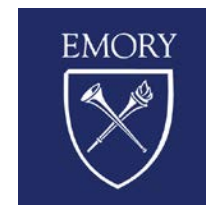


Acute Care Management of Viral Hemorrhagic Fevers

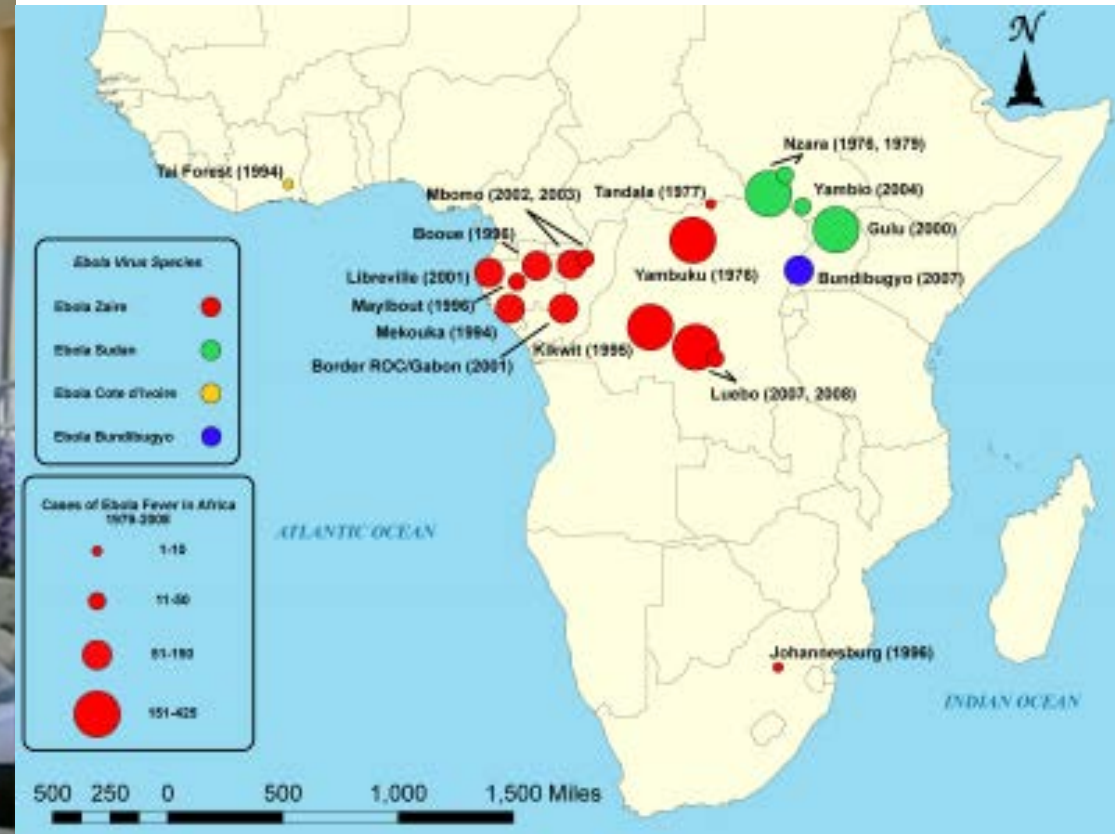
September 1, 2022

Colleen S. Kraft, MD, MSc

Emory University Hospital

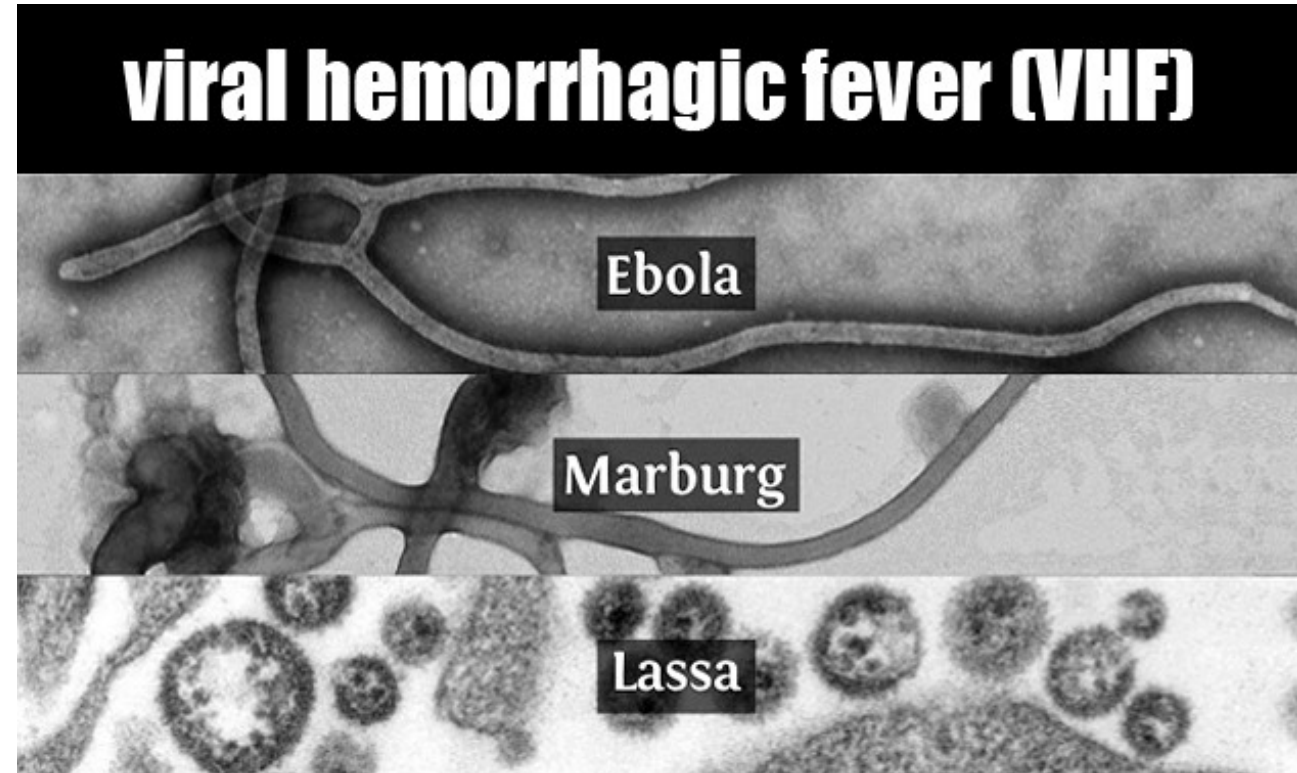


Before 2014, Ebola virus disease was a rural disease and containment worked



Description of VHF

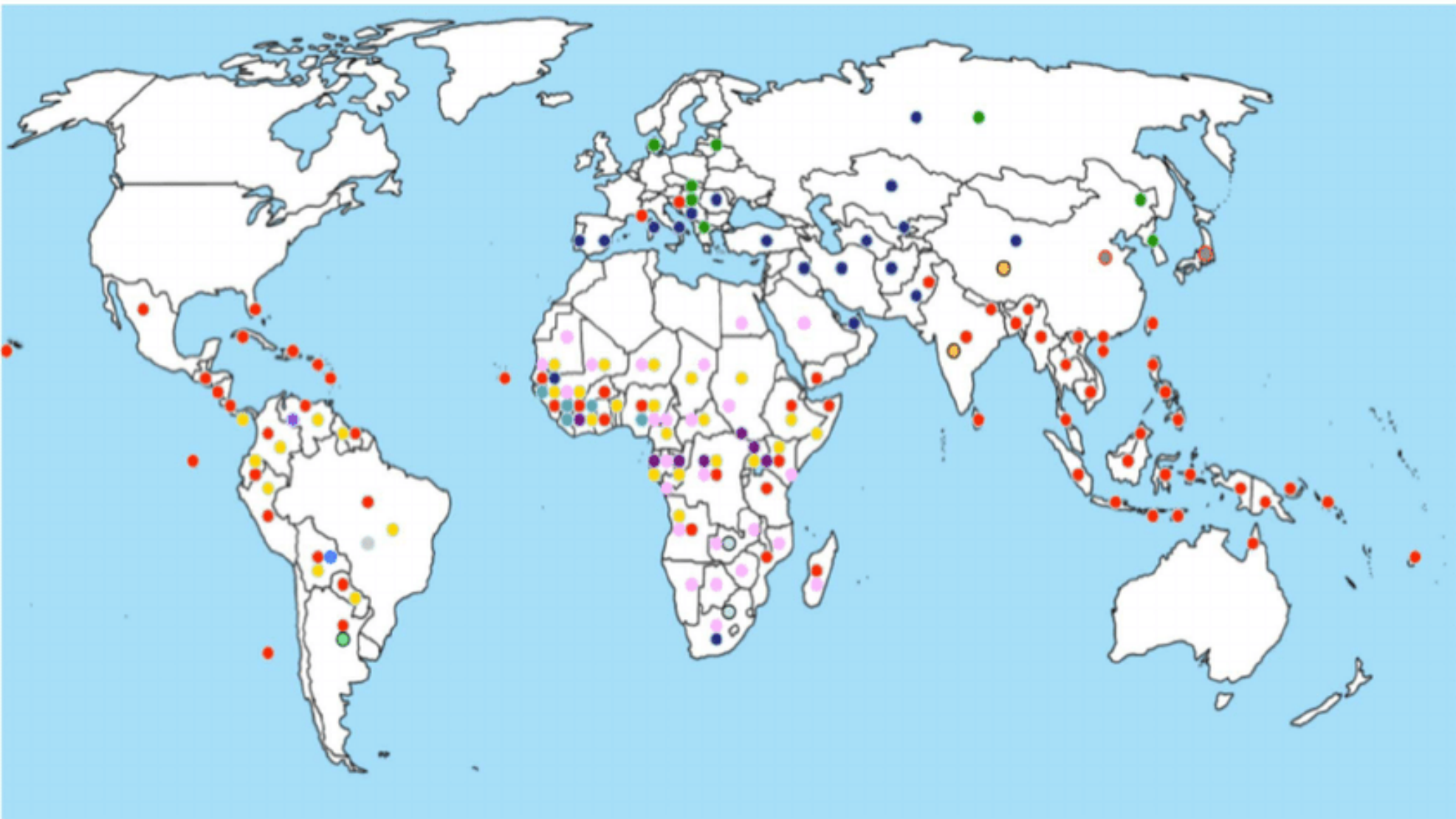
- They are RNA viruses
- They are enveloped, in a lipoprotein outer layer, making it easier to destroy these viruses
- They naturally exist in animal or insect populations, restricted to the geographical areas where the host species live
- They spread to people when a person encounters an infected animal or insect host
- Outbreaks of VHF in people can be difficult to prevent since they can occur sporadically and cannot be easily predicted



Unique clinical challenges with VHF

- More of the world's population is at risk for VHFs
- Person-to-person transmission of some VHFs can occur
- Confirmation of VHF cases can take time
- Prevention of VHF outbreaks is difficult
- Availability of vaccines and treatments are limited





Flaviviridae

- Dengue virus
- Yellow fever virus
- Kyasanur forest disease

Bunyaviridae

- CCHF virus
- Hantavirus HFRS
- Rift valley fever virus
- SFTS virus

Arenaviridae

- Lassa virus
- Lujo virus
- Junin virus

Filoviridae

- Machupo virus
- Ebola and Marburg
- Guaranito virus
- Sabiá virus

Ebola virus disease as a critical illness?

44 year old health care worker evacuated from Kenema, Sierra Leone in early September

- Admitted to Emory Hospital on day 5; received first dose of experimental medication in country
- High fever, rigors, copious diarrhea, high transaminases, mild coagulopathy, encephalopathy

Day 6: Severe gastroenteritis and hepatitis

Day 9: Acute kidney injury and respiratory distress

- Intubation and Mechanical ventilation

Day 11: Cardiac arrhythmias and worsening acidosis

- Continuous Renal Replacement Therapy

Day 21: Extubated → Delirium

Day 29: Improving mental status

Day 35: Dialysis held

- Blood tests negative for EBOV by RT-PCR

Day 40: Discharged home

- 30 lb weight loss, easy fatigability, proximal muscle weakness + unsteady gait → difficulty ambulating, word-finding difficult



Table 1. Similarities between Severe and Fatal EBOV and Classical Sepsis.*

Parameter	Similarities	References
Systemic Inflammation	Increased levels of pro-inflammatory cytokines (e.g., interleukin 6 [IL-6]), chemokines (IL-8), and the anti-inflammatory cytokine IL-10	Classical Sepsis: [5,10,11] ; EBOV: [17,19,20]
Immune Dysfunction	Increased susceptibility to secondary bacterial infections, lymphocyte apoptosis	Classical Sepsis: [4,14] ; EBOV: [23,28]
Coagulopathy	Increased D-dimers, thrombomodulin, ferritin, disseminated intravascular coagulation, thrombocytopenia	Classical Sepsis: [9,12] ; EBOV: [17,18,20]
Endothelial Dysfunction	Vascular leak with hypovolemia	Classical Sepsis: [13] ; EBOV: [23–25,27]
Organ Dysfunction	Renal insufficiency, hepatic dysfunction, respiratory failure, neurologic dysfunction	Classical Sepsis: [6,8,11] ; EBOV: [21–25]

* Classical sepsis is defined as bacterial and fungal sepsis

doi:10.1371/journal.ppat.1005088.t001

Outbreaks have led to modernization of treatment



Pamoja Tulinde Maisha (PALM) trial

- Zmapp™ (MappBio) - 3 antibodies, c13C6FR1, c2G4, and c4G7, expressed in a species of tobacco, *Nicotiana benthamiana*
- Remdesivir (Gilead Sciences) – novel nucleotide analog prodrug
- MAb114 (Merck) - human IgG1 MAb targeted to the Zaire ebolavirus (EBOV) glycoprotein (GP)
- REGN-EB3 (Regeneron) – 3 antibodies



Ebola-specific therapies

- Atoltivimab, maftivimab, and odesivimab (REGN-EB3) and ansuvimab (mAb114) are two antibody-based therapies that are effective for the treatment of *Zaire ebolavirus* infection. The WHO included the use of these antibodies in its response to an outbreak of Ebola virus disease in the DRC in 2021, and these antibodies are both approved for use by the US Food and Drug Administration.
 - **Atoltivimab, maftivimab, and odesivimab (REGN-EB3)** – In October 2020, the US Food and Drug Administration (FDA) approved the triple-monoclonal antibody (mAb) product, which contains atoltivimab, maftivimab, and odesivimab (sold as Inmazeb). This combination of three mAbs targets three nonoverlapping epitopes on the Ebola virus surface glycoprotein, providing potent virus neutralization.
 - **Ansuvimab (mAb114)** – In December 2020, the FDA approved the monoclonal antibody ansuvimab (sold as Ebanga). This mAb was isolated from a survivor of Ebola virus disease and neutralizes the virus.



BRIEF REPORT

Molecular Evidence of Sexual Transmission of Ebola Virus

S.E. Mate, J.R. Kugelman, T.G. Nyenswah, J.T. Ladner, M.R. Wiley, T. Cordier-Lassalle, A. Christie, G.P. Schroth, S.M. Gross, G.J. Davies-Wayne, S.A. Shinde, R. Murugan, S.B. Sieh, M. Badio, L. Fakoli, F. Taweh, E. de Wit, N. van Doremalen, V.J. Munster, J. Pettitt, K. Prieto, B.W. Humrighouse, U. Ströher, J.W. DiClaro, L.E. Hensley, R.J. Schoepp, D. Safronetz, J. Fair, J.H. Kuhn, D.J. Blackley, A.S. Laney, D.E. Williams, T. Lo, A. Gasasira, S.T. Nichol, P. Formenty, F.N. Kateh, K.M. De Cock, F. Bolay, M. Sanchez-Lockhart, and G. Palacios

SUMMARY

Days since Second Blood Sample from S Tested Negative for EBOV

207 Days

175 Days

155 Days

Oct. 3
S: Second blood
sample tests
EBOV-negative

Sept. 29
S: First blood
sample tests
EBOV-negative

Sept. 23
S: Enters
ETU

Oct. 7
S: Exits
ETU

March 7
S and P engage in
sexual intercourse

March 14
P: EVD
onset

March 27
S: First semen
sample tests
EVD-positive;
P: Dies from
EVD

March 19
P: Enters
ETU

March 20
P: Blood sample
tests EBOV-positive

April 28
S: Second semen
sample tests
EBOV-negative

May 2
S: Third
semen
sample
tests
EBOV-
negative

September 2014

October 2014

November 2014—
February 2015

March 2015

April 2015

May 2015

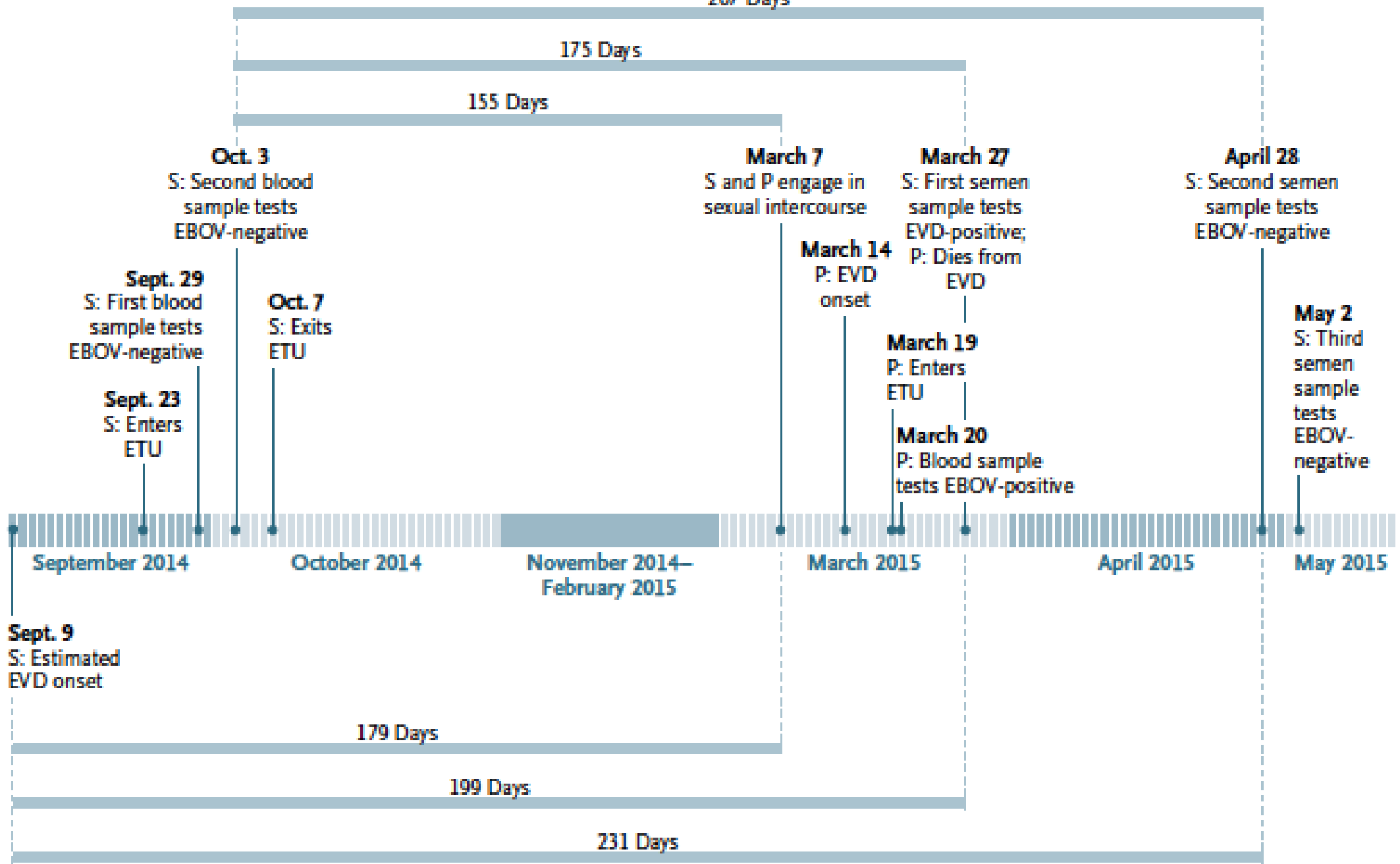
Sept. 9
S: Estimated
EVD onset

179 Days

199 Days

231 Days

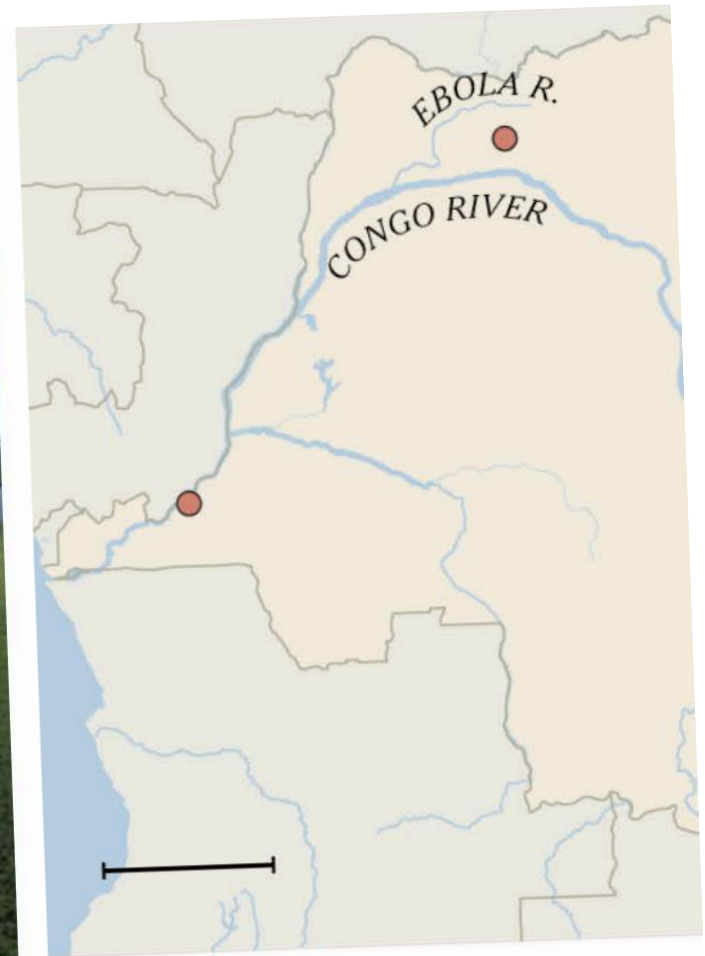
Days since Estimated Date of EVD Onset in S



Vaccination strategies

- Ervebo[®] (rVSV-ZEBOV)
 - >350,000 people in Guinea, DRC under compassionate use and safe and effective against Zaire Ebolavirus
 - Global stockpile started January 2021
 - U.S. indications: outbreak response, laboratorians and healthcare personnel
- Zabdeno-and-Mvabea
 - Granted marketing authorization by European Medicines Agency
 - 2 dose regimen, and not suitable for an outbreak response

Questions?



The Ebola River, D.R. of Congo