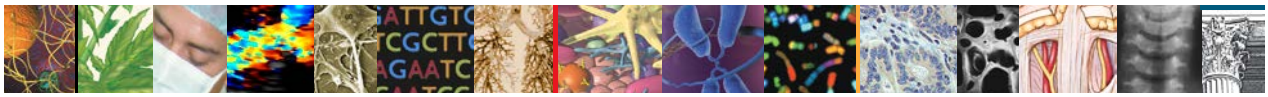

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Perspective

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Ebola 2014 — New Challenges, New Global Response and Responsibility

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Since Ebola virus was first identified in 1976, no previous Ebola outbreak has been as large or persistent as the current epidemic, and none has spread beyond East and Central Africa.[1] To date, more than 1000 people, including numerous health care workers, have been killed by Ebola virus disease (EVD) in 2014, and the number of cases in the current outbreak now exceeds the number from all previous outbreaks combined. Indirect effects include disruption of standard medical care, including for common and deadly conditions such as malaria, and substantial economic losses, insecurity, and social disruption in countries that were already struggling to recover from decades of war.

The outbreak's spread to densely populated Lagos, Nigeria, is worrisome, and the situation there is evolving rapidly. Lagos has a population roughly equivalent to that of Guinea, Sierra Leone, and Liberia combined, and it took nearly 2 weeks to establish the first effective isolation and treatment facilities there. Nigeria has since greatly improved its response, but whether it acted in time to stop a large outbreak is not yet clear. Given the extensive mobility and air travel in West Africa, EVD could reach other countries in the region and beyond. Every day that disease transmission remains uncontrolled, the likelihood of spread to unaffected countries increases.

The Centers for Disease Control and Prevention (CDC) is working intensively with partners to help stop the outbreak at its source in Africa. We are also assisting the four affected countries to improve their exit-screening protocols to help protect the rest of the world, including the United States. Each month, several thousand travelers from affected areas enter the United States, and even more people travel to and from Europe, other parts of Africa, and Asia. As long as Ebola is spreading in these regions, clinicians need to be alert to the possibility of EVD, take a travel history, and promptly isolate and test ill travelers who have returned from these regions in the past 21

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days and have symptoms consistent with EVD. The CDC has issued detailed guidelines regarding identifying, isolating, diagnosing, and treating patients.[2] There is also specific guidance for airline flight crews, cleaning personnel, and cargo personnel to minimize their risk of exposure.[3]

Stopping the outbreak at the source in Africa will take many months. Three core interventions have stopped every previous outbreak and can stop this one as well: exhaustive case and contact finding, effective response to patients and the community, and preventive interventions.

Identifying infected persons quickly requires accessible diagnostic and treatment facilities. In the current outbreak, the number of patients has far exceeded local capacity, which has resulted in a vicious cycle in which more cases lead to overloading of facilities which leads to more cases. Laboratory testing with real-time polymerase chain reaction is sensitive and specific and can return results within hours; it is now becoming more widely available in the affected areas.

Responding to cases involves isolation and treatment of patients, contact tracing, and monitoring each contact for 21 days after exposure. It is difficult to isolate and care for patients with EVD, not because the disease is particularly infectious or the virus particularly hardy, but because a single lapse can be devastating. Neither negative air flow nor special respirators are essential; meticulous attention to gown, glove, mask, and eye protection and great care while removing protective equipment are key. Improved hospital infection control throughout the region would prevent a substantial number of EVD and other illnesses. Soap and water or alcohol-based hand sanitizers readily disrupt the envelope of this single-stranded RNA virus, and decontamination with dilute bleach is effective and readily available even in remote settings.

Provision of supportive care, particularly fluid and electrolyte management and treatment of bacterial superinfections, can significantly improve survival.

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Contacts need to be identified and their temperature monitored daily for 21 days after exposure; if they develop fever, they will also need to be immediately isolated, tested, and if tests are positive, interviewed to identify contacts, each of whom must then be followed for 21 days. Social mobilization and culturally appropriate health education efforts are critical to successful case identification and tracking of contacts.

There are three key preventive interventions. The first is meticulous infection control in health care settings. The greatest risk of transmission is not from patients with diagnosed infection but from delayed detection and isolation. Since the early symptoms of EVD — fever, nausea, vomiting, diarrhea, and weakness — are nonspecific and common, patients may expose family caregivers, health care workers, and other patients before the infection is diagnosed.

Second, educating and supporting the community to modify long-standing local funeral practices to prevent contact with body fluids of people who have died from EVD, at least temporarily until the outbreak is controlled, will close the second major route of propagation of the virus. This is a culturally sensitive issue that requires culturally appropriate outreach and education.

And third, avoiding handling of bush meat (wild animals hunted for sustenance) and contact with bats (which may be the primary reservoir of Ebola virus) can reduce the risk of initial introduction of Ebola virus into humans. Bush meat consumption could be reduced through socioeconomic development that increases access to affordable protein sources. Where bush meat consumption continues, safer slaughter and handling can be encouraged. The potential effect of deforestation and other environmental changes on increasing human–bat contacts needs to be further studied and addressed.

These are straightforward interventions, but Ebola virus is a formidable enemy. If a single case is missed, a single contact becomes ill and isn't isolated, or a single lapse in infection control or funeral-practice safety occurs, another chain of transmission can start.

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Elements of the Global Health Security Agenda and Their Application to the Ebola Outbreak.

Global Health Security	Stopping the Ebola Outbreak
Prevention	
Promote biosafety	Provide infection-control education and supplies for hospitals and ambulances
Reduce the number of disease outbreaks	Provide leadership for behavioral change, including safe burial methods and supplies; communicate with community members and health workers
Minimize spillover of zoonotic diseases into human populations	Reduce contact with bats; increase food security; reduce unsafe handling of bush meat
Detection	
Implement or improve disease surveillance	Improve systems for disease and syndrome reporting (e.g., connectivity and networked data systems)
Implement or improve laboratory testing for virulent pathogens	Provide diagnostics and transport systems for specimens
Create accurate data systems and ensure timely reporting	Improve disease reporting and information systems in ministries of health (e.g., trained staff, connectivity, networked data systems)
Ensure presence of trained workforce	Hire and train personnel to find cases and contacts, to manage outbreak detection and response, and to care for patients safely
Response	
Establish emergency operations centers	Staff emergency operations centers in each country and each area within the country affected by outbreak to oversee case detection and diagnosis, contact elicitation and follow-up, and establishment and management of safe isolation and treatment facilities, as well as to promote safe burial practices
Receive and deploy countermeasures	Establish isolation and treatment centers in each country and provide them with effective personal protective equipment and trained staff, logistic support, and other essential supplies

In addition to implementing stringent control efforts, we need to accelerate development and deployment of vaccines and antiviral treatment. Supportive medical care can reduce case fatality rates substantially (and probably contributed to the much lower — 23% — case fatality rate in the Marburg virus outbreak in Germany[4]), but there are promising antiviral treatments and vaccines currently in development.[5] Ethical issues have been raised about using experimental treatments and vaccines that are in very limited supply, but a vaccine that is safe and effective would further protect health care workers and potentially others in outbreak situations. Phase 1 clinical trials are expected to begin in the coming weeks, and intensive discussions are under way regarding how to evaluate and provide these vaccine candidates, with informed consent, for pre- or post-exposure prophylaxis.

In addition to acting to stop this outbreak, we should put systems in place to prevent another one. Earlier this year, the United States joined partner governments, the World Health Organization, and other multilateral organizations and nongovernmental actors to launch the Global Health Security Agenda (see table), which aims to better protect all people from health threats. As the world faces the major threats of emerging or reemerging organisms, increased drug resistance, and the intentional or unintentional spread of virulent pathogens, we have three critical advances that will enable further action: increased societal commitment on a global scale; new technologies that allow us to work better, faster, and cheaper; and successes, ranging from better control of EVD in Uganda to the rapid and effective response to H7N9 influenza in China. The current EVD outbreak is a tragic illustration of the importance of improving global health security (see table). The components of this strategy — prevent wherever possible, detect rapidly, and respond effectively — match the framework for stopping the EVD outbreak.

EVD is a painful reminder that an outbreak anywhere can be a risk everywhere. The Global Health Security Agenda aims to strengthen public health systems in countries that need it most in order to stop outbreaks before they become emergencies. We believe that stopping outbreaks in a

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way that leaves behind stronger systems to identify, stop, and prevent future health threats is a moral imperative.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Centers for Disease Control and Prevention, Atlanta.

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1. Outbreaks chronology: Ebola hemorrhagic fever. Atlanta: Centers for Disease Control and Prevention, 2014 (http://www.cdc.gov/vhf/ebola/resources/outbreak-table.html#eighteen).
2. Infection prevention and control recommendations for hospitalized patients with known or suspected Ebola hemorrhagic fever in U.S. hospitals. Atlanta: Centers for Disease Control and Prevention, 2014 (http://www.cdc.gov/vhf/ebola/hcp/infection-prevention-and-control-recommendations.html).
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The International Ebola Emergency

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On August 8, 33 weeks into the longest, largest, and most widespread Ebola outbreak on record, the World Health Organization (WHO) declared the epidemic to be a Public Health Emergency of International Concern (PHEIC). This declaration was not made lightly. A PHEIC is an instrument of the International Health Regulations (IHR) — a legally binding agreement made by 196 countries on containment of major international health threats.

The August 8 statement made by WHO Director-General Margaret Chan followed advice from the independent IHR Emergency Committee. Reviewing all the available evidence, the committee concluded that further international spread of Ebola could have serious consequences. Their concern was based on the continuing transmission of Ebola in West African communities and health facilities, the high case fatality rate of Ebola virus disease (EVD), and the weak health services of Guinea, Liberia, Sierra Leone, Nigeria, and other neighboring countries at risk for infection.

An interactive map of the Ebola outbreak is available at NEJM.org

A Public Health Emergency carries immediate consequences for all IHR signatories (see Box 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). For the four currently affected countries, the Emergency Committee made several recommendations. Heads of state should declare a national emergency, activate national disaster-management mechanisms, and establish emergency operations centers. There should be no international travel of infected persons or their contacts. In areas of intense transmission — especially the border areas of Sierra Leone, Guinea, and Liberia — the provision of clinical care to affected populations could be used as a basis for reducing people's movement. Funerals and burials should be conducted in the presence of fully trained personnel so as to reduce the risk of spreading infection. And extraordinary supplementary measures, such as quarantine, may be implemented if necessary. These recommendations constitute a robust response to an extraordinary event but are not intended to be coercive. Rather, they should be introduced with the understanding and collaboration of affected communities.

The current outbreak has caused more cases and deaths than any previous EVD epidemic (see graph in the Supplementary Appendix). It appears to have started in the Guéckédou district of Guinea. The first case was recorded in December 2013, but that case was probably not the first in this outbreak.[1,2] Until the end of April 2014, most cases were reported from Guinea, with a small number in bordering parts of Liberia and Sierra Leone (see graph). In late April, a dip in reported cases in Guinea gave hope that the epidemic was beginning to subside and could be confined largely to one country. That hope was abandoned as the number of confirmed cases in Liberia and Sierra Leone rose sharply during May. By August 16, the cumulative number of confirmed, probable, and suspected cases of EVD in the three worst-affected countries plus Nigeria was 2240, with 1229 deaths. The ratio of deaths to cases implies a case fatality rate of 55%. However, this estimate is approximate, since some

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