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Vice President, Programs and Government Relations
Samaritan's Purse

Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

Update on the U.S. Public Health Response to the Ebola Outbreak
November 17, 2014

Chairman Murphy, esteemed members of this council and fellow guests of the committee, it is a privilege to testify before you today regarding the developments of the Ebola outbreak in West Africa.

Since Ebola entered Liberia in March, through its explosion onto the international spotlight in July, and even now when it appears the disease may have crested in Liberia, the world has learned much about Ebola. We have also discovered there are important questions for which we simply do not have factual answers.

I believe it is important to highlight just a few questions that remain unanswered and therefore continue to pose significant risk to Americans and the world:

- How are the doctors who are returning to the USA becoming infected?
- Can the virus live in other mammals besides primates, bats, rodents, and humans? (Attachment 1) For example, could it live in dogs, cats, cows, swine, and groundhogs?
- As with other viruses, could Ebola continue to be carried by a human who has no fever but enough viral load to be contagious?

An article in *The New England Journal of Medicine* (Attachment 2) reports that 95% of Ebola cases fully incubate in less than 21 days, but 5% of cases can remain asymptomatic for up to 42 days (Attachment 3). What does that mean for the United States and the world?

The media coverage is already decreasing as if the disease itself is burning out. I hope it is, but we cannot assume that Ebola will now just go away because of the measures that have been implemented so far. The United States, and the international community, needs to relentlessly pursue all reasonable means to fight the spread of the virus in West Africa.

Many public health experts are telling us that we know the disease, how to fight it, and how to stop it. Everything we have seen in this current outbreak, however, suggests that we do not know the science of Ebola as well as we think we do.

No one can predict the path this virus will take or the number of innocent lives that will ultimately be lost. Estimates from the Centers for Disease Control (CDC) state that up to 1.5 million persons in West Africa will be infected by mid-January. The World Health Organization (WHO) recently announced that we will likely see 10,000 cases per week by early December. Every time proclamations are made based on the current understanding of the science, the agile virus surprises the best minds in the world and teaches us new things. Now the disease has entered Mali and it is likely to enter other countries that border Sierra Leone, Liberia, and Guinea. Samaritan's Purse is concerned that will happen soon.

I want to stress the strategic need to stop the disease in West Africa, and the United States government should base all of its policy decisions on stopping the disease there for the sake of the entire world. This must be our primary focus.

My organization, Samaritan's Purse, has had an office in Liberia for 11 years. When Ebola was first identified there in March of this year, we immediately mobilized a large-scale public awareness and infection prevention effort that is ongoing and has so far reached over one million people. Just two months later, we had assumed primary responsibility for all of the direct clinical care of Ebola patients in the country. In late July, one of our physicians, Dr. Kent Brantly, who has since testified before this committee, contracted the disease. The ensuing media frenzy upon his evacuation to the United States, then awoke the world to Ebola and its dangers.

From the beginning, we knew that we were dealing with an unprecedented Ebola outbreak. We were one of the first organizations to sound alarms while pleading with the international donors and the relief community for more resources. Our warnings were not heeded, and the struggling governments and crumbling healthcare systems in Liberia, Guinea, and Sierra Leone were left to manage a deadly epidemic that threatens the world. Over 5000 have since died and more lives are being lost every day.

Today, we are seeing what appears to be improvement in Liberia. Data reporting on the disease has been grossly inaccurate from the outset, yet there is a noteworthy trend as evidenced by fewer burials, a substantial number of empty clinic beds, and fewer cases found in some of the early hottest spots of the epidemic.

While this is positive news, I fear that some in the international community are already beginning to breathe a sigh of relief and pat themselves on the back. It is too early for that, as Ebola has repeatedly shown itself to be insidious, nimble, and deceptive.

At the same time as we see declines in patient loads and death rates in Liberia, there are significant increases in patient loads and deaths in the neighboring country of Sierra Leone. And in Liberia, there are numerous new outbreaks in remote rural communities, including in areas along the border with Cote d'Ivoire. Nearly every single district bordering Cote D'Ivoire has confirmed Ebola cases. Samaritan's Purse is deeply concerned the disease will soon appear there. The disease has also now been confirmed in Mali.

As an organization that has been on the frontlines of fighting the current outbreak, we have learned that there are things we know about Ebola, but many things we don't know. The disease has been underestimated from day one. Every time we learn something new, it comes at a terrible price, whether that is in Monrovia, Dallas, New York, or Spain. We must not assume that we have a complete grasp on its trajectory, in Liberia or anywhere else, and we should not be content to accept that our capabilities are fully sufficient.

We don't know exactly why the numbers have decreased in Liberia. The Ebola treatment unit for healthcare workers ordered by President Obama in mid-September was just opened last week, and it has not treated any patients as of the 15th of November. Only a small percentage of the new Ebola Treatment Units have been completed, and none of the 1,700 beds that were committed are open yet.

USAID and others have mobilized about 65 burial teams, and that has made real progress in removing infection sources as have public awareness campaigns and infection control programs. Liberians are now much more accepting of the knowledge that contact with corpses is deadly. Social change has also happened through public messaging and personal observation. These are all good things, but no one can state conclusively why the disease is decreasing in Liberia and increasing in Sierra Leone. It has descended in both countries before and then returned with intensity.

We should not be lulled into thinking that the fight is over or even has peaked. On the contrary, we must remain steadfastly committed to stopping the disease in Africa or seeing it turn into an even larger global crisis. Dr. Peter Piot, the man who co-discovered Ebola in 1976, recently said, "I am more worried about the many people from India who work in trade or industry in West Africa. It would only take one of them to become infected, travel to India to visit relatives during the virus' incubation period, and then, once he becomes sick, go to a public hospital there. Doctors and nurses in India, too, often don't wear protective gloves. They would immediately become infected and spread the virus." An article in the New York Times dated Sunday, November 16 reports on serious sanitation and hygiene issues in Mumbai (Attachment 4).

Is the world ready for the disease to hit the Indian subcontinent? What would it mean to see the virus spread in these densely populated countries where public health systems are wholly inadequate to contain the outbreak? If this seems like a far-fetched question, just think that between 1,500 and 3,000 people travel by air

from West Africa to India every week (Attachment 5). A single case in India similar to Mr. Duncan in Dallas would have a vastly different outcome.

The theoretical became a real possibility for me just last week. One of our Liberian team staff members, of Indian nationality, planned to take leave and return home to India for Christmas. This staff person has lived in a "no touch" environment for over two months and serves in a zero-risk position. Yet, I was faced with the decision of whether to send him home with the protocols of WHO and CDC, which are essentially to monitor your temperature twice daily and report to a hospital if your fever spikes or you have other symptoms of Ebola. For the sake of public health we decided not to allow immediate return to India but to isolate the person for 21 days first. Despite scientific claims, the consequences of being wrong are unimaginable.

There has been much discussion about restricting travel from West Africa. Two American allies, Canada and Australia, have essentially closed their borders to non-resident travelers from Sierra Leone, Liberia, and Guinea. Prohibitions or severe restrictions from about two-dozen other countries have hurt the ability to travel commercially in and out of the three countries. There is no cohesive global policy however just like there is no unified protocol within the US for returning relief workers or members of the US military.

We need to seriously consider whether travel restrictions could stop or slow the spread of the disease to America, or more significantly, other parts of the globe. Our health system has shown that, although with pain, panic and great expense, we

are able to trace contacts and quickly shut down the spread of the virus. Would India, Bangladesh, or China have the same capacity?

We must do more than just screen departing passengers for fever. We have to be willing to consider implementing a policy of "essential" travel only that would be coordinated internationally. Those who argue that it will bring these countries to financial ruin perhaps fail to recognize that these nations have already suffered enormous economic pain because of the outbreak. The internationally accepted premise of fighting Ebola is to identify and isolate. Why would we not include air travel in that discussion?

Commercial airlines have already severely cut back and restricted their flights. British Air, Air France, Delta, Kenya Air and others have ceased flights in and out of these countries. Today in Liberia there are only two commercial carriers left flying, Brussels Air and Royal Air Maroc. Each makes two flights per week into Monrovia. It can take up to two weeks to get a booking out. The flight crews have come under pressure from their unions to stops flying there. If the companies should decide it is not in their commercial interest to continue these flights, Liberia will be effectively quarantined.

If the commercial flights come to a halt, what is the back-up plan? How would the relief effort continue to be supported with personnel and supplies? Given the recent international track record in timeliness, would we be looking at four or six or eight weeks to get an air bridge set up to fly relief workers and emergency cargo? Instead, a trustworthy system dedicated to flying solely for the Ebola response should be established now.

We often hear that the 21-day isolation will hamper efforts to recruit staff to join the fight against Ebola. It would be much more of an onerous challenge to convince personnel to go if they did not have assurance of their flight home. A dedicated air bridge for humanitarian workers would also provide the ability to fully monitor and land a large group if needed in case of crisis.

Strong diplomatic pressure must be continued on the governments in Guinea, Liberia, and Sierra Leone to put aside their local politics and engage in this fight in a more serious way. As we struggle to work in Liberia, we see government bureaucracy hampering efforts. In one area, we finished construction on a new Community Care Center two weeks ago, but we are still waiting for the government to inspect it so that it can care for the Ebola patients around it. Liberia removed their emergency decree last week and announced their desire to reopen schools soon. We hope those measures are timely and not premature.

I want to emphasize the incredible need for a vaccine and effective treatments. This cannot be overstated. Finding an effective vaccine is in the interest of the United States and the entire world.

We should be asking ourselves if we are truly seeing a turn in the tide or merely the calm before the storm. This disease is a formidable enemy, and it has already caught us off-guard more than once. Its patterns of transmission are not fully understood and have not been fully controlled. We should not take the chance of having our response come up short again. The stakes are too high. If we let our guard down now, the consequences could be much more catastrophic than what we have already seen.

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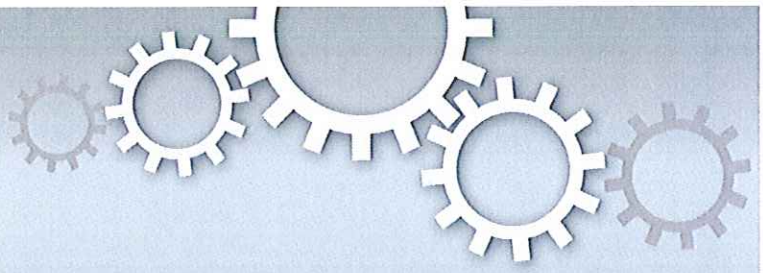
Attachment 1

SCIENTIFIC REPORTS



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Transmission of Ebola virus from pigs to non-human primates

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Ebola viruses (EBOV) cause often fatal hemorrhagic fever in several species of simian primates including human. While fruit bats are considered natural reservoir, involvement of other species in EBOV transmission is unclear. In 2009, Reston-EBOV was the first EBOV detected in swine with indicated transmission to humans. In-contact transmission of Zaire-EBOV (ZEBOV) between pigs was demonstrated experimentally. Here we show ZEBOV transmission from pigs to cynomolgus macaques without direct contact. Interestingly, transmission between macaques in similar housing conditions was never observed. Piglets inoculated oro-nasally with ZEBOV were transferred to the room housing macaques in an open inaccessible cage system. All macaques became infected. Infectious virus was detected in oro-nasal swabs of piglets, and in blood, swabs, and tissues of macaques. This is the first report of experimental interspecies virus transmission, with the macaques also used as a human surrogate. Our finding may influence prevention and control measures during EBOV outbreaks.

Ebola viruses belong to the family *Filoviridae,* genus *Ebolavirus*. Those endemic to Africa cause severe hemorrhagic fever with frequent fatal outcome in humans, great apes and several species of non-human primates (NHPs). Fruit bats are considered to be the natural reservoir for EBOV in Africa[1]. In 2009, the only non-African known species of EBOV, Reston Ebola virus (REBOV), was isolated from swine in Philippines, with antibodies against the virus detected in pig farmers[2,3]. However REBOV did not cause clinical signs in experimentally inoculated pigs[4]. In contrast to African species of EBOV, REBOV does not cause clinical symptoms in humans, although the infection may be fatal in cynomolgus macaques[5]. We have previously demonstrated that Zaire-EBOV (ZEBOV) can infect pigs, cause disease, and transmit to in-contact pigs[6]. While primates develop systemic infection associated with immune dysregulation resulting in severe hemorrhagic fever, the EBOV infection in swine affects mainly respiratory tract, implicating a potential for airborne transmission of ZEBOV[2,6]. Contact exposure is considered to be the most important route of infection with EBOV in primates[7], although there are reports suggesting or suspecting aerosol transmission of EBOV from NHP to NHP[8–10], or in humans based on epidemiological observations[11]. The present study was design to evaluate EBOV transmission from experimentally infected piglets to NHPs without direct contact.

Results

Six four-week old Landrace piglets (*Sus scrofa*) were oronasally inoculated with 10^6 $TCID_{50}$ of ZEBOV (Kikwit 95) per animal. The piglets were transferred to a separate room for the inoculations, and then moved back into the room containing four cynomolgus macaques. This age group was selected based on the previous observation of differences in severity of the disease in ZEBOV inoculated piglets[6] to ensure sufficient survival time of the piglets potentially needed for virus transmission, and to determine whether piglets without an overt clinical disease could transmit the virus. The macaques were housed in two levels of individual cages inside the pig pen, and separated from the piglets by wire barrier placed about 20 cm in front of the bottom cages to prevent direct contact between the two species. Bottom cages housing NHPs Nos. 07M and 20F were about 10 cm above the ground, top cages housing NHPs Nos. 34F and 51M were about 1.4 m above the ground. The NHP cages were located immediately to the side of the air exhaust system. The cubicle layout respective to the airflow (ten complete air exchanges per hour) in the room is schematically indicated in Supplemental Figure S1. During the husbandry, piglets were moved away from the cages and enclosed by the gate system. The floor was washed, taking care that the water is sprayed at low pressure and away from the NHP cages, to avoid any splashes into the bottom cages. Also the

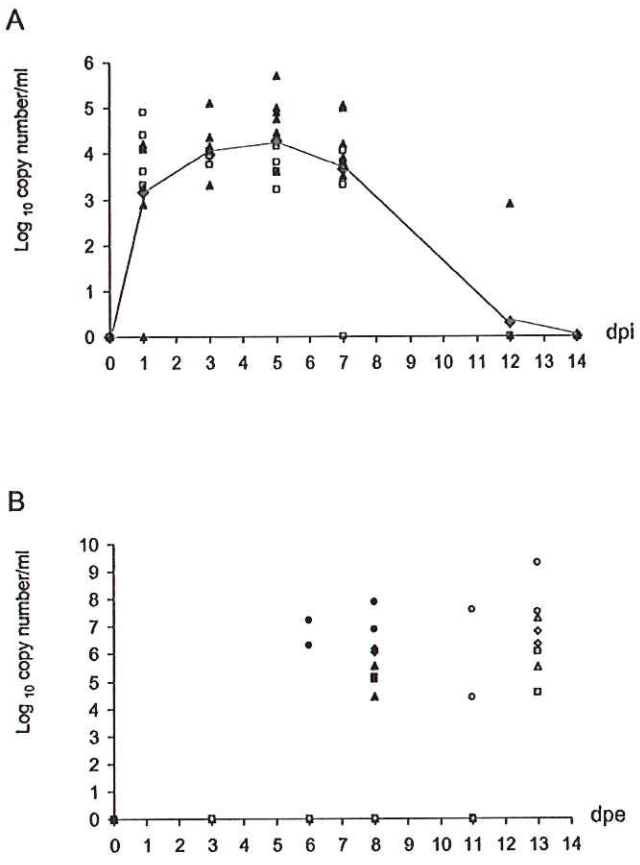

Figure 1 | Detection of EBOV RNA in swabs and blood. (A) Shedding in pigs. Squares represent the oral swabs and triangles illustrate the nasal swabs. Gray line with diamonds shows the general trend of the oro-nasal shedding. (B) Non-human primates: square markers represent the oral swabs, diamonds represent the rectal swabs, triangles represent the nasal swabs, circles represent blood samples. Gray markers-NHP No. 51M and 20F, black markers-NHP 07M and 34F. "dpi" (days post inoculation) and "dpe" (days post exposure) on the X axis are equivalent.

20 cm space between the wire barrier and the cages was cleaned separately with running water prior to proceeding with NHP cage cleaning. Both animal species were fed after the cleaning, providing new clean dishes for the macaques, with staff changing disposable outer gloves between procedures and animals. The design and size of the animal cubicle did not allow to distinguish whether the transmission was by aerosol, small or large droplets in the air, or droplets created during floor cleaning which landed inside the NHP cages (fomites). The husbandry flow during the sampling days was: cleaning, followed by sampling, then feeding, with staff changing disposable outer gloves between procedures and animals. Pigs and NHPs were sampled on alternative days except for day 3 post infection, when NHPs were sampled in the morning and the piglets in the afternoon.

Clinical signs and gross pathology in swine, following the inoculation with EBOV, were comparable to previous infection study in piglets of this age group[6]. Increase in respiratory rate (up to 80 breaths/min) and in rectal temperatures (40.2–40.5°C) was observed between 5 and 7 days post infection (dpi). All piglets apparently recovered from the disease by 9 dpi. Piglets Nos. 1, 2 and 4 were euthanized at 12 dpi, and piglets Nos. 3, 5 and 6 at 14 dpi, based on experimental schedule. Clinical scores and parameters are provided in the Supplementary Information (Supplemental Figure 2A, Supplemental Table 1). No significant lesions were observed at the necropsy. Microscopic lung lesions were focal and not extensive,

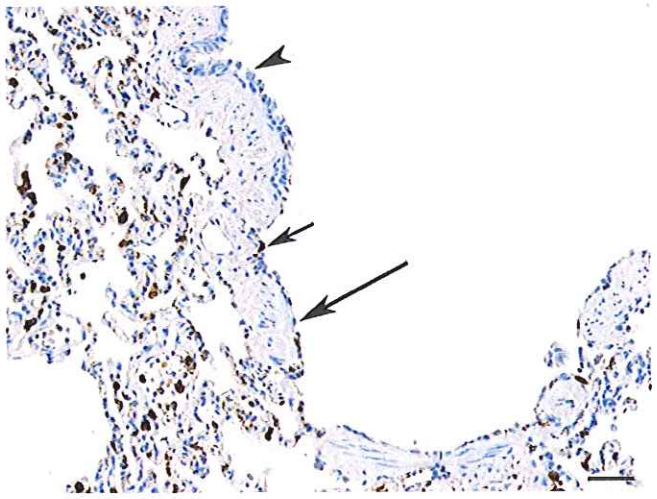

Figure 2 | Lungs, macaque No.34F. Segmental attenuation and loss of respiratory epithelium in the bronchiolar wall (large arrow) with some areas of the lungs relatively unaffected (arrowhead). Immunostaining for Ebola virus antigen was detected in occasional respiratory epithelial cells (small arrow) as well as within alveolar and septal macrophages. Bar=50 μm.

characterized by broncho-interstitial pneumonia with a lobular pattern, similar to those described in our previous report[6]. Virus antigen was detected by immunohistochemistry in three piglets (No. 2, 4, and week signal in No. 5), primarily within the areas of necrosis often adjacent to bronchioles (Supplemental Figure S3A). The presence of virus in the lung was confirmed by detection of EBOV RNA employing real-time RT-PCR targeting the L gene, and by virus isolation on Vero E6 cells for piglet No. 2 and No. 4. Virus isolation was also attempted from lung associated lymph nodes, based on detection of viral RNA, yielding one, successful isolation. Viral RNA was detected in submandibular lymph nodes of all piglets, and in the spleen and liver of two piglets. Low level of viremia based on RNA levels was detected in blood of four piglets at 5 and 7 dpi. EBOV RNA was detected in nasal and oral swabs of piglets from 1 dpi until 7 dpi, inclusively (Figure 1A), and from rectal swabs on day 1 and 5, but not at 3, 7 and 12 dpi (Supplemental Table 1). Viral isolation was attempted on all swabs. Out of 45 oral and nasal swabs positive by RT-PCR, 16 were positive on virus isolation, while two out of 11 RNA-positive rectal swabs tested positive for virus. Presence of EBOV RNA in cell culture supernatants from the isolates with observed CPE was confirmed by real time RT-PCR (Supplemental Table 1; Supplemental Table 2).

Air sampling was conducted on day 0, 3, 6, 8 and 11 post inoculation. Real time RT-PCR targeting the L gene detected viral RNA on days 6 and 8 post inoculation. Location in front of the bottom cages at about 75 cm above the floor was sampled in 30 min triplicates following husbandry, during the NHP sampling. Average values of 4.4 $\log_{10}$ copies/ml and 3.85 $\log_{10}$ copies/ml of the sampling buffer were detected at 6 and 8 dpi, respectively. Virus isolations were not successful, likely due to the sampling buffer composition (0.1% Tween 20).

All four NHPs (*Macaca fascularis*) were alert and in good apparent health until 7 days post exposure (dpe - corresponding to dpi of piglets) with ZEBOV. At 8 dpe, macaques 07M (bottom left cage) and 34F (upper right cage), housed in cages located within an air flow towards the exhaust system, were euthanized based on clinical signs typical for EBOV infection in NHPs. Both had petechial hemorrhages on the skin of the chest and along internal surfaces of the arms and legs. Macaques 51M and 20F were visually healthy until 12 dpe, when early clinical signs were noted, and both animals were

euthanized the next day (13 dpe). The NHPs were euthanized when convincing clinical signs typical for EBOV infection became apparent, preferably prior to the humane endpoint (Supplemental Figure S2B; Supplemental Table 1). Examination of internal organs at the necropsy exposed damages mainly to the lung (Supplemental Figure S4) and liver. Microscopic lesions and antigen distribution in the organs were similar to previous reports[12–14], except for the lesions and antigen distribution in lungs. Interstitial pneumonia was characterized by thickened and hypercellular alveolar septa due to infiltration by primarily macrophages (Supplemental Fig. 3B), with multifocal areas of alveolar hemorrhage and edema. EBOV antigen was detected extensively in alveolar and septal macrophages using double immunostaining (Supplemental Fig. 3C), as well as within pneumocytes and endothelial cells. Viral antigen was also observed within bronchiolar epithelial cells with adjacent segmental loss of epithelial cells (Figure 2.) and within respiratory epithelial cells of the trachea. The pattern of lesions and immunostaining for EBOV antigen in lungs suggests infection of the lungs both, via respiratory epithelium and due to viremic spread of the virus.

There was a remarkable difference in the type and quantity of cells infiltrating the lungs between the macaques and the pigs, although viral antigen was detected only in alveolar macrophages of both species. Monocytes/macrophages were essentially the only leukocyte type infiltrating the lungs in non-human primates, while large quantities of non-infected lymphocytes were recruited into the pig lungs. This phenomenon can be linked to different clinical picture in the two animal species: respiratory distress in pigs (severe in a specific age group[6]) versus systemic disease with no major respiratory signs in NHPs. It will be important to identify differences and similarities in ZEBOV-induced pathogenesis and pathology between the two species in future studies.

Infection of the NHPs with ZEBOV was confirmed by detection of viral RNA (real time RT-PCR targeting the L gene), and in all samples collected at euthanasia by virus isolation. The first detection of ZEBOV RNA was in the blood of NHPs 34F and 07M at 6 dpe, with virus isolation from macaque 07M. This was followed by ZEBOV RNA detection in nasal, oral and rectal swabs from the same NHPs at 8 dpe (Figure 1B). A similar pattern was observed for macaques 51M and 20F, starting at 11 dpe with detection of RNA in blood and virus isolation from animal 20F, followed by RNA and virus detection in swabs at 13 dpi. Detection of viral RNA and infectious virus in blood, swabs and tissues of the macaques (summarized in Supplemental Table 4) confirmed systemic spread of the virus. Whole genome sequencing performed on virus nucleic acid from selected swab and lung samples from pigs and NHPs confirmed identity of the virus.

Discussion

Pigs were the source of ZEBOV at a time of infection of NHPs euthanized at 8 dpe (07M and 34F) since shedding from the macaques was not detected at dpe 3 or 6. NHPs euthanized at 13 dpe (20F, 51M) could have contracted ZEBOV from the environment contaminated by either species, considering previous reports on development of disease following aerosol exposure[10], or other inoculation routes[5,15,16], although pigs can generate infectious short range large aerosol droplets more efficiently then other species[17]. We have also never observed transmission of EBOV from infected to naive macaques, including in an experiment employing the same cage setting as in the current study, where three NHPs intramuscularly inoculated with EBOV did not transmit the virus to one naive NHP for 28 days, the duration of the protocol. During another study, three EBOV infected NHPs cohabiting with 10 naive NHPs in adjacent cage systems did not transmit the virus to naive animals for 28 days (unpublished data). The exact route of infection of the NHPs is impossible to discern with certitude because they were euthanized at a time when EBOV had already spread systemically. However, the segmental attenuation and loss of bronchiolar epithelium and the presence of Ebola virus antigen in some of the respiratory epithelial cells in the lungs of all macaques suggest that the airways were one of the routes involved in the acquisition of infection, consistent with previous reports[9,10]. Other routes of inoculation generally did not lead to lesions in the respiratory tract comparable to those observed in this study[12,13].

Under conditions of the current study, transmission of ZEBOV could have occurred either by inhalation (of aerosol or larger droplets), and/or droplet inoculation of eyes and mucosal surfaces and/or by fomites due to droplets generated during the cleaning of the room. Infection of all four macaques in an environment, preventing direct contact between the two species and between the macaques themselves, supports the concept of airborne transmission.

It is of interest, that the first macaques to become infected were housed in cages located directly within the main airflow to the air exhaust system. The experimental setting of the present study could not quantify the relative contribution of aerosol, small and large droplets in the air, and droplets landing inside the NHP cages (fomites) to EBOV transmission between pigs and macaques. These parameters will need to be investigated using an experimental approach specifically designed to address this question.

The present study provides evidence that infected pigs can efficiently transmit ZEBOV to NHPs in conditions resembling farm setting. Our findings support the hypothesis that airborne transmission may contribute to ZEBOV spread, specifically from pigs to primates, and may need to be considered in assessing transmission from animals to humans in general. The present experimental findings would explain REBOV seropositivity of pig farmers in Philippines[2,3] that were not involved in slaughtering or had no known contact with contaminated pig tissues. The results of this study also raise a possibility that wild or domestic pigs may be a natural (non-reservoir) host for EBOV participating in the EBOV transmission to other species in sub-Saharan Africa.

Methods

Virus. ZEBOV strain Kikwit 95 was produced on VERO E6 cells in minimal essential medium (MEM) supplemented with 2% fetal bovine serum and antibiotics (Penicillin/Streptomycin). Virus titers were determined by standard $TCID_{50}$ and/or immunoplaque assays on VERO E6 cells. Procedures for the production and propagation of ZEBOV and all subsequent experiments involving infectious materials were performed in the Containment Level (CL) 4 facilities of the Canadian Science Center for Human and Animal Health (CSCHAH).

Animal experiments. Four cynomolgus macaques were acclimatized in the BSL4 animal facility for two weeks, and housed in the same room for one week prior to the swine inoculation. The macaques were housed in two levels of individual cages inside the pig pen, and separated from the piglets by wire barrier placed about 15 cm in front of the cages to prevent direct contact between the two species. Bottom cages housing NHPs Nos. 07M and 20F were about 20cm above the ground, while top cages housing NHPs Nos. 34F and 51M were about 1.4 m above the ground. The NHP were sampled at 3 and 6 dpi (nasal, oral rectal swabs, blood) as per experimental schedule. Two macaques were euthanized for humane reasons at 8 days post exposure (dpe), and all animals were sampled at that time. Two remaining NHPs were in addition sampled at 11 dpe, and at13 dpe when they were euthanized. The animals were euthanized when typical clinical signs of Ebola infection became apparent, if possible prior to reaching the humane endpoint. Lung, lung associated lymph nodes, liver, spleen and intestine were collected at the necropsy.

Pigs (breed Landrace) were obtained from a high health status herd operated by a recognized commercial supplier in Manitoba, Canada. Three-week old piglets, designated as animal No. 1–6, were acclimatized for seven days prior to the inoculation in an animal cubicle already housing the non-human primates. The six piglets were inoculated oro-nasally with 2 ml of 10^5 $TCID_{50}$ total per animal (0.5 ml per each nostril and 1 ml orally) in a room adjacent to the BSL4 animal cubicle and subsequently housed in proximity to cages with four non-human primates (NHP). Swine rectal temperatures were taken during the sampling performed under anesthesia on days 0, 1, 3, 5, 7, 12 and 14, when blood and rectal, oral and nasal swabs were collected. Three piglets were euthanized on day 12 post inoculation (no. 1M, 2M. 4F), and three on day 14 (3M, 5F, 6F), as per experimental schedule. Muscle, lung, liver, spleen, trachea, and submandibular, lung associated and mesenteric lymph nodes were collected at necropsy.

All animal manipulations were performed under CL4 conditions and followed Animal Use Document No. CSCHAH AUD# C-11-004 approved by the Animal Care

Committee of the Canadian Science Centre for Human and Animal Health, according to and following the guidelines of the Canadian Council on Animal Care.

Virus isolation. Swabs collected into 1 ml of cMEM, blood, and tissues homogenized in MEM using a bead mill homogenizer according to the manufacturer's protocol (Tissue Lyser, Qiagen) were used for virus isolation and real time RT-PCR analysis. All NHP samples and swine rectal swabs were plated in 10-fold serial dilutions of supernatant on Vero E6 cells with six replicates per dilution. At 72–96 h post-infection the plates were scored for cytopathic effect (CPE) and $TCID_{50}$ virus titers were calculated using the Reed and Muench method. Swine rectal swabs had to be however carried over onto replica plates for three passages prior to reading the CPE. Swine nasal and oral swabs, blood and tissues were first analyzed by real time RT-PCR targeting the ZEBOV L gene, followed by virus isolation on Vero E6 cells in P6 plates on selected samples.

Virus RNA detection. NHP samples: Total RNA was isolated from tissues preserved and homogenized in RNA later employing the RNeasy Mini Kit (QIAGEN). RNA from nasal washes and swabs was isolated using the QIAamp Viral RNA Mini Kit (QIAGEN, GmbH).

Swine samples: RNA was isolated using Tripure Reagent (Roche Applied Science) according to the manufacturer's recommendations from swabs, blood or 10% w/v tissue homogenates in cMEM. One-Step real-time RT-PCR was carried out using following primers and probe:

ZebovForward -CAGCCAGCAATTTCTTCCAT;

ZebovReverse- TTTCGGTTGCTGTTTCTGTG;

ZebovProbe FAM-ATCATTGGCGTACTGGAGGAGCAG-NFQ.

Armoured enterovirus RNA (Asuragen) was used as external extraction/reaction control. Quantitect Reverse Transcriptase Real-time PCR kit (Qiagen) was employed for the PCR reactions according to the manufacturer's specifications. Reaction conditions for the RT-PCR were as follows: 50°C for 30 minutes; 95°C for 15 minutes; 45 cycles of 95°C for 15 seconds followed by 60°C for 45 seconds. The samples were run on the Rotor-Gene 6000 (Qiagen) or on the the LightCycler 480 (Roche Applied Science). Copy numbers were determined based on the L-gene Ebola plasmid standard control curve. Cut off value for samples to be considered positive were 3 log_{10} copies/ml (Rotorgene) or 3.15 log_{10} copies/ml (LightCycler 480).

Air sampling. The air was sampled using BioCapture 650 Air Sampler (FLIR, Arlington, VA) on days 0, 3, 6, 8 and 11 post inoculation of the piglets. The air sampling started after husbandry, concurrent to NHP sampling, later in the morning before noon. Location in front of the bottom cages at about 75 cm above the floor was sampled in 30 min triplicates. The collection took place over a span of about two hours in total (three 30 min collection times with changes of cartridges in between). The air sampler device collects particles by bubbling the air through a pre-loaded buffer (0.74% Tris/0.1 Tween 20) provided in a sealed cartridge by the manufacturer. This solution is not optimal for recovery of live enveloped viruses, and virus isolation attempts were unsuccessful. ZEBOV RNA was detected by real time RT-PCR targeting the L gene.

EBOV sequencing. Viral RNA previously extracted for real time PCR was sequenced by first generating cDNA with the use of Omniscript reverse transcriptase (Qiagen) and random hexamers along with specific EBOV primers followed by PCR with iProof high fidelity DNA polymerase (Bio-Rad) with specific primers (available upon request). DNA sequencing was carried out using the 3730xl DNA Analyzer (ABI).

Histology and immunohistochemistry. Tissues were fixed in 10% neutral phosphate buffered formalin, paraffin embedded using standard procedures, sectioned at 5 m, and stained with hematoxylin and eosin (HE) for histopathologic examination. Detection of viral antigen was performed using A 1:2000 dilution of rabbit polyclonal anti-ZEBOV VP40 antibody as described previously[6]. Identification of macrophages in the lungs was performed by immunostaining for the macrophage/monocyte marker L1 using Clone Mac387 (Dako, USA) primary antibodies. The tissue sections were quenched for 10 minutes in aqueous 3% hydrogen peroxide, prior to retrieval of epitopes using high pH AR10 (BioGenex, CA) in a BioCare Medical Decloaking Chamber. Antibody Clone Mac 387 was applied for 10 minutes at a dilution of 1:3200, and visualized using an AP-polymer kit, Mach 4 Universal (BioCare Medical, CA) for 30 minutes, and reacted with Vulcan Fast Red (BioCare Medical, CA) substrate. For the Mac387/Ebola double stain, antibody Clone Mac 387 was applied for 10 minutes at a dilution of 1:3200, and visualized using a multilink horseradish peroxidase labeled kit, Super Sensitive Link-Label IHC Detection System (BioGenex, CA), reacted with the chromogen diaminobenzidine (DAB). The sections were then incubated with a denaturing solution (1 part A, 3 parts B, BioCare Medical, CA) for 5 minutes, pretreated with proteinase K enzyme for 10 minutes, and rabit polyclonal anti-Ebola Zaire VP40 antibody was applied to the sections at a 1:2,000 dilution for one hour. The anti-EBOV antibody was visualized using an AP-polymer kit, Mach 4 Universal (BioCare Medical, CA) for 30 minutes and reacted with Vulcan Fast Red (BioCare Medical, CA) substrate. All sections are counterstained with Gill's hematoxylin.

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Author contributions

H.M.W. and G.K. conceived the study, design experiments, performed the animal experiments, analyzed and interpreted data, and wrote the manuscript. C.E-H. provided analysis of histopathology and data interpretation; A.L., G.S. and C.N. performed *in vitro* experiments and analyzed related data.

Additional information

Supplementary information accompanies this paper at http://www.nature.com/scientificreports

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Vice President, Programs and Government Relations
Samaritan's Purse

Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

Update on the U.S. Public Health Response to the Ebola Outbreak
November 17, 2014

Attachment 2

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Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections

WHO Ebola Response Team*

ABSTRACT

BACKGROUND

On March 23, 2014, the World Health Organization (WHO) was notified of an outbreak of Ebola virus disease (EVD) in Guinea. On August 8, the WHO declared the epidemic to be a "public health emergency of international concern."

METHODS

By September 14, 2014, a total of 4507 probable and confirmed cases, including 2296 deaths from EVD (Zaire species) had been reported from five countries in West Africa — Guinea, Liberia, Nigeria, Senegal, and Sierra Leone. We analyzed a detailed subset of data on 3343 confirmed and 667 probable Ebola cases collected in Guinea, Liberia, Nigeria, and Sierra Leone as of September 14.

RESULTS

The majority of patients are 15 to 44 years of age (49.9% male), and we estimate that the case fatality rate is 70.8% (95% confidence interval [CI], 69 to 73) among persons with known clinical outcome of infection. The course of infection, including signs and symptoms, incubation period (11.4 days), and serial interval (15.3 days), is similar to that reported in previous outbreaks of EVD. On the basis of the initial periods of exponential growth, the estimated basic reproduction numbers (R_0) are 1.71 (95% CI, 1.44 to 2.01) for Guinea, 1.83 (95% CI, 1.72 to 1.94) for Liberia, and 2.02 (95% CI, 1.79 to 2.26) for Sierra Leone. The estimated current reproduction numbers (R) are 1.81 (95% CI, 1.60 to 2.03) for Guinea, 1.51 (95% CI, 1.41 to 1.60) for Liberia, and 1.38 (95% CI, 1.27 to 1.51) for Sierra Leone; the corresponding doubling times are 15.7 days (95% CI, 12.9 to 20.3) for Guinea, 23.6 days (95% CI, 20.2 to 28.2) for Liberia, and 30.2 days (95% CI, 23.6 to 42.3) for Sierra Leone. Assuming no change in the control measures for this epidemic, by November 2, 2014, the cumulative reported numbers of confirmed and probable cases are predicted to be 5740 in Guinea, 9890 in Liberia, and 5000 in Sierra Leone, exceeding 20,000 in total.

CONCLUSIONS

These data indicate that without drastic improvements in control measures, the numbers of cases of and deaths from EVD are expected to continue increasing from hundreds to thousands per week in the coming months.

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As of September 14, 2014, a total of 4507 confirmed and probable cases of Ebola virus disease (EVD), as well as 2296 deaths from the virus, had been reported from five countries in West Africa — Guinea, Liberia, Nigeria, Senegal, and Sierra Leone. In terms of reported morbidity and mortality, the current epidemic of EVD is far larger than all previous epidemics combined. The true numbers of cases and deaths are certainly higher. There are numerous reports of symptomatic persons evading diagnosis and treatment, of laboratory diagnoses that have not been included in national databases, and of persons with suspected EVD who were buried without a diagnosis having been made.[1]

The epidemic began in Guinea during December 2013,[2] and the World Health Organization (WHO) was officially notified of the rapidly evolving EVD outbreak on March 23, 2014. On August 8, the WHO declared the epidemic to be a "public health emergency of international concern."[3] By mid-September, 9 months after the first case occurred, the numbers of reported cases and deaths were still growing from week to week despite multinational and multisectoral efforts to control the spread of infection.[1] The epidemic has now become so large that the three most-affected countries — Guinea, Liberia, and Sierra Leone — face enormous challenges in implementing control measures at the scale required to stop transmission and to provide clinical care for all persons with EVD.

Because Ebola virus is spread mainly through contact with the body fluids of symptomatic patients, transmission can be stopped by a combination of early diagnosis, contact tracing, patient isolation and care, infection control, and safe burial.[1] Before the current epidemic in West Africa, outbreaks of EVD in central Africa had been limited in size and geographic spread, typically affecting one to a few hundred persons, mostly in remote forested areas.[4] The largest previous outbreak occurred in the districts of Gulu, Masindi, and Mbarara in Uganda.[5] This outbreak, which generated 425 cases over the course of 3 months from October 2000 to January 2001,[6] was controlled by rigorous application of interventions to minimize further transmission — delivered through the local health care system, with support from international partners.[5,7,8]

We now report on the clinical and epidemiologic characteristics of the epidemic in Guinea, Liberia, Nigeria, and Sierra Leone during the first 9 months of the epidemic (as of September, 14, Senegal had reported only a single case). We document trends in the epidemic thus far and project expected case numbers for the coming weeks if control measures are not enhanced.

METHODS

SURVEILLANCE

Full details of the methods, along with sensitivity and uncertainty analyses, are provided in Supplementary Appendix 1, available with the full text of this article at NEJM.org; a summary is provided here. Case definitions for EVD have been reported previously by the WHO.[9] In brief, a suspected case is illness in any person, alive or dead, who has (or had) sudden onset of high fever and had contact with a person with a suspected, probable, or confirmed Ebola case or with a dead or sick animal; any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, anorexia or loss of appetite, diarrhea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccupping; or any person who had unexplained bleeding or who died suddenly from an unexplained cause. A probable case is illness in any person suspected to have EVD who was evaluated by a clinician or any person who died from suspected Ebola and had an epidemiologic link to a person with a confirmed case but was not tested and did not have laboratory confirmation of the disease. A probable or suspected case was classified as confirmed when a sample from the person was positive for Ebola virus in laboratory testing.

Clinical and demographic data were collected with the use of a standard case investigation form (see Supplementary Appendix 1) on confirmed, probable, and suspected EVD cases identified through clinical care, including hospitalization, and through contact tracing in Guinea, Liberia, Nigeria, and Sierra Leone. To create the fullest possible picture of the unfolding epidemic, these data were supplemented by information collected in informal case reports, by data from diagnostic laboratories, and from burial records. The data recorded for each case included the district of residence, the district in which the disease was reported, the patient's age, sex, and signs

and symptoms, the date of symptom onset and of case detection, the name of the hospital, the date of hospitalization, and the date of death or discharge. A subgroup of case patients provided information on potentially infectious contacts with other persons who had Ebola virus disease, including possible exposure at funerals. We present here the results from analyses of detailed data on individual confirmed and probable cases recorded by each country in databases provided to the WHO as of September 14, 2014; analyses of confirmed and probable cases, together with suspected cases, are provided in Supplementary Appendix 1.

ETHICAL CONSIDERATIONS

This study is based on data collected during surveillance and response activities for EVD in Guinea, Liberia, Nigeria, and Sierra Leone. All information on individual patients has been anonymized for presentation.

CLINICAL MANIFESTATIONS AND CASE FATALITY RATE

We report on the frequency of symptoms in patients with confirmed and probable EVD cases overall and by country. We evaluated potential risk factors for a fatal outcome, including sex, age group (<15 years, 15 to 44 years, and ≥45 years), general and hemorrhagic symptoms, and occupation (whether the patient was or was not a health care worker). We performed the analysis using logistic-regression models, with data on patients for whom there was a definitive outcome (death or recovery) by August 17, 2014.

The case fatality rate was calculated as the percentage of fatal EVD cases among reported cases with a known definitive clinical outcome (see Supplementary Appendix 1). For comparison, we also calculated a case fatality rate that was based only on the ratio of reported deaths to reported cases, including in the denominator cases for which the clinical outcome is unknown.

KEY TIME PERIODS

We investigated five key time periods that characterize the progression of infection, the detection, care, and recovery or death of a person with Ebola virus disease, and the transmission of infection: the incubation period, which is the time between infection and the onset of symptoms (information that is relevant for assessing the length of time that case contacts have to be followed up); the interval from symptom onset to hospitalization (which is indicative of the infectious period in the community); the interval from hospital admission to death and the interval from hospital admission to discharge (both of which are relevant to assessing the demand for beds in relation to hospital capacity); the serial interval, which is defined as the interval between disease onset in an index case patient and disease onset in a person infected by that index case patient; and the generation time, which is the time between infection in an index case patient and infection in a patient infected by that index case patient (required to estimate the reproduction number, or R, of the epidemic).

The incubation period was estimated retrospectively (by having patients with confirmed cases recall the likely source of infection), with a distinction made between persons with single exposures and those with multiple exposures. In the case of multiple exposures, all the times of exposure were used to fit a parametric distribution (see Supplementary Appendix 1 for a sensitivity analysis). The interval from symptom onset to hospitalization is summarized as the mean, rather than the median, number of days to reflect the average person-days of infectiousness in the community. The mean duration of hospitalization was estimated as the average number of days from hospitalization to discharge and the average number of days from hospitalization to death, weighted by the proportion of patients who died. For each statistic we calculated the mean, median, and interquartile range and fitted a gamma probability distribution to model the variation among persons (see the results in Supplementary Appendix 1). Separate estimates were obtained for health care workers and for all other adults. The serial interval was estimated from a subgroup of patients for whom information was available on the time of symptom onset in known or suspected chains of transmission. For EVD, we expect the generation time distribution to be nearly identical to the serial interval distribution (result derived in Supplementary Appendix 1).

QUANTIFICATION OF THE SPREAD OF INFECTION AND PROJECTION OF FUTURE CASES

The basic reproduction number (R_0) is the average number of secondary cases that arise when one primary case is introduced into an uninfect-

ed population. These secondary cases arise after a period measured by the serial interval or by the generation time. When R_0 is greater than 1, infection may spread in the population, and the rate of spread is higher with increasingly high values of R_0. The doubling time (the time required for the incidence to double) was estimated on the basis of the reproduction number and the serial interval.[11] After the early phase of exponential growth in case numbers, once infection has become established, the number of people still at risk declines, so the reproduction number falls from its maximum value of R_0 to a smaller, net reproduction number, R_t. When R_t falls below 1, infection cannot be sustained. Estimates of R_0 and R_t help in evaluating the magnitude of the effort required to control the disease, the way in which transmission rates have fluctuated through time, and the effectiveness of control measures as they are implemented.

We estimated R_t over time from the time series of incidence of cases (i.e., a plot of the number of new cases per week over the course of the epidemic) and from our estimate of the serial interval distribution.[12] We then estimated R_0 for the early stages of the epidemic, when transmission rates were at their highest, on the basis of the date of symptom onset. As described in Supplementary Appendix 1, average estimates of R_t for the period from July 28 to September 7, 2014, which were made on the basis of the date of report to facilitate comparison with future cases, were used to project future cases, allowing for both uncertainty in the estimates of R_t and stochastic variability in the transmission process.

RESULTS

An animated map with timeline is available at NEJM.org

SCALE OF THE EPIDEMIC

A total of 4507 confirmed and probable EVD cases were reported to the WHO between December 30, 2013, and September 14, 2014 — a 37-week period. A total of 718 confirmed and probable cases and 289 deaths were reported in the week of September 8 through September 14 alone. The numbers of confirmed and probable cases reported by each country over time are shown in Figures 1 and 2. Detailed information was available on 3343 confirmed and 667 probable cases; these cases were used in all our analyses, with the exception of projections (results of analyses based on confirmed, probable, and suspected cases are provided in Supplementary Appendix 1). The median age of persons with EVD was 32 years (interquartile range, 21 to 44), and there were no significant differences in the age distribution of persons with EVD among countries. The majority of persons with EVD (60.8%) were between 15 and 44 years of age (this age group makes up only 44% of the population) (Table 1). There were also no significant differences among countries in the total numbers of male and female persons with EVD reported (49.9% of the total were male patients; within-country differences have not yet been fully investigated). EVD has taken a heavy toll among health care workers in Guinea, Liberia, and Sierra Leone. By September 14, a total of 318 cases, including 151 deaths, had been reported among health care workers.

GEOGRAPHIC ORIGIN AND THE SPREAD OF INFECTION

In December 2013, the first cases occurred in Guéckédou and Macenta districts, the focus of the epidemic in Guinea. During March 2014, a rise in the numbers of cases in these two districts, in addition to the first reports from Lofa and other districts in Liberia, was followed by the discovery of cases in the capital, Conakry. A second increase in case incidence in Guinea — first in Guéckédou and Macenta and then in the capital — occurred in May and June.

During May, the focus of the epidemic in Guinea expanded to the neighboring districts of Kenema and Kailahun in Sierra Leone, and in June further cases were reported in Lofa district in Liberia. These five districts have remained the focus of transmission in the border areas of the three countries. From July onward, there were sharp increases in case numbers at the epidemic foci in all three countries, at other sites away from the epicenter, and in the capital cities of Conakry, Freetown, and Monrovia (Fig. 1, and animated map and timeline at NEJM.org). However, although EVD has spread to many parts of Guinea, Liberia, and Sierra Leone, it has not been reported in all districts in the countries: among the total of 67 districts in the three countries, only 43 have reported one or more confirmed, probable, or suspected cases, and more than 90% of cases have been reported from just 14 districts.

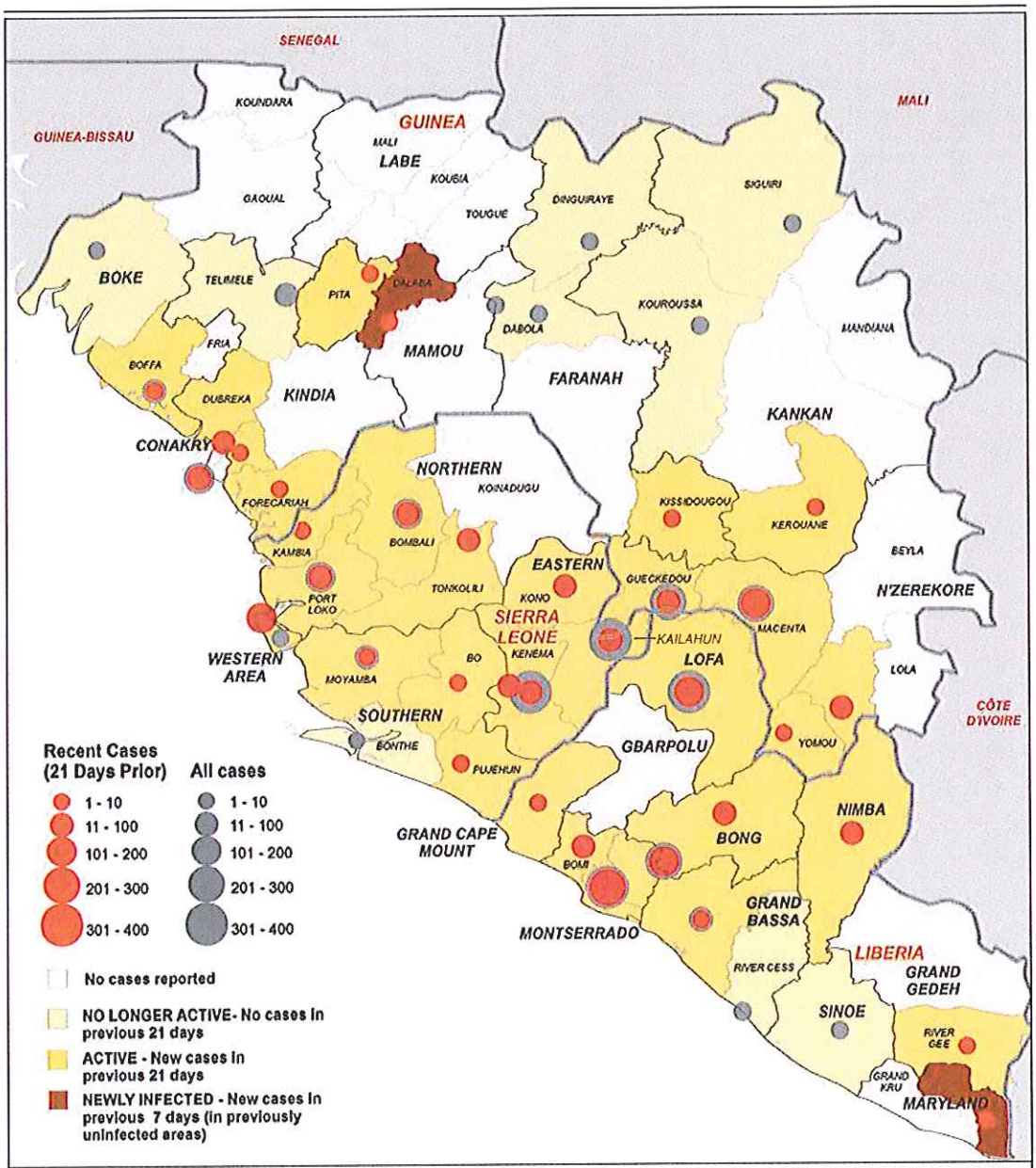

Figure 1. Districts Affected by Ebola Virus Disease in Three Countries in Africa.

The map shows the districts that have been affected by Ebola virus disease in Guinea, Liberia, and Sierra Leone. Gray circles indicate the total numbers of confirmed and probable Ebola cases reported in each affected district, and red circles the number reported during the 21 days leading up to September 14, 2014.

CLINICAL MANIFESTATIONS AND CASE FATALITY RATE

Table 1 provides information on demographic characteristics and symptom frequency in patients with confirmed or probable EVD with a definitive outcome in Guinea, Liberia, Nigeria, and Sierra Leone. The most common symptoms reported between symptom onset and case detection included fever (87.1%), fatigue (76.4%), loss of appetite (64.5%), vomiting (67.6%), diarrhea (65.6%), headache (53.4%), and abdominal pain (44.3%). Specific hemorrhagic symptoms were rarely reported (in <1% to 5.7% of patients). "Unexplained bleeding," however, was reported in 18.0% of cases. These patterns are similar in each country (see Supplementary Appendix 1).

Assessing the case fatality rate during this

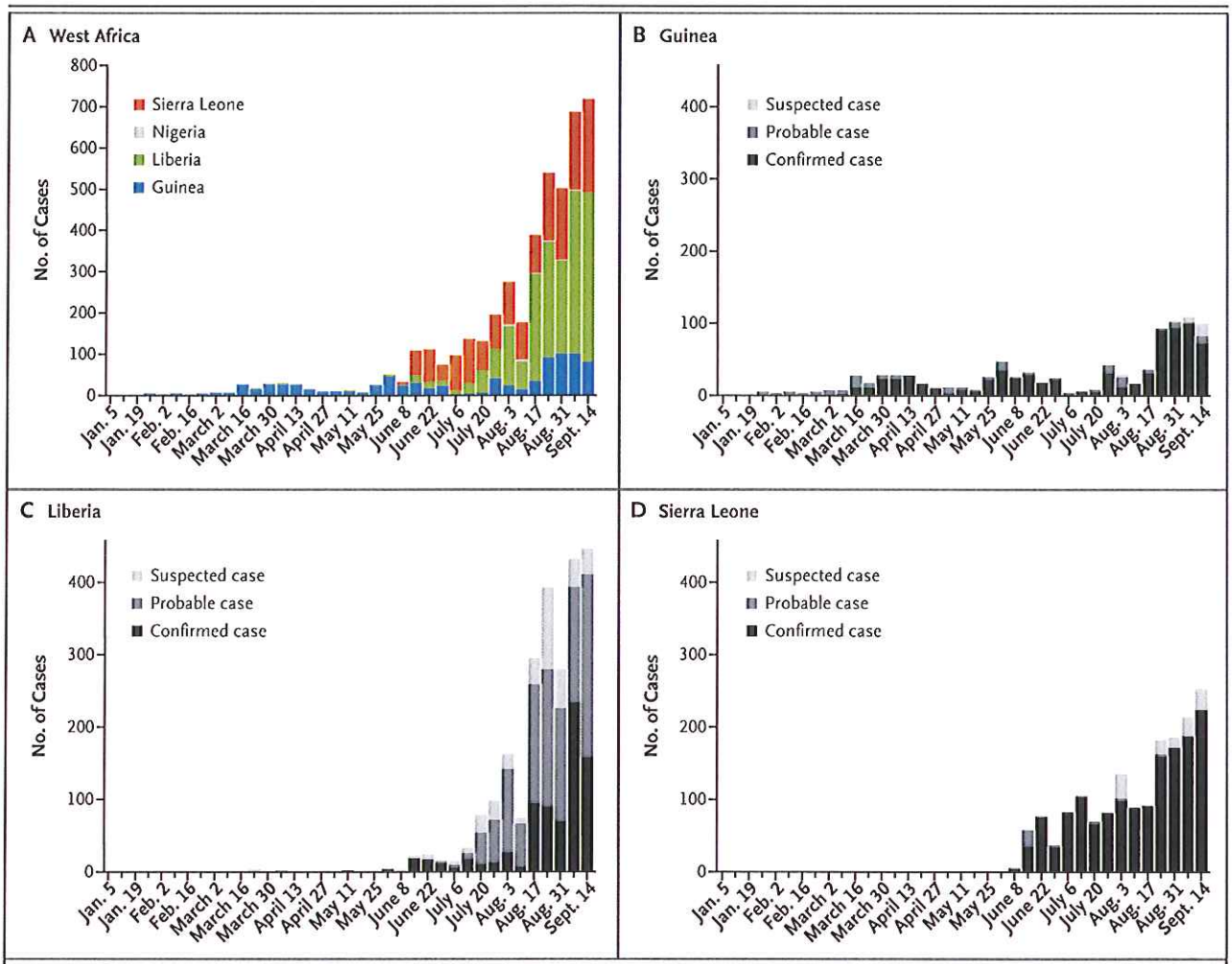

Figure 2. Weekly Incidence of Confirmed, Probable, and Suspected Ebola Virus Disease Cases.

Shown is the weekly incidence of confirmed, probable, and suspected EVD cases, according to actual or inferred week of symptom onset. A suspected case is illness in any person, alive or dead, who has (or had) sudden onset of high fever and had contact with a person with a suspected, probable, or confirmed Ebola case or with a dead or sick animal; any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, anorexia or loss of appetite, diarrhea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccupping; or any person who had unexplained bleeding or who died suddenly from an unexplained cause. A probable case is illness in any person suspected to have EVD who was evaluated by a clinician or any person who died from suspected Ebola and had an epidemiologic link to a person with a confirmed case but was not tested and did not have laboratory confirmation of the disease. A probable or suspected case was classified as confirmed when a sample from the person was positive for Ebola virus in laboratory testing.

epidemic is complicated by incomplete information on the clinical outcomes of many cases, both detected and undetected. Estimates of the case fatality rate (Table 2) derived by calculating the ratio of all reported deaths to all reported cases to date are low in comparison with historical outbreaks and are highly variable among the affected countries. However, estimating the case fatality rate using only the 46% of cases with definitive recorded clinical outcomes gives higher estimates that show no significant variation among countries (Table 2). This analysis shows that by September 14, a total of 70.8% (95% confidence interval [CI], 68.6 to 72.8) of case patients with definitive outcomes have died, and this rate was consistent among Guinea, Liberia, and Sierra Leone (Table 2). The case fatality rate in Nigeria was lower (45.5%), though this estimate is based on only 11 recent cases. The case fatality rate among hospitalized case

patients was 64.3% (95% CI, 61.5 to 67.0) lower than that among all patients with definitive outcomes and was consistent among countries. The case fatality rate among health care workers ranged from 56.1% (95% CI, 41.0 to 70.1) in Guinea to 80.0% (95% CI, 68.7 to 87.9) in Liberia (Table 2). Risk factors for a fatal outcome, after adjustment for country, are provided in Table 1. Significant risk factors for death include an age of 45 years or older as compared with 44 years of age or younger (odds ratio, 2.47; 95% CI, 1.79 to 3.46) and a number of general symptoms (diarrhea, conjunctivitis, difficulty breathing or swallowing, confusion or disorientation, and coma) and hemorrhagic symptoms (unexplained bleeding, bleeding gums, bloody nose, bleeding at the injection site, and bleeding from the vagina) (odds ratios and 95% confidence intervals for these factors are provided in Table 1).

KEY TIME PERIODS

The mean incubation period was 11.4 days (Table 2 and Fig. 3A), and did not vary by country (Fig. 3B, 3C, and 3D). Approximately 95% of the case patients had symptom onset within 21 days after exposure (Fig. 3A), which is the recommended period for follow-up of contacts. The estimated mean (±SD) serial interval was 15.3±9.3 days (Table 2 and Fig. 3E), which is the same as the estimated mean generation time (see Supplementary Appendix 1). The mean time from the onset of symptoms to hospitalization, a measure of the period of infectiousness in the community, was 5.0±4.7 days (Table 2), and was no shorter for health care workers than for other case patients. The mean time to death after admission to the hospital was 4.2±6.4 days, and the mean time to discharge was 11.8±6.1 days. The mean length of stay in hospital was 6.4 days in Guinea, Liberia, and Sierra Leone (Table 2).

QUANTIFICATION OF THE SPREAD OF INFECTION AND PROJECTION OF FUTURE CASES

Estimates of the basic reproduction number, R_0, were 1.71 (95% CI, 1.44 to 2.01) for Guinea, 1.83 (95% CI, 1.72 to 1.94) for Liberia, 1.20 (95% CI, 0.67 to 1.96) for Nigeria, and 2.02 (95% CI, 1.79 to 2.26) for Sierra Leone (Table 2, and Fig. S7 in Supplementary Appendix 1). Although R_0 reflects the maximum potential for growth in case incidence, Figure S7 in Supplementary Appendix 1 shows the variation in the estimated net reproduction number, R_t, during the course of the epidemic. Between March and July 2014, the R_t for Guinea fluctuated around the threshold value of 1 but appeared to increase again in August, reflecting the rise in case incidence in Macenta district. In Sierra Leone, the value of R_t dropped between June and August as the case incidence stabilized in Kenema and Kailahun. In Liberia, the R_t remained above 1 for most of the period between March and August, reflecting the consistent increase in case incidence (Fig. S9) in that country.

The growing numbers of cases reported from Guinea, Liberia, and Sierra Leone in August and early September suggest that the R_t remains above 1 in a still-expanding epidemic (reliable estimates of R_t could be obtained only to early September owing to reporting delays). As of September 14, the doubling time of the epidemic was 15.7 days in Guinea, 23.6 days in Liberia, and 30.2 days in Sierra Leone (Table 2). We estimate that, at the current rate of increase, assuming no changes in control efforts, the cumulative number of confirmed and probable cases by November 2 (the end of week 44 of the epidemic) will be 5740 in Guinea, 9890 in Liberia, and 5000 in Sierra Leone, exceeding 20,000 cases in total (Fig. 4, and Table S8 in Supplementary Appendix 2). The true case load, including suspected cases and undetected cases, will be higher still.

DISCUSSION

Although the current epidemic of EVD in West Africa is unprecedented in scale, the clinical course of infection and the transmissibility of the virus are similar to those in previous EVD outbreaks. The incubation period, duration of illness, case fatality rate, and R_0 are all within the ranges reported for previous EVD epidemics.[7,13-18] Our estimates of R_0 are similar to other recent estimates for this West Africa epidemic.[19-23] The combination of signs and symptoms recorded between symptom onset and clinical presentation is also similar to that in other reports.[14,17,24-26] We infer that the present epidemic is exceptionally large, not principally because of the biologic characteristics of the virus, but rather because of the attributes of the affected populations and because control efforts have been insufficient to halt the spread of infection.

Certain characteristics of the affected populations may have led to the rapid geographic dissemination of infection. The populations of Guinea, Liberia, and Sierra Leone are highly interconnected, with much cross-border traffic at the epicenter and relatively easy connections by road between rural towns and villages and between densely populated national capitals. The large intermixing population has facilitated the spread of infection, but a large epidemic was not inevitable. In Nigeria, the number of cases has so far been limited, despite the introduction of infection into the large cities of Lagos (approximately 20 million people) and Port Harcourt (>1 million people). The critical determinant of epidemic size appears to be the speed of implementation of rigorous control measures.

Previous experience with EVD outbreaks, though they have been limited in size and geographic spread, suggests that transmission can

Table 1. Demographic Characteristics and Signs and Symptoms in Confirmed and Probable Ebola Case Patients with a Definitive Clinical Outcome in Guinea, Liberia, Nigeria, and Sierra Leone.*

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Demographic characteristics				
Male sex	685/1415 (48.4)	515/1056 (48.8)	170/359 (47.4)	0.93 (0.73–1.19)
Age group				
<15 yr	190/1378 (13.8)	145/1021 (14.2)	45/357 (12.6)	1.18 (0.83–1.71)
15–44 yr	838/1378 (60.8)	577/1021 (56.5)	261/357 (73.1)	0.48 (0.36–0.62)
≥45 yr	350/1378 (25.4)	299/1021 (29.3)	51/357 (14.3)	2.47 (1.79–3.46)
Health care worker	158/1429 (11.1)	112/1067 (10.5)	46/362 (12.7)	0.86 (0.60–1.27)
Signs and symptoms				
General symptoms				
Fever‡	1002/1151 (87.1)	746/846 (88.2)	256/305 (83.9)	1.34 (0.92–1.95)
Fatigue	866/1133 (76.4)	633/829 (76.4)	233/304 (76.6)	0.94 (0.68–1.28)
Loss of appetite	681/1055 (64.5)	498/778 (64.0)	183/277 (66.1)	0.92 (0.69–1.23)
Vomiting	753/1114 (67.6)	566/816 (69.4)	187/298 (62.8)	1.19 (0.89–1.59)
Diarrhea	721/1099 (65.6)	555/813 (68.3)	166/286 (58.0)	1.42 (1.06–1.89)
Headache	553/1035 (53.4)	407/757 (53.8)	146/278 (52.5)	1.03 (0.78–1.36)
Abdominal pain	439/992 (44.3)	311/715 (43.5)	128/277 (46.2)	0.85 (0.64–1.13)
Muscle pain	385/990 (38.9)	293/728 (40.2)	92/262 (35.1)	1.24 (0.92–1.67)
Joint pain	374/950 (39.4)	283/695 (40.7)	91/255 (35.7)	1.32 (0.98–1.80)
Chest pain	254/686 (37.0)	196/488 (40.2)	58/198 (29.3)	1.53 (1.07–2.20)
Cough	194/655 (29.6)	150/462 (32.5)	44/193 (22.8)	1.74 (1.18–2.61)
Difficulty breathing	155/665 (23.3)	123/472 (26.1)	32/193 (16.6)	1.68 (1.10–2.63)
Difficulty swallowing	169/514 (32.9)	138/375 (36.8)	31/139 (22.3)	2.22 (1.41–3.59)
Conjunctivitis	137/658 (20.8)	109/465 (23.4)	28/193 (14.5)	2.03 (1.29–3.29)
Sore throat	102/467 (21.8)	82/339 (24.2)	20/128 (15.6)	1.94 (1.13–3.46)
Confusion	84/631 (13.3)	68/446 (15.2)	16/185 (8.6)	2.00 (1.14–3.71)
Hiccups	108/947 (11.4)	91/699 (13.0)	17/248 (6.9)	2.15 (1.27–3.82)
Jaundice	65/627 (10.4)	52/443 (11.7)	13/184 (7.1)	1.83 (0.99–3.63)
Eye pain	48/622 (7.7)	39/438 (8.9)	9/184 (4.9)	1.95 (0.95–4.40)
Rash	37/642 (5.8)	30/453 (6.6)	7/189 (3.7)	1.90 (0.86–4.83)
Coma or unconsciousness	37/627 (5.9)	34/445 (7.6)	3/182 (1.6)	4.59 (1.61–19.34)

Table 1. (Continued.)

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Unexplained bleeding	168/932 (18.0)	140/693 (20.2)	28/239 (11.7)	1.83 (1.20–2.90)
Hematemesis	26/670 (3.9)	20/503 (4.0)	6/167 (3.6)	1.07 (0.44–3.01)
Blood in stool	48/843 (5.7)	35/614 (5.7)	13/229 (5.7)	0.98 (0.52–1.96)
Bleeding gums	19/837 (2.3)	18/608 (3.0)	1/229 (0.4)	6.69 (1.35–121.32)
Bloody nose	16/836 (1.9)	15/610 (2.5)	1/226 (0.4)	8.02 (1.54–148.62)
Bloody cough	20/831 (2.4)	16/605 (2.6)	4/226 (1.8)	1.63 (0.58–5.82)
Other bleeding	8/657 (1.2)	5/493 (1.0)	3/164 (1.8)	0.45 (0.11–2.23)
Bleeding at injection site	20/833 (2.4)	19/605 (3.1)	1/228 (0.4)	6.51 (1.32–118.04)
Blood from vagina§	14/431 (3.2)	13/290 (4.5)	1/126 (0.8)	6.0 (1.11–112.4)
Blood in urine	10/827 (1.2)	9/601 (1.5)	1/226 (0.4)	5.14 (0.90–98.73)
Bleeding under skin	5/827 (0.6)	5/604 (0.8)	0/223	NA

* Data are as of September 14, 2014. Patients with date of onset up to August 17, 2014, were included. Total numbers are the numbers of patients with data on the variable in question. NA denotes not applicable.
† Odds ratios are adjusted for country. CI denotes confidence interval.
‡ Fever was defined as a body temperature above 38°C; however, in practice, health care workers at the district level often do not have a medical thermometer and simply ask whether the person's body temperature is more elevated than usual.
§ Percentages reflect only female patients.

be interrupted, and case incidence reduced, within 2 to 3 weeks after the introduction of control measures.[1,5,7,14-17,24,27-31] This view is reinforced by the estimates of case reproduction number presented in this analysis. We estimate the R_0 to have varied between 1.71 (upper boundary of the 95% confidence interval, 2.01) in Guinea to 2.02 (upper boundary of the 95% confidence interval, 2.26) in Sierra Leone. This means that transmission has to be a little more than halved to achieve control of the epidemic and eventually to eliminate the virus from the human population. Considering the prospects for a novel Ebola vaccine, an immunization coverage exceeding 50% would have the same effect. Greater reductions in transmission would, of course, be desirable, but minimum requirements for the containment of EVD are far less severe than for the containment of more contagious diseases, such as measles. Between March and July 2014, the reproduction number in Guinea fluctuated around the threshold value of 1, suggesting that modest further intervention efforts at that point could have achieved control.

The analyses in this paper can be used to inform recommendations regarding control measures. The measured duration of the incubation period, and its variation, imply that the advice to follow case contacts for 21 days[1] is appropriate. To curtail transmission in the community, the period from symptom onset to hospitalization (a mean of 5 days but a maximum of >40 days) clearly needs to be reduced. Surprisingly, the mean was not shorter among health care workers, who are at risk both of acquiring and transmitting the infection to others. The average length of hospital stay of about 1 week (6.4 days) means that the number of beds required to treat EVD patients is roughly equal to the rising weekly case incidence. Even without allowing for underreporting, 995 patients with confirmed, probable, or suspected infection were known to need clinical care in the week of September 8 through 14 alone, which far exceeds the present bed capacity in Guinea, Liberia, and Sierra Leone (approximately 610 beds in total).

The data used in these analyses were collected in the field by various field teams across Guinea, Liberia, Nigeria, and Sierra Leone. Although they provide an excellent opportunity to better understand the current EVD epidemic in Africa, they understate the magnitude of the

Table 2. Estimates of Epidemiologic Variables for Confirmed and Probable Ebola Cases, According to Country, as of September 14, 2014.*

Variable	All Countries		Guinea		Liberia		Nigeria		Sierra Leone	
	no. of days	no. of patients with data	no. of days	no. of patients with data	no. of days	no. of patients with data	no. of days	no. of patients with data	no. of days	no. of patients with data
Incubation period										
Single-day exposures										
Observed†	9.4±7.4	500	10.7±8.7	35	9.5±6.6	259	NC	<10	9.0±8.1	201
Fitted‡	9.1±7.3	500	9.9±9.8	35	9.4±6.7	259	NC	<10	8.5±7.6	201
Multi-day exposures										
Observed†	11.4±NA	155	10.9±NA	20	11.7±NA	79	NC	<10	10.8±NA	48
Fitted‡	9.7±5.5	155	8.3±4.5	20	9.9±5.7	79	NC	<10	9.9±5.6	48
Serial interval§										
Observed	15.3±9.1	92	19.0±11.0	40	13.1±6.6	26	NC	<10	11.6±5.6	25
Fitted¶	15.3±9.3	92	19.0±11.2	40	13.1±7.8	26	NC	<10	11.6±6.3	25
R_0‖										
Mean (95% CI)	—		*1.71 (1.44–2.01)*		*1.83 (1.72–1.94)*		*1.2 (0.67–1.96)*		*2.02 (1.79–2.26)*	
Doubling time — days (95% CI)	—		*17.53 (13.18–26.64)*		*15.78 (14.4–17.37)*		*59.75 (13.27–∞)*		*12.84 (10.92–15.66)*	
R**										
Mean (95% CI)	—		*1.81 (1.60–2.03)*		*1.51 (1.41–1.60)*				*1.38 (1.27–1.51)*	
Doubling time — days (95% CI)	—		*15.7 (12.9–20.3)*		*23.6 (20.2–28.2)*		*NC*		*30.2 (23.6–42.3)*	
Interval from symptom onset										
To hospitalization	5.0±4.7	1135	5.3±4.3	484	4.9±5.1	245	4.1±1.4	11	4.6±5.1	395
To hospital discharge	16.4±6.5	267	16.3±6.1	152	15.4±8.2	41	NC	<10	17.2±6.2	70
To death	7.5±6.8	594	6.4±5.3	248	7.9±8.0	212	NC	<10	8.6±6.9	128
To WHO notification	6.1±8.5	2185	7.5±10.4	743	6.0±8.7	797	3.9±2.3	11	4.5±5.0	634
Interval from WHO notification										
To hospital discharge	11.8±7.2	312	11.1±5.8	164	11±8.0	41	NC	<10	12.7±8.4	102
To death	−3.0±13.8	584	−4.4±14.4	300	−1.8±13.6	221	NC	<10	−1.6±9.2	58
Interval from hospitalization										
To hospital discharge	11.8±6.1	290	11±5.4	159	12.8±8.1	40	NC	<10	12.4±5.8	86
To death	4.2±6.4	121	2.5±3.4	36	4.5±6.0	63	NC	<10	4.4±6.0	17
Duration of hospital stay — days††	6.42		4.99		6.72		NC		6.88	

	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data
Case fatality rate										
All cases, based on current status	37.7 (36.1–39.2)	3747	57.5 (53.7–61.1)	677	34.7 (32.4–37.1)	1616	40.0 (19.8–64.3)	15	31.6 (29.3–34.1)	1439
All cases, based on definitive outcome	70.8 (68.6–72.8)	1737	70.7 (66.7–74.3)	542	72.3 (68.9–75.4)	739	45.5 (21.3–72.0)	11	69.0 (64.5–73.1)	445
Before August 18	71.3 (68.7–73.7)	1244	68.7 (64.3–72.8)	454	79.8 (75.7–83.4)	416	50.0 (23.7–76.3)	10	65.4 (60.4–70.1)	364
August 18–September 14	59.9 (54.7–64.9)	354	80.7 (71.2–87.6)	88	41.1 (34.3–48.2)	190	NC	<10	84.0 (74.1–90.6)	75
All hospitalized cases, based on definitive outcome	64.3 (61.5–67.0)	1153	64.7 (60.1–68.9)	450	67.0 (62.0–71.7)	361	40.0 (16.8–68.7)	10	61.4 (56.1–66.5)	332
According to sex										
Male	72.2 (69.1–75.1)	874	68.5 (62.6–73.9)	254	74.9 (70.4–79.0)	395	NC	<10	71.9 (65.7–77.5)	221
Female	69.9 (66.7–73.0)	818	72.7 (67.3–77.6)	286	71.6 (66.4–76.3)	317	NC	<10	64.4 (57.7–70.6)	208
According to age group										
<15 yr	73.4 (67.2–78.8)	218	78.1 (67.3–86.0)	73	70.7 (60.1–79.5)	82	NC	<10	71.4 (59.3–81.1)	63
15–44 yr	66.1 (63.1–69.0)	1012	64.9 (59.5–69.9)	319	70.6 (66.1–74.8)	422	NC	<10	61.4 (55.4–67.0)	264
≥45 yr	80.4 (76.2–84.0)	398	78.6 (71.1–84.6)	140	81.1 (74.4–86.4)	164	NC	<10	82.2 (73.1–88.8)	90
According to occupation										
Health care worker	69.4 (62.1–75.8)	170	56.1 (41.0–70.1)	41	80.0 (68.7–87.9)	65	NC	<10	68.4 (55.5–79.0)	57
Non–health care worker	70.9 (68.6–73.1)	1567	71.9 (67.8–75.6)	501	71.5 (68.0–74.8)	674	NC	<10	69.1 (64.3–73.5)	388

* Plus–minus values are means ±SD. NA denotes not available, NC not calculated, and WHO World Health Organization.

† Contacts on day 0 (i.e., on the day of symptom onset) were excluded.

‡ Contacts on day 0 (i.e., on the day of symptom onset) were excluded. Gamma probability distributions were fitted to confirmed and probable cases.

§ The serial interval is the interval between disease onset in an index case patient and disease onset in a person infected by that index case patient. In this category, the number of patients with data is the number of epidemiologically linked pairs in which the later case patient reported only one direct contact.

¶ Gamma probability distributions were fitted to confirmed and probable cases.

‖ The basic reproduction number (R_0) is the average number of secondary cases that arise when one primary case is introduced into an uninfected population. We estimated the R_0 and associated mean doubling time, using a serial interval of 15.3 days, for the period up to March 30, 2014, for Guinea; up to August 24, 2014, for Liberia and Nigeria; and up to July 6, 2014, for Sierra Leone. This number was estimated for individual countries only and not for the combined data.

** We estimated R_t (the estimated net reproduction number), and associated mean doubling time, using a serial interval of 15.3 days, for the period of July 21 to August 31, 2014. This number was estimated for individual countries only and not for the combined data.

†† The mean duration of hospital stay was calculated as the weighted average of the observed means from the hospitalization-to-discharge and hospitalization-to-death distributions. This variable was not calculated in Nigeria because there were fewer than 10 case patients with data.

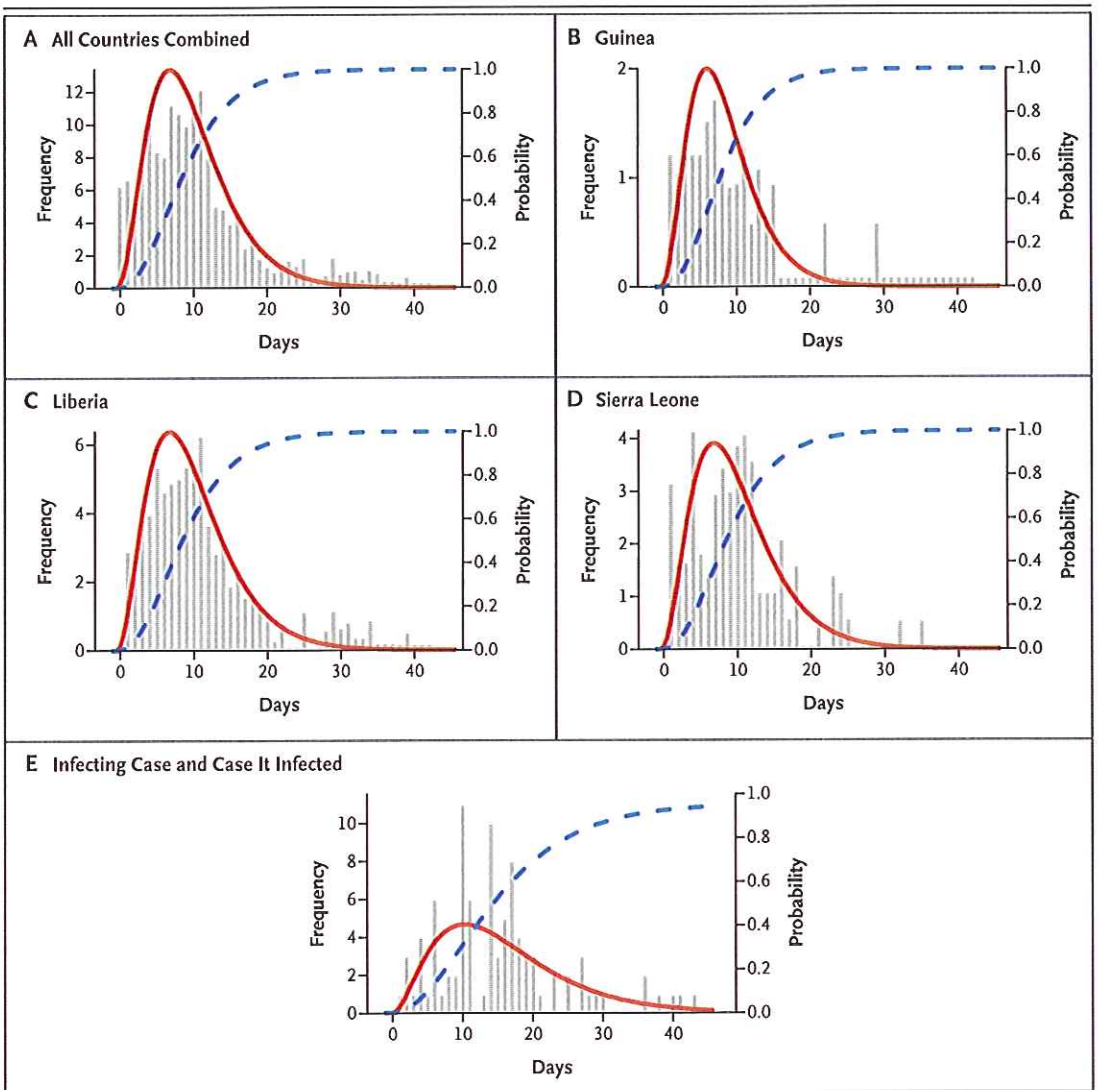

Figure 3. Time between Exposure and Disease Onset.

Panel A through D show the observed times (>0) between exposure and disease onset for all countries, Guinea, Liberia, and Sierra Leone, respectively, including only cases with multiple exposure days (histograms in gray), best-fit (gamma) probability density function (red curves) and cumulative distribution for the incubation period (blue curves). Panel E shows the observed times between disease onset in an index case patient and disease onset in the person infected by the index case patient (histograms in gray) and best-fit (gamma) probability density function (red curve) and cumulative distribution (blue curve) for the serial interval.

problem. It is likely that many cases have not been detected, and for those cases that have been reported, case records are often incomplete. Therefore, interpretation of the available case data requires care. We recognize, however, that data are being collected under extreme conditions, and the top priorities are patient care, contact tracing, and limiting transmission in the community, rather than epidemiologic investigations. In addition, in this initial assessment it was not possible to consider all the sources of heterogeneity (e.g., geographic and health care–related) affecting the development of this epidemic. Thus the future projections provided here should be regarded as indicative of likely future trends more than precise predictions. Despite these limitations and the resulting uncertainties, the results presented here help us to understand the spread of infection and the potential for control.

Some details of the current analysis remain

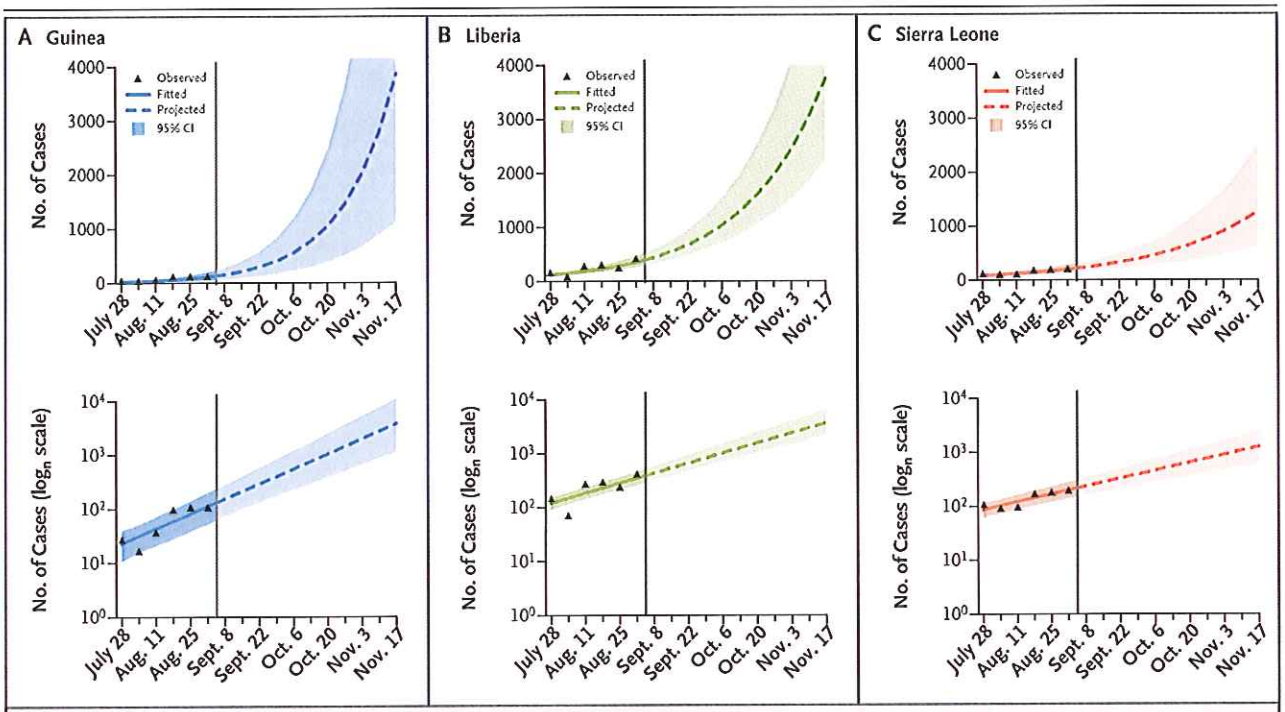

Figure 4. Observed and Projected Case Incidence.

Observed and projected weekly case incidence in Guinea (Panel A), Liberia (Panel B), and Sierra Leone (Panel C) are shown on linear (upper panels) and logarithmic (lower panels) scales

to be confirmed by further investigation. For example, our estimate of 15.3 days for the serial interval is slightly longer than past estimates.[32,33] This may reflect the difficulties of collecting temporally unbiased data on exposure through contact tracing, either in the current outbreak or during previous outbreaks. Alternatively, a longer serial interval may indicate that case isolation has been less effective in the current epidemic, resulting in a higher proportion of transmission events occurring late in the course of illness.

Case fatality is among the most important topics for further investigation. Our estimates of case fatality are consistent in Guinea (70.7%), Liberia (72.3%), and Sierra Leone (69.0%) when estimates are derived with data only for patients with recorded definitive clinical outcomes (1737 patients). Estimates for hospitalized patients with recorded definitive clinical outcomes are also consistent across countries but are lower than those for all patients with definitive clinical outcomes. In contrast, simply taking the ratio of reported deaths to reported cases gives estimates that differ among countries (Table 2). These discrepancies perhaps reflect the challenges of clinical follow-up and data capture. The lower case fatality rate among hospitalized patients than among all persons with EVD could indicate that hospitalization increased survival, that cases of EVD in nonhospitalized persons were more likely to be detected if they were fatal, or that some persons died before they could be admitted to the hospital. In each of the countries studied, the case fatality rate is lowest among persons 15 to 44 year of age, and highest among persons 45 years of age or older, and some limited variation in the case fatality rate among health care workers was observed among countries. The reasons for this variation are not yet known. Moreover, the case fatality rate among hospitalized patients may differ from that among patients who are never seen by a physician. Liberia has reported an unusually high proportion of deaths among patients with suspected (but not probable or confirmed) EVD cases (58% [440 of 754 patients]), as compared with Guinea (13% [4 of 30 patients]) and Sierra Leone (35% [74 of 213 patients]). The implication is that many true EVD case patients in Liberia may have died before receiving a definitive diagnosis.

Notwithstanding the geographic variation in case incidence within and among Guinea, Liberia, and Sierra Leone, the current epidemiologic outlook is bleak. Forward projections suggest that unless control measures — including improvements in contact tracing, adequate case isolation, increased capacity for clinical management, safe burials, greater community engagement, and support from international partners — improve quickly, these three countries will soon be reporting thousands of cases and deaths each week, projections that are similar to those of the Centers for Disease Control and Prevention. Experimental therapeutics and vaccines offer promise for the future but are unlikely to be available in the quantities needed to make a substantial difference in control efforts for many months, even if they are proved to be safe and effective. Furthermore, careful assessment of the most effective means of utilizing such interventions (e.g., vaccination or treatment of contacts versus health care workers) will be required while stocks remain limited. For the medium term, at least, we must therefore face the possibility that EVD will become endemic among the human population of West Africa, a prospect that has never previously been contemplated. The risk of continued epidemic expansion and the prospect of endemic EVD in West Africa call for the most forceful implementation of present control measures and for the rapid development and deployment of new drugs and vaccines.

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APPENDIX

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Update on the U.S. Public Health Response to the Ebola Outbreak
November 17, 2014

Attachment 3

naturalnews.com printable article

Originally published October 15 2014

Shock W.H.O. report: Ebola has 42-day incubation period, not 21 days!

by Mike Adams, the Health Ranger, NaturalNews Editor

(NaturalNews) A jaw-dropping report released by the World Health Organization on October 14, 2014 reveals that 1 in 20 Ebola infections has an incubation period longer than the 21 days which has been repeatedly claimed by the U.S. Centers for Disease Control.

This may be the single most important -- and blatantly honest -- research report released by any official body since the beginning of the Ebola outbreak. The WHO's "Ebola situation assessment" report, found here, explains that only 95% of Ebola infections experience incubation within the widely-reported 21-day period. Here's the actual language from the report:

95% of confirmed cases have an incubation period in the range of 1 to 21 days; 98% have an incubation period that falls within the 1 to 42 day interval. [1]

Unless the sentence structure is somehow misleading, this passage appears to indicate the following:

- 95% of Ebola incubations occur from 1 - 21 days
- 3% of Ebola incubations occur from 21 - 42 days
- 2% of Ebola incubations are not explained (why?)

If this interpretation of the WHO's statistics are correct, it would mean that:

- 1 in 20 Ebola infections may result in incubations lasting significantly longer than 21 days

- The 21-day quarantine currently being enforced by the CDC is entirely insufficient to halt an outbreak

- People who are released from observation or self-quarantine after 21 days may still become full-blown Ebola patients in the subsequent three weeks, **even if they have shown no symptoms of infection during the first 21 days**. (Yes, read that again...)

Any declaration that an outbreak is over requires 42 days with no new infections

Underscoring the importance of the 42-day rule, the WHO document openly states that **a 42-day observation period with no new outbreaks is required before declaring the outbreak is under control**. In the WHO's own words:

WHO is therefore confident that detection of no new cases, with active surveillance in place, throughout this 42-day period means that an Ebola outbreak is indeed over. [1]

W.H.O. "alarmed" over false pronouncements of negative Ebola tests

Just as disturbing is the WHO's open warning that government health officials who are announcing negative Ebola findings in patients mere hours after them being tested are grossly misleading the public and essentially practicing quack medicine.

As explained by the WHO:

WHO is alarmed by media reports of suspected Ebola cases imported into new countries that are said, by government officials or ministries of health, to be discarded as "negative" within hours after the suspected case enters the country. ***Such rapid determination of infection status is impossible****, casting grave doubts on some of the official information that is being communicated to the public and the media.* [1]

In other words, WHO is telling us that all those public pronouncements by government health authorities are meaningless. An Ebola infection determination cannot be made in mere hours, it turns out. In fact, as WHO explains, a suspected case of Ebola must be observed and tested **for 48 hours** before any degree of certainty can be reached about the Ebola infection status:

Two negative RT-PCR test results, at least 48 hours apart, are required for a clinically asymptomatic patient to be discharged from hospital, or for a suspected Ebola case to be discarded as testing negative for the virus. [1]

"No signs" that outbreaks are under control

Finally, this WHO report goes on to conclude that the Ebola outbreaks of Guinea, Liberia and Sierra Leone are multiplying out of control. The report even cites the curious phenomenon of unexpected outbreak surges taking place in areas once thought to be eradicated:

In Guinea, Liberia, and Sierra Leone, new cases continue to explode in areas that looked like they were coming under control. An unusual characteristic of this epidemic is a persistent cyclical pattern of gradual dips in the number of new cases, followed by sudden flare-ups. WHO epidemiologists see no signs that the outbreaks in any of these 3 countries are coming under control. [1]

Is it possible that these resurging outbreaks are being caused by governments failing to monitor potentially infected Ebola victims for a full 42 days? If they only observe them for 21 days, then 1 out of 20 infected victims may be cleared as "clean" and allowed back into the population where they soon become symptomatic and spread the disease even further.

U.S. doctors and health officials have been taught the wrong number: 21 days is only HALF the duration

It is extremely disturbing to realize that, to our best knowledge, every single person in the United States who has been suspected of harboring Ebola has been instructed to monitor symptoms for only 21 days, not the necessary 42 days.

This means that **Ebola-infected U.S. citizens who are "cleared" of Ebola may still erupt with the deadly virus for a period of three more weeks.**

Why hasn't anyone reported this until now? How is this not one of the single most important pieces of information in the world at this moment when all human life on our planet is now legitimately threatened by an uncontrolled viral outbreak with a 70 percent fatality rate and no recognized treatments or cures?

Prepare yourself now with the free downloadable MP3 audio files at www.BioDefense.com

Sources for this article include:

[1] http://www.who.int/mediacentre/news/ebola/14...

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Attachment 4

The New York Times | http://nyti.ms/1BF9ENV

THE OPINION PAGES | OP-ED CONTRIBUTOR

In India, Growth Breeds Waste

By JERRY PINTO NOV. 16, 2014

MUMBAI, INDIA — There is, we are told, a small island of plastic in the middle of the Pacific Ocean. There was, we are told, a fatberg plucked out of the sewers of London. But nowhere in the world is dirt as visible as in India. It is so visible that for many Indians who return from America, even from New York, it isn't the Grand Canyon or the Met they remember. It's how clean the streets were.

That's because you can't get away from the dirt of India. My city, Mumbai, has an estimated 20 million people. According to one estimate, we produce 630 grams of garbage per person per day — that's 12.6 million tons every day. Mumbai is also the richest city in the country, with one-third of the national income tax revenue coming from here. The richer you are, the more waste you produce.

And that's only talking about the garbage we see. A doctor told me she can't measure her patients' Vitamin B levels accurately because fecal contamination through the tap water skews the numbers too much. The city's 19th-century sewers often run right next to the water pipes and both are porous, and as you learned in Chemistry 101, if two liquids with different degrees of concentration are separated by something with teeny-tiny holes, osmosis will do the rest.

India now has its own clean-up campaign, inaugurated by a new-broom prime minister. This is well and good. No one can deny that being clean is. "Cleanliness is next to godliness," my grandmother would say to my mother. "Then let's be godly instead," my mother would answer, tapping some more ash from a bidi on the floor. No one agreed with her. We Indians are cleanly people, we like to think. Hindus and Muslims alike bathe every day because it's in the scriptures. We wash our homes every day, and the urban middle class throws out yesterday's drinking water because it is "stale." But that's the private sphere.

In the public sphere, we are consistently awful. Arthur Koestler once said that breathing the air in Mumbai felt like "a wet, smelly diaper was being wrapped around my head." I returned from Delhi recently, and there I felt like my head had been stuck in the exhaust of a truck. Hundreds of ministers and bureaucrats and workers travel around the city in hundreds of cars, each one in a single car with his or her own driver, each one sighing at the density of the traffic, each one complaining about the quality of the air, not one admitting to being part of the problem.

In 1901, Mahatma Gandhi, the father of the nation, as we like to call him, was struck by how the delegates at a meeting of the Indian National Congress in Calcutta had made the toilets of the house they were living in too filthy to use. Then they turned a verandah into an open-air latrine. Young Gandhi chided them but was told that cleaning the toilets was the sweepers' job.

Sweepers in India aren't people who choose to be sanitation engineers. They're people who are born to be sanitation engineers, and they are not supposed to hope to be anything else. They're the outcasts of Indian society; "untouchables," they used to be called, unseeables. Then Gandhi started calling them Harijans, People of God. They have since renamed themselves Dalits, the Broken People or the Oppressed People. Reservations — the Indian word for the affirmative action measures prescribed by the Constitution — may have helped many of them become doctors and lawyers and engineers, but most of the people who clean latrines in India still come from the Dalits. (When you take a dump on an Indian train, it falls onto the tracks. After the train has passed a manual scavenger, usually a Dalit, comes by and cleans up.) It is always going to be someone else's job to keep things clean.

Dirt, it is said, is matter in the wrong place. Then what is the right place for it? We have garbage policies to deal with this, but they are not implemented. Although in Mumbai the government asks residents to segregate rubbish into wet and dry waste, municipal workers often mix everything into the same dumpster.

There are still rag pickers and raddiwallas, the men who buy your old papers, bottles and whatever else you don't want. Some of these things go back into the system. Old clothes are bought in the cities and sold in the villages. Used electronics get refurbished and returned into the market. CDs are painted over with religious symbols and hung in cars. We continue to recycle and upcycle.

But we can no longer keep up. There's too much stuff being made now, thanks to the backwash of globalization. Plastic was once an exotic substance, and plastic bags were hoarded and exchanged with ritual solemnity. When I was in the third grade, in 1975, we used chalk on slate for rough calculations. We would write out our lessons in pencil, and every so often would be told to erase them and reuse the notebooks. At the end of every academic year, we would tear out all the unused pages and get them bound as a "rough note" book. No child would be caught dead with one of those now. We're richer, we're more style-conscious and we're dirtier.

I remember my sister's friend, Alice, and her love affair with the Marlboro Man, circa 1978-81. Alice's cousin was in the airlines and he once brought their family some goodies in a plastic bag that had the Marlboro Man doing his macho thing on the outside. Alice used the bag for years, carrying her college books in it. One day, I went over to her house and her mother was at the sewing machine. The bag had split at the seam and was being repaired. Today, it would have ended up on the garbage heap or by the edge of a national highway. It would have become someone else's responsibility.

Jerry Pinto is the author of "Em and the Big Hoom."

A version of this op-ed appears in print on November 17, 2014, in The International New York Times.

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Attachment 5

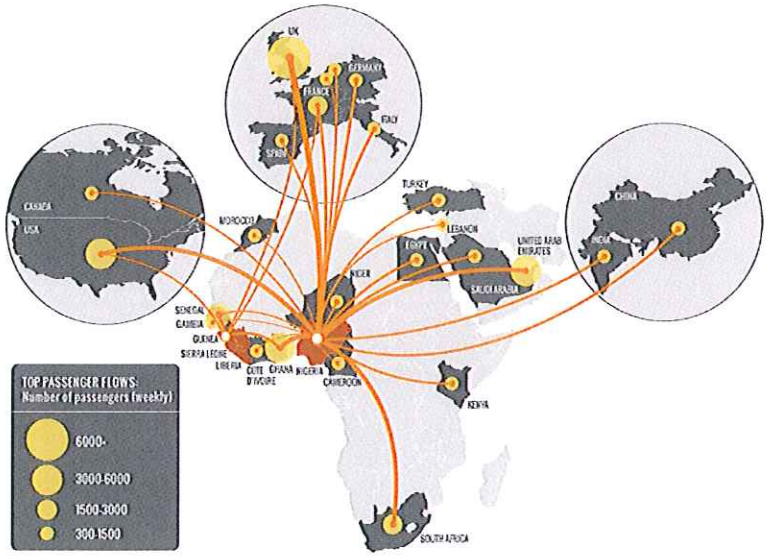
Forbes http://onforb.es/1rrlhfS

JV ChamaryContributor
I cover the science of life
Opinions expressed by Forbes Contributors are their own

INNOVATION & SCIENCE 10/13/2014 @ 7:00PM | 223,040 views

Ebola Is Coming. A Travel Ban Won't Stop Outbreaks

Comment Now



Air traffic connections from West African countries to the rest of the world (Image CC BY 4.0: Alessandro Vespignani / PLOS Currents Outbreaks)

Ebola has officially gone global.

The World Health Organization recently confirmed that a Spanish nurse was the first case of transmission outside Africa. Now it seems the first patient diagnosed in the United States transmitted the disease before he died.

More outbreaks are on their way.

While nations struggle to contain the epidemic in West Africa, other countries are discussing how to protect their own citizens, with governments and health authorities repeatedly asked the same question:

Why don't we just ban flights from Africa?

The idea seems logical. Prevent sick people entering the country, keep your loved ones safe. It's selfish, but understandable. A survey of over 1000 people by NBC News found that the majority of Americans (58%) support a ban on flights from countries where the Ebola virus has broken out.

Dr Tom Frieden, director of the US Centers for Disease Control and Prevention, has tried to explain why he doesn't support a travel ban:

> **Importantly, isolating countries won't keep Ebola contained and away from American shores. Paradoxically, it will increase the risk that Ebola will spread in those countries and to other countries, and that we will have more patients who develop Ebola in the US. People will move between countries, even when governments restrict travel and trade. And that kind of travel becomes almost impossible to track.**

Simply put: you can't seal the country. If you blocked air travel, it would force desperate individuals to use alternative routes – over land and sea – to escape the epidemic. They'll still end up in the US, except you won't know where.

An attempted travel ban would be like locking yourself in a cabin on a sinking ship and praying the flood doesn't seep through the gaps, and that the water pressure won't be enough to burst through the door.

There are many reasons why a flight ban would be practically impossible to implement. For example, remember that Thomas Eric Duncan, the US patient who caught the Ebola virus in his native Liberia, flew to Texas via Brussels in Belgium. An effective ban would require international coordination. Would every nation agree to quarantine West Africa, to cripple their economy and choke them of humanitarian aid? Unlikely.

But for the sake of argument, what happens when you reduce air travel?

Air traffic reduction

Professor Alex Vespignani, a physicist at Northeastern University in Boston, MA, has developed a computer model that predicts how air traffic affects the spread of Ebola.

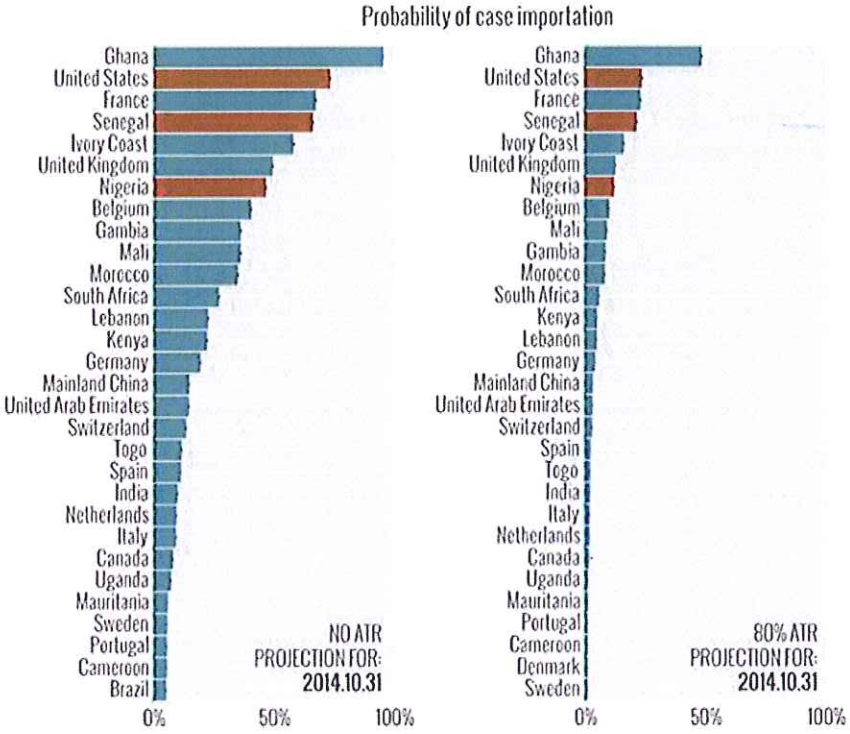
His team at the Laboratory for the Modeling of Biological and Socio-technical Systems used a high-resolution map of human populations (3300 locations in 220 countries) and added daily airline passenger traffic. This model considers connecting flights and final destinations, plus details of the disease dynamics, such as incubation time of the Ebola virus and the fact a susceptible individual can only be infected by someone who shows symptoms of illness.

"All the people who have been exposed to the disease but are not yet in the symptomatic state can in principle travel," says Vespignani. "So since we have this model that puts people on a plane, we can assess the probability of getting an infectious individual in countries around the world."

Air traffic connections is a key factor influencing the chances of importing a case of Ebola. Over 6000 passengers normally flow into the United Kingdom every week, while the US and Ghana each receive over 3000 travellers (see

image at the top of this page). The nations affected by the epidemic have urban areas with international airports, or are connected to West Africa's travel hub, Nigeria, which has had one outbreak of 20 cases from a single importation from Liberia.

Vespignani's computer model simulates a virtual world in which billions of individuals move around, come into contact with one another, and potentially spread disease. The aim is to predict cases like that of Thomas Eric Duncan.



Countries ranked by risk (relative probability) of importing a case of Ebola by 31 October. Red bars are nations that have already experienced case importation. LEFT: No air traffic reduction (ATR) reflects travel before the 2014 epidemic in West Africa. RIGHT: 80% ATR approximates the current reduction in air traffic to and from countries with Ebola. (Image: Alessandro Vespignani / www.mobs-lab.org)

The model calculates the risk of importing at least one Ebola case after running millions of simulations. They're run under two scenarios: no air traffic reduction (ATR) to mirror travel before the epidemic, and reducing air travel by 80% to reflect airlines suspending flights and passengers avoiding travel.

The number of simulations in which a virtual country ends up with an outbreak gives a statistic for the risk of importing an Ebola case in the real world. So if a country gets the disease in half of them, the probability of case importation is 50%. That's the prediction in October for Ghana, which lies between the affected nations – Guinea, Liberia and Sierra Leone – and Nigeria.

Big risks

For most countries, the results indicate that an 80% air traffic reduction more than halves the probability of importing a case of Ebola. For the US, the risk is reduced from around 75% to 25%.

But those risks don't stay static.

An 80% reduction in air traffic only postpones the inevitable. "This is just delaying by four weeks what would have happened without those travel restrictions," Vespignani explains. What about a 90% reduction? It would only buy you another month or two.

Like weather forecasts, Vespignani's virtual model is calibrated using real-world data. As conditions change, the model is revised and simulations are re-run. To make accurate predictions, it needs to be regularly updated with the number of cases and deaths at each geographical area. Like weather, there's higher confidence in forecasts for next month than further into the future.

The predictions above are for October, calibrated from recent data. In the original study, the model was calibrated with data from 6 July to 9 August to predict how an 80% air traffic reduction affects risks for September. The results showed that outside Africa, the risk was tiny – under 5% probability for every country except the UK, which has the most connections. (England's chief medical officer says the UK should expect a handful of cases.) A dozen countries have since joined the UK with a risk over 5%.

As the number of Ebola cases continues to rise in West Africa, so too will the risk of case importation. "We're a little safer for a finite amount of time, but then you are not really solving the problem," says Vespignani.

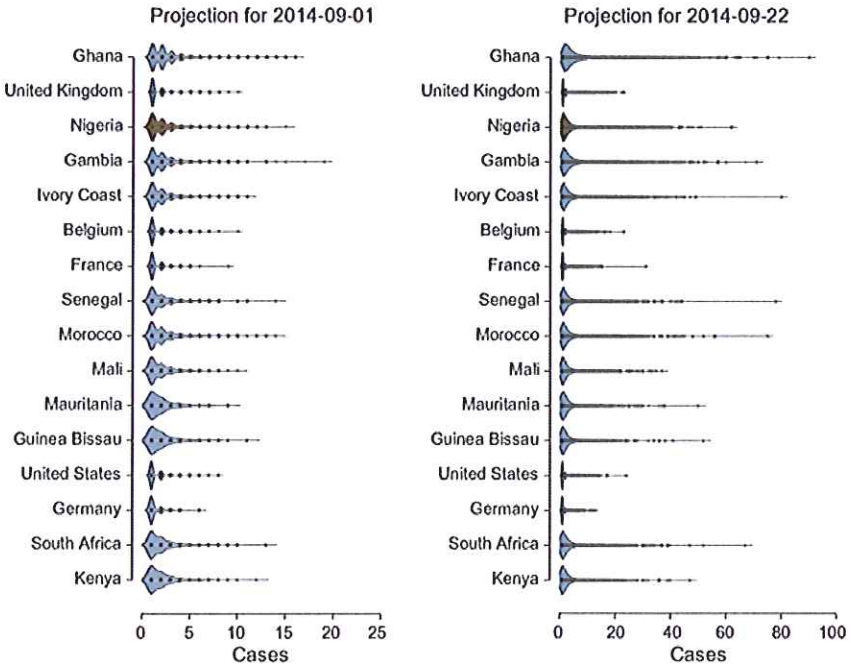
Small outbreaks

The forecasts aren't all doom and gloom though.

As well as modelling the global spread of Ebola, Vespignani's simulations also predict local transmissions within a community, in hospitals and at funerals. And the numbers for secondary infections from imported cases are reassuring.

"These outbreaks should be very, very small – 2 or 3 cases," he says. "I won't panic if tomorrow we hear that in Texas there is another case. This is totally normal."

[Note: A prophetic quote, given that I interviewed Vespignani before it was revealed Thomas Eric Duncan had transmitted the virus.]



Projections for outbreak size (number of cases) after a country imports Ebola. LEFT: 1 September. RIGHT: 22 September. (Image CC BY 4.0: Alessandro Vespignani / PLOS Currents Outbreaks)

One thing that computer simulations can't predict is human error. In the two cases of person-to-person transmission outside Africa (the Spanish nurse and second US patient), there might have been a breach in proper safety protocols.

"But these mistakes are very rare, and again this is not going to give rise to large outbreaks," says Vespignani. "Obviously what is happening in Liberia, Sierra Leone and Guinea is something that is of a totally different scale, with a healthcare system that we cannot even think of in our countries."

Vespignani is confident that the healthcare systems in Europe and North America are strong enough to stop outbreaks from ever reaching epidemic proportions, but says Asia is another matter. "If you ask me about India, China, other countries, then there are a lot of question marks."

Worse for the world

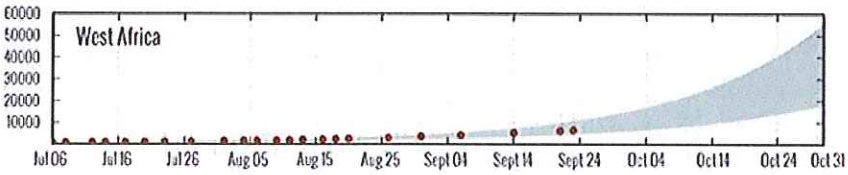
An Ebola epidemic in two countries with a combined population of 2.6 billion is not only terrifying, it further highlights the futility of attempting a travel ban. Could the US ban all flights from Asia and Africa? Where would it end, isolating the North American subcontinent from the rest of the world?

A travel ban is short-sighted, and would be ineffective in the long run. It's the epidemiological equivalent of an ostrich sticking its head in the sand: ignore the problem and hope it goes away.

And the Ebola epidemic isn't going anywhere. It's actually getting worse: the number of cases in West Africa continues to increase at an exponential rate.

Read: 4000 Deaths And Counting: The Ebola Epidemic In 4 Charts

Projections based on current trends using a dozen different models give future figures in the same ballpark: WHO predicts the total number will exceed 20,000 by 2 November, for example, while Vespignani's simulations say 18,100 to 55,400 cases by the end of October.



Projection for the total number of Ebola cases in West Africa by 31 October. Red circles are reported cases. Gray area is the range of projected cases, based on a worst-case scenario where the epidemic continues to grow exponentially. (Image: Alessandro Vespignani / www.mobs-lab.org)

According to a projection by the CDC, by late January 2015 there could be up to 1.4 million cases in West Africa alone.

War on Ebola

As Vespignani's computer simulations show, Ebola can easily spread across the globe. "This epidemic has pandemic potential," he warns. "What happens next year depends on what we are able to do in Africa. If we win this battle, it's okay. If we lose the battle there, then this thing is serious."

The only way to stop Ebola going truly global is to beat the epidemic in West Africa. Governments get this: the US is deploying 4000 troops to Liberia and the UK is sending 750 soldiers to Sierra Leone. Nonetheless, according to the NBC survey, over half (51%) of Americans disapprove of sending US troops to fight the spread of Ebola.

The survey also revealed that most Americans (72%) understand that the Ebola virus is transmitted via contact with bodily fluids, which suggests that health authorities like the CDC and WHO have successfully educated the public on how the disease spreads from person to person.

Calls for a travel ban illustrate that there's yet another battle to be won over Ebola: explaining how the disease spreads between populations.

Ebola in Four Charts

JV Chamary is a biologist and writer – read more of his stories on Forbes and follow him on Google+ and Twitter