CD Alert

National Centre for Disease Control,
Directorate General of Health Services, Government of India

December, 2022

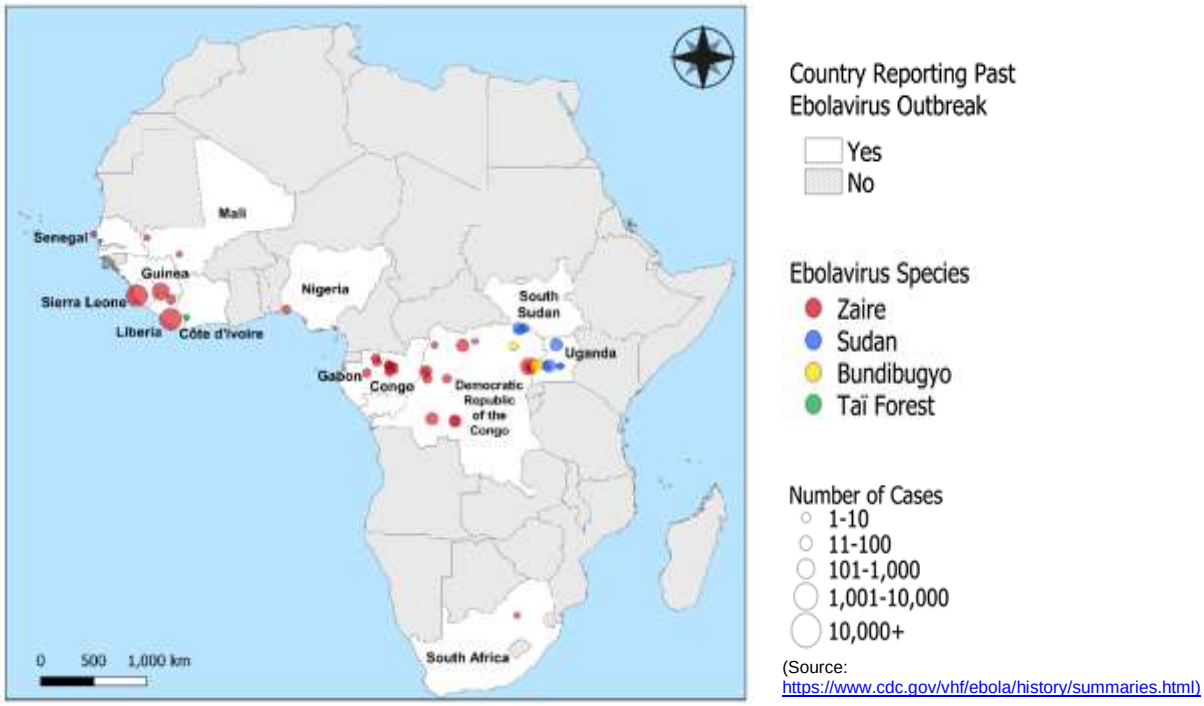
Ebola Virus Disease

INTRODUCTION

Ebola virus disease (EVD), is a viral disease caused by Ebola virus a member of the filovirus family, which occurs in humans and other primates. It was formerly known as Ebola hemorrhagic fever, which is a severe, often fatal illness in humans. Ebola virus was first described in 1976 near the Ebola River in what is now the Democratic Republic of the Congo. Since then, the virus has emerged periodically and infected people in several African countries. The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. It is regarded as one of the world's most virulent diseases and its outbreaks have been recognized with increasing frequency.

HISTORICAL BACKGROUND

First identified in 1976, in simultaneous outbreaks in Democratic Republic of Congo (DRC) and Sudan. Between 1979-94, no cases were detected. However, since 1994, its outbreaks are being increasingly reported. Until 2014, outbreaks of EVD were primarily reported from remote villages close to tropical rainforests in C. & W. Africa. Most confirmed cases were reported from DRC, Gabon, Congo, Sudan and Uganda. In 2014, an EVD outbreak was reported in W. Africa (Guinea, Liberia & Sierra Leone). During this outbreak, between 2014-16, there was intense transmission in urban areas, resulting in >28,000 cases. Multiple countries including Italy, Mali, Nigeria, Senegal, Spain, UK & US, reported EVD cases related to this outbreak.



(Source: https://www.cdc.gov/vhf/ebola/history/summaries.html)

Ebola Virus Outbreaks by Species and Size, Since 1976

EPIDEMIOLOGY

Burden Worldwide

Global Situation

Since its discovery in 1976, most cases and outbreaks of Ebola Virus Disease have occurred in Africa. The outbreaks of past decade are enlisted in table below:

Indian Situation:

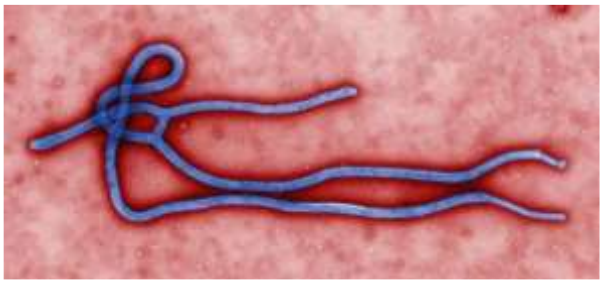
A 26-year-old male, Indian, had travelled from Liberia to India and reached Delhi on 10th November 2014. He underwent the mandatory screening at the Delhi Airport. He carried a certificate of medical clearance from the Ministry of Health and Social Welfare, Government of Liberia mentioning that 'he has successfully undergone care and treatment related to Ebola Virus Disease and after post treatment assessment he has been declared free of any clinical signs and symptoms and confirmed negative by laboratory analysis'.

As a matter of abundant caution, he was isolated at the Airport Health Organization's Quarantine Centre at Delhi Airport. Although as per WHO and CDC specifications, he was deemed to be cured. However, as has been reported in the past, the virus may continue to be positive in secretions like urine and semen for a longer time. Before releasing him from quarantine, a decision was taken to test his other body fluids and release him only when they turned negative.

However, till date no indigenous case of Ebolavirus disease has been found in our country.

THE CAUSATIVE AGENT: EBOLA

Ebolavirus is one of 3 members of the Filoviridae family (filovirus), along with genus Marburgvirus and Cuevavirus.



Pic courtesy: https://www.cdc.gov/vhf/ebola/index.html

Genus Ebolavirus comprises 6 distinct species:

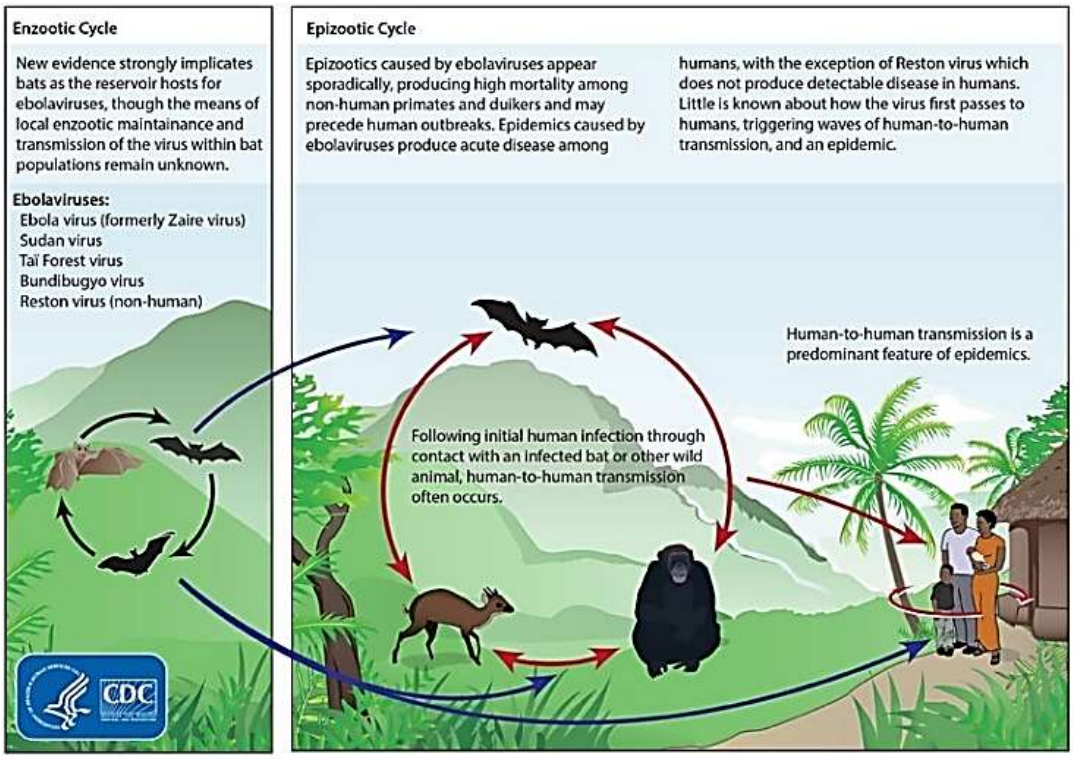
- Ebola virus (species Zaire ebolavirus)
- Sudan virus (species Sudan ebolavirus)
- Taï Forest virus (species Taï Forest ebolavirus)
- Bundibugyo virus (species Bundibugyo ebolavirus)
- Reston virus (species Reston ebolavirus)
- Bombali virus (species Bombali ebolavirus)

Of these, only four (Ebola, Sudan, Taï Forest, and Bundibugyo viruses) have caused disease in humans. Zaire ebolavirus is the most fatal Ebola virus.

Country	Cases	Deaths	Species	Year
Uganda	141*	55*	*Sudan ebolavirus*	2022
Guinea	23	12	*Zaire ebolavirus*	2021
Dem. Rep of the Congo	12	6	*Zaire ebolavirus*	2021
Dem. Rep. of the Congo	130	55	*Zaire ebolavirus*	2020
Dem. Rep. of the Congo, Uganda	3470	2287	*Zaire ebolavirus*	2018-2020
Dem. Rep. of the Congo	54	33	*Zaire ebolavirus*	2018
Dem. Rep. of the Congo	8	4	*Zaire ebolavirus*	2017
Dem. Rep. of the Congo	66	49	*Zaire ebolavirus*	2014
Multiple countries	28646	11323	*Zaire ebolavirus*	2014-2016
Uganda	6*	3*	*Sudan ebolavirus*	2012
Dem. Rep. of the Congo	36*	13*	*Bundibugyo ebolavirus*	2012
Uganda	11*	4*	*Sudan ebolavirus*	2012

Table: Outbreaks of Ebola Virus Disease *Numbers reflect laboratory confirmed cases only

Source: https://www.cdc.gov/vhf/ebola/history/distribution-map.html



Hosts and Sources of Infection Image courtesy: CDC

Source of Infection

- Ebola is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals, chimpanzee, gorilla, fruit bats, monkeys, forest antelopes and porcupines.
- The virus is likely maintained in the environment by spreading from host to host or through intermediate hosts or vectors.

Natural host

- In Africa, fruit bats, particularly species of the genera Hypsignathus monstrosus, Epomops franqueti and Myonycteris torquata, are considered possible natural hosts for Ebola virus.
- As a result, the geographic distribution of Ebola viruses may overlap with the range of the fruit bats.
- The most recent Ebola virus to be detected, Bombali virus, was identified in samples from bats collected in Sierra Leone.

Incubation period: 2-21 days. The average is 8 to 10 days. A person can only spread Ebola to other people after they develop signs and symptoms of Ebola, thus there is no asymptomatic transmission.

Infectious Period

- People are infectious as long as their blood and secretions contain the virus. The virus can be transmitted through semen of affected person up to 7 weeks after recovery from illness.
- The virus can remain in areas of the body that are immunologically privileged sites after acute infection. These are sites where viruses and pathogens, like the Ebola virus, are shielded from the survivor's immune system, even after being cleared elsewhere in the body. These areas include the testes, interior of the eyes, placenta, and central nervous system, particularly the cerebrospinal fluid.

ROUTES OF TRANSMISSION

Human-to human transmission, with infection resulting from direct contact (through broken skin or mucous membranes e.g. the eyes, nose, or mouth, with the blood or secretions, organs or body fluids (urine, saliva, sweat, feces, vomit, breast milk, amniotic fluid, and semen) of an infected person or who died with it.

- Health-care workers have frequently been infected while treating patients with suspected or confirmed EVD. This has occurred through close contact with patients when infection control precautions are not strictly practiced.
- With objects like needles that have been contaminated with the virus, or infected animals.
- Indirect contact with environments contaminated with such fluids. Ebola virus can survive on dry surfaces, like doorknobs and countertops for several hours; in body fluids like blood, the virus can survive up to several days at room temperature.
- Ebola is not spread through the air or by water or, in general, by food.
- There is no evidence that mosquitoes or other insects can transmit Ebola virus
- In Africa Ebola may spread because of hunting, processing, and consuming infected animals (e.g., bushmeat which is often consumed raw or minimally processed)

Bushmeat hunting in Africa

Case Fatality Rate (CFR): Ebolavirus has multiple strains with varying severity of the disease. The average EVD case fatality rate is around 50%. Case fatality rates have varied from 25% to 90% in past outbreaks. CFR in the recent Uganda outbreak of 2022 has been 39%.

Risk assessment in disease-endemic areas is difficult because the natural reservoir host of Ebola viruses, and the way transmission of the virus to humans occurs remains unknown. Those at highest risk include:

- Healthcare workers
- Family and friends of patients with Ebola
- handlers of body dead of an EVD patient

Ebola poses little risk to travellers or the public who have not cared for or been in close contact (within 3 feet or 1 meter) with someone sick with Ebola.

CASE DEFINITION

Suspected (clinical) case:

Any person ill or deceased who has or had fever with acute clinical symptoms and signs of haemorrhage, such as bleeding of the gums, nose-bleeds, conjunctival injection, red spots on the body, bloody stools and/or melena (black liquid stools), or vomiting blood (hematemesis) with the history of travel to the affected area. Documented prior contact with an EBVD case is not required.

Probable case (with or without bleeding):

Any person (living or dead) having had contact with a clinical case of EHF and with a history of acute fever.

OR

Any person (living or dead) with a history of acute fever and three or more of the following Symptoms: headache/ vomiting/nausea/ loss of appetite/ diarrhea/ intense fatigue/ abdominal pain/ general muscular or articular pain/ difficulty in swallowing/ difficulty in breathing/hiccoughs.

OR

Any unexplained death.

The distinction between a suspected case and a probable case in practice relatively unimportant as far as outbreak control is concerned.

Contact:
A person without any symptoms having had physical contact with a case or the body fluids of a case within the last three weeks. The notion of physical contact may be proven or highly suspected such as having shared the same room/bed, cared for patient, touched body fluids, or closely participated in a burial (e.g. physical contact with the corpse).

Confirmed Case:
A suspected or probable case with laboratory confirmation (positive IgM antibody, positive PCR or Viral isolation).

SURVEILLANCE STRATEGIES

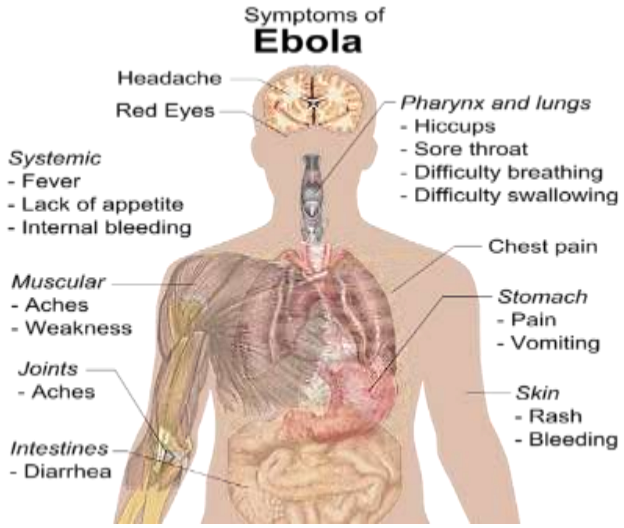
- As cases have not been reported from India, so the surveillance strategies should be more focused at the point of entry in the country.
- Adequate measures shall be instituted at Points of Entry's (PoEs) to make travellers aware of the signs & symptoms of EVD.
- Any person coming from Ebola affected areas or coming in contact with suspected or confirmed EBVD and develops symptoms within 21 days should immediately report to the designated health care facility.
- Contact tracing shall be carried out by IDSP and all identified contacts shall be quarantined as per the protocol.

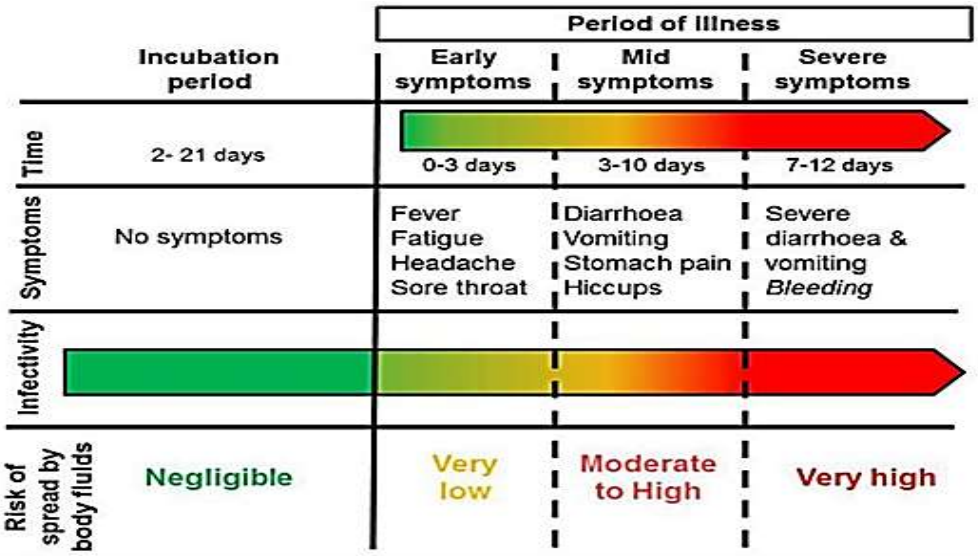
CLINICAL FEATURES

EVD is a severe acute viral illness often characterized by the sudden onset of:

- fever
- intense weakness
- muscle pain
- headache
- sore throat
- vomiting
- diarrhoea
- rash
- impaired kidney and liver function
- in some cases, both internal and external bleeding.

Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes.





DIAGNOSIS

Other diseases that should be ruled out before a diagnosis of EVD can be made include malaria, typhoid fever, shigellosis, cholera, leptospirosis, plague, rickettsiosis, relapsing fever, meningitis, hepatitis and other viral hemorrhagic fevers.

Ebola virus infections can be diagnosed definitively in a laboratory through several types of tests:

- Antibody-capture enzyme-linked immunosorbent assay (ELISA)
- Antigen detection tests
- Serum neutralization test
- Reverse transcriptase polymerase chain reaction (RT-PCR) assay
- Electron microscopy
- Virus isolation by cell culture.
- Samples from patients are an extreme biohazard risk; testing should be conducted under maximum biological containment conditions.

TREATMENT

Timely treatment of EVD is important but challenging because the disease is difficult to diagnose clinically in the early stages of infection. Because early symptoms, such as headache and fever, are nonspecific to Ebola viruses, cases of Ebola VD may be initially misdiagnosed. However, if a person has the early symptoms of Ebola VD and there is reason to believe that Ebola VD should be considered, the patient should be isolated and public health professionals notified.

EVD patients require intensive supportive therapy, including intravenous fluids or oral rehydration with solutions including electrolytes and maintenance of oxygen status and blood pressure.

Two monoclonal antibodies, REGN-EB3 (Inmazeb™) and mAb114 (Ebanga™) are available for the treatment of EVD caused by Zaire ebolavirus. There are currently no licensed therapeutics for the treatment of EVD caused by Sudan ebolavirus.

Pregnant and breastfeeding women with Ebola should be offered early supportive care.

PREVENTIVE MEASURES

Risk of infection with Ebola virus and how to avoid it

Casual contact in public places with people that do not appear to be sick do not transmit Ebola. One cannot contract Ebola virus by handling money, groceries or swimming in a pool. Mosquitoes do not transmit the Ebola virus.

Ebola virus is easily killed by soap, bleach, sunlight or drying. Ebola virus survives only a short time on surfaces that have dried in the sun.

Reducing the risk of Ebola infection in people

In the absence of effective treatment and a human vaccine, raising awareness of the risk factors for Ebola infection and the protective measures individuals can take is the only way to reduce human infection and death.

Reducing the risk of wildlife-to-human transmission from contact with infected fruit bats or monkeys/apes and the consumption of their raw meat. Animals should be handled with gloves and other appropriate protective clothing. Animal products (blood and meat) should be thoroughly cooked before consumption.

Reducing the risk of human-to-human transmission in the community arising from direct or close contact with infected patients, particularly with their body fluids. Close physical contact with Ebola patients should be avoided. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home and should be disposed after use as per biosafety guidelines. Regular hand washing is required after visiting patients in hospital, as well as after taking care of patients at home.

Dead patients to be handled for cremation/burial under biosafety precautions.

Controlling infection in health-care settings

Health-care workers always apply standard precautions consistently with all patients – regardless of their diagnosis – in all work practices. These include basic hand hygiene, respiratory hygiene, use of personal protective

equipment (according to the risk of splashes or other contact with infected materials), safe injection practices and safe handling after death of infected patient.

Health-care workers caring for patients with suspected or confirmed Ebola virus should apply, in addition to standard precautions, other infection control measures to avoid any exposure to the patient's blood and body fluids and direct unprotected contact with the possibly contaminated environment. When in close contact (within 1 meter) of patients with EBV, health-care workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown, and gloves (sterile gloves for some procedures).

Well-equipped isolation wards (adequate infection control practices in place) for patients with symptoms suggestive of highly infectious/contagious diseases, such as Ebola, are essential to reduce the risk of the spread of nosocomial infection in hospital settings. The state must ensure that suspect cases of highly pathogenic infectious diseases do not go to routine referral healthcare systems but must be managed at designated tertiary care facilities with appropriate infection control and biomedical waste management practices. Proper cleaning and disposal of instruments, such as needles and syringes, is also important. If instruments are not disposable, they must be sterilized before being used again.

Laboratory workers are also at risk. Samples taken from suspected human and animal Ebola cases for diagnosis should be handled by trained staff and processed in suitably equipped laboratories.

If travelling to an area with known Ebola cases:

- Practice hygiene. Avoid direct contact with blood and body fluids.
- Do not handle items that may have come in contact with an infected person's blood or body fluids.
- Avoid funeral or burial rituals that require handling the body of someone who has died from Ebola.
- Avoid contact with bats and nonhuman primates or blood, fluids, and raw meat prepared from these animals.
- Avoid hospitals where Ebola patients are being treated.
- After return, one should monitor his/her health for 21 days and seek medical care immediately if develop symptoms of Ebola.

Vaccines:

Commercial vaccines have been used to contain the spread of ebolavirus disease outbreaks caused by Zaire strains. Available commercial vaccines against EVD have been developed for Zaire strain of Ebola virus and hence have not been proved effective to control Uganda outbreak[1]. WHO is working on three vaccine candidates to be tested in a vaccination trial in Uganda[2] Ebola trial candidate vaccines for Sudan ebolavirus have been developed. None of these vaccines are available in India.

1. FDA approved rVSV-ZEBOV vaccine (ERVEBO®) protects against EVD caused by Zaire ebolavirus and is used for adults over 18 years old. This recommendation includes adults who are responding or planning to respond to an outbreak of EVD; Laboratorians or other staff working at biosafety-level 4 facilities that work with live Ebola virus.

2. The second vaccine available to protect against EVD caused by Zaire ebolavirus is delivered as 2 doses. The first dose, Ad26.ZEBOV-GP (Zabdeno), is given followed by a second dose, MVA-BN-Filo (Mvabea), 8 weeks later is EU approved. The 2 doses are administered as injections into the muscle (intramuscular) around the shoulder or thigh.

Ad26.ZEBOV-GP and MVA-BN-Filo can be used in adults and children over one year old. The vaccine requires 2 doses and is therefore not suitable for use in outbreak response where immediate protection is necessary.

CONCLUSION

Ebola virus disease (EVD), is a severe, often fatal illness in humans and its outbreaks have been recognized with increasing frequency in Africa with frequent exportation to other countries. Factors like population growth, encroachment into forested areas, and direct interaction with wildlife (such as bushmeat consumption) may have contributed to the spread of the Ebola virus. Community engagement is key to successfully controlling outbreaks. The most effective way to save lives is to inform people about how the disease spreads, and how they can protect themselves. Good outbreak control relies on applying a package of interventions, namely case management, infection prevention and control practices, surveillance and contact tracing, a good laboratory service, safe and dignified burials and social mobilization. Early supportive care with rehydration, symptomatic treatment improves survival. More research is warranted regarding its occurrence, transmission, therapeutics and vaccines.

….about CD Alert

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[1] https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-high-level-emergency-ministerial-meeting-on-cross-border-collaboration-for-preparedness-and-response-to-ebola-virus-disease---12-october-2022

[2] https://cdn.who.int/media/docs/default-source/blue-print/who-vaccine-prioritization-report-uganda-ebola-trial-nov-16-2022.pdf?sfvrsn=cf4542ba_3&download=true