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Lessons Learned from the Ebola Outbreak

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1st Qatar workshop for the "Assessing the Threats to Public Health
2-3 November 2016

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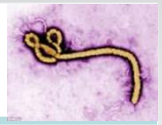
Outline



- History
- Reservoir
- How does the disease spread
- The Epidemic
- The Disease
- Lessons Learned

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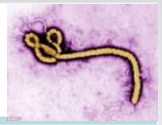
History



- Ebola virus disease (EVD) (formerly known as Ebola haemorrhagic fever) is a severe disease caused by a virus of the filovirus family, which occurs in humans and non-human primates
- 1976: It first appeared simultaneously in Nzara, Sudan and Yambuku in the Democratic Republic of Congo (DRC)
- Two strains were identified; Sudan & Zaire
- 1989: The third strain, was discovered in Reston, VA
- It caused severe illness in non-human primates but not in humans. Virus was found in a colony of monkeys imported from the Philippines
- Subsequently caused outbreaks in non-human primates in Pennsylvania (Philadelphia), Texas (Alice) and Italy (Sienna)
- Several research workers became infected with the virus during these outbreaks, but did not become ill

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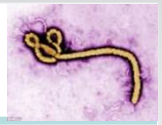
History



- 1994: The forth strain was discovered during necropsy in Cote D'Ivoire, and outbreaks have been occurring with increasing frequency since.
- 2008: A fifth strain, from Uganda called the Bundibugyo was identified.
- In Africa, outbreaks of EVD primarily occur in remote villages close to tropical rainforests in Central and West Africa
- Confirmed cases of EVD were reported in the Democratic Republic of the Congo (DRC, formerly Zaire), Sudan, Gabon, Uganda, Republic of Congo, Cote d'Ivoire, and for the first time in Guinea, Liberia and Sierra Leone in 2014.

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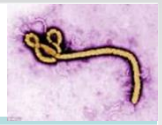
The 5 species of Ebola virus



- Human Disease:
  - Zaïre ebolavirus (EBOV)
  - Sudan ebolavirus (SUDV)
  - Tai Forest (TAFV) (formerly known as Ebola Ivory Coast)
  - Bundibugyo ebolavirus (BDBV)
- Non-Human Primate Disease
  - Reston ebolavirus (RESTV)

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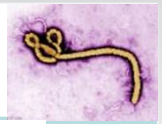
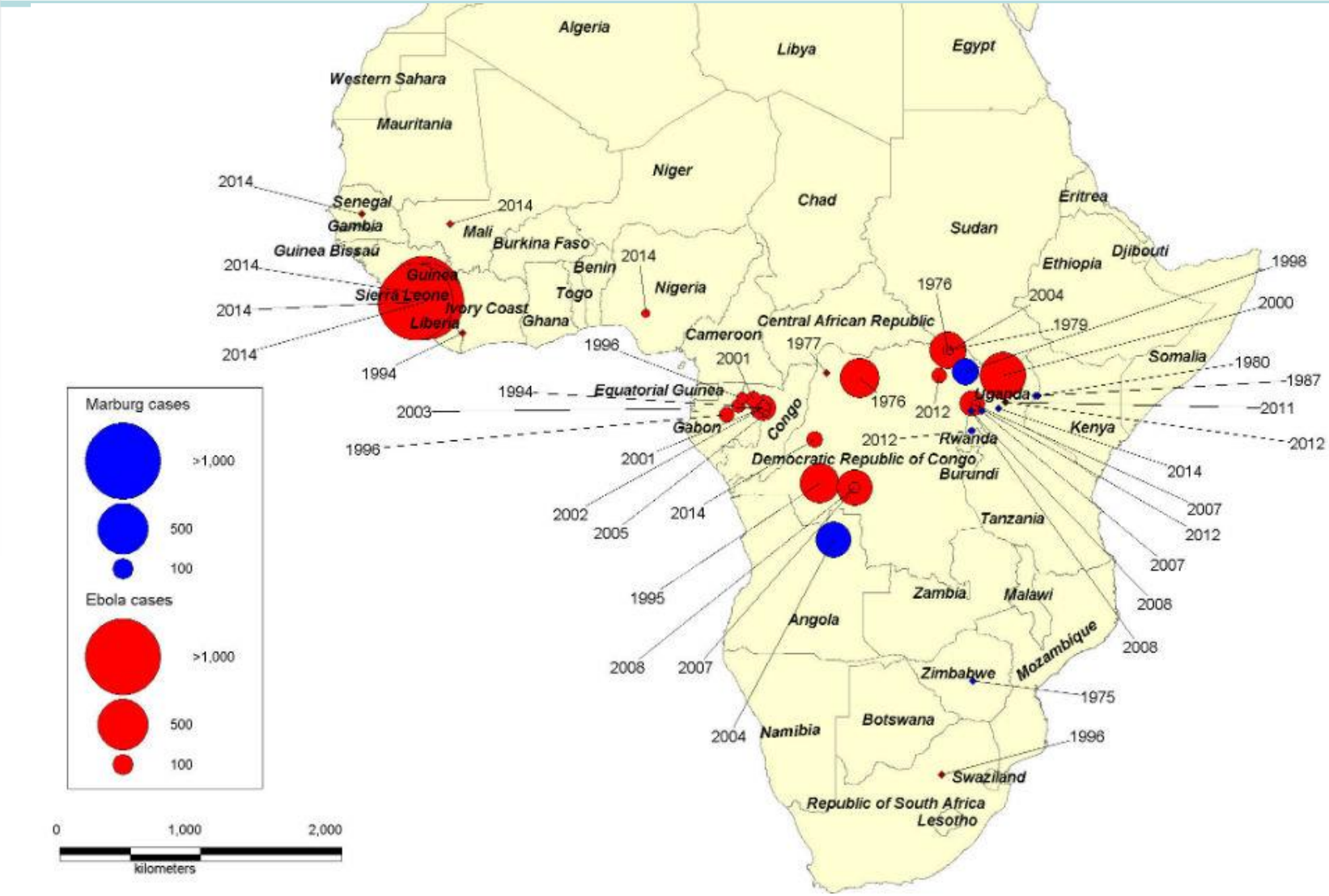
Year	Country	Ebola virus species	Cases	Deaths	Case fatality rate
1976	Zaire (DRC)	Zaire	318	280	88%
1976	Sudan	Sudan	284	151	53%
1976	England	Sudan	1	0	0%
1977	Zaire (DRC)	Zaire	1	1	100%
1979	Sudan	Sudan	34	22	65%
1989	USA	Reston	0(a)	0	0%
1990	USA	Reston	0(a)	0	0%
1992	Italy	Reston	0(a)	0	0%
1994	Gabon	Zaire	52	31	60%
1994	Côte d'Ivoire	Tai Forest	1	0	0%
1995	Zaire (DRC)	Zaire	315	254	79%
1996	Gabon	Zaire	31	21	57%
1996	Gabon	Zaire	60	45	75%
1996	South Africa	Zaire	1	1	100%
2000-1	Uganda	Sudan	425	224	53%
2001-2	Gabon and Zaire (DRC)	Zaire	124	97	78%
2002-3	Zaire (DRC)	Zaire	143	128	89%
2003	Zaire (DRC)	Zaire	35	29	83%
2004	Sudan	Sudan	17	7	41%
2005	Zaire (DRC)	Zaire	12	10	75%
2007	Zaire (DRC)	Zaire	264	187	71%
2007	Uganda	Bundibugyo	149	37	25%
2008	Philippines	Reston	0(b)	0	0%
2008-9	Zaire (DRC)	Zaire	32	14	47%
2011	Uganda	Sudan	1	1	100%
2012a	Uganda	Sudan	24	17	70%
2012b	Uganda	Sudan	7	4	40%
2012	Zaire (DRC)	Bundibugyo	57	29	55%
Total			2388	1590	67%

Ebola & Marburg Outbreaks in Africa 1976 to 2014





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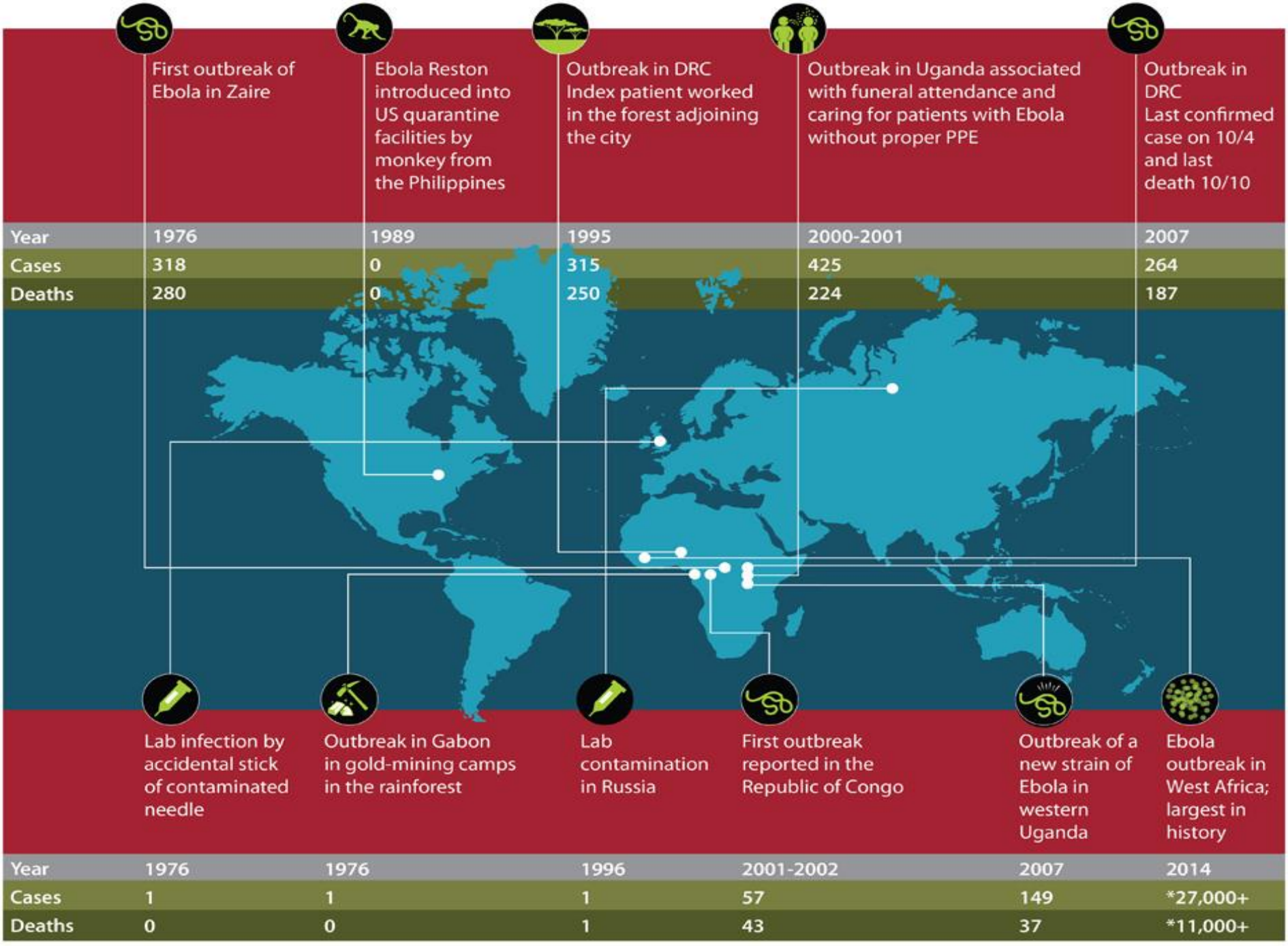
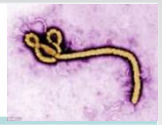
Source: WHO



CS 252971

* As of July 18, 2015

Reservoir



- Evidence strongly implicated fruit-bats as the reservoir host for ebolavirus, thought the means of local enzootic maintained and transmission within bat population remains unknown
- Epizootics caused by ebolavirus appear sporadically, causing high mortality among non-human primates and duikers and may precede human outbreaks
- Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and epidemics
- With the current evolving epidemic there is an urgent need to better understand the ecology of Ebola virus in nature.

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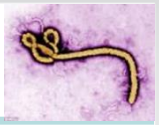
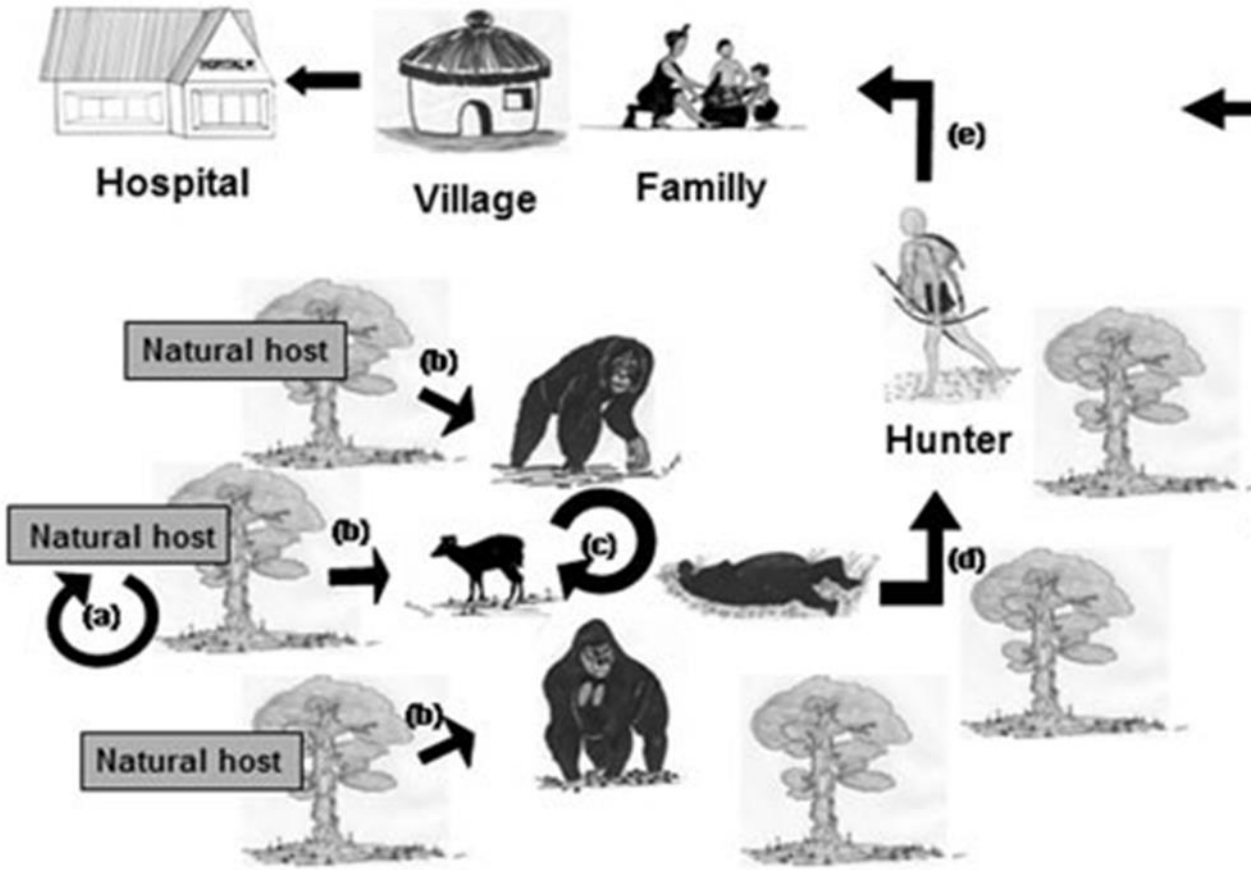
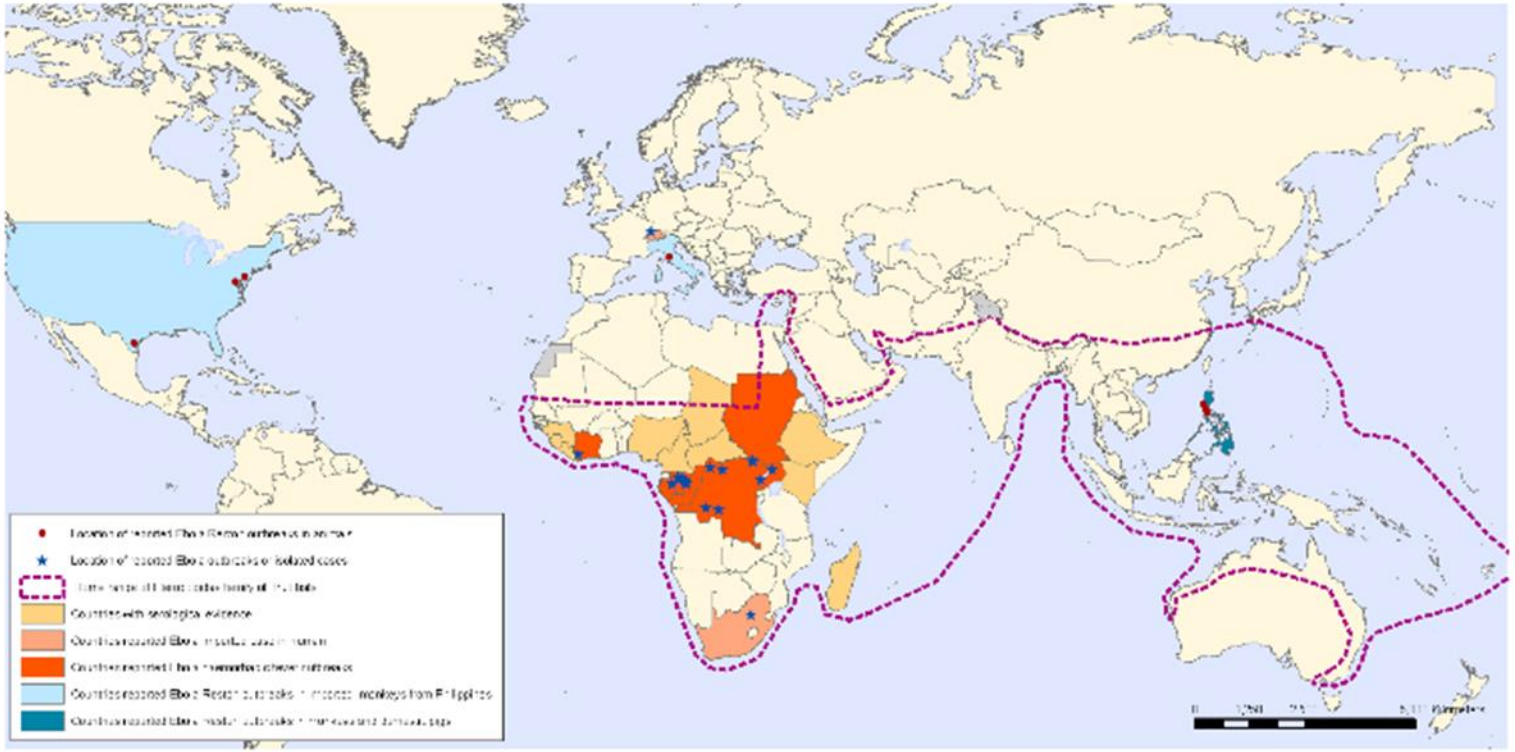
How Does the Disease Spread?





Geographic Distribution of EVD and Fruit Bats of Pteropodidae Family



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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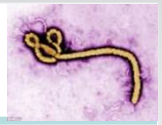
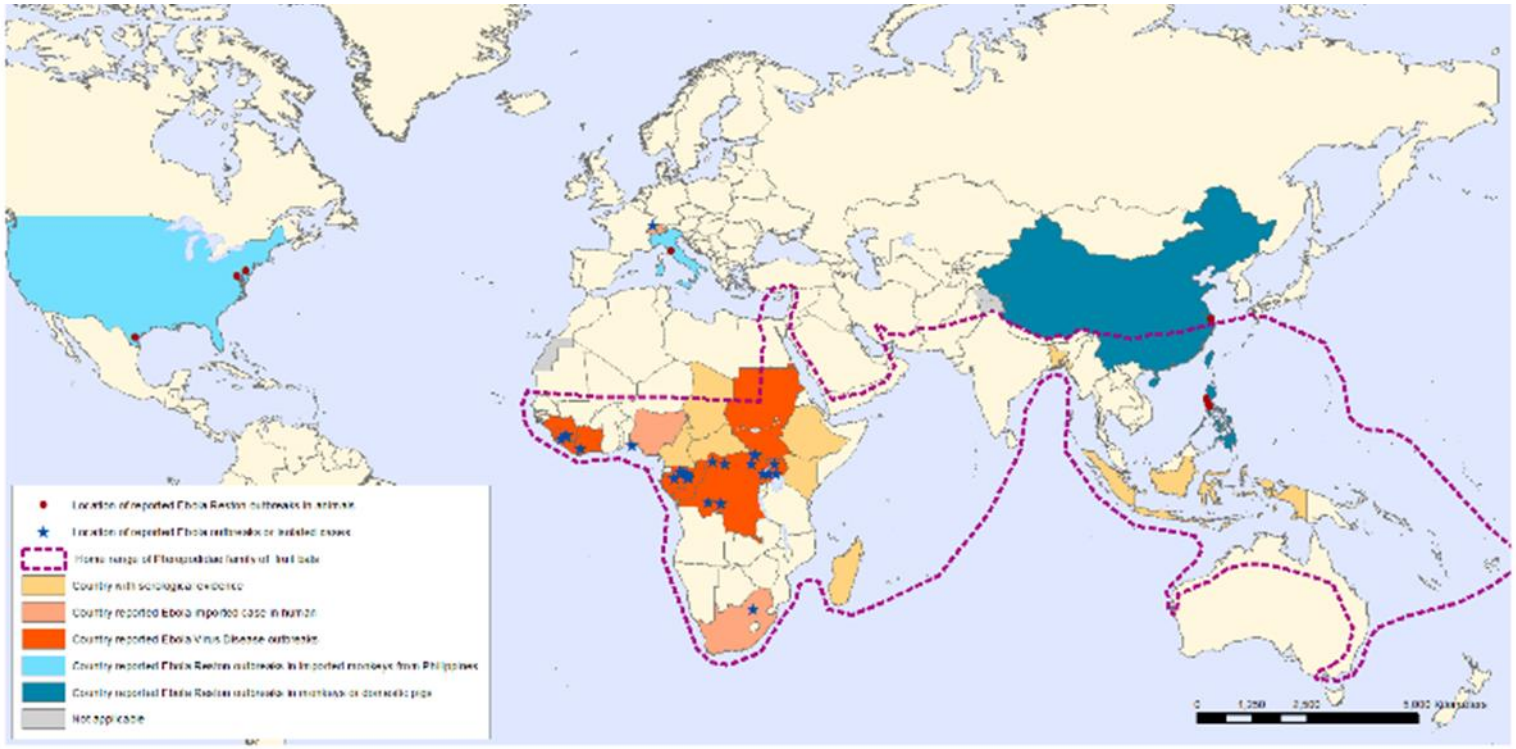
Geographic Distribution of EVD Outbreaks in Humans & Animals





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Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
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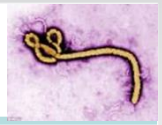
Human to Human Transmission



- The way in which the virus first appears in a human at the start of an outbreak is unknown
- The first patient becomes infected through contact with an infected animal, such as a fruit bat or primate (apes and monkeys), which is called a spillover event
- Person-to-person transmission follows and can lead to large numbers of affected people
- In some past Ebola outbreaks, primates were also affected by Ebola, and multiple spillover events occurred when people **touched or ate infected primates**.

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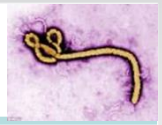
Human to Human Transmission



- Once infection occurs in humans, the virus can be spread in several ways to others:
  - Through direct contact
    - Broken skin or mucous membranes in, for example, the eyes, nose, or mouth
  - Through blood or body fluids of a person who is sick with Ebola
    - Including but not limited to urine, saliva, sweat, feces, vomit, breast milk, and semen
  - Objects
    - Like needles and syringes that have been contaminated with the virus
  - From infected fruit bats or primates
    - Apes and monkeys

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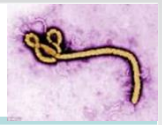
Human to Human Transmission



- Ebola is not spread through the air or by water, or in general, by food
- In Africa, Ebola may be spread as a result of handling bushmeat (wild animals hunted for food) and contact with infected bats
- There is no evidence that mosquitos or other insects can transmit Ebola virus
- Only a few species of mammals (for example, humans, bats, monkeys, and apes) have shown the ability to become infected with and spread Ebola virus
- Once someone recovers from Ebola, they can no longer spread the virus. However, Ebola virus has been found in semen for up to 3 months
  - Abstinence from sex (including oral sex) is recommended for at least 3 months. If abstinence is not possible, condoms may help prevent the spread of disease.

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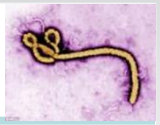
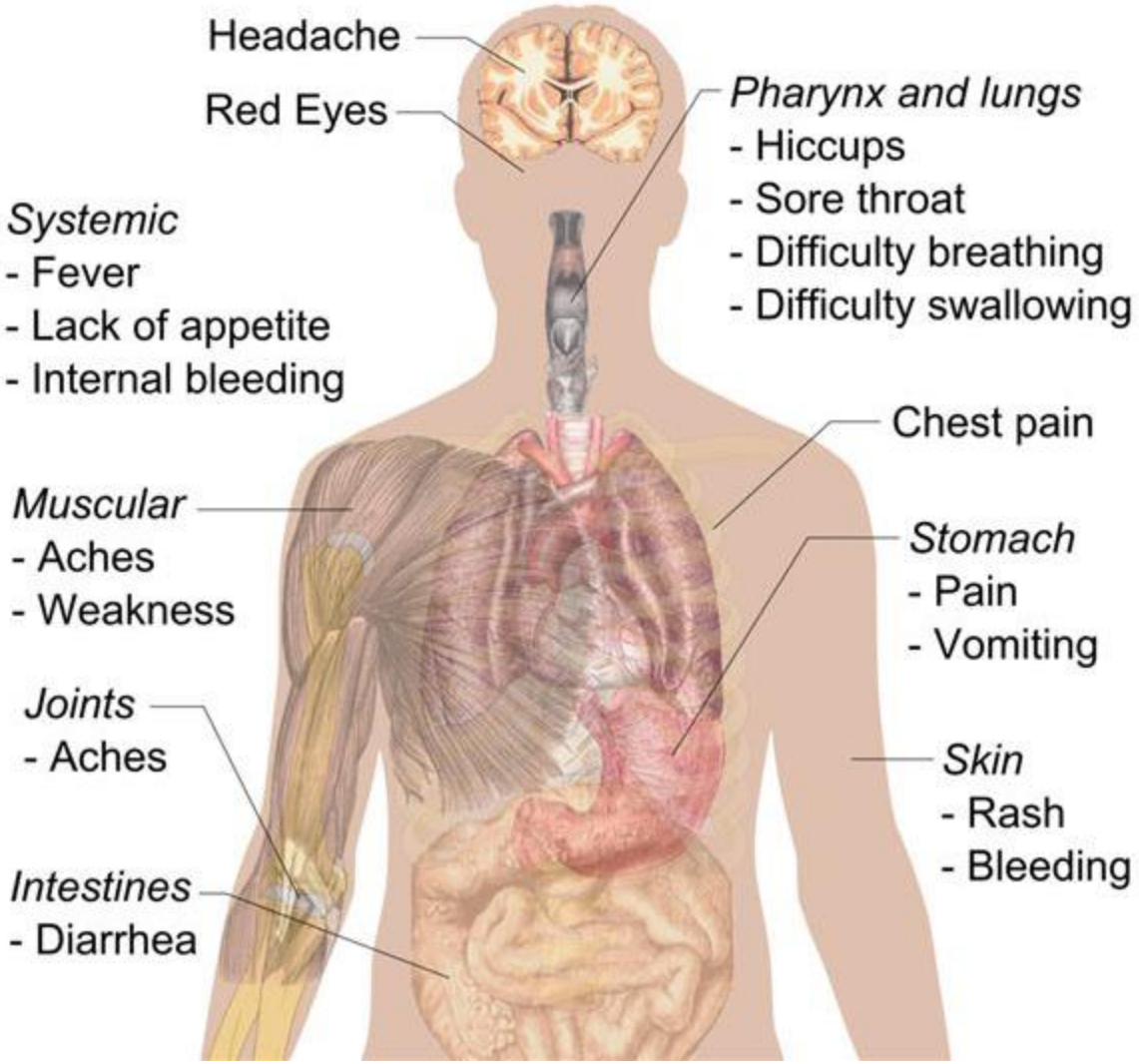
Symptoms of Ebola





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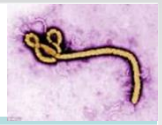
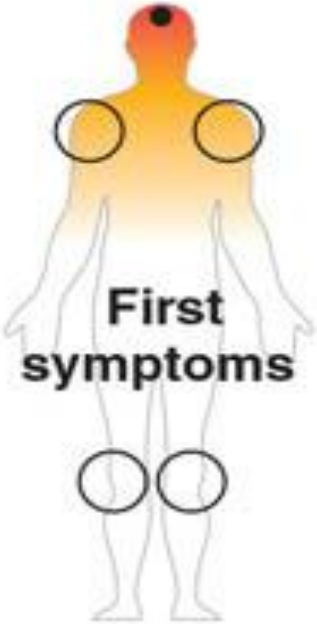
Ebola virus' typical path through humans



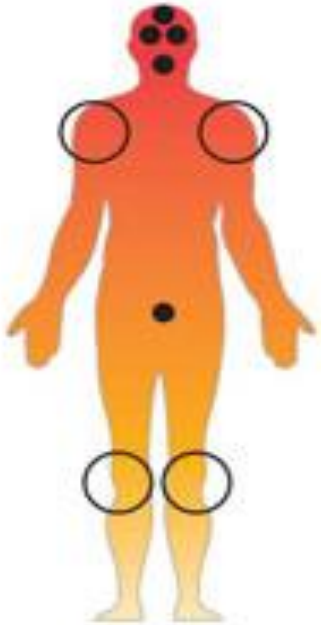


Day 7-9

Headache, fatigue, fever, muscle soreness

Day 10

Sudden high fever, vomiting blood, passive behavior



Day 11

Bruising, brain damage, bleeding from nose, mouth, eyes, anus

Day 12

Loss of consciousness, seizures, massive internal bleeding, death

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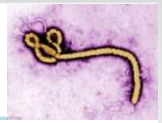
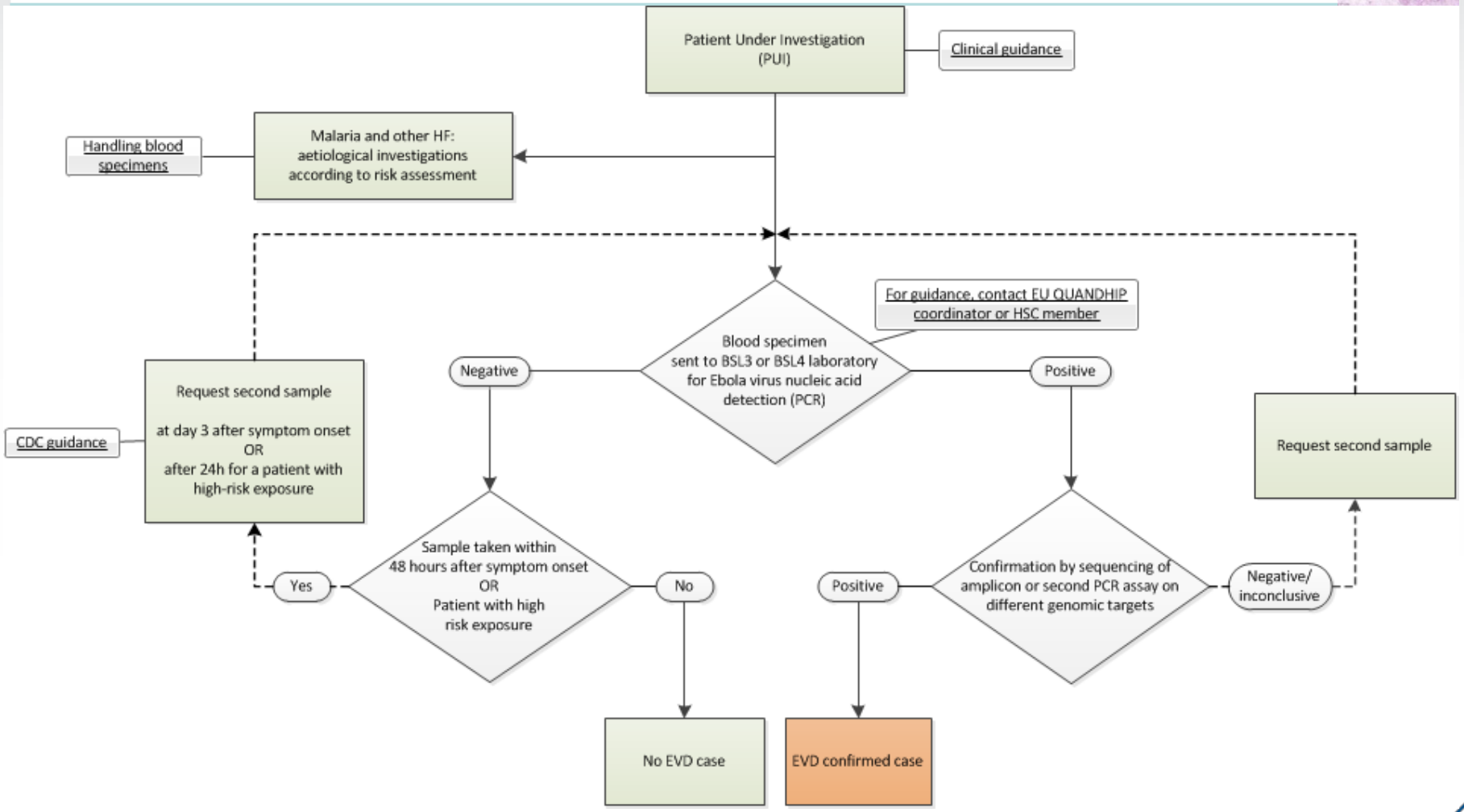
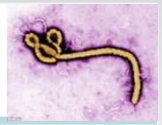
EVD Laboratory Diagnostic Algorithms





Source: CDC

Laboratory Findings



- Leukopenia frequently with lymphopenia followed later by elevated neutrophils and a left shift
- Platelet counts are often decreased in the 50,000 to 100,000 range
- Amylase may be elevated, reflecting pancreatic involvement (inflammation/infection)
- Hepatic transaminases are elevated with aspartate aminotransferase (AST) exceeding alanine aminotransferase (ALT); these values may peak at more than 1,000 IU/L.
- Proteinuria may be present
- Prothrombin (PT) and partial thromboplastin times (PTT) are prolonged and fibrin degradation products are elevated, consistent with disseminated intravascular coagulation (DIC).

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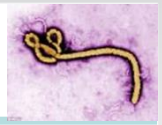
Source: CDC

Diagnostics Test



Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	• Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing • IgM ELISA • Polymerase chain reaction (PCR) • Virus isolation
Later in disease course or after recovery	• IgM and IgG antibodies
Retrospectively in deceased patients	• Immunohistochemistry testing • PCR • Virus isolation

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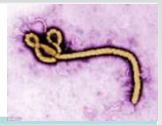
Source: CDC

Treatment



- No FDA-approved vaccine or medicine is available for Ebola.
- Symptoms of Ebola and complications are treated as they appear. The following basic interventions, when used early, can significantly improve the chances of survival:
  - Providing intravenous fluids (IV) and balancing electrolytes (body salts).
  - Maintaining oxygen status and blood pressure.
  - Treating other infections if they occur.
- Experimental vaccines and treatments for Ebola are under development, but they have not yet been fully tested for safety or effectiveness.
- Recovery from Ebola depends on good supportive care and the patient's immune response.
- People who recover from Ebola infection develop antibodies that last for at least 10 years, possibly longer.
- Some people who have recovered from Ebola have developed long-term complications, such as joint and vision problems.

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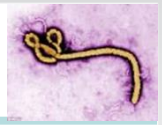
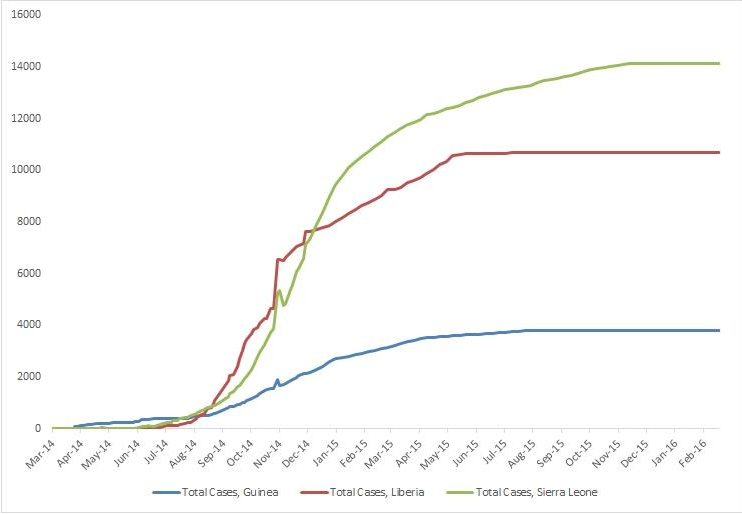
Source: CDC

Status as of EVD as of 10 June 2016 (WHO)

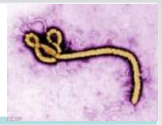


- The Public Health Emergency of International Concern (PHEIC) related to Ebola in West Africa was lifted on 29 March 2016.
- A total of **28,616** confirmed, probable and suspected cases have been reported in Guinea, Liberia and Sierra Leone, with **11,310** deaths.
- Guinea and Liberia declared the end of the most recent outbreak of EVD on 1 and 9 June, respectively.
- There are over 10,000 survivors.



Source: WHO

Lessons Learned



1. Health System

- There is a critical need to reinforce basic public health systems, including primary health care facilities, laboratories, surveillance systems, and critical care facilities, among other components.
- Ebola has spread much faster and more widely in countries whose health systems, especially whose primary care systems, were severely weakened by years of armed conflict and neglect.
- Without a functioning health system, it is very hard for a country to end the cycle of disease and poverty.
- **It is imperative to build and improve health systems worthwhile. This helps our ability to confront epidemics.**

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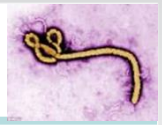
Source: Bill Gates

Lessons Learned



2. Surveillance System

- There was no systematic disease-surveillance process in place today in most poor countries, which is where a naturally occurring epidemic seems most likely to break out.
- Even once the Ebola crisis was recognized , there weren't resources to effectively map where cases were occurring and in what quantity.
- **It is critical to invest in better disease-surveillance and laboratory-testing capacity, for normal situations and for epidemics**.
- Routine surveillance systems should be designed in such a way that they can detect early signs of an outbreak beyond their sentinel sites and be quickly scaled up during epidemics.
- They should be linked with national public health laboratories to enable robust monitoring and response.
- Data derived from such testing need to be made public immediately.

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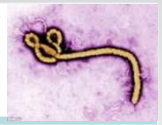
Source: Bill Gates

Lessons Learned



3. Human Resources

- There were no trained personnel ready to deal with the outbreak. Some countries stepped forward with volunteers within 2 to 3 months, but they were needed within days. It was fortunate that Médecins sans Frontières could mobilize volunteers more quickly than any government.
- **Trained personnel need to be ready to confront and contain an epidemic quickly: incident managers; experts in epidemiology, disease surveillance, and other relevant fields who can provide surge capacity; respected community leaders who can lead local engagement efforts; and community workers who speak local languages.**

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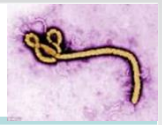
Source: Bill Gates

Lessons Learned



4. Transportation

- Transportation and equipment are also key. When an epidemic strikes, roads and airports in affected areas are overwhelmed by people trying to get out.
- **All countries could identify trained military resources that would be available for epidemics; in a severe epidemic, the military forces of many or all middle- and high-income countries might have to work together.**

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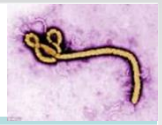
Source: Bill Gates

Lessons Learned



5. Supplies

- During severe epidemics, responders also need tents, portable power sources, medical supplies, and other materials.
- **A list of the supplies that would be needed to stop an epidemic affecting 10 million people — 100 times the population affected by the Ebola epidemic — could be developed, and experts could determine which items would need to be stockpiled or be subject to commandeering.**

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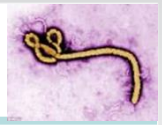
Source: Bill Gates

Lessons Learned



6. Data

- It is critically important to have good data about the ground situation.
- During the epidemic, the case database has not always accurate or up to date, due to the chaotic situation, but also because good technology and training was not available and there are no clear rules regarding making data accessible.
- **WHO, the U.S. CDC, and others — could recommend specifications, and some combination of foundations and technology companies could build such a system within the year.**

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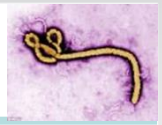
Source: Bill Gates

Lessons Learned



7. Predictive Analysis

- Computer predictive models were needed to predict what might happen and which interventions should be prioritized.
- With access to satellite photography and cell-phone data, movement of populations and individuals in the affected region could have been monitored.
- **Internet and cell-phone capacity need to be improved. Key centers should have high-bandwidth Internet capacity through satellite, and Wi-Fi capacity should be added so that digital tools can help with reporting data and coordinating.**

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Source: Bill Gates

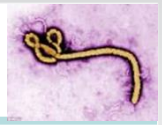
Lessons Learned

8. Medical and Public Health Tools

- With the possible exception of influenza vaccines, there is not enough capacity for developing adaptable platforms, partly because there are opportunity costs for private-sector organizations in shifting resources away from more commercially viable projects to work on tools for epidemics that may not happen.
- **Need an international funding system that factors in these opportunity costs.**

Source: Bill Gates

Lessons Learned



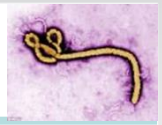
8. Medical and Public Health Tools

- Plasmapheresis should have been used in the Ebola epidemic, but its application wasn't approved and scaled up until it was too late for this intervention to have a large impact.
- **Develop rules to expedite drug approvals in future epidemics and establish clear guidelines for approving studies and treatments, including experimental ones.**
- Three different Ebola vaccine constructs were being developed in the summer of 2014. This work made us more prepared for Ebola than we would be for an entirely new pathogen
- **Vaccine research would be funded in such a way that during an outbreak, a vaccine could be designed, tested for safety, and ready for manufacture at scale within a few months.**

IEM

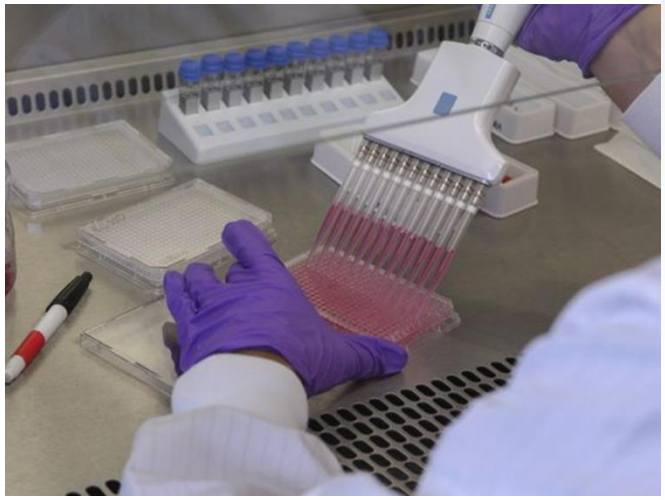
Source: Bill Gates

Lessons Learned



8. Medical and Public Health Tools

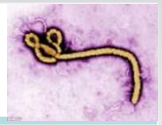
- There are drugs that work against viruses similar to Ebola, and some of them have been shown in test assays to have an effect against Ebola. However, they were not tested in patients with Ebola until after the epidemic had peaked as there was no clear process for approving a novel trial format or for providing indemnity against legal liability.
- **Clear set of guidelines (and testing and regulatory pathways) need to be developed for determining whether existing drugs could be repurposed to help stop a particular epidemic.**



IEM

Source: Bill Gates

Lessons Learned



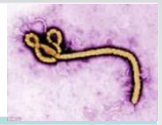
8. Medical and Public Health Tools

- The diagnostic approach used during the Ebola epidemic has involved sending blood samples for quantitative polymerase-chain-reaction (qPCR) analysis. But qPCR machines are expensive and not widely available, so on average it has taken 1 to 3 days to get test results.
- **An adequate number of qPCR machines should be made available while novel diagnostic methods are rapidly developed. We also need a clear process for developing and manufacturing accurate diagnostic tests rapidly.**

IEM

Source: Bill Gates

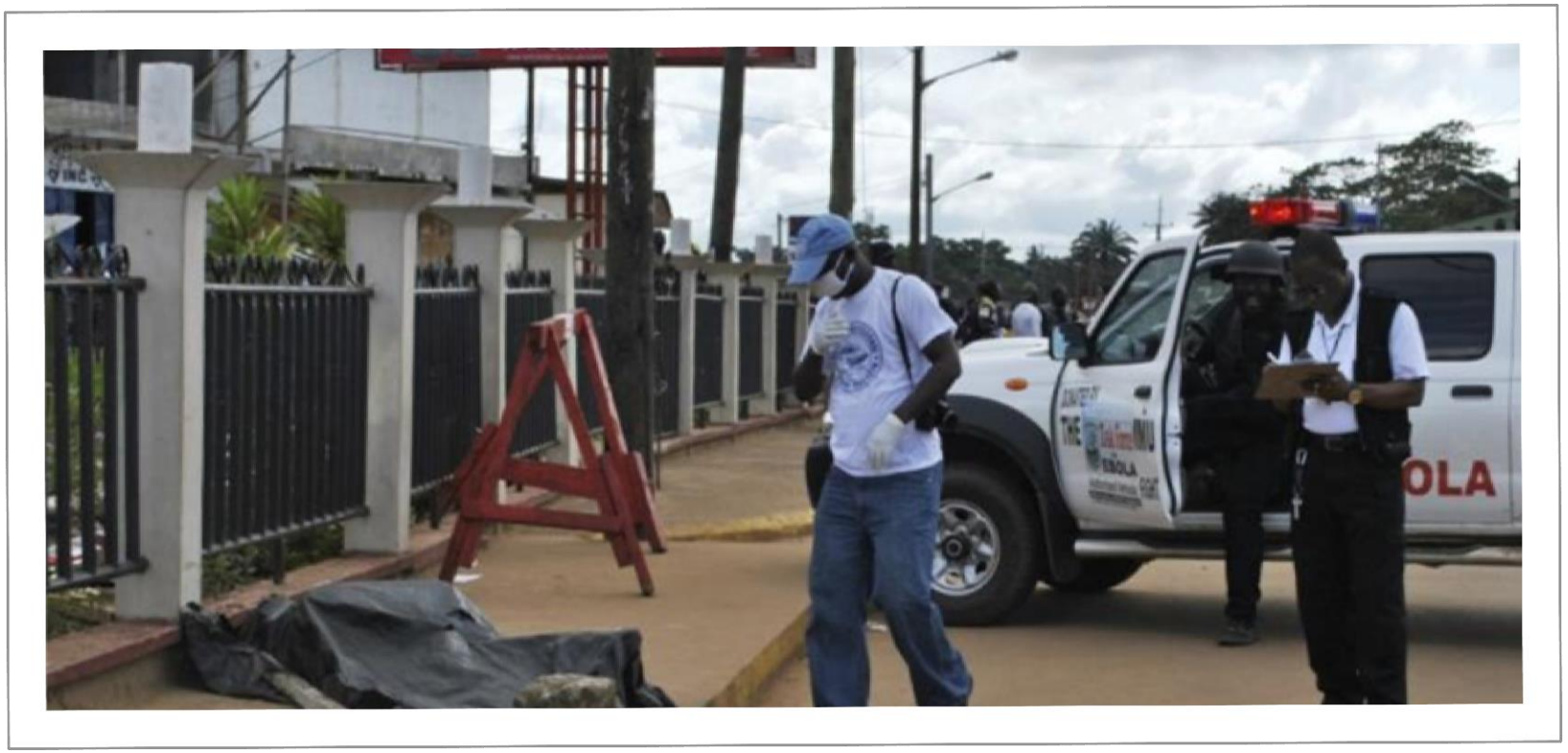
Conclusion



- Lessons from the Ebola epidemic may pave the way to improve international crisis management.
- These lessons can serve as a starting point for discussions of ways to strengthen the WHO's capacity and to distinguish parts of the process other organizations such as the World Bank or the G7 countries could lead in close coordination.
- Military alliances such as NATO, should make epidemic a priority and be part of the response.
- A reserve corps of experts needs to be developed with the broad range of skills needed in an epidemic.
- **A comprehensive global warning and response system needs to be built.**

IEM

Source: Bill Gates



!!!!Remember diseases do not observe boundaries!!!!