboratory methods, laboratory capacity building, and surveillance for measles and rubella. These experts conducted a site visit to NPHRL to interview laboratory personnel, evaluate facilities, and review key documents. Two laboratory assessment tools were used to capture information on public health functions. The first tool used was the WHO Laboratory Assessment Tool (*10*), which broadly captures all aspects of laboratory services. The second tool used was the new CDC International Measles and Rubella Laboratory Review Tool, which focuses on measles and rubella–specific laboratory testing activities, such as virus isolation, confirmation of measles and rubella infection, and genotyping of measles and rubella viruses.

Results obtained with the WHO tool indicated that NPHRL is well organized and has a functioning quality management system (Figure 1). However, equipment, reagents, and supplies are usually insufficient, mostly because of a lack of funding coupled with unavailability of reagents in the country. Some critical reagents and supplies have to be ordered from outside Ghana, and this factor results in delay. Major challenges include inadequate financial resources for laboratory activities and maintenance of equipment and lack of political commitment (e.g., policies, budget) to support the laboratory (Figure 2).

Results obtained with the CDC tool showed good capacity for specimen handling (100%) and biosafety and safety (81%) (Figure 3). However, there was little capacity for virology (0%) or molecular biology (2%) (Figure 3). The NPHRL was proficient in serologic testing for measles and rubella because this laboratory passed its 2015 ELISA proficiency test as part of the GMRLN proficiency

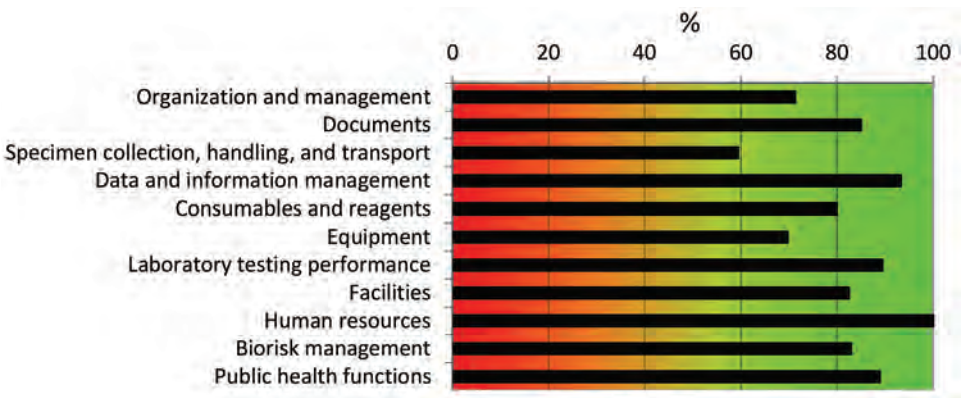

Figure 1. Summary of assessment results for the National Public Health and Reference Laboratory, Accra, Ghana, determined by using the World Health Organization Laboratory Assessment Tool. Capacity score (0%–100%) of each section of the tool is indicated and color coded. Red (<50%) indicates need for major improvement; orange (50%–80%), some improvement is necessary; green (>80%), the laboratory is in good standing.

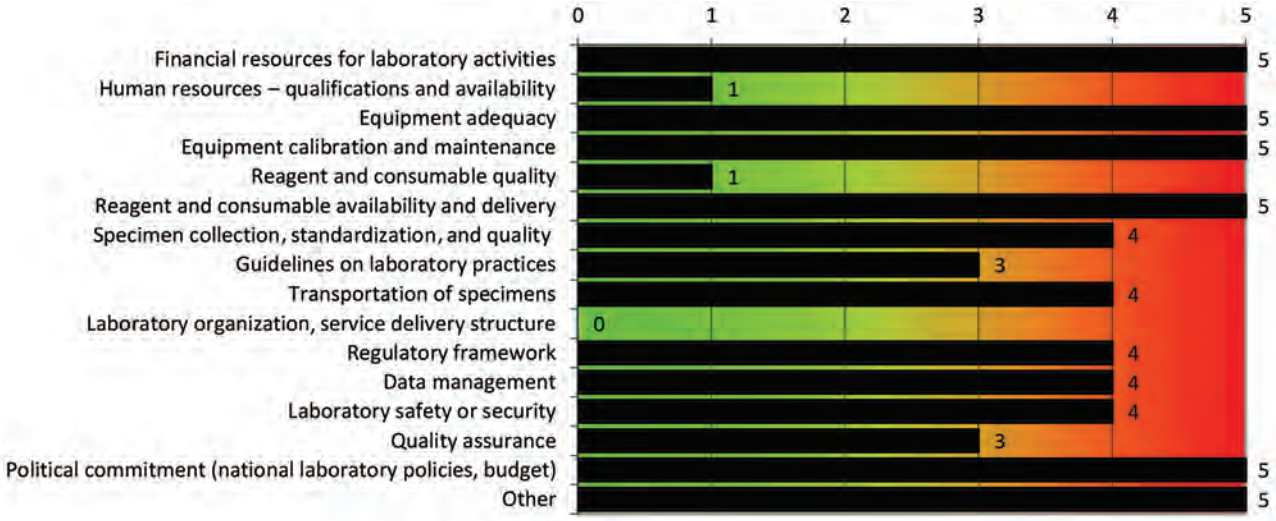

Figure 2. Gap score analysis of the National Public Health and Reference Laboratory, Accra, Ghana, performed by using the World Health Organization Laboratory Assessment Tool. Gaps are indicated on the basis of a score of 0–5. Results are indicated with a color code for each section of the laboratory. Green (0–1), no gaps found; orange (2,3), needs some improvement; red (4,5), requires major improvement. Other, lack of political commitment.

testing program coordinated by WHO. None of the NPHRL staff assigned to measles and rubella serologic testing was trained in molecular biology techniques for measles and rubella surveillance.

Since 2012, the NPHRL has been involved in the Strengthening Laboratory Management Toward Accreditation (SLMTA) program (*11*). The SLMTA scored checklist quantifies the quality status of a laboratory by using a 0–5-star rating (*12*). The NPHRL has received 1 SLMTA star since December 2013. Overall, NPHRL had a score of 72% by the CDC tool (Figure 3) and a score of 71% by the WHO tool (Figure 1). Furthermore, both tools confirmed weakness in maintenance of laboratory equipment and showed the highest gap score (5) by the WHO tool (Figure 2) and the lowest capacity score by the CDC tool (0%) (Figure 3). Gap score analysis with the WHO tool (Figure 2) resulted from a set of questions asked to laboratory staff to highlight and prioritize the biggest needs or weaknesses of the laboratory. Thus, gap scores might be interdependent and not directly proportional to the capacity score observed (Figure 1).

For NPHRL, lack of financial resources, which had the highest gap score (5), directly affected the possibility of performing regular calibration and maintenance of equipment and the availability of equipment, reagents, and consumables (Figure 2). In addition, lack of political commitment made it difficult to maintain the facilities (shown as "other" in Figure 2). Specimen collection, which had the lowest score (59%) (Figure 1), was classified as a second priority, with a gap score of 4 (Figure 2).

The main advantage of the CDC tool is its specificity in regards to measles and rubella laboratory activities. Therefore, recommendations based on assessment results covered all requirements needed to strengthen measles and rubella laboratory surveillance. This new tool could also be quickly adapted to assess laboratory activities for surveillance of other viral diseases.

This study had some limitations. Both tools did not capture the same information. Therefore, it is difficult to fully compare these tools. The CDC tool does not capture laboratory testing activities for diseases other than measles and rubella, whereas the WHO tool captures these laboratory activities. Thus, there were some discrepancies observed between results obtained with the WHO tool compared with those obtained with the CDC tool regarding specimen handling, for which the scores were 60% and 100%, respectively. Such a difference was also found in laboratory testing performance, for which the score was 80% with the WHO tool (Figure 1) compared with 0%–2% (virology laboratory and molecular biology laboratory) with the CDC tool (Figure 3).

The CDC tool was critical in capturing laboratory-specific activities needed for measles and rubella surveillance and to rapidly identify related laboratory needs, such as specific equipment required for molecular and virologic testing, training of laboratory personnel for molecular methods for case confirmation and genotyping, and the need for training for tissue culture and virus isolation. The CDC and WHO tools complemented each other in providing a more complete picture of the capacity of NPHRL. For example, the WHO tool provided information on human resources, consumables, and reagents, as well as public health functions of the NPHRL. The CDC tool focused on information related to laboratory

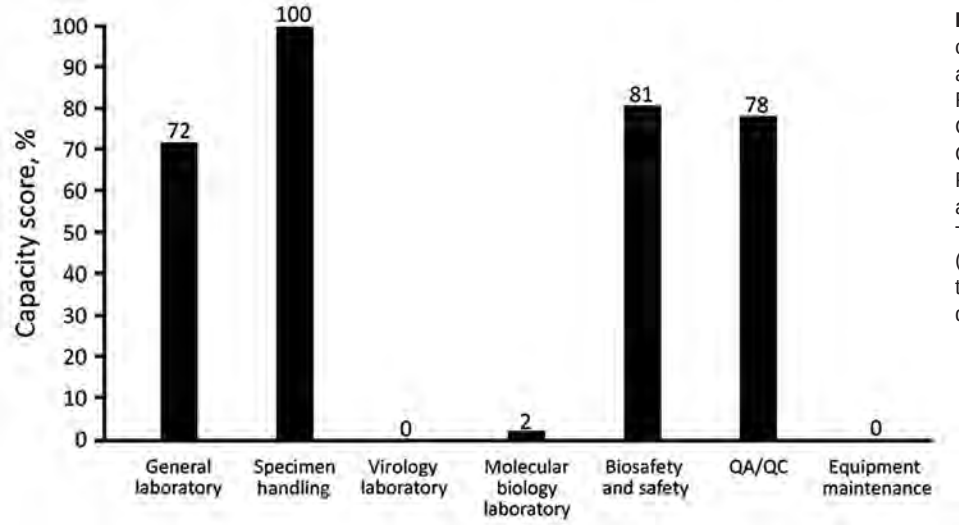

Figure 3. Indicators of laboratory capacity for measles and rubella at the National Public Health and Reference Laboratory, Accra, Ghana, analyzed by using the Centers for Disease Control and Prevention International Measles and Rubella Laboratory Review Tool. Capacity score is indicated (0%–100%) for each section in the tool. QA, quality assurance; QC, quality control.

activities, such as virology and molecular biology for measles and rubella surveillance.

The assessment results were used to develop a working plan for improving molecular surveillance of measles and rubella in Ghana, which is needed to support achievement of the 2020 measles elimination goal. Laboratory activities will focus on implementation of molecular methods for case confirmation and genetic characterization of measles and rubella virus strains. Equipment and reagent needs will be supported, and laboratory personnel will be trained by the end of 2017, with support from the GHSA and CDC GSL. The data produced from this set of activities will be sent to the Ghana Ministry of Health, the WHO country office, and the WHO Regional Laboratory Coordinator for the West African Region. These data can be used to advocate for more financial resources from the Ghana Ministry of Health, WHO, and other partners to ensure the sustainability of laboratory surveillance of measles and rubella at NPHRL.

Continual reassessment by using the same tools will help to measure the effect of GHSA support at NPHL. The new CDC tool (which is available upon request to the corresponding author) will also be used to assess measles and rubella laboratories in other countries within the GMRLN as needed by WHO, and could be adapted to assess laboratory capacity for other vaccine-preventable diseases worldwide. Building laboratory capacity and especially building molecular biology capacity for measles and rubella surveillance will strengthen the NPHRL platform for detection of other diseases and increase the capacity of a country to rapidly detect, respond, and contain public health emergencies at their source, thereby enhancing global health security.

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- Estimation of Severe MERS-CoV Cases in the Middle East, 2012–2016
- Hypervirulent Clone of Group B *Streptococcus* Serotype III Sequence Type 283, Hong Kong, 1993–2012
- Chikungunya Virus in Febrile Humans and *Aedes aegypti* Mosquitoes, Yucatan, Mexico
- Daily Reportable Disease Spatiotemporal Cluster Detection, New York, New York, USA, 2014–2015
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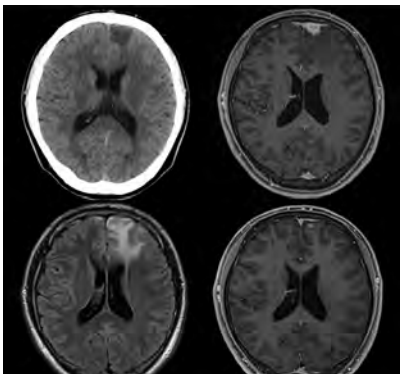
- African Tick-Bite Fever in Traveler Returning to Slovenia from Uganda
- Synovial Tissue Infection with *Burkholderia fungorum*



EMERGING INFECTIOUS DISEASES https://wwwnc.cdc.gov/eid/articles/issue/22/10/table-of-contents

Enhancing Laboratory Response Network Capacity in South Korea

J. Todd Parker, Ann-Christian Juren, Luis Lowe, Scott Santibañez, Gi-eun Rhie, Toby L. Merlin

Laboratory Response Network (LRN) laboratories help protect populations from biological and chemical public health threats. We examined the role of LRN biological laboratories in enhancing capacity to detect and respond to public health infectious disease emergencies in South Korea. The model for responding to infectious disease emergencies leverages standardized laboratory testing procedures, a repository of standardized testing reagents, laboratory testing cooperation among hospital sentinel laboratories and reference laboratories, and maintenance of a trained workforce through traditional and on-demand training. Cooperation among all network stakeholders helps ensure that laboratory response is an integrated part of the national response. The added laboratory testing capacity provided by the US Centers for Disease Control and Prevention LRN assets helps protect persons who reside in South Korea, US military personnel and civilians in South Korea, and those who reside in the continental United States.

The US Centers for Disease Control and Prevention (CDC), in cooperation with the Federal Bureau of Investigation (FBI) and the Association of Public Health Laboratories, developed the Laboratory Response Network (LRN) as part of the strategic infrastructure that keeps the United States safe from intentional and naturally occurring public health threats (*1*). The LRN has a broad capacity to detect biological and chemical public health threats. LRN laboratories that detect and identify biological threat agents, such as *Bacillus anthracis*, ricin toxin, or variola virus, are referred to as LRN-B laboratories; those that detect chemical agents are called LRN-C laboratories. The LRN-B comprises clinical, food, veterinary, environmental, and agricultural laboratories that work together to detect and identify agents that have historically been considered potential weapons of mass destruction (*2*). The LRN-B currently has 139 reference microbiology laboratories; ≈100 laboratories are in the United States, and member laboratories (which have access to LRN-B assets) are in Canada, Australia, and South Korea (Figure 1). Increasing the number of LRN-B laboratories worldwide can help countries more rapidly detect, respond to, and contain public health emergencies at their source and thereby enhance global health security.

South Korea (also called the Republic of Korea) is geographically situated in a region at high risk for a state-sponsored release of biological or chemical agents (*3*,*4*). In addition to the estimated 50 million South Korea residents, >28,500 US military personnel and 136,600 US civilians live and work there (*5*). Risks for a deliberate biological agent release in South Korea affect the local population (*1*), US military personnel and civilians who live and work on the Korean peninsula (*2*), and the population of the continental United States through imported cases and secondary transmission (*3*).

The establishment of LRN-B laboratories in South Korea enables these laboratories to access the standardized LRN testing procedures and reagents. This access helps leverage US response assets in the event of a biological agent release, thereby assisting in the protection of all 3 populations described above. We describe the development of the LRN model in the United States (*1*), how the US LRN model works by using a 3-tiered system (*2*), and collaborative efforts to enhance international–US CDC LRN capacity in South Korea (*3*).

Development of the LRN Model

In 1999, the US LRN was founded as a collaboration among CDC, the Association for Public Health Laboratories, and the FBI. The initial focus of the LRN-B centered on identification of potential bioterrorism pathogens (*6*). The LRN subsequently developed into an integral component of detection and response to outbreaks of severe acute respiratory syndrome (2003), monkeypox (2003), Middle East respiratory syndrome (MERS; 2013), Ebola (2014–2015), and Zika virus infection (2016).

LRN-B laboratories use a 3-tiered system. The first tier comprises ≈5,000 sentinel microbiology laboratories, located mainly in hospitals and clinics. The role of a sentinel laboratory is not to confirm the identity of a particular suspected bioterrorism pathogen but rather to identify frequently encountered bacteria with similar culture characteristics or to refer the specimen to an LRN reference-level microbiology laboratory (*7*,*8*).

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The second tier of the LRN-B comprises reference-level microbiology laboratories, typically state, city, or local public health laboratories, or military, veterinary, and agriculture laboratories (*9*). LRN-B reference laboratories follow testing algorithms to rapidly identify specific presumed and confirmed bioterrorism pathogens.

The third tier of the LRN-B comprises agencies such as CDC and the US Army Medical Research Institute of Infectious Diseases. The LRN reference-level laboratories can refer isolates that require further characterization to these laboratories.

In addition to the 3-tiered system, the LRN program office at CDC manages several network assets that facilitate national preparedness. These assets include secure access to standardized pathogen-detection procedures, a repository of quality pathogen-detection reagents, a robust proficiency-testing program, secure laboratory communication and reporting processes, and expertise in Emergency Use Authorizations for emergency response (*10*). The Food and Drug Administration (FDA) can authorize (FDA approval) pathogen-detection testing of human clinical specimens for the duration of a declared emergency. The LRN

Figure 1. Locations of Laboratory Response Networks in South Korea. BAACH, Brian Allgood Army Community Hospital, US Army Yongsan Garrison, Seoul; KCDC, Korea Center for Disease Control, Osong.

program office has worked with FDA for Emergency Use Authorizations deployment and to predeploy assays for severe acute respiratory syndrome, MERS, Ebola, and Zika virus infection.

During the US LRN membership enrollment process, foreign and domestic laboratories self-determine the extent of the LRN-B testing portfolio that their laboratory will implement, based on their resources and the threats that they are most likely to encounter. LRN member laboratories are tested on their proficiency to respond to test challenges, based on self-reported biological agent–specific testing capability. In addition, training in regulatory compliance and documentation is essential for those laboratories that ship pathogens and pathogen-derived material used for proficiency testing and specimen/sample referral.

Building International–US CDC LRN Capacity in South Korea

In 2011, the CDC LRN program office and the US Department of Defense began establishing an international–US CDC LRN member laboratory in South Korea. Since 2002, the Korea Centers for Disease Control and Prevention (KCDC) had already been operating a laboratory response network similar in structure to that of the US LRN, using its own procedures and reagents. However, establishing a US LRN presence in South Korea enabled its use of US LRN-B procedures and reagents, in addition to other US LRN assets, which are accessible only to US LRN member laboratories.

To establish an international–US LRN-B presence, KCDC and the US Department of Defense identified 2 locations: 1 on a joint US/South Korea military facility (the Brian Allgood Army Community Hospital [BAACH] at Yongsan US Army Garrison in Seoul) and 1 at a South Korea public health facility (KCDC Division of High-Risk Pathogen Research in Osong). The BAACH functions as a sentinel and reference-level laboratory for the base personnel and their families; the Division of High-Risk Pathogen Research is a public health laboratory within the KCDC.

The initial steps for adding the US LRN capability were provision of training for confirmatory procedures that use standard culture and biochemical techniques and rapid procedures for presumptive identification that use molecular and antigen-detection technologies. Critical portions of training documents were translated into Korean. These portions included laboratory job aids and specific laboratory procedures such as data interpretation and assay limitations. Biological select agents and toxins have the potential to pose a severe threat to public, animal, or plant health or to animal or plant products. The LRN program office worked with the US LRN Army Medical Command partners to select laboratory personnel who were fluent in the Korean language, security-risk assessment (SRA) approved (i.e., authorized to directly handle cultures of select agent organisms), and able to take the course themselves and partner with KCDC laboratory course students at the LRN confirmatory microbiology course to assist with language barriers. The logistics for an LRN Conventional Methods course are complicated. Only students with prior SRA approval from the FBI may directly handle cultures or material considered a select agent, and the class may be held only in a select agent registered laboratory (*11*). Using SRA-approved, Korean-fluent US Army laboratory course students enabled the LRN course trainers to provide one-on-one translation and direct laboratory observance of bacterial select agent culture characteristics by the KCDC course students, without compromising compliance with US select agent regulations. The LRN program office selected the US Hawaii public health laboratory to host the LRN Conventional Methods training course. This laboratory was chosen because it is an LRN-member laboratory, uses cultures of select agent bacteria, is registered to handle select agent pathogens, and is relatively near South Korea and the US mainland. During 2012–2013, two training courses were completed by 9 persons from the Korea-based International–US CDC LRN laboratories (Figure 2). In 2013, the Yongsan Garrison facility hosted an LRN Rapid Methods course, which focuses on sample processing, and a Rapid Molecular/Antigen Detection course for co-participating US Army and KCDC students. The Rapid Methods course did not use select agents during the training, which simplified the importation of materials and course implementation.

In 2016, a CDC team including members of the LRN program office, an infection prevention practitioner, a CDC poxvirus subject matter expert, and a high containment laboratory (HCL) manager traveled to South Korea to help develop training similar to that used at other LRN-B facilities to further enhance emerging infectious diseases (EID) response

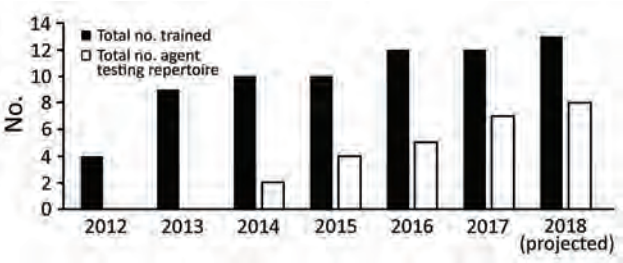

Figure 2. Training and testing capacity building for Laboratory Response Networks in South Korea. Training and expanded testing capability are synergistic. Total number trained indicates the number of laboratory personnel from the Brian Allgood Army Community Hospital, US Army Yongsan Garrison, and from the Korea Centers for Disease Control and Prevention facility trained on either rapid diagnostics or confirmatory conventional microbiology. Total number of agents in testing repertoire indicates the biological threat agent testing capability when Laboratory Research Network procedures, as determined by proficiency testing, are used.

capability. At the KCDC HCL, the CDC poxvirus subject matter expert and CDC HCL manager helped develop training for safe HCL entry and exit and man-down emergency HCL exit training. Emergency man-down training involves a simulated emergency involving a person who needs immediate medical intervention because of a life-threatening incident (e.g., collapsing while at work). In such a situation, a person might need to be extracted from an HCL facility as rapidly as possible without compromising overall safety.

The BAACH hospital and laboratory are unique to the LRN because they function as a primary care hospital and as both sentinel-level and reference-level LRN laboratories. To assist BAACH in its preparedness for an EID outbreak, members of the LRN program office and a CDC infection prevention practitioner held discussion-based EID training and assessment of best practices and information sharing for the medical and laboratory staff. The EID training for BAACH followed the same model as the US Ebola Risk Assessment training. This format, which is the usual type of training used in other LRN-B laboratories, integrates hospital, LRN sentinel-level laboratory, and LRN reference-level laboratory personnel to understand roles, responsibilities, and communication among stakeholders. The discussion was based on review of the laboratory component of a 2015 MERS outbreak in South Korea and hospital laboratory preparedness for an EID event.

Leveraging Technology to Enhance Laboratory Capacity

A valuable component of this collaborative effort is the leveraging of technology for continuing education. On-demand technology resources include offering additional training resources to LRN-B domestic and international partners in the form of a mobile smartphone or tablet application (app) and online proficiency assessments. Our standard for on-demand training is the LRN Rule-Out and Refer mobile app (Figure 3). This app is a support tool for sentinel laboratories, providing integrated agent-specific, bacterial biological threat rule-out and refer testing flowcharts and additional information to assist the laboratorians (*11*). The testing algorithms derive from American Society for Microbiology guidelines and are available for tablet devices, which can be sequestered for in-laboratory use only and can access updates by wireless connection (*2*). This mobile app can work as a quick reference and as a formative training tool. The bacterial agent–specific rule-out and refer flowcharts in the app have been translated into Korean.

Recently, the LRN-B program office added virtual online proficiency assessments as a complement to existing training resources. The proficiency assessments are used during hands-on laboratory courses, to reinforce learning, and as an on-demand informative training tool. The proficiency assessments are accessed through a secure online link that provides instantaneous feedback to participants and allows for tailored knowledge remediation from the training providers. These tools were first used in the 2016 Conventional Methods training classes and are currently being translated into Korean. The content of the proficiency assessments are expanding to include content for the rapid presumptive procedures and other agent-specific EID training for participating LRN laboratories. The intrinsic value of these technologies as training tools is increased by their accessibility and versatility, providing optimum functionality in the global context of the LRN-B and the goal of maintaining a trained workforce.

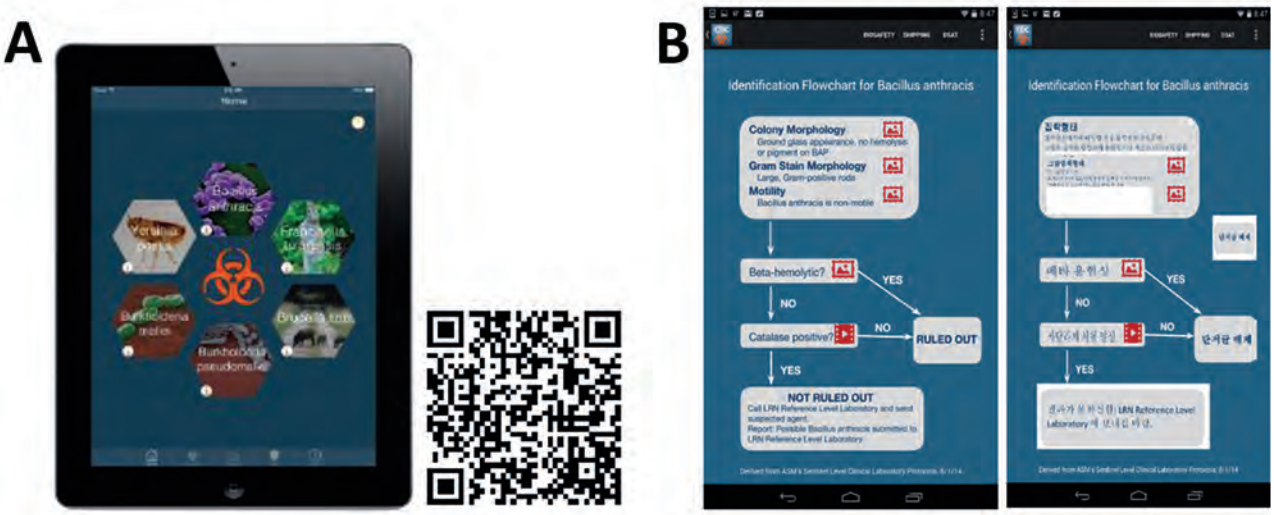

Figure 3. On-demand training tools sustain and enhance laboratory pathogen identification as part of the Laboratory Research Network. A) The Laboratory Research Network Rule-Out and Refer mobile application, available for download on Apple tablets via QR code or the Apple App store. B) Flowcharts provide easy agent-specific rule-out and refer information, including images and videos in English and Korean.

Future Steps for Increasing Capacity

Enhancing LRN capacity in South Korea helps protect the population of South Korea, US military personnel and civilians in South Korea, and the population of the continental United States, and thereby enhances global health security. In addition, South Korea is geographically and technologically poised to serve as a hub for public health functions in Southeast Asia. These functions could include enhancing infectious disease detection capability and providing leadership on global health security initiatives. Continued collaboration with partners in South Korea provides a mechanism for rapidly disseminating processes, procedures, and reagents before and during a public health crisis. The LRN-B collaboration in South Korea and the use of standardized procedures, which lead to an added assurance of laboratory results, could provide a catalyst for engaging partners in other Southeast Asia countries. Combined, these partnerships and sharing of information benefit the public health for residents of South Korea and for US personnel serving in Southeast Asia.

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EMERGING INFECTIOUS DISEASES®

Real-Time Surveillance in Emergencies Using the Early Warning Alert and Response Network

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Humanitarian emergencies often result in population displacement and increase the risk for transmission of communicable diseases. To address the increased risk for outbreaks during humanitarian emergencies, the World Health Organization developed the Early Warning Alert and Response Network (EWARN) for early detection of epidemic-prone diseases. The Centers for Disease Control and Prevention has worked with the World Health Organization, ministries of health, and other partners to support EWARN through the implementation and evaluation of these systems and the development of standardized guidance. Although protocols have been developed for the implementation and evaluation of EWARN, a need persists for standardized training and additional guidance on supporting these systems remotely when access to affected areas is restricted. Continued collaboration between partners and the Centers for Disease Control and Prevention for surveillance during emergencies is necessary to strengthen capacity and support global health security.

Humanitarian emergencies are events that disrupt the function of a society, cause harm, and overwhelm routine capacity for response. The causes vary greatly, including those resulting from natural hazards or epidemics in unstable or low-income countries, food insecurity, and complex emergencies related to civil strife or armed conflict with increased civilians deaths (*1*). In 2015 alone, an estimated 125 million persons were in need of humanitarian assistance (*2*). Humanitarian emergencies are often characterized by population displacement, which has predictable consequences and health impacts (*3*). Those persons displaced often settle in crowded, temporary shelters or camps, many of which have inadequate access to safe water and sanitation and limited health infrastructure. In addition, existing health infrastructure in areas of resettlement often are severely strained, putting displaced and host populations at risk for public health emergencies, including communicable disease outbreaks. Because of increased globalization, acute public health threats are at greater risk for crossing international borders and can have implications for countries worldwide. Providing assistance at the source protects the health of the local population and supports global health security to prevent international public health emergencies.

The World Health Organization (WHO) provides leadership and support for ministries of health (MOHs) to mitigate public health threats during humanitarian emergencies, including health sector coordination, support for clinical care delivery, implementation of surveillance systems, and technical leadership for outbreak responses (*4*). WHO's role is especially important in fragile states, which are disproportionately affected by disasters and where national or regional health authorities often are unable to cope with the public health consequences of population displacement. The WHO Health Emergencies Programme works with countries and partners to prepare for and respond to hazards that can lead to health emergencies, including disaster and conflict (*5*). At the Centers for Disease Control and Prevention (CDC), the Emergency Response and Recovery Branch (ERRB), part of the Division of Global Health Protection, Center for Global Health, is responsible for coordinating the international response to humanitarian emergencies for the CDC. ERRB provides technical assistance at the request of WHO or MOHs to support various activities during humanitarian emergencies, such as rapid assessments of

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health facilities and basic services, vaccination campaign planning and coverage surveys, and communicable disease surveillance and response.

Early Warning Alert and Response Network

In humanitarian emergencies, routine public health surveillance systems can be disrupted. To rapidly identify and respond to outbreaks when routine surveillance is not functional, WHO developed the concept of an early warning surveillance system for diseases of epidemic potential during emergencies called the Early Warning Alert and Response Network (EWARN). Versions of EWARN have been implemented in emergencies throughout the world under different names; these systems were similar in concept but were implemented using various methods and tools depending on the implementing partner. EWARN was first implemented by WHO in South Sudan in 1999 after a 6-month delay occurred in the response to a relapsing fever outbreak, which resulted in >2,000 deaths (*6*). The primary objective of EWARN is to rapidly detect and respond to potential outbreaks of epidemic-prone diseases. EWARN is intended to be implemented during the acute phase of a humanitarian emergency, either as an adjunct to existing surveillance or as a new system in a setting where no routine surveillance is operational. Implementation of EWARN is done in coordination with the MOH or with nongovernmental organizations in conflict areas outside government control. Implementation requires identifying diseases under surveillance and thresholds for triggering public health action, protocol development, recruitment of surveillance staff, identification of reporting sites, training of staff, community education for alert reporting, and initiation of system reporting as soon as possible after the acute phase of a humanitarian emergency. EWARN is not intended to be a permanent substitute for a comprehensive national surveillance system, and its activities should be reintegrated with routine surveillance once the emergency is over.

Although EWARN focuses on epidemic-prone communicable diseases, the system is intended to be sensitive to all potential cases of priority diseases. It detects any unusual conditions or health events in order to pick up potential outbreaks or public health concerns. EWARN relies on syndromic case definitions adapted for each emergency because laboratory confirmation might be delayed or unavailable in these settings. Surveillance activities in EWARN consist of 2 reporting components: 1) an immediate alert component for cases of potential outbreaks, and 2) a weekly reporting component for aggregation of total cases of priority conditions at participating health facilities. The response component of EWARN facilitates rapid implementation of the necessary public health measures in response to a potential or evolving public health event.

EWARN systems have been successful in detecting several disease outbreaks. Syria has been polio-free since 1999, and Somalia since 2007 (*7*,*8*). However, because of conflict, displacement, insecurity, and the collapse of the public health infrastructure, polio reemerged in both countries in 2013; the initial cases were reported by the EWARN systems (*9*). EWARN systems have also detected outbreaks in other emergencies, such as hepatitis E in South Sudan (*10*), measles in Iraq, and suspected dengue in the Darfur region of Sudan. Building on these successes, EWARN has become an essential paradigm for communicable disease surveillance in emergencies.

Early EWARN Work

ERRB has been supporting EWARN in numerous countries since 2004 (Figure 1). Activities have included initial implementation of systems, trainings of surveillance staff, evaluations, and development of standardized guidance (Figure 2).

ERRB's initial involvement with EWARN was in system evaluations, specifically the evaluation of the Early Warning Alert and Response System (EWARS) in Darfur in 2004, 6 months postimplementation (*11*). Since then, ERRB has conducted 2 follow-up evaluations of EWARS in Darfur, in 2009 and 2016, to document system progress during the protracted humanitarian emergency. Despite challenges, EWARS in Darfur has continued to operate, detecting outbreaks and providing epidemiologic data from an area where very little information would be available otherwise. ERRB also conducted evaluations in South Sudan, before and after independence (2009 and 2012). South Sudan has a long history of civil conflict and displacement, placing the population at increased risk for epidemic-prone diseases. Common problems that emerged from these early evaluations were 1) emphasis on weekly reporting over outbreak detection, 2) inadequate staff training resulting in poor data quality, 3) large amounts of data collection that were not used for public health action, and 4) lack of a clear exit strategy. These evaluations provided recommendations to strengthen systems and enhance programmatic support; they also increased the evidence base to guide future EWARN implementations.

In addition, ERRB has supported the implementation of EWARN systems in emergencies. In collaboration with MOHs and the Pan American Health Organization, ERRB helped establish the Internally Displaced Persons Surveillance System, an EWARN-type surveillance system, after the 2010 earthquake in Haiti that displaced ≈2 million persons. The system monitored communicable disease outbreaks from nongovernmental organizations' clinics operating in the camps housing internally displaced (IDP) persons (*12*). Lessons learned from this experience included 1) the need to shift from daily to weekly reporting

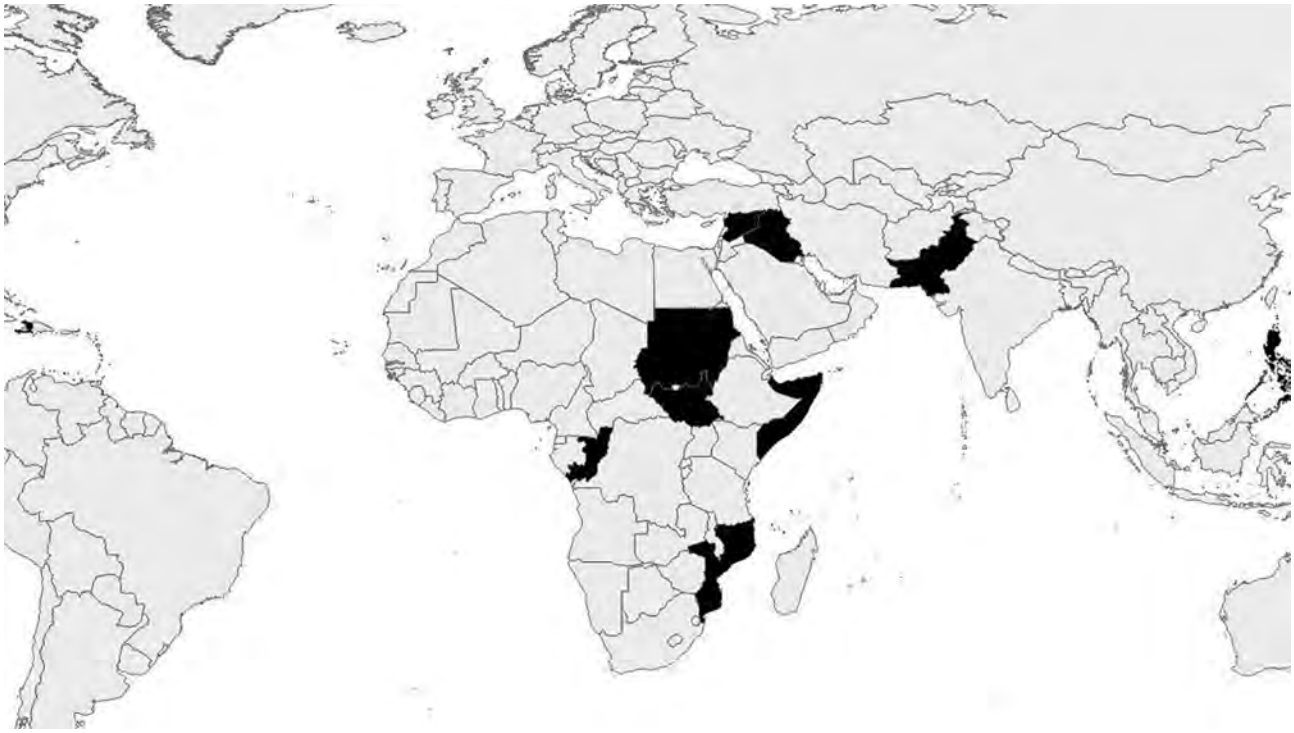

Figure 1. Countries (shown in black) where the US Centers for Disease Control and Prevention's Emergency Response and Recovery Branch (Division of Global Health Protection, Center for Global Health), with the World Health Organization's Health Emergencies Program, has provided support for implementation or evaluation of early warning surveillance systems in response to humanitarian emergencies.

to reduce the burden on clinic staff and to allow for data-quality checks and 2) the need to use proportional morbidity to analyze disease trends because of the lack of accurate denominator data.

That same year, Pakistan experienced its worst flooding in history, affecting ≈18 million persons. ERRB provided support to strengthen and rapidly expand the Disease Early Warning System (DEWS), an EWARN-based emergency surveillance system, across the affected area. Emergency surveillance systems might remain in place even after emergencies are over, as was the case with DEWS. The Pakistan MOH, the Pakistan National Institute of Health, and WHO worked with ERRB staff to revise DEWS, removing chronic conditions such as hypertension and diabetes to focus on 13 epidemic-prone priority conditions (*13*). Varied application of the case definitions and use of nonstandard reporting forms made the identification of disease trends difficult. In addition, not all partners delivering health services contributed data to the system. These challenges highlighted the importance of including key stakeholders in the revision process and the need for standardized training on EWARN to increase acceptability of the system by all partners and end users. Nevertheless, early detection and proactive preparedness activities helped prevent a major cholera outbreak in Pakistan after the flooding.

Development of Implementation Guidelines

On the basis of these early experiences, WHO, ERRB, and others played important roles in developing EWARN implementation guidelines. Lessons learned from previous EWARN implementations provided the foundation for the strategic development and operational perspective of the guidelines. ERRB is an active member of the EWARN technical working group, which is led by WHO and includes other governmental and nongovernmental partners (*14*,*15*).

The first standardized guidelines for establishing EWARN, titled Outbreak Surveillance and Response in Humanitarian Emergencies: WHO Guidelines for EWARN Implementation, were published in 2012 (*16*). These guidelines included several key points identified during the 2009 technical working group meeting, such as the necessity of focusing on few epidemic-prone diseases, emphasizing immediate alerts and their verification over weekly trend reporting, and reducing the type and amount of data collected (*14*). The guidelines also emphasized using weekly reporting rather than daily, with the exception of immediate notifiable conditions, and the need for determining an exit strategy at the time of initial system implementation.

Continued Support

After the development of the implementation guidelines, ERRB has continued to play a critical role in EWARN

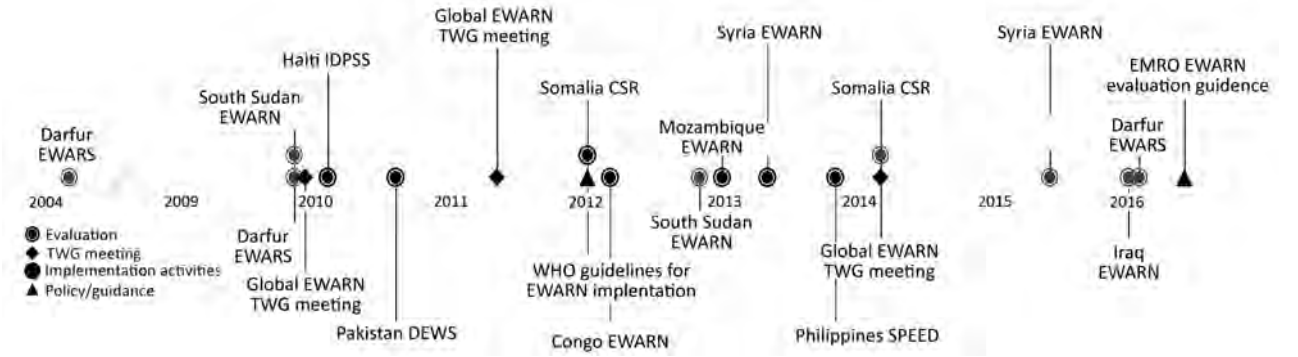

Figure 2. Timeline of EWARN activities conducted by the Centers for Disease Control and Prevention's Emergency Response and Recovery Branch (Division of Global Health Protection, Center for Global Health), with the WHO Health Emergencies Program. CSR, Communicable Disease Surveillance and Response; DEWS, Disease Early Warning System; EMRO, World Health Organization's Eastern Mediterranean Region Office; EWARS, Early Warning Alert and Response System; EWARN, Early Warning Alert and Response Network; IDPSS, Internally Displaced Persons Surveillance System; TWG, Technical Working Group; WHO, World Health Organization.

activities during more recent emergencies. This role has included the implementation and evaluation of systems in several countries.

In 2011, Somalia faced a severe drought that resulted in famine, exacerbated by the ongoing civil conflict (*16*–*18*), that led to mass population displacement, reduced access to basic services, and an increased risk for disease. Before 2011, numerous disease surveillance systems had been implemented within Somalia. To simplify surveillance, WHO Somalia and ERRB combined 4 separate systems into 1, the revised Communicable Diseases Surveillance and Response, to provide information on communicable diseases among displaced and affected populations. This system was fully implemented in January 2012 and was the first system to follow the principles outlined in the 2012 WHO Guidelines for EWARN Implementation (*16*). ERRB's technical support was conducted remotely from the WHO Liaison Office for Somalia based in Nairobi, Kenya, and this experience would later inform subsequent remote work. To address concerns regarding the impact of remote implementation on data quality, tools were developed to assist with data-quality checks and remote monitoring at each level of the system on weekly and monthly bases, as well as guidance for biannual facility assessments. Although ongoing conflict, restricted access, and limited resources have hampered outbreak response activities, the Communicable Diseases Surveillance and Response system has successfully detected several outbreaks in Somalia, including the first new cases of polio in 2013 (6 years after the country had been declared polio-free). Since the implementation of this system in 2012, ERRB has provided ongoing remote support, including an evaluation in 2014 and support for analysis and creation of system reports (*9*).

An explosion at the munitions depot in Brazzaville, Republic of the Congo, in March 2012, forced ≈125,000 displaced persons to relocate into 8 makeshift camps. The Republic of the Congo MOH requested assistance to implement emergency surveillance. An expanded version of EWARN, with the additional capability for laboratory confirmation of diseases, was implemented in IDP camps as an adaptation of the Integrated Disease Surveillance and Response system used for routine surveillance in the country. The system was streamlined from 61 diseases to 8 reportable conditions, reduced daily reporting to weekly to lessen the reporting burden on the limited number of surveillance staff, and increased supervisory checks to improve data quality. EWARN benefited from good collaboration between partners and strong preexisting laboratory support provided by the national laboratory in Brazzaville and from regional laboratories in the Democratic Republic of the Congo and Gabon.

After the onset of civil crisis in 2011, the Syria MOH initiated EWARS in 2012 with the aid of WHO Syria; however, system coverage was limited to government-controlled areas. To address limited system coverage, the Syrian Coalition's Assistance Coordination Unit (ACU), with support from ERRB staff, established EWARN in the opposition-controlled areas of northern Syria in June 2013. The system was established remotely from ACU headquarters in Turkey because of security concerns. To date, the EWARN in nongovernmental areas collects data on 13 syndromes and has expanded coverage from 8 to 11 governorates, covering a population of ≈9.8 million. Regular trainings by ACU and ERRB have contributed to the expansion of EWARN, despite numerous challenges. Ongoing insecurity has limited access and outbreak response capacity, including laboratory access and capacity. However, EWARN successfully detected the reemergence of polio in 2013. The dedicated staff and innovative use of technology for communication between field staff and headquarters have enabled the system to remain useful and detect several other outbreaks. ERRB remotely evaluated EWARN in the

opposition-controlled areas of Syria in 2015, two years after system implementation. Some interviews were conducted in-person with participants attending a workshop and training in Turkey coinciding with the evaluation period, whereas interviews with staff unable to leave Syria were conducted remotely. The Syria MOH EWARS and ACU EWARN continue to operate independently within Syria but are seen as complementary, providing a more complete profile of epidemic-prone disease burden.

Later in 2013, ERRB staff provided assistance for implementation and information management of emergency surveillance in the Philippines after Typhoon Haiyan (Yolanda), which displaced ≈4 million persons (*19*). The Philippines Department of Health uses Surveillance in Post Extreme Emergencies and Disasters, an EWARN-type system activated in response to humanitarian crises. The widespread damage resulting from the typhoon presented challenges, including destruction of health facilities and limited power and communication; however, a total of 411 facilities were ultimately able to report (*20*). Areas with the most severely damaged infrastructure initially used messengers on motorbikes to rapidly send reports. Early detection of an increase in cases for conditions like suspected measles and suspected dengue enabled rapid response (*21*).

In January 2013, flooding in Mozambique displaced ≈200,000 persons. Nine accommodation centers were established to house the displaced population. The Mozambique MOH requested assistance for surveillance activities. The affected region quickly entered recovery phase, and routine surveillance was promptly reestablished. Although EWARN was never fully implemented, the National Institute of Health within the MOH, in partnership with WHO, CDC's Mozambique office, and ERRB, worked to draft EWARN guidelines for the country. These guidelines were translated into Portuguese and remain with the National Institute of Health in the event of future emergencies. Working with the National Institute of Health S to develop guidelines provided an opportunity to strengthen public health capacity through preemergency preparedness.

ERRB staff routinely provide training during EWARN implementation. In inaccessible areas, such as Somalia and Syria, ERRB has conducted several offsite trainings in neighboring countries, such as Kenya, Djibouti, Turkey, and Jordan. To ensure capacity building of local and national EWARN staff in protracted emergencies, ERRB has provided long-term, ongoing support through trainings and data analysis. ERRB has also developed train-the-trainer modules for staff unable to travel because of security concerns, logistics, or other reasons. At the request of the WHO Eastern Mediterranean Region Office (EMRO), ERRB is currently developing standardized EWARN trainings to be used by all EMRO partners implementing EWARN in emergencies.

Development of Evaluation Guidance

Despite the numerous EWARN evaluations conducted by WHO, ERRB, and other partners, no standard method existed to evaluate these systems. Evaluators used varying methods and tools developed ad hoc for each evaluation and calculated different indicators. These differences highlighted the need for standardized evaluation methodology to allow comparison of findings and demonstrate system evolution over time. In addition, as a result of the crisis in Syria, several new EWARN systems were implemented in the EMRO region, including the 2 systems in Syria and 1 each in Lebanon and Iraq. To better understand response efforts to the crisis and inform future implementations, WHO EMRO decided to pursue the development of standard EWARN evaluation guidance with assistance from ERRB. The initial draft was developed in 2015 and included components for planning the evaluation (e.g., methods for site selection, key stakeholders to interview, and relevant documents to collect), activities during the evaluation and tools for data collection (e.g., standardized questionnaires for interviews), and methods for reporting findings and making recommendations. The draft also included guidance for conducting evaluations remotely.

The first draft of the evaluation guidance was piloted in early 2016 in northern Iraq and Darfur. Because of security restrictions and limited access, both evaluations included remote components. The standardized guidance enabled identification and organization of relevant documents before the evaluation. The questionnaires and tools enabled standardized data collection and entry. Challenges within the remote components of the evaluations, such as difficulties with document transfer and the necessity of in-country support, were not adequately addressed in the draft guidelines. These findings were discussed during a technical working group meeting in Cairo, Egypt, where the evaluation guidance was updated based on feedback and lessons learned.

Moving Forward

Since 2004, ERRB has evaluated 8 EWARN systems in 5 countries, implemented the system in 7 countries (in 2 of them remotely), and led efforts to publish the first implementation and evaluation guidelines in collaboration with WHO. This work, and the gaps identified in the systems, will inform and guide next steps for EWARN.

Standardized EWARN evaluation guidance has currently been provided only to the EMRO region because these tools were a collaborative effort between WHO EMRO and ERRB. This guidance has not been introduced to other WHO regions, but it is hoped the tools will be adopted globally and serve as a catalyst for WHO headquarters to develop standardized global guidelines for EWARN evaluations. To this end, workshops involving other WHO regions are in negotiation.

The EWARN implementation guidelines have not been revised since they were first published in 2012. Because the evidence base has grown during subsequent implementations and evaluations, the 2012 implementation guidelines need to be revised to address the issues and gaps of operationalizing the guidelines and to adapt to new technologies and changing requirements, such as working remotely, improving outbreak detection and response, and providing better point-of-care methods to confirm syndromic case definitions, among other changes.

At the most recent EWARN technical working group meeting in 2014, participants identified the need for the development and operationalization of standardized training materials, a standardized EWARN toolkit, and electronic reporting solutions. WHO EMRO is working with ERRB to develop standardized training packages in English and Arabic that can be modified for each the country and system. The organizations are also working to develop a standardized package for train-the-trainer modules, because many areas in which EWARN is implemented have limited accessibility, and often only a small group is able to travel to receive in-person training.

Experiences in Somalia, Syria, Iraq, and Sudan showed that working remotely can make communicating objectives, obtaining documents, providing supervision, and translating interviews more difficult. In each of the locations, new or redirected local staff with great understanding of the challenges and security concerns were hired to facilitate data collection and data-quality monitoring from reporting sites. Regardless of the dedication and strength of international staff, EWARN is only as successful as the local staff who make up the backbone of the surveillance and response, often at great danger to themselves. Continued insecurity and increasing travel restrictions necessitate improved guidance for supporting EWARN remotely. This remote work is included in the new evaluation guidance and will be an important component of the future standardized training and implementation guidance.

Conclusions

Strengthening capacity for simplified early warning surveillance for diseases of epidemic potential enhances countries' abilities to detect events affecting public health and acute threats to global health security during emergencies. EWARN systems have been useful sources of information where no other data were available during many emergencies, including conflicts and natural disasters, in more than a dozen countries around the world since 1999 and have identified numerous outbreaks. Early detection and control of outbreaks has prevented their spread and is an important component of global health security efforts. At-risk countries should invest in EWARN-type systems or strengthen the early warning component of their current system through preemergency preparedness to ensure they are able to detect public health threats in the event of an emergency. Although EWARN is implemented during humanitarian emergencies, principles of the system and lessons learned can inform surveillance during large outbreaks in nonemergency settings, such as the Ebola outbreak in West Africa, to ensure continued detection of other outbreak-prone diseases. Continued collaboration within the WHO EWARN technical working group and with other partners has improved the knowledge base for communicable disease surveillance and response during emergencies. Continuing to revise guidelines and develop standardized evaluation and training tools is essential to strengthen these systems and protect the health of those directly affected by emergencies as well as populations around the world.

Ms. Cordes is a fellow with the Centers for Disease Control and Prevention, Atlanta, Georgia, USA. Her primary research interests are surveillance and epidemiologic methods in humanitarian emergencies.

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Global Disease Detection—Achievements in Applied Public Health Research, Capacity Building, and Public Health Diplomacy, 2001–2016

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The Centers for Disease Control and Prevention has established 10 Global Disease Detection (GDD) Program regional centers around the world that serve as centers of excellence for public health research on emerging and reemerging infectious diseases. The core activities of the GDD Program focus on applied public health research, surveillance, laboratory, public health informatics, and technical capacity building. During 2015–2016, program staff conducted 205 discrete projects on a range of topics, including acute respiratory illnesses, health systems strengthening, infectious diseases at the human–animal interface, and emerging infectious diseases. Projects incorporated multiple core activities, with technical capacity building being most prevalent. Collaborating with host countries to implement such projects promotes public health diplomacy. The GDD Program continues to work with countries to strengthen core capacities so that emerging diseases can be detected and stopped faster and closer to the source, thereby enhancing global health security.

Infectious disease outbreaks present a serious health threat that requires early detection and effective preventive action to avoid regional or even global spread. Such actions enhance global health security by protecting the health of persons in the affected regions and in the United States. Recent epidemics, including severe acute respiratory syndrome (SARS) during 2002–2003, pandemic influenza A(H1N1) in 2009, Ebola virus disease in 2014, and Zika virus infection during 2015–2016, underscore this risk and highlight the critical need for building core global public health capacity for detection and response.

In 2001, the Centers for Disease Control and Prevention (CDC) established the International Emerging Infections Program (IEIP) to conduct applied public health surveillance and research aimed at preventing infectious disease outbreaks with pandemic potential. IEIP placed CDC staff in key overseas locations to work with national public health institutes and their partners to establish sentinel surveillance and conduct applied research on emerging infectious diseases. The program was modeled after the US-based Emerging Infections Program, a network of state health departments and their partners that conduct surveillance of certain infections and thereby provide a foundation for various epidemiologic studies to explore risk factors, spectrum of disease, and prevention strategies (*1*). IEIP had a similar objective but on a global platform; namely, to conduct applied public health research in strategic global locations to prevent, detect, and control emerging and reemerging pathogens.

CDC established the Global Disease Detection (GDD) Program in 2004 by using existing research programs within IEIP as the scientific backbone of its GDD regional centers; this effort was made in response to data gaps identified during the SARS epidemic. The GDD Program mission was to ensure that infectious diseases were detected and stopped at the source before crossing international borders (*2*). The GDD Program, like IEIP, set up a network of CDC technical experts stationed in GDD regional centers located in multiple countries across the World Health Organization (WHO) regions. GDD regional centers were initially set up in countries with IEIP presence (Thailand, Kenya, Guatemala, Egypt, China, and Kazakhstan). Subsequently, new GDD regional centers were established in Bangladesh, India, South Africa, and Georgia (*3*). These centers serve as regional resources for neighboring countries and are a framework for improving public health and global health security through close collaboration with local partners. To date, the 10 GDD regional centers have supported ≈90 countries around the world, including the United States (Figure). The GDD regional centers have assisted US domestic public health institutions in response to

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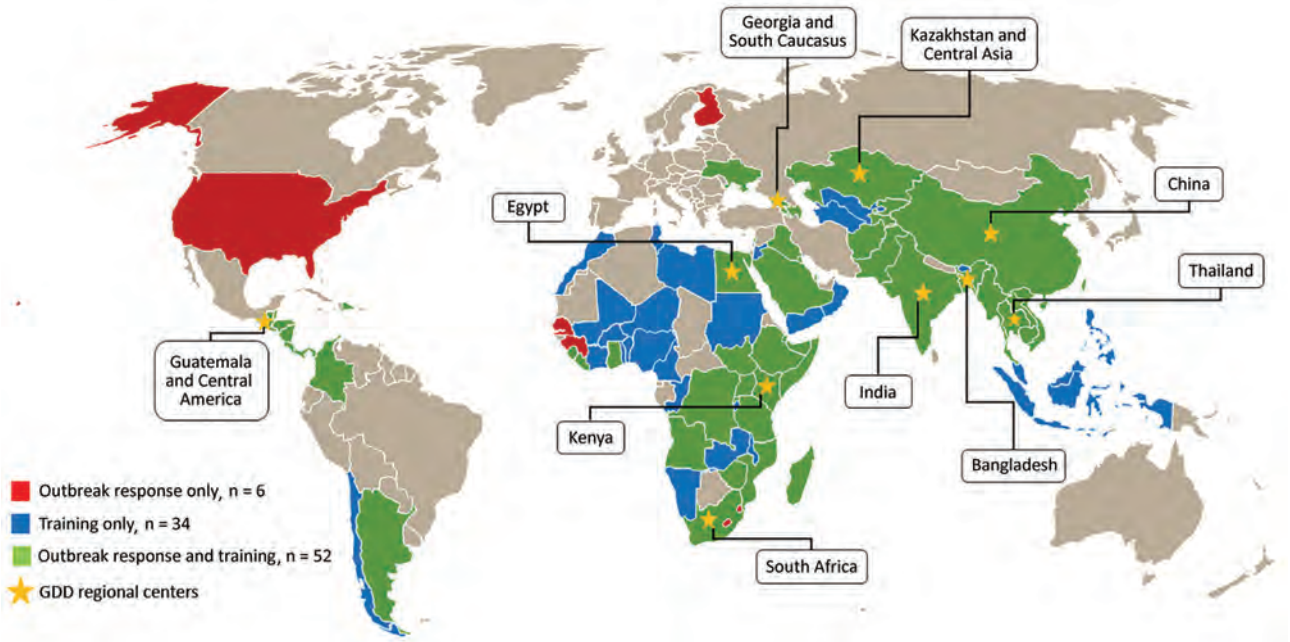

Figure. Geographic range of technical support provided by Global Disease Detection Program regional centers, 2006–2016. GDD, Global Disease Detection.

infectious diseases that affected international visitors while in the United States and US citizens while abroad.

The GDD Program promotes intersectoral public health responses and applied epidemiologic research that include ministries of health and agriculture, academic institutions, other US government programs, and international and nongovernmental organizations. These established and trusted relationships with national governments enable more effective prevention and detection of emerging infectious diseases. The GDD regional centers also provide an in-country infrastructure that enables CDC to respond rapidly to public health threats. A critical strength of the GDD Program is the long-term assignment (i.e., 2–6 years) of epidemiologists, laboratorians, statisticians, and other diverse technical staff at GDD regional centers in host countries. The GDD technical staff work alongside locally hired technical staff to foster close collaboration and bilateral knowledge transfer with host country partners. These strategically placed GDD technical staff can have localized information for early detection of unusual infectious disease events. During public health emergencies, where time lost often equals lives lost, the ability to leverage trusted international public health scientific partnerships is essential for life-saving action. GDD field staff are often a first line of response during an epidemic. During the 2014–2016 West Africa Ebola outbreak, ≈30 GDD field-assigned staff, including US and local personnel, deployed from GDD regional centers to assist with establishing diagnostic, contact tracing, and data analysis capacity. GDD field staff's experience in international settings was critical to the response and facilitated quick integration into ongoing response and prevention efforts. GDD's sustained capacity-building efforts enabled these forward-deployed assets to respond quickly not only in their own regions but also across the globe.

Activities and Accomplishments

The core activities of the GDD Program focus on applied public health research, surveillance, laboratory, public health informatics, and technical capacity building. Applied public health research refers to activities that generate data to answer a research question; test a hypothesis; evaluate a program or programmatic element (e.g., a public health practice, a surveillance system, data quality); or provide information for evidence-based decision making. Surveillance refers to activities that collect health-related data in a systematic manner over time to inform public health action. Laboratory refers to activities that collect specimens for laboratory analyses. Informatics refers to any activity that collects and aggregates data (paper-based or electronic) that could be used for further analysis. Capacity building refers to activities that increase the skills, infrastructure, or resources of individuals or partnering organizations. Current GDD Program projects incorporate multiple core activities, with technical capacity building, laboratory, and public health research being most common (Table 1). These activities are essential for the identification of new health threats, monitoring and tracking of health threats over time, and for conducting applied research and pathogen discovery. At times, regional centers

Table 1. Number of projects conducted by Global Disease Detection Program regional centers, by activity type and year center was founded, fiscal years 2015 and 2016*

Year center founded	Country/region	No. projects	Activity type				
			PHR	S	L	PHI	CB
2004†	Thailand	20	8	13	11	13	7
2004	Kenya	36	12	10	9	9	19
2006	China	14	10	5	8	10	8
2006	Egypt	11	3	2	3	3	11
2006	Guatemala and Central America	22	15	11	14	15	10
2008	Kazakhstan and Central Asia	13	3	2	4	2	13
2009	India	13	4	4	5	3	13
2010	South Africa	28	9	5	12	5	20
2011‡	Bangladesh	31	22	14	17	1	11
2012	Georgia and South Caucasus	17	6	9	12	11	13
Total no. projects		205	92	75	95	72	125

*October 1, 2014–September 30, 2016. Activities do not sum across the rows because activity types are not mutually exclusive. CB, technical capacity building; IEIP, International Emerging Infections Program; L, laboratory; PHI, public health informatics; PHR, applied public health research; S, surveillance.
†IEIP-Thailand founded in 2001.
‡IEIP-Bangladesh founded in 2008.

might conduct studies of noninfectious causes of illnesses because it is not always clear whether the etiologic agent is a pathogen, a toxin, or some other cause at the beginning of an outbreak (*4*,*5*). The GDD Program also provides a robust framework for public health diplomacy and the development and implementation of coordinated multisite activities and studies (*6*).

GDD by the Numbers

In 2015, the GDD Program performed a portfolio review of activities in the 10 GDD regional centers for fiscal years 2015 and 2016 (October 1, 2014–September 30, 2016). The unit of analysis was a GDD Program–funded project. Multiyear projects were counted once. Projects were not weighted by the size or scope of a project; thus, a small research study was equivalent to a large, multiyear, population-based surveillance project. We excluded projects that listed HIV (n = 2) or noncommunicable disease (n = 1) as their primary focus. We classified projects into core activity areas: technical capacity building, surveillance, applied public health research, laboratory, and informatics. Activity areas were not mutually exclusive, so a project could be classified in multiple areas.

Overall, the 10 GDD regional centers engaged in 205 discrete projects during October 2014–September 2016 (Table 1). The number of projects per GDD regional center ranged from 11 to 36. The variability in number of projects per center was attributable to a combination of factors, including the age of the center, the geographic region covered by the center, and funding and staffing resources available for the center. Capacity-building projects (n = 125) were most common (Table 1). We also classified technical projects into topical areas based on the key focus of the project. Topical areas were collated and categorized by major groupings (Table 2). The variability in the range of topical areas was attributable to a combination of factors, including the epidemiology of the disease (nationally and globally); available funding; the technical capacity at the local level; and the changing priorities of the United States and local partners (e.g., ministries of health, national public health institutes, and research institutes). Of 205 projects with a defined topical area, 24% (n = 50) were focused on acute respiratory illness (Table 2), which is expected given that respiratory disease surveillance has been a core function since the inception of the program. Health system strengthening (n = 36), One Health (n = 30), and emerging infectious disease (n = 22) were the next most common topical areas. The increasing prevalence of these new topical areas indicates an expansion of the breadth of projects being conducted by GDD regional centers.

GDD Core Activities

Applied Public Health Research

The GDD Program has a broad portfolio of applied public health research and special epidemiologic studies, ranging from ensuring infection control practices for Nipah virus in Bangladesh to evaluating antimicrobial drug–resistant invasive salmonellosis in Thailand (Table 3). Conducting applied public health research and epidemiologic studies in international settings can address important knowledge gaps in infectious disease issues. Many of these issues would be difficult to examine in the United States, primarily because of low prevalence of many infectious diseases. International public health research studies contribute to the scientific knowledge base and help answer questions that can influence US public health policy. Examples range from gathering data for the issuance of travel notices to conducting vaccine studies needed to guide domestic vaccination guidelines (*7*,*8*).

GDD regional centers work closely with the international partners, often a ministry of health or national public health institute, to identify common areas of research

Table 2. Number of projects conducted by Global Disease Detection Program regional centers, by topical area and activity type assessed, fiscal years 2015 and 2016*

Topical area	Definition	No. projects	Activity type*				
			PHR	S	L	PHI	CB
Acute respiratory illness	Syndromic surveillance focusing on respiratory pathogens (e.g., influenza, severe acute respiratory infections, pneumonia)	50	37	25	32	24	19
Health system strengthening	Incorporating any components of training, guidelines and protocol development, or capacity building to enhance the national disease surveillance system, workforce development, epidemiologic research, or information systems	36	7	2	7	6	34
One Health	The intersection of animal and human health, zoonotic diseases, or program development around zoonoses	30	13	14	15	10	16
Emerging infectious disease	Emerging or reemerging infectious disease within the regional center (e.g., hepatitis in Egypt and Georgia, polio in Kenya, neglected tropical diseases in Guatemala)	22	8	12	13	10	12
Emergency preparedness and response	Emergency preparedness and response efforts focusing on risk communication, pathogen detection, and outbreak investigation	19	2	1	0	2	19
Vectorborne infections	Vectorborne infections (e.g., malaria, dengue, Japanese encephalitis, Crimean-Congo hemorrhagic fever)	12	5	5	7	4	5
Hospital-associated infections	Healthcare infection and control	9	5	4	4	1	4
Tuberculosis	Tuberculosis infection, case findings, control, and treatment	9	7	1	5	4	3
Enteric disease	Diarrheal diseases or infection	8	3	6	6	6	6
Antimicrobial resistance	Antimicrobial drug–resistant pathogens	6	1	1	2	1	5
Acute febrile illness	Syndromic surveillance focusing on acute febrile or neurologic illness	4	4	4	4	4	2
Total no. projects		205	92	75	95	72	125

*October 1, 2014–September 30, 2016. Activities do not sum across the rows because activity types are not mutually exclusive. CB, technical capacity building; L, laboratory; PHI, public health informatics; PHR, applied public health research; S, surveillance.

interests and national priorities. The data generated from these collaborations have been used by host governments to quantify the public health issue and, ultimately, to guide and inform public health policy. Implementing high-quality research studies also serves as a hands-on training mechanism for international partners. Projects are conducted in collaboration with the in-country hosts, from developing the concept, writing the research protocol, implementing the study, analyzing and interpreting the data, and publishing the results. A tangible way that highlights the results of these collaborations is dissemination of findings in the scientific literature. Since the inception of the GDD Program, GDD staff have authored or coauthored ≈875 peer-reviewed scientific articles (*9*).

Surveillance

GDD regional centers partner with host countries to develop and strengthen surveillance for key illnesses and to limit spread of disease to the point of origin. Projects integrate laboratory, clinical, and epidemiologic information that can guide public health interventions and other control measures. GDD centers achieve this objective through several types of surveillance strategies, such as syndromic, laboratory-based, population-based, and sentinel systems (*10*–*15*). Population-based surveillance provide a framework for applied public health research that can help to characterize the burden, risk factors, and transmission characteristics of new or emerging infectious diseases and to assess the effectiveness of prevention strategies (*3*). Sentinel surveillance in a few key sites/facilities for specific or syndromic infectious diseases can help to identify emerging or reemerging pathogens (*16*).

Outbreaks of SARS and avian influenza A(H5N1) highlighted the need to have systems in place for detecting emerging pathogens (*3*). Thus, establishing population-based infectious disease surveillance for pneumonia and acute respiratory infections was a primary goal of the GDD Program (*3*). The resulting surveillance activities also provide a platform for other GDD core activities. Moreover, the GDD respiratory surveillance research projects have helped quantify burden of illness for pneumonia and influenza-associated acute respiratory illness, especially among children, and a high incidence of several respiratory pathogens, including respiratory syncytial virus, parainfluenza, and adenoviruses (*6*,*11*,*12*,*17*–*23*).

Table 3. Selected ongoing projects presented at the Global Disease Detection Program annual science meeting, by country and activity type assessed, June 2016, Atlanta, Georgia, USA*

Country	Title of presentation	Activity type				
		PHR	S	L	PHI	CB
Bangladesh	Ensuring infection control is feasible and acceptable: identifying high-intensity interventions for Nipah-like illness and low-intensity interventions for routine use in Bangladesh	X			X	X
	Making the case for rotavirus vaccination in Bangladesh: surveillance impacting public health interventions	X		X	X	
	Spatial heterogeneity for dengue risk in Bangladesh: significance for other arthropodborne infections such as Zika	X		X	X	
China	Verification of patients reported as central line–associated bloodstream infections (CLABSI) in a healthcare-associated infections surveillance system evaluation in Beijing	X			X	
	Risk factors for *Vibrio parahaemolyticus* infection in a southern coastal region in China	X			X	
Egypt	National surveillance of healthcare-associated infections and antimicrobial resistance in Egypt		X	X	X	
	Overview of GDD Egypt's population-based syndromic surveillance—Damanhur, Egypt, 2009–2016	X	X	X	X	
	Rickettsia typhi as an underrecognized cause of acute undifferentiated febrile illness—Damanhour, Egypt, 2010–2014	X			X	
Georgia	Bloodborne disease prevalence in the blood supply, Georgia, 2012–2014	X			X	
	Hepatitis C elimination in Georgia: a one-of-a-kind program providing a golden opportunity to strengthen public health systems	X		X	X	
Guatemala	Influenza-like illness and influenza vaccination during pregnancy in Quetzaltenango, Guatemala	X	X	X	X	
	Participatory development of a congenital Chagas disease screening strategy after the vector control attack phase in Guatemala	X		X	X	
India	Acute encephalitis syndrome in Assam, India: importance of Japanese encephalitis in the adult population, 2014–2015	X		X	X	
	Redrawing the boundaries of Kyasanur Forest Disease (KFD) in India: early results of GHSA-supported acute febrile illness surveillance	X		X	X	
Kazakhstan	Strengthening the capacity of the Republic of Uzbekistan to combat antimicrobial resistance		X		X	
	Implementation of the CCHF surveillance enhancement activities in Kazakhstan, 2012–2015				X	X
Kenya	Epidemiology of brucellosis and MERS-CoV in linked human and animal populations in Kenya	X		X	X	
	Indirect effects of 10-valent pneumococcal conjugate vaccine (PCV10) against adult pneumococcal pneumonia in rural western Kenya	X	X	X	X	
South Africa	Application of a simple differential diagnostic tool for solving febrile, neurologic and heamoragic fever cases in Southern Africa			X	X	
	Decline in syphilis seroprevalence among females of reproductive age in Northern Cape Province, South Africa, 2003–2012: utility of laboratory-based information	X			X	
Thailand	Spotted fever group, typhus group rickettsioses and Sennetsu neorickettsiosis in rural Thailand	X		X	X	
	Enhanced surveillance for severe pneumonia, Thailand 2010–2014		X	X	X	
	Epidemiology and antimicrobial resistance of invasive salmonellosis, rural Thailand, 2006–2014	X		X	X	
No. presentations by activity type		18	6	15	23	2

*CB, technical capacity building; CCHF, Crimean-Congo hemorrhagic fever; GDD, Global Disease Detection; GHSA, Global Health Security Agenda; L, laboratory; MERS-CoV, Middle Eastern respiratory syndrome coronavirus; PHI, public health informatics; PHR, applied public health research; S, surveillance.

As GDD regional centers have matured, existing surveillance platforms have increasingly been adapted to include emerging pathogens, special noncommunicable disease studies, and projects focused on the animal–human interface (i.e., zoonotic diseases) (*24–28*). In 2014, the GDD regional centers began efforts to link common acute febrile illness (AFI) syndromic surveillance strategies across 5 regional sites (Egypt, Guatemala, India, Kenya, and Thailand) to gain a global perspective on AFI. Conducting AFI surveillance at GDD regional centers is of public health importance because AFI represents a common clinical syndrome for multiple diseases of outbreak potential or emerging zoonotic infections and provides an opportunity to evaluate novel diagnostics. Unlike respiratory illness syndromes such as severe acute respiratory illness and influenza-like illness, no international consensus case definition exists for AFI surveillance, although recommendations for improving methods have been

proposed (*29*,*30*). In addition, very few published AFI etiology studies have been conducted in multiple countries. A literature review currently under way has found that, of 169 AFI studies aiming to identify etiology and published during 2005–2016, only 6 (4%) had enrolled cases in multiple countries (G. Kharod and C. Rhee, unpub. data).

A multisite research effort has the potential to catalyze historically disparate AFI syndromic surveillance systems toward globally comparable data of high utility at all levels for public health response. Network activities across different GDD regional centers that represent diverse disease risks enhanced the ability to study a range of infectious diseases for which a single country might not have the capacity or incidence of disease to study for evidence-based public health decision making. The GDD effort, to date, has included consistent case definition use with a focus on undifferentiated AFI, multipathogen detection of local and globally significant infectious diseases, use of standard and investigational diagnostics where feasible, and prospective sentinel health facility–based surveillance methods of ≥1 year in duration to evaluate seasonal epidemic trends. Barriers to launch and harmonization to a common research protocol have included variation in local priority pathogens, resource availability, and time required for integration into existing public health surveillance and healthcare networks. Established enhanced AFI surveillance has thus far provided a useful platform for investigating emerging infections with a febrile illness component, such as Zika virus and scrub typhus.

Laboratory

Effective public health requires close collaboration between epidemiologists and laboratory scientists. GDD works with partner countries to strengthen diagnostic technical capacity for priority diseases; evaluate new laboratory diagnostics; establish frameworks for national laboratories that include quality assurance and specimen referral systems; improve biosafety/biosecurity; and train laboratory personnel on benchtop skills, laboratory management, and public health laboratory functions. These efforts have improved the capacity of GDD host countries and their regions to detect and respond to emerging infectious disease threats and to sustain these efforts through a strong cadre of laboratory scientists dedicated to improving the global public health laboratory infrastructure (*31*).

Research at the GDD regional centers has assisted in the detection and identification of 12 novel strains and pathogens that were new to the world and 62 novel strains or pathogens that were new to the region where they were discovered (*9*). GDD laboratorians have helped implement capacity to conduct >380 new diagnostic tests in 59 countries, improving disease detection capability and contributing to faster response times within the region.

Public Health Informatics

Informatics is the application of public health information systems to capture, manage, analyze, and use information to improve public health practice (*32*). Examples of the key activities include the use of electronic databases, either as the source of data or as a method to collate data, for expediting the time between data collection and use. At GDD regional centers, public health informatics is a cross-cutting activity for disease surveillance, laboratory studies, and applied epidemiologic research to ensure that data are collected and managed in a systematic and reliable manner. Most GDD data-collecting projects currently under way have an informatics component (Table 3).

Capacity Building

Strengthening the local public health capacity and workforce are key for improving the detection and response to infectious diseases globally. The transfer of epidemiology, laboratory, and emergency preparedness skills to local public health professionals is necessary for sustainability, both nationally and across regions. Capacity building is another cross-cutting activity at the GDD regional centers and ranges from establishing or strengthening existing surveillance, laboratory, emergency preparedness, and health systems to conducting high-quality epidemiologic research studies to address knowledge gaps. This capacity is achieved through on-the-job training of local partners, providing technical expertise, conducting high-quality research studies, and collaborating on analysis of information to inform evidence-based decision making.

Public Health Diplomacy

Scientific exchange can play a strong role in building bonds across countries. Because health is an area of concern for all nations, international projects that address a common threat, such as infectious diseases that easily cross borders, can open avenues of communication and ease tensions between the United States and other nations (*33*). GDD China serves as an example of how 2 strong national public health institutes (1 in China and 1 in the United States) can collaborate and benefit. During the West Africa Ebola outbreak in 2014, China CDC had the resources and willingness to respond but not necessarily the US CDC experience or technical expertise with Ebola outbreaks and response. Since 2006, Chinese laboratorians have worked alongside US colleagues to build greater diagnostic testing capacity throughout China. Because of this preexisting relationship, the 2 countries were able to forge a new type of collaboration in Sierra Leone; scientists from both countries worked together to offer critical training and resources to Sierra Leone to help stop the spread of the largest Ebola outbreak in history (*34*). By building strong partnerships and scientific systems, GDD

protects the United States and countries around the world from threats to health, safety, and security.

Lessons Learned and the Future

The GDD Program promotes the prompt detection and mitigation of disease threats globally. GDD works with multiple countries (Figure) to conduct applied public health research and develop and enhance public health capacity to rapidly detect, accurately identify, and promptly contain emerging and reemerging infectious diseases. The activities of the GDD Program are critical to help countries improve their disease surveillance networks and enhance laboratory capabilities for detection of emerging pathogens. The program also has greatly expanded epidemiology workforce networks to meet their commitment to global health security and the International Health Regulations 2005.

The activities of the GDD Program have developed needed technical capacity, advanced science, and provided critical information for policy change. Activities of the GDD regional centers have allowed a greater understanding of what infections or conditions are of concern in the countries and regions in which they work. They have increased awareness of the emergence of antimicrobial resistance and the growing threat of infections that can be acquired in healthcare settings (*35*,*36*). Strengthening disease surveillance, applied public health research, and laboratory capacity have allowed for a better understanding of pathogens associated with illnesses that present with acute fever. The activities established serve as a base or launch pad for the rapid and timely implementation of surveillance for emerging infections like Zika virus and applied epidemiologic research studies to better understand which populations are being affected and to enumerate potential factors associated with infection and spread of illness.

As new laboratory techniques for the detection of pathogens are developed, the GDD regional centers have served as a platform to examine the performance of these new tests in multiple settings and promote the adoption of the new techniques in multiple countries. Because of ongoing surveillance and routine collection of epidemiologic information, GDD regional centers and the countries they work with have the tools needed to best characterize pathogens that are circulating and explore potential reservoirs and sources associated with these infections. Increased informatics capacity is concurrently enabling the active linkage of information and interfacing of data housed in multiple data systems within the countries and regions.

GDD regional centers make critical contributions to global disease detection by improving infectious disease detection capacity through integration of applied public health research and laboratory capacity building, which in turn will generate quality data that can inform high-level policy. The GDD Program has matured and transformed over the past 10 years and continues to evolve. Further advancing the technical capacity that has already been developed is allowing the GDD Program to focus on needed research and generation of data to develop and evaluate interventions and inform policies needed to reduce burden of multiple conditions worldwide. Examples of research activities needed include studies to understand the actual burden of conditions at play, assessments of the impact of multiple conditions on local and global populations, quantification of the societal and economic costs of illnesses, and evaluation of control measures.

Threats posed by emerging pandemics and other infectious diseases will remain a challenge to global health security, endangering economies and decreasing political stability. GDD will continue to work with countries to strengthen core capacities and conduct applied public health research so that emerging and reemerging diseases and conditions can be detected and stopped faster and closer to the source, thereby enhancing global health security.

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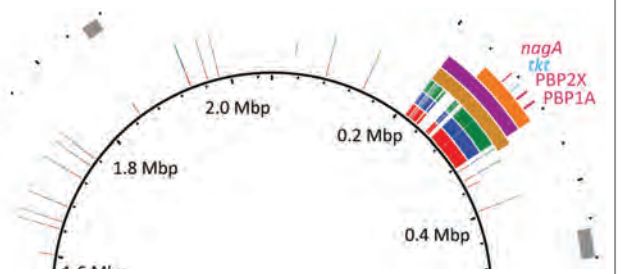

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Enhancing Surveillance and Diagnostics in Anthrax-Endemic Countries

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Naturally occurring anthrax disproportionately affects the health and economic welfare of poor, rural communities in anthrax-endemic countries. However, many of these countries have limited anthrax prevention and control programs. Effective prevention of anthrax outbreaks among humans is accomplished through routine livestock vaccination programs and prompt response to animal outbreaks. The Centers for Disease Control and Prevention uses a 2-phase framework when providing technical assistance to partners in anthrax-endemic countries. The first phase assesses and identifies areas for improvement in existing human and animal surveillance, laboratory diagnostics, and outbreak response. The second phase provides steps to implement improvements to these areas. We describe examples of implementing this framework in anthrax-endemic countries. These activities are at varying stages of completion; however, the public health impact of these initiatives has been encouraging. The anthrax framework can be extended to other zoonotic diseases to build on these efforts, improve human and animal health, and enhance global health security.

Anthrax is a zoonotic bacterial disease caused by *Bacillus anthracis*, which primarily inhabits herbivorous wildlife and livestock and is usually fatal among these animals. Human infections can result in a high mortality rate if not diagnosed and treated promptly. Humans contract cutaneous anthrax through direct contact of skin or mucosal membranes with *B. anthracis*–infected animals as they are slaughtered or butchered or by handling by-products (*1*–*3*). Ingestion anthrax results from consuming raw or undercooked meat salvaged from infected animals. Inhalation anthrax causes severe disease but rarely occurs naturally in humans; it is acquired through inhaling *B. anthracis* spores aerosolized during contact with or processing of contaminated hides, bones, hair, or wool (*2*). In addition, an incident of injection anthrax, associated with the use of *B. anthracis*–contaminated heroin, has been reported in Europe (*4*). Among these forms, cutaneous anthrax is the most common, comprising ≈95% of naturally occurring human infections (*3*). In addition to the naturally acquired forms of anthrax, *B. anthracis* is designated as a potential bioweapon, and the risk of acquiring anthrax from laboratory-produced *B. anthracis* spores emphasizes the importance of anthrax surveillance, prevention, and control in anthrax-endemic countries (*5*,*6*).

B. anthracis spores can survive in the soil for many years and are distributed worldwide, although the disease is endemic to Africa, Central Asia, the Middle East, and South America (*7*,*8*). The pathogen has a substantial economic and public health impact in countries with limited resources for the development of anthrax control and outbreak response programs. In anthrax-endemic areas, the high mortality rate among livestock can disrupt the subsistence livelihood for families and distress the local agricultural sector. Contact with *B. anthracis*–infected carcasses and by-products routinely leads to human infections and can affect whole communities through the practice of slaughtering sick animals to recoup income or food from the lost animals (*3*,*9*).

The foundation of anthrax control is vaccination of livestock accompanied by rapid outbreak response to limit environmental contamination and human exposure. Animal outbreak response relies heavily on effective surveillance and availability of rapid and reliable laboratory diagnostics. However, countries with underresourced public and veterinary health surveillance programs and laboratory capacity are disproportionately affected by this disease (*8*).

The need to strengthen global capacity to prevent, detect, and respond to public health threats such as anthrax is increasingly being recognized by endemic countries because of their desire to meet requirements under the International Health Regulations 2005 (*10*) and Global Health Security Agenda (GHSA) (*11*). One component of the Centers for Disease Control and Prevention (CDC) GHSA (*12*) activities is an effort to prioritize zoonotic diseases on the

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basis of criteria selected by the host country (*13*). In the 7 countries where this prioritization has occurred, 4 countries ranked anthrax as 1 of the top 5 zoonotic diseases of major public health concern (*14*). CDC is committed to building anthrax prevention and control capacity in countries prioritizing anthrax as a public health threat or otherwise requesting assistance.

Framework for Enhancing Anthrax Prevention and Control

CDC's Bacterial Special Pathogens Branch, part of the Division of High-Consequence Pathogens and Pathology in the National Center for Emerging and Zoonotic Infectious Diseases, works with governments and other international partners to support activities in anthrax-endemic countries that strengthen human and animal anthrax surveillance, enhance laboratory capacity, develop control strategies, and foster collaborative outbreak investigations. The goal of these activities is to reduce anthrax in persons who come in contact with infected animals or their by-products and to reduce the economic effect associated with livestock loss. To achieve these goals, CDC developed a comprehensive framework compiled from multiple published guidelines that outlines a start-to-finish approach to prevent and control anthrax (*15*). The principles and methods described in the framework can be applied in any anthrax-endemic country and can be modified to address specific gaps.

The framework is subdivided into 2 phases, assessment and implementation (Table), and includes instructions on performing assessments (laboratory, epidemiologic, situational); providing recommendations; and implementing interventions to prevent and control anthrax. Anthrax-endemic countries have already started applying the framework principles and have successfully completed some activities, with some ongoing (online Technical Appendix Table, https://wwwnc.cdc.gov/EID/article/23/13/17-0431-Techapp.pdf).

Table. Framework for enhancing anthrax prevention and control in endemic countries

Phase no., title	Activities
Phase I—assessment	Establishment of partnerships Surveillance and outbreak response assessment Laboratory assessment Vaccination assessment
Phase II—implementation	Project identification Enhancement of surveillance Enhancement of outbreak response capacity Enhancement of diagnostic capacity Development of targeted studies Implementation of prevention and control measures Development and dissemination of educational materials

Phase I—Assessment

Establishment of Partnerships

CDC collaborates with anthrax-endemic countries that request assistance to improve surveillance and diagnostic capacity. Upon request, CDC identifies key working partners in these countries to initiate collaborations. Cooperative agreements are established with host country partners to strengthen existing and develop new anthrax-related activities and provide technical and financial assistance. The One Health approach, involving both human and animal health stakeholders, is used for the promotion of cross-sectoral integration and coordination of activities for the detection, prevention, and response to endemic anthrax (*16*). CDC works with host country representatives to identify a complete cadre of partners and stakeholders to collaborate on anthrax activities. This cadre might include the ministries of health, agriculture, wildlife, and forestry; national institutes; local universities; hospitals; animal industry; and professional organizations. In addition, international organizations like the World Health Organization, the World Organisation for Animal Health, and the Food and Agriculture Organization of the United Nations are usually identified as partners for in-country activities.

Partnering with CDC country offices and local Field Epidemiology and Laboratory Training Programs (FELTPs) has proven to be an effective mechanism for building collaborations on anthrax. Work in the countries of Georgia, Ghana, India, and Bangladesh was facilitated by CDC country offices and FELTP staff, who provided expertise and assistance with forging relationships with multiple agencies, navigating the political environment, assisting with the outbreak response, and promoting needed and beneficial proposed studies. CDC usually engages with national-level partners; however, anthrax is typically endemic only in focal regions. Thus, control programs are most useful when targeting disease-endemic areas. In countries with >1 disease-endemic region, phased implementation improves the likelihood of success. Factors such as status of surveillance, burden of disease, partners, security, and funding should be considered when selecting a region for initial implementation. Once partnerships and agreements are in place, appropriate assessments of ongoing anthrax-related activities and capacities can be conducted.

Surveillance and Outbreak Response Assessment

Surveillance assessments progress according to the published protocols for the assessment of disease surveillance and response that are modified to be anthrax-specific and address each country's needs (*17*,*18*). The initial assessment includes a review of information collected by the

surveillance systems for both human and animal anthrax; a report of flow and timeliness; the distribution of anthrax-affected areas throughout the country; the burden of disease (number of outbreaks, illnesses, hospitalizations, deaths, associated costs); and available studies and reports describing anthrax in the country. It is critical to discuss the existing national anthrax surveillance systems' strengths, weaknesses, and barriers, with a focus on anthrax case definitions, case reporting processes, surveillance data quality, outbreak investigation protocols, and intersectoral collaboration, which provide valuable information on areas for collaboration and project development to enhance anthrax surveillance.

Laboratory Assessment

Similar to surveillance assessments, laboratory assessments were developed by modifying existing assessment tools and incorporating evaluations for anthrax diagnostic procedures (*2*,*3*). Assessment of laboratory capacity includes identifying existing national, regional, and local laboratories performing anthrax diagnostics. Then, various aspects of the laboratories are evaluated, such as the existing workforce, established diagnostic and logistic capacity, available equipment, facility infrastructure, and waste management. Laboratory assessment findings and the diagnostic capacity that countries request for use within their laboratory system are used to determine the needs for appropriate training, facility improvements, and diagnostic algorithms to ensure the safety of all facility staff.

Numerous diagnostics ranging from basic Gram stains to more specialized culture and molecular diagnostics (e.g., PCR) are available for identifying *B. anthracis.* Each has varied sensitivity and specificity and requires varied technological skills and laboratory resources. Diagnostic capacity varies by country. Most underresourced countries will base their outbreak response on clinical signs and microbiological stains and culture. However, some countries have successfully developed PCR and culture capability to detect and confirm anthrax from clinical specimens. Fortunately, the absence of costly Biosafety Level 3 laboratory facilities is not a limiting factor for safely conducting *B. anthracis* diagnostics. Diagnostic procedures, including molecular diagnostics and bacterial culture, can be safely conducted by trained laboratory staff under Biosafety Level 2 conditions, with handling of infectious material in certified biosafety cabinets (*19*,*20*).

Vaccination Assessment

Animal vaccination is a vital tool to prevent and control anthrax in animals and, thus, prevent infection in humans (*3*). During vaccination assessments, information is collected on the following: the type of vaccine and bacteria strain used; production site; vaccination coverage of livestock; affordability; and logistics for storage, distribution, and delivery. Although the vaccine is available and subsidized through the government in some countries, vaccine cost is often the livestock owners' responsibility. Information on vaccination policies and regulations, such as timing, frequency of administration, record keeping, vaccine administration personnel, and minimum age of animals at vaccination, are also collected. Assessment of animal vaccination status is laborious and the information is rarely readily available. Collaboration with vaccine production agencies and commercial partners is essential to obtain these data.

Phase II—Implementation

Project Identification

After the assessments, convening multisectoral meetings to discuss priority activities for enhancing anthrax surveillance, diagnostic, and outbreak response capacities and prevention and control measures can ensure a more efficient use of available resources and government ownership of activities. Anthrax stakeholder workshops can help to identify high-risk areas to implement activities and to define and discuss in-country surveillance and laboratory capacity. For example, CDC collaborated with international partners to engage key stakeholders in the country of Georgia through a series of workshops held during 2013–2015 to improve existing systems, promote integration of human and animal anthrax surveillance, and promote rigorous scientific investigations. Similarly, in 2017, CDC organized the Anthrax Surveillance, Prevention, and Control in Ethiopia Meeting, which provided government agencies representing both human and animal health the opportunity for technical discussions of ongoing anthrax activities in Ethiopia, including surveillance, outbreak response, and laboratory diagnostic capacity. The workshop facilitated intersectoral discussions and collaboration to enhance anthrax surveillance and control and identify priority needs for anthrax work in Ethiopia. In addition, CDC assisted partners to coordinate the Bangladesh-India Cooperative Workshop on Anthrax with the goal to strengthen anthrax detection and diagnostics through a coordinated international approach.

Enhancement of Surveillance, Outbreak Response, and Diagnostic Capacity

During stakeholder meetings, CDC and other partners offer ideas and assistance on activities countries could undertake to enhance their anthrax-related activities, with a focus on improving the areas identified as gaps or weaknesses during assessments. Surveillance can be enhanced by developing an organized reporting system agreed upon by stakeholders, encouraging local (human and animal) health

providers to report cases, conducting training courses, providing resources and equipment, and integrating human and animal surveillance data. Anthrax outbreak response can be improved by supporting activities, such as training of response personnel, developing standard operational procedures for joint outbreak investigations, and establishing joint-investigation response teams. Defining clear roles and responsibilities for each agency before an outbreak investigation is critical for an efficient outbreak response. On-site training sessions on outbreak investigations and anthrax diagnostics can target identified gaps and support surveillance of other diseases. In 2016 in Bangledesh, CDC conducted a training on field collection methods for cutaneous lesions and eschars, which included training for sample collection of not only cutaneous anthrax but also other eschar-associated diseases such as poxviruses.

Enhancing outbreak response and surveillance capacity directly affects the country's ability to detect and contain anthrax outbreaks. In 2012, a national, intersectoral working group was formed in Georgia to investigate a human anthrax outbreak. This group evolved into a One Health surveillance team to improve intersectoral communication and provide more rapid response to anthrax investigations in Georgia. Later, the team promptly identified a human anthrax case in Tbilisi linked to illegally sold meat and traced it back to the seller, preventing a possible outbreak in a dense urban setting (*21*). This team also spurred development of regional rapid response teams to improve surveillance and outbreak response at the local level and developed and disseminated educational materials throughout Georgia. The team affected anthrax control nationwide when they identified animal anthrax reporting issues, which led to targeted interventions in the highest risk districts. These interventions included reinstatement of animal vaccination campaigns in these areas, which resulted in a decline of human anthrax cases (*22*). Furthermore, in 2009 and 2010, CDC assisted the Bangladesh Ministry of Health with its response to multiple anthrax outbreaks, affecting >270 persons. Since this time, CDC has maintained collaborations providing technical support, consultation, and laboratory confirmation for annually occurring anthrax outbreaks throughout Bangladesh (*23*,*24*).

Development of standard operational procedures for specimen collection and transportation, as well as establishment of laboratory diagnostics that are reliable, appropriate, safe, and sustainable, are necessary steps for enhancing anthrax surveillance. Standard diagnostics include microscopy and culture, which are both relatively reliable and sustainable diagnostic techniques. However, biosafety concerns are inherent to culturing bacteria, and identification of culture isolates typically requires confirmation by either PCR or susceptibility to gamma phage, which are not typically available in many anthrax-endemic countries. Increasing a country's ability to perform molecular diagnostics decreases the turnaround time for specimen processing and diagnostic results (*12*). Thus, CDC encourages the use of molecular methods such as PCR for confirmation at the national reference laboratories. While these diagnostic protocols are being developed and implemented, CDC offers confirmatory testing, such as culture and PCR, for human specimens at the CDC Zoonoses and Select Agent Laboratory in Atlanta, Georgia, USA (*24*). CDC also performs anthrax serologic assays not available in most anthrax-endemic countries, including assays that detect anthrax lethal factor (LF) and anti-protective antigen IgG and measure anthrax lethal toxin neutralization activity levels. CDC has conducted these tests to confirm human outbreaks in Bangladesh; they are specifically useful for identifying outbreaks after implementation of antimicrobial drugs (*23*).

In Bangladesh, CDC used laboratory assessments to identify public health and veterinary laboratories capable of conducting various diagnostic methods and those requiring training and resources to improve methodology, biosafety, and biosecurity to ensure their anthrax diagnostic capabilities. CDC has assisted Bangladesh with diagnostics during anthrax investigations since 2009. A variety of diagnostic methods, including M'Fadyean staining, culture, immunohistochemistry, anti-protective antigen ELISA, toxin neutralization assays, and LF detection by mass spectrometry, were used during outbreaks. This collaborative effort was of great benefit to both CDC and Bangladesh. CDC testing allowed for the first confirmation of human cutaneous anthrax cases in Bangladesh since 1986 and provided CDC invaluable data on the performance of newer tests such as the LF detection test. Unlike patients with inhalation and ingestion anthrax, patients with cutaneous anthrax often do not display systemic illness or bacteremia; thus, the value of testing patient blood for antibodies and LF was unclear. However, these assays were found useful even for diagnosis of cutaneous cases; 18 of 26 probable and confirmed cases of cutaneous anthrax were positive (*23*).

A 2015 assessment of the anthrax diagnostics and laboratory facilities at the Veterinary Services of Ghana, Ghana Health Services, and the Noguchi Memorial Institute for Medical Research in Ghana identified the need for confirmatory diagnostics at the national level. This need was confirmed during discussions with national anthrax surveillance staff, as was the need for a rapid diagnostic test (RDT) to presumptively diagnose animal cases. CDC assisted in training 6 veterinarians from the Veterinary Services of Ghana to use the RDT and collect specimens from animals suspected of dying of anthrax for confirmation and RDT validation. In 2016, the 6 newly trained veterinarians conducted 3 regional training courses,

extending capacity to 61 veterinarians. Technology transfer of confirmatory diagnostic methods is planned for 2017–2018. These efforts to improve diagnostic capacity in Ghana have prompted the development of an electronic notification system for more rapid response to suspected anthrax animal deaths, with the aim to improve surveillance and outbreak response. The use of gamma phage was recently introduced by CDC to veterinary partners in India as a method for diagnostic confirmation of culture-positive isolates in laboratories without PCR capabilities. The use of simple nonmolecular methods, such as infection with gamma phage, has the potential to widen surveillance efforts to bacteriology laboratories where molecular diagnostic capacity is not present.

Development of Targeted Studies

CDC supports activities aimed at understanding anthrax epidemiology in endemic countries. After a human anthrax outbreak in 2012, CDC collaborated with national and international partners in Georgia to conduct epidemiologic studies to determine the probable sources of environmental and animal exposure. The studies found that humans who had contact with sick or dead animals were at greatest risk of developing anthrax (*25*). CDC also provided technical support for the development and implementation of a matched case–control study to identify risk factors for animal anthrax deaths in Georgia during 2013–2015. This study confirmed the need for regular vaccination of livestock, which was reinstated by the Ministry of Agriculture (*22*). In Bangladesh, CDC are co-investigators with country partners on a study to identify host risk factors associated with cutaneous anthrax infections, aiming to identify vulnerable populations. In this study, risk factors related to animal husbandry practices, socioeconomics, and the geographic distribution of *B. anthracis* are being investigated with the goal to focus future surveillance, prevention, and control strategies in Bangladesh.

Improving Implementation of Prevention and Control Measures

In Georgia and Bangladesh, surveillance assessments and historical outbreak data were used to target anthrax prevention and control in specific, high-prevalence regions. Spatial modeling of disease distribution can help improve identification and prediction of high-risk areas for anthrax. CDC provided support to partners in Ghana and at the University of Florida (Gainesville, FL, USA) to hold trainings on Geographic Information Systems and spatial modeling for anthrax surveillance. These trainings included 6 Geographic Information Systems webinars with 31 regular participants, followed by 6 days of in-person class to solidify the spatial analytic methods. This same collaboration also resulted in an anthrax predictive risk map for Ghana created by using ecologic niche and random forest modeling. The model is guiding renewed efforts to train medical staff on case identification in high-risk areas and will be used to guide targeted anthrax vaccination campaigns (*26*).

Development and Dissemination of Educational Materials

Healthcare and community education materials are another aspect of the prevention and control of anthrax. The CDC framework for enhancing anthrax surveillance provides an outline for assessing and implementing anthrax prevention activities in endemic countries. The manual is provided in both English and French and has been distributed to human and animal health partners. In addition, international collaborations have improved communications between CDC and anthrax subject matter experts in anthrax-endemic countries, enabling a more direct, efficient, and mutually beneficial exchange of expertise on anthrax surveillance. Therefore, CDC developed an anthrax toolkit including a series of culturally specific illustrations to communicate anthrax prevention messages. In Cameroon and Mali, these illustrations were used successfully in field manuals for anthrax outbreak control to disseminate a clear One Health message that informs high-risk groups of the health implications of anthrax.

Impact and Next Steps

Anthrax causes serious public health problems and has high economic significance in affected countries (*9*,*21*). Enhancing surveillance, outbreak response, and diagnostics will prevent anthrax cases in both animals and humans and, thus, will reduce death, illness, and economic losses associated with anthrax. The framework for the control and prevention of anthrax promoting the One Health approach developed by CDC has shown positive public health effects in anthrax-endemic countries (*16*,*27*). The epidemiology of anthrax involves animal, human, and environmental components. Linking human and animal anthrax surveillance and tracing animal outbreaks to their source is imperative for the implementation of effective control measures. Laboratories with enhanced diagnostic capabilities can serve as regional reference facilities, and trained staff can assist with regional anthrax and other zoonotic outbreaks. This work also enhances global health security by supporting the GHSA, which aims to rapidly detect, respond, and control public health emergencies such as anthrax outbreaks.

CDC has provided support for the activities discussed and has seen substantial progress in anthrax prevention and control efforts in each partnering country. Despite the success of the framework activities, additional operational research and other capacity-enhancing activities can and should still be considered. These include assisting countries with building integrated human and animal anthrax

surveillance, testing vaccine efficacy, investigating best practices for carcass disposal, and partnering for community education campaigns. In addition, field testing novel, point-of-care diagnostic methods can advance rapid disease detection and biosecurity and enhance diagnostic capacity in endemic areas. Overall, on the basis of positive outcomes from past and ongoing activities, we recommend the continuation of ongoing efforts to support enhancement of anthrax surveillance and diagnostics. The anthrax framework can be adjusted to improve One Health surveillance, prevention, and control of multiple zoonotic diseases in anthrax-endemic countries.

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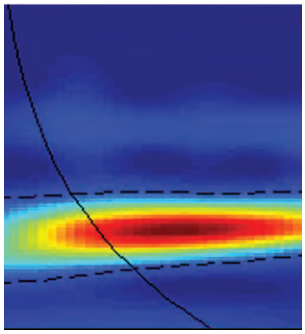
August 2015: **Surveillance**

- Drivers of Emerging Infectious Disease Events as a Framework for Digital Detection
- *Escherichia coli* O157 Outbreaks in the United States, 2003–2012
- Real-time Microbiology Laboratory Surveillance System to Detect Abnormal Events and Emerging Infections, Marseille, France



- Underrecognition of Dengue during 2013 Epidemic in Luanda, Angola
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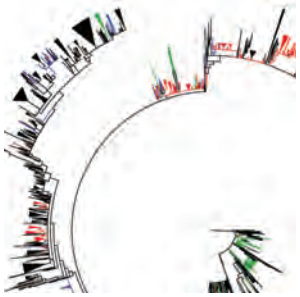

EMERGING INFECTIOUS DISEASES

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Cholera Mortality during Urban Epidemic, Dar es Salaam, Tanzania, August 16, 2015–January 16, 2016[1]

Lindsey S. McCrickard,[2] Amani Elibariki Massay,[2] Rupa Narra, Janneth Mghamba, Ahmed Abade Mohamed, Rogath Saika Kishimba, Loveness John Urio, Neema Rusibayamila, Grace Magembe, Muhammud Bakari, James J. Gibson, Rachel Barwick Eidex, Robert E. Quick

In 2015, a cholera epidemic occurred in Tanzania; most cases and deaths occurred in Dar es Salaam early in the outbreak. We evaluated cholera mortality through passive surveillance, burial permits, and interviews conducted with decedents' caretakers. Active case finding identified 101 suspected cholera deaths. Routine surveillance had captured only 48 (48%) of all cholera deaths, and burial permit assessments captured the remainder. We interviewed caregivers of 56 decedents to assess cholera management behaviors. Of 51 decedents receiving home care, 5 (10%) used oral rehydration solution after becoming ill. Caregivers reported that 51 (93%) of 55 decedents with known time of death sought care before death; 16 (29%) of 55 delayed seeking care for >6 h. Of the 33 (59%) community decedents, 20 (61%) were said to have been discharged from a health facility before death. Appropriate and early management of cholera cases can reduce the number of cholera deaths.

Cholera is an acute diarrheal illness caused by infection with the bacterium *Vibrio cholerae* (*1*). Severe cholera can be rapidly fatal; patients who do not receive appropriate treatment could die within hours (*1*). Prompt replacement of fluids and electrolytes through the use of oral rehydration solution (ORS) and intravenous fluids can prevent cholera death (*2*). With appropriate care, case-fatality rates for cholera should be <1% (*1*).

Tanzania reported an outbreak of cholera on August 15, 2015 (*3*,*4*). At that time, 6 of 8 countries bordering Tanzania were experiencing cholera outbreaks (*5*). Cholera outbreaks can spread rapidly, crossing national borders, and are a major global health security problem.

Early in the Tanzania outbreak, most cases and deaths were reported in Dar es Salaam, where 3,371 cases and 36 deaths (case-fatality rate 1.1%) had been recorded by October 31, 2015. Deaths were exclusively reported from cholera treatment centers (CTCs), but additional deaths in the community were rumored. When cholera deaths in the community were suspected, an environmental health officer was required to visit the decedent's house, prepare a burial permit, obtain a rectal swab for culture, and assist with the disposal of the body. The burial permit included the decedent's name, suspected cause of death, and date of death. We conducted a cholera mortality evaluation to identify unreported deaths, investigate household cholera management practices, and describe healthcare-seeking behaviors.

The Study

We obtained a list of persons who were suspected to have died of cholera (decedents) from the CTCs and obtained the burial permits from the CTCs, referral hospitals, and municipal offices (for complete description of methods, see online Technical Appendix 1, https://wwwnc.cdc.gov/EID/article/23/13/17-0529-Techapp1.pdf). The case definition for suspected cholera death was death of a person ≥2 years of age with acute watery diarrhea with or without vomiting with illness onset after August 15, 2015, in Dar es Salaam. A confirmed cholera death was defined as death of a person ≥2 years of age whose stool was positive for *Vibrio cholerae* O1 (*6*). All suspected and confirmed cholera deaths identified from CTC reports and burial permits were included in the evaluation.

We developed survey instruments with the Open Data Kit software (https://opendatakit.org/). Written informed

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[1]Preliminary results from this study were presented at the American Society of Tropical Medicine and Hygiene Annual Meeting; November 13–17, 2016, Atlanta, Georgia, USA.

[2]These first authors contributed equally to this article.

consent to take surveys was obtained, and then trained enumerators completed surveys with caregivers or relatives of the deceased (online Technical Appendix 2, https://wwwnc.cdc.gov/EID/article/23/13/17-0529-Techapp2.pdf). During January 19–23, 2016, these data were collected electronically on Galaxy Tablets (Samsung, Seoul, South Korea).

During August 16, 2015–January 16, 2016, the cholera surveillance system in Dar es Salaam identified 48 cholera deaths, all reported by CTCs. These deaths included persons who died at CTCs and persons who were dead on arrival. The burial permit assessment identified an additional 53 cholera deaths for a total of 101 total deaths (Figure 1); therefore, 52% of the total deaths were not captured by the existing surveillance system.

Cholera cases and deaths peaked in late September, with fewer deaths reported from November through January (Figure 2, panels A, B). The decrease in deaths coincided with a decrease in reported cholera cases. Of 101 decedents, 45 (45%) were not included in the study: for 35 (87.5%), caretakers could not be located; for 3 (7.5%), the caretakers had moved; 2 (5%) were an entire family unit with no respondent to give a survey; and 5 were misclassified (2 were <2 years of age and 3 had negative cultures with clinical signs inconsistent with cholera). Anecdotal reports suggested that many of the decedents for whom family members and caretakers could not be found were migrant workers who lived alone in single rented rooms, and the homes of others were not disclosed because of the stigma associated with cholera and local political pressure not to report.

Caretakers interviewed for this evaluation were family members (73%), landlords and neighbors (21%), employees (4%), and friends (2%) of the 56 decedents. The median age of decedents was 23 (range 2–80) years, and 32 (57%) were men or boys (Table).

Fecal samples from 39 (70%) decedents yielded *V. cholerae*. Laboratory results from 16 (29%) decedents were not available. The location of death was the community or en route to a health facility for 33 (59%) decedents, a health facility for 22 (39%), and an unknown location for 1 (2%) (Table). Of the 51 respondents who reported that decedents received home treatment, 5 (10%) said ORS was consumed. Reasons the decedents did not take ORS at home included not knowing what ORS was (38%) and not thinking that ORS would help (33%). Of 56 decedents, 26 (46%) consumed fluids other than ORS, including water (30%), soft drinks (13%), and porridge (5%), at home before their deaths.

Of 55 decedents with a reported time of death, 44 (80%) died within 24 hours of symptom onset, and of the 51 (93%) decedents who sought care before death, 16 (31%) waited >6 h from symptom onset to seek care. All decedents were able to reach a health facility from their home within 1 hour. Of 33 decedents who died in the community or en route to a health facility, 20 (61%) had previously been discharged alive from a health facility.

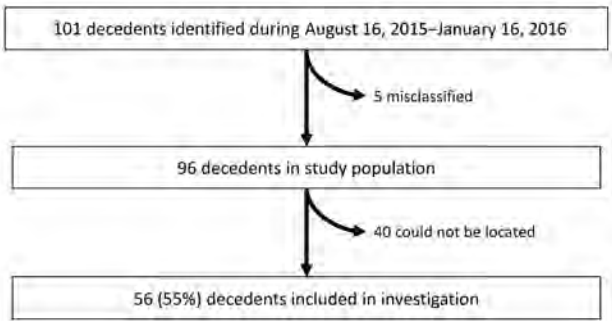

Figure 1. Study population for cholera mortality evaluation, Dar es Salaam, Tanzania, August 16, 2015–January 16, 2016.

Conclusions

More than half of the records of cholera deaths in Dar es Salaam were missing from the existing surveillance system, which only captured patients who arrived at CTCs. Deaths that occurred in other treatment locations

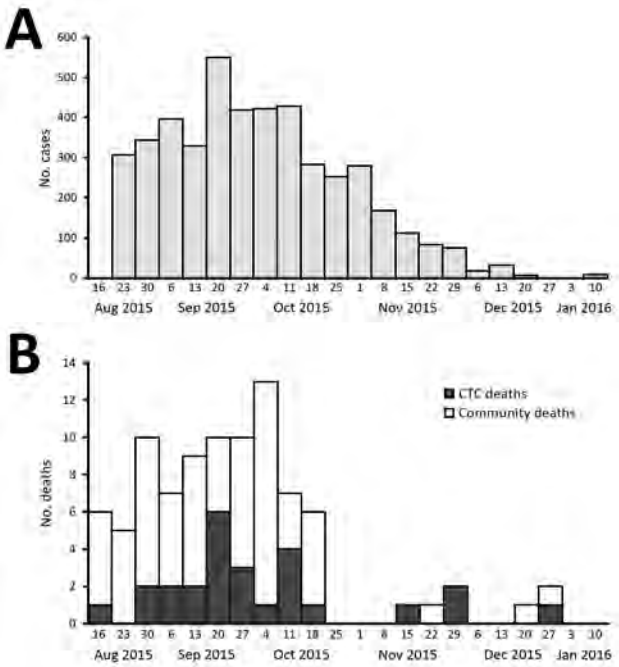

Figure 2. Suspected and confirmed cholera cases (A) and deaths (B) from cholera mortality evaluation and burial permit assessment, by week, Dar es Salaam, Tanzania, August 16, 2015–January 16, 2016. CTC deaths are deaths in patients ≥2 years of age with suspected or confirmed cholera who died following admission to a hospital or CTC. Community deaths were deaths in persons ≥2 years of age highly suspected of having cholera or having culture-confirmed cholera who died in the community or en route to a CTC. The date of death could not be determined for 6 decedents who were therefore excluded from the epidemic curves. CTC, cholera treatment center.

Table. Demographic characteristics of cholera decedents from cholera mortality evaluation, Dar es Salaam, Tanzania, August 16, 2015–January 16, 2016*

Characteristic	Total, N = 56	Confirmed, n = 39	Suspected, n = 17
Median age, y (range)†	23 (2–80)	21 (2–80)	25.5 (3–73)
Sex			
M	32 (57)	24 (62)	8 (47)
F	24 (43)	15 (38)	9 (53)
Location of death			
Health facility	22 (39)	11 (28)	11 (65)
Community	33 (59)	28 (72)	5 (29)
Unknown	1 (2)	0 (0)	1 (6)
Clinical signs/symptoms			
Vomiting	42 (75)	28 (72)	14 (82)
Diarrhea‡	43 (77)	28 (72)	15 (88)
Headache	9 (16)	7 (18)	2 (12)

*Values are no. (%) decedents except as indicated.
†Age was unknown for 7 persons.
‡One respondent did not know if the patient had diarrhea. Caretakers of 2 persons with suspected cases did not report diarrhea but met the burial permit assessment case definition.

or in the community were not reported. Underreporting of deaths during cholera epidemics, a phenomenon not unique to Tanzania (*5*,*7*,*8*), poses a threat to global health security.

We identified 3 anecdotal barriers to reporting cholera deaths. One barrier was political pressure; because of the electoral campaign ongoing during the epidemic, healthcare workers might have been discouraged from reporting cholera cases (*9*,*10*). Similarly, in 2008, underreporting of cholera deaths was observed during an electoral campaign in Kenya (*8*). Another barrier was influence from local leaders; because of the stigma associated with cholera, these leaders might have wished to deny the presence of the disease in their communities and created an environment discouraging others from reporting (*11*,*12*). The third barrier was lack of communication with immigrants; some decedents reported to be migrant workers who lived alone did not have social contacts who could serve as caregivers or report the decedent's cause of death. Similar observations have been described in another cholera mortality investigation (*13*).

This evaluation suggested that most caregivers of decedents lacked knowledge of ORS. Other studies have observed that the use and knowledge of ORS (*7*,*8*,*14*) has plateaued or declined in countries of sub-Saharan Africa and Asia since the 1990s (*15*,*16*). This decline or plateau was associated with decreased funding for diarrhea control projects, declining commercialization of ORS, and inconsistent messaging regarding homemade ORS (*16*). In addition, >30% of cholera decedents delayed seeking care by >6 h. Although other cholera mortality studies have not directly addressed the effect of delays in seeking care, several studies have identified distance to health facilities or lack of transportation as barriers to timely care in rural populations (*14*,*17*,*18*). In this urban epidemic, all decedents were able to reach a health facility within 1 hour. The failure to seek timely care was probably a matter of inadequate messaging to the public.

More than 60% of community decedents were reportedly discharged from a health facility before dying, suggesting inadequate management by health workers or premature discharge. The Tanzanian Ministry of Health initiated healthcare provider training in November 2015 to address cholera case management problems; starting around that time, cholera deaths became infrequent (Figure 2, panel B). The use of rectal swabs to confirm cholera in decedents might be a useful practice especially in the context of unexplained deaths during cholera outbreaks.

Enhanced surveillance, cholera case management training, and robust community education focused on destigmatizing the disease, as well as encouraging persons on the margins of society to seek medical attention for cholera-like symptoms, are needed to manage cholera epidemics. These practices can help expedite outbreak detection and response, facilitate the control of cholera at its source, and prevent deaths, enhancing global health security.

Acknowledgments

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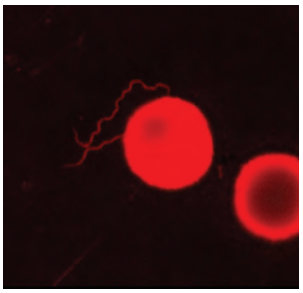
September 2016: Antimicrobial Resistance



- Co-Infections in Visceral Pentastomiasis, Democratic Republic of the Congo
- Multistate US Outbreak of Rapidly Growing Mycobacterial Infections Associated with Medical Tourism to the Dominican Republic, 2013–2014
- Virulence and Evolution of West Nile Virus, Australia, 1960–2012
- Phylogeographic Evidence for 2 Genetically Distinct Zoonotic *Plasmodium knowlesi* Parasites, Malaysia
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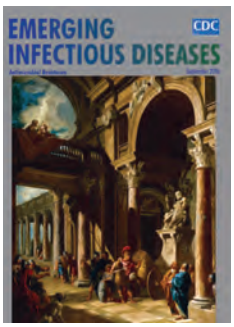
- Middle East Respiratory Syndrome Coronavirus Transmission in Extended Family, Saudi Arabia, 2014
- Exposure-Specific and Age-Specific Attack Rates for Ebola Virus Disease in Ebola-Affected Households, Sierra Leone
- Outbreak of Achromobacter *xylosoxidans* and *Ochrobactrum anthropi* Infections after Prostate Biopsies, France, 2014
- Human Babesiosis, Bolivia, 2013
- Assessment of Community Event–Based Surveillance for Ebola Virus Disease, Sierra Leone, 2015
- Probable Rabies Virus Transmission through Organ Transplantation, China, 2015



- Cutaneous Melioidosis Cluster Caused by Contaminated Wound Irrigation Fluid
- Possible Role of Fish and Frogs as Paratenic Hosts of *Dracunculus medinensis*, Chad
- Time Lags between Exanthematous Illness Attributed to Zika Virus, Guillain-Barré Syndrome, and Microcephaly, Salvador, Brazil

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EMERGING INFECTIOUS DISEASES

Building Global Epidemiology and Response Capacity with Field Epidemiology Training Programs

Donna S. Jones, Richard C. Dicker, Robert E. Fontaine, Amy L. Boore, Jared O. Omolo, Rana J. Ashgar, Henry C. Baggett

More than ever, competent field epidemiologists are needed worldwide. As known, new, and resurgent communicable diseases increase their global impact, the International Health Regulations and the Global Health Security Agenda call for sufficient field epidemiologic capacity in every country to rapidly detect, respond to, and contain public health emergencies, thereby ensuring global health security. To build this capacity, for >35 years the US Centers for Disease Control and Prevention has worked with countries around the globe to develop Field Epidemiology Training Programs (FETPs). FETP trainees conduct surveillance activities and outbreak investigations in service to ministry of health programs to prevent and control infectious diseases of global health importance such as polio, cholera, tuberculosis, HIV/AIDS, malaria, and emerging zoonotic infectious diseases. FETP graduates often rise to positions of leadership to direct such programs. By training competent epidemiologists to manage public health events locally and support public health systems nationally, health security is enhanced globally.

In 1951, in response to the threat of biological warfare during the Korean War, the Communicable Disease Center (now the US Centers for Disease Control and Prevention; CDC) established the Epidemic Intelligence Service (EIS) to respond to infectious disease outbreaks (*1*). The 2-year training program used a learning-while-doing approach to develop field epidemiologists (or disease detectives) capable of rapidly investigating and curtailing public health threats. The EIS has served as the model for developing a similar program, called the Field Epidemiology Training Program (FETP), around the world (*2*).

In 1975, the first FETP outside the United States was established in Canada. In 1980, Thailand launched the first FETP outside of North America, with CDC support (*3*). Since then, FETPs have been established in ≈65 countries around the world, many with assistance from CDC, the World Health Organization (WHO), the European Centre for Disease Prevention and Control, and other public health organizations. In many countries, FETPs have proven to be successful models for building public health workforce capacity (*4*); however, critical gaps remain in epidemiologic capacity including, for example, the 3 countries in West Africa where the 2014–2015 Ebola epidemic arose and propagated widely (*5*).

In 2003, the outbreak of severe acute respiratory syndrome (*6*) highlighted the continued worldwide vulnerability to infectious disease threats brought by ever-expanding global travel and trade. In response to severe acute respiratory syndrome and similar threats, WHO revised the International Health Regulations in 2005 (IHR 2005) to define core capacities necessary for countries to detect and respond to public health threats (*7*). Unfortunately, many countries remain unprepared to meet IHR 2005 requirements. In 2014, the Global Health Security Agenda (GHSA) was launched by the United States with 28 partnering nations, WHO, the Food and Agriculture Organization, and the World Organisation for Animal Health. The GHSA purpose was to accelerate progress toward implementation of IHR 2005 so that all countries are able to rapidly detect, respond to, and control public health emergencies at their source and thereby ensure global health security (*6*). One of these core elements is adequate human resources, which is essential for achieving each of the other IHR 2005 capacities. Highlighting the role of workforce development in accelerated IHR 2005 implementation, WHO revised the IHR 2005 monitoring framework and the Joint External Evaluation tool (which is used to measure progress toward IHR 2005 and GHSA implementation) to include specific public health workforce targets that rely on having an "applied epidemiology training program in place such as FETP" (*8*). By 2014, however, nearly 70% of countries had still not achieved IHR 2005 compliance, and few countries had achieved the Joint External Evaluation target of having 1 trained field epidemiologist (or equivalent) per 200,000 population.

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We describe the traditional 2-year FETP that has been supported by CDC in many countries. We also describe the effect of FETPs; their role in the development of a public health workforce; and how FETPs are enhancing the capacity of countries to rapidly detect, respond to, and control public health threats and thereby enhance global health security.

Building Field Epidemiology Capacity Globally

CDC supports FETP development to strengthen countries' epidemiology, surveillance, and response capacity, thereby enhancing global health security through a well-trained public health workforce. CDC support has included placement of a resident advisor in the country, technical support, and financial support. The resident advisor is an experienced applied epidemiologist, usually a graduate of the CDC EIS program or another FETP, who is placed in the country during the first few years of a new FETP to guide training and provide technical assistance. Since 1980, CDC has supported the launch of ≈45 FETPs with participants from ≈64 countries; numbers have increased since 2000 (Figure 1). Almost all of these FETPs continue to recruit and train epidemiologists, and many function independently of CDC funding. As of December 2016, there were 65 FETPs in 90 countries, and CDC was supporting 30 FETPs-Advanced serving 49 countries (Figure 2); ≈3,900 field epidemiologists have graduated from these CDC-supported programs.

FETPs traditionally have been 2-year programs that are based in ministries of health and that provide advanced field epidemiology training and service; however, shorter FETP models now exist. Participants (residents) in the FETPs-Advanced, usually ministry of health physicians and other professional staff, learn and practice epidemiologic skills while delivering essential epidemiologic services (training through service) to the ministry at the national or subnational level. FETP residents contribute to ministry missions by reviewing and analyzing surveillance data, detecting and responding to disease outbreaks and other public health emergencies, and conducting planned studies of public health priorities. They also develop skills to conduct public health research, improve communication of scientific findings, translate those findings into public health action, and contribute to the network of field epidemiologists locally and worldwide (*9*,*10*).

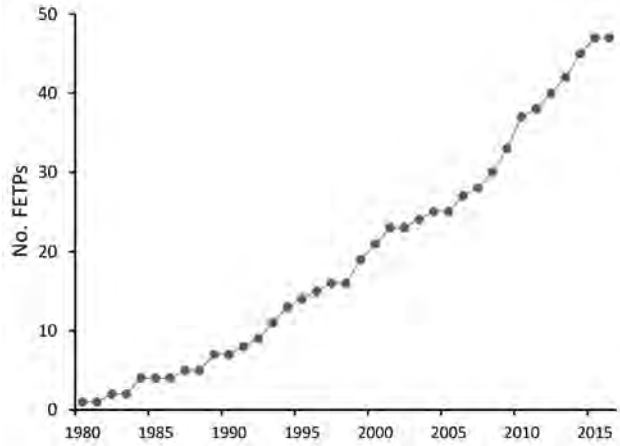

Figure 1. No. Field Epidemiology Training Programs (FETPs) established with US Centers for Disease Control and Prevention engagement (previous and current), 1980–2016.

As a fundamental feature, FETPs use the learning-by-doing approach with mentored public health practice for ≥70% of program time (*4*,*11*). However, programs are tailored to suit the needs and conditions of individual countries and regions. For example, although the focus for most programs is national, for a few programs it is regional (e.g., Central America, French-speaking West Africa, central Asia) (*12*,*13*), and some national programs accept residents from smaller neighboring countries. Many FETPs partner with a university to provide a postgraduate degree to residents who successfully complete the field and academic requirements, and some offer medical board qualification in community medicine or epidemiology. Some programs have included a laboratory track (Field Epidemiology and Laboratory Training Program; FELTP) (*14*), a veterinary track, or both, and 1 has a parallel veterinary FETP for animal health. The Central America program addressed the need for improved surveillance and epidemiology practice at all levels of the public health system by developing a 3-tiered FETP training model (Basic/Frontline, Intermediate, and Advanced) to build capacity at each level (*12*,*15*). Each tier aims to improve competency of public health workers in the same 4 essential domains of field epidemiology—surveillance, field investigation and response, data collection and analysis, and scientific communication—but the expectations are tailored to the public health skills needed at that level. FETP-Frontline training for surveillance officers has been implemented throughout Africa, Latin America, and elsewhere in response to the Ebola epidemic in West Africa, the Zika virus threat in the Americas, and the adoption of the GHSA (a global initiative to strengthen capacity to prevent, detect, and respond to public health threats). As of the end of 2016, a total of 24 new Frontline programs had been established and 1,354 surveillance staff had been trained (*16*).

During the 1990s, directors of several FETPs and similar programs organized themselves into a global network to expand program reach and to ensure program quality. In 1997, the network was formalized as the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) (*17*). TEPHINET now has 69 member programs in its global network. Over the years, as the number of FETPs has expanded, regional networks have been developed to support program implementation and strengthening. The African Field Epidemiology Network formed in 2005 (*18*), the Eastern Mediterranean Public

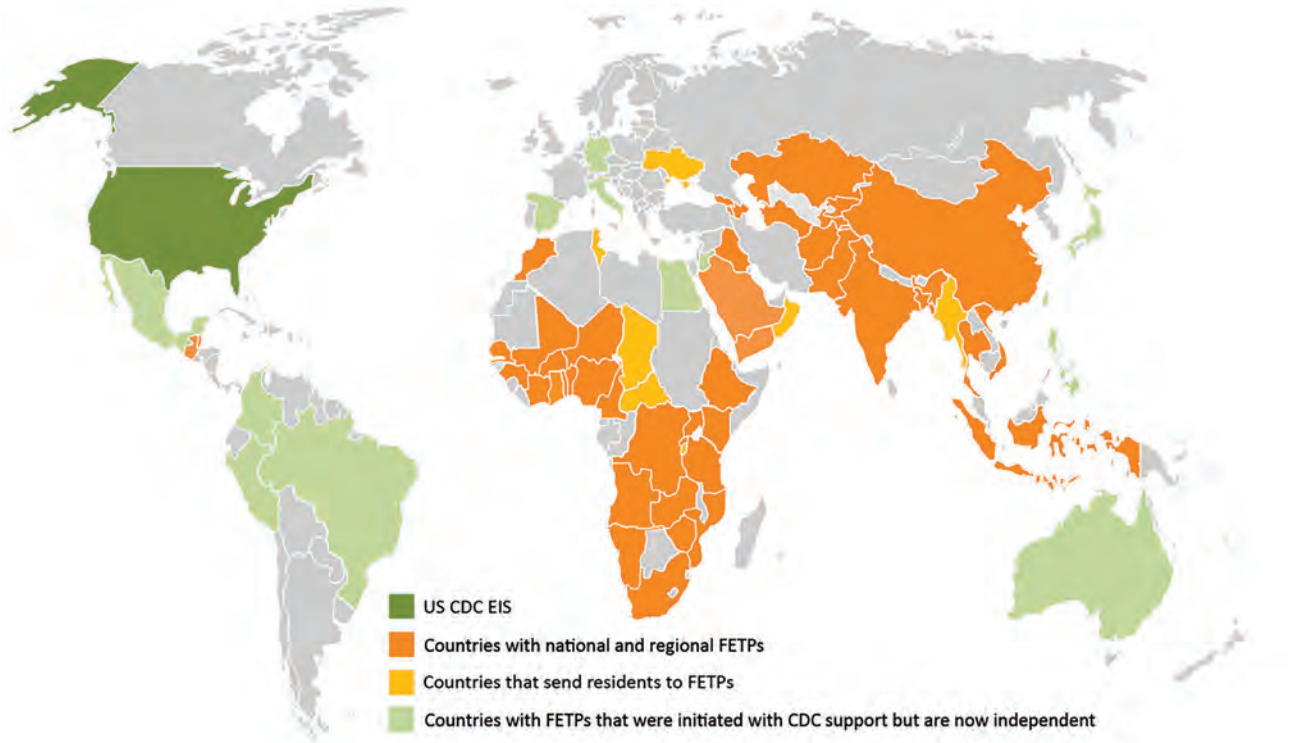

Figure 2. FETPs-Advanced presently or previously associated with CDC, as of December 2016. India supports 2 FETPs-Advanced; both were initiated with CDC support, and 1 is now independent. Central America has had an FETP-Advanced that was paused in 2015 and restarted in August 2017 with Guatemala and Belize. CDC, US Centers for Disease Control and Prevention; EIS, Epidemic Intelligence Service; FETP, Field Epidemiology Training Program.

Health Network (*19*) and the South East Asia Field Epidemiology and Technology Network in 2009, and the South American Field Epidemiology Training Programs Network and the Association of Southeast Asian Nations Plus Three Field Epidemiology Training Networks in 2011.

TEPHINET, along with its member programs and CDC, has recently developed and implemented an accreditation process for FETPs-Advanced (http//:www.tephinet.org/accreditation). Accreditation was initiated in response to the increasing numbers of programs and the variations in their implementation. Its goal is to maintain and improve program quality (*20*,*21*). The process has received wide support from FETP program directors (D. Herrera, TEPHINET, pers. comm., 2017 Feb 28). The first 3 programs (EIS, Canadian Field Epidemiology Program, and the UK FETP) were accredited in 2016, and more programs have applied for accreditation in 2017.

Outcomes and Effects of FETPs

The goal of FETPs is to develop competent field epidemiologists who can assume priority public health positions while strengthening countries' outbreak response capacity, surveillance systems, and use of data to inform prevention and control measures for priority public health problems. The following examples demonstrate the value of a strong public health workforce and improved surveillance, outbreak response, and data use capacity for greatly enhancing national, regional, and global health security.

Outbreak Investigations and Emergency Responses

Since 2005, FETP residents have responded to ≈3,300 outbreaks (Figure 3). Although many of these outbreaks were local, the experience prepared FETP residents to handle problems of national and international concern.

During the recent Ebola epidemic in West Africa, ≈70 FETP residents and graduates from ≥9 African nations and Haiti participated in investigation and response activities. They served as epidemiologists, surveillance officers, contact tracing supervisors, and laboratorians in support of epidemic control (*22*) (L. Boulanger, CDC Ethiopia, pers. comm., 2017 Mar 23). In 2015, the residents and graduates of the Nigeria FELTP supported a contact tracing effort that prevented a major Ebola epidemic in that country, in contrast to the unchecked spread in neighboring countries without FETPs (*23*,*24*).

In February 2015, the 10 residents of the Uganda FETP were called to investigate an outbreak of a strange

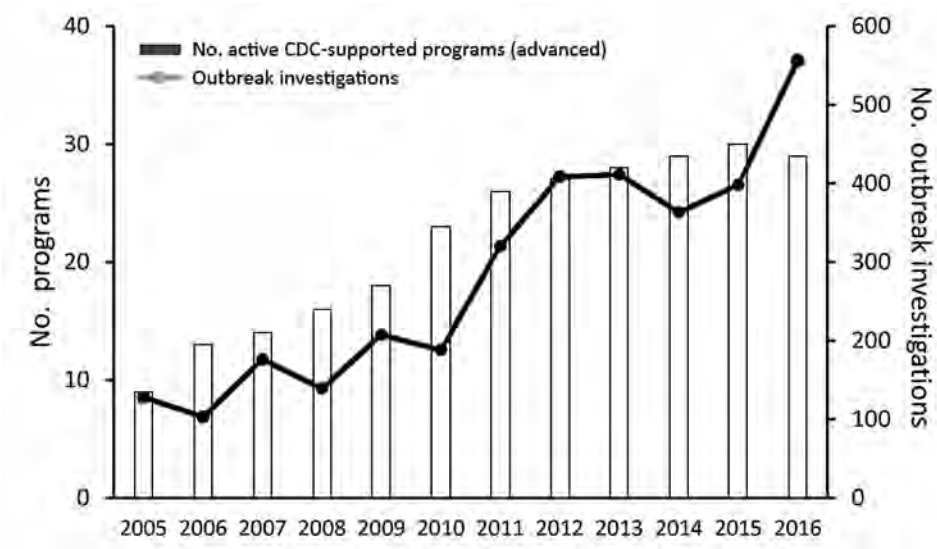

Figure 3. Outbreak investigations conducted by residents (participants) in US Centers for Disease Control and Prevention (CDC)–supported Field Epidemiology Training Programs, 2005–2016.

disease that had killed 1 person and sickened 24 more in Kampala, the capital of Uganda. Investigation by the residents uncovered a much more widespread outbreak of typhoid fever that had spread insidiously throughout Kampala. They identified the cause as contaminated water from uncontrolled underground sources (*25*). Guided by this epidemiologic investigation, international institutes and organizations from Uganda and elsewhere mounted a major coordinated response and contained the outbreak.

In May and June 2013, the India Epidemic Intelligence Service (India EIS), an FETP in India, investigated an outbreak of unexplained encephalopathy in which 133 children were hospitalized and 59 (44%) died. Similar outbreaks had been noticed since 1995, but multiple attempts to find a cause and control the disease had failed. The India EIS noted that many of the affected children were hypoglycemic, a characteristic of patients with ackee fruit encephalopathy. They also noted that litchi (also called lychee) fruit, a relative of the ackee, was commercially cultivated in the area. When the outbreak recurred in 2014, the India EIS demonstrated a strong epidemiologic association between encephalopathy and litchi consumption; laboratory testing confirmed the presence of the toxins methylenecyclopropylglycine and hypoglycin A in affected children and in litchi. Evidence-based recommendations were developed to prevent future seasonal outbreaks and associated deaths (*26*).

In 2007 in China, paraplegia suddenly developed in leukemia and lymphoma patients while they were receiving weekly intrathecal injections of drug. Without an identified cause, the intrathecal drugs were embargoed, thus limiting treatment availability. Investigation by epidemiologists and residents of the China FETP led to the identification of contamination with minute quantities of vincristine, a potent neurotoxin (*27*). These findings enabled correction of the problem and resumption of intrathecal drug production and use.

Surveillance System Support

During their training, all FETP residents are expected to analyze, use, and improve surveillance data. Surveillance systems addressed by FETP residents include those for routinely reported notifiable diseases; specific diseases, such as HIV infection; and noncommunicable conditions such as maternal death, injury, and birth defects (*28*,*29*).

During the 2014 outbreak of Middle East respiratory syndrome (MERS) in Jeddah, Saudi Arabia, several graduates from the Saudi Arabia FETP were asked to strengthen the surveillance system for MERS. The graduates tackled numerous issues such as nonuse of the case definition for selection of laboratory testing, delayed laboratory reporting, and inconsistent case counts among sources. The FETP team redesigned the system to enable simultaneous real-time electronic reporting of suspected and confirmed cases to public health professionals who needed to take essential control and preventive actions on new cases. The system, now run by another FETP graduate, provides real-time data on MERS in Saudi Arabia and is used to populate the widely distributed, weekly Saudi MERS report that is redistributed by WHO (A. Alzahrani, King Faisal Specialist Hospital and Research Center, pers. comm., 2017 Feb 7).

FETPs also develop and support surveillance and response systems during mass gatherings for sporting, religious, and other events. During the Fédération Internationale de Football Association World Cup held in South Africa in 2010, FETP residents helped establish and run surveillance and response systems to protect the public health during these events. The 22 FETP residents supported the collation and analysis of data from

the 9 provinces and participated in investigation of ≈20 suspect public health events (*30*) (L. Kuonza, South Africa FETP, pers. comm., 2017 Feb 2). Similarly, during religious mass gathering events in Saudi Arabia, Pakistan, Morocco, Iraq, and Jordan, FETP residents in those countries supported surveillance and other public health activities (*31–34*).

FETP-trained personnel also participate in surveillance activities during national disasters. In 2010, when floods covered 20% of Pakistan, FETP-trained officials were mobilized to help their provincial departments of health. They developed and maintained surveillance and responded to outbreaks in the camps of displaced populations. This workforce provided vital public health services, including planning; coordination; data collection, analysis, and interpretation; emergency preparedness and response; and outbreak investigations in multiple districts (*35*).

FETPs have also strengthened laboratory surveillance. The South Caucasus FELTP expanded the existing anthrax surveillance to include poxviruses, leading to improved diagnosis and control for anthrax and identification of a novel poxvirus (*36*).

Control and Prevention of Priority Public Health Problems

FETPs play critical roles in addressing priority public health problems in countries, often with the collaboration and support of international initiatives such as the US President's Emergency Plan for AIDS Relief (*37*,*38*), the President's Malaria Initiative (*39*,*40*), and the Global Polio Eradication Initiative (*41*,*42*). This approach ensures that residents' work supports national and global priorities while the residents practice applying epidemiologic methods to these programs and providing public health service.

As an example, FETP residents have broadly supported polio elimination in Nigeria and Pakistan through National Stop Transmission of Polio (N-STOP) programs. FETP Pakistan designed the first N-STOP program to meet the need for local public health staff to fight polio in that country. The North Waziristan area, a highly security-compromised area, reported 20% of all global cases of polio in 2014. Despite ongoing military operations and human displacement, FETP Pakistan placed 2 residents as N-STOP officers in the North Waziristan area and the adjoining South Waziristan area. The residents, working under difficult and hazardous conditions, rebuilt the infrastructure for surveillance and polio eradication activities and persuaded other staff to return. The transmission of polio virus was interrupted in the North Waziristan area (cases decreased from 70 in 2014 to 0 in 2016) and substantially reduced in the South Waziristan area (cases decreased from 24 in 2014 to 2 in 2016) (*42*).

In Nigeria, the N-STOP program has developed innovative strategies to address polio eradication challenges. One N-STOP initiative focused on locating and vaccinating children <5 years of age in remote, nomadic, scattered, and border populations in northern Nigeria where low polio vaccination coverage probably contributed to ongoing transmission of wild polio virus. During August 2012–April 2013, N-STOP conducted field outreach activities that enumerated ≈40,000 remote settlements, including 4,613 settlements never visited by vaccination teams during previous polio supplemental immunization activities (*41*,*43*).

Graduates

Training competent field epidemiologists for a country builds long-term capacity only if the country uses FETP graduates in appropriate positions of public health responsibility. Some countries have developed specific positions for graduates, such as provincial epidemiologist. Other countries have modified the requirements for certain positions to include FETP certification. Overall, most FETP graduates are retained within their country's public health systems, and many rise to positions of public health responsibility. We estimate that ≈80% of recent graduates continue to work for the national ministry of health or equivalent. In many countries, this figure approaches 100%. Graduates have served as permanent secretaries for health; ministers of health; and program directors for epidemiology, surveillance, and specific disease control programs. Others have held responsible positions with WHO (e.g., national professional officers) and nongovernmental public health–associated organizations.

A valued role for graduates is leadership within the FETP itself. The national FETP director and other technical staff are usually FETP graduates. Graduates serving in national and other public health positions are specifically groomed to serve as mentors for the residents during their field placements. Experienced graduates have also been hired to serve as resident advisors of newly developed FETPs in other countries.

Building Institutionalized and Sustainable FETPs

Most FETPs were initiated with financial and technical support from external donors and partners (*3*,*4*). The costs for developing programs vary widely and, among other considerations, depend on the size, model, and partners involved (*10*). To ensure their continuity and long-term contribution toward strengthening public health, the programs are anchored within the ministries of health or other public health institutions. This national ownership ensures that the FETPs contribute to tangible and relevant delivery of essential epidemiologic services from the outset.

Recognizing FETPs as valuable for addressing national health priorities has helped to institutionalize and sustain FETPs (*11*,*44*). Many programs have been operating independently for years and have become national resources for disease surveillance, public health emergency response, and priority public health disease prevention and control programs (*45*,*46*).

Of the 19 programs that were established during 1980–2000 with CDC engagement, 17 continue to produce graduates and provide service. The principal elements for program institutionalization and sustainability include establishment of an organizational structure and institutional ownership within the ministry of health or other public health institution, national leadership from FETP graduates, focus on priority- and science-based training, communication of findings and recommendations to the public health leadership, assurance of a recognized career path for graduates, and continued engagement between graduates and the FETP (*20*). CDC works with programs to support these elements and to help ensure their long-term success.

Challenges

Despite progress in building sustainable institutionalized programs, several challenges remain. New FETPs commonly struggle to identify sufficient numbers of qualified epidemiologists to serve as mentors until graduates can become mentors at least 2 years later. Ministries of health commonly wrestle with the challenge to develop and maintain appropriate career paths for FETP graduates. In the absence of appropriate available positions, graduates often resume their pretraining roles, which probably underutilize their new epidemiologic skills. Committed ministries of health have had varying levels of success in addressing this problem, depending on the structure and limitations of their human resources systems (*47*,*48*). A final challenge is that uncertain political support within the health system, funding limitations in the face of competing priorities, and weaknesses in the healthcare infrastructure can threaten support for FETPs and prevent establishment of a sufficient institutional framework to ensure long-term survival. CDC works with programs to identify and engage numerous disease initiatives and multisectoral global health activities to develop new partnerships to support programs as they develop (*49*). To highlight the contribution of FETPs and promote their sustainability in countries around the world, continuous advocacy is essential.

Conclusions

In this age of globalization and the emergence of new and resurgent communicable diseases (e.g., Ebola, Zika, MERS) and the increasing global effects of known diseases (e.g., yellow fever, dengue fever), qualified field epidemiologists are needed more than ever. There is a critical need for good epidemiologic science in all countries to support prevention and control programs for communicable and noncommunicable diseases, injuries, and environmental hazards. The adoption of the IHR 2005 standards and the development of the GHSA have made clear that every country needs at least a minimum capacity in field epidemiology to rapidly detect, respond to, and control public health emergencies and thereby keep its population safe, protect other countries from the spread of illness, and ensure global health security. The development of FETPs across the globe is recognized as being critical for meeting that need and therefore for enhancing global health security (*50*). It will be crucial to maintain and continue to improve the quality and reach of FETPs in countries through expanding the number of countries with access to these programs and expanding the tiered training within countries. The global public health community, working together with international partners and the global network of FETPs, can be instrumental in building on the strengths of the existing programs to broaden the beneficial effects of these critical capacity-building efforts.

Acknowledgments

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Baylisascaris procyonis, the common intestinal roundworm of raccoons, has increasingly been recognized as a source of severe, often fatal, neurologic disease in humans, particularly children. Although this devastating disease is rare, lack of effective treatment and the widespread distribution of raccoons in close association with humans make baylisascariasis a disease that seriously affects public health. Raccoons infected with *B. procyonis* roundworms can shed millions of eggs in their feces daily. Given the habit of raccoons to defecate in and around houses, information about optimal methods to inactivate *B. procyonis* eggs is critical for the control of this disease. However, little information is available about survival of eggs and effective disinfection techniques. Additional data provide information on thermal death point and determining the impact of desiccation and freezing on the viability of *B. procyonis* eggs to provide additional information for risk assessments of contamination and guide attempts at environmental decontamination.

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EMERGING INFECTIOUS DISEASES

Frontline Field Epidemiology Training Programs as a Strategy to Improve Disease Surveillance and Response

A. McKenzie André, Augusto Lopez, Samantha Perkins, Stephanie Lambert, Lesley Chace, Nestor Noudeke, Aissatou Fall, Biagio Pedalino

Since 1980, Field Epidemiology Training Programs (FETPs) have trained highly qualified field epidemiologists to work for ministries of health (MOH) around the world. However, the 2013–2015 Ebola epidemic in West Africa, which primarily affected Guinea, Liberia, and Sierra Leone, demonstrated a lack of field epidemiologists at the local levels. Trained epidemiologists at these levels could have detected the Ebola outbreak earlier. In 2015, the US Centers for Disease Control and Prevention (CDC) launched FETP-Frontline, a 3-month field training program targeting local MOH staff in 24 countries to augment local public health capacity. As of December 2016, FETP-Frontline has trained 1,354 graduates in 24 countries. FETP-Frontline enhances global health security by training local public health staff to improve surveillance quality in their jurisdictions, which can be a valuable strategy to strengthen the capacity of countries to more rapidly detect, respond to, and contain public health emergencies at the source.

Since their inception in 1980, Field Epidemiology Training Programs (FETPs) have been 2-year applied training programs focused on the practice of epidemiology in a mentored environment, with a focus on "learning by doing" (*1*). FETPs, which are adapted to the host country context, are designed to produce highly skilled epidemiologists who will work at the ministry of health (MOH) in each country to strengthen surveillance systems and respond to public health threats. The primary distinguishing characteristic of FETP is that most of the learning (≈75%) occurs in the field, at district- or national-level health offices. Trainees conduct fieldwork that simultaneously increases their capacity to apply epidemiologic concepts while strengthening the health system through the production of useful epidemiologic field products that provide information for decision making.

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The Centers for Disease Control and Prevention (CDC) has a long history of providing technical assistance for FETPs (*1*,*2*), which were mostly modeled on CDC's 2-year applied training through service program, the Epidemic Intelligence Service (EIS). Currently, CDC provides technical assistance to >765 FETPs throughout the world. These programs have been successful in strengthening epidemiologic and surveillance capacity at the national levels, but most programs did not address gaps at the subnational level.

Even before the West Africa Ebola outbreak, there were efforts to start a modified training program that could strengthen other levels of the public health system. In 2000, six Central American countries recognized a need for training of surveillance staff at the subnational level to collect quality surveillance data in a timely manner. The countries were part of a regional FETP that used a pyramidal approach to training; the 3 levels were dubbed basic, intermediate, and advanced and targeted local, regional, and national levels of the surveillance system (*3*). The curriculum of the 3-tiered training program was based on fundamental competencies of field epidemiology needed at each level of the surveillance system (*4*), with the purpose of improving the quality of surveillance and the ability to use surveillance data for action.

The Ebola outbreak in 2014 underscored the need for field epidemiology capacity at all levels of the healthcare system, in both affected and nonaffected countries in West Africa. Deficits in the public health surveillance system to identify cases and contacts at the local level and to respond in a timely manner were factors that contributed to the expansion and prolonged nature of the Ebola outbreak (*5*,*6*). Until the Ebola epidemic, most of the experience with FETP in Africa had been with the 2-year advanced-level program, which trained staff to work at national surveillance and disease control programs (*7*,*8*). This approach did not address the need to have adequately trained staff at the local level to detect outbreaks and respond appropriately.

In January 2015, in response to the urgent need for local capacity during the outbreak, CDC and several partners organized and conducted the emergency implementation of Surveillance Training for Ebola Preparedness (STEP). This program was designed to rapidly build surveillance capacity along the border districts and regions in the 4 countries sharing a land border with the heavily Ebola-affected countries, Guinea-Bissau, Senegal, Mali, and Côte d'Ivoire (*9*). The program was a simpler, shorter, and more focused version of the basic FETP, with an emphasis on the early identification of Ebola virus disease (EVD).

Shortly thereafter, longer-term planning to support surveillance capacity in the region began. Based on experience with basic FETP training and the successful emergency intervention of STEP, CDC developed a new strategy called FETP-Frontline. This training strategy targets public health staff working in surveillance at the local level to strengthen the capacity of countries to more rapidly detect, respond to, and contain public health emergencies at their source, preventing the spread of diseases and thereby enhancing global health security. FETP-Frontline development corresponded with the launch of the Global Health Security Agenda (GHSA). GHSA is an international collaboration between governments, international organizations, and implementing partners to help countries build the capacity to prevent, detect, and respond to public health threats from infectious diseases and achieve competencies necessary for compliance with the World Health Organization (WHO) International Health Regulations 2005 (IHR 2005) (*10*). Workforce development, which focuses on practical field-based epidemiology training, is 1 of the 11 Action Packages identified for strengthening to help countries to meet GHSA goals. This article describes the process and early results on the implementation of FETP-Frontline.

Program Implementation

CDC staff visited each country and met with representatives of each MOH to describe the program and explore the value and feasibility of implementing FETP-Frontline. Upon agreement to launch the program, CDC staff, along with MOH colleagues, assessed the country's training needs and priorities, gathering information from site visits and interviews with surveillance workers at multiple levels within the health system. Shortly thereafter, a 1- to 2-day implementation workshop was held with key stakeholders from relevant ministries within the country and key nongovernmental partners. During the meeting, leaders and stakeholders discussed strategic elements of program implementation, such as defining the subnational unit targeted for training and the personnel or job classes to be prioritized for training. In this article, we refer to the targeted administrative unit as the health district, even though the nomenclature varies across countries, because this is where data are first aggregated within the surveillance system. We also determined at the workshop possible sources of mentors to supervise participants in the field. Each country then developed a plan to cover all subnational units with ≥1 FETP-Frontline–trained person.

In each country, a FETP team was established to work closely with the MOH, implementing partners, and the CDC country office to implement FETP-Frontline. Each team was led by a resident advisor, a senior-level epidemiologist who was either a CDC staff member or a contractor, usually from another country and a graduate of a 2-year FETP-Advanced. Other staff included a field coordinator, usually from the host country, who was most often a physician with experience in surveillance and epidemiology; and an administrator to assist with the logistics of program implementation. The resident advisor provided overall technical leadership for the program and worked closely with an identified MOH person to manage the program. The teams were often embedded within the MOH offices to facilitate planning and operation of the program.

Trainees and Mentors

The persons targeted for the training were those responsible for collecting and analyzing health surveillance information, often called district surveillance officers. However, participants from other administrative levels were also eligible for training. In each country, the resident advisor and MOH counterparts identified mentors to provide onsite technical assistance to participants during the field stages. Mentors were ideally from within the MOH, with a ratio of 1 mentor to 5 participants. Once the strategic model was established, identified mentors were introduced to the FETP-Frontline curriculum and some basic adult-learning principles before the launch of the first training. The pretraining process typically took 3–6 months from the first meeting with the MOH to the first day of training for participants.

Curriculum

The standardized curriculum and program schedule, incorporating both classroom workshops and on-the-job fieldwork, were originally developed in English and then translated into French and Portuguese to accommodate Francophone and Lusophone countries. Training materials also incorporated the Integrated Disease Surveillance and Response (IDSR) framework, which is used in 43 of 46 countries in the WHO Regional Office for Africa for disease surveillance and response reporting (*11*). In each country, the curriculum was then adapted to the country context, incorporating national reporting guidelines and practices. The classroom training is reinforced by the completion of field projects designed to help participants develop competencies related to specific job functions (Table 1).

Table 1. Fieldwork requirements as part of FETP-Frontline workshops*

Stage	Projects
Fieldwork stage 1, weeks 2–6: participants must complete both activities and present their findings at workshop 2	
Weekly surveillance report	Complete a weekly surveillance summary report based on health facility reports
	Record reporting timeliness and completeness; record key notifiable diseases
	Create graphs and figures that describe data
Data quality report	Examine the surveillance data collected in ≥3 different health facilities
	Conduct interviews with health facility staff; review log books, case forms, and posted bulletin boards
	Collect and review health facility weekly reports
	Complete a worksheet that organizes the findings from their data quality audit
Fieldwork stage 2, weeks 7–11: participants must complete 2 of the 4 activities and present their findings at workshop 3	
Case investigation report	Conduct a case investigation and interview a case or contact, using country-specific procedures when available
	Present details of the case investigation, including any public health action taken
Outbreak investigation report	Assist in outbreak investigation and develop an outbreak investigation report
	Maintain a rumor log book of suspected outbreaks
	Present report and findings
Expanded surveillance summary report	Continue creating weekly surveillance summary reports
	Analyze data to identify trends and gain a comprehensive view of the surveillance system
	Summarize the data and highlight trends or interesting characteristics at final workshop
Analysis of surveillance quality with recommendations	Critically examine a weakness that has been identified in the surveillance system during FETP-Frontline fieldwork
	Form a team with the surveillance personnel who are close to the issue in question; identify the critical causes of the problem
	Create a suitable solution to the problem that will lead to a direct improvement of the surveillance system

*FETP, Field Epidemiology Training Program.

The program schedule (Figure 1) for FETP-Frontline consists of an initial 5-day workshop introducing basic epidemiology principles and importance of disease surveillance. The participants then return to their regular job sites for 5 weeks. There, they receive onsite and remote mentoring from program staff to review local surveillance data and conduct a data quality audit around a priority disease in their coverage area. All FETP-Frontline participants create a weekly surveillance report using real-world data derived from their home districts. The FETP resident advisors and mentors then guide the participants to aggregate and analyze the data at the district level. The participants return for a second 5-day workshop to present their work and receive feedback from the staff and their peers on their projects. During the second workshop, participants learn how and when to conduct field investigations and how to effectively communicate results. Participants then return to the field for the second 5-week field stage to put in practice what they have learned under the guidance of the mentors and to complete 2 of 4 possible field activities: conducting a field investigation to confirm or rule out a reportable disease, participating in an outbreak investigation, developing an expanded surveillance summary report, or completing an analysis of surveillance quality with appropriate recommendations. In the third workshop, participants present their final projects and receive a certificate of course completion cosigned by MOH and CDC representatives. At the end of each module and in between cohorts, the technical staff conducted internal evaluations. Participant feedback is gathered through questionnaires. Program staff are encouraged to review the feedback and work with the MOH to tailor the curriculum materials and training schedule as needed.

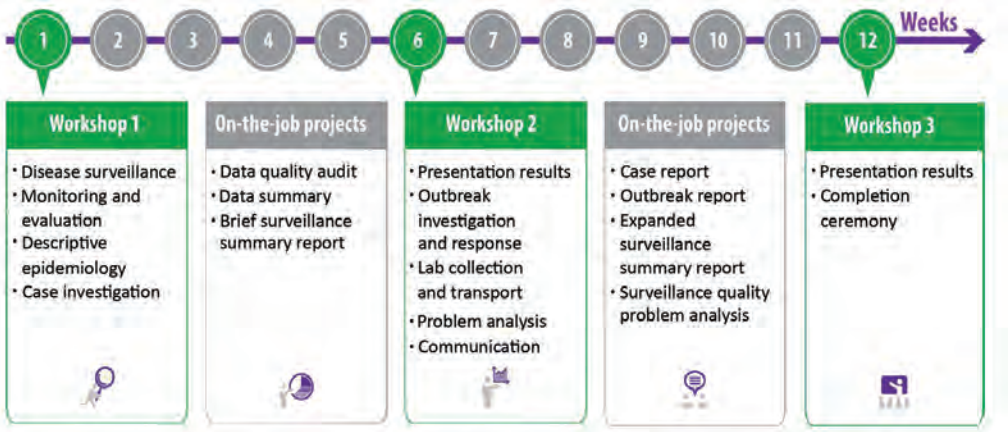

Figure 1. General program schedule showing the 3 classroom workshops (green boxes) and 2 field stages (gray boxes) in a standard Frontline Field Epidemiology Training Program curriculum.

Results (Status)—Principles of FETP-Frontline Implementation

The first FETP-Frontline cohort began in Tanzania in July 2015. All the FETPs-Frontline that started in 2015 and 2016 were in Africa and southern Asia, with a heavy concentration in West Africa (Figure 2). The FETP-Frontline underwent a rapid expansion across these countries, with most programs launching their first cohort during the first 6 months of 2016 (Figure 3).

From the program's launch in July 2015 through the end of 2016, a total of 1,354 persons completed FETP-Frontline training (Figure 3). Participants were almost all MOH employees and represented a variety of backgrounds: data managers, nurses, physicians, environmental health officers, veterinarians, laboratorians, and public health officials. The proportion of districts in each country with ≥1 FETP-Frontline–trained surveillance officer has expanded steadily. Four countries (Sierra Leone, Guinea-Bissau, Liberia, and Senegal) achieved complete or near-complete district-level coverage by the end of 2016 (Table 2).

Weekly surveillance data were collected from 3 countries for the duration of FETP-Frontline. The timeliness of surveillance reporting, defined as the proportion of weekly surveillance reports delivered to the district level by a predetermined deadline, from these 3 programs increased from an average timeliness rate of 33% in week 1 to 96% in week 12. An example can be seen in the reported timeliness data from the first cohort in the Benin program, in which the average reported timeliness went from 37% on-time to 85% on-time (Table 3).

FETP-Frontline participants have used their training to identify gaps and promote change in the public health systems in which they work. Guinea-Bissau FETP-Frontline participants made policy recommendations to improve the way in which dog bites are tracked, in terms of follow-up with rabies testing, and to improve data confidentiality and protection for patients. In The Gambia, under the resident advisor's guidance, members of the first cohort created recommendations for improving the surveillance system; among these were appointing district surveillance officers where there were none previously, training new staff in basic epidemiology, implementing and revising protocols to match IDSR recommendations, and including private health clinics in the national surveillance strategy. Liberia realized a need to appoint surveillance personnel between the community and regional levels.

In Côte d'Ivoire, only 4 of the 36 participants in the first 2 cohorts had ever conducted a field investigation before the training; upon program completion, 20 had conducted a field investigation with the assistance of a field mentor. Investigations included suspected cases of yellow fever, measles, and rabies (Table 4). In Liberia, participants conducted outbreak investigations on conditions such as food poisoning, suspected acute flaccid paralysis, and measles. In the Democratic Republic of the Congo, participants investigated typhoid fever, yellow fever, and cholera outbreaks. In Benin and Burkina Faso, program participants have mobilized from their home districts to respond to outbreaks in other parts of the country, serving as a trained, in-country pool of epidemiologists from which to draw during emergencies. In Côte d'Ivoire, Senegal, and Togo, where

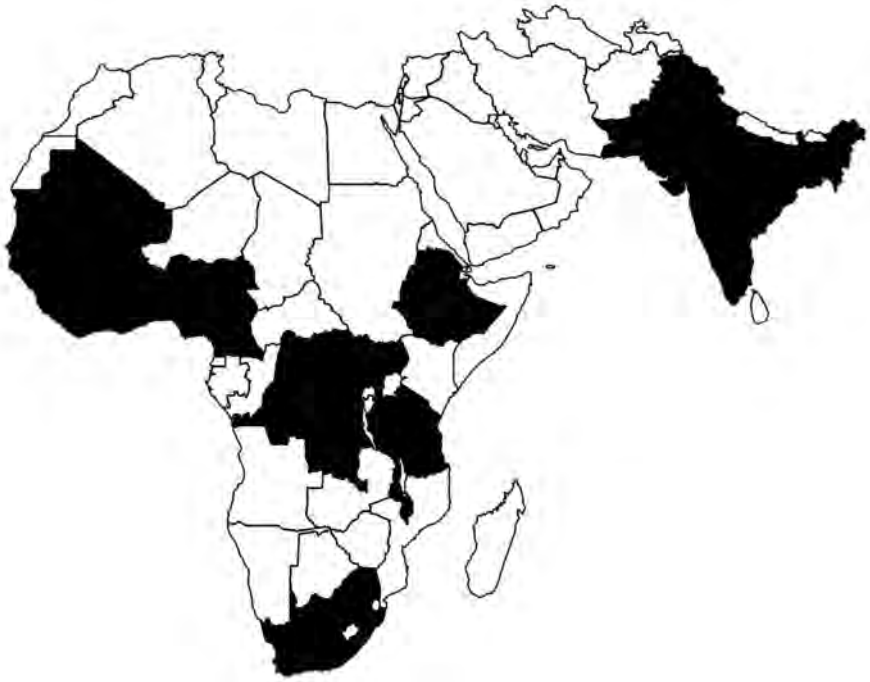

Figure 2. Geographic coverage of Frontline Field Epidemiology Training Programs established (black), July–December 2016.

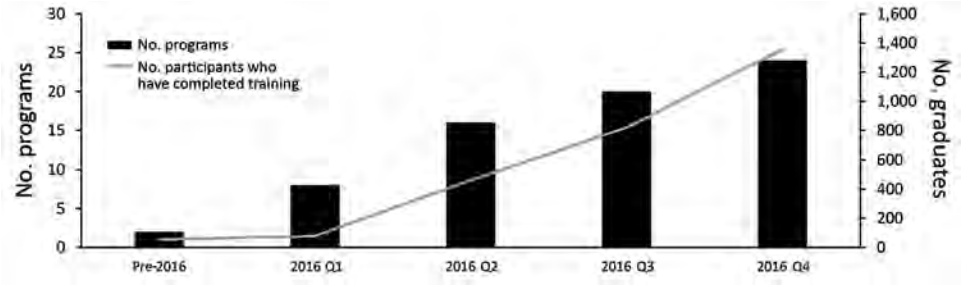

Figure 3. Frontline Field Epidemiology Training Programs launched and cumulative number of participants trained by quarter (Q) of program launch through Q4 2016. Quarter of launch is defined by the date of the first classroom session.

training has included participants from both the human and animal health sectors, trainees have worked together to conduct coordinated joint investigations to combat rabies.

Discussion

As countries address gaps in surveillance and begin to develop the core capacities for surveillance and response as set by the IHR 2005, they will need to ensure that there is capacity at the local level "to detect unusual public health events, to report key epidemiological information to relevant intermediate and national authorities, and to immediately implement primary control measures" (*12*). The FETP-Frontline was initiated as a response to identified gaps in surveillance and response capacity at the local level. In many developing countries, district-level surveillance officers have historically only passed information on to the national level, without taking the opportunity to analyze the data locally or respond immediately. These missed opportunities can contribute to delays in disease recognition and timely interventions. By tailoring a training program and field products to the routine responsibilities and expected job duties of a district surveillance officer, participants develop relevant and practical competencies in field epidemiology.

FETP-Frontline has targeted the district level for training because, quite simply, this is where the action is. In most countries, the district level is the point at which surveillance data first enter the formal public health system and also the point at which data are aggregated and can be analyzed to detect abnormalities and represents the first opportunity to mount a public health intervention. Preliminary data from FETP-Frontline have shown improvements in local detection and response capacity within weeks of initiating the training. This capacity can be seen in the local functioning of the public health surveillance system. There have been improvements in the timeliness of surveillance reporting and an increase in field activity that result in quicker identification of diseases in the community. The purpose of FETP-Frontline is not only to improve the timeliness of the

Table 2. Proportion of districts or other designated subnational health unit with ≥1 trained FETP-Frontline graduate for 24 participating countries, 2016*

Country	Total no. districts	% Districts with ≥1 Frontline FETP graduate			
		Q1	Q2	Q3	Q4
Sierra Leone	14	0	100	100	100
Guinea-Bissau	11	0	73	100	100
Liberia	90	0	57	76	76
Senegal	76	0	53	53	74
Côte d'Ivoire	82	NA	15	15	29
Benin	82	0	28	28	28
Nigeria	774	NA	14	23	26
South Africa	52	NA	0	4	17
Cameroon	178	NA	8	8	15
Ghana	216	NA	13	13	13
Uganda	112	NA	4	13	13
Tanzania	169	NA	7	12	12
Burkina Faso	70	NA	0	11	11
Bangladesh	490	4	4	4	9
Malawi	29	NA	3	3	7
Democratic Republic of the Congo	517	NA	3	3	3
India	687	2	2	2	2
Ethiopia	880	NA	NA	0	0
Mauritania	55	NA	NA	0	0
Gambia	43	NA	0	0	0
Guinea	33	NA	NA	NA	NA
Mali	49	NA	NA	NA	NA
Pakistan	149	NA	NA	NA	NA
Togo	40	NA	NA	NA	NA

*Most programs target participants at the district level or its equivalent. This is typically the first surveillance level at which data are aggregated (immediately above the health facility level). FETP, Field Epidemiology Training Program; NA, no coverage data available because the first cohort of FETP-Frontline had not yet graduated; Q, quarter.

Table 3. Effect of FETP-Frontline training on timeliness of surveillance reporting by health district, Benin, epidemiologic weeks 25–36, 2016*

	Epidemiologic week											
		Workshop 1			Fieldwork 1				Workshop 2	Fieldwork 2		
Health district	25	26	27	28	29	30	31	32	33	34	35	36
NIKKI	94	94	88	56	31	31	38	38	44	75	94	94
SO-AVA	56	56	56	78	100	100	100	100	100	100	100	100
PEV d'Abomey-Calavi	25	25	38	50	63	75	75	88	100	100	100	100
Save	0	0	42	83	83	92	100	100	100	100	100	100
Zagnanado	25	0	0%	50	100	100	100	100	100	100	100	100
Malanville	100	100	100	100	100	100	100	100	100	100	100	100
Allada	25	25	50	75	100	100	25	50	25	75	100	75
Cotonou 6	NR	NR	NR	NR	NR	NR	50	50	100	75	100	100
Aguégués	0	0	0	0	100	100	100	100	100	100	100	100
Pobe	67	83	100	83	83	83	100	100	100	100	100	100
Abomey-Calavi	25	25	38	50	63	75	75	88	100	100	100	100
Ze	50	75	100	100	100	100	100	100	100	100	100	100
Sèmè-Podji	30	20	30	40	60	80	90	90	100	100	100	100
Ifangni	9	27	9	9	9	36	9	9	9	9	9	45
Adja-Ouèrè	100	100	100	100	100	100	100	100	100	100	100	100
Adjarra	14	29	43	43	57	57	71	57	71	57	57	57
Tchaourou	31	54	46	46	46	62	100	100	100	100	100	100
Perere	0	0	27	36	36	36	45	36	36	45	18	36
Kalale	27	27	40	53	87	93	67	80	87	87	87	93
Cotonou V	0	0	0	0	75	75	75	75	75	75	75	75
Segbana	100	100	100	100	100	100	100	100	100	100	100	100
Cotonou I and IV	0	0	0	0	0	0	0	0	0	0	0	0
Weekly average	37	40	50	55	71	76	74	75	79	82	84	85

*Timeliness is defined as the percentage of reports from the health facility level that are delivered to the district by a predetermined deadline (typically weekly). FETP, Field Epidemiology Training Program; NR, not reported.

surveillance data that are collected but also to improve the quality of the data and to promote critical thinking by district-level surveillance officers who are responsible for the data. In conducting data quality analysis, trainees identify gaps and propose recommendations to improve surveillance in their locales. During the third workshop, higher-level members of the surveillance system are invited to attend the presentations and react to some of the findings, ensuring that the problems identified during the fieldwork are brought to the attention of MOH leadership. Some of the recommendations formulated by FETP-Frontline participants have already led to local changes in surveillance systems such as the adoption and utilization of rumor logs, increased distribution of standardized case definitions for diseases under surveillance, and increased emphasis on surveillance data during monthly district management meetings.

The successful implementation of FETPs-Frontlines occurred simultaneously across several countries and demonstrated that a large-scale, multicountry capacity-building program could be implemented quickly with external support and country engagement. This effort did not take staff away from their jobs in-country and provided benefits in a short timeframe by addressing actual problems at individual work sites. However, for the program to be sustainable, countries will ultimately have to take on the technical and logistical leadership of the program. The implementation of FETP FETP-Frontlines is not without challenges. This initiative was greatly supported by the CDC and several partners including WHO, the African Field Epidemiology Network (AFENET), Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET), and the Defense Threat Reduction Agency (DTRA). Because the FETP-Frontline model is continuing education for existing public health personnel, it requires the involvement and commitment of the host country's MOH. During the training, each participant received ≥1 day of onsite mentoring and supervision during each of the 2 field stages. Mentorship in the field requires both financial and technical

Table 4. Field products completed by the first 2 cohorts of FETP-Frontline participants in Côte d'Ivoire, May–December 2016*

Field product	Total no.
Expanded weekly surveillance report	36
Topics for the problem analysis report	17
Late-reporting or underreporting of surveillance data	6
Nonapplication of case definitions	3
Poor community notification of cases	2
Inadequate local surveillance data analysis	2
Underreporting of maternal deaths	2
Other	2
Conditions identified for field investigation report	20
Suspected case of yellow fever	6
Suspected case of measles	4
Other vaccine-preventable disease	4
Gastrointestinal illness/diarrhea	3
Rabies	2
Suspected case of hemorrhagic fever	1
Cluster of acute respiratory illness	1

*FETP, Field Epidemiology Training Program.

resources. The costs for implementing FETP-Frontline varied from US $5,000 to $8,000 per student (data not shown) based on many factors, including the existence of locally trained personnel.

Several countries had difficulty identifying professionals with the appropriate skills and experience in field epidemiology who could devote the time required to mentor participants. Several strategies were used to address this gap, including providing an orientation on effective mentoring techniques for staff, fully training a small group of central-level candidates in the first cohort to familiarize them with the field-based training approach and then having them serve as mentors for later cohorts, and engaging mentors from outside the country for the first few cohorts.

There is a concern that, once trained, graduates may leave their posts for better opportunities outside the public health system. A few countries have addressed this issue through the following mechanisms: making participation in the program contingent upon staying in that position for a set period, setting an upper age limit for participants so that newly trained staff will not retire shortly after the course, and designating new and more appropriate positions for those who are trained in FETP-Frontline. FETP-Frontline will need to continue until there is a critical mass of trained personnel representing each district or other identified subnational unit in every country. MOHs are responsible for continuing to support the training to address staff turnover and to make available the resources for the field activities of effective public health surveillance.

Although comparing the outcomes of FETP-Frontline implementation between countries is complicated due to the wide variability in public health systems, there are important lessons and implications for other countries from each implementation. Currently, standard indicators across programs are in development. The national IDSR indicators and the results of efforts such as the independent Joint External Evaluation process will enable countries to track progress in detecting and responding to emergencies (*13*). It is likely that other countries can learn from the lessons in FETP-Frontline implementation we have described and embark upon efforts to launch the program for themselves.

In-service FETP-Frontline training can be an effective strategy to improve the functioning of a public health surveillance system in a short time with immediate benefits. Trainees are working in their home districts, analyzing their own data, addressing their local health priorities, and identifying ways to better detect and respond to public health emergencies given their unique local constraints. By empowering actors to analyze and intervene at the district level, the program helps decentralize some of the initial analysis and decision making, which leads to more accurate communication within the system and a timelier public health response. In some countries, the veterinary and laboratory sectors were included in training cohorts to foster local cross-sector collaboration and a One Health approach to surveillance and response activities. This initiative should be viewed not as a training program but as part of a larger workforce development strategy to improve a country's local surveillance and response capacity that complements FETP training activities at the intermediate and advanced levels. Participants who have completed the training are contributing to enhanced global health security by being able to detect outbreaks sooner, respond faster, and, through quick response, limit the spread of infectious disease outbreaks at the source.

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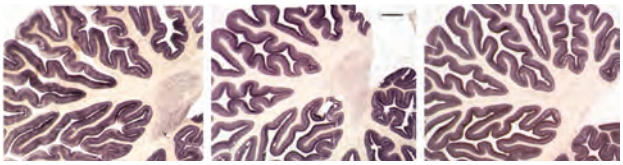

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Surveillance Training for Ebola Preparedness in Côte d'Ivoire, Guinea-Bissau, Senegal, and Mali

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The 2014–2015 epidemic of Ebola virus disease in West Africa primarily affected Guinea, Liberia, and Sierra Leone. Several countries, including Mali, Nigeria, and Senegal, experienced Ebola importations. Realizing the importance of a trained field epidemiology workforce in neighboring countries to respond to Ebola importations, the Centers for Disease Control and Prevention Field Epidemiology Training Program unit implemented the Surveillance Training for Ebola Preparedness (STEP) initiative. STEP was a mentored, competency-based initiative to rapidly build up surveillance capacity along the borders of the at-risk neighboring countries Côte d'Ivoire, Mali, Senegal, and Guinea-Bissau. The target audience was district surveillance officers. STEP was delivered to 185 participants from 72 health units (districts or regions). Timeliness of reporting and the quality of surveillance analyses improved 3 months after training. STEP demonstrated that mentored, competency-based training, where learners attain competencies while delivering essential public health services, can be successfully implemented in an emergency response setting.

By January 2016, 2 years after the beginning of the epidemic of Ebola virus disease in West Africa, 28,616 cases and 11,310 deaths had been reported (*1*). Nearly all cases occurred in 3 countries (Guinea, Sierra Leone, and Liberia); however, several countries experienced Ebola importations, including Mali, Nigeria, and Senegal. Rapid response in Nigeria prevented catastrophic widespread Ebola transmission in one of the most densely populated areas in Africa (*2*). Containing and ultimately eliminating widespread transmission in the heavily affected countries required an unprecedented collaboration of global partners working closely with ministries of health (MOHs) in epidemiology and surveillance; this included laboratory support, infection prevention and control (including isolation), treatment, safe burials, risk communication, and training of local workers in each domain. A notable contribution to the response was the emergency implementation of the Surveillance Training for Ebola Preparedness (STEP) initiative, led by the Centers for Disease Control and Prevention (CDC) Field Epidemiology Training Program (FETP) unit, to rapidly build up surveillance capacity along border districts and regions in the 4 countries (Guinea-Bissau, Senegal, Mali, and Côte d'Ivoire) sharing land borders with the 3 heavily Ebola-affected countries. STEP was urgently needed because of the exponential human-to-human spread of Ebola, porous borders, massive seasonal population movements, and limited epidemiologic surveillance infrastructure.

CDC has a long history of assisting MOHs in building the capacity of their public health workforces. For over 35 years, CDC's FETP has helped countries strengthen disease surveillance and epidemiology through mentored, competency-based training in which trainees attain competencies while delivering essential public health services (*3*). Integrated Disease Surveillance and Response (IDSR), a program CDC developed jointly with the World Health Organization (WHO) and widely adopted in Africa, provides guidelines and trainings to improve

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disease surveillance at local and district levels (*4*). STEP integrated the principles of FETP (mentored, training-in-service approach) with the IDSR framework to implement a 5-week, highly focused training with 2 goals: increase timeliness and quality of surveillance data reports, and increase the number of facilities reporting.

STEP received its funding from an Ebola-focused emergency US congressional appropriation. The time from funding availability to implementing partners to initiation of onsite training (including conceptual design, partnership formation, materials development and translation) was approximately 10 weeks. CDC led the implementing partnership consisting of MOHs in Guinea-Bissau, Côte d'Ivoire, Mali, and Senegal; the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET); the African Field Epidemiology Network (AFENET); and WHO (*5,6*). We report on the STEP experience in Guinea-Bissau, Senegal, Mali, and Côte d'Ivoire, highlighting successes, challenges, and lessons for the future. We also describe an initiative to implement daily, short message service (SMS) text-based reporting for suspected Ebola cases, an activity added to STEP training in response to an acute need for improved situational awareness along border districts (*7*).

Methods

Partner Collaboration

Each partner in the STEP initiative played a critical role. CDC led the overall initiative and provided technical expertise. TEPHINET, a global, professional network of FETPs, was responsible for recruiting and providing transport for 1–2 senior epidemiologists with field epidemiology expertise and language skills, who served as trainers and mentors in each country (e.g., Brazilian mentors in Guinea-Bissau, a Rwandan mentor in Côte d'Ivoire). AFENET, with its extensive experience with strengthening FETPs in Africa, was responsible for training logistics, including providing transport for participants, identifying and securing training venues, and translation and printing of materials. In each country, CDC partnered with the entity within the MOH responsible for disease surveillance: in Côte d'Ivoire, Institut National d'Hygiene Publique (INHP); in Guinea-Bissau, Instituto Nacional Saúde Pública (INASA); in Senegal, Centre des Opérations d'Urgence Sanitaire (COUS); and in Mali, Centre National d'Appui à la lutte contre la Maladie (CNAM). An MOH representative served as the point of contact, working closely with CDC to ensure country engagement, identify the appropriate training audience, and provide in-depth knowledge of the country's surveillance system. Disease Prevention and Control Officers from the WHO Regional Office for Africa (AFRO) provided vital information about disease surveillance in-country.

Country Engagement

Initial communication with country representatives about the training was conducted through CDC country offices where present (Côte d'Ivoire, Mali) and the High-Risk Unaffected Countries Team (a component of CDC's Ebola response) (*8*). The project description document, curriculum plan, and country planning worksheet were shared as part of this initial communication, and customized in accordance with each country's input. Countries sent letters inviting CDC and its partners to conduct the training, indicating the MOH's point of contact, and including a list of proposed districts/regions and participants.

Curriculum

The curriculum integrated classroom instruction with field assignments, mentorship, and SMS daily reporting to achieve STEP's overarching goals. The project team finalized the proposed program objectives based on each country's MOH planning discussion. The target audience was surveillance officers at the first level of the health system where data from local health facilities are aggregated and reported up. Materials from the IDSR and FETP library were adapted to the country context (e.g., surveillance infrastructure, notifiable disease list) and the urgent needs of the outbreak. The classroom component emphasized specific desired competencies to which each MOH had agreed during the initial country meetings. An Ebola case study, complementary field guidelines, and mentor guides were developed. All materials were created in English and translated into French and Portuguese.

In-Country Training

STEP training was led by senior CDC epidemiologists with support from TEPHINET mentors and MOH and AFRO representatives. The training lasted 5 weeks and had 3 distinct components (Table 1). Two cohorts were trained in each country, except for Mali, where only 1 cohort was trained due to security constraints.

During Workshop 1, which lasted 5 days, participants engaged in interactive learning on IDSR, Ebola virus disease, investigation and contact tracing, surveillance system monitoring, and daily SMS zero-reporting. After Workshop 1, participants returned to their respective districts/regions for 3 weeks to review processes for surveillance data collection, data analysis, and disease notification. They completed 2 field projects: 1) conducting a data quality audit by visiting a minimum of 3 health posts in their district, and 2) drafting a surveillance summary report of nationally reportable diseases. During the 3 weeks of field assignments, participants were supported by TEPHINET mentors through site visits, phone calls, and emails. The final component of the training consisted of a 3-day workshop in the fifth week (Workshop

Table 1. Surveillance Training for Ebola Preparedness 5-week program timeline

Week 1	Weeks 2–4	Week 5
Workshop 1 Interactive learning based on Integrated Disease Surveillance and Response Ebola virus disease, case investigation, and contact tracing Surveillance system monitoring Magpi (http://home.magpi.com) daily short message service reporting Draft goals	On-the-job fieldwork Data analysis and quality audit Surveillance summary report	Workshop 2 Present results Engage in continuing education on outbreak response, report writing, additional topics per local requirements Self-assess goal progress Draft plan to improve local surveillance

2), during which participants presented findings from the field to trainers and ministry officials, received feedback from the trainers, and developed plans for improving local surveillance.

Daily SMS Zero-Reporting

Daily SMS zero-reporting was designed as a management tool to supplement, not replace, the MOHs' existing systems for immediate reporting. The process allowed STEP participants to implement the principles of zero-reporting of suspected Ebola cases using Magpi, a cloud-based mobile data collection application that works with simple phones, smartphones, tablets, and computers (http://home.magpi.com). Zero-reporting means the reporting of the absence or presence of a disease or syndrome at a regular interval and is critical for the surveillance of a rapidly spreading infectious disease. The pilot implementation of daily SMS reporting in Guinea-Bissau has been previously reported (*7*). In Guinea-Bissau, Senegal, and Mali, 1 participant (the reporter) from each border district or region (and other districts/regions specifically requested by MOHs) was provided with a simple cell phone for sending daily SMS texts indicating the number of newly identified cases under investigation for Ebola in the previous 24 hours. System setup and SMS training occurred during Workshop 1. The countries generally used the standard WHO suspected Ebola case definition (Case Under Investigation): any person who has traveled to or stayed in a country that has reported ≥1 confirmed case of Ebola virus disease within ≤21 days of the onset of symptoms and who reports sudden onset of high fever and any of the following symptoms: headache, vomiting, diarrhea, anorexia/loss of appetite, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, hiccups; or inexplicable bleeding/hemorrhaging; or who died suddenly and inexplicably.

The SMS text was received by a smartphone connected to the MOH office's wireless network and uploaded automatically to the Magpi cloud in real time. An Epi Info cloud–Magpi bridge application (http://eicloudmagpibridge.codeplex.com) was used to extract collected data from the Magpi cloud. An Epi Info cloud data analytics application (http://www.cdc.gov/epiinfo/cloud.html) was used to generate tables, charts, and maps that were available on a real-time, web-based dashboard. CDC distributed to MOH points of contact a weekly summary indicating each district's reporting rate for the preceding week and for the entire reporting period. Daily zero-reporting was closely monitored from the date of first report submission in each country through November 1, 2015, after which the risk of Ebola importation was very low due to the disease disappearing in affected countries.

Evaluation Plan

The program evaluation plan consisted of 2 strategies: 1) a pretraining (baseline) and posttraining Surveillance Practices Self-Assessment (SPSA), and 2) a Predictive Evaluation framework (*9*) which linked STEP objectives to anticipated behavior changes on the job. At the beginning of Workshop 1, participants completed the baseline SPSA to provide data about their current work responsibilities, assessing whether participants met target audience criteria. The respondents were also asked about the content and quality of surveillance reports (e.g., "What percentage of routine summary surveillance reports include tables, graphs, or maps?"). After 3–6 months, an evaluator would conduct in-person interviews to reassess their surveillance practices and elicit information about key competencies attained from the training course, deliverables achieved posttraining, progress made toward their goals, and other changes resulting from STEP.

The Predictive Evaluation framework approach uses specific performance objectives defined by the country and establishes a committee to design workshop content. Stakeholders predict the new or changed behaviors they expect to see after a successful workshop. At the end of the workshop, participants develop statements describing specific actions they intend to do with their new knowledge, and their statements are compared with the stakeholders' expectations. In accordance with the Predictive Evaluation framework, participants were instructed at the end of Workshop 1 to draft 1–2 goals describing specific actions they would take upon returning to the workplace, and to align these goals with classroom

learning objectives. The STEP staff analyzed goal statements for quality, based on the four criteria of specific, observable, impactful, and directly related to the training content. Participants were asked about their progress toward their goals upon return from their fieldwork for Workshop 2.

Results

The implementation of STEP in Côte d'Ivoire, Guinea-Bissau, Senegal, and Mali occurred during an 8-month period, beginning with the first training in Côte d'Ivoire on January 12, 2015, and ending with the last training in Mali on August 19, 2015. STEP trained 185 participants from 72 health units (61 districts and 11 regions) in these 4 countries (Table 2). Among the participants were 47 district surveillance officers, 45 district medical officers, and other district-level staff who were responsible for frontline analysis and reporting of surveillance data. Although STEP was primarily designed for surveillance officers at the first level of the health system, 42 regional surveillance officers also participated in the training to reinforce the work of the district-level surveillance officers whom they supervised.

The results of the baseline SPSA confirmed that the appropriate participants had been recruited, with 155 (84%) of the 184 participants responding that they performed surveillance activities as part of their routine work when they began the training. Participants' responses to questions about current reporting practices indicated that pretraining surveillance practices were not optimal (Table 3).

The 307 goal statements that the 185 participants drafted for the Predictive Evaluation were categorized by the learning objective with which they are most closely associated (Figure 1). Examples of goal statements included the following:

- "After the data [are] collected, I will ensure that I do an analysis with diagrams, tables, and graphs, and present it to staff, service supervisors to show the utility of the data and to altogether improve the data."
- "I will encourage providers to make and transmit the report on time, and make a telephone reminder."
- "[I will] reduce wrong diagnosis through the use of definition of cases by training health specialists in this field."

Across countries, participants consistently demonstrated strong intent to improve the methods used for data analysis. Reducing misdiagnosis through the use of standard case definitions and improving reporting of epidemic-prone diseases were also frequently declared goals. Participants were less likely to make plans to improve reporting compliance or data quality. During the follow-up assessment in Workshop 2, most (110/133, 83%) sampled participants reported achieving (61 participants) or making significant progress toward (49 participants) their goal during 3 weeks of fieldwork (Table 4).

Due to resource constraints, the team was only able to conduct the posttraining SPSA in Côte d'Ivoire (Table 5). Three months after the training was completed, the SPSA was readministered to 21 respondents from Côte d'Ivoire, with 1–2 graduates from each of the districts bordering Ebola-affected countries assessed. Surveillance practices improved in several ways between the onset of STEP and the 3-month posttraining follow-up. A substantial number of participants reported taking actions to strengthen the data flow from health facilities. All 21 participants (100%) reported working with health facility staff to strengthen awareness of case definitions, with 18 (86%) participants stating they had provided flyers with case definitions and distributed disease notification sheets to all health centers. We also found very little tolerance for late reporting, with 20 (95%) respondents stating they routinely follow up via phone call, SMS, or a personal visit with health facilities that do not report on time. Eighteen (86%) participants submitted weekly surveillance reports. Ten respondents (48%) reported training others in data analysis techniques or using analysis methods themselves to improve surveillance.

Daily zero-reporting for suspected Ebola cases was implemented in 3 of the high-risk border countries; this included 13 sites in 11 regions and 1 national laboratory in Guinea-Bissau, 20 sites in 20 districts in Senegal, and 25 sites in 15 districts in Mali (Figure 2). The setup of the phones and SMS reporting system during Workshop 1 of the training took <8 hours in each country. Mean reporting rates among the countries ranged 53%–68% (Table 6), with slightly lower rates for countries reporting over a longer time (suggesting that reporting drops off with time). Eight suspected Ebola cases, 6 in Senegal (Figure 3) and 2 in Mali (not shown), were detected through the SMS system during the reporting periods, but none was confirmed.

Table 2. Surveillance Training for Ebola Preparedness training information for 4 countries in West Africa, 2015*

Country	Training dates	No. cohorts	No. participants	No. health units, districts, or regions
Côte d'Ivoire	Jan 12–Mar 18	2	54	25 districts
Guinea-Bissau	Jan 19–Mar 25	2	53	11 regions
Senegal	Apr 7–Jun 10	2	52	21 districts
Mali	Jul 20–Aug 19	1	26	15 districts†
Total		7	185	61 districts, 11 regions

*The number of Ebola-related deaths in West Africa peaked during October–December 2014.
†For purposes of this program, the 6 communes in Bamako, Mali, are counted as 6 distinct health districts, yielding a total of 15.

Table 3. Overall baseline Surveillance Practices Self-Assessment results from Surveillance Training for Ebola Preparedness program for 4 countries in West Africa, 2015*

Surveillance practice	No. (%) participants			
	Côte d'Ivoire n = 54†	Guinea-Bissau n = 52†	Senegal n = 52	Mali n = 26
Participant performs surveillance work as part of routine work responsibilities	53 (98)	39 (75)	43 (83)	20 (77)
Most routine surveillance reports submitted to the district/region:‡				
Were submitted on time	43 (80)	25 (48)	34 (65)	19 (73)
Were complete	34 (63)	17 (33)	36 (69)	20 (77)
Contained data on EVD indicating its presence or absence	37 (69)	11 (21)	19 (37)	20 (77)
Most summary surveillance reports developed by the participants:				
Included tables, graphs, or maps	14 (26)	5 (10)	6 (12)	12 (46)
Were analyzed using computer software	19 (35)	11 (21)	12 (23)	15 (58)
Included interpretations of the data	16 (30)	9 (17)	13 (25)	16 (62)
Included analyzed case-based data	5 (9)	4 (8)	11 (21)	15 (58)

*EVD, Ebola virus disease.
†One participant did not complete assessment.
‡Most indicates ≥50%.

Discussion

The STEP initiative successfully completed its emergency mission to scale up border preparedness to mitigate potential spread of disease from Ebola virus–affected countries. The training was highly valued and well accepted by the MOHs that received it. The evaluation suggested important changes in the self-reported work behaviors of several participants. At 83%, the percentage of participants reporting either substantial progress or goal completion in our study shows the immediate impact of the training on surveillance behaviors (*10*). The rate of daily SMS-text zero-reporting, albeit declining with time, demonstrated the feasibility of this technology for active monitoring of suspected Ebola cases several months post-STEP training.

Little has been published on real-time training during disasters, emergencies, and disease outbreaks for healthcare or public health professionals. Historically, workforce trainings for disaster, emergency, and outbreak response efforts have targeted clinical health professionals to identify, diagnose, and treat affected persons in healthcare settings. Published trainings primarily used exercises, simulations, and online certification of healthcare workers for purposes of preparedness and response planning either hypothetically or in anticipation of a real event. The unprecedented magnitude and severity of the 2014–2015 Ebola epidemic in West Africa required a novel training approach focused on the public health workforce's emergency response during the epidemic. It is important to understand the lessons

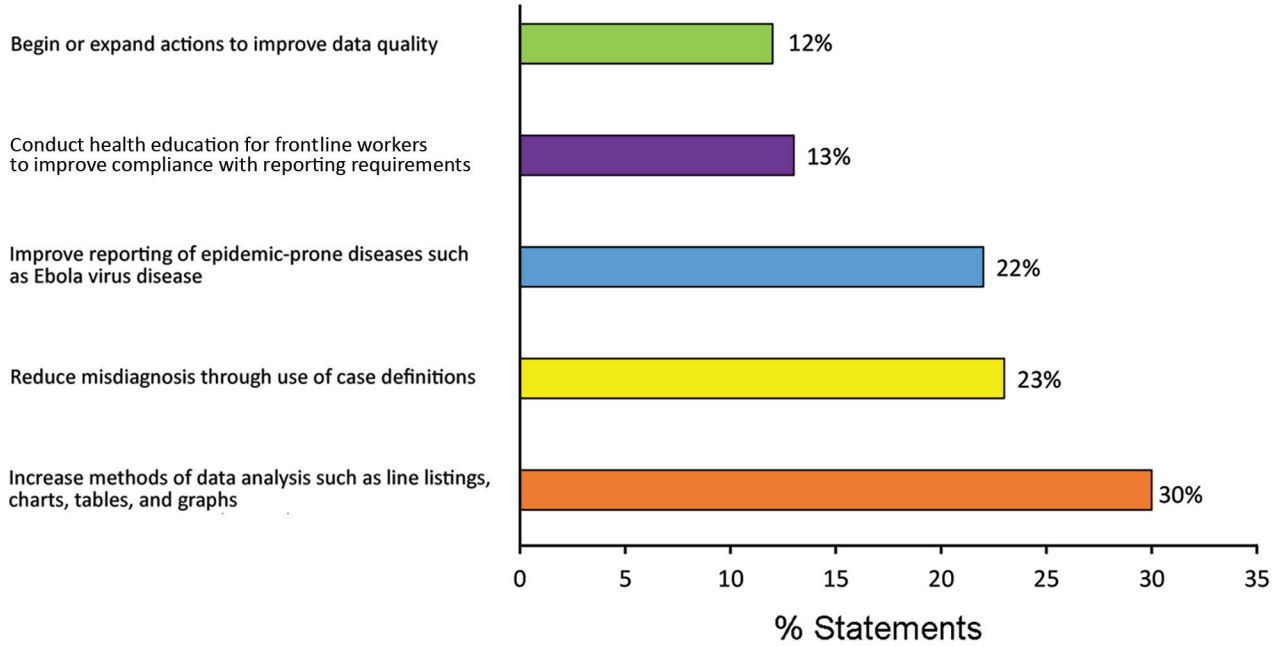

Figure 1. Distribution of 307 goal statements drafted by participants in Surveillance Training for Ebola Preparedness program in 4 countries in West Africa, categorized by related objective, January–August 2014.

Table 4. Participant-reported goal progress during fieldwork for Surveillance Training for Ebola Preparedness program in 4 countries in West Africa, 2015

	No. (%) participants				
Progress toward ≥1 goal	Côte d'Ivoire, n = 54	Guinea-Bissau, n = 26	Senegal, n = 26	Mali, n = 26	Overall, n = 133
Achieved goal	28 (52)	10 (38)	10 (38)	13 (50)	61 (46)
Significant progress toward goal	18 (35)	9 (35)	12 (46)	10 (38)	49 (37)
Some progress toward goal	2 (4)	5 (19)	3 (12)	3 (12)	13 (10)
No progress toward goal	0	2 (8)	0	0	2 (2)
Forgot/lost goal	0	0	0	0	0
No response	6 (11)	0	1 (4)	0	8 (6)

learned and limitations of our approach. These lessons can be divided into the areas of MOH political buy-in, preparatory country visits and planning, multilevel partnerships, and training and curriculum approach.

Political buy-in was a challenge easily met in the emergency context of the Ebola virus epidemic. Two of the countries (Mali and Senegal) had previously experienced Ebola virus importations, and there was general recognition of the need to fortify porous country borders that were susceptible to Ebola virus spread. It was vital that the formal letter of invitation from each MOH recognize the multilateral partnership involved in the technical assistance as well as identify a principal MOH point of contact. The contact, generally a high-level decision maker, was key to leading in-country efforts such as identifying dates and venues for training, prioritizing districts and participants, and coordinating logistics planning with partner organizations. Planning was greatly facilitated in countries in which CDC had an office. In countries with no office, CDC's Ebola Response High-Risk Unaffected Countries Team provided valuable support through its in-country deployed field staff. A 2-day preparatory in-person visit by CDC FETP and partner staff with each MOH was important to ensure a common understanding of training objectives, the appropriate STEP participants, and the surveillance context in each country.

The collaboration of CDC FETP with many of its longstanding partners (TEPHINET, AFENET, WHO [in-country and AFRO]) was key to the speedy recruitment of mentors and handling of logistics; the project team members had previously worked together and understood administrative mechanisms for moving financial resources, participants, and mentors. Also, these organizations could more readily ensure that decisions were consistent with the FETP approach of field-based, mentored training.

We tailored the training curriculum to the requirements of the emergency within each country's context. We supplemented STEP classroom instruction with a continuum of activities (including group work, goal statements, action plans, field assignments, mentor supervision) that have been shown in previous evaluation research to be associated with posttraining work application (*10*). Participants enhanced existing skills and developed new ones to identify problems affecting disease surveillance systems in their districts and to propose practical solutions. The STEP approach directly linked technical expertise about surveillance and Ebola to country priorities and performance-based learning. We believe that this approach, supported by quality mentorship, was a key factor of success and is applicable to other diseases and surveillance efforts.

This program had several important limitations and challenges. We had insufficient resources to conduct posttraining evaluation in all 4 countries. Although the evaluation in Côte d'Ivoire was encouraging, the interpretation is limited because the data were self-reported and nonrandomized, and we do not know how long the positive work behaviors continued. We had also hoped to implement SMS text–based reporting in all 4 countries. In the 3

Table 5. Surveillance Practices Self-Assessment results before and 3 months after Surveillance Training for Ebola Preparedness program, Côte d'Ivoire Border Districts*

	No. (%) participants	
Surveillance practice	Before program, n = 21†	3 mo after program, n = 21
Participant performs surveillance work as part of routine work responsibilities	20 (95)	21 (100)
Most routine surveillance reports submitted to the district/region:‡		
Were submitted on time	19 (90)	20 (95)
Were complete	16 (76)	18 (86)
Contained data on EVD indicating its presence or absence	17 (81)	10 (48)
Most summary surveillance reports developed by the participants:		
Included tables, graphs, or maps	5 (24)	10 (48)
Were analyzed using computer software	7 (33)	14 (67)
Included interpretations of the data	5 (24)	13 (62)
Included analyzed case-based data	2 (10)	3 (14)

*EVD, Ebola virus disease.
†The 21 respondents are a subset of the initial 54 participants.
‡Most indicates ≥50%.

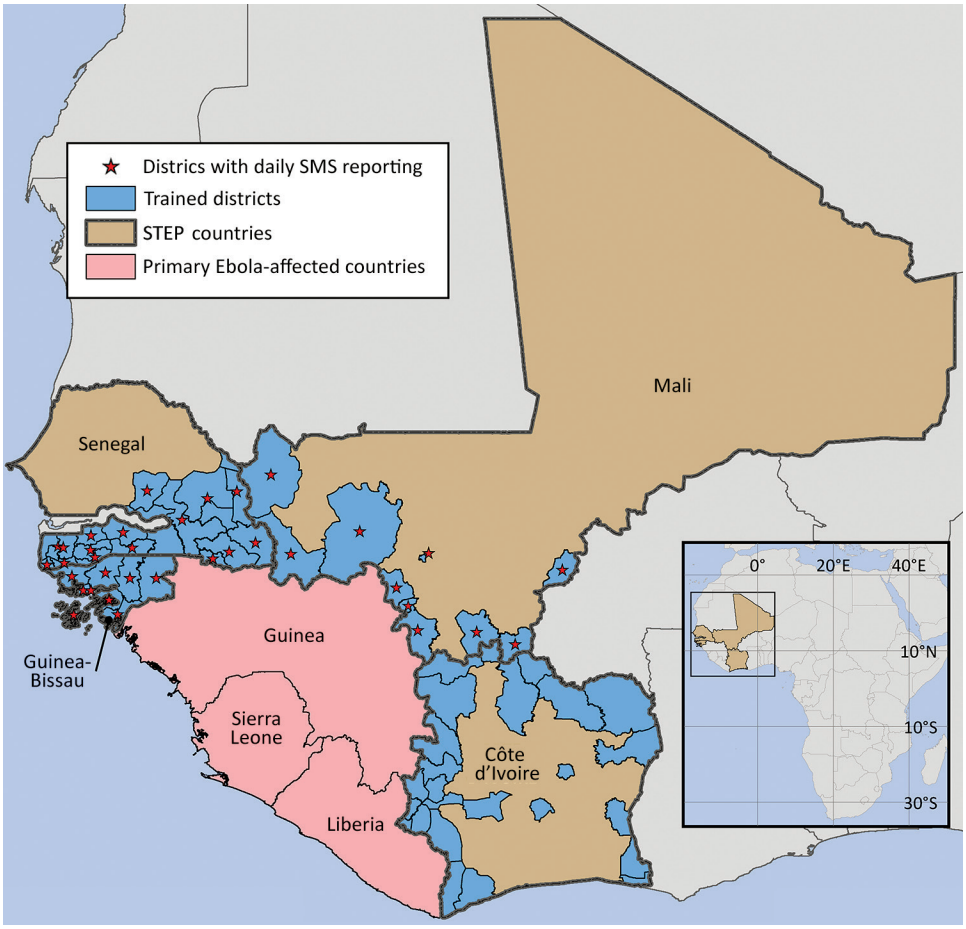

Figure 2. Districts and regions in 4 countries in West Africa participating in program training and daily SMS zero-reporting, 2015. The city of Bamako in Mali is administratively divided into 6 discrete communes, each equivalent to 1 health district. These are too small to individually illustrate on the map, so only Bamako, comprising all 6 communes, is shown. STEP, Surveillance Training for Ebola Preparedness; SMS, short message service. Map created by Andrew Berens. Sources: Global Administrative Areas (http://gadm.org); ERSI Data & Maps 2005.

countries that implemented the system, we were encouraged by the generally high rates of reporting (Table 6). The system took only a few hours to set up in each country and worked without major disruptions. Working in countries with different official languages also presented challenges, both in timely translation of materials and in the recruitment of mentors with appropriate language skills. Travel to hard-to-reach areas and situational awareness of security-related developments were mitigated by having MOH supervisory staff accompany mentors on site visits and by communicating closely with the embassies.

The Ebola crisis brought to light the large gap in the number of epidemiologists needed in West Africa. In addition, we noted the lack of epidemiologic skills at the district (operational) level. In most countries, these staff are responsible for aggregating and reporting surveillance data and often are the first with the opportunity to analyze, communicate, and respond to local events. The Ebola epidemic underscored the importance of WHO's International Health Regulations (IHR 2005) and the Global Health Security Agenda (GHSA) (*11*). The GHSA, started in 2014, is an "international collaboration that aims to support all countries in meeting IHR regulations and ensuring global health security" (*12*). One of the major activities of GHSA is to support workforce development activities to better prevent, detect, and respond to public health emergencies (*13*). With the conclusion of STEP and the Ebola epidemic, CDC's FETP unit is building on the work we report here by continuing to work with MOHs throughout the region to build sustainable epidemiologic and surveillance capacity through implementation of the FETPs-Frontline program. FETPs-Frontline targets district-level surveillance officers for a 3-month competency-based training;

Table 6. Daily zero-reporting rates for suspected Ebola cases using short message service texting for Surveillance Training for Ebola Preparedness program in 4 countries in West Africa, 2015

Country	No. reporters	Reporting dates	No. days	Mean reporting rate (range), %
Guinea-Bissau	14	Jan 24–Nov 1	282	53 (22–78)
Senegal	20	April 1–Nov 1	215	65 (23–93)
Mali	15	July 25–Nov 1	100	68 (24–98)

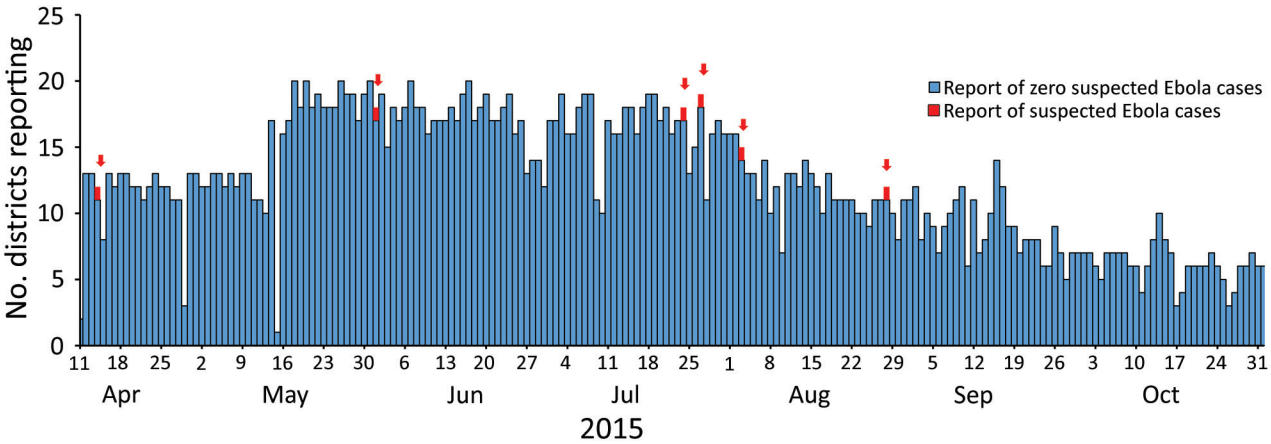

Figure 3. Number of districts reporting suspected cases of Ebola per day, Senegal, April 11–November 1, 2015 (n = 20).

it has been conducted in 14 countries in West Africa and recently expanded to other parts of the world. The experience of STEP demonstrates that rapid scale-up of surveillance capacity and daily zero-reporting in the midst of an epidemic can be successfully executed by leveraging established partnerships, simple technologies, and mentored, field-based training.

Members of STEP Working Group include Roodley Archer, Richard Dicker, Eric Brenner, Meredith G. Dixon, Erika Meyer, Rachel Rhodes, Samuel Twinomugisha, Anthony Kimuli, Sachin Agnihotri, Kenneth Johnson.

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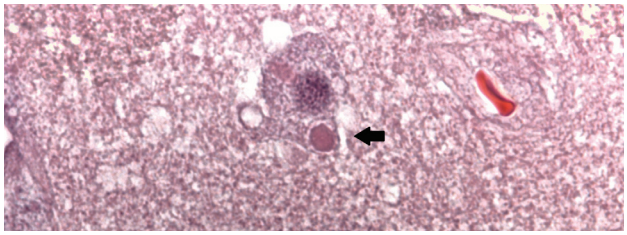
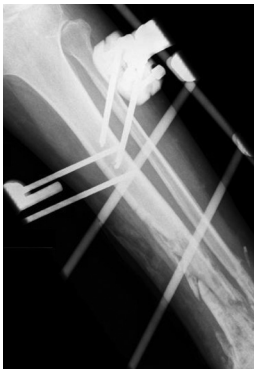
September 2014: **Emerging Pathogens**

- Molecular Epidemiology of Reemergent Rabies in Yunnan Province, Southwestern China
- Encephalitis Caused by Pathogens Transmitted through Organ Transplants, United States, 2002–2013
- Confirmed *Bacillus anthracis* Infection among Persons Who Inject Drugs, Scotland, 2009–2010
- Distance from Construction Site and Risk for Coccidioidomycosis, Arizona, USA
- Swine-to-Human Transmission of Influenza A(H3N2) Virus at Agricultural Fairs, Ohio, USA, 2012
- Genomic Epidemiology of *Salmonella enterica* Serotype Enteritidis based on Population Structure of Prevalent Lineages

- *Pneumocystis jirovecii* Pneumonia in Patients with or without AIDS, France
- Passive Surveillance for Azole-Resistant *Aspergillus fumigatus,* United States, 2011–2013
- Feeding Period Required by *Amblyomma aureolatum* Ticks for Transmission of *Rickettsia rickettsii* to Vertebrate Hosts
- Methicillin-Sensitive *Staphylococcus aureus* CC398 in Intensive Care Unit, France
- Household-Level Spatiotemporal Patterns of Incidence of Cholera, Haiti, 2011
- Incidence of *Cronobacter* spp. Infections, USA, 2003–2009



- Novel Circovirus from Mink, China
- Investigation and Control of Anthrax Outbreak at the Human–Animal Interface, Bhutan, 2010
- Family Cluster of Middle East Respiratory Syndrome Coronavirus Infections, Tunisia, 2013
- Pork Consumption and Seroprevalence of Hepatitis E Virus, Thailand, 2007–2008
- Asymptomatic, Mild, and Severe Influenza A(H7N9) Virus Infection in Humans, Guangzhou, China
- Mutations of the Novel Influenza A(H10N8) Virus in Chicken Eggs and MDCK Cells
- Genetic Variation among African Swine Fever Genotype II Viruses, Eastern and Central Europe
- Factors Contributing to Decline in Foodborne Disease Outbreak Reports, United States
- Risk Factors for Severe Influenza A Virus Pneumonia in Adult Cohort, Mexico, 2013–14
- Common Exposure to STL Polyomavirus During Childhood
- Enhanced MERS Coronavirus Surveillance of Travelers from the Middle East to England
- Live Poultry Market Closure and Control of Avian Influenza A(H7N9), Shanghai, China



EMERGING INFECTIOUS DISEASES https://wwwnc.cdc.gov/eid/articles/issue/20/9/table-of-contents

CDC Support for Global Public Health Emergency Management

Daniel J. Brencic,[1] Meredith Pinto,[1] Adrienne Gill, Michael H. Kinzer, Luis Hernandez, Omer G. Pasi

Recent pandemics and rapidly spreading outbreaks of infectious diseases have illustrated the interconnectedness of the world and the importance of improving the international community's ability to effectively respond. The Centers for Disease Control and Prevention (CDC), building on a strong foundation of lessons learned through previous emergencies, international recognition, and human and technical expertise, has aspired to support nations around the world to strengthen their public health emergency management (PHEM) capacity. PHEM principles streamline coordination and collaboration in responding to infectious disease outbreaks, which align with the core capacities outlined in the International Health Regulations 2005. CDC supports PHEM by providing in-country technical assistance, aiding the development of plans and procedures, and providing fellowship opportunities for public health emergency managers. To this end, CDC partners with US agencies, international partners, and multilateral organizations to support nations around the world to reduce illness and death from outbreaks of infectious diseases.

Recent public health events, such as the 2016 Zika outbreak and 2009 influenza A(H1N1) pandemic, have illustrated the interconnectedness of the world and the importance of global health security. Outbreaks of new and highly infectious diseases that start in remote parts of the world can quickly spread to large, urban populations. When Ebola virus disease appeared in Nigeria in 2014, what could have been an explosion of cases was quickly contained, in part because of prior emergency management investment by the government of Nigeria, with assistance from the US Centers for Disease Control and Prevention (CDC) and other organizations. Nigeria's ability to use public health emergency management (PHEM) principles to rapidly detect and respond proved invaluable in quickly and effectively stopping the spread of Ebola throughout the country and illustrates the effect of a strong PHEM program (*1*,*2*).

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In 2004, in response to the changing landscape of public health emergencies, the World Health Organization (WHO) led an effort, with support from CDC and other international organizations, to update the International Health Regulations (IHR), leading to adoption of the IHR 2005 (*3*) (Figure 1). According to WHO, "One of the most important provisions in the IHR is the obligation for all States Parties to establish core capacities to detect, assess, notify and report events, and to respond to public health risks and emergencies" (*4*). All member countries had until 2012 to conduct self-assessments and report their progress to WHO. In 2014, WHO, CDC, and other partners launched the Global Health Security Agenda (GHSA) to further advance national capacities to rapidly detect, respond to, and control public health emergencies and thereby comply with IHR 2005 (*5*). Although many countries were able to manage small outbreaks within their borders, the introduction of new diseases and the increased spread of disease from international travel exposed the need for a more purposeful and streamlined approach to manage these public health emergencies.

In the same timeframe that IHR 2005 was being written, CDC began to build its own preparedness and response program as a direct result of the increasing risk for public health threats and increased terrorism around the world (*6*). Using foundational emergency management principles, including the Incident Management System (IMS), CDC established its first permanent Emergency Operations Center (EOC) in 2003 and activated it soon after for the agency's response to the 2003 outbreak of severe acute respiratory syndrome (*7*). Since then, CDC has aimed to strengthen its emergency management program through exercises and responses to meet industry emergency response standards and, in 2013, became the first federal agency to receive full accreditation from the Emergency Management Accreditation Program (*8*). Building on a strong foundation of lessons learned through previous emergencies, national accreditation, international recognition, and technical expertise, CDC has established itself as a world leader in PHEM and begun to help other entities strengthen their capacity. CDC, as outlined in its Global Health Strategy (2012–2015), now collaborates "with host country

[1]These authors contributed equally to this article.

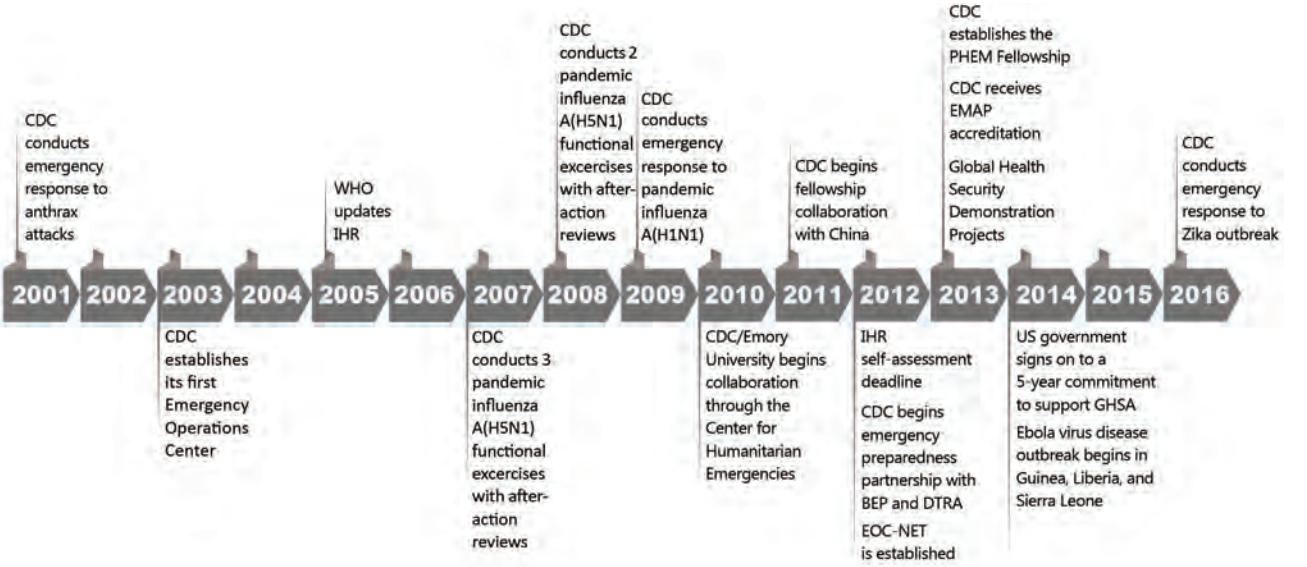

Figure 1. Timeline of CDC's support for development of global public health emergency management, 2001–2016. BEP, Biosecurity Engagement Program; CDC, Centers for Disease Control and Prevention; DTRA, Defense Threat Reduction Agency, US Department of Defense; EMAP, Emergency Management Accreditation Program; EOC-NET, Public Health Emergency Operations Centre Network; GHSA, Global Health Security Agenda; IHR, International Health Regulations; PHEM, public health emergency management; WHO, World Health Organization.

governments and partner organizations to strengthen health security by improving the ability of countries to prepare for and respond to disease threats on a global scale" (*9*).

History of CDC's Global PHEM Work

CDC's global footprint has grown considerably during the past 2 decades. As of 2016, CDC has 342 staff stationed in ≈50 countries and ≈40 staff detailed to international organizations and is supported by ≈1,368 locally employed staff from host countries (*10*). Starting in 2009, CDC hired local emergency coordinators in Guatemala, Kenya, Egypt, Kazakhstan, Thailand, and China. As CDC's EOC became increasingly involved in managing public health responses, and the role of the emergency coordinators evolved, CDC began to focus on assisting host country ministries of health with institutionalizing emergency preparedness and response activities. The objectives were to train on IMS and risk communication, complete public health capacity assessments, develop emergency preparedness plans, conduct tabletop exercises, and advise about EOC facility development. Through these efforts, CDC laid the foundation for further technical assistance.

The CDC emergency coordinators have been a valuable asset in this endeavor by providing technical knowledge in emergency preparedness and cultural understanding of the local contexts. In particular, during 2011–2015, the emergency coordinator based at the CDC Central America Regional Office supported the Risk Management Departments of 8 ministries of health in the Central American Region through the Council of Ministries of Health of Central America cooperative agreement. The development of public health emergency response plans and the development of EOCs led to ≈3,800 hours of training to ≈400 staff from 9 countries in Central and South America. As a result of these collaborations with CDC, Central America is better prepared to manage public health emergencies.

Fellowships and Delegations

CDC's growing role providing PHEM technical assistance coincided with countries' self-assessments for the 2012 deadline to report on progress toward achieving core capacities outlined in IHR 2005. During this time, requests increased to CDC for PHEM technical assistance, and CDC began to provide short-term, in-country emergency preparedness trainings and to host international delegations at the CDC EOC. During 2008–2011, the number of in-country delegations visiting CDC and learning about the US national-level PHEM program increased by 41%. CDC continues to host delegations and collaborates with local partners in Atlanta to enable visitors to observe PHEM at federal, state, and local levels.

Because of the benefits gained through the visits to CDC, several countries expressed interest in comprehensive fellowship opportunities to learn how CDC manages public health emergencies. In 2011, through a cooperative agreement between CDC, the Chinese Center for Disease Control and Prevention, and the National Health and Family Planning Commission of the People's Republic of China, CDC hosted fellows from China for a year-long study tour. As Chinese institutions became more advanced in their

plans and training, they sent staff for shorter fellowships to be embedded with CDC emergency management teams and receive specialized training in the areas of emergency plan development, EOC management and operations, and exercises and evaluation.

The interest of sending international public health staff to CDC to learn about public health emergency preparedness and response continued to grow, and in 2013 CDC established the Public Health Emergency Management Fellowship (PHEMF) program in Atlanta to build PHEM capacity among members of the international public health community through residential training and mentorship. Fellows complete a comprehensive, standardized study program in core emergency management functions that includes operations, planning, risk communications, and logistics. They observe CDC EOC responses and conduct site visits to improve their familiarity with PHEM in the field. The program enables fellows to interact with, and learn from, stakeholders of CDC's emergency management system, including federal, state, and local partners.

The PHEMF curriculum is guided by a global PHEM Core Competency Model, currently in development, which encompasses 7 competencies: leadership, emergency management frameworks, emergency management functions, emergency management communication, partnership and collaboration, training development and facilitation, and evaluation. With mentorship from CDC subject matter experts, fellows apply their learning to develop a personalized toolkit of products to be used by their ministries of health. Specific products in the toolkits may include standard operating procedures (SOPs), draft all-hazards or hazard-specific plans, or Web-based systems for EOC messaging.

By December 2016, CDC had trained 39 fellows from 25 countries. As leaders within their respective organizations, returning fellows facilitate the expansion of PHEM within their countries and have assumed key roles as leaders and managers of emergency response units in Africa, Asia, and the Middle East.

Building a Community of Practice

In the years leading up to the 2012 self-assessment on IHR 2005 capacities, worldwide need increased for guidelines and standards for building PHEM capacity. In fact, by June 2012, only "42 of 193 [21.76%] States Parties declared that they had met their core capacity requirements" (*4*), and most countries had requested a 2-year extension. To fill this need, CDC and other international organizations focused their global technical assistance on countries' IHR 2005 requirements. However, after 2 years of such support, in 2014, WHO reported that "at the time of…[the] second Review Committee meeting, 64 States Parties [33.16%] had indicated that they met the minimum core capacity standards" (*4*), which indicated that additional effort was needed.

Ongoing reviews of countries' PHEM capabilities demonstrated a lack of clear international guidelines for program implementation. Therefore, WHO, with support from CDC, the Chinese Center for Disease Control and Prevention, the European Centre for Disease Prevention and Control, and others, established the Public Health Emergency Operations Centre Network (EOC-NET), which strives to identify best practices in PHEM and promote EOC capacity-building activities in member states (*11*). As a member of EOC-NET, in 2013 CDC supported WHO's systematic review of EOCs and technical consultations through 4 working groups that aimed to develop guidance and standards for building, maintaining, and managing Public Health EOCs (PHEOCs).

The direct result of the EOC-NET work was publication of the Framework for a Public Health Emergency Operations Centre in 2015 as a first step in creating internationally recognized minimum common standards for PHEOCs. The Framework "outlines the key concepts and essential requirements for developing and managing… a PHEOC in order to achieve a goal-oriented response to public health emergencies and unity of effort among response agencies" (*12*). These guidelines provide a framework for public health emergency managers and practitioners to build the core capacity elements necessary for effective responses to public health emergencies.

Initiatives in Global Public Health Emergency Management

In 2013, CDC partnered with the ministries of health in Uganda and Vietnam as part of the Global Health Security Demonstration Project to show what public health capacity could be developed in 6 months with a concentrated commitment of technical assistance and resources. Although each country faced unique hazards and challenges, both projects focused on 3 main areas: 1) strengthening laboratory systems, 2) improving information gathering and sharing, and 3) developing a highly functioning PHEOC (*13*,*14*). CDC worked with the countries to develop SOPs and provide emergency management training for their PHEOC staff. At the culmination of the project, each country underwent a series of drills to demonstrate its increased capacity in the 3 target areas and showed significant improvements.

In 2014, the US government signed on to a 5-year commitment to support GHSA, an international collaboration among partner nations and international organizations intended to serve as a roadmap for countries to reach the capacities outlined in IHR 2005 (*5*). The goal of GHSA is to prepare nations around the world to more quickly and effectively detect and respond to infectious disease threats to reduce morbidity and mortality and prevent the global spread of disease (*15*). Eleven GHSA Action Packages are organized around Prevent, Detect, and Respond (*16*),

and CDC's strong foundation in PHEM has positioned the agency to provide effective technical assistance for the Respond 1 Action Package: Emergency Operations Centers.

The Respond 1 goal is for a country to have "a PHEOC functioning according to minimum common standards and trained EOC staff capable of activating a coordinated emergency response within 120 minutes of the identification of a public health emergency" (*16*). Although the Action Package goal highlights the need for each country to have a functioning PHEOC, what the Global Health Security Demonstration Project showed was that a fully coordinated response can be accomplished only through a comprehensive PHEM program. Through GHSA, CDC provides technical assistance to 17 countries in 3 areas: training and mentoring of PHEM staff; reinforcing sufficient PHEOC infrastructure; and developing streamlined systems, including plans, SOPs, and connections with other ministries of health (Figure 2).

At the same time CDC began to support GHSA, the Ebola virus disease outbreak struck West Africa. Using the lessons learned in the Global Health Security Demonstration Project, in September 2014, CDC provided emergency management technical assistance to develop PHEOCs in Guinea, Liberia, and Sierra Leone and the surrounding countries (*17*). The Ebola outbreak substantially weakened the already limited public health systems in the 3 affected countries. CDC's emergency management assistance focused on developing IMS goals and objectives, coordinating infrastructure improvements for increased collaboration, assisting with logistics, and training staff on PHEM principles. The progress in these 3 countries demonstrated that "rudimentary emergency management capacities can be rapidly established in countries with the application of focused technical assistance" (*17*). The response to this outbreak provided CDC with a unique opportunity to understand and overcome the challenges of providing technical assistance to countries with limited emergency management capacity, which would inform the approach for GHSA.

Throughout 2015, US government interagency delegations composed of officials from the Department of State (DOS), US Agency for International Development (USAID), Department of Defense (DOD), and CDC participated in GHSA launch meetings in 17 countries. As part of the implementation of the GHSA, countries developed 1-year work plans based on 5-year roadmaps that outlined a country's priorities, objectives, and activities and how the US government, other foreign governments, and international organizations would provide financial support and technical assistance. CDC developed a standardized package of technical assistance activities using a variety of foundational emergency management documents, including the International Organization for Standardization 22300 Societal

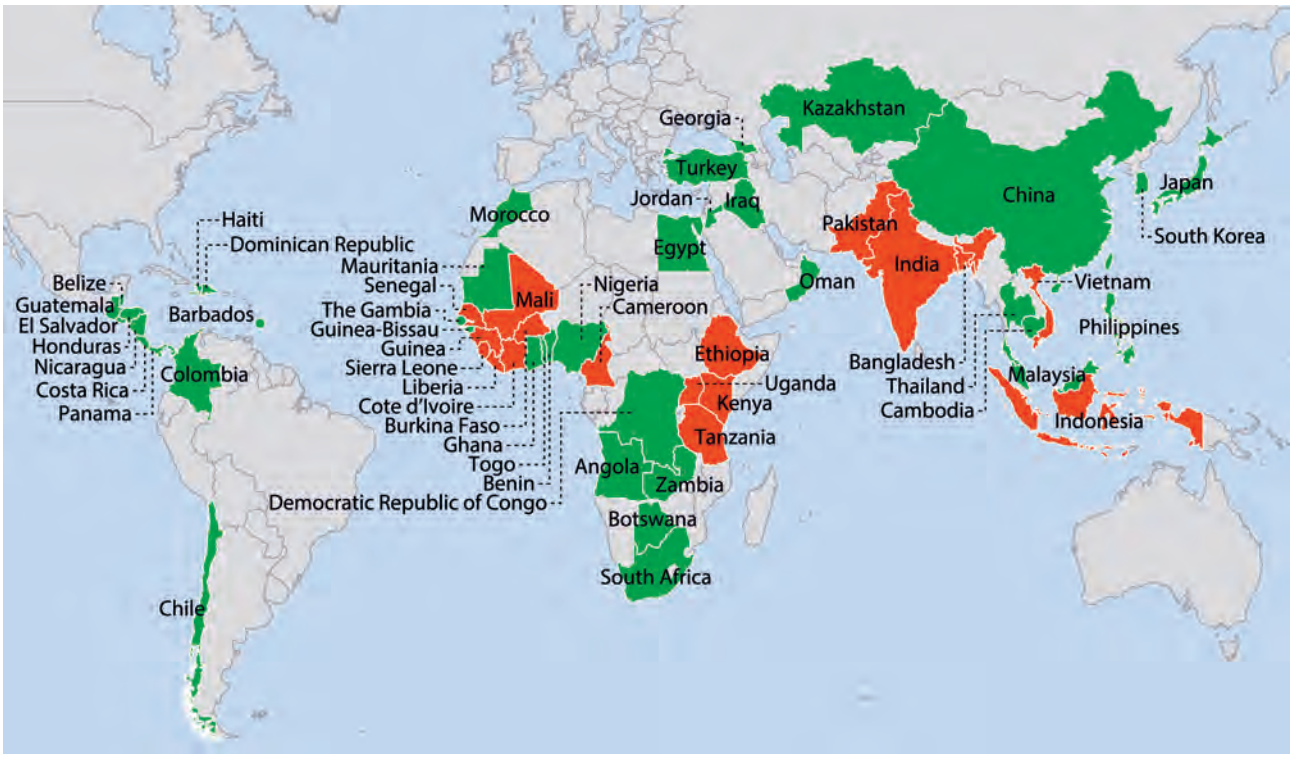

Figure 2. Centers for Disease Control and Prevention public health emergency management (PHEM) engagements, 2008–2016. Red indicates Global Health Security Agenda PHEM engagement; green indicates other PHEM engagement; gray indicates no PHEM engagement.

Security series (*18–20*); the WHO EOC Framework (*10*); and industry-specific standards, such as the National Fire Protection Association 1600 Standard on Disaster/Emergency Management and Business Continuity/Continuity of Operations (*21*). CDC then worked with ministries of health to customize work plans based on the country's baseline capacity and 5-year strategic goals for a PHEOC.

Through collaboration with in-country partners, CDC assists countries with public health threat and hazard identification and risk assessments; design of PHEOC policies, protocols, and guidelines; strategic and operational plans; planning for the physical design of a PHEOC; training PHEOC staff; and developing and executing exercises to validate activities. The effect of this work has been demonstrated in multiple ways. For example, in Cameroon, 33 Ministry of Health staff received basic PHEM training and participated in a follow-up exercise, and 26 participated in a workshop to develop and validate 11 priority SOPs for the PHEOC. A PHEMF graduate served as the incident manager for an influenza A(H5N1) outbreak and applied newly acquired skills in IMS to coordinate and manage the Ministry of Health's emergency response (*22*). In 2016 alone, Cameroon has seen a decrease in the time it takes to activate the PHEOC from 8 weeks (cholera outbreak) to 1 week (Lassa fever outbreak) to 24 hours (H5N1 outbreak), and coordination between animal and human health stakeholders has substantially improved.

Senegal needed a PHEM program early in the West Africa Ebola outbreak when an Ebola-positive person traveled from Guinea to the capital, Dakar. Since that time, emergency management has improved substantially through development of a PHEOC with support from CDC, the DOD's Defense Threat Reduction Agency (DTRA), and USAID. The Ministry of Health has trained permanent PHEOC staff, developed plans and procedures, and participated in 2 simulation exercises. The PHEOC assets also have been linked to national systems in public health surveillance, laboratory, human resources, and other sectors through joint strategic planning and simulation exercises. Both Cameroon and Senegal are emerging as regional PHEM leaders and are leading initiatives to share resources and exchange lessons learned from emergency responses with other West Africa countries. Of the 17 GHSA countries, 16 have received in-country CDC technical assistance and completed data collection for planning emergency management technical assistance, and 12 have held in-country CDC emergency management trainings.

Leveraging Partnerships to Increase PHEM Impact

Emergency management principles strive to streamline coordination and collaboration. Therefore, CDC works with US agencies and international partners to reach the goals of IHR 2005. CDC coordinates with DOS, DOD, USAID, and others to leverage resources and partnerships to expand emergency management technical assistance to countries. For example, since 2012, CDC has partnered with the DOS Biosecurity Engagement Program (BEP) to support biosecurity-related emergency preparedness. In India, CDC collaborated with the National Centre for Disease Control to develop a national-level PHEOC and is further strengthening emergency management capacity by developing PHEOCs at the state and district levels in Tamil Nadu. This network of PHEOCs will help India be better prepared to respond to biosecurity/biosafety threats. In Jordan, CDC partners with DTRA and DOS in 2 separate initiatives; through BEP, CDC has been working with the Ministry of Health Crisis Management Unit to develop a national-level PHEOC and provide training for Ministry of Health staff on the principles of emergency management. In addition, CDC has partnered with DTRA to bring different entities of the government of Jordan together for emergency preparedness planning, EOC training, and exercises focusing on civil–military coordination during humanitarian crises and health emergencies. These activities can streamline emergency management across Jordan's government.

CDC's partnerships and technical assistance also extend to large multilateral organizations and entities. CDC participates in WHO-led initiatives as subject matter experts in Joint External Evaluations, which assess a country's capacity to prevent, detect, and respond to public health threats (*23*), and partners with WHO to conduct GHSA activities. CDC also provides the African Union with emergency management training and technical assistance in developing a continent-level PHEOC. CDC partners with other nations' public health organizations, such as Public Health England and Public Health Agency of Canada, to leverage technical and language expertise and has joined with Emory University (Atlanta, GA, USA) through its Rollins School of Public Health Center for Humanitarian Emergencies to help develop the next generation of public health practitioners in humanitarian emergencies, emergency preparedness, and response (*24*).

Public Health Impact

Countless examples throughout the past few years have shown that diseases know no borders and can rapidly spread across land and sea. Increasing the international community's ability to rapidly and effectively respond to public health threats ensures the broader global health security of all people. In resource-limited environments, emergency response is centered on achieving the biggest public health impact. PHEM components, like preparedness plans, SOPs, and EOCs, contribute to faster and more efficient responses during emergencies which enable a greater reduction in morbidity and mortality.

Limitations

Successes have occurred in capacity development in some countries; however, challenges and limitations remain to building PHEM capacity around the globe. Although the WHO EOC Framework provides guidelines for countries on how to build a PHEM program, each country faces unique circumstances and challenges in implementing these programs. Laws, policies, and authorities vary substantially, and because PHEM is still a relatively new concept for most developing countries, high-level support must be cultivated. Countries with limited financial and human resources must prioritize planning for the most immediate and dire threats, and preparedness planning can seem an unaffordable luxury of time and resources. CDC and other international partners have provided technical assistance and resources, but transitioning to managing public health emergencies through a PHEOC still requires major commitment and input from a ministry of health to progress from having functionality to being fully operational. It is often expensive for countries to dedicate staff to work only on PHEM without drawing resources from other parts of the ministry of health. Efforts to strengthen PHEM capacity must build on existing emergency response structures. Any augmentation of technology and infrastructure also should improve nonemergency capability to be sustainable and effective.

Conclusions and Next Steps

The ability to detecting and respond locally to public health threats has been needed for generations. However, as the world becomes more interconnected, countries are realizing an increased need to prepare for public health threats from across the globe. Furthermore, global health security relies on the capacity of all countries to comply with IHR 2005 and rapidly detect, respond to, and control public health emergencies. This realization has increased the demand for PHEM technical assistance in building countries' sustainable capacity. Although CDC has focused on providing PHEM technical assistance to a select number of countries through programs such as the GHSA and partners such as BEP and DTRA, the need for PHEM assistance exceeds current support. The Zika outbreak in Central and South America is just one example of how nations outside these programs are susceptible to threats previously limited only to countries on other continents.

Providing technical assistance to countries during an outbreak or public health emergency is important; however, CDC encourages countries to invest in preparing for emergencies by highlighting the effect of an effective PHEM program on a response. CDC is focusing on regional workshops to bring together neighboring countries for trainings to increase communication and collaboration to leverage expertise across nations with similar threats and hazards. Continued close collaboration and partnership across the US government and with international organizations will enable more to be accomplished through leveraging individual institutional strengths. CDC aims to standardize the PHEM approach to respond to public health emergencies by continuing to assist WHO, through initiatives such as EOC-NET, to create global standards for PHEM. With this effort, CDC aims to reach its goal of saving lives and protecting people while making the world a safer place from disease outbreaks and other public health threats.

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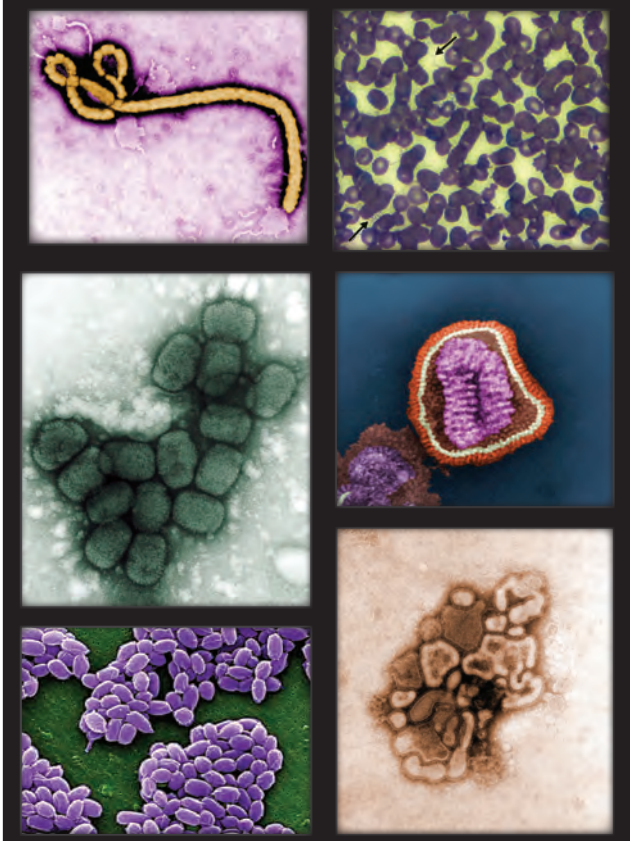

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Sustainable Model for Public Health Emergency Operations Centers for Global Settings

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Capacity to receive, verify, analyze, assess, and investigate public health events is essential for epidemic intelligence. Public health Emergency Operations Centers (PHEOCs) can be epidemic intelligence hubs by 1) having the capacity to receive, analyze, and visualize multiple data streams, including surveillance and 2) maintaining a trained workforce that can analyze and interpret data from real-time emerging events. Such PHEOCs could be physically located within a ministry of health epidemiology, surveillance, or equivalent department rather than exist as a stand-alone space and serve as operational hubs during nonoutbreak times but in emergencies can scale up according to the traditional Incident Command System structure.

Every country needs a system for responding to emergencies and managing emergency response. Emergency Operations Centers (EOCs) are increasingly viewed as necessary components of emergency preparedness and are used for multiagency coordination and response to a variety of hazards, including natural disasters, chemical spills, radionuclear incidents, humanitarian emergencies, and disease outbreaks. Public health EOCs (PHEOCs) are physical spaces with the ability to monitor events using various sources of data, improve communication between public health and emergency management personnel, facilitate coordination with multiple response partners, and provide space for members of the incident command team to gather and work (*1*–*7*).

When activated, a PHEOC is a location for the coordination of information and resources and is staffed with teams of subject matter experts, analysts, logisticians, and support staff (*2*,*3*). During activation, PHEOCs monitor epidemiologic data and field reports from a variety of sources using data technologies and informal networks of public health professionals (*1*,*8*). Scalability is essential for maintaining the effectiveness of a PHEOC (*2*), and it can be partially or fully activated according to situational needs (*9*). When inactive, many PHEOCs reduce in size or become dormant, and routine surveillance activities continue elsewhere within a ministry or department of public health (*3*,*6*,*10*).

In the United States, the Centers for Disease Control and Prevention (CDC) has a 24,000-square-foot PHEOC staffed by trained personnel 24 hours per day, 365 days per year, on CDC's main campus in Atlanta, Georgia (*1*). The CDC PHEOC may be notified about potential public health threats through its watch desk, which receives calls primarily from clinicians and other state and local entities, including PHEOCs. Notification also can come from public health partner briefings, field operations intelligence, reports from media and the Internet, and the International Health Regulations reporting system maintained by the World Health Organization (WHO) (*11*).

Although the CDC PHEOC houses a unit that monitors a wide variety of media sources for reports of outbreaks, most routine domestic surveillance data are collected and analyzed by the states and individual pathogen- or disease-specific programs within CDC. For instance, CDC's Influenza Division collects, compiles, and analyzes information about influenza activity year-round in the United States. This information is communicated to the public in FluView (*12*), a weekly influenza surveillance report, and FluView Interactive (*13*), which enables in-depth exploration of influenza surveillance data. The CDC PHEOC can access and view FluView 24/7 but relies on experts in the Influenza Division to analyze and interpret data and identify major aberrations. If an aberration in the data was thought to represent an event with public health consequences, such as the emergence of a new influenza virus rapidly spreading among humans, the PHEOC would be activated and all influenza surveillance activities moved into it during the period of activation.

Since its official launch in 2003, the CDC PHEOC has been central to CDC's timely and efficient coordination of public health threats and has responded to ≈60 domestic and international public health threats, including hurricanes;

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foodborne disease outbreaks; the 2009 A(H1N1) influenza pandemic; the Haiti cholera outbreak; and the outbreaks of Middle East respiratory syndrome, Ebola virus infection, and Zika virus infection (*9*). Although the CDC PHEOC has been a successful model in the United States, it might be less relevant for resource-limited countries. Maintaining a freestanding, constantly staffed PHEOC with a large dedicated workforce might be prohibitively expensive. In addition, recruiting a highly skilled epidemiologic workforce for an EOC might be challenging in these countries. Furthermore, the CDC PHEOC conducts surveillance on a global scale, whereas some countries may prioritize a more regional or national focus and thus might not have the ability or the need to scale up human and technical resources to tackle public health threats on the international stage.

Countries face challenges with surveillance and outbreak response because of 1) fragmented data streams that do not enable easy access to raw data for timely analyses and data use, 2) a small workforce that is responsible for most surveillance and response-related activities, 3) poor coordination during outbreaks resulting in slow response, and 4) limited resources dedicated to public health (*4,10,14,15*). To mitigate these challenges, PHEOCs in global settings can serve as epidemic intelligence hubs by receiving, analyzing, and visualizing multiple data streams, including surveillance data, and being staffed with a trained workforce capable of analyzing and interpreting data in real time. Such PHEOCs can be embedded within a ministry of health epidemiology, surveillance, or equivalent department, rather than existing as a standalone space, and can operate continuously for routine health surveillance.

The Global Health Security Agenda (GHSA), officially launched in 2014, was developed to strengthen countries' capacity to prevent, detect, and respond to human and animal biologic threats (*16,17*). The 5-year target for GHSA's Emergency Operations Centers Action Package is that "Every country will have a public health Emergency Operations Center functioning according to minimum common standards; maintaining trained, functioning, multi-sectoral rapid response teams (RRTs), 'real-time' bio-surveillance laboratory networks and information systems; and trained EOC staff capable of activating a coordinated emergency response within 120 minutes of the identification of a public health emergency" (*18*).

With the launch of GHSA and the need to develop PHEOCs and surveillance response capacities in countries around the world, we outline a sustainable model for PHEOC operations. Such PHEOCs will operate continuously by maintaining routine surveillance activities and serving public health needs during outbreak and nonoutbreak periods, thereby ensuring sustainability and helping address other national needs, such as routine analyses and use of surveillance data. We illustrate this approach with 2 case studies.

Case Study 1: Vietnam

Vietnam has 4 technically strong regional institutes with moderately advanced laboratory and epidemiologic capacity, resulting in scores of 3 or 4 out of 5 for laboratory and surveillance capacity indicators using the Joint External Evaluation of the International Health Regulations Core Capacities tool (*19*). These institutes oversee public health activities in their respective regions (North, South, Central Coast, and Central Highland), including the response and management of outbreaks that are beyond the capacity of local health departments. Nationally, the General Department of Preventive Medicine (GDPM), an agency within the Ministry of Health, provides public health policy and the strategic direction of public health activities, including surveillance. The GDPM developed a national PHEOC with the support of CDC and the US Defense Threat Reduction Agency's Cooperative Biologic Engagement Program as part of a GHSA demonstration project in 2013. Since then, the PHEOC has been used to manage responses and risk assessments to several different threats, including a nationwide measles outbreak, concerns about the importation of Ebola virus infection and Middle East respiratory syndrome, and recently, the emergence of Zika virus infection. The national PHEOC conducted and coordinated several training sessions for Ministry of Health and regional institute personnel on basic Public Health Emergency Management, facilitated participation for GDPM and regional institute staff in CDC's Public Health Emergency Management Fellowship training program, and has conducted several tabletop exercises and drills. A comprehensive PHEOC operational handbook was also developed and recently disseminated throughout the country's public health system (*20*).

Vietnam has several surveillance systems that generate data from a variety of sources. Hospitals are required to routinely report notifiable diseases, including several high-risk illnesses that must be reported within 24 hours. Typically these data are transmitted through the public health system from communes and districts to the province level, and then the regional institutes, through aggregated reports, submit these data to an electronic Communicable Disease Surveillance software. Since July 1, 2016, the Ministry of Health has been rolling out a system of case-based reporting on the established backbone of aggregated data reporting. In addition, multiple separate sentinel surveillance networks monitor for Japanese encephalitis virus; hand, foot, and mouth disease; influenza-like illness; severe acute respiratory infections; and dengue virus infection. Each system has an independent reporting mechanism, but all are monitored by the same small group of regional institute–level epidemiologists. Surveillance for malaria, tuberculosis, and HIV infection also have separate reporting systems. Each regional institute has a public health laboratory system, but the laboratories are not directly connected to the epidemiology or disease

control departments that monitor for outbreaks. In addition to these indicator-based surveillance systems, event-based surveillance systems recently have been improved in Vietnam, where community health workers and healthcare providers can report unusual events through public health reporting networks. The fragmentary nature of the surveillance data available through diverse reporting sources impedes timely detection of outbreaks, making the creation of integrated data systems critical to the success of these PHEOCs.

To help mitigate these challenges, the Vietnam Ministry of Health envisioned a network of PHEOCs that will be an interlinked system of information hubs, one at each regional institute. Each PHEOC will be connected to the network through its own data warehouse, which is in turn connected to the national data warehouse at the national PHEOC at GDPM. The warehouses incorporate and integrate data from multiple surveillance sources and enable analyses with the District Health Information System 2 software platform (*21*). For immediate accessibility, data dashboards with automated analyses are being created for each high-priority disease, enabling surveillance staff to instantly see the status of disease cases in their region. Alert thresholds for specific endemic seasonal diseases, such as dengue and influenza, have been designed to trigger notifications to the regional institutes.

The National Institute of Hygiene and Epidemiology (NIHE) in Hanoi and the Pasteur Institute of Ho Chi Minh City (PI-HCMC) lead the surveillance and outbreak response for the North and South regions, respectively, and collaborate with GDPM. NIHE has completed the establishment of a PHEOC, and PI-HCMC is in the process of doing the same. Vietnam plans to develop 2 additional PHEOCs in the remaining regional institutes in 2017. Both PHEOCs (NIHE and PI-HCMC) are situated physically and administratively in departments of epidemiology or disease control at the regional institutes and are staffed by epidemiologists within those departments, the same epidemiologists responsible for routine surveillance. A small number of support staff, including full-time PHEOC managers and information technology staff, are being recruited. During nonoutbreak times, the PHEOCs will be surveillance hubs where data from notifiable disease reporting from healthcare facilities, sentinel surveillance sites, and public health laboratory systems are all available through the data warehouse and displayed on data dashboards that automate routine analyses. Epidemiologists in each PHEOC will monitor and interpret the various streams of surveillance data to define usual patterns of disease transmission and monitor for aberrations. Data also are summarized for weekly distribution to policy makers in the MOH. The PHEOCs also will receive and incorporate event reports from the media, community, healthcare facilities, and event-based surveillance systems, enabling more timely detection of emerging or small outbreaks. Separate real-time data dashboards are in place for priority diseases, such as Zika virus infection (online Technical Appendix Figure, https://wwwnc.cdc.gov/EID/article/23/13/17-0372-Techapp1.pdf).

After WHO declared Zika virus infection as a Public Health Emergency of International Concern, the national PHEOC at GDPM began operating as a nerve center for Zika virus preparedness and response (*22*). Through the institution of a national preparedness and response plan, ongoing data surveillance, and multiagency meetings, the Vietnam PHEOC network has monitored and documented the Zika epidemic in the Americas and tracked cases within Vietnam. The Vietnam PHEOCs also are training centers for Vietnam's Field Epidemiology Training Program (FETP). That program recently inducted full-time fellows for the first time in 2016. These fellows rotate through the PHEOCs, where they are responsible for analyzing surveillance data and writing data summaries.

Ultimately, the development of Vietnam's PHEOC policies and operating procedures had to be tailored to the specific context of the country's existing legislative background. Formal PHEOC activation at CDC mobilizes financial resources for outbreak response and mobilizes personnel from other departments within the organization, which expedite the processes usually required for travel authorization and the clearance of communications materials. In Vietnam, however, these same actions are accomplished by the formal declaration of an "outbreak," which carries a specific legal meaning. This legislation, which long preceded development of a PHEOC, had to be taken into account when the EOC guidelines and manual of operations were drafted.

Case Study 2: Cameroon

Cameroon has experienced nearly annual cholera outbreaks and 3 separate outbreaks of measles in 2014 and continues to encounter major challenges in containing these outbreaks. Obstacles to efficient containment of outbreaks include reporting lags from the field, delays in information sharing of outbreak data through the public health system, inefficient coordination of outbreaks, and slow response at the central level (*23*,*24*).

The Integrated Disease Surveillance and Response (IDSR) system is the framework for Cameroon's disease surveillance and response. Public health policies, supervision and management of the health system, and IDSR at the central level are the responsibility of Ministère de la Santé Publique (MINSANTE), the Cameroon Ministry of Health. Cameroon has 10 regions with regional health delegations, and each is responsible for public health surveillance and response. Each region is further divided into districts, and the districts are additionally divided into health center catchment areas. These health center catchment areas are the outmost peripheral health units and may have community

health volunteer networks. Aggregated reports of IDSR notifiable diseases are sent weekly from the districts to MINSANTE, and the process is completed by manual data entry shared by email.

In 2014, Cameroon began developing a PHEOC, and MINSANTE prioritized its establishment to improve outbreak coordination, management, and response. The PHEOC was developed in the capital city, Yaoundé. It was created after several trainings of MINSANTE personnel, including training on the Incident Management System, participation in CDC's Public Health Emergency Management Fellowship training program, and the execution of several tabletop exercises and simulations. This knowledge was shared within the country, through a course taught by the newly hired PHEOC manager, with support from CDC subject matter experts.

The PHEOC was activated in May 2016 in response to an avian influenza virus A(H5N1) outbreak on a poultry farm in Yaoundé to enable the early detection of human cases, respond rapidly to interrupt human transmission, and oversee case management. A veterinary FETP fellow served as the liaison between the PHEOC and MINEPIA, Cameroon's Ministry of Livestock, Fisheries, and Animal Industries, coordinating seamless communication between the National Veterinary Laboratory and the PHEOC. When the PHEOC was deactivated in June 2016, none of the human contacts had tested positive (*25*).

During the avian influenza outbreak, the PHEOC faced a challenge in securing Tamiflu (oseltamivir phosphate) (Genentech, South San Francisco, CA, USA), an antiviral medication used to treat persons with symptoms caused by influenza. Early in the PHEOC's activation, all existing national stocks of Tamiflu were recognized to have expired, leaving the country unprepared for human cases. Working with WHO, the PHEOC obtained Tamiflu.

When GHSA was launched in Cameroon, MINSANTE understood that Cameroon could not wait for another outbreak and needed to begin operating the national PHEOC immediately. MINSANTE positioned the PHEOC as a hub to coordinate resources, information, and communication for data receipt, integration, analyses and interpretation, and coordination, with less focus on the physical infrastructure. Thus, the PHEOC runs out of a small multipurpose room within the MINSANTE facility, and a new facility is being built mearby. The lack of a dedicated physical place has not hindered the PHEOC's operation. In 2016 alone, the PHEOC responded to a cholera outbreak; prepared for a Lassa fever outbreak when it broke out in neighboring Nigeria; responded to measles, monkeypox, and avian influenza virus A(H5N1) outbreaks; elaborated on contingency plans for Zika virus; fine-tuned monkeypox plans when human cases and fatalities were registered in neighboring Central African Republic; and preventively activated for wild poliovirus detected in Nigeria. Most recently, the PHEOC responded to a train derailment in the Ezeka district, demonstrating all-hazards response capability. All of these opportunities helped Cameroon improve its preparedness, reducing its response time from 8 weeks to 24 hours during the recent H5N1 influenza outbreak (Table).

Engaging Cameroon's FETP within the newly created PHEOC was a critical component of the design of the country's PHEOC. The FETP trainees are forming the critical workforce that regularly analyze IDSR data from the district, interpret results, and present the results to stakeholders each week. These epidemiologic meetings are led by FETP trainees at the PHEOC and include stakeholders from WHO, UNICEF, the National Public Health Laboratory, Centre Pasteur of Cameroon, International Medical Corps, Metabiota, MaSanté, CDC, various officers from concerned directorates, and surveillance teams from MINSANTE, among others. This ethos of cooperation and stakeholder engagement was crucial for coordination meetings later, during the H5N1 influenza activation.

As the concept of incident command started to take shape, it became apparent that 2 major gaps in the Cameroon health system had been secondarily bridged: more accountability and better coordination. The lack of these 2 attributes previously were the major cause of poor initial response to the wild poliovirus outbreak (2013–2015) (*26*).

Cameroon's PHEOC faces many challenges, including a time lag in data availability from districts because of manual collection and reporting of data and limited information systems capacity to collect and analyze information from diverse data sources. To address this challenge, MINSANTE is investing in a data warehouse and an automated software platform at the district, regional, and national levels to make data available in near real time to decision makers at each level and to enable information flow into the PHEOC. Work is also under way to build capacity for automated data analysis and visualization at the PHEOC.

A Sustainable, Optimal, and Continuous Use Model for PHEOCs for Global Settings

Developing PHEOCs to facilitate appropriate coordination, response, and management of public health events is essential for building countries' emergency response capacity. Experience gained from developing PHEOC capacity in Vietnam and Cameroon demonstrated the following as a recommended sustainable path for PHEOC development:

1. PHEOCs benefit from being housed physically and administratively in close proximity to or within the epidemiology or surveillance departments of the ministry of health. This closeness establishes the PHEOC as a working hub readily accessible by epidemiologic staff.
2. PHEOCs should be epidemic intelligence hubs to receive, interpret, and visualize surveillance data from

Table. PHEOC activations illustrating improvements in time to activation, Cameroon, 2015–2016*

Date	Outbreak/disaster	Type	Event/outbreak location	Activation time	Comments/action taken
2015 Nov–2016 Jan	Cholera	Infectious disease outbreak	Gider District, Cameroon	8 wk	Major delays because of lack of coordination and accountability
2016 Mar–Apr	Measles	Infectious disease outbreak	Cameroon	4 wk	Delays because of lack of accountability
2016 May–Jun	Influenza A(H5N1)	Infectious disease outbreak	Cameroon	24 h	Benefit from lessons learned for first time. EOC's Incident Manager is ministry of health staff member who graduated from CDC PHEOC fellowship
2016 Aug	Lassa fever	Infectious disease outbreak	Nigeria	2 wk	Outbreak in neighboring country provided opportunity to test preparedness and set up contingency plans for bordering districts
2016 Aug	Monkeypox	Infectious disease outbreak	Cameroon	24 h	Collaboration between CDC, Defense Threat Reduction Agency, and WHO to provide PPE to government of Cameroon
2016 Sep	Zika virus	Infectious disease outbreak	Latin America	2 wk	New opportunity to test preparedness and set up national contingency plan
2016 Oct	Camrail train accident	National disaster	Ezeka, Cameroon	1 h	Using PHEOC for other public health–related events that are not infectious diseases
2016 Oct	Monkeypox	Infectious disease outbreak	Central African Republic	24 h	Outbreak with human cases and deaths
2016 Nov	African Women Cup of Nations	National major event	Limbé and Yaoundé, Cameroon	Pre-event	Centre and Littoral Regions' rapid response teams

*CDC, Centers for Disease Control and Prevention; EOC, Emergency Operations Center; PHEOC, public health EOC; PPE, personal protective equipment; WHO, World Health Organization.

multiple sources. These hubs make information systems development a critical part of PHEOC operations. Mechanisms should be created that integrate data streams and develop data dashboards, automate routine analyses to improve the value and utility of surveillance data, and establish the continuous operations of the PHEOC.

3. Rotating FETP trainees through the PHEOCs provides the epidemiologic workforce needed for analysis and interpretation of surveillance data. This rotation can augment epidemiology workforce capacity, especially in ministries of health where epidemiology staffing is limited. It also provides a valuable training experience for FETP fellows.
4. PHEOCs should function during nonoutbreak periods, and surveillance data should routinely be interpreted by an epidemiologic workforce. Such an "always on" PHEOC facilitates the rapid transition to response mode during outbreaks and improves the cost-effectiveness of the infrastructure investment. Routine use of PHEOCs during outbreaks and during nonoutbreak periods helps ensure sustained technical capacity for data analyses, interpretation, and visualization tools and equipment, as well as the knowledge to analyze and interpret incoming health information.
5. Each PHEOC must be tailored to the legislative context in which it is situated. The result is a PHEOC that fits within local legislation and more fully meets the needs of the ministries of health.

The 2015 WHO Framework for a Public Health Emergency Operations Centre provides valuable information about the role, function, and construction of PHEOCs (*2,7*). A critical gap exists in guidance, however, regarding how PHEOCs maintain readiness between periods of activation. This gap in guidance is particularly relevant for resource-limited nations that might not be capable of readily scaling up human resources and technical capacity in the event of an emergency. It is more sustainable for PHEOCs in these countries to initially be established in departments or institutions that are already responsible for monitoring public health data and responding to disease outbreaks. Illustrations from Vietnam and Cameroon present the implementation of this approach and its associated successes and challenges.

The approach described here could enable rapid establishment of a PHEOC with minimal infrastructure and available workforce. Such a PHEOC will serve well in resource-limited settings as a continuously operational hub for surveillance, yet ready for activation during emergencies. As additional resources become available, this PHEOC model can expand to fit international standards and be capable of addressing all emergency hazards.

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Centers for Disease Control and Prevention Public Health Response to Humanitarian Emergencies, 2007–2016

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Humanitarian emergencies, including complex emergencies associated with fragile states or areas of conflict, affect millions of persons worldwide. Such emergencies threaten global health security and have complicated but predictable effects on public health. The Centers for Disease Control and Prevention (CDC) Emergency Response and Recovery Branch (ERRB) (Division of Global Health Protection, Center for Global Health) contributes to public health emergency responses by providing epidemiologic support for humanitarian health interventions. To capture the extent of this emergency response work for the past decade, we conducted a retrospective review of ERRB's responses during 2007–2016. Responses were conducted across the world and in collaboration with national and international partners. Lessons from this work include the need to develop epidemiologic tools for use in resource-limited contexts, build local capacity for response and health systems recovery, and adapt responses to changing public health threats in fragile states. Through ERRB's multisector expertise and ability to respond quickly, CDC guides humanitarian response to protect emergency-affected populations.

The number of persons affected by humanitarian emergencies worldwide is unprecedented; in 2016, the United Nations Office for the Coordination of Humanitarian Affairs estimated that 125 million persons needed humanitarian assistance (*1*). More than half of these, 65.3 million persons, have been forcibly displaced as a result of armed conflict, civil strife, or human rights violations. The number displaced has increased by 75% during the past 20 years and by 50% in just the past 5 years (*2*). Among these are 21.3 million refugees and 40.8 million internally displaced persons (IDPs) (*2*). Displaced persons might settle in temporary shelters or camps in resource-limited or politically unstable areas, straining local capacity to provide services. The effects of humanitarian emergencies can be exacerbated by political instability and weak governance associated with fragile states or areas of conflict (*3*), and this instability directly undermines global health security. In such unstable settings, the humanitarian community calls these crises complex emergencies (CEs) (Table) (*4*).

Although the underlying causes of humanitarian emergencies and CEs specifically are highly varied, the population displacement and health systems destabilization associated with emergencies have predictable public health consequences. A hallmark of CEs is increased mortality rates, sometimes ≥10-fold above baseline rates (*3,6,7*). Historically, the cause of the high morbidity and mortality rates have been infectious disease outbreaks; exacerbation of endemic infectious diseases; and acute malnutrition, often in high-density settlements with inadequate water, sanitation, shelter, and access to food (*3,7–10*). Increased availability of interventions for these conditions, coupled with a rise in conflicts in higher-income countries, have led to an increasing burden from chronic conditions such as tuberculosis, cardiovascular disease, and diabetes (*3,8,9*). Conflict-affected populations also have an elevated risk for injury from violence, including sexual and gender-based violence, and mental health conditions are common (*3,9*). Most displaced persons live in host communities, rather than in separate camps, contributing to poor or uncoordinated access to healthcare services (*9*). This inconsistent access continues to be problematic in protracted emergencies, during which public health services might be strained for years. Responding to the wide-ranging public health effects of CEs requires expertise in diverse sectors, such as vaccine-preventable and other infectious diseases;

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Table. Definitions of terms related to disasters and humanitarian emergencies

Term	Definition
Disaster	A serious disruption of the functioning of a community or a society involving widespread human, material, economic, or environmental losses and impacts that exceeds the ability of the affected community or society to cope using its own resources
Natural disaster	A disaster brought about by natural hazards
Human-made disaster	A disaster brought about by human activities or events (*4*)
Humanitarian emergency	A disaster resulting in the need for international support (humanitarian assistance) to meet the basic needs of the affected population (*4*)
Complex emergency	A humanitarian emergency associated with fragile states or areas of conflict, in which a total or considerable breakdown of authority has occurred (*4*)
Global health security	A state of collective protection of health through ensuring all countries can effectively prevent, detect, and respond to public health emergencies (*5*)

water, sanitation, and hygiene (WASH); nutrition; noncommunicable diseases; injury; sexual and reproductive health; and mental health. Equally varied are the epidemiologic approaches needed to effectively respond to CEs, including development of novel epidemiologic methods, rapid needs assessments, surveillance implementation and evaluation, outbreak investigations, and capacity building, often in resource-restricted and insecure environments.

The Centers for Disease Control and Prevention (CDC) has long been a leader in developing and understanding the epidemiology and public health effects of humanitarian emergencies and CEs specifically. CDC's work in CEs began during the 1968 war-induced famine in Biafra in West Africa, during which staff documented the extent of severe malnutrition (*11*). CDC's assessment of the health effects of the 1970 Bangladesh cyclone established epidemiologic approaches in humanitarian emergencies triggered by natural disasters (*12*). CDC published a compendium of disease control and public health surveillance programs used among Khmer refugees from Kampuchea (Cambodia) in Thailand during 1979–1980 (*13*), followed by a synthesis of accumulated knowledge about public health issues in CEs (*14*). In 1990, Toole and Waldman, among the first CDC staff dedicated to studying the epidemiology of CEs, published a paper on mortality rates among displaced populations, which established the use of a crude mortality rate (CMR) threshold to quantitatively define CEs (*15*). In 1994, CDC staff, as part of the Goma Epidemiology Group, conducted rapid cluster sample population surveys to document the unprecedented mortality rate among Rwanda refugees in Goma, Zaire (now Democratic Republic of the Congo) (*6,8*). After a systematic review of nutritional surveys in Somalia during the 1991–1992 famine, CDC staff provided recommendations for standardizing nutritional assessments in CEs (*16*). Toole et al. published on measles control in refugee settings in 1989 with special attention to how measles prevention policies during CEs differ from measles control in standard settings (*17,18*). In the 1990s and 2000s, CDC staff emphasized the burden of chronic diseases in CEs (*19*) and documented adverse mental health outcomes and social functioning among refugee and CE-affected populations (*20–23*) and, later, among national and international aid workers (*24–26*). In all activities, CDC worked to address the unique characteristics of humanitarian emergencies through development of epidemiologic methods, strengthening local capacity, improvement of surveillance, and evaluation of interventions.

CDC continues its work on humanitarian emergencies through its humanitarian emergency response branch, the Emergency Response and Recovery Branch (ERRB), in the Division of Global Health Protection, Center for Global Health. ERRB includes the Global Disease Detection Operations Center, the Global Rapid Response Team, the Global Response Preparedness Team, the Global WASH Team, and the Humanitarian Health Team, thus unifying CDC's humanitarian emergency preparedness, alert, and response activities into a single program. Staff members work with the international humanitarian community to apply public health and epidemiologic science, develop tools and methods to understand health needs, and build the capacity and resilience of public health systems within these fragile settings. This article focuses on ERRB's work in humanitarian emergency response over the past decade; its collaboration with response partners; the broad lessons that can be drawn from its work; and how it and other humanitarian health responders are adapting to address new threats to global health security, new needs of populations affected by CEs, and humanitarian emergencies at large.

Response Descriptions

We retrospectively examined ERRB responses during 2007–2016. To compile the responses that occurred during 2007–2014, we abstracted data from past branch activities databases and publications. To ensure the completeness of this dataset, we compared it with a previously compiled comprehensive database of all emergencies worldwide, including CEs and natural disasters, for the same period (A. Culver, Emory University, pers. comm., 2015 Aug 4). Sources of CEs included in this database were the Center for Research on the Epidemiology of Disasters Complex Emergency Database (http://cedat.be) and the United Nations Office for the Coordination of Humanitarian Affairs Central Emergency Response Fund archives of funded responses (http://www.unocha.org/cerf/cerf-worldwide/allocations-country/2006-2017-country). Included events were those that affected ≥10,000 persons and had a documented

CMR of >1 death/10,000 persons/day. Sources for natural disasters were the Center for Research on the Epidemiology of Disasters international disaster database (http://www.emdat.be) and Central Emergency Response Fund archives; inclusion required that the event affected ≥10,000 persons. To compile emergency responses for 2015 and 2016, we abstracted data from branch administrative and travel records. Responses were selected to reflect ≥1 response/year and to include those in which branch staff had a major role.

Of 14 selected emergencies over the past 10 years, nearly two thirds were CEs; the rest were natural and human-made disasters (online Technical Appendix Table, https://wwwnc.cdc.gov/EID/article/23/13/17-0473-Techapp1.pdf). Responses were conducted in Africa, Asia, Latin America and the Caribbean, Europe, and the Middle East; activities included providing technical assistance or directly conducting assessments and investigations, implementing and evaluating surveillance systems, developing guidelines, providing trainings, and coordinating interventions. All responses featured extensive collaboration with a variety of partners, including the US government, UN agencies, governmental health entities, and both national and international nongovernmental organizations (NGOs). To illustrate the breadth and impact of the CDC and its partners' work in humanitarian emergency responses, we highlight activities performed in 3 cases (online Technical Appendix Table).

Case Studies

Haiti Earthquake Response, 2010

On January 12, 2010, a 7.0 magnitude earthquake struck central Haiti, killing >200,000 persons and injuring another 300,000. The quake also created 1 million IDPs and massively disrupted public health and other basic services within an already fragile state. ERRB staff worked with the Pan American Health Agency and the Haiti Ministry of Public Health and Population to establish sentinel site surveillance for epidemic-prone infectious diseases at 51 health facilities across the country and in IDP camp clinics; these systems were instrumental in detecting the cholera outbreak that began in October 2010 (*27*,*28*). Recognizing that population displacement could exacerbate Haiti's already poor access to improved water sources and sanitation facilities, ERRB staff and the Haiti National Directorate for Potable Water and Sanitation performed a rapid assessment of access to WASH services in 308 IDP settlements in February 2010 and found that <10% of sites met the minimum Sphere Project standards for emergency sanitation (≤50 persons/latrine) (*29*). This work provided the impetus for the Haiti National Directorate for Potable Water and Sanitation and the humanitarian WASH sector to increase emphasis on improving WASH in IDP sites, actions that likely reduced the number of cases among IDPs early in the cholera epidemic (*30*,*31*).

The cholera epidemic was also the basis for a series of ERRB activities focused on improving access to clean water and proper sanitation in Haiti. Although WASH had been a core sector within ERRB, this epidemic led to an increased CDC emphasis on implementing and evaluating WASH interventions in CEs. In light of the ongoing burden of thousands of cholera cases in Haiti annually, WASH activities in Haiti are now a focus of health systems recovery work of ERRB and the CDC Haiti country office.

Horn of Africa Famine and Displacement Response, 2011–2014

In 2011, a drought in the Horn of Africa led to severe food insecurity for 13 million persons, contributing to 30% acute malnutrition rates and declaration of famine in 3 regions of Somalia (*32*). Nearly 1 million Somali refugees fled to camps in Kenya and Ethiopia, and an additional 1.5 million persons were internally displaced within Somalia. Host populations in Kenya also experienced emergency rates of ≥25% acute malnutrition, and outbreaks of measles and cholera occurred.

In response, ERRB staff worked with the UN High Commissioner for Refugees (UNHCR) to strengthen its Health Information System (HIS) disease surveillance (http://www.unhcr.org/en-us/protection/health/4a3374408/health-information-system-toolkit.html), which led to identification of measles outbreaks in 2 refugee camps. Staff review of demographic profiles of outbreak cases led to an expansion of the target age group for vaccination from 6 months–14 years of age to 6 months–30 years of age (*33*,*34*). In a retrospective survey of deaths among 753 refugee families arriving at Dadaab, Kenya, ERRB staff and partners noted a doubling of CMR among refugees in transit (CMR 1.94, 95% CI 0.50–3.37) compared with that before departure (CMR 0.86, 95% CI 0.57–1.15), leading to aid agencies intervening during refugees' journeys (*35*). ERRB's evaluation of a blanket supplementary feeding program in northern Kenya, conducted with several collaborators, pointed out the need for more regular distribution of rations and strengthened interventions for acutely malnourished children (*36*). ERRB staff and UN partners reviewed and validated all aid groups' nutrition and mortality surveys conducted in Somalia to ascertain the severity of the famine in some affected areas, thus directing aid (*32*). Until 2014, ERRB supported the Somalia communicable disease reporting surveillance system, designed to optimize early warning of outbreaks, by providing analysis and training; this system identified an outbreak of polio in 2013, enabling swift intervention (*37*).

For ERRB, the response to the Horn of Africa famine and displacement indicated the value of enhancing public

health information quality, thereby guiding the allocation of humanitarian resources. ERRB's response to this emergency also sharpened CDC's capacity to respond to protracted emergencies over the course of several years, adapting responses to the changing public health needs across several sites simultaneously within a destabilized region. In addition, this response represented one of the first instances of ERRB's providing remote support and monitoring of emergency public health activities.

Syria Displacement Response, 2012–Present

Antigovernment protests in Syria in 2011 devolved into an ongoing, multisided armed conflict that has devastated a previously middle-income country and destabilized the region. The UN Office for the Coordination of Humanitarian Affairs estimated, as of October 2016, that 13.5 million persons across the region were in need of humanitarian assistance. The war has caused the displacement of 4.8 million persons outside the country and 6.1 million within, totaling more than half of Syria's population (*38*). The displacement crisis has strained resources in neighboring countries and beyond.

As in other protracted emergencies, ERRB's work has spanned several years and multiple sectors. Branch staff helped UNHCR implement HIS for disease surveillance in Za'atari refugee camp in Jordan, including introduction of an outbreak response protocol. Thereafter, when HIS showed a decline in child vaccination rates in the camp area from 90% to 50%, aid partners conducted a measles vaccination campaign of 660,000 children. Working with the US Agency for International Development's Office of Foreign Disaster Assistance and the Assistance Coordination Unit, staff also established and trained local users on the Early Warning Alert and Response Network in northern Syria, playing a fundamental role in establishing disease surveillance in non–government-controlled areas and increasing local public health capacity. This system detected a polio outbreak in 2013, initiating a vaccination campaign, and provided information on suspected cholera cases and measles and typhoid fever outbreaks. ERRB assisted UNHCR, UNICEF, and other partners in conducting cross-sectional representative cluster surveys of nutritional status of refugee children and women of reproductive age, finding a high prevalence of anemia in both groups and providing evidence to support a micronutrient fortification food program for refugees (*39*). ERRB and multiple collaborators performed an assessment of the Minimum Initial Services Package for reproductive health among the refugees from Syria residing in Jordan and instituted a protocol for clinical management of survivors of sexual violence after noting a lack of such services (*40*).

This response in Syria indicated the importance for the emergency health response community to support public health guideline and strategy development and program implementation across regional public health systems. The Syria displacement crisis also pointed out the need to develop responses for emergencies in middle-income regions of the world, where demographics, disease burden, and functionality of public health systems are different from those of sites of historic CEs.

Discussion

Reflecting on these 3 case studies and the other listed ERRB humanitarian emergency responses, several overarching lessons for effective public health humanitarian emergency response emerge. First, because humanitarian emergency response requires engaging in a broad range of public health work within resource-limited, fragile, or insecure environments, successful response requires developing close working relationships with other humanitarian response organizations. For CDC, these partnering organizations include national governments; ministries of health; US government agencies (especially the Agency for International Development's Office of Foreign Disaster Assistance and the Department of State Bureau of Populations, Refugees, and Migration); UN agencies, including the World Health Organization, UNHCR, and UNICEF; and national and international NGOs. At a basic level, these close relationships allow ERRB and other humanitarian responders access to CE settings. These collaborations encourage standardization of approaches across the international humanitarian emergency response community (*29*) and improved coordination of response (*6,18*). The common use of these standardized practices has been facilitated by the dissemination of the epidemiologic approaches and methods championed by CDC during humanitarian emergency responses and through CDC-trained staff going on to senior positions at UN agencies. Finally, these collaborations permit ERRB and similar organizations to provide technical assistance while partners such as national ministries of health, UN agencies, and NGOs take the lead in implementation of interventions.

Second, because public health emergency responses often take place within the context of mass population displacement and fragile states, CDC and other responders must develop and apply epidemiologic methods and tools to be used in challenging and resource-limited settings. ERRB has contributed to several such tools. In the nutrition sector, ERRB enhanced the application of the emergency nutrition assessment software that facilitates survey planning, data collection, and analysis of anthropometric indices (http://smartmethodology.org/survey-planning-tools/smart-emergency-nutrition-assessment) and led the technical development of the Community-based Management of Acute Malnutrition report for monitoring programs to manage malnutrition in emergencies (*41*). In the communicable diseases sector, ERRB helped develop the evaluation tool

for tuberculosis in resource-limited, refugee, and postconflict settings (https://www.cdc.gov/globalhealth/healthprotection/errb/researchandsurvey/tbtool.htm). In the sexual and gender-based violence sector, branch staff contributed to the guidelines for integrating gender-based violence interventions in humanitarian action (http://gbvguidelines.org/wp/wp-content/uploads/2015/09/2015-IASC-Gender-based-Violence-Guidelines_lo-res.pdf). Across these and other sectors, in settings where the evidence base for interventions is limited, CDC focuses on strengthening the accuracy of data to build a solid evidence base for interventions to guide humanitarian response, enhance global health security, and prevent morbidity and mortality.

Third, effective emergency responses must adapt to changing needs of emergency-affected populations. Humanitarian emergencies, especially CEs, which exacerbate the fragility of politically weak and unstable regions, could last several years without a clear endpoint. Although dramatically elevated mortality rates might decrease as a CE moves from an acute emergency to a postemergency phase, populations continue to be vulnerable to many of the same health risks. As the humanitarian response evolves and becomes better established, responders might need to strengthen disease surveillance, review and interpret public health data, and improve capacity of local or national public health systems. Responders must maintain a commitment to improving the function and resilience of public health systems within these fragile settings.

Fourth, ERRB's work supports the work of CDC to prevent, detect, and respond to public health threats in fragile states under conditions that can result in regionally destabilizing effects and threaten global health security. Responding effectively requires that ERRB and other responders recognize 3 global patterns in population displacement: urbanization of the displaced, a shifting disease burden that includes noncommunicable diseases, and increasing security restrictions in areas of displacement. Understanding the unique aspects of urbanization of the displaced, moving away from the rural camp–based models of the past, suggests the need to change epidemiologic methods of surveillance and population assessment. In addition, because the displaced are increasingly likely to need assistance for noncommunicable, chronic diseases and access to long-term health services, compared with displaced populations in the past (*9*), the humanitarian emergency response community's areas of expertise must expand to include this sector. Increasing security restrictions have sometimes prevented, and will likely continue to prevent, CDC staff and the humanitarian community from physically accessing certain displaced populations. Furthermore, CDC is the public health agency of the US government and not a humanitarian agency, and thus, ERRB's responses are limited in ways that those of humanitarian agencies are not. These limitations include where, under what circumstances, and with which partners CDC staff can work. To address these limitations, ERRB staff is working to formalize remote support and program evaluation without sacrificing quality or comprehensiveness of assistance. More broadly, however, ERRB relies on humanitarian agencies to continue using epidemiologically sound public health approaches to guide evidence-based, effective interventions when CDC is precluded from responding.

Finally, ERRB responses show that response expertise is most useful when deployed early in an emergency and with a sustained presence. To that end, ERRB's Global Rapid Response Team quickly matches needs in the field with expertise available from within ERRB and across the entire CDC, and these responders can provide longer-term support. In its first year of existence, the Global Rapid Response Team deployed >200 staff members to various emergency responses, including for Hurricane Matthew in Haiti in October 2016.

As the numbers affected by and intensity of humanitarian emergencies increase, ERRB and other response organizations must provide broader assistance. To that end, ERRB collaborates with partners; contributes to epidemiologic tools to be used in humanitarian emergencies; and, through the Global Rapid Response Team, responds more quickly and with more staff. The next steps for ERRB and other responders include improving capacity and resilience of public health systems in fragile states; understanding the public health implications of long-term, urban-based displacements; adding a focus on noncommunicable diseases; and providing remote epidemiologic support in a systematic way. In settings where ERRB staff, as representatives of a US government agency, cannot respond, CDC's evidence-based interventions for emergencies are still implemented because of branch efforts in building local capacity for emergency response and training public health practitioners who then move on to work with humanitarian agencies. In these ways, ERRB continues to apply public health science to save lives in humanitarian settings while also working on the forefront of response-purposed detection and preparing a global health response workforce.

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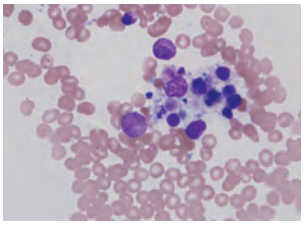
February 2014: **High-Consequence Pathogens**

- Poxvirus Viability and Signatures in Historical Relics
- *Anncaliia algerae* Microsporidial Myositis
- Human Antibody Responses to Avian Influenza A(H7N9) Virus, 2013
- Seven-Valent Pneumococcal Conjugate Vaccine and Nasopharyngeal Microbiota in Healthy Children
- Novel Paramyxovirus Associated with Severe Acute Febrile Disease, South Sudan and Uganda, 2012
- Subtyping *Cryptosporidium ubiquitum*, a Zoonotic Pathogen Emerging in Humans

- Monitoring Human Babesiosis Emergence through Vector Surveillance, New England, USA
- Genomic Variability of Monkeypox Virus among Humans, Democratic Republic of the Congo
- Lymphocytic Choriomeningitis Virus in Employees and Mice at Multipremises Feeder-Rodent Operation, United States, 2012
- Fungal Endophthalmitis Associated with Compounded Products

- Andes Hantavirus Variant in Rodents, Southern Amazon Basin, Peru
- Human Cutaneous Anthrax, Georgia 2010–2012
- Melioidosis Caused by *Burkholderia pseudomallei* in Drinking Water, Thailand, 2012
- Fatal Systemic Morbillivirus Infection in Bottlenose Dolphin, Canary Islands, Spain
- Co-circulation of West Nile Virus Variants, Arizona, USA, 2010
- Replicative Capacity of MERS Coronavirus in Livestock Cell Lines
- Investigation of Inhalation Anthrax Case, United States
- Genetic Characterization of Coronaviruses from Domestic Ferrets, Japan
- Crimean-Congo Hemorrhagic Fever Virus, Greece
- Trace-Forward Investigation of Mice in Response to Lymphocytic Choriomeningitis Virus Outbreak



- Rift Valley Fever Outbreak, Southern Mauritania, 2012

EMERGING INFECTIOUS DISEASES https://wwwnc.cdc.gov/eid/articles/issue/20/2/table-of-contents

Establishment of CDC Global Rapid Response Team to Ensure Global Health Security

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The 2014–2016 Ebola virus disease epidemic in West Africa highlighted challenges faced by the global response to a large public health emergency. Consequently, the US Centers for Disease Control and Prevention established the Global Rapid Response Team (GRRT) to strengthen emergency response capacity to global health threats, thereby ensuring global health security. Dedicated GRRT staff can be rapidly mobilized for extended missions, improving partner coordination and the continuity of response operations. A large, agencywide roster of surge staff enables rapid mobilization of qualified responders with wide-ranging experience and expertise. Team members are offered emergency response training, technical training, foreign language training, and responder readiness support. Recent response missions illustrate the breadth of support the team provides. GRRT serves as a model for other countries and is committed to strengthening emergency response capacity to respond to outbreaks and emergencies worldwide, thereby enhancing global health security.

The need to detect and respond to disease outbreaks before they spread has long been recognized as a priority because uncontained outbreaks can rapidly proliferate into international emergencies (*1*–*3*). A jarring example was provided by the 2014–2016 Ebola virus disease (Ebola) epidemic in West Africa, in which ≈29,000 cases were identified and ≈11,000 patients died (*1*,*4*). Although most cases occurred in 3 countries, imported and locally transmitted cases were confirmed in 7 others, including the United States (*5*). This experience highlighted needs for improved international collaboration and coordination and stronger national response capacity to rapidly detect and control major health threats at their source to ensure global health security (*3*,*6*–*10*).

The 2005 International Health Regulations (IHR 2005), adopted by the World Health Organization, dictate that all member states should be prepared to detect and respond to public health threats and emergencies (*11*). However, by 2012, <20% of countries reported full compliance with IHR 2005 (*12*). To accelerate progress, several member states and international partners launched the Global Health Security Agenda, which outlines specific actions that countries can take to meet IHR 2005 requirements (*6*,*7*,*13*–*15*). The US Centers for Disease Control and Prevention (CDC), in coordination with other US government agencies and global partners, is using its expertise and the Global Health Security Agenda framework to assist partner countries and strengthen global health security (*16*).

CDC has a long history of responding to global public health emergencies, including polio and severe acute respiratory syndrome. It is internationally recognized for its expertise in disease detection, investigation, diagnosis, monitoring, and control, as well as management of public health emergencies (*16*). Several groups within CDC work closely to identify and respond to public health threats. The Global Disease Detection Operations Center (GDDOC) is dedicated to the detection and monitoring of global public health events of international importance (*17*). GDDOC links external requests for assistance with the appropriate disease-specific CDC subject matter experts, who respond frequently to domestic and international outbreaks of diseases in their program domains. GDDOC also serves as an agency liaison to the Global Outbreak Alert and Response Network (GOARN) and supports the mobilization of subject matter experts through GOARN. In the field, responders work closely with governments and partners, including within Incident Management System structures or health clusters when established. Although mobilized CDC responders do not provide medical care, such activities are coordinated with organizations providing patient care.

Before the Ebola epidemic, when response operations exceeded subject matter expert program capacity, surge staff from the Epidemic Intelligence Service and other CDC programs were engaged and coordinated by the CDC Division of Emergency Operations (DEO). For larger, complex public

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health responses, the CDC director can authorize the activation of an agency-level Incident Management System, supported by the CDC emergency management subject matter experts in DEO and ordinarily based in the CDC Emergency Operations Center (EOC) (*18*). DEO also provides logistical and other support to response operations funded by GDDOC without activating the Incident Management System. At the time of the Ebola epidemic, CDC lacked a formal pool of on-call, trained responders who could rapidly mobilize for extended periods and in large numbers.

In July 2014, CDC activated its Incident Management System in response to the Ebola epidemic; as the largest agencywide response ever, it tested the limits of the agency response capacity (*19*). During July 9, 2014–March 31, 2016, ≈4,000 CDC staff participated in the response in Ebola-affected countries; in countries at high risk for Ebola introduction; from CDC headquarters in Atlanta, Georgia, USA; or through other partner organizations (*1*). By March 31, 2016, CDC had supported ≈2,000 mobilizations of 1,400 personnel providing wide-ranging technical support, for ≈80,000 person-days of mobilization time (*19–23*).

The size, scale, severity, and duration of the Ebola response highlighted key challenges to the efficiency and effectiveness of international emergency response efforts (Table). Specifically, greater support from the international community was needed because of limited national capacity of affected countries to detect and respond to the outbreak, fundamental aspects of IHR 2005, and the diminishing healthcare capacity over the course of the epidemic (*1*). Despite CDC experience regularly providing assistance for smaller, shorter outbreaks, sustaining support over 21 months proved difficult. Because of limited CDC presence before the epidemic, weak or underdeveloped relationships with governments and partner organizations in affected countries hindered response coordination. Short mobilizations (typically 30 days) and frequent staff rotation in the field also disrupted development of long-standing relationships and continuity of response. However, longer mobilizations of such a large workforce could hamper staff members' regular duties, potentially affecting other CDC programs (*1*,*19*,*20*). Additional challenges included identifying staff with the appropriate technical skills and foreign language abilities who were mentally and emotionally prepared for the austere conditions and ready and available to mobilize (*19*,*20*).

The challenges observed during the Ebola response underscored the need for a cadre of highly trained and experienced personnel who can rapidly mobilize to respond for extended periods (*20*). To address these challenges, CDC established the Global Rapid Response Team (GRRT). We describe the establishment of GRRT, team structure, main activities, case studies, and lessons learned.

Establishment of GRRT

Before the Ebola epidemic ended, CDC began investing in its capacity to rapidly respond to public health emergencies.

Table. Challenges encountered during response to the 2014–2016 Ebola epidemic in West Africa and GRRT mitigation strategies

Challenge	GRRT strategy
Limited in-country capacity to detect and respond to disease outbreaks (*1*)	Support the development of national outbreak detection and response systems
Wide range of technical expertise required to address needs of a large outbreak response (*1*)	Recruit team members with a wide range of technical expertise and experience Train responders in multiple technical areas for high-risk diseases
Establishing working partnerships with governments and partner organizations for more efficient coordination (*1*,*19*,*20*)	Train responders on working with partner organizations, incident management systems, cultural sensitivity, and foreign languages Recruit dedicated, ready responders who can mobilize for up to 6 mo for stronger partner relationships and improved coordination
Short mobilizations (traditionally 30 d) and frequent rotation of staff disrupted continuity of response activities (*19*,*20*)	Recruit dedicated responders who are available and ready to mobilize for up to 6 mo if needed Expand the typical mobilization length of those in leadership roles Develop best practices and systems for information management in field response
Responder preparation and readiness (*19*)	Strengthen safety, security, and responder wellness training through a GRRT orientation Support continuous learning by offering frequent technical trainings on priority topics Track responder international travel–related mobilization requirements, training, and clearance compliance Obtain supervisor preapproval for mobilizations during on-call months
Identifying appropriate responders (*19*)	Roster GRRT responders and tracking skills and experience to match staffing needs
Limited foreign language capacity (*20*)	Develop a program to develop and validate foreign language capacity
Logistical support for field efforts (*19*)	Roster a group of dedicated and surge logisticians who can mobilize to provide support directly to responders in the field or coordinate with Atlanta-based logistics personnel to provide support

*GRRT, Global Rapid Response Team.

In June 2015, CDC launched GRRT to address many of the challenges recognized during the Ebola response and to support other countries when their national response capacity is overwhelmed. Housed within the Emergency Response and Recovery Branch (ERRB), Division of Global Health Protection, at the CDC Center for Global Health, GRRT is an agencywide asset mandated to strengthen emergency response capacity. GRRT stands ready to provide technical and nontechnical support for public health responses worldwide; it is the result of collaboration across CDC.

GRRT Team Structure

GRRT comprises a small group of dedicated responders and a large group of agencywide surge staff. This model enables effective response to common events with a small number of experts while the team prepares for larger, rare events that necessitate substantial response. A total of 18 dedicated responders with public health emergency response expertise can immediately mobilize and remain in the field for extended periods. Included on this Atlanta-based team are multilingual epidemiologists with expertise in public health and humanitarian emergencies, logisticians who support GRRT activities and coordinate with DEO during a response, highly experienced team leaders, and support staff. Outside Atlanta, 1 regional emergency advisor in West Africa is tasked with engaging national, regional, and global partners to build capacity to detect and respond to health threats in the region. This group of dedicated responders answers the need to improve response time for emergencies, establish stronger long-standing relationships with governments and key partners, and reduce disruption to the continuity of response activities from staff turnover in the field.

GRRT surge capacity comprises >400 CDC staff members from around the agency; the goal is to support an emergency response with up to 50 staff members on short notice. Nearly 40 of the surge staff members routinely respond to humanitarian emergencies and build public health capacity as part of their regular duties in ERRB. They provide expertise in nutrition, emergency preparedness, surveillance, mental health, reproductive health, water, sanitation, and hygiene. The remaining surge staff vary widely in technical, language, and leadership skills and experience levels. They were recruited from 15 CDC centers, field personnel staff with state and local health departments, and overseas offices. International experience of the surge staff is a median of 2 years (mean 5 years), totaling 1,577 years combined. More than half have emergency response experience and ≈13% report having expertise in ≥1 foreign language. The most common occupations are epidemiologist, health scientist, public health advisor, and health communicator; surge staff have experience in nearly 30 different occupational areas.

Balancing the need to mobilize large numbers of agency staff, thereby possibly hindering their regular duties, with the need to ensure that existing programs maintain their operations is challenging (*19*). To address both needs, surge staff are on call 2 months each year for emergency mobilizations. The assignment of these on-call months is determined by staff availability (avoiding months in which regular duties or personal needs require the staff to be in the home office) while evenly distributing the technical skills, foreign language, and experience levels across months. The resulting roster lists at least 50 surge staff with a similar distribution of skills and experience who are on call for mobilization each month.

GRRT Activities

Requests for assistance come from within CDC and from external partners. After receipt, requests are evaluated to determine the appropriate response mechanism. Requests meeting specific criteria are addressed through standard response mechanisms (e.g., GDDOC or subject matter expert mobilizations). GRRT reviews requests that do not meet the criteria or exceed capacity of other CDC groups. Decisions to respond are based on, among other considerations, the urgency, public health impact, and availability of appropriate staff to fill the request. After the decision to respond is made, responders are selected according to their skills, experience, and availability.

From September 1, 2015, through December 31, 2016, GRRT responders were mobilized 291 times for 10,148 person-days to work in 35 countries, territories, and the CDC EOC (Figure). Most of the mobilization time was spent responding to outbreaks of Zika virus infection (65.0%), yellow fever (9.4%), Ebola (4.3%), cholera (3.9%), polio (0.5%), and measles (0.5%). The remaining time went to natural disasters (Hurricane Matthew [12.8%] and wildfires in Indonesia [3.2%]). Responders aligned themselves with existing response activities, working directly with ministries of health, the World Health Organization (WHO), CDC country offices, and other partners.

In addition to response activities, GRRT collaborated with ministries of health and external partners, such as the Africa CDC and the West African Health Organization, to assess and build national and international capacity to detect and respond to health threats, improving IHR compliance (320 person-days mobilized; median mobilization length 9 days). Activities included supporting the WHO Joint External Evaluations (*24*), developing rapid response team guidance, and facilitating response-related trainings.

Within CDC, GRRT works to build a sustainable, trained workforce. GRRT has designed a comprehensive training curriculum for surge staff that includes safety, security, soft skills, and technical training. GRRT increases responder readiness for rapid mobilization by defining and tracking training and logistical criteria. Continuing education

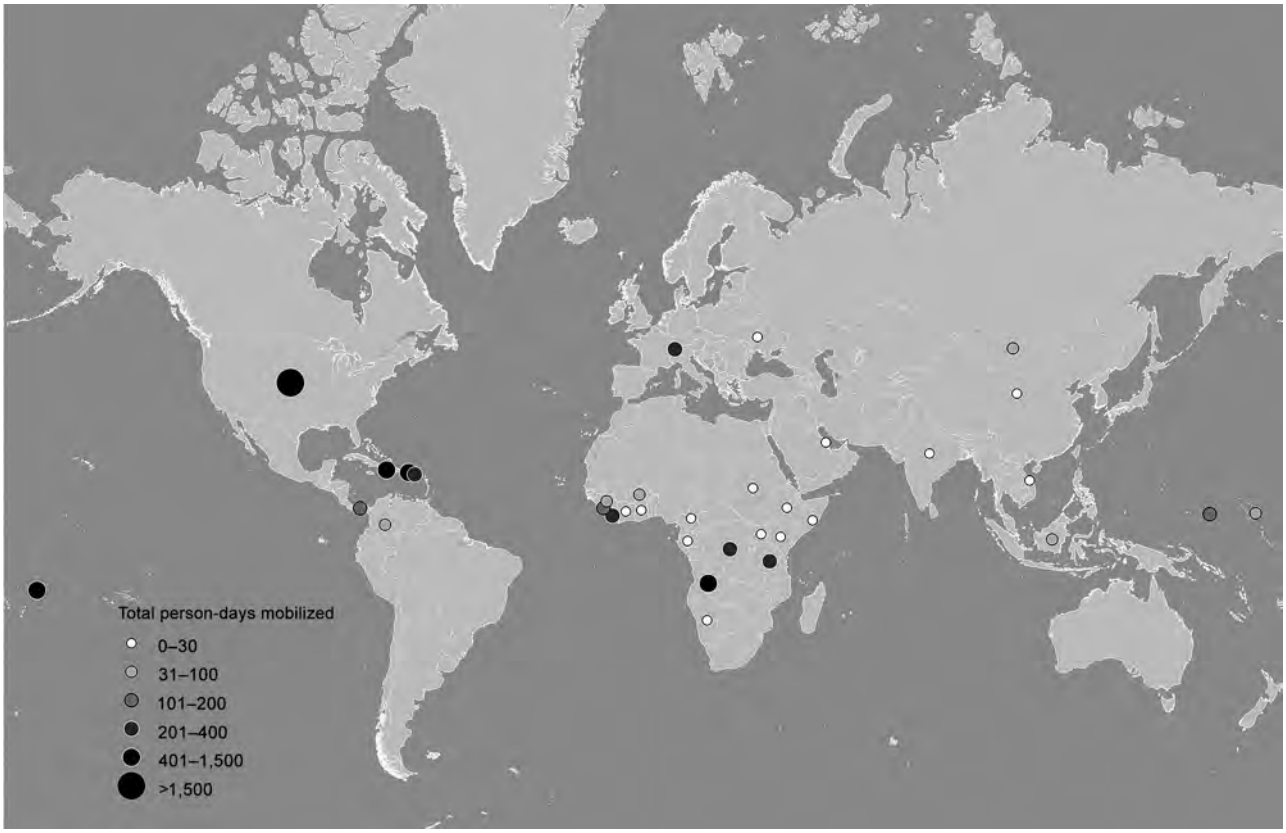

Figure. Global Rapid Response Team personnel mobilizations, September 2015–December 2016.

is provided monthly for additional training opportunities beyond the baseline training received during a 1-day orientation. These trainings are hosted by subject matter expert groups throughout the agency and feature a combination of scientific topics, role-specific technical content for the field, interpersonal skills, and situational awareness updates depending on current emergency context. GRRT is also developing training focused on the principles of field team leadership in international response; the aim is preparing leaders to apply Incident Management System principles during mobilization while navigating the nuances of international field response. To enhance the agency's foreign language capacity, GRRT provides foreign language training opportunities online and in classrooms. Efforts to standardize foreign language testing are under way.

Case Studies

To illustrate the breadth of GRRT's response work and its influence on agency response capacity, we describe selected responses to the Zika virus epidemic, urban outbreaks of yellow fever, and Hurricane Matthew in Haiti. Case studies demonstrate GRRT ability to support large complex outbreak responses, fill response needs when CDC expert capacity is strained, and manage smaller responses without EOC activation.

2015–2016 Zika Virus Response

In May 2015, an outbreak of Zika virus disease was reported in Brazil. In October, unusually high rates of birth defects, particularly microcephaly, were reported in areas with Zika virus transmission (*25*). By January 2016, Zika virus had spread to 14 countries and territories in Latin America and the Caribbean, and CDC activated an Incident Management System to respond to the outbreak (*26*). To support the response and address external requests for assistance, GRRT coordinated closely with subject matter experts, GDDOC, and DEO.

The complex Zika virus response, with its expansive affected geographic area and multidisciplinary technical needs, tested the CDC emergency response capacity soon after the Ebola experience. Investigations into the modes of transmission, birth defects associated with infection, and effective interventions required subject matter experts in vectorborne diseases, maternal and child health, reproductive health, and birth defects. Laboratorians strengthened Zika virus testing capacity and improved existing diagnostic tools. Health communication specialists developed messages in multiple languages for varied audiences, balancing the relatively mild symptoms of infection experienced by most persons with the devastating consequences of infection during pregnancy (*26*).

GRRT supported the agency response by mobilizing 117 responders to 9 countries and territories for 151 mobilizations and 6,597 person-days. A total of 69 mobilizations and more than half of the response time (3,556 person-days) were in the CDC EOC, where responders worked in Incident Management System leadership positions and as subject matter experts. The GRRT primary focus is international response, and responders are trained to work within varying cultural and environmental conditions outside the continental United States; however, the needs for assistance resulted in ≈90% of GRRT response time occurring in affected US territories and freely associated states. The GRRT roster, searchable by technical and language skills, facilitated the rapid identification of appropriate responders to fill response needs, particularly for speakers of Spanish and Portuguese, key languages in many of the affected areas. Although WHO declared the end of the emergency in November 2016 (*27*), GRRT will support CDC Zika virus response activities until no longer needed.

2016 Yellow Fever Response

In January 2016, the Angola Ministry of Health alerted WHO of an urban outbreak of yellow fever in Luanda Province (*28*). Because of active cross-border travel in the region, yellow fever cases spread to neighboring Democratic Republic of the Congo (DRC). In March 2016, the DRC Ministry of Health notified WHO of another yellow fever outbreak.

The CDC GDDOC closely monitored the evolution of the outbreak and coordinated mobilization needs with GRRT. Traditionally, the CDC response to a request for support would be led directly by subject matter experts; however, at the time, these experts were already fully engaged in the CDC Zika virus response and had limited capacity to lead another vectorborne disease response. Therefore, GRRT, in close coordination with GDDOC and anchored by expert guidance from CDC subject matter experts, contributed to the requested technical assistance and surge presence in the field.

During April–November 2016, GRRT mobilized 15 responders to Angola for 742 person-days and 7 responders to DRC for 211 person-days. Responders, working closely with expert guidance from headquarters, provided epidemiologic and management support to country ministries of health; led the interagency Incident Management System in the field on behalf of WHO; led field investigations and epidemiologic surveillance activities; and supported logistical needs, border health assessments, and a mass vaccination campaign. Four responders were mobilized to WHO headquarters to coordinate with and support the WHO yellow fever outbreak response. By August 2016, the last confirmed cases of yellow fever were reported, and the disease did not spread to additional countries. The last GRRT mobilization ended in November 2016.

The yellow fever response highlighted the benefits of agency surge capacity, particularly when specialized technical expertise is needed for multiple responses in multiple locations. The response also underscored the benefits of accurately identifying responders with high-level foreign language fluency but demonstrated the need to strengthen language capacity. Fluent speakers of Portuguese and French were identified for mobilization to Angola and DRC, respectively. However, because insufficient numbers of Portuguese speakers were available, fluent Spanish speakers partially filled the language gap.

2016 Haiti Hurricane Matthew Response

On October 4, 2016, Hurricane Matthew, a category 4 storm, made landfall in southwestern Haiti, causing major damage and flooding, killing at least 540 persons, and displacing ≈175,000 persons (*29*,*30*). Torrential rains washed away roads, bridges, and crops, threatening food security, water safety, telecommunication capabilities, and medical services (*29*). The hurricane devastated healthcare facilities, including 46 cholera treatment centers (*29*), and disrupted key public health programs.

After the 2010 earthquake in Haiti, GRRT surge staff, particularly ERRB responders, had experience in Haiti, and a field response was coordinated with the CDC Haiti Country Office. Because the CDC EOC was already coordinating 3 simultaneous activations for Ebola, Zika virus, and polio, GRRT and ERRB implemented the Incident Management System in the field and in ERRB workspace at CDC headquarters. Simultaneously, the CDC National Center for Environmental Health activated an Incident Management System to coordinate the domestic response for the expected effects to the US coastline. To foster coordination within the agency, both activations, outside of the CDC EOC, were supported by DEO in the early phases of the response.

GRRT mobilized the first wave of responders to Haiti 2 days after the hurricane struck. In total, GRRT mobilized 31 responders to Haiti, 26 members to the Atlanta-based Incident Management System structure, and 2 liaisons to the US Agency for International Development Office of Foreign Disaster Assistance and the Pan American Health Organization. In total, 1,302 person-days were spent responding to Hurricane Matthew.

GRRT responders supported the response in a diversity of roles. Early in the response, while physical access to affected areas was still limited, GRRT members organized a rapid phone assessment to provide critical information on the current needs of affected populations. CDC responders partnered with the Haiti Ministry of Health to investigate cholera cases, assess damage to healthcare

facilities, and reestablish affected disease surveillance systems. Atlanta-based support staff mobilized to the CDC Haiti Country Office to support the Incident Management System structure, enabling the Haiti-based staff to fulfill their regular duties. At CDC headquarters, responders worked as Incident Management System staff coordinating the agency response and information managers for the CDC Haiti Country Office.

The Hurricane Matthew response demonstrated successful coordination of international and domestic response activities across the agency without burdening EOC staff. The GRRT/ERRB Incident Management System deactivated in November 2016, and the last mobilization for the Hurricane Matthew response ended in December 2016. An after-action review was conducted to evaluate the response and improve GRRT processes for future activations.

Lessons Learned

The lessons learned from the Ebola epidemic forced many national and international organizations to reevaluate their emergency response capacity and processes. At CDC, these lessons contributed to the development of GRRT, a cadre of highly trained and experienced staff members and resources that provide response and surge capacity for CDC international emergency response operations. GRRT dedicated response staff enable rapid and longer mobilizations to establish and sustain working relationships with governments and partner organizations and to improve continuity of response activities. The large roster of >400 team members fosters a diversity of skills and experiences, and tracking of team member profiles facilitates matching technical skills and language capacity with response needs. GRRT support for CDC staff preparation and deployment readiness improves the speed at which qualified responders can be mobilized. GRRT capacity-building activities support countries' progress toward IHR 2005 compliance, particularly around workforce development, personnel deployment, and emergency operations, in alignment with DEO and subject matter expert activities for other action packages.

Despite progress, several challenges remain. The Zika virus and yellow fever responses highlighted the need for strengthened language capacity. GRRT language training and targeted recruitment of highly proficient staff aim to address this gap; other language training options are being explored. CDC response capacity can be developed further by providing additional disease-specific technical training, particularly for high-risk pathogens and epidemic-prone diseases that may warrant a large-scale response. This training will build disease-specific response capacity and enable a limited set of subject matter experts to guide response activities in multiple areas, as was seen during the yellow fever response.

Moving forward, GRRT continues to evolve and seek new ways to improve international response capacity in coordination with international partners. Ongoing identification and rostering of responders with appropriate technical and language skills to fill response needs is critical for rapid response. The GRRT surge capacity roster will need to be maintained to keep responder information current and replenished with future qualified staff. CDC response mechanisms can be further improved through continued coordination with agency emergency response personnel and streamlined mobilization processes. To ensure a cohesive approach, GRRT will continue coordinating with external partners during emergency responses by identifying clear roles and responsibilities for staff (*20*). In addition, GRRT will continue supporting Global Health Security Agenda activities; building local, national, and regional response capacities; and supporting WHO, GOARN, and other international partners in global efforts toward development of international and regional public health rapid response teams. The lessons learned from the establishment of GRRT at CDC can serve as a model for the creation of similar response units in other countries.

Conclusions

The CDC GRRT was established to address lessons learned during the 2014–2016 Ebola epidemic. Since June 2015, GRRT has been actively engaged in strengthening agency and partner emergency response capacity by developing a capable emergency workforce. However, continuing these activities and sustaining the momentum of global health security requires ongoing resources to ensure that GRRT is ready to respond to future health threats. CDC is one of many global organizations that respond to outbreaks and emergencies; no one organization alone can effectively control global health threats. As the international emergency response community coordinates to build capacity around the world, GRRT will work diligently so that disease threats are rapidly detected, responded to, and controlled at their source, thereby ensuring global health security.

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Lessons Learned from Emergency Response Vaccination Efforts for Cholera, Typhoid, Yellow Fever, and Ebola

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Countries must be prepared to respond to public health threats associated with emergencies, such as natural disasters, sociopolitical conflicts, or uncontrolled disease outbreaks. Rapid vaccination of populations vulnerable to epidemic-prone vaccine-preventable diseases is a major component of emergency response. Emergency vaccination planning presents challenges, including how to predict resource needs, expand vaccine availability during global shortages, and address regulatory barriers to deliver new products. The US Centers for Disease Control and Prevention supports countries to plan, implement, and evaluate emergency vaccination response. We describe work of the Centers for Disease Control and Prevention in collaboration with global partners to support emergency vaccination against cholera, typhoid, yellow fever, and Ebola, diseases for which a new vaccine or vaccine formulation has played a major role in response. Lessons learned will help countries prepare for future emergencies. Integration of vaccination with emergency response augments global health security through reducing disease burden, saving lives, and preventing spread across international borders.

In emergency settings, countries must be prepared to respond to public health threats. Prompt vaccine delivery can be a major component of emergency response, especially for populations vulnerable to epidemic-prone, vaccine-preventable diseases (VPDs). Public health emergencies might be triggered by natural disaster; humanitarian emergency; a disease pandemic leading to health systems breakdown, as in the recent Ebola epidemic in West Africa in 2014; or by a specific VPD outbreak not contained by ongoing immunization services. During emergencies affecting health systems in general, vaccination services are frequently disrupted. Emergency vaccination campaigns aim to control VPD outbreaks, reducing the possibility of international spread and thereby enhancing global health security.

For countries to respond rapidly in emergency situations, planning for appropriate and effective vaccine delivery to at-risk populations is essential. The decision to engage in a vaccination response depends on several factors, including the risk for a VPD in the emergency situation, characteristics and availability of vaccines for response, and prioritization of vaccination in relation to other public health interventions (*1*). Once a decision is made for a vaccination response, additional issues need to be addressed, including regulatory barriers for unlicensed products, vaccine supply and stockpile access, appropriate cold chain capacity, and designation of roles and responsibilities based on in-country capacity and global partner involvement. Key responsibilities include overall emergency management, coordination of vaccination response, communications and social mobilization, monitoring and evaluation of vaccine implementation, and enhancement of surveillance for adverse events after immunization. To enable countries to respond rapidly to future emergencies, clearly outlining the command structure beforehand for these key responsibilities is essential.

Evaluation of emergency vaccination activities is a major component of the overall response efforts, necessary to refine ongoing activities and document lessons learned. Implementation research can close evidence gaps between licensure and programmatic use of new vaccines (*2*). Emergency vaccination has been well-described and evaluated for outbreak-prone VPDs such as polio, measles, meningitis, yellow fever, cholera, and hepatitis A (*3*). However, as new vaccines, new formulations, or new routes of administration for existing vaccines are developed, licensed, and prequalified by the World Health Organization (WHO), vaccination strategies must be evaluated and reevaluated to ensure the greatest effect for protecting vulnerable populations and preventing spread of disease.

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Prevention (CDC) is committed to supporting countries in emergency vaccine delivery planning, implementation, and evaluation in collaboration with other CDC divisions and with international partners. In this report, we highlight the work CDC has conducted to generate evidence that will shape future outbreak response vaccination strategies by using lessons learned specifically from cholera, typhoid, yellow fever, and Ebola. For these diseases, a new vaccine or new vaccine formulation has played a major role in emergency response. Lessons learned will help countries prepare for future emergency outbreak response and contribute to the broader goal of more rapidly containing public health emergencies caused by VPDs, thereby enhancing global health security.

Cholera

Cholera is an acute diarrheal infection caused by ingestion of toxigenic serogroups O1 and O139 of the bacterium *Vibrio cholerae*. The global burden of cholera is estimated to be 2.9 million cases and 95,000 deaths annually; most cases are reported to WHO from sub-Saharan Africa (*4*). More recently, since 2010, Haiti has made a major contribution to the global burden. Although cholera prevention and control measures have traditionally focused on cholera treatment and improving access to safe water, sanitation, and hygiene (WaSH), oral cholera vaccines (OCVs) have gained prominence as a major complementary tool in comprehensive cholera prevention and control. In 2010, WHO recommended the use of existing OCVs, preemptively in cholera-endemic settings to target high-risk areas or populations or reactively as part of outbreak response activities (*5*). In June 2013, WHO established a global OCV stockpile with an initial stock of 2 million doses with funding from multiple partners (*6*). In November 2013, the Global Alliance for Vaccines and Immunization endorsed funding support for the stockpile for 2014–2018 (*7*). As of March 2017, a total of 41 OCV campaigns have been conducted in 14 countries with vaccine from the global stockpile (*8*).

Three inactivated, whole-cell OCVs are prequalified by WHO and available for global use: Dukoral (killed whole-cell monovalent [O1] cholera vaccine with cholera toxin B subunit; Valneva, Lyon, France); Shanchol (modified killed bivalent [O1 and O139] whole-cell–only cholera vaccines; (Shantha Biotechnics, Hyderabad, India); and Euvichol (modified killed bivalent [O1 and O139] whole-cell–only cholera vaccines; Eubiologics, Seoul, South Korea) (*9*). Two of these vaccines, Shanchol and Euvichol, are available through the global stockpile. Shanchol and Euvichol are recommended for persons ≥1 years of age, including pregnant women (*10*), in a 2-dose schedule given ≥14 days apart. Both OCVs are safe, efficacious, and effective in multiple settings (*5,11,12*). Recently, a single dose of Shanchol showed an efficacy of 63% against severely dehydrating cholera in the short term (6 months), which has major implications for outbreak control (*13*).

CDC has conducted several evaluations of OCV use in emergency settings. In 2010, CDC collaborated with partners including WHO, the Pan American Health Organization, and others to review current evidence for OCV use in emergency settings and conduct real-time modeling to estimate the effect of using a limited supply of available OCV doses during a cholera outbreak in Haiti after the 2012 earthquake (*14*). In the postemergency period in Haiti, CDC conducted additional evaluations of the cholera response to inform future vaccination campaigns. These evaluations included OCV coverage surveys and precampaign and postcampaign knowledge, attitude, and practice (KAP) surveys (*15,16*). A postcampaign KAP survey showed an increase in availability of soap and handwashing stations but a decrease in reported treatment of drinking water, highlighting the need for comprehensive communication messages for cholera control during and, if feasible, after OCV campaigns.

In 2013, CDC supported the Thailand Ministry of Public Health in implementing and evaluating a preemptive 2-dose OCV campaign in a refugee camp. Coverage and precampaign and postcampaign KAP surveys showed a high degree of acceptability of the campaign, as well as improvements in WaSH behaviors (*17,18*). In 2015, a 2-dose OCV campaign was conducted in Iraq in response to a cholera outbreak affecting ≈255,000 persons living in selected refugee camps, internally displaced persons camps, and collective centers. After the campaign, CDC conducted a coverage survey in collaboration with WHO and the Iraq Ministry of Health; overall, 2-dose coverage was 87%, and 55% of respondents reported receiving other cholera prevention messages (*19*). This evaluation demonstrated the feasibility of successfully implementing an OCV vaccination campaign in a conflict setting as part of an integrated approach to cholera control.

Most recently, 1 million doses of Euvichol were released for use in hurricane-affected departments in Haiti after Hurricane Matthew in October 2016, the first release of Euvichol from the global stockpile. Approximately 830,000 persons in 18 communes were targeted for vaccination with a single dose, the largest single-dose campaign as well as the largest emergency stockpile release to date. CDC was part of the Haiti OCV taskforce that led monitoring and evaluation of the campaign. This effort included improving laboratory capacity for stool cultures and planning for a coverage survey and a single-dose effectiveness study in collaboration with the Ministry of Public Health and Population and other partners. Because of delays, the evaluations were not conducted; however, in-country staff were trained on field survey techniques and laboratory

methods for evaluation, which increased their capacity for future evaluation activities.

Athough OCV campaigns have clearly been demonstrated as feasible in emergency and cholera-endemic settings, additional evaluations will address evidence gaps. These gaps include single-dose effectiveness, effect of OCV (1 and 2 doses) on halting an outbreak and reducing disease burden, the effectiveness of a second dose in the setting of a prolonged dosing interval, and how to optimize the integration of OCV and WaSH for both short-term and longer-term cholera control in emergency and cholera-endemic settings. A single OCV dose might be particularly useful in emergency settings and might enable vaccination of a larger population in a shorter timeframe when a 2-dose delivery is challenging.

Typhoid

Typhoid (typhoid fever), which is caused by the bacterium *Salmonella enterica* serovar Typhi, is responsible for ≈11 million illnesses and 129,000 deaths globally each year (*20*). As is true for cholera, typhoid primarily occurs in southern Asia, sub-Saharan Africa, and parts of the Middle East and Latin America, where limited access to safe water, inadequate sanitation infrastructure, and poor hygiene practices, often as a result of rapid urbanization, favor transmission. Although most disease is endemic, these same factors give typhoid a high epidemic potential, and outbreaks occur periodically, including outbreaks caused by antimicrobial drug-resistant strains (*21–24*). Although most typhoid prevention and control efforts have focused on primary measures of WaSH, vaccines are a major complementary strategy. In 2008, WHO recommended use of existing typhoid vaccines for endemic disease control and outbreak control (*25*). More recently, however, a rapid global increase in antimicrobial drug resistance (*26,27*) has emphasized the need for more prompt, short-term prevention and control efforts using existing and newer-generation typhoid vaccines.

Two typhoid vaccines have been available for use in several countries since the 1990s. The first vaccine is a single-dose injectable polysaccharide vaccine based on the purified Typhi Vi antigen (ViPS vaccine), which is for use in persons ≥2 years of age. The second vaccine is a multidose, live attenuated, oral Ty21a vaccine available as a capsule formulation for persons ≥5 years of age. Both vaccines are safe, efficacious, and effective in multiple settings. A recently available newer-generation, single-dose, injectable typhoid conjugate vaccine (TCV) has several advantages over current polysaccharide vaccines, including a higher level of vaccine effectiveness, a longer duration of protection, an added booster response, and approval for use in children <2 years of age. Detailed information on the various vaccines is available elsewhere (*25,28,29*). Despite the large body of evidence and availability of the current typhoid vaccines, vaccine adoption and use has been limited globally.

CDC has been working with partners to plan, monitor, and evaluate emergency use of typhoid vaccine. In 2010, after a category 4 tropical cyclone in Fiji, the Ministry of Health of Fiji conducted an emergency typhoid vaccination campaign with the ViPS vaccine that targeted cyclone-affected areas as part of the postdisaster response. A small proportion of vaccine was also used in an area not affected by the cyclone but that had experienced a typhoid outbreak during the same period. CDC conducted an impact evaluation in collaboration with partners that showed reduction of disease burden in areas where a large proportion of the population was vaccinated compared with unvaccinated areas (*30*).

In a protracted outbreak in Kasese District in Uganda during 2008–2011, CDC coordinated discussions with multiple partners, including the Coalition Against Typhoid, the Uganda Ministry of Health Expanded Program on Immunization, and Sanofi Pasteur (Lyon, France), regarding vaccine use for outbreak control. CDC investigated the protracted nature of the outbreak (*31*) and conducted a cost-effectiveness modeling exercise to support the need for emergency vaccination (*32*). However, a global vaccine shortage caused by a recall on certain lots of the Sanofi ViPS vaccine precluded vaccine use.

CDC is working with WHO in India; Stanford University (Stanford, CA, USA); local hospitals in Navi Mumbai, India; and the Municipal Corporation (local government body) to evaluate the planned introduction of TCV in a public sector program targeting ≈400,000 children 9 months–14 years of age. Although vaccine introduction will occur in a disease-endemic setting, evaluation findings, including safety, effectiveness, acceptability, and impact will provide information for future targeting and use of TCV in emergency settings.

Yellow Fever

Yellow fever is a viral hemorrhagic fever caused by the yellow fever virus (genus *Flavivirus*), which is transmitted by *Haemagogus* and *Aedes* spp. mosquitoes. Yellow fever is endemic to tropical regions of 47 countries in Africa and South and Central America; >90% of cases and deaths are in Africa (*33*). The number of reported cases is believed to be greatly underestimated because of challenges in surveillance and diagnosis. Yellow fever caused ≈51,000–380,000 severe cases and 19,000–180,000 deaths in Africa in 2013 (*34*).

Current yellow fever vaccines are live attenuated vaccines manufactured from 2 substrains of the 17D strain. A standard 0.5-mL dose is highly efficacious; ≈97.5% of recipients showed development of protective levels of antibodies (*35*) and life-long protection. Many disease-

endemic countries have introduced yellow fever vaccine into their childhood immunization schedules since the late 1990s, with or without a preventive mass vaccination campaign for all ages near the time of introduction. However, there are huge gaps in population immunity because some countries have not introduced yellow fever vaccine, coverage in routine immunization programs of many countries is suboptimal, and most adults in countries that did not conduct mass preventive campaigns are unprotected. Furthermore, recent changes in environmental and agricultural conditions have contributed to a worldwide resurgence in the *Ae. aegypti* mosquito, the primary vector in urban settings (*33*). Large urban outbreaks can occur when infected persons move to densely populated urban settings in which population immunity is low and *Ae. aegypti* mosquitoes are present (*33*).

Because outbreak response needs are difficult to predict, a global stockpile of yellow fever vaccine has been maintained since 2001; >90 million doses have been distributed (*36*). The 6 million–dose stockpile had to be replenished multiple times in 2016 because of outbreak response vaccinations in Angola and the Democratic Republic of the Congo (DRC), which led to the use of almost 30 million doses of vaccine (*37*). During the response, a large-scale campaign targeted 8 million persons in Kinshasa, the capital of the DRC, in August 2016. At that time, however, an insufficient vaccine supply was available globally. Fractional-dose yellow fever vaccine administered by subcutaneous and intramuscular injections was evaluated in 2 small, controlled studies in healthy adults (*38,39*), but its use in a mass campaign had never been evaluated. With guidance from WHO, the DRC decided to administer a fractional (1/5; 0.1 mL) dose of yellow fever vaccine to all nonpregnant adults and children ≥2 years of age. Pregnant women and children 9 months–2 years of age received the full dose.

To evaluate whether the immunogenic response observed in persons vaccinated during the mass campaign was sufficient to confer protection against yellow fever virus, CDC partnered with the US Agency for International Development and the Institut Nationale de Recherche Biologique (Kinshasa), the national reference laboratory in the DRC, to conduct a cohort study of 760 persons eligible for vaccination during the campaign. Participants provided blood samples before and 28 days after vaccination; another sample will be collected 1 year after vaccination. If the fractional dose is found to induce a sufficient immune response to confer protection, this result would provide supporting evidence for fractional-dose yellow fever vaccination as a strategy to control outbreaks of yellow fever.

The evaluation in the DRC will provide immunogenicity data on adults and children ≥2 years of age. However, this evaluation will not provide immunogenicity data for fractional-dose vaccination in children <2 years of age. CDC has partnered with the Uganda Viral Research Institute (Entebbe, Uganda) and the Infectious Diseases Institute of Makerere University (Kampala, Uganda) to conduct a randomized controlled trial of fractional-dose yellow fever vaccination in children 9–23 months of age. This trial will provide immunogenicity data needed to determine whether fractional-dose vaccination performs similarly to a full dose in the youngest age group eligible for yellow fever vaccination, further adding to the body of knowledge on the use of fractional-dose vaccination for outbreak response.

Ebola Virus Disease

Human infection with Ebola virus causes hemorrhagic fever disease with a high case-fatality rate (*40*); sporadic outbreaks have been reported since 1976 (*41*). Within the genus *Ebolavirus* (family *Filoviridae*), 4 species are known to cause human disease: *Zaire ebolavirus* (ZEBOV), *Sudan ebolavirus*, *TaiïForest ebolavirus*, and *Bundibugyo ebolavirus*. Human-to-human transmission occurs through percutaneous or mucous membrane contact with blood or other body fluids of infected persons (*42,43*).

The Ebola outbreak in West Africa during 2014–2016 was the largest filovirus disease outbreak recorded and was caused by a ZEBOV strain. Over 24 months, this outbreak caused >28,000 suspected cases and >11,000 deaths in Guinea, Liberia, and Sierra Leone (*44*). Ebola vaccine delivery to at-risk populations during final stages of the outbreak was possible because of expedited vaccine development driven by the gravity of the public health emergency. During the outbreak, several clinical trials or investigational expanded access protocols used a single-dose, recombinant, replication-competent, vesicular stomatitis virus (VSV)–based vector encoding the ZEBOV glycoprotein (rVSV-ZEBOV). WHO and partners conducted a cluster-randomized ring vaccination trial in Guinea that showed 100% efficacy (95% CI 68.9%–100.0%) for randomized clusters of at-risk adults in rings, including contacts and contacts of contacts, of an infected person (*45*). Most adverse events were mild and self-limited; 2 serious adverse events (fever and anaphylaxis) were judged to be related to vaccination, and both case-patients recovered. This vaccine was offered to healthcare workers (HCWs) as part of clinical trials and as part of expanded access emergency ring vaccination for new clusters that arose in all 3 countries. The CDC Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE) evaluated the largest safety sample in which no vaccine-associated adverse events were observed for nearly 8,000 participants (*46*). Although the vaccine has not yet been licensed, available evidence supports the efficacy and safety of the rVSV-ZEBOV vaccine in ring vaccination. Thus, rapid access to vaccine for at-risk groups is regarded by the public health

community as a major adjunctive measure for consideration in future outbreak response.

CDC is engaged in assisting countries to incorporate vaccination delivery into emergency response plans. The development of guidelines and protocols for Ebola vaccination response will help ensure that activities are standardized, evidence-based, and well-coordinated with overall Ebola outbreak response efforts. Availability of a standard protocol approved for at-risk countries would facilitate evaluation of the vaccination response during an emergency.

CDC will support implementation research needed to inform policy decisions about use of an unlicensed Ebola vaccine, including additional regulatory approvals and requirements needed in the setting of expanded access, feasibility of vaccine introduction, potential interaction with ongoing immunization procedures or schedules, and vaccine acceptability and hesitancy in communities. Strategies to ensure adequate cold chain capacity for vaccine storage and transport to field sites will also need evaluation because the rVSV-ZEBOV vaccine requires storage at -60°C, which is not a standard capacity for national immunization programs in Africa. Stability data from the manufacturer (Merck & Co., Kenilworth, NJ, USA) suggest that single-dose vials (2×10^7 PFU/mL) are stable for 2–8 days at 4°C (Merck & Co., pers. comm., 2017), which would improve the feasibility of using standard cold chain equipment to implement vaccination in remote areas.

Ring vaccination is the only vaccination strategy for Ebola with available effectiveness data to support its use (*45*). Additional response strategies include geographically targeted and HCW vaccination, but more research is needed to explore the effect of these strategies if used in the future. Geographically targeted vaccination may be most appropriate if areas of transmission are well-defined and densely populated. Vaccination strategies targeted geographically or focused on HCWs are also likely to be more feasible to implement quickly from fixed vaccination sites and would not require the high-quality contact tracing needed for ring vaccination. Postvaccination coverage evaluations would be used to assess success of the vaccination strategy. Preemptive vaccination for HCWs in high-risk countries is a strategy that might prevent another large-scale outbreak; data to support duration of effectiveness are needed to inform timing of revaccination and potential effects.

Licensure of the rVSV-ZEBOV vaccine is not expected until 2019, and additional candidate vaccines continue to be studied in clinical trials (*47–51*). During the prelicensure period, plans for emergency ring vaccination with the rVSV-ZEBOV vaccine should take into account new evidence and guidance to support use of alternate vaccine candidates or strategies. CDC has contributed to the development of preliminary guidance for implementation of a licensed Ebola vaccine as part of the Global Ebola Vaccine Implementation Team led by WHO (*52*).

Conclusions

CDC emergency vaccine implementation activities enhance global health security by enabling more rapid containment of VPD outbreaks at their source. These activities have built in-country response capacity and have provided valuable evidence to inform future emergency vaccine delivery for the countries involved and globally for other countries at risk for VPD outbreaks. CDC has contributed to development and updating of guidelines that countries and partners use for response planning efforts; examples include an updated WHO position paper for cholera vaccines expected in 2017, an updated WHO position paper for typhoid vaccines expected in 2018, and the WHO Global Ebola Vaccine Implementation Team guidance document for Ebola vaccine implementation (*50*). Planning and evaluation of emergency vaccination present distinct challenges for predicting needs before an emergency, anticipating ways to expand vaccine availability during critical global shortages, and delivering and evaluating new products. The Ebola epidemic accelerated vaccine clinical trials and could set a precedent for rapid clinical development of countermeasures for future infectious disease outbreaks. Integration of vaccination with emergency response to VPD outbreaks will continue to augment global health security by reducing disease burden and mortality rates for vulnerable populations and by averting pathogen spread across international borders. Lessons learned from emergency vaccine implementation might inform response with new vaccines in the development pipeline, such as vaccines against Middle East respiratory syndrome coronavirus, Lassa virus, Marburg virus, and Zika virus, for which rapid response would also be required.

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CDC Safety Training Course for Ebola Virus Disease Healthcare Workers

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Response to sudden epidemic infectious disease emergencies can demand intensive and specialized training, as demonstrated in 2014 when Ebola virus disease (EVD) rapidly spread throughout West Africa. The medical community quickly became overwhelmed because of limited staff, supplies, and Ebola treatment units (ETUs). Because a mechanism to rapidly increase trained healthcare workers was needed, the US Centers for Disease Control and Prevention developed and implemented an introductory EVD safety training course to prepare US healthcare workers to work in West Africa ETUs. The goal was to teach principles and practices of safely providing patient care and was delivered through lectures, small-group breakout sessions, and practical exercises. During September 2014–March 2015, a total of 570 participants were trained during 16 course sessions. This course quickly increased the number of clinicians who could provide care in West Africa ETUs, showing the feasibility of rapidly developing and implementing training in response to a public health emergency.

In 2014, epidemic Ebola virus disease (EVD) rapidly spread throughout West Africa; by August of that year, ≈2,600 EVD cases and 1,400 deaths had been reported (*1*). Widespread EVD transmission occurred in Guinea, Sierra Leone, and Liberia for several reasons. First, these countries had undergone years of civil war and unrest, which damaged an already fragile healthcare infrastructure and reduced the healthcare workforce (*2–4*), gravely limiting the countries' ability to rapidly respond to a growing epidemic (*5*). Second, EVD is a hemorrhagic fever readily transmissible in the absence of rigorous infection prevention and control (IPC) (*6*). Ebola virus is spread by direct contact with body fluids of patients or contaminated fomites (*7*). For outbreak control, isolation of patients from the community is essential (*8*). EVD patients can arrive at healthcare facilities with severe symptoms such as substantial dehydration from vomiting, diarrhea, or hemorrhage, requiring aggressive intravenous resuscitation (*9*). Third, the EVD epidemic placed medical workers themselves at risk. Few healthcare workers have cared for patients with such a severe and highly transmissible disease requiring this degree of stringent IPC. The close patient interactions that were needed put healthcare workers at risk for infection (*9*,*10*).

Personal protective equipment (PPE) serves as a physical barrier and can protect healthcare workers when used properly. However, PPE is only one IPC measure used to protect healthcare workers from EVD (*11*). Moreover, availability of PPE alone is not adequate for preventing infection. Without strict adherence to the complex processes of donning and doffing PPE and proper conduct while wearing PPE, transmission can still occur. Improper donning and doffing of PPE can result in self-contamination if unprotected mucous membranes or broken skin are exposed to infected body fluids (*12*). PPE doffing, in particular, carries high risk for self-contamination because of its complexity combined with healthcare worker fatigue after tiring shifts in an ETU (*12–14*). Fourth, the setting of this epidemic was unusual. Unlike previous Ebola outbreaks, which occurred predominantly in rural areas, the 2014 EVD epidemic occurred primarily in densely populated urban areas. Previous rural outbreaks had been controlled by isolating EVD patients from the community through early admission to healthcare facilities capable of managing the disease. In 2014, the rapid increase in the number of EVD patients early in the epidemic quickly overwhelmed the number of trained clinicians and healthcare facilities that could care for them (*5*).

By late August 2014, a total of 240 registered healthcare workers had acquired EVD and 120 had died (*15*). As the number of infected healthcare workers rose, medical staff became increasingly fearful of contracting EVD from

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patients. The World Health Organization (WHO) found risk of contracting EVD during this epidemic to be 21–32 times higher among healthcare workers than among non–healthcare workers (*16*). Some clinics and hospitals closed because of staff shortages or healthcare workers' unwillingness to work, exacerbating the lack of facilities (*17*).

Transmission models developed by the US Centers for Disease Control and Prevention (CDC) indicated that to halt the epidemic, ≈70% of EVD patients should be isolated in appropriate treatment facilities (*18*). The models projected that if transmission were not rapidly reduced, EVD cases in Liberia and Sierra Leone could reach 550,000 by January 2015 (*18*). A key component of the international response to the epidemic entailed deploying trained volunteer healthcare workers to EVD-affected areas to reduce community transmission by isolating EVD patients and providing care in a safe healthcare setting. To support this urgent need, CDC developed and implemented an introductory EVD safety training course to prepare volunteer US healthcare workers to work in West Africa Ebola treatment units (ETUs).

Few deploying clinicians had been trained in the infection control practices needed to provide EVD care safely in limited-resource settings, which are distinctly different from US hospitals. In August 2014, the only structured EVD training for healthcare workers was a 2-day course held in Brussels, Belgium, by Médecins Sans Frontières (MSF) (*19*). MSF acquired extensive EVD care experience in Africa and developed this course to share knowledge with staff deploying to respond to the epidemic (*20*–*22*). Given the urgency and need for international healthcare volunteers, demand quickly exceeded course availability. On August 26–27, 2014, three CDC members attended the MSF course in Brussels in anticipation of developing a US-based version of the training. After rapid course planning and development, CDC launched its first EVD Safety Training Course in Anniston, Alabama, USA, on September 22, 2014. We summarize the development and operation of the course.

Course Concept

The course objective was to introduce deploying healthcare workers to principles and practices of safely providing patient care in a West Africa ETU. Key learning objectives included understanding of the following: EVD modes of transmission, ETU structure and operation, ETU IPC procedures (proper PPE donning and doffing techniques, disinfection, sharps and waste management), and personal safety within ETUs (psychologic preparation, stress management, overheating while wearing PPE). The various organizations with which trainees would deploy stocked different types of PPE. Thus, our training strategy centered on teaching sound principles and methods to prevent disease transmission, rather than focusing on a particular type of PPE or protocol. We wanted to prepare volunteers for the complex and changing clinical and social environment in the center of a transmissible disease epidemic of unprecedented scope and severity. The course included classroom instruction and practical hands-on training in a realistically constructed mock ETU. At the time, West Africa ETUs were simple healthcare isolation units that combined a specific layout with rigorous IPC practices and offered patient isolation, diagnosis, and oral and intravenous rehydration therapy and medications. Therefore, we focused clinical management instruction on these topics.

The course provided introductory training as the first stage of a more comprehensive process, which involved further in-country mentoring under direct supervision of local or international staff with previous EVD experience. We designed a sustainable, repeatable course model that enabled efficient course implementation by sequential cohorts of instructors. Beginning in September 2014, the US-based 3-day course was offered weekly at the same location.

Staff and Setting

The initial course design team was a multidisciplinary 15-person unit comprising members who had attended the MSF Brussels course, infectious disease physicians, medical epidemiologists, instructional designers, and healthcare workers recently deployed to West Africa who had worked in ETUs or EVD-affected communities (returning responders). Course development incorporated input from experts in public health and EVD from CDC, MSF, and WHO and from US-based infection control experts. When the pilot course was launched, the team had grown to a 40-person unit including data managers, communication specialists, and logisticians.

The course was held at the US Federal Emergency Management Agency (FEMA) Center for Domestic Preparedness (CDP) in Anniston (https://cdp.dhs.gov/). CDP is an all-hazards training center equipped with classrooms, audiovisual equipment, dormitory-style lodging, and food and transportation services. The 124-acre campus has buildings and outdoor spaces well suited for the construction of austere mock West Africa ETUs for simulated exercises. CDP trains ≈45,000 emergency responders yearly and efficiently supported the rapidly expanding course. The location, 90 miles from CDC headquarters in Atlanta, Georgia, USA, enabled relatively convenient transportation of staff, supplies, and trainees.

Trainees

We assigned high priority to US healthcare workers scheduled to deploy to West Africa. We required that trainees have a license to provide clinical care, recent experience providing direct patient care, and affiliation with a governmental or nongovernmental organization responsible for travel to and

from West Africa. Healthcare workers included nurses, physicians, paramedics, physician assistants, and others who would work directly with EVD patients in ETUs (Table 1). Additional participants included representatives of organizations who were interested in designing similar courses or assessing the course's suitability for their deploying staff.

Operations and Logistics

The 3-day course consisted of lectures, small-group discussions, and practical exercises requiring trainees to perform simulated patient care activities in a mock ETU (Figure 1). Course days lasted ≈9 hours. During September 2014–March 2015, a total of 16 courses were held. Trainees traveled to Atlanta independently; CDC provided bus transport from Atlanta to Anniston, private dormitory rooms, on-site transport, and 3 meals per day. The environment promoted easy monitoring of trainees and emotional bonding and support among course participants.

The most valuable supplies for the course, and the most challenging to obtain, were PPE. Other materials were supplied by CDP or purchased locally. A list of supplies can be found at http://www.cdc.gov/vhf/ebola/hcp/safety-training-course/training-toolkit.html.

PPE for trainees consisted of coverall (protective suit), eye protection (goggles or full face shield), N95 respirator or surgical mask, 2 pairs of latex gloves, hood covering the head and neck, apron, gum boots, and surgical scrubs (Figure 2). PPE procurement was challenging for 2 reasons. First, protocols dictating which PPE supplies were needed had to be established. However, in 2014, consensus on optimal PPE for use in West Africa ETUs was lacking (*23*). Consequently, experts from CDC, MSF, and WHO used preexisting MSF and WHO PPE guidelines to develop protocols for the course (*24*,*25*). Protocols balanced the anticipated availability of specific PPE in West Africa with safe IPC practices. The goal was to impart a fundamental understanding of infection control measures necessary to avoid self-contamination and assess the safety of PPE that trainees might encounter in West Africa ETUs. Within 2 weeks, we procured a combination of MSF- and WHO-style PPE and supplies from local manufacturers, international distributors, and medical supply companies. Second, worldwide shortages of fluid-resistant coveralls and specially made hoods required rapid substitutions to best emulate what participants might encounter in West Africa ETUs (*26*). To conserve PPE in short supply, over the 3-day course, trainees reused fluid-resistant suits and aprons.

Table 1. Professions of 570 trainees attending Ebola Virus Disease Safety Training Course, Anniston, Alabama, USA, 2014–2015

Profession	No. (%)
Healthcare worker	387 (68)
Nurse	180 (32)
Physician	169 (30)
Physician assistant/nurse practitioner	20 (3)
Paramedic/emergency medical technician	18 (3)
Non–clinical care provider	185 (32)
Public health official	44 (8)
Pharmacist	25 (4)
Scientist	21 (4)
Mental health professional	17 (3)
Other	76 (13)

Course Content

As the course development team, we drew course content from materials from MSF, WHO, and CDC. We referenced technical manuals (*27*,*28*), online resources, videos, and other materials from the MSF Brussels EVD course, as well as input from returning responders and Ebola experts. Course materials included lectures, EVD case scenarios, step-by-step PPE protocols, and practical exercise instruction. Course materials underwent CDC institutional clearance, which entailed detailed review of each topic by CDC-designated experts, and were made available to trainees in paper and electronic formats.

Because healthcare workers in West Africa needed to strictly adhere to infection control principles to minimize the risk of contracting EVD, we focused most course content on IPC. Crucial IPC components for preventing EVD transmission are methodical PPE donning and doffing, proper patient flow and triage, injection and sharps safety, environmental cleaning and waste disposal, safe handling of laboratory samples, and safe management of the dead (*11*). We taught these principles through lectures, small-group breakout sessions, and practical exercises.

Lectures and Classroom Exercises

Morning sessions were devoted to lectures and small-group activities. Lecture topics included EVD epidemiology, transmission, and pathophysiology; elementary clinical management of patients; IPC; proper ETU design; disinfection and waste management in ETUs; mental health resilience; occupational health; community health promotion; and experimental treatments and vaccines for EVD. Small-group activities consisted of discussions with recently returned EVD responders and a series of tabletop exercises: 1) interactive case studies on EVD recognition and triage; 2) designing safe ETUs, including patient care areas, placement of handwashing stations, and healthcare worker flow; and 3) cultural sensitivity exercises, including techniques for interacting with community members while recognizing and respecting local customs.

Exercises in a Mock ETU

Afternoon sessions consisted of practical exercises that involved real-life scenarios, which comprised 50% of the course. Practical exercises requiring trainees to be in

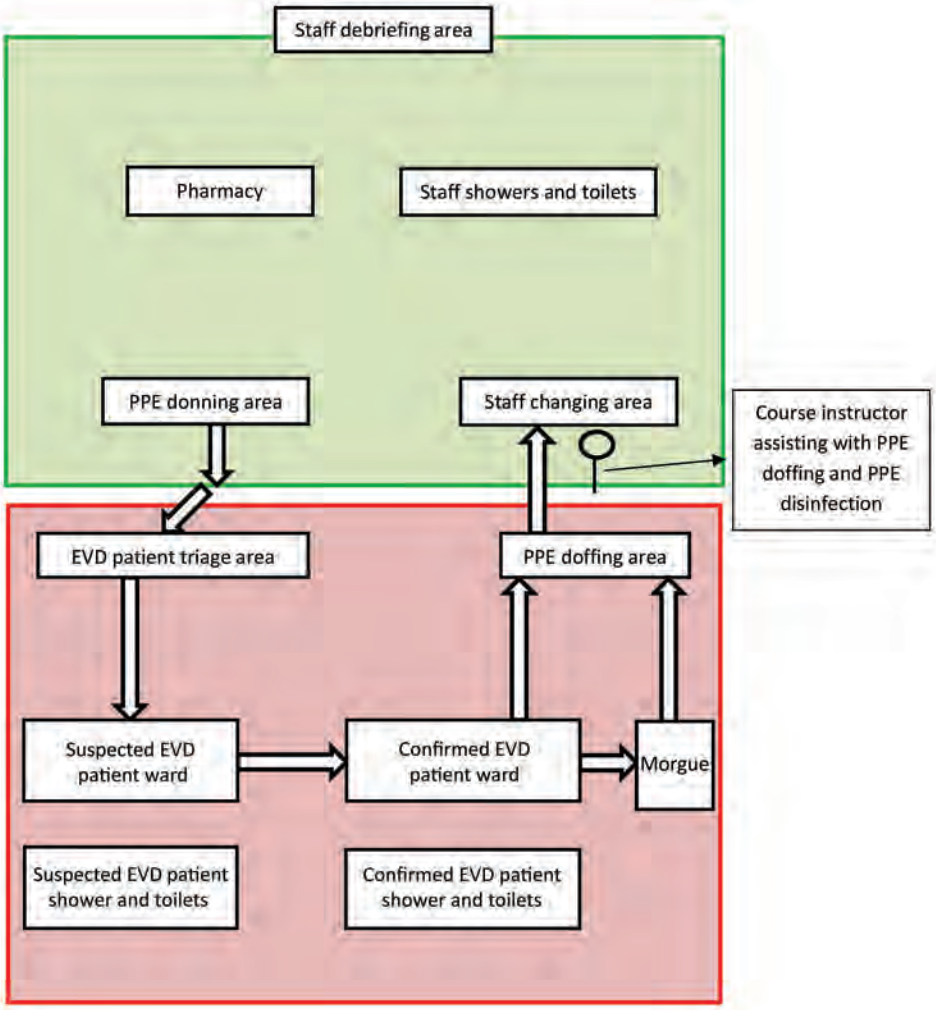

Figure 1. Layout of mock Ebola Treatment Unit used during the Centers for Disease Control and Prevention Ebola Safety Training Course, held at the US Federal Emergency Management Agency Center for Domestic Preparedness in Anniston, Alabama, USA, 2014–2015. Green indicates low-risk zone, which included staff PPE donning area, the staff changing area (after PPE doffing), pharmacy, staff showers and toilets, and a staff debriefing area; red indicates high-risk zone, which included EVD patient triage area, wards for patients with suspected and confirmed EVD, patient showers and toilets, and the morgue. Arrows indicate staff unidirectional movement from lower to higher risk zones. EVD, Ebola virus disease; PPE, personal protective equipment.

full PPE were a foundation of this course. We focused on repetitive practical exercises involving donning PPE with a partner, performing simulated high-risk patient-care activities, and doffing PPE under close supervision. Anecdotal observations indicated that trainees entering the mock ETU experienced increased concentration and anxiety, suggesting a level of realism in the simulated training setting.

In West Africa, healthcare workers faced additional challenges of harsh conditions, such as high temperatures, inconsistent electricity, poor lighting and visibility, and overcrowded ETUs (*12*). Returning responders described overworked staff in West Africa, covered in layers of PPE in sweltering heat, who experienced excessive sweating, dehydration, fogged eye protection, and decreased dexterity while caring for and transporting critically ill and dying patients. As core body temperatures rise while wearing PPE, overheating can lead to motor and cognitive impairment, further increasing healthcare worker vulnerability to breaches of safety practices (*29*). Thus, we constructed 2 mock ETUs to simulate the challenging conditions trainees might face in West Africa. Our mock ETUs had clearly designated low- and high-risk zones, stocks of PPE with changing areas, simulated chlorine footbaths and hand-washing stations, weighted patient dummies, a triage area, and a unidirectional flow pattern from low- to high-risk zones (Figures 1, 3).

Teams of 4–6 trainees entered mock ETUs, where they received a focused orientation and then donned PPE under direct supervision of a course instructor. According to MSF protocol, we taught a buddy system during practical exercises, whereby partners observed each other during PPE donning and regularly checked for breaches in PPE or infection control protocol. Trainees then entered the patient-care area, where they conducted instructor-guided simulated patient-care activities, including collecting and preparing blood specimens for transport, transporting a patient into the ETU, performing environmental decontamination and waste management, and transporting a deceased patient from a patient care area to a morgue. After these

Figure 2. Example of personal protective equipment (PPE) used during the Centers for Disease Control and Prevention Ebola Safety Training Course, held at the US Federal Emergency Management Agency Center for Domestic Preparedness in Anniston, Alabama, USA, 2014–2015. From top to bottom: head covering, eye protection, N95 respirator, apron over coverall, 2 pairs of latex gloves, gum boots.

activities, trainees learned a regimented doffing process in a designated area of the mock ETU, performing the structured PPE removal sequence under direct supervision of course instructors and the observing partner.

Course Evaluation

Trainee Demographics

By March 25, 2015, 570 trainees had attended a total of 16 course sessions. Trainees came from US governmental agencies (n = 352, 62%); 43 nongovernmental organizations, (n = 164, 29%); and other organizations, including foreign governments, private healthcare organizations, and academic institutions (n = 54, 9%) (Table 2). Trainees traveled from 36 states and 20 countries to attend the course. To our knowledge, although most deployed to ETUs in West Africa, some for months at a time, none of the trainees acquired EVD during deployment.

Figure 3. Constructed mock Ebola Treatment Unit used during the Centers for Disease Control and Prevention Ebola Safety Training Course, held at the US Federal Emergency Management Agency Center for Domestic Preparedness in Anniston, Alabama, USA, 2014–2015. Trainees prepare to place a simulated deceased patient into a body bag.

Costs and Staff Resources

A course of this scale required substantial resources. As the course evolved, the number of trainees increased each week. To ensure close supervision during practical exercises, we added course graduates to the staff to maintain an instructor:trainee ratio of 1:4. Over the life of the course, a total of 193 staff (89 CDC, 104 non-CDC) provided the training: 26 experts in infectious diseases and 117 practical exercise course instructors.

We estimate that 30,000 staff person-hours were required for course development (12,000 hours), 16 sessions of course instruction (10,000 hours), and course material revision (8,000 hours). The average total cost for a 3-day course was approximately US$27,000, or $750 per trainee for meals, lodging, transport, administrative coordination, and PPE and other supplies (Table 3). Course development and implementation relied on a multidisciplinary team; outside experts with ETU experience were essential. Because no mechanism existed to rapidly establish a training course of this scope, assembling and maintaining this large, diverse team was time-consuming and challenging. Institutional support was critical for creating interagency collaborations. Modifying an existing interagency agreement with the Oak Ridge Institute for Scientific Education (https://orise.orau.gov/) was instrumental in finding and supporting the travel of many trainers, and a new interagency agreement between CDC and FEMA provided access to the CDP campus and infrastructure.

Table 2. Sponsoring agencies of 570 trainees attending Ebola Virus Disease Safety Training Course, Anniston, Alabama, USA, 2014–2015

Agency	No. (%)
US government	352 (62)
Public Health Service	296 (52)
Centers for Disease Control and Prevention	26 (5)
Armed Forces	18 (3)
Other	12 (2)
Nongovernmental organizations	164 (29)
Partners in Health	38 (7)
Samaritan's Purse	24 (4)
International Medical Corps	15 (3)
Americares	11 (2)
Other	76 (13)
Academic institutions, foreign governments, and other	54 (9)

Feedback and Observations

Feedback from course graduates and returning responders during and immediately after each course session confirmed that the most crucial aspects of the course were hands-on, practical exercises, especially donning and doffing PPE. We therefore constructed a second mock ETU where students were able to don and doff PPE, practice dexterity exercises in double-gloved hands, and develop and discuss other potential ETU layouts while waiting to perform the practical exercises in the main ETU. This second mock ETU enabled trainees to practice, ask additional questions, and further discuss infection control procedures.

To improve trainees' understanding of the systematic process, our teaching model also incorporated trainees as instructors during the practical exercises. We asked trainees to identify breaches in their partner's PPE and instruct fellow trainees during the doffing process. To better understand PPE doffing, trainees replaced course instructors during the doffing process and gave explicit step-by-step instructions to fellow trainees as they removed PPE piece by piece. To ensure that proper techniques and procedures were followed, course instructors supervised all activities.

We encouraged flexibility in course instructors and trainees in various scenarios but still stressed the value of recognizing a safe work environment. International support for control of the 2014 West Africa EVD epidemic entailed aid from hundreds of international organizations. Healthcare workers who deployed to West Africa therefore encountered a wide variety of PPE supplies, ETU layouts, and safety protocols. Hence, rather than focusing our training on mastering a specific protocol, we attempted to instill a general culture of safety by providing trainees with the knowledge and skills to work safely in ETUs, identify and correct safety deficiencies, and feel empowered to withdraw from unsafe situations.

Table 3. Estimated cost per Ebola Virus Disease Safety Training Course, Anniston, Alabama, USA, 2014–2015*

Expense	Cost, US$
Meals	5,182.92
Lodging	5,700.00
Administrative and program costs	4,386.24
Transportation	5,355.00
Personal protective equipment	6,468.32
Total	27,092.48

*3-day course, 36 trainees.

Course Sustainability

Given the relative rarity of EVD, limited formal training courses exist worldwide. Several organizations and institutions, including foreign ministries of health, have expressed interest in establishing their own EVD training courses and requested our training materials. In response to these requests and to make course content easily accessible and reproducible, we created a Web-based toolkit that included all lectures, facilitator guides for small-group exercises, comprehensive trainer guides with video tutorials of practical exercises, supply checklists, and administrative templates required to implement the course. The toolkit went through extensive review and clearance by representatives of CDC, MSF, and WHO; on April 2, 2015, the complete toolkit was posted on the CDC Ebola website (https://www.cdc.gov/vhf/ebola/hcp/safety-training-course/training-toolkit.html). The step-by-step instructions and detailed materials in the toolkit might enable other organizations and countries to reproduce this training, given appropriate resources. The kit could help other countries, particularly those with a history of EVD outbreaks, better prepare for and respond to future outbreaks.

Conclusions

Establishment of the CDC EVD Safety Training Course was a relatively low-cost but high-impact activity that required an exceptional time commitment and flexibility from an evolving multidisciplinary team and dedicated trainees. Effective course execution required staff with diverse specialties, specialized supplies, transportation and housing for trainees, specific facilities for training, rapid access to funding, and complex interagency agreements. The implementation challenges included rapid hiring, contracting, and management of nearly 200 staff; recruitment and selection of course trainees and instructors; and development and review of course materials, including PPE protocols for ETUs in West Africa, when no international consensus existed.

Sudden public health emergencies can demand intensive and specialized training. The CDC EVD Safety Training Course was an innovative and extensive US training effort designed specifically to fill the previously unmet need to prepare clinicians to deploy to West Africa in response to the 2014 EVD epidemic. As was the case for the Haiti cholera epidemic of 2010, rapid development of a specialized clinical training course was a fundamental component

of the public health response to epidemic disease (*30*). The CDC EVD Safety Training Course quickly increased the number of clinicians who could provide care in West Africa ETUs, showing the feasibility of rapidly developing and implementing focused training in response to a public health emergency. Course graduates could use these specialized skills for future outbreaks of hemorrhagic fevers, although setting-specific components of the course addressing epidemiologic, cultural, and other issues would need to be adapted. Moreover, several key components of the EVD Safety Training Course (i.e., IPC procedures such as proper PPE donning and doffing, personal safety measures such as stress management in ETUs) might have considerable applicability to outbreaks of other pathogens that affect resource-limited settings.

In the following ways, advance preparation could greatly help rapidly mobilize a multifaceted training course as part of the response to future complex infectious disease emergencies. First, having a standing cadre of dedicated staff and a plan for developing training courses would increase the efficiency and speed of course development and implementation. The plan would include maintaining lists of staff specialized in instructional design, infectious diseases, public health, healthcare infection control, and logistics, who could fill needs depending on the course and contact lists of supplemental staff and contractors. Second, having contact and ordering information for various local and international manufacturers with detailed resource estimates could expedite supply procurement. Third, having established training sites with active partnership agreements in place would bypass the time-consuming and burdensome process of site identification and contract negotiation. Fourth, reliable funding sources and high-level institutional support is critical for quickly overcoming barriers.

The 2014 Ebola epidemic provides a reminder that the threat of global outbreaks of emerging infectious diseases is real and immediate. It is with these threats in mind that CDC and public health partners developed the Global Health Security Agenda (https://www.cdc.gov/globalhealth/security/index.htm), which supports capacity-building in ≈40 countries to prevent, detect, and respond to infectious disease threats. The CDC EVD Safety Training Course is a relevant and timely example of how international partners can work collaboratively to meet the Global Health Security Agenda objectives of more rapidly detecting, responding to, and controlling public health emergencies at their source and thereby enhancing global health security. Maintaining institutional memory of this effort, by establishing a core team of educators who could serve as a dedicated rapid training team, would help preserve expertise gained by development of this course, which in turn would enable a more nimble response to future urgent training needs with regard to new or emerging pathogens.

Acknowledgments

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Global Health Security—An Unfinished Journey

Michael T. Osterholm

This supplement is a timely, comprehensive compendium of the critical work being done by the Centers for Disease Control and Prevention and various partners to enhance and expand the Global Health Security Agenda. This perspective provides a review of, and comments regarding, our past, current, and future challenges in supporting the Global Health Security Agenda.

"It's no use saying, 'We're doing our best.'
You have got to succeed in doing what is necessary."
—Sir Winston Churchill (*1*)

We have witnessed numerous global public health achievements over the past century, resulting in major gains in life expectancy. These achievements resulted primarily from our unprecedented ability to prevent and control infectious diseases. Because of technological advances, such as electricity, we were able to provide safe water and sewage systems (*2*). We manufactured vaccines and antimicrobial drugs and, in some situations, stored and distributed them via reliable cold chains around the world. We began to refrigerate our pathogen-vulnerable food. Pasteurization of milk supplies became commonplace. Smallpox eradication, the near elimination of *Aedes aegypti* mosquitoes from the Americas, and major gains against killer childhood vaccine-preventable diseases led some to proclaim in the 1970s that we had beaten infectious diseases.

However, as we entered the 1980s, any sense of celebration ended as the HIV/AIDS pandemic took hold and outbreaks of emerging pathogens were increasingly recognized. Key victories began to fade as the growing number of failed states around the world made basic public health activities like vaccination extremely difficult and sometimes dangerous. Furthermore, the more than quadrupling of the human population since 1900, especially skyrocketing growth in megacities of the developing world, and the unprecedented level of global trade and travel (3.6 billion international air passengers in 2016) have ensured that emerging microbial pathogens could navigate the globe quickly. Finally, growing awareness of the looming threat of antimicrobial drug resistance has changed our view about being able to successfully manage and treat many life-threatening infections.

The outbreak of severe acute respiratory syndrome in 2003 was a wake-up call to the global public health community that it lacked an international vehicle for rapidly detecting and responding to a multicountry outbreak, particularly one caused by a respiratory-transmitted agent. Despite the World Health Organization's (WHO's) adoption of the International Health Regulations 2005 to address this concern, the 2009 pandemic of influenza A(H1N1) was a "live fire demonstration" that the world was still ill-prepared for global public health emergencies. Subsequent emerging microbial threats, including cholera in Haiti (2010), Middle East respiratory syndrome coronavirus (MERS-CoV) in the Middle East and Korea (2012), chikungunya in 2013 and Zika in 2015 in the Americas, yellow fever in Africa in 2015–2016 and in South America in 2016–2017, and cholera in Yemen (2017), highlight the challenges in accomplishing effective global public health preparedness. Most notably, the Ebola epidemic in West Africa in 2014–2016 provided a case study of our numerous global response deficiencies (*3*–*5*).

What has changed to make the world a safer place against infectious diseases, given the cumulative lessons learned from severe acute respiratory syndrome, influenza A(H1N1), Ebola, and other emerging threats? The Global Health Security Agenda (GHSA) was launched by 29 countries, WHO, the Food and Agriculture Organization of the United Nations, and the World Organisation for Animal Health in February 2014, just as the Ebola outbreak was unfolding (*6*). GHSA is now a growing partnership of more than 60 nations and organizations designed to help build countries' capacity to elevate global health security. GHSA pursues a multisectoral approach to strengthen global and national capacity to prevent, detect, and respond to human and animal infectious disease threats, whether occurring naturally or accidentally or deliberately spread.

The Centers for Disease Control and Prevention (CDC) supports staff in 35 countries. In 2017, CDC supported work in 49 countries conducting broad-based

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capacity-building efforts to help ensure global health security. It is critical to consider that although CDC's mission is to protect Americans, we cannot ensure domestic preparedness without ensuring that global infectious disease threats are contained at the source before they reach the United States. The number of countries that are currently strengthened through these CDC health security programs is, however, dependent on intermittent US government funding. Moreover, the 1-time, 5-year emergency congressional funding in 2014 to end the West Africa Ebola epidemic and implement GHSA in US-supported countries ends in 2019.

This supplement of *Emerging Infectious Diseases* is a timely, comprehensive compendium of the critical work being done by CDC and various partners to enhance and expand global health security. The article by Tappero and colleagues (*7*) presents an overview drawing from several articles in this issue and also provides an excellent historical summary of CDC's invaluable contributions to global health security. This supplement contains articles on GHSA progress, the Joint External Evaluation process, the recent West Africa Ebola outbreak, and building capabilities in disease surveillance, workforce, emergency response and preparedness, laboratory partnerships, and national public health institutes.

One of CDC's finest hours in its entire 71-year history was its response to the West Africa Ebola outbreak. Many international organizations responded to the outbreak, including WHO and key nongovernmental organizations, but CDC's effort, with >3,500 staff deployments, was consequential to bringing the epidemic under control and preventing the emergence of a major outbreak in Nigeria. WHO is the international lead agency for global outbreak response, but CDC's technical expertise, epidemiologic and laboratory workforce development training, and disease detection programs are cornerstones for ministry of health and WHO health security activities globally.

Will GHSA and WHO's and CDC's efforts help create a world safer from infectious disease threats and elevate global health security as a priority? Can the international public health community effectively prevent, detect, and respond to human and animal infectious disease threats? These programs help advance the global agenda for infectious disease prevention and control, but we still need to garner greater political will for additional progress. Recently, in our book *Deadliest Enemy: Our War Against Killer Germs* (*2*), Mark Olshaker and I detailed a 9-point crisis agenda if the world is to minimize, if not eliminate, the risk of catastrophic pandemics, outbreaks of critical regional importance, and intentional use of biologic weapons, including genetically altered pathogens.

At the top of our crisis agenda are 2 frightening scenarios: the rapidly emerging consequences of a 1918-like influenza pandemic and the slow-moving tsunami of antimicrobial drug resistance. Outbreaks of critical regional importance include diseases such as Ebola, Lassa fever, Nipah, MERS, and mosquito-borne diseases like Zika. Finally, the prospect for the intentional use of biologic agents cannot be understated. This scenario is often seen through the lens of the 22 cases of anthrax, including 5 deaths, that occurred on the heels of the September 11, 2001, attacks in the United States. This limited number of cases does not portend the public health crisis this attack triggered and the extensive public health resources required to respond to it. A future, much larger bioterrorism attack with a highly lethal agent, such as drug-resistant *Bacillus anthracis*, variola virus, or some other genetically altered pathogen, is not only possible but also highly likely. For true global health security, governments and philanthropic organizations must support Manhattan Project–like initiatives in research, development, manufacturing, and distribution of game-changing vaccines for high-priority pathogens. The new Coalition for Epidemic Preparedness Innovations is a good start, but we need to greatly expand these and related efforts to quickly address the types of objectives outlined in our crisis agenda. For example, we need a similar initiative for developing new antimicrobial drugs and alternative therapies, like phage treatment, for antimicrobial drug–resistant infections. Point-of-care diagnostics to enhance early appropriate antimicrobial therapy are also urgently needed.

All countries need to have the laboratory, trained workforce, surveillance, and emergency operations capabilities to prevent, detect, and respond to disease threats. Only when these accomplishments are realized can we truly be on the road to global health security for infectious diseases. Until then, the goal of global health security remains an unfinished journey.

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Alana Mermin-Bunnell (b. 2001), *28,616,* 2017 (detail). Watercolor and pen on paper, 16 in x 20 in/40.64 cm x 50.8 cm. Digital image courtesy of the artist/private collection, Atlanta, Georgia, USA.

Unseen Faces, Lingering Storylines

Byron Breedlove

Unlike previous outbreaks of Ebola virus disease that occurred in difficult to reach rural settings, the 2014–2016 West Africa Ebola epidemic involved major urban areas and thereby increased the potential to escalate from a regional epidemic to a pandemic. The West Africa Ebola outbreak was unprecedented in its scope, resulting in 28,616 reported cases and 11,300 deaths among adults and children. In all, Ebola cases were treated in 10 different countries during this outbreak.

Approximately 800 confirmed and suspected cases of Ebola virus disease occurred among healthcare workers. According to the World Health Organization, these workers had a "critical yet high risk role in responding to the Ebola epidemic and in working to meet the health needs of their communities during the epidemic. Many paid for this with their lives."

The title of this supplement issue's cover art, *28,616,* by American artist Alana Mermin-Bunnell, corresponds to

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the number of Ebola cases that were reported during the 2014–2016 West Africa epidemic. The painting depicts one moment during the outbreak. The artist uses a pallet of bright watercolors dominated by searing yellows, reds, and oranges that evoke both the urgency of the response and the caution essential to protect responders and patients.

A healthcare worker sheathed in yellow personal protective equipment (hood, goggles, and gloves) commands the viewer's attention. Standing before one of the Ebola treatment centers built in West Africa during the international public health response, this unknown worker clutches a young child to his or her shoulder with one hand and grips a bright blue bag in the other. The healthcare worker looks toward the ground, shoulders slumped, while walking between strands of plastic barrier fencing that look like a bright tapestry sagging under relentless sun and heat.

Multiple questions and potential storylines converge in this painting. Some are simple curiosity. What is inside the blue bag the healthcare worker clutches? Why is the child wearing a medical bracelet on his or her right wrist? Is the child being quarantined and separated from an infected parent sequestered in the treatment center? Did the child and his or her parents survive? The image also raises other complex questions. For instance, how is the responder handling the ethical and moral dilemmas that arise from decision making with regard to triage, quarantine, surveillance, and burial rituals and ceremonies? How is the local population reacting to restrictions and disruptions? Are these reactions endangering the public health responders and community and villages? How are responders handling the task of following up with people who may have been in contact with an individual with Ebola?

Mermin-Bunnell notes, "The Ebola epidemic forced a layer of separation between caretaker and patient. My painting, of a person in PPE (personal protective equipment) holding a child, tries to convey the humanity and emotion of healthcare workers that has been evident throughout the epidemic despite the dehumanizing use of PPE." (All quotes from A. Mermin-Bunnell, pers. comm., 2017 Aug 9.) The faces of the child and the healthcare worker are unseen, making the viewers guess at what their emotions are at this moment.

The artist had a direct, personal connection to the events in West Africa. During the fall of 2014, both of her parents were deployed to Sierra Leone to fight the Ebola epidemic. That experience, she explained, "was transformative for our family, and I gained a greater perspective of the process of fighting for global health security. There are sides to the effects of the Ebola epidemic that are harder to see than the obvious tragic death toll."

The West Africa Ebola epidemic brought heightened awareness of the need to enhance health security in all countries worldwide. The late D.A. Henderson wrote, "Today, cases and outbreaks of disease, whatever their cause and wherever they occur, pose a threat to people throughout the world. No major city in the world is more than 36 hours distant from any other." A lingering storyline from this issue's cover art from the West Africa Ebola outbreak is the need to strengthen global health security should the next epidemic become a pandemic and potentially overwhelm infrastructures, cripple economies, and claim millions of lives.

Pandemics have been a dark part of global history. The Black Death, an outbreak of bubonic plague that occurred during 1346–1353, was the most devastating pandemic in history and "swept away around 60 per cent of Europe's population" according to researcher Ole Jørgen Benedictow. The Spanish flu emerged during the final phases of World War I, during 1918–1920, and spread throughout the world, killing between 50 and 100 million people, and sickening more than 500 million people.

To protect the world from infectious disease threats, public health agencies, nations, international organizations, and public and private stakeholders need to cooperate and coordinate to prevent and reduce outbreaks, detect threats, and respond effectively. Those unseen faces and lingering storylines from the painting *28,616* remind us of what is at stake.

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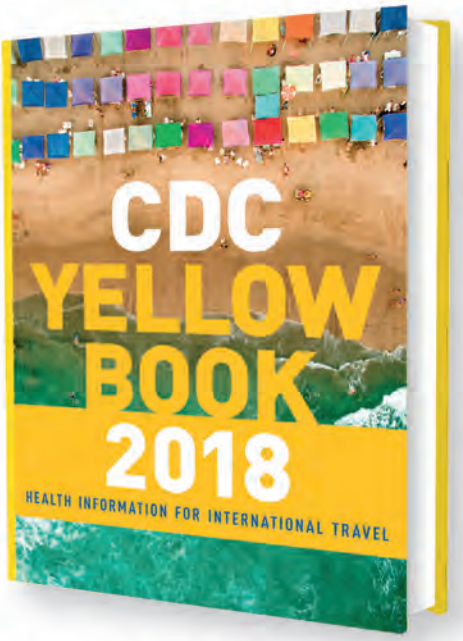

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Types of Articles

Perspectives. Articles should not exceed 3,500 words and 50 references. Use of subheadings in the main body of the text is recommended. Photographs and illustrations are encouraged. Provide a short abstract (150 words), 1-sentence summary, and biographical sketch. Articles should provide insightful analysis and commentary about new and reemerging infectious diseases and related issues. Perspectives may address factors known to influence the emergence of diseases, including microbial adaptation and change, human demographics and behavior, technology and industry, economic development and land use, international travel and commerce, and the breakdown of public health measures.

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Research. Articles should not exceed 3,500 words and 50 references. Use of subheadings in the main body of the text is recommended. Photographs and illustrations are encouraged. Provide a short abstract (150 words), 1-sentence summary, and biographical sketch. Report laboratory and epidemiologic results within a public health perspective. Explain the value of the research in public health terms and place the findings in a larger perspective (i.e., "Here is what we found, and here is what the findings mean").

Policy and Historical Reviews. Articles should not exceed 3,500 words and 50 references. Use of subheadings in the main body of the text is recommended. Photographs and illustrations are encouraged. Provide a short abstract (150 words), 1-sentence summary, and biographical sketch. Articles in this section include public health policy or historical reports that are based on research and analysis of emerging disease issues.

Dispatches. Articles should be no more than 1,200 words and need not be divided into sections. If subheadings are used, they should be general, e.g., "The Study" and "Conclusions." Provide a brief abstract (50 words); references (not to exceed 15); figures or illustrations (not to exceed 2); tables (not to exceed 2); and biographical sketch. Dispatches are updates on infectious disease trends and research that include descriptions of new methods for detecting, characterizing, or subtyping new or reemerging pathogens. Developments in antimicrobial drugs, vaccines, or infectious disease prevention or elimination programs are appropriate. Case reports are also welcome.

Another Dimension. Thoughtful essays, short stories, or poems on philosophical issues related to science, medical practice, and human health. Topics may include science and the human condition, the unanticipated side of epidemic investigations, or how people perceive and cope with infection and illness. This section is intended to evoke compassion for human suffering and to expand the science reader's literary scope. Manuscripts are selected for publication as much for their content (the experiences they describe) as for their literary merit. Include biographical sketch.

Research Letters Reporting Cases, Outbreaks, or Original Research. EID publishes letters that report cases, outbreaks, or original research as Research Letters. Authors should provide a short abstract (50-word maximum), references (not to exceed 10), and a short biographical sketch. These letters should not exceed 800 words in the main body of the text and may include either 1 figure or 1 table. Do not divide Research Letters into sections.

Letters Commenting on Articles. Letters commenting on articles should contain a maximum of 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article's publication.

Commentaries. Thoughtful discussions (500–1,000 words) of current topics. Commentaries may contain references (not to exceed 15) but no abstract, figures, or tables. Include biographical sketch.

Books, Other Media. Reviews (250–500 words) of new books or other media on emerging disease issues are welcome. Title, author(s), publisher, number of pages, and other pertinent details should be included.

Conference Summaries. Summaries of emerging infectious disease conference activities (500–1,000 words) are published online only. They should be submitted no later than 6 months after the conference and focus on content rather than process. Provide illustrations, references, and links to full reports of conference activities.

Online Reports. Reports on consensus group meetings, workshops, and other activities in which suggestions for diagnostic, treatment, or reporting methods related to infectious disease topics are formulated may be published online only. These should not exceed 3,500 words and should be authored by the group. We do not publish official guidelines or policy recommendations.

Photo Quiz. The photo quiz (1,200 words) highlights a person who made notable contributions to public health and medicine. Provide a photo of the subject, a brief clue to the person's identity, and five possible answers, followed by an essay describing the person's life and his or her significance to public health, science, and infectious disease.

Etymologia. Etymologia (100 words, 5 references). We welcome thoroughly researched derivations of emerging disease terms. Historical and other context could be included.

Announcements. We welcome brief announcements of timely events of interest to our readers. Announcements may be posted online only, depending on the event date. Email to eideditor@cdc.gov.

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