Science in the Time of Crisis: The Global Response to Viral Hemorrhagic Fever in Africa

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Learning Objectives

1. **Analyze the epidemiologic and clinical characteristics of the 2024 Marburg virus outbreak in Rwanda and its diagnostic and infection-control challenges.**

2. **Explain the processes and infrastructure that enabled rapid initiation of therapeutic and vaccine trials during the outbreak, and evaluate their implications for future outbreak-associated research.**

3. **Apply the principles of the One Health framework to strengthen clinical training and global-health collaboration for emerging-pathogen preparedness.**

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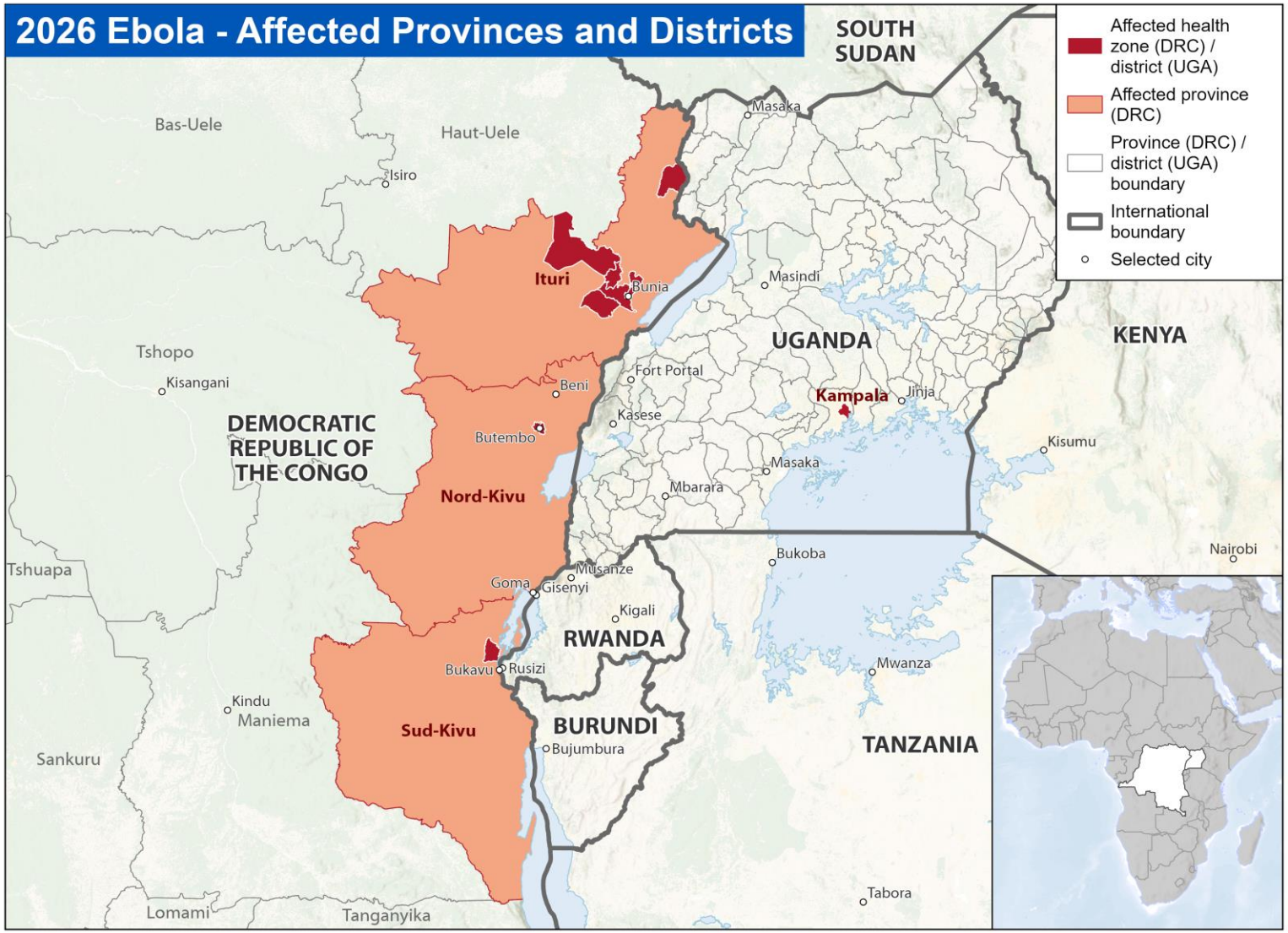
Ebola Outbreak – Situation Update



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Ebola Outbreak – Situation Update

Ebola disease (Bundibugyo virus)

Data as of 26 May 2026						
Affected countries	**Suspected cases**	**Suspected deaths**	**CFR (%) suspected**	**Confirmed cases**	**Confirmed deaths**	**CFR (%) confirmed**
Democratic Republic of the Congo#	1077	238	22%	121	17	14%
Uganda	0	0	0	7	1	14%
Total	**1077**	**238**	**22%**	**128**	**18**	**14%**

#Data source: Centre des opérations d'urgences de sante publique (COUSP-DRC)

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Ebola Outbreak – Wisconsin DHS Resources

WISCONSIN DEPARTMENT of HEALTH SERVICES

https://www.dhs.wisconsin.gov/disease/han.htm

Bureau of Communicable Diseases Information Update

CDC Health Alert Network (HAN) Health Advisory: Ebola Disease Outbreak in the Democratic Republic of the Congo and Uganda

This message is being sent to the health alert network, travel health network, and infection preventionists.

Summary

On May 19, 2026, the CDC (Centers for Disease Control and Prevention) issued a Health Alert Network (HAN) Health Advisory providing information about a new outbreak of Ebola disease in the Democratic Republic of the Congo (DRC) and Uganda caused by the Bundibugyo virus (species *Orthoebolavirus bundibugyoense*). **The risk of spread to the United States is considered low at this time.**

Background

Ebola disease is a rare but severe viral hemorrhagic fever (VHF). The investigation of a cluster of severe illness that began in early May among health care workers in DRC identified Ebola Bundibugyo virus disease (BVD) as the cause. On May 17, the World Health Organization determined this outbreak to be a public health emergency of international concern.

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Clinician Outreach and Communication Activity (COCA)

EXPLORE THIS TOPIC

SEARCH

What Clinicians Should Know about Ebola Bundibugyo Virus

For Health Care Providers
MAY 28, 2026

https://www.cdc.gov/coca/hcp/about/index.html

AT A GLANCE

During this COCA Call, learn more about this outbreak, the history and ecology of Bundibugyo virus, what U.S. clinicians should know about preparing for, diagnosing, and managing patients with suspect or confirmed Ebola disease, and how to prevent Ebola viruses from spreading.

Rwanda

- Population (2024): 13.6 Million
- Area: 26,798 sq. km (~ Maryland)
- Capital: Kigali City (Pop: 1.7 Million)

Fulbright Public Policy Fellowship

- August 1, 2024 – May 30, 2025
- Sabbatical from UW-Madison
- Leave of absence from Wisconsin DHS
- Assigned to Rwanda Ministry of Health (MOH), Department of Health Workforce Development

King Faisal Hospital – Rwanda

- Academic, tertiary care center in Kigali
- Regional referral hub for advanced care
- Clinical home of the new Africa Health Sciences University (AHSU) – 6 new residency programs started July 2024
- Infectious Disease Fellowship planned to launch in 2025

Presentation of 2 Cases

King Faisal Hospital Intensive Care Unit

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Case 1 – September 24

Male – Age 24

CC: Fever/Chills + Headache

- Admitted to ED 9/20/2025 – fever x 5d
- Exam: Abdominal tenderness, conjunctivitis
- AST 262, ALT 151, LDH 710, Tbili 5, Cr nl

Hospital Course:

- Empiric IV antibiotics, artesunate
- Day 2: bilirubin 8
- Day 3: bilirubin 23, ALT 2300, Cr 1.7, INR 2.1
- Day 5: seizures, intubated, shock

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PERSPECTIVE

Fight or Flight — Facing the Marburg Outbreak in Rwanda

Author: Jean Pierre Sibomana, M.D. Author Info & Affiliations

Published November 20, 2024 | N Engl J Med 2024;391:2070-2072 | DOI: 10.1056/NEJMp2413951
VOL. 391 NO. 22 | Copyright © 2024

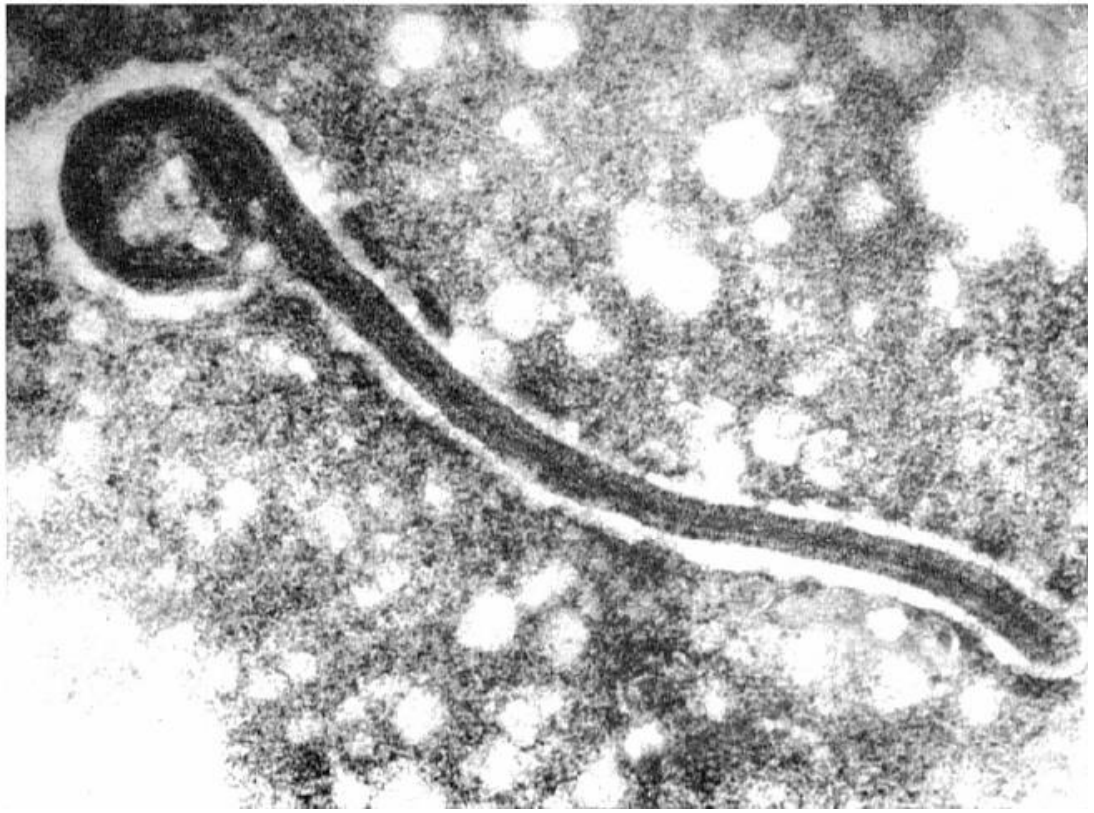
"Given their significantly reduced oxygen saturation, I decided to intubate them to protect their airways, and I asked the on-call anesthesiologist to intubate the second patient while I intubated the first. As I opened his oropharynx with a laryngoscope, I observed that the source of bleeding was not the oral cavity but the esophagus and airway, and I was immediately filled with fear and anxiety regarding the possible cause."

Jean Pierre Sibomana, M.D.
ICU Physician, King Faisal Hospital

Viral Hemorrhagic Fever – Testing

- September 24 – Blood specimens from 4 patients sent to Rwanda National Reference Lab
  - 2 case patients
  - 1 ED nurse with AKI & acute hepatitis
  - 1 Medical assistant who died on Sept 16 with malaria
- September 25 – RT-PCR **negative** for dengue, Rift Valley fever, ebola virus
- September 26 –RT-PCR **positive** for Marburg virus – in 4/4
- September 27 – MVD Outbreak Declared

Marburg Virus - History



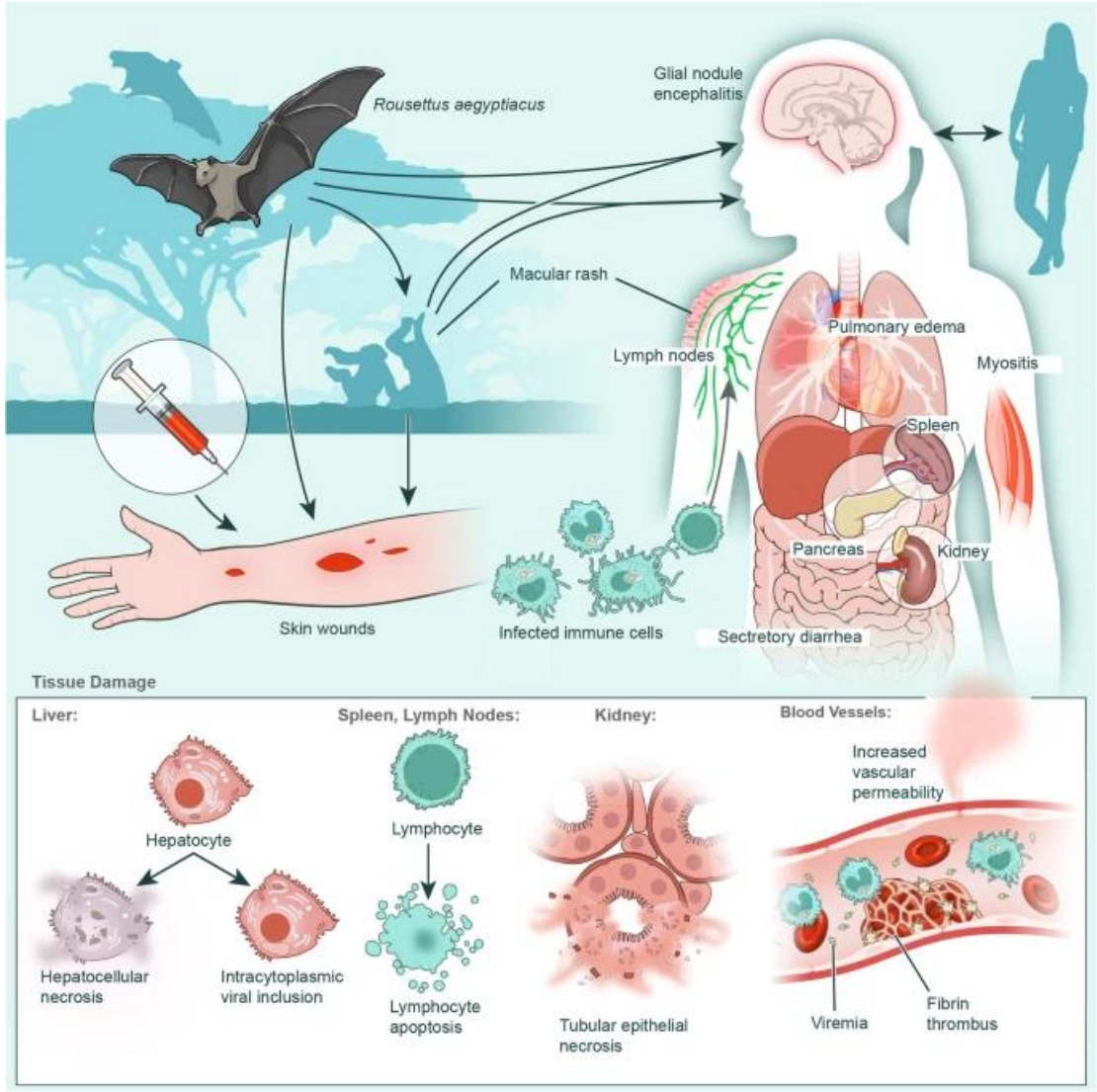
The first electron micrograph of a Marburg virion from 1967. Image courtesy of W. Slenczka, University of Marburg, Germany.

- Family *Filoviridae*
  - Genus ***Marburgvirus***
  - Genus ***Ebolavirus*** (6 species)
- 1967 – Hemorrhagic fever outbreak among lab workers in Marburg, Germany
- African green monkey exposure
- 31 cases of acute febrile illness

Viruses 2012, 4, 1878-1927; doi:10.3390/v4101878

Marburg Virus - Pathophysiology

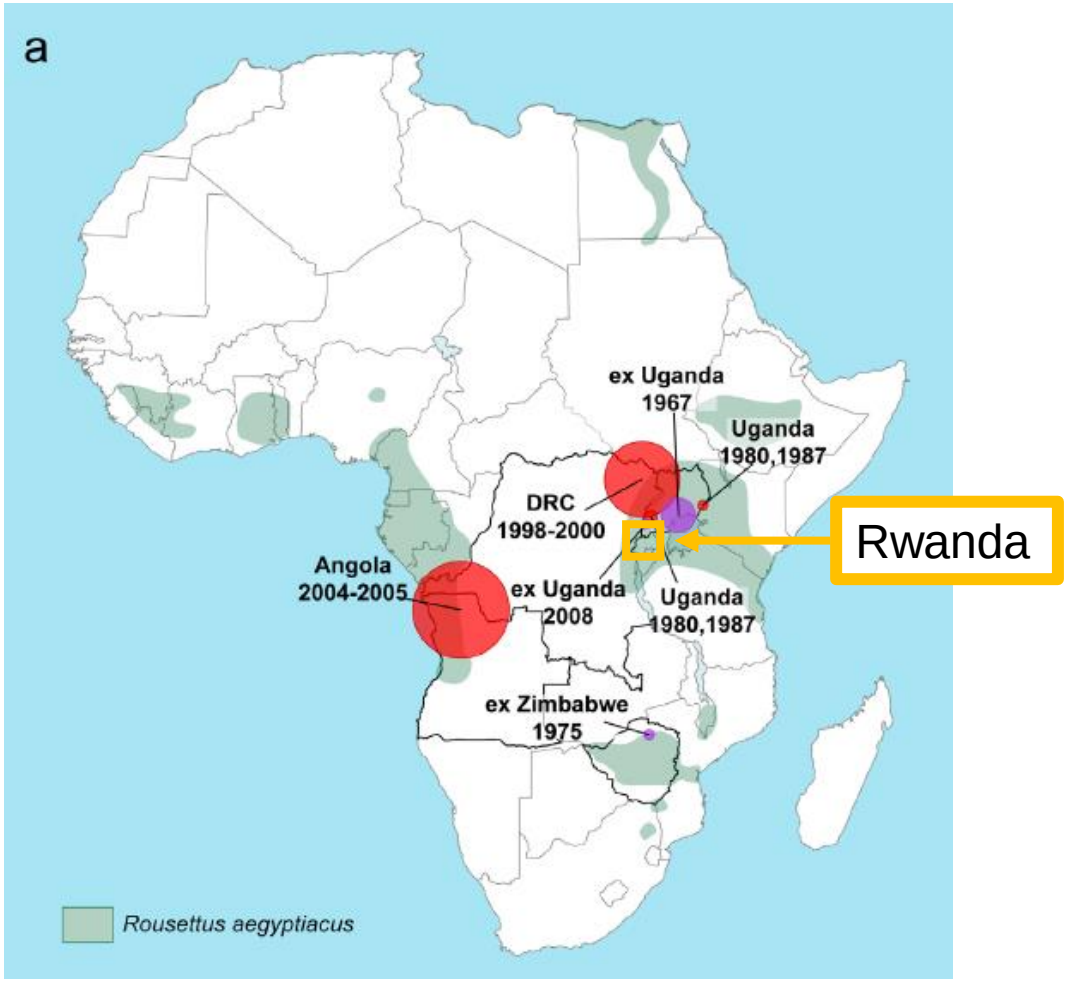
- Infects macrophages, dendritic cells, and endothelial cells,
- Viral spread to liver and spleen → hepatocellular necrosis and coagulopathy.
- Cytokine storm and tissue-factor release → systemic inflammation and DIC.
- Endothelial injury → capillary leak, hypovolemia, and shock.
- Multiorgan failure: hepatic, renal, and adrenal dysfunction.



Virology Journal (2019) 16:165

Marburg Virus Ecology

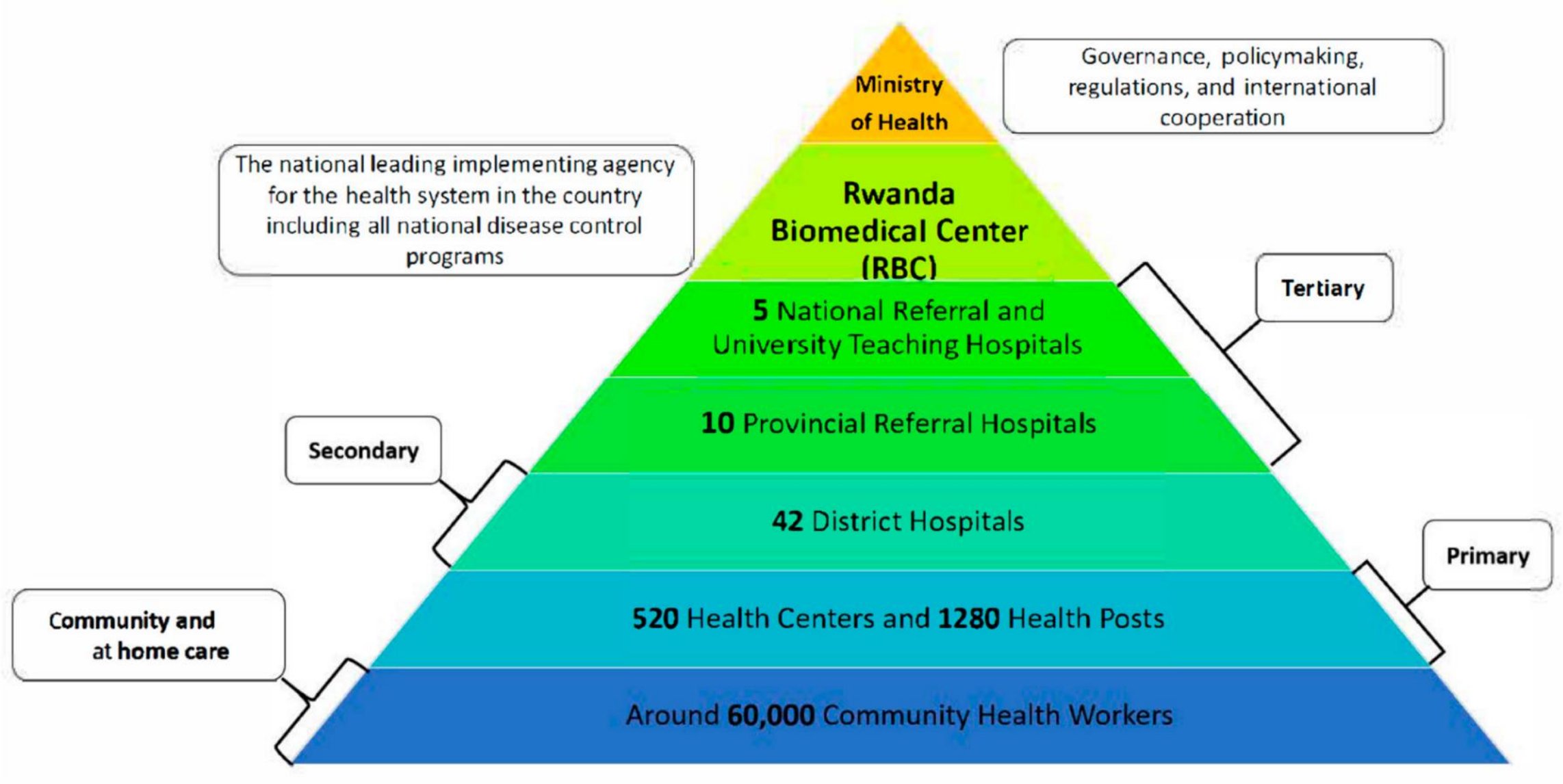
Marburg virus reservoir. Egyptian fruit bats (*Rousettus aegyptiacus*), the putative reservoir of MARV, roosting in the Python Cave in Maramagambo Forest, Uganda.



Year(s)	City	Country	Origin (apparent or suspected)/ mode of infection	Fatalities/ number of cases (case fatality rate)
2004–2005	Uíge	Angola	Uíge Province, Angola/ unknown	227/252 (90%)
1998-2000	Durba, Watsa (multiple	Democratic Republic of the Congo	Durba, Democratic Republic of the Congo/ Gold mining in Goroumbwa cave	128/154 (83%)

Viruses 2012, 4, 1878-1927; doi:10.3390/v4101878

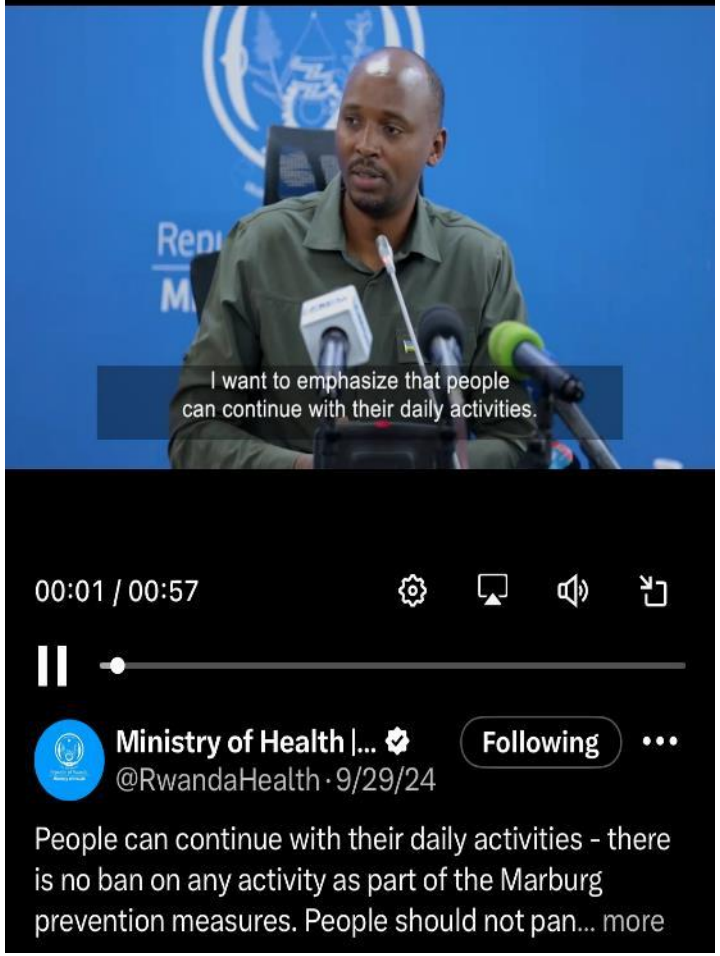
Structure of Rwanda's Health Care System



National Command Post:

The comprehensive, all-of-government outbreak response

- Leadership and Coordination
- Surveillance
- Risk Communication and Community Engagement (RCCE)
- Laboratory
- Clinical Case Management
- Vaccination
- Infection Prevention and Control (IPC)/Safe and Dignified Burial (SDB)
- Operations
- Strategic Information



Multi-Layered Surveillance Strategy for Marburg Virus Detection

- Case investigations and contact tracing
- Universal symptom screening in clinical settings
- Door-to-Door symptom screening and education by CHW
- Mortality Surveillance (MVD testing for all decedents)

- Chart review “deep dive” to find the index case
- Ecological assessment

National MVD surveillance system components

Case-investigations & contact tracing

- **1,497 contacts** identified through contact tracing
- Evaluated in person, daily active symptom monitoring using a mobile phone app
- Outbreak linked back to a zoonotic source

Community & household-level surveillance

- Door-to-Door symptom screening and education by CHW in all 30 districts
- 1,288,205 households reached
- 4,793,212 persons screened for MVD symptoms (37% of the population)
- 24 suspect cases identified
- **No positive RT-PCR tests**

Centralized Data System (RBC)

National MVD screening & triage

- Universal symptom screening in clinical settings from Sept 23 – Nov 22:
  - 6,340 suspect cases tested
  - **66 positive tests**
  - **77% were healthcare workers**

National mortality surveillance system

- Mandated RT-PCR testing for all deaths in the community from Sept 25 – Nov 8
- 240 decedents tested
- **No positive RT-PCR tests**

Finding the index case

Reconstructing the First Chain of Transmission

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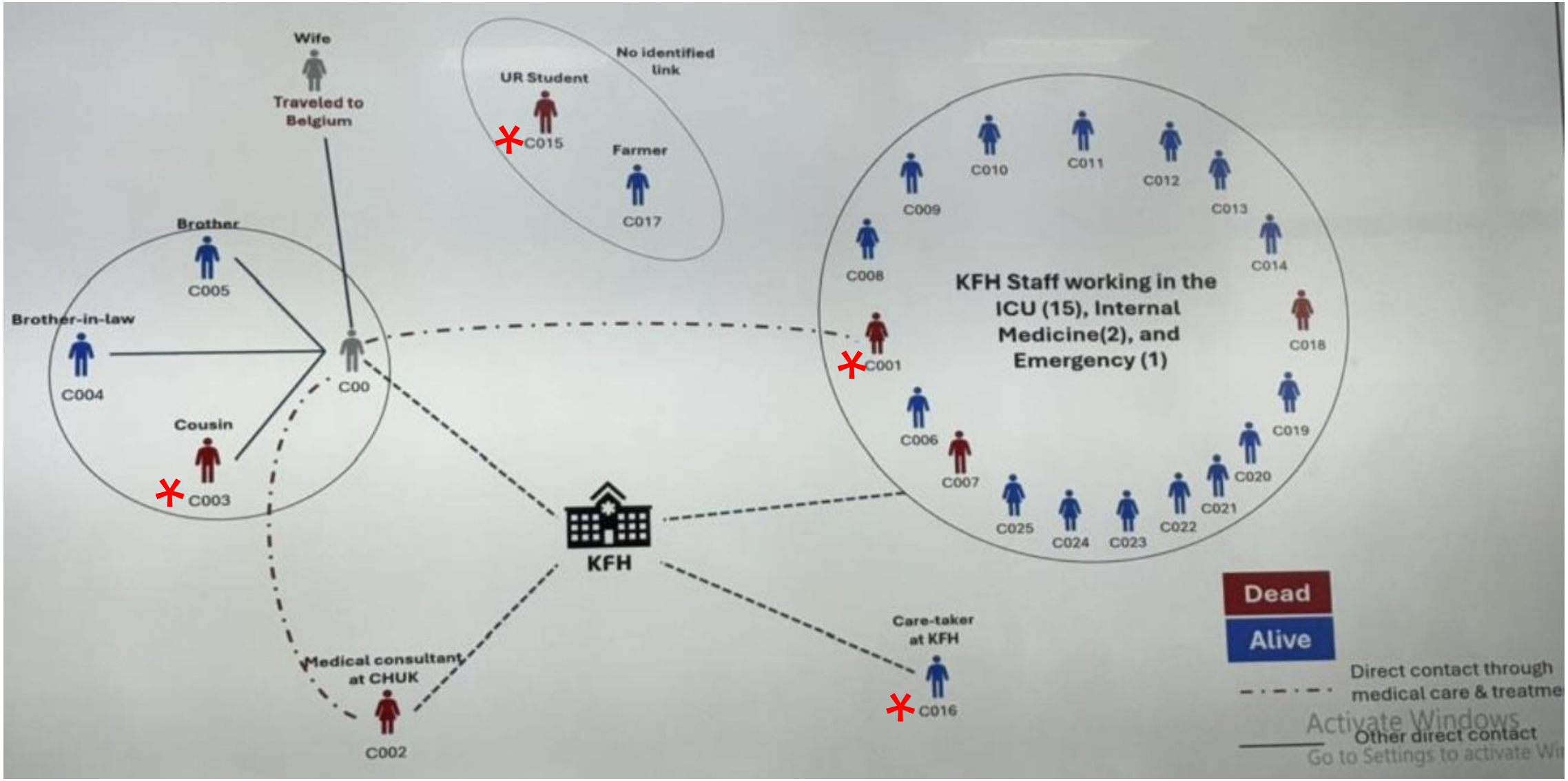
Early sketch of MVD transmission – Week 1



Overlooked MVD Cases?

- In-depth, retrospective review of hospital records at KFH
- Used standardized case definition to identify suspect cases
- Team of 3 physicians + 1 epidemiologist x 18h

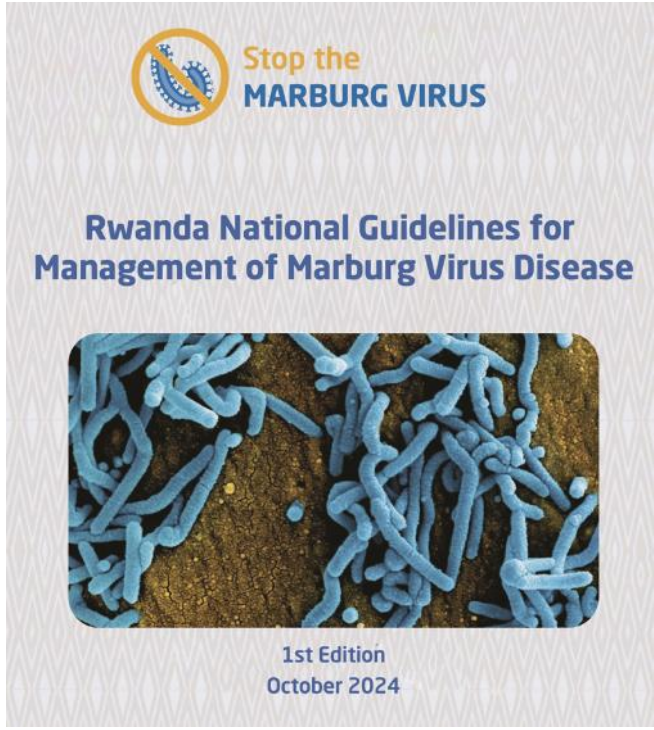
3.1.1. Standard case definitions used in a MVD outbreak

i) Suspect case

- Any person who has an unexplained sudden onset of acute fever of ≥38ºC and with one or more of the following symptoms: fatigue, acute flu-like illness, sore throat, headache, nausea, loss of appetite, hiccups, stomach/abdominal pain, vomiting, diarrhea, muscle pain, joint pain, difficulty swallowing or difficult breathing, unexplained bleeding not related to injury, skin rash, conjunctivitis, unexplained visual loss

OR

- Any person, alive or dead, suffering or having suffered from a sudden onset of fever (≥38°C) **AND/OR** having had contact with one or more of the following within 3 weeks before onset of symptoms:
  - A suspected, probable, or confirmed MVD case (alive or dead)
  - An endemic area or area with active transmission of MVD
  - A mine



“Marburg Masquerades as Malaria”

Comment

When Malaria Masks Marburg: Lessons from the Early Recognition of Rwanda’s First Marburg Virus Outbreak

Zainab Ingabire[a,b], Gloria Shumbusho[a,b], Ahmed Aboubasha[a], Jean Pierre Sibomana[a,c], Ahmed Moharam[a], Janvier Murayire[a,b], Mariska Jacoba Kreuger[a,b], Tsion Firew[a,b,d,,e], Lambert Ingabire[a], Menelas Nkeshimana[e], Kara L. Neil[a,b], Alexis Manishimwe[f], Jean Luc Benimana[f,e], Frederick Ntabana[f], Edson Rwagasore[e], John Baptist Nkuranga[a,b], Augustin Sendegeya[a,b], Zerihun Abebe[a,b], Ryan P. Westergaard[a,c,g]

Table 1. Clinical features of patients admitted to ICU with febrile illness

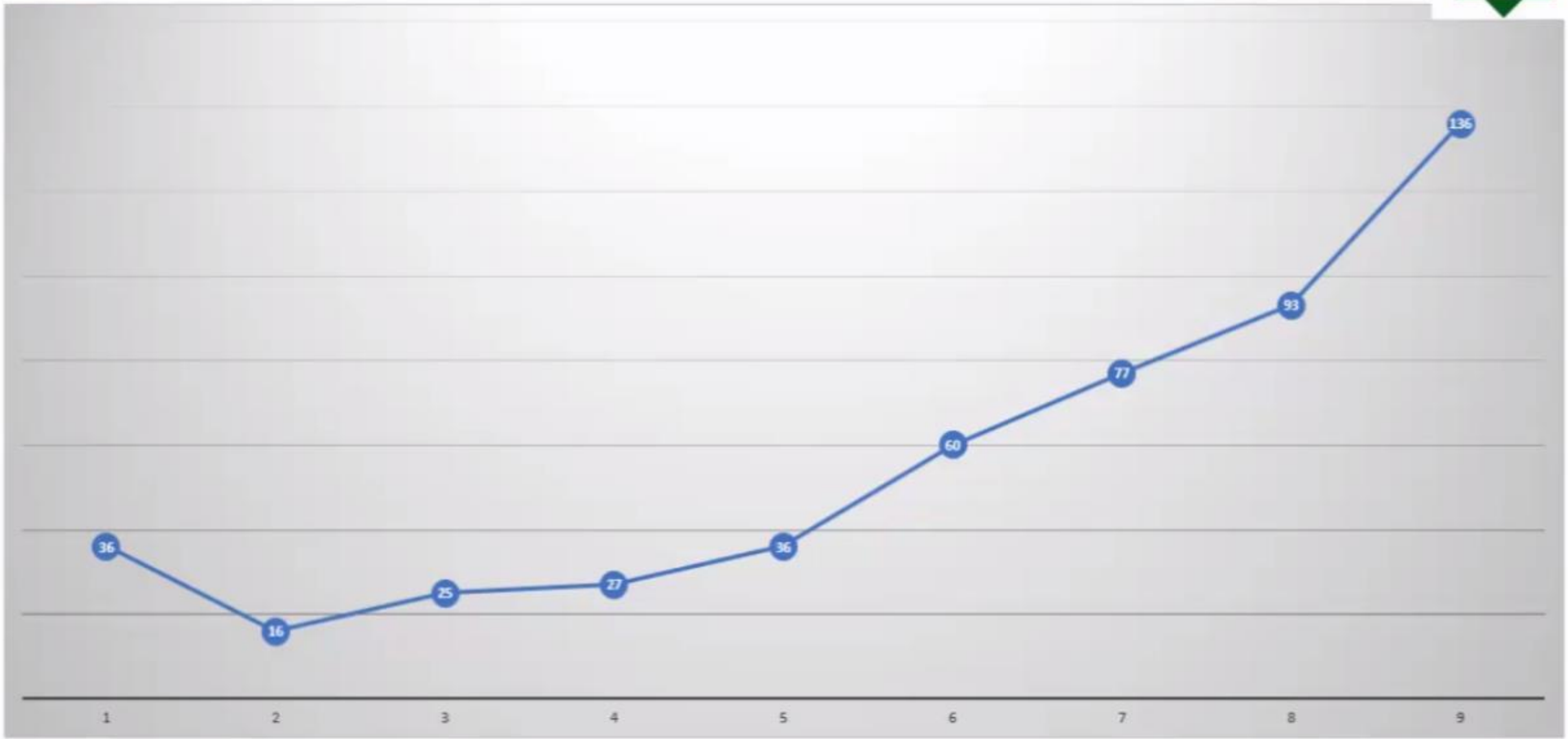
ID	Age/Sex	Admit Date	Discharge Date	Clinical Features	Diagnosis	Outcome
1	14M	19 Jul	23 Jul	Fever, headache, vomiting	Malaria	Recovered
2	38M	21 Jul	23 Jul	Fever, respiratory failure	Malaria, ARDS	Recovered
3	26M	27 Jul	31 Jul	Fever, headache, vomiting	Malaria	Died
4	38M	27 Jul	28 Jul	Fever, multi-organ system failure	Malaria	Died
5	46M	28 Jul	30 Jul	Fever, seizure, thrombocytopenia	Malaria	Recovered
6	30M	30 Jul	31 Jul	Fever, headache, kidney failure	Malaria	Recovered
7	1F	5 Aug	8 Aug	Fever, diarrhea, coagulopathy	Septic shock	Died
8	71F	5 Aug	6 Aug	Fever, confusion, low platelets	Cerebral malaria	Died
9	25F	27 Aug	27 Aug	Fever, pregnancy, liver failure, low platelets	Malaria, Probable MVD*	Died
10	35M	29 Aug	9 Sep	Fever, DKA, elevated liver tests	Probable MVD	Died
11	33F	11 Sep	16 Sep	Fever, liver/kidney injury	Malaria, Confirmed MVD	Died
12	24 M	24 Sep	25 Sep	Fever, liver/kidney injury	Confirmed MVD**	Died
13	24 M	25 Sep	26 Sep	Fever, liver/kidney injury	Confirmed MVD**	Died

“Patient Zero”

Known laboratory-confirmed MVD cases

Unpublished data

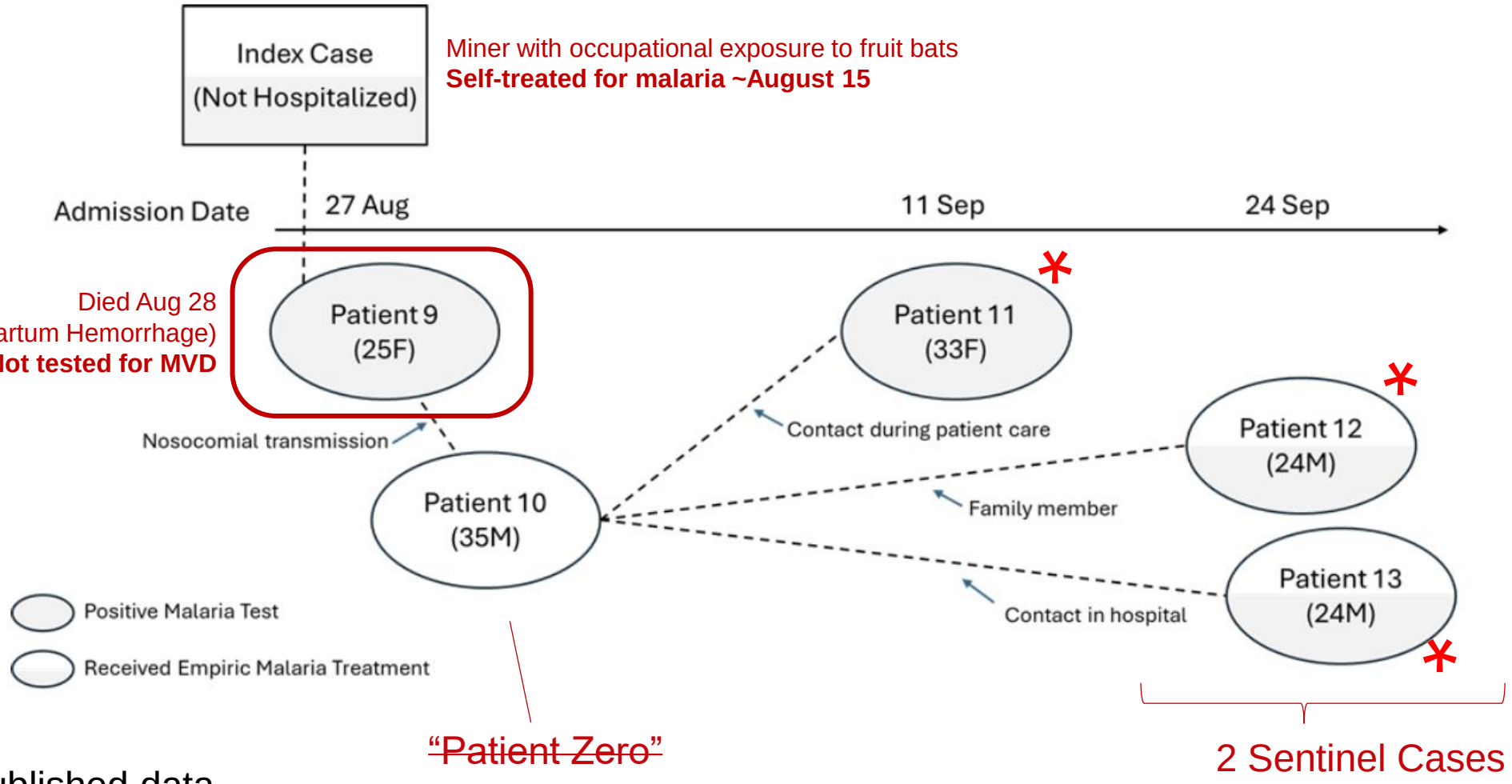
Malaria cases at KFH Jan-Sept 2024



Slide courtesy of Dr. Edgar Kalimba

“Marburg Masquerades as Malaria”

Figure 1: Suspected transmission linkage among first 5 confirmed cases in Rwandan MVD outbreak



Unpublished data

Ecological Assessment Plan

Risk-based geographic mapping

Understanding bat ecology and their movement patterns

VHF surveillance in bats and other intermediate hosts

Community-based surveillance networks and awareness campaigns

Gamico Mining Site

1931

The Belgian mining company began exploiting tin in Rwanda

April 2021

Gamico Mining Company began mining activities in different sites including Nyarugenge site

December 2021

Closing of all Exit and use Fire and Chemicals to chase bats

2021-2025

Increase in the number of bats in Tunnel 12 & Gamico sought advise to RMB on the approach to terminate bats increase

05 August 2024

Probable index case exposures - One of Gamico mining company staff working in T12

27 Sept 2024

MVD outbreak confirmed in KFH and later in CHUK staff

15 Oct - 01 Nov 2024

14 Gamico staff have been confirmed positive for IgG during Serology testing performed

MVD Treatment and Prevention

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Patients hospitalized
= 100%

Patients who received an investigational therapy **= 79%**

Overall Case-fatality rate **= 23%**

Table 2. Characteristics of Patients with Laboratory-Confirmed MVD According to Outcome.*

Characteristic	Patients with Confirmed MVD (N = 66)	Outcome†	
		Recovered	Died
Age — no./total no. (%)			
<35 yr	40/66 (61)	31/40 (78)	9/40 (22)
≥35 yr	26/66 (39)	20/26 (77)	6/26 (23)
Sex — no./total no. (%)			
Female	21/66 (32)	15/21 (71)	6/21 (29)
Male	45/66 (68)	36/45 (80)	9/45 (20)
Median initial Ct value on RT-PCR (IQR)	25.8 (21.5–28.8)	26.5 (21.5–28.7)	19.4 (16.3–23.0)
Initial RT-PCR Ct value — no. (%)			
<25	27/66 (41)	14/27 (52)	13/27 (48)
≥25	39/66 (59)	37/39 (95)	2/39 (5)
Median time from first known contact to symptom onset (IQR) — days	10 (8–13)	10 (7–12)	9 (7–11)
Median time from symptom onset to hospital admission (IQR) — days	2 (1–3)	1 (1–3)	3 (3–5)

N Engl J Med 2025;393:983-93.

First MVD Isolation Unit, Nyamata

First MVD Isolation Unit, Nyamata

“The best treatment center I have ever seen”

- Dr. Tedros Ghebreyesus,
- W.H.O. Director General

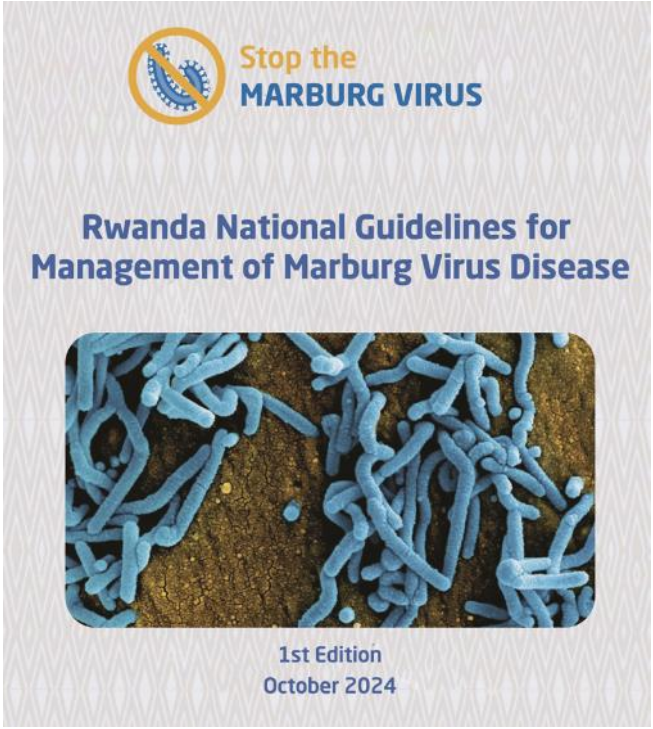
MVD Case Management Pillar – Key Activities

- Completion & dissemination of national MVD guideline
- Daily huddle to discuss management of specific cases
- Liaison with W.H.O. Clinical Team
- Treatment & Clinical Research Protocols

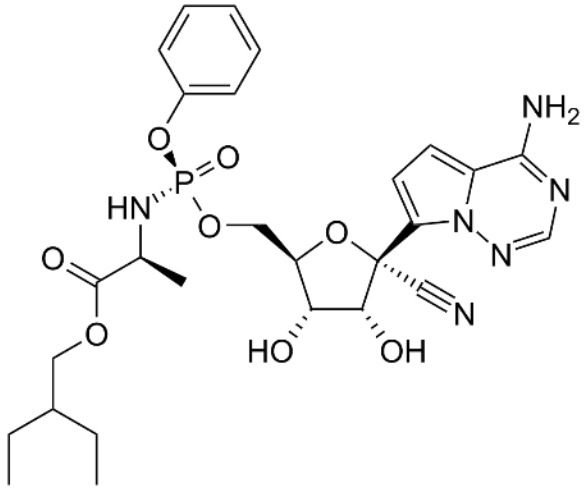
Remdesivir

ChAd3-MARV Vaccine

MBP-091



Remdesivir



- Broad spectrum antiviral drug – Gilead Sciences
- Prodrug of GS-41524, an ATP-analog that interferes with RNA-dependent RNA polymerase
- Developed for hepatitis C virus in 2014 → poor activity
- Repurposed for emerging RNA viruses
  - Ebola
  - Middle East Respratory Syndrome (MERS)
  - SARS-CoV-2
  - Antiviral activity in vitro and animal models against Marburg virus

- PALM Study – RCT of 4 investigational therapeutics for EVD
- 1:1:1:1 randomization, no placebo
- Remdesivir significantly inferior than 2 monoclonal antibody products

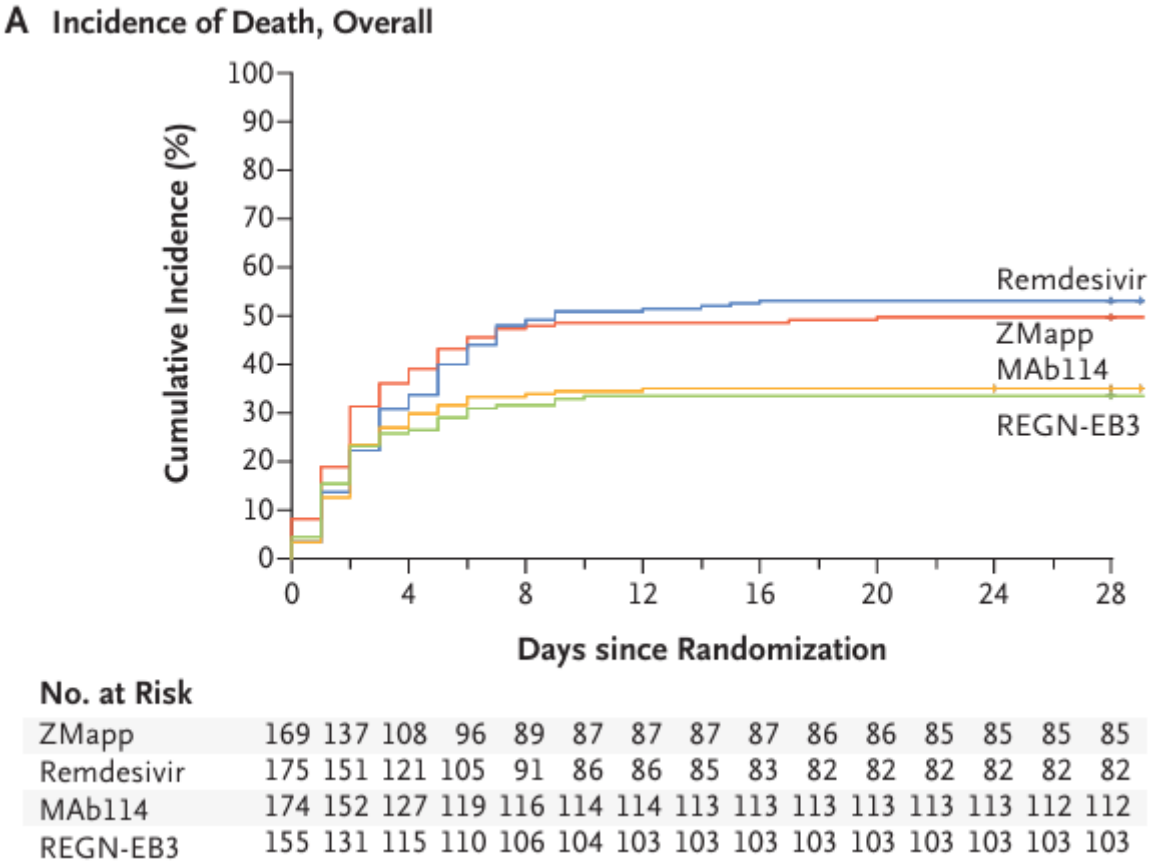
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 12, 2019 VOL. 381 NO. 24

A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics

Sabue Mulangu, M.D., Lori E. Dodd, Ph.D., Richard T. Davey, Jr., M.D., Olivier Tshiani Mbaya, M.D., Michael Proschan, Ph.D., Daniel Mukadi, M.D., Mariano Lusakibanza Manzo, Ph.D., Didier Nzolo, M.D., Antoine Tshomba Oloma, M.D., Augustin Ibanda, B.S., Rosine Ali, M.S., Sinaré Coulibaly, M.D., Adam C. Levine, M.D., Rebecca Grais, Ph.D., Janet Diaz, M.D., H. Clifford Lane, M.D., Jean-Jacques Muyembe-Tamfum, M.D., and the PALM Writing Group, for the PALM Consortium Study Team*

ABSTRACT

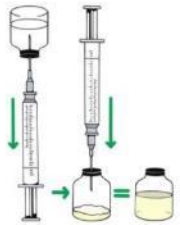


Remdesivir – Use in Rwanda MVD Outbreak

Remdesivir Preparation and Administration

1- Remdesivir comes in a 100mg vial that requires reconstitution prior to use. Each dose will use the entire vial.

2- Using 19mL of sterile water, reconstitute the Remdesivir. Swirl until all of the powder has dissolved. This can take a minute or two.



3- The Remdesivir solution from the vial will be further diluted into a 100mL, or 250mL bag of normal saline. The concentration will depend on the patient, and may account for kidney function or other factors. Both concentrations are acceptable.

4- Educate the patient on potential side effects and reasons to notify medical providers. These will include shortness of breath, rash, palpitations, lip or tongue swelling, lower back pain or fever.

5- Initiate the infusion. The dose can run between 30-120 minutes as ordered by the provider.

- Loading Dose: 200 mg IV x 1, administered as early after diagnosis as possible
- Maintenance Dose: 100 mg IV every 24 hours
- Duration of therapy: 10 days (minimum); Extend to 14 days if the patient has not had a negative RT-PCR test by day 10

Remdesivir – Use in Rwanda MVD Outbreak

I. Therapeutic Use

- Administered to 52 patients (First on Sept 29, then routine)
- 3 of 52 patients who received remdesivir died (6%)
- 12 of 14 patients who received no remdesivir died (86%)

II. Prophylactic Use

- Offered to exposed HCWs under a research protocol
- Experience Presented at ID Week - October 2025

Remdesivir for Post-Exposure Prophylaxis of Marburg Virus Disease: A Retrospective Cohort Study Assessing Safety, Clinical, and Immunologic Outcomes.

Presenter: Dr Tsion Firew, MD,MPH,FACEP
Chair, Department of Emergency Medicine, Africa Health Sciences University and King Faisal Hospital Rwanda, Kigali, Rwanda

Methods

Study Design

- A retrospective analysis of HCWs
- PEP Recipients between (October 2nd –30 Oct 2024)
- 380 exposed HCWs were offered post-exposure prophylaxis (PEP) with intravenous Remdesivir
- Intervention: IV Remdesivir (200 mg Day 1; 100 mg Days 2–3)

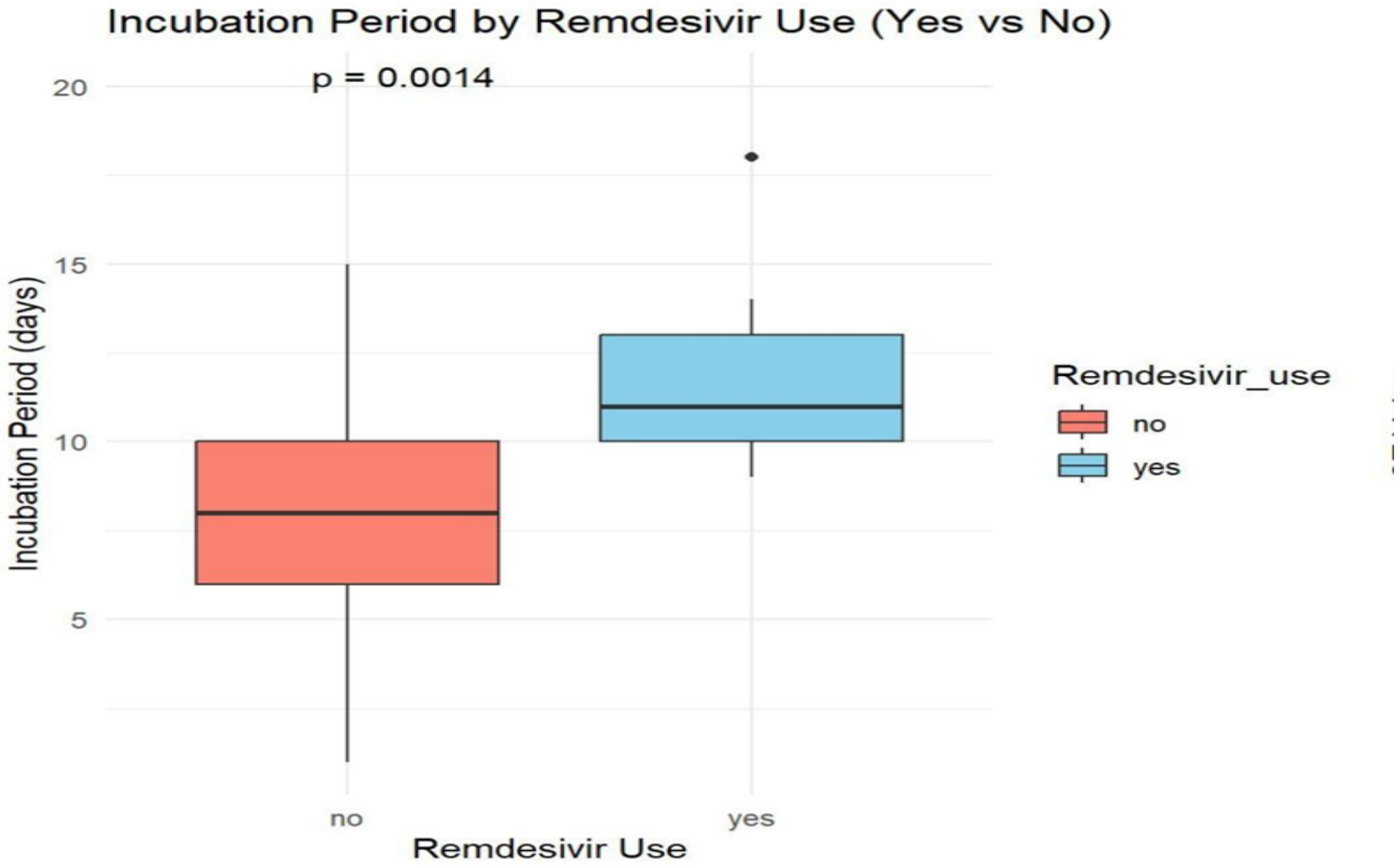
Remdesivir PEP for HCWs - Results

Demographics:	• 380 HCWs were enrolled
	  • 194 (51%) opted for PEP
	  • 186 (49%) opted out PEP
	• Most HCWs were under 40 years (65%) and male (51%)

Testing & Disease Course:	• 261 (68.7%) reported MVD testing
	  • 11 (3.2%) tested positive
	  • 20 (5.3%) were hospitalized with MVD-like symptoms (some tested positive for malaria and negative for MVD)

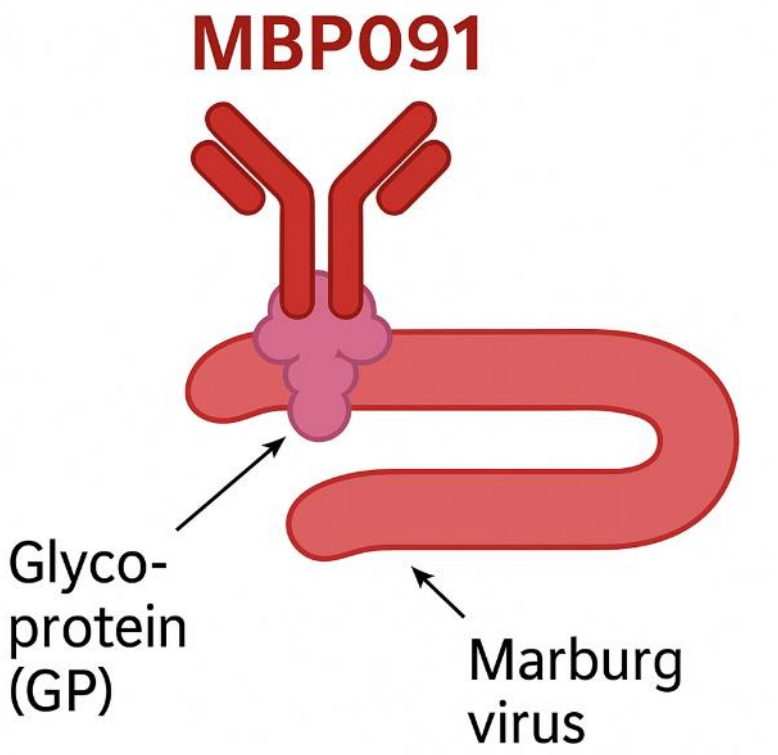
Abstract #176, IDWeek 2025

Remdesivir PEP for HCWs - Results



Abstract #176, IDWeek 2025

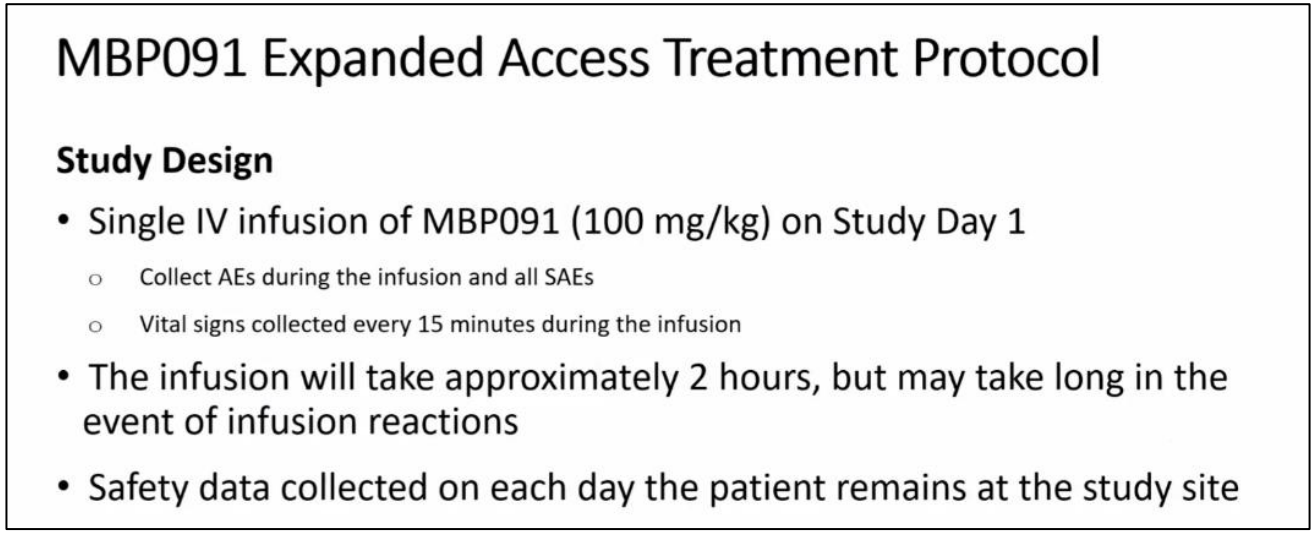
MBP091 Monoclonal Antibody



- Human monoclonal antibody (IgG1 λ) derived from a Marburg survivor
- Targets the viral glycoprotein (GP) → blocks host-cell attachment and fusion
- Developed by Mapp Biopharmaceutical with support from U.S. Biomedical Advanced Research and Development Authority (BARDA)
- Demonstrated clinical activity against MVD in macaque models

MBP091 – Use in Rwanda MVD Outbreak

- Not FDA approved for any indication; a single phase 1 study in healthy volunteers showed no SAEs
- Mapp Biopharmaceuticals submitted protocol for use under expanded access program to U.S. DHHSA, Rwanda FDA and Rwanda National Ethics Committee
- Shipped 5 doses from Washington DC to Kigali on Oct 4



Accessing Investigational Therapies – MBP091

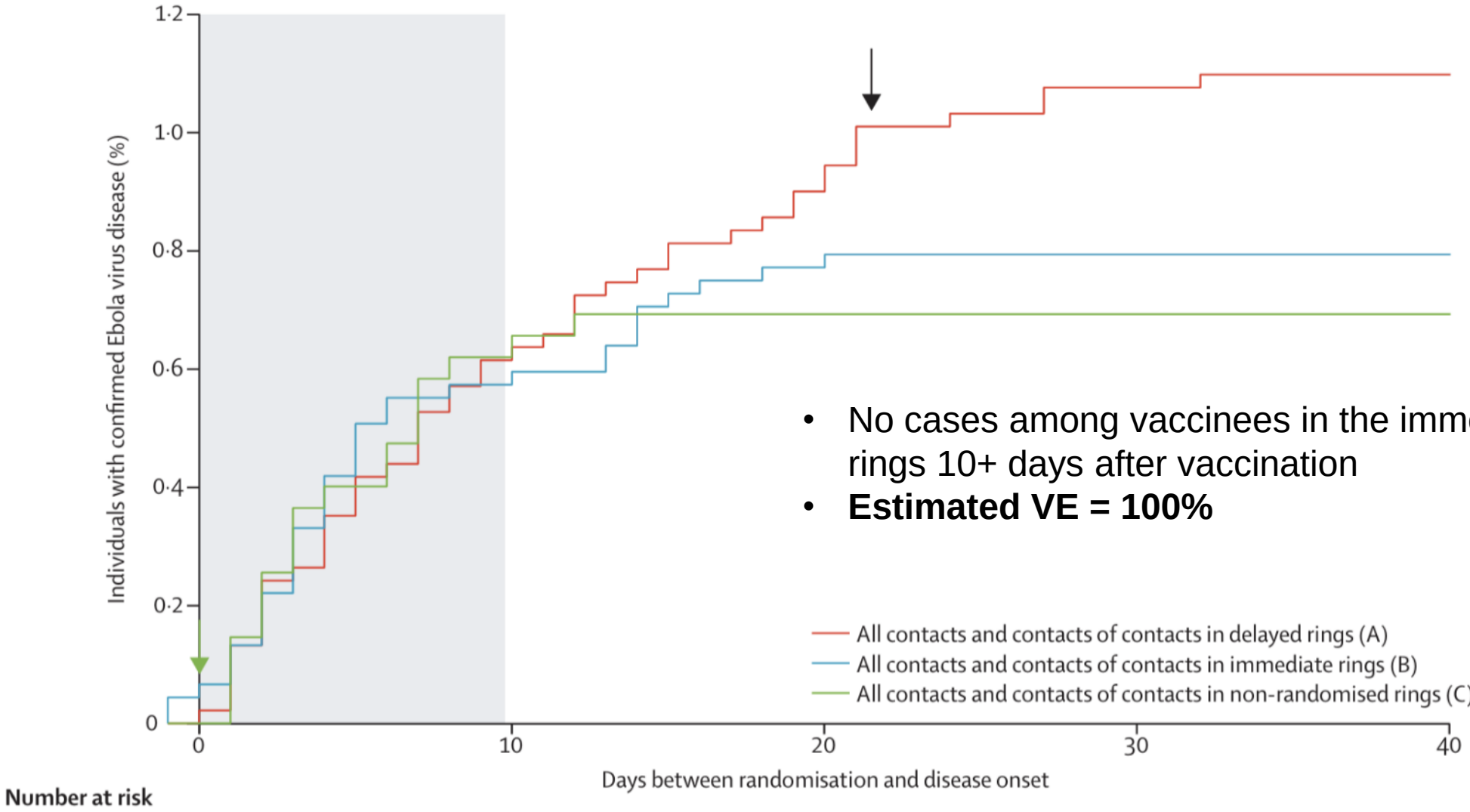
MBP091 – Use in Rwanda MVD Outbreak

- Administered to 10 patients:
  - 5 under expanded access protocol (prioritized the patients with most severe illness)
  - 5 enrolled in RCT after approval of WHO-led trial on October 15
- 2 patients who received MBP091 died (20%), and 8 recovered

ChAd3-MARV: Filovirus Vaccine Candidate

- Developed by Sabin Institute, Washington D.C.
- Replication-defective chimpanzee adenovirus type 3 vector expressing MARV glycoprotein (GP)
- Single-dose immunization conferred 100% protection against lethal MARV challenge in macaques
- Never used in humans in an outbreak setting

Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!)



- No cases among vaccinees in the immediate rings 10+ days after vaccination
- **Estimated VE = 100%**

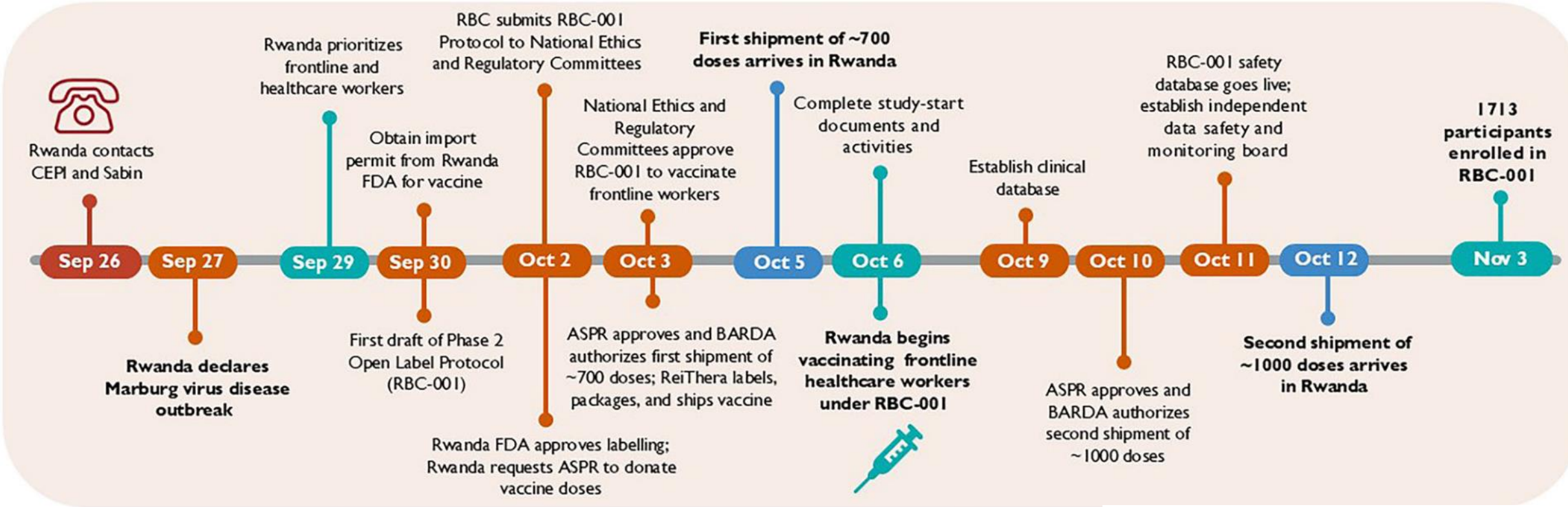
Lancet 2017; 389: 505–18

CEPI & The 100 Day Mission

- Coalition for Epidemic Preparedness Innovations (CEPI)
- Created in the aftermath of the 2014–2016 Ebola epidemic in West Africa
- Goal:

“To have vaccines ready for use with initial emergency authorization within 100 days from the identification of a novel pathogen with pandemic potential”

From Outbreak Declaration to Trial in 13 days

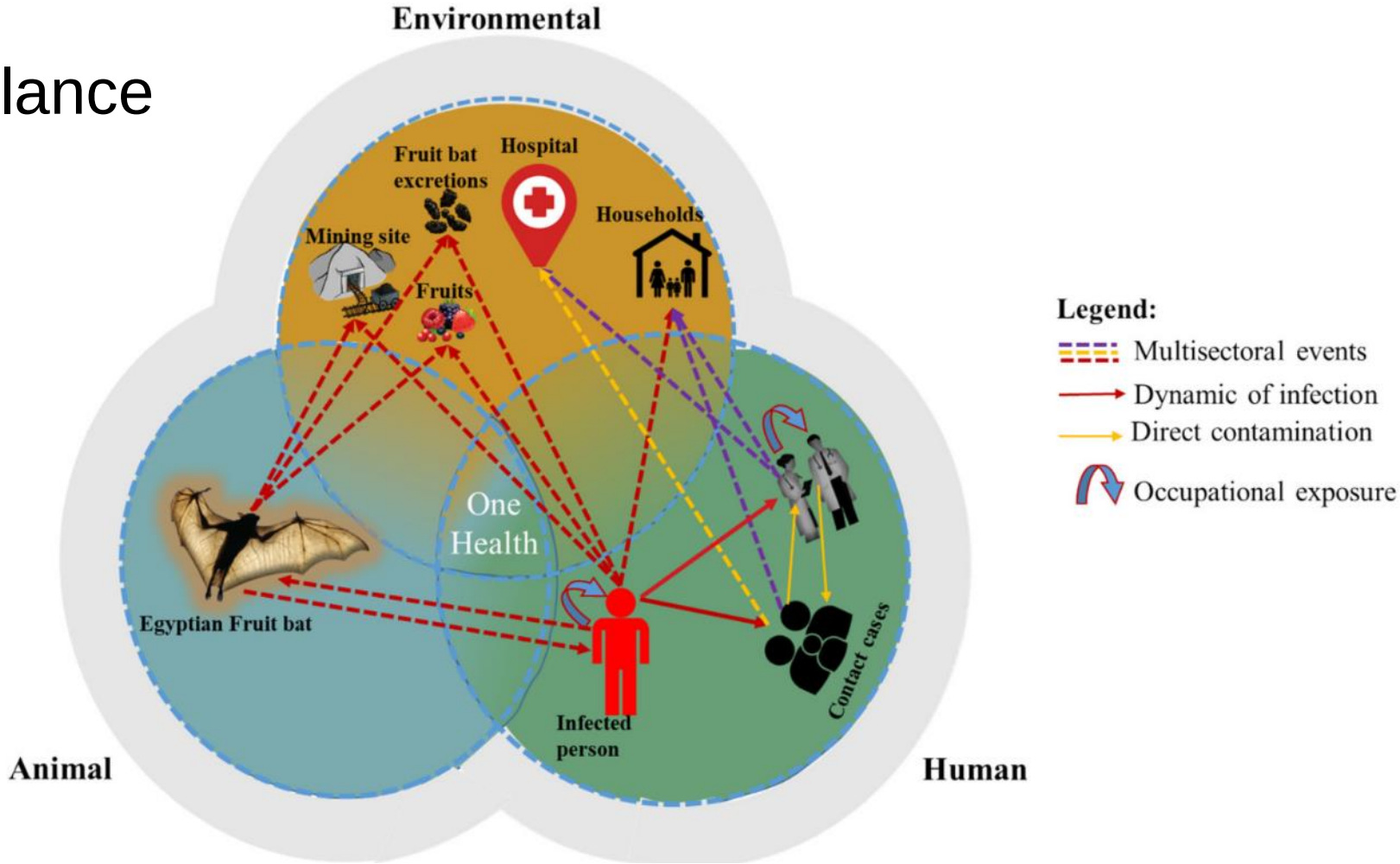


Nsanzimana et al, *NPJ Vaccines* (2025) 10:178

The “One Health” Paradigm

Outbreak preparedness requires a holistic view of public health

- Multi-Method Surveillance
- Laboratory Capacity
- Clinical Acumen
- Rapid Response Protocols
- Clinical Research Infrastructure



Summary – Lessons Learned

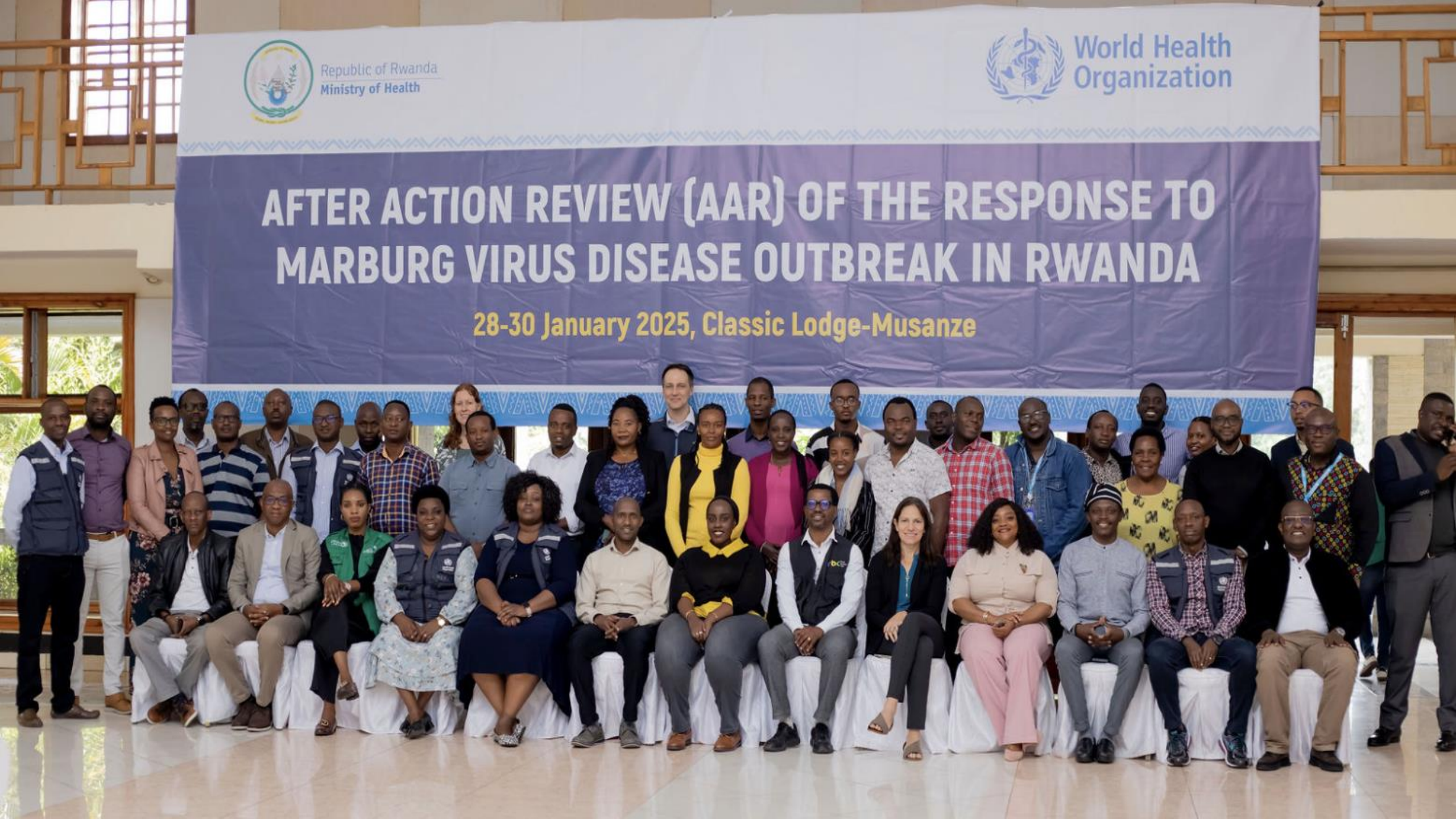
#1. MVD has a wider spectrum of clinical severity than previously recognized, including asymptomatic and mild, self-limited infection

#2. Early receipt of supportive care as soon as possible after symptom onset is likely key to improved survival

#3. Antivirals and monoclonal antibodies must be studied rigorously to understand their impact on VHF disease outcomes.

#4. Infection control strategies to minimize risk to HCWs before recognition of a VHF outbreak is an unresolved challenge

#5. Capacity building for VHF outbreak preparedness requires clinical excellence, laboratory excellence, and strong public health partnerships


Republic of Rwanda
Ministry of Health
World Health Organization
AFTER ACTION REVIEW (AAR) OF THE RESPONSE TO MARBURG VIRUS DISEASE OUTBREAK IN RWANDA
28-30 January 2025, Classic Lodge-Musanze

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