Epidemiology of Ebola virus disease

Conference on new epidemic and pandemic phenomena: socio-economic impacts and policy responses
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Animals = reservoir of diseases

- Zoonosis, also called zoonotic diseases, are diseases that can be transmitted from animals, whether wild or domesticated, to humans
- 60% of pathogens are zoonotic and 3/4 of emerging diseases are zoonotic
- **Human population** 7.3 billions **Farmed animals** 24.4 billions
  - Every person 2.5 chicken
  - Every 5 persons 1 cow
  - Every 7 persons 1 sheep
  - Every 8 persons 1 pig

Most common zoonosis: influenza

easonal flu about 40 000 people dying each year in the European countries due to he seasonal influenza

6.2 million vaccinated in EU, about 9% of total population

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ARS 2002 (coronavirus) 775 deaths in 17 countries

I1N1 2009 (swine flu): 2900 deaths in Europe, 15300 deaths in the rest of the world

I5N1 2013 (avian flu): 380 deaths in 15 countries

MERS 2012 -to date: 571 deaths in 26 countries

Epidemics

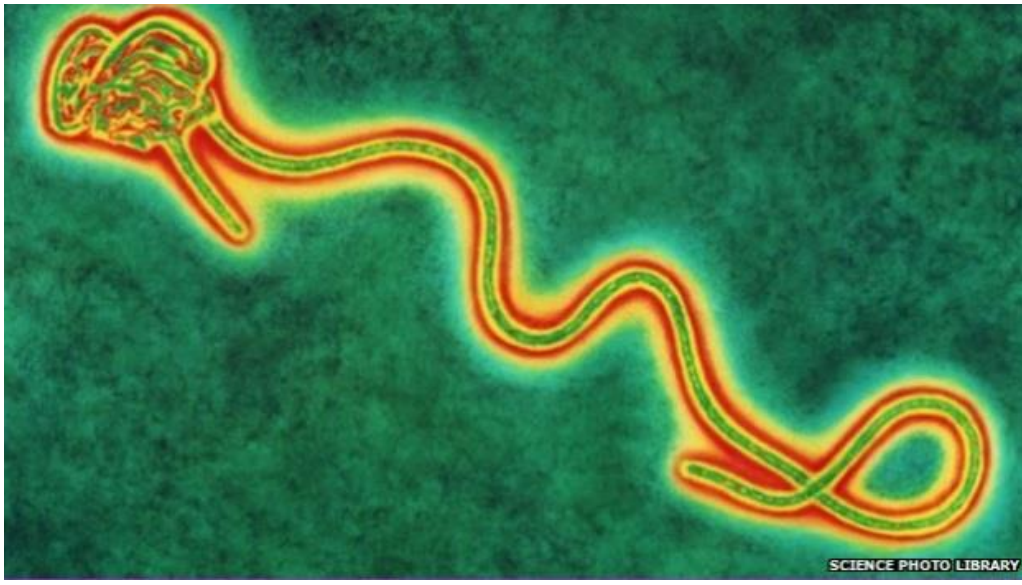
Epidemic: the spreading of an infectious disease rapidly and extensively, affecting many individuals in an area or a population at the same time

Pandemia: when a new infectious diseases appears against which the human population has no immunity, resulting in several simultaneous epidemics worldwide with high numbers of deaths and illness

Example

- Middle East Respiratory Syndrome (MERS) is a viral respiratory illness that is new to humans. It was first reported in Saudi Arabia in 2012 and has since spread to several other countries, including Europe
- Coronaviruses are a large family of viruses that can cause diseases ranging from the common cold to Severe Acute Respiratory Syndrome (SARS).
- 26 countries have reported cases, the great majority is in Saudi Arabia
- Total cases 1595, deaths 571 (Arabia 688 cases, 282 deaths) (36% patients have died)
- No vaccine or specific treatment is currently available. Treatment is supportive and based on the patient's clinical condition

Ebola virus



Filoviridae Family

Morphology: enveloped RNA filaments up to 14 000 nm, diameter 80 nm

Virus can survive in liquid or dried material for many days

Five different kind of viruses with different pathogenicity

Sensitive to sodium hypochlorite and other disinfectants

Pathogen of Group risk 4 which trigger special containment measures and barrier protection, particularly for health care workers

Epidemiological features of Ebola virus

bats are considered natural reservoir; monkeys and chimpanzees can
the virus.

nal-to-person transmission: contact with living or dead infected
nals (e.g. primates, bats) or material infected by animals

on-to-person transmission: through direct contact with organs, blood
ther bodily fluids (e.g. saliva , urine, vomit) of living or dead infected
ons

incubation period (the time from infection to the onset of symptoms) is
etween 2 to 21 days

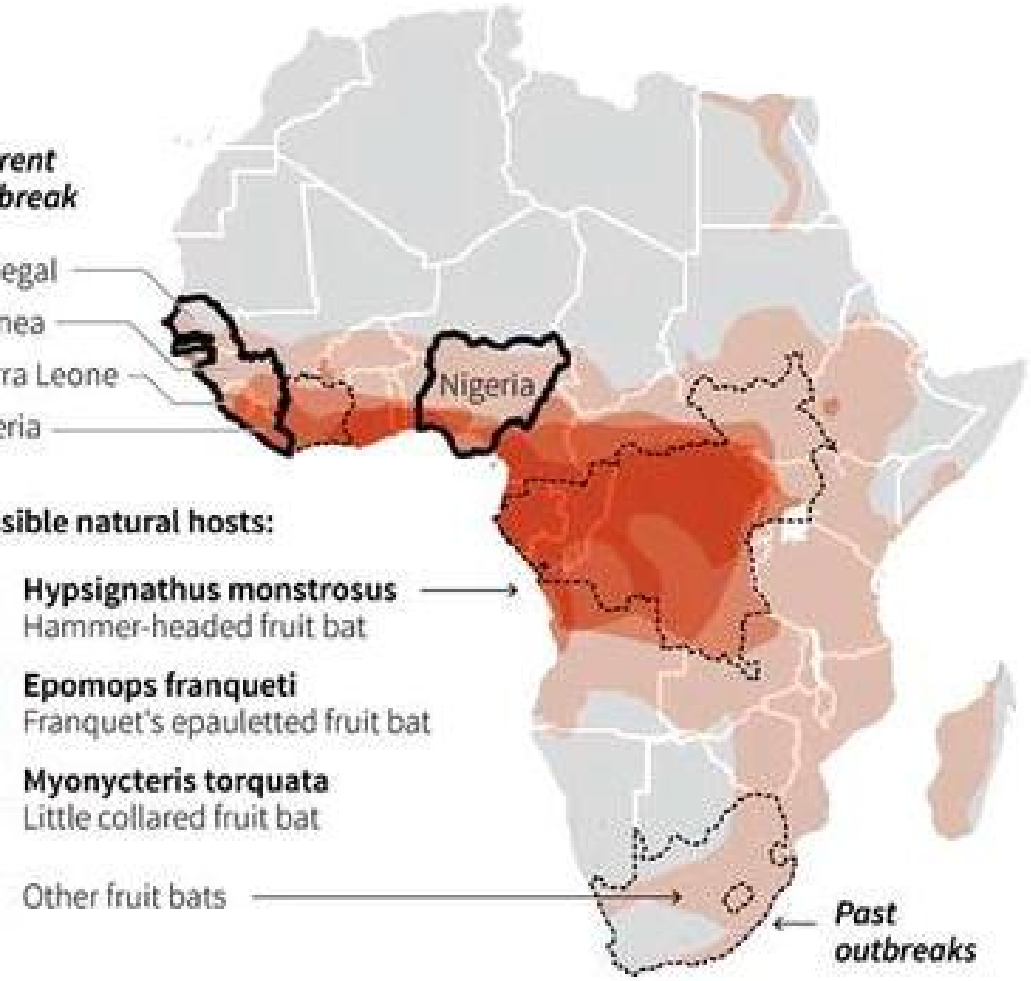
on is infectious from the onset of symptoms and as long as their blood
nd secretions contain the virus (sometimes weeks sometimes months)

al ceremonies and health care settings without proper protection are
articularly dangerous, underestimated until the 2014 outbreak

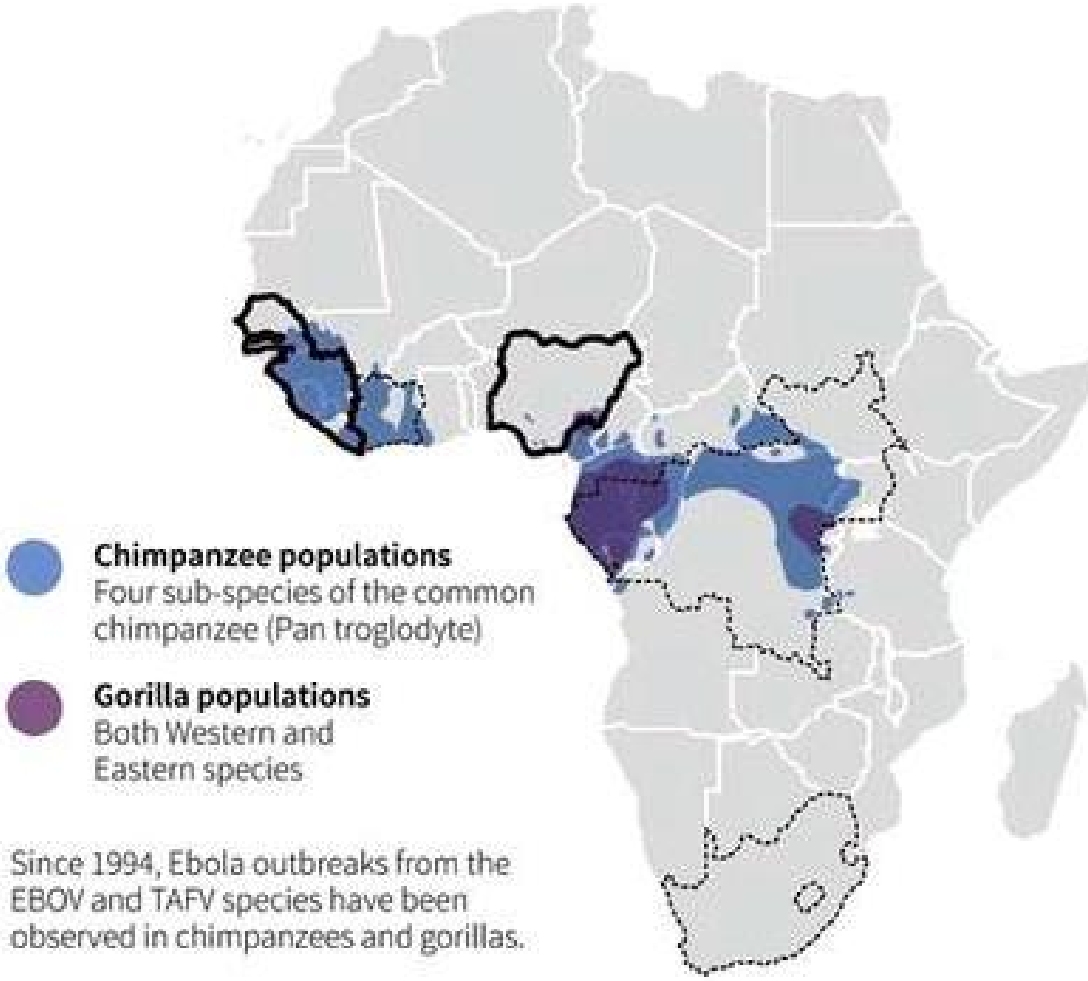
bola outbreak

ough fruit bats are considered possible natural hosts of the Ebola virus, direct transmission to humans is rare. However, animals that may fruit dropped by infected bats, like chimps and gorillas, have been linked to spreading the disease in communities that eat them.

ge of fruit bats in Africa



Range of chimpanzees and gorillas in Africa



e: International Union for Conservation of Nature and Natural Resources (IUCN); World Wide Fund for Nature (WWF); World Health Organization

Clinical presentation of the Ebola virus disease

Sudden onset of flu-like illness: fever, muscle pain, weakness, headache and sore throat

Followed by various clinical symptoms, including:

- gastrointestinal - abdominal pain, anorexia, diarrhoea, vomiting; hypovolemic shock
- neurological - headaches, confusion;
- vascular - conjunctival/pharyngeal injections;
- cutaneous - maculopapular rash and
- respiratory - cough, chest pain, shortness of breath

One week later, haemorragic manifestations in >50% of patients:

bloody diarrhoea/vomiting, nosebleeds, petechiae, ecchymosis and puncture bleeding, fatal internal hemorrhage

Laboratory confirmation assays

Detection and sequencing of viral RNA in blood (by quantitative PCR) from onset of fever up to 10-12 days
Can be negative during the two first days of illness

Viral isolation: only conducted in laboratories of Biological Safety Level 4
From onset of fever up to 8-10 days

Serology: blood tests for detection of specific immunoglobulins (IgM and IgG)
No validated assays

History of Ebola virus disease

1976: epidemics of severe haemorrhagic fever simultaneously in the Democratic Republic of Congo and Sudan
The new virus was identified and named after a small river

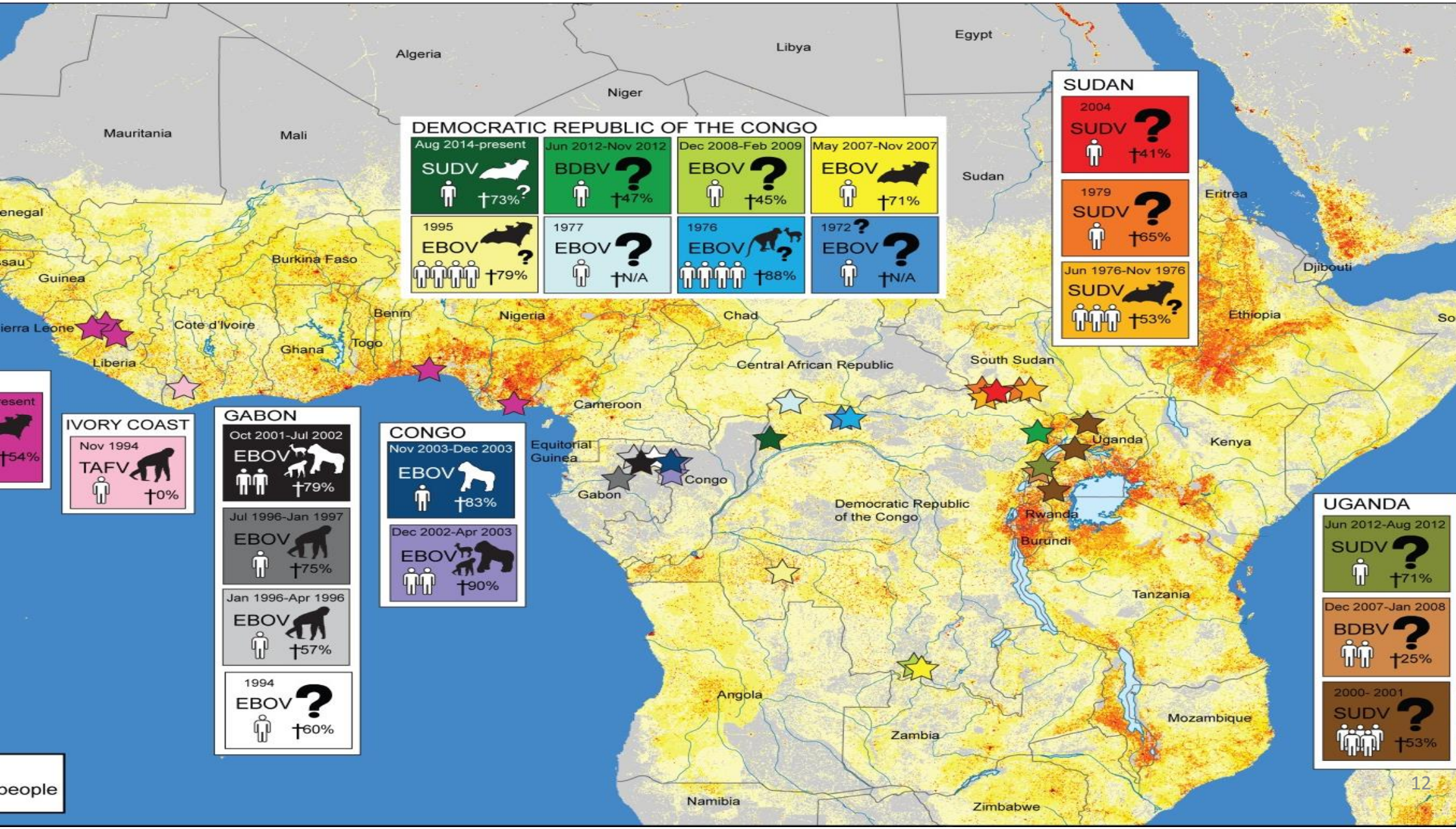
Several Ebola viruses identified:
- *Zaïre* and *Sudan* (1976) in Congo and Sudan
- *Taï Forest* (1994) in Ivory Coast
- *Bundibugyo* (2007) in DRC
- *Reston* (1989) in the Philippines: non-pathogenic for humans

Up to 2012 outbreaks in Congo, DRC, Gabon, Sudan and Uganda
In total **2387 cases** and **1590 deaths** reported

Biggest outbreaks of Ebola

ÅSudan 1976	284 cases -151 deaths
ÅDemocratic Republic of Congo 1976	318 cases – 280 deaths
ÅDemocratic Republic of Congo 1995	315 cases -254 deaths
ÅUganda 2000	425 cases - 224 deaths
ÅDemocratic Republic of Congo 2007	530 cases – 380 deaths

Factors leading to the Ebola Outbreaks (Source PLOS Neglected Tropical Diseases)



Ebola epidemic in West Africa in 2014

The largest ever documented outbreak of Ebola Virus Disease
both in terms of numbers and geographical spread

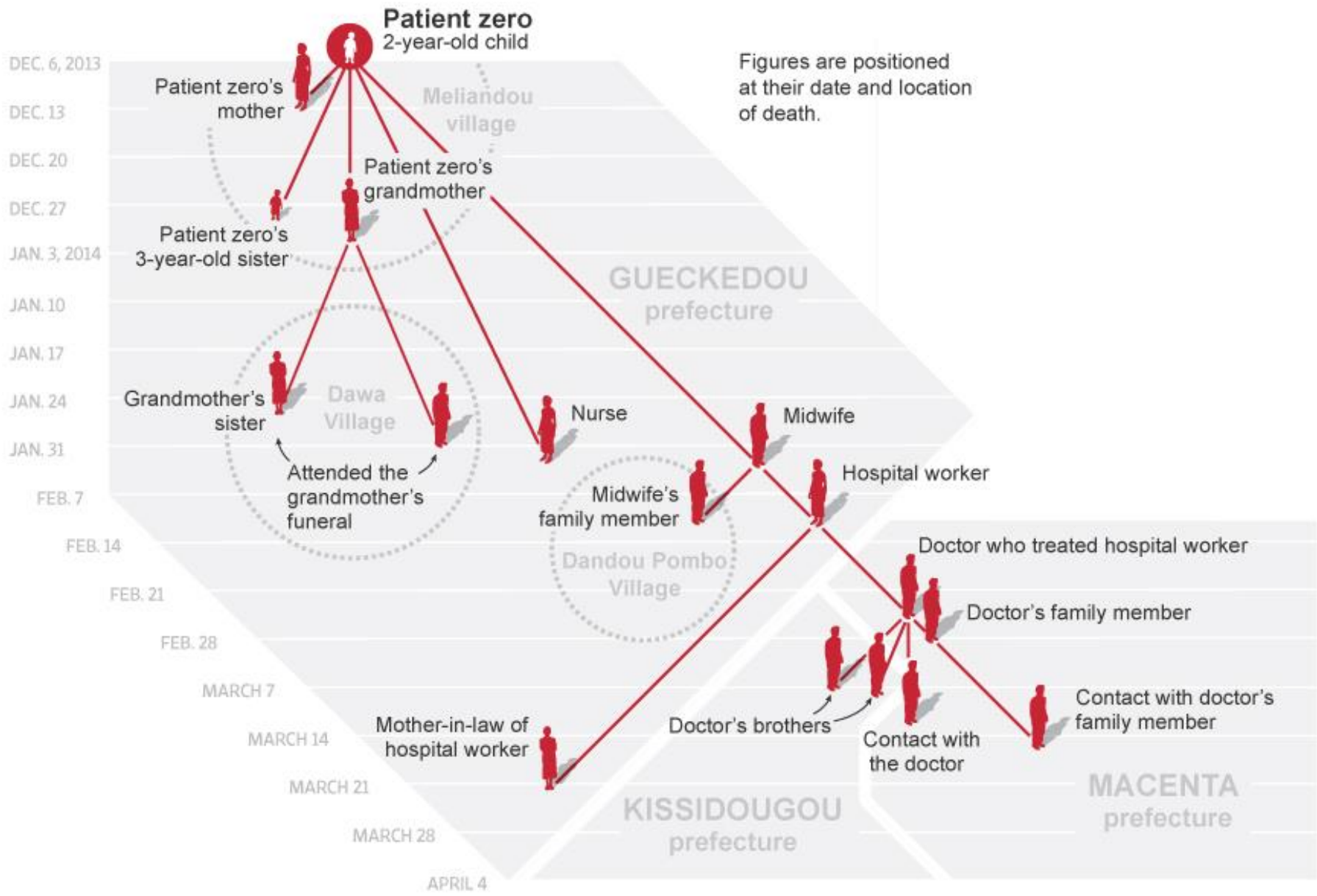
Sierra Leone, Liberia and Guinea	Cases 28 476	Deaths 11 298
Other countries	Cases 36	Deaths 15

The first outbreak of Ebola Virus in West Africa

Zaïre ebolavirus related but distinct from the previous isolations in Africa

An area is declared Ebola-free when there has been no cases for a 42-day period (the double of the incubation period of 21-days)

Ebola epidemic in West Africa ï How did it start?



Sources: New England Journal of Medicine

The Wall Street Journal

Events of Ebola epidemic in West Africa (1)

March 2014: Guinea notified WHO about rapidly evolving outbreak. First cases indeed December 2013 (population: 10,6 millions)

Late March 2014: Cases reported in Liberia (population: 4 millions)

April 2014: Cases reported also in Sierra Leone (6,2 millions)

July 2014: An imported case in Nigeria from Liberia - Subsequent local transmission

8 Aug 2014: WHO declared "Public Health Event of International Concern (PHEIC)"

9 Aug 2014: One confirmed case in Senegal – native of Guinea - No local transmission

18 Sep 2014: United Nations Security Council declared "threat to international peace and security"

Events of Ebola epidemic in West Africa (2)

9 Sep 2014: The first imported case in the USA from Liberia

Oct 2014: A confirmed case in Spain

9 Oct 2014: Health worker at Texas hospital tested positive for Ebola (had provided re for the first imported case); few days later a second case

7 Oct 2014: WHO declares outbreak in Senegal over (13,6 millions)

9 Oct 2014: WHO declares outbreak in Nigeria over (174 millions)

3 Oct 2014: Mali reports its first confirmed case of EVD: a child originally from uinea, dies in Kayes hospital

3 Oct 2014: USA reports its fourth case of EVD medical aid worker

Events of Ebola epidemic in West Africa (3)

8 Oct 2014: WHO approved a new Ebola vaccine trial

Nov 2014: UN worker medically evacuated from Sierra Leone to France

2 Nov 2014: Mali reports three plus two additional cases, not linked to he first case reported on 23 October 2014

0 Nov 2014: MSF health worker was medically evacuated from Mali to pain

1 Nov 2014: WHO declares outbreak in the Democratic Republic of ongo over (67,5 millions)

5 Nov 2014: Two additonal cases in Mali

Events of Ebola epidemic in West Africa (4)

Dec 2014: UN peace corp worker medically evacuated from Liberia to Netherlands

9 Dec 2014: a UK health worker coming back from affected areas tested positive for Eb

18 Jan 2015: WHO declares Mali Ebola free (15,3 millions)

May 2015: WHO declares Liberia Ebola free

2 May 2015: an Italian nurse coming back from Sierra tested positive for Ebola

0 June 2015: the Italian nurse has been declared Ebola free. All his contacts have ende
1-days follow-up

Experimental therapies used to treat Ebola

Prioritized for consideration based on the availability of NHP efficacy data with a filovirus challenge and justification for a human dose based on clinical data of the product or comparable products within that class.

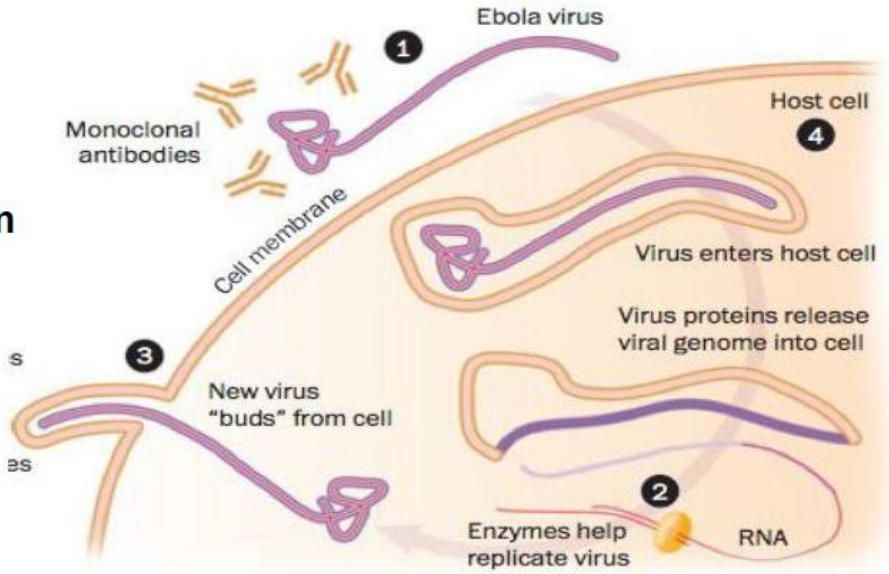
1- Targets the virus before it enters the cell

Zmapp A cocktail of three monoclonal antibodies, which block or neutralises the virus by binding to or coating a different site on the covering or "envelope" of the virus

Hyperimune globulin Antibodies that can neutralize the different EVD strains.

4- Bolsters human cells

Interferons - Induce an antiviral state in exposed cells and regulates the immune system



3- Prevents virus from exiting host cells

5- Testing existing drugs approved for other purposes

All drugs Screening all licensed drugs.

6- Whole blood transfusions and convalescent plasma

2- Interferes with viral production

TKM 100802Ebola Target two essential viral genes to stop the Ebola from replicating.
AVI 7537 Sarepta Molecules that bind viral RNA, blocking gene function.
Favipiravir T705 Disrupts enzymes that the virus uses to make copies of himself.
BCX4430 Biocryst Disrupts enzymes that the virus uses to make copies of himself.
Brincidofovir Disrupts enzymes that the virus uses to make copies of himself.

Source: Adapted from the Washington Post, Oct 7, 2014

Source: Current treatment approaches for EVD in European hospitals. WHO Ebola Clinical Team. Nahoko Shindo MD PhD, Coordinator, Epidemic Clinical Management, World Health Organization, Department of Pandemic and Epidemic Disease

Development of Ebola virus disease vaccines

Vaccines best instrument to fight a new pandemia

Presently no vaccines to protect against EVD licensed for use in humans

Clinical trials for several candidate vaccines are in various phases

A safe and effective vaccine is hoped for early 2016

Main problem in vaccine development : lower levels of transmission so not enough people at risk to evaluate efficacy.

Clinical pipeline now

5 Jan 2015

J&J

BAVARIAN NORDIC

Ad26/MVA

NOVAVAX
Creating Tomorrow's Vaccines

VLP

12 Feb 2015

gsk

2 Sep 2014

ChAd3 +/- MVA

NewLink GENETICS

MERCK
Be well

17 Oct 2014

rVSV-ΔG

Chinese Ad5 candidate – no NHP efficacy data

World Health Organization

Source: Clinical Pipeline now, from Ebola Vaccine Development. What went well. What lessons can be learned for vaccine R&D before the next emergency and for when the next emergency occurs? By Vasee Moorthy MD PhD

Vaccines in Clinical trials

1.VSV-EBOV, developed by NewLink Genetics and Merck Vaccines USA in collaboration with the Public Health Agency of Canada, is now tested in Phase II and III Clinical trials in Guinea, Sierra Leone and Liberia

2.ChAd3-ZEBOV, developed by GlaxoSmithKline (GSK) in collaboration with the US National Institute of Infectious Diseases

3.Johnson & Johnson, in association with Bavarian Nordic, has developed a 2-dose vaccination approach for Ebola using different vaccines for the first and second doses which has been tested in Phase I Clinical trials The two vaccine candidates are known as Ad26-EBOV and MVA-EBOV.

4.Novavax, a biotech company in the US, has developed a recombinant protein Ebola vaccine candidate based on the Guinea 2014 Ebola virus strain and has completed a Phase I human clinical trials in Australia.

5.An additional vaccine candidate has recently finished early stage human clinical testing in China

Projection of economic losses for 2015

Guinea	US$ 540 million
Liberia	US$ 180 million
Sierra Leone	US$ 920 million
Total three Countries	**US$ 1.640 billion**
Sub-Saharan Africa	US$ 550 million

Source: World Bank, January 2015

What to expect now?

- In the last three months transmission of the virus geographically confined to several small areas in Western Guinea and Sierra Leone (case incidence at 5 confirmed cases or fewer per week), marking a transition to a distinct, third phase of the epidemic
- Three new confirmed cases of Ebola virus disease were reported in the week to 18 October, all of which were reported in Guinea. Hundreds of contacts remain under follow-up in Guinea and few contacts in Sierra Leone: so there is still a risk of further cases among both registered and untraced contacts
- Aim is to drive case incidence to zero, and ensure a sustained end to EVD transmission
- Risk of a reintroduction either from an area of active transmission or from an animal reservoir, or re-emergence of virus from a survivor
- Vaccines will bring the real solution