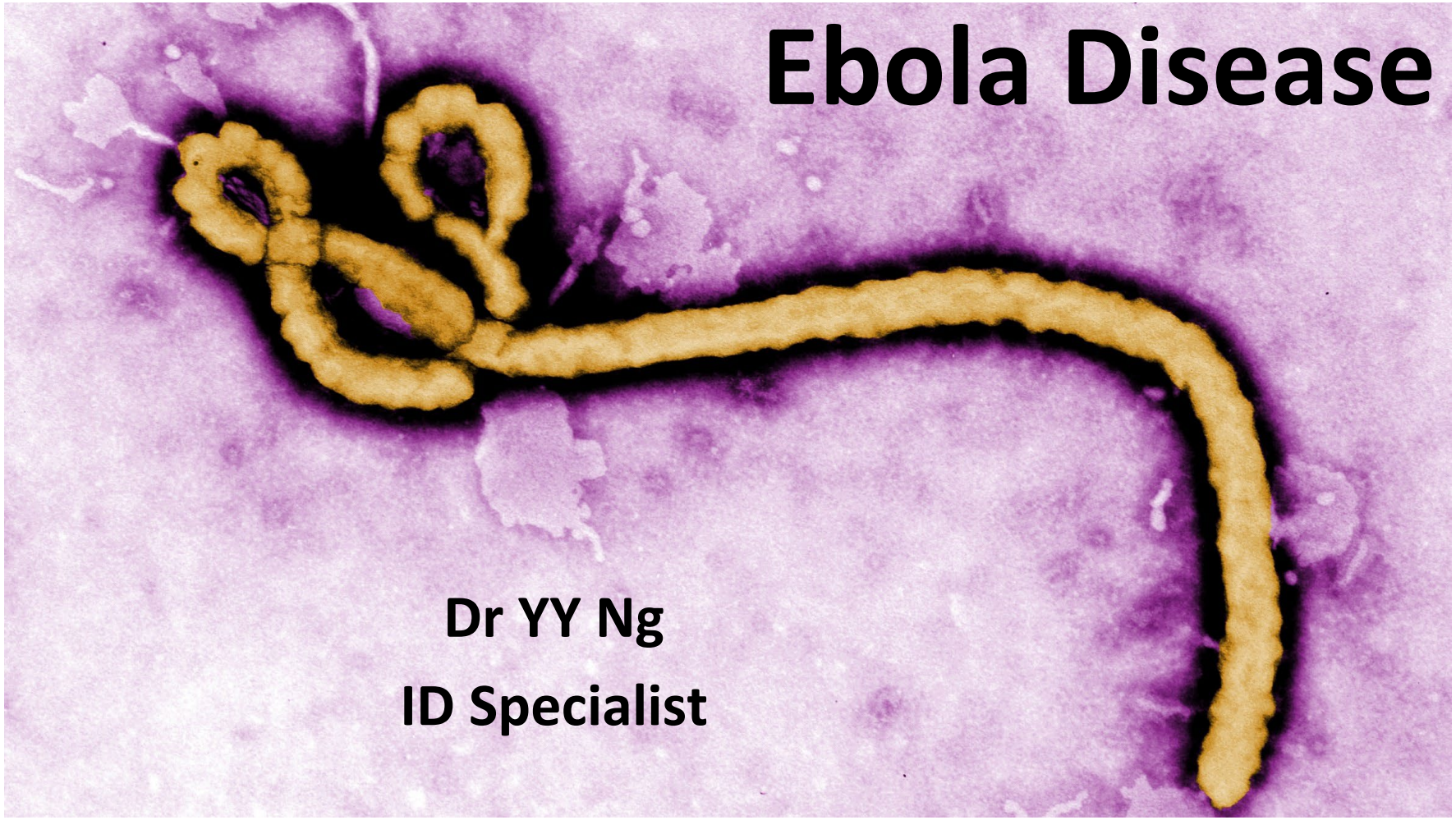
Clinical Management on Ebola Disease



Dr YY Ng

ID Specialist

TO DO LIST:

- Clinical Presentation
- Diagnosis
- Management
- Vaccine

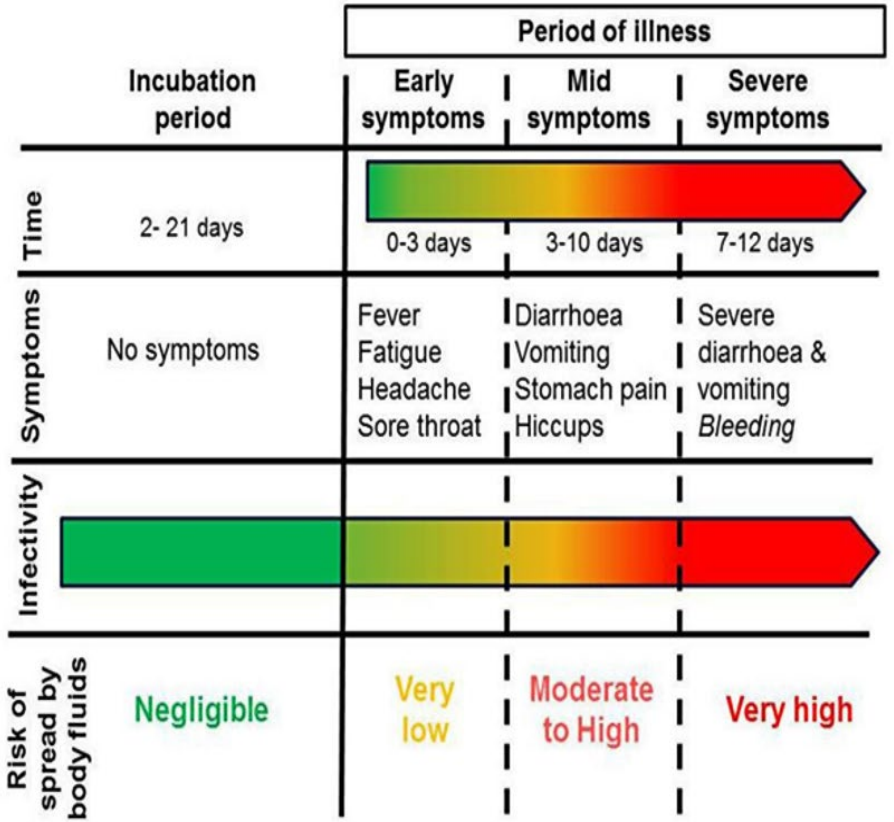
Clinical Presentation – Incubation Period 2-21 days

Early Symptoms (DRY Symptoms)

- Fever
- Aches and pains in the muscles and joints
- Severe headache
- Weakness and fatigue
- Sore throat

Late Symptoms (WET Symptoms) – after 4-5 days of illness

- Unexplained bleeding
  (both internal and external bleeding can occur e.g. petechiae, ecchymoses, oozing from venipuncture sites, mucosal bleeding or blood in stool)
- GI symptoms
  - Nausea
  - Abdominal pain
  - Diarrhea
  - Vomiting
- Loss of appetite
- Other symptoms - chest pain, shortness of breath, confusion, red eyes, skin rash, hiccups and seizures.



Clinical Presentation

Clinical Features of Ebola Virus Disease.

Phase of Illness	Time since Symptom Onset	Clinical Features
Early febrile	0–3 days	Fever, malaise, fatigue, body aches
Gastrointestinal	3–10 days	Primary: epigastric pain, nausea, vomiting, diarrhea Associated: persistent fever, asthenia, headache, conjunctival injection, chest pain, abdominal pain, arthralgias, myalgias, hiccups, delirium
Shock or recovery	7–12 days	Shock: diminished consciousness or coma, rapid thready pulse, oliguria, anuria, tachypnea Recovery: resolution of gastrointestinal symptoms, increased oral intake, increased energy
Late complications	≥10 days	Gastrointestinal hemorrhage, secondary infections, meningoencephalitis, persistent neurocognitive abnormalities*

* Secondary infections are presumptive diagnoses based on clinical features of distributive shock, oral or esophageal candidiasis, and oral ulcers; meningoencephalitis is a presumptive diagnosis based on clinical features of unconsciousness and stiff neck.

The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

Clinical Presentation of Patients with Ebola Virus Disease in Conakry, Guinea

Authors: Elhadj Ibrahima Bah, M.D., Marie-Claire Lamah, M.D., Tom Fletcher, M.R.C.P., Shevin T. Jacob, M.D., M.P.H., David M. Brett-Major, M.D., M.P.H., Amadou Alpha Sall, Ph.D., Nahoko Shindo, M.D., Ph.D., +20, and Robert A. Fowler, M.D.C.M. Author Info & Affiliations

Published January 1, 2015 | N Engl J Med 2015;372:40-47 | DOI: 10.1056/NEJMoa1411249 | VOL. 372 NO. 1

Table 1. Characteristics, Symptoms, Vital Signs, and Time Course of Clinical Progression of 37 Patients with Confirmed Ebola Virus Disease (EVD).*

Variable	Value
Median age (IQR) — yr	38 (28–46)
Male sex — no. (%)	24 (65)
Health care worker — no. (%)	
Yes	14 (38)
No	23 (62)
Known mechanism of contact — no./total no. (%)†	
Health care	12/34 (35)
Household	23/37 (62)
Funeral	6/37 (16)
Known coexisting medical condition — no. (%)	
Hypertension	2 (5)
Human immunodeficiency virus	2 (5)
Diabetes	1 (3)
Renal insufficiency	1 (3)
Tuberculosis	1 (3)
Malaria at presentation — no. (%)	4 (11)
Symptoms — no./total no. (%)	
Fever	31/37 (84)
Fatigue	24/37 (65)
Diarrhea	23/37 (62)
Headache	12/21 (57)
Vomiting	21/37 (57)
Anorexia	16/37 (43)
Vital signs at admission	
Temperature — °C	38.6±1
Heart rate — beats/min	93±14
Systolic blood pressure — mm Hg	125±25
Median interval from onset of symptoms (IQR) — days	
To hospital admission	5 (3–7)
To death	8 (7–11)

* Plus–minus values are means ±SD. IQR denotes interquartile range.
† Some patients had more than one exposure.

Laboratory Abnormalities

- Low white blood cell
- Low platelet counts
- Abnormal haematocrit (↑ or ↓)
- Elevated liver enzymes (ALT and AST)
- Elevated creatine kinase (CK), >50% rhabdomyolysis
- Coagulation abnormalities
- Renal abnormalities including proteinuria
- Electrolyte abnormalities secondary to GI symptoms

Differential Diagnoses

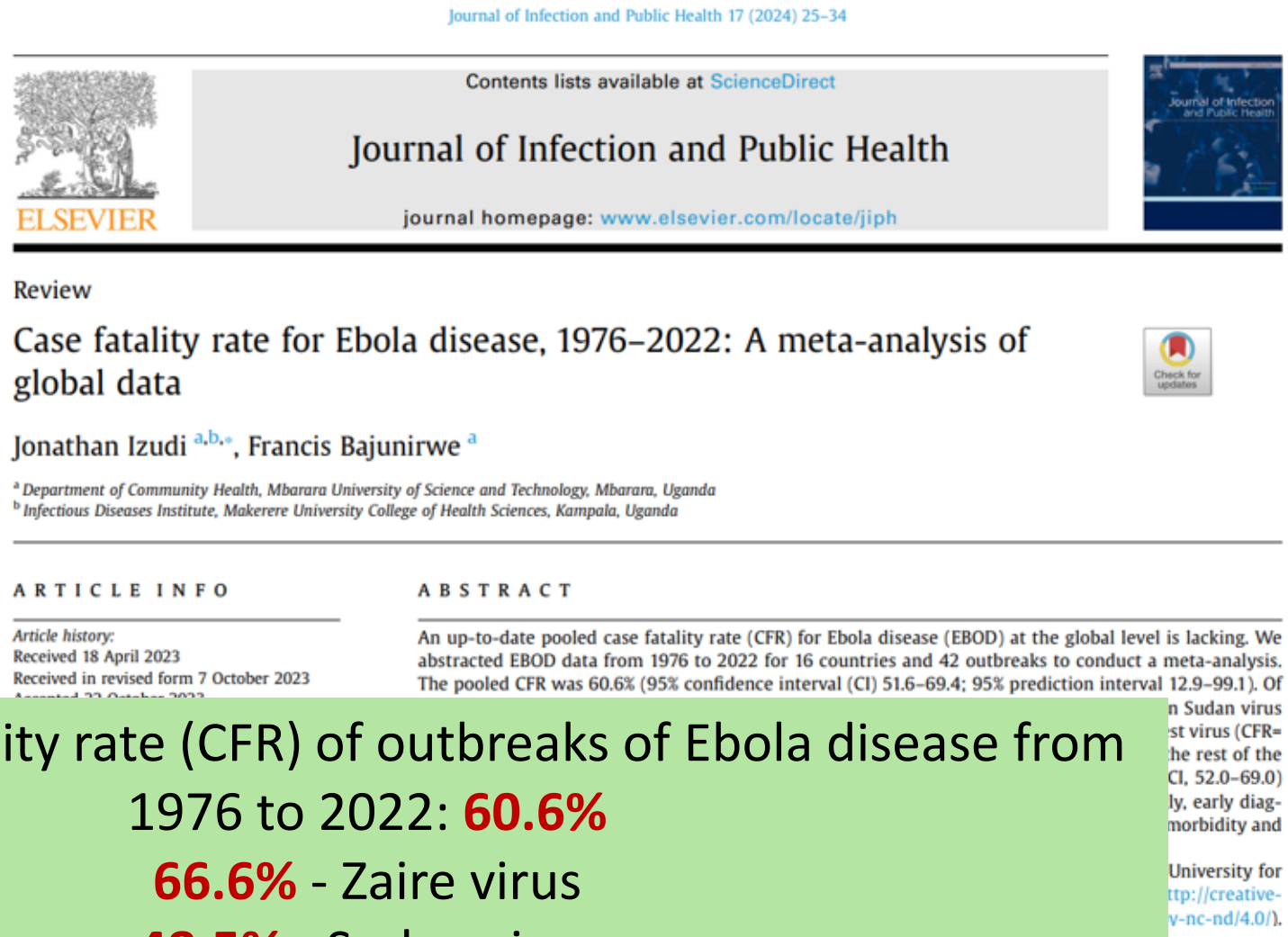
- **Exclusion of malaria is essential**

- Other differential diagnoses:
  - Other forms of viral haemorrhagic fever e.g. Marburg virus, Lassa fever, Crimean Congo haemorrhagic fever
  - Typhoid fever
  - Yellow fever
  - Dengue
  - Influenza
  - Measles
  - Traveler’s diarrhea
  - Staphylococcal or streptococcal infection +/- toxic shock syndrome
  - Gram-negative sepsis, meningococcemia
  - Leptospirosis

Disease Course

- **Fatal disease** has been characterized by more severe clinical signs and symptoms early during infection, with progression to multiorgan failure with death typically occurring in the 2nd week.

- **Survivors** typically begin to improve during the 2nd week of illness.



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Review

Case fatality rate for Ebola disease, 1976–2022: A meta-analysis of global data

Jonathan Izudi [a,b,*], Francis Bajunirwe [a]

[a] Department of Community Health, Mbarara University of Science and Technology, Mbarara, Uganda
[b] Infectious Diseases Institute, Makerere University College of Health Sciences, Kampala, Uganda

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ABSTRACT

An up-to-date pooled case fatality rate (CFR) for Ebola disease (EBOD) at the global level is lacking. We abstracted EBOD data from 1976 to 2022 for 16 countries and 42 outbreaks to conduct a meta-analysis. The pooled CFR was 60.6% (95% confidence interval (CI) 51.6–69.4; 95% prediction interval 12.9–99.1). Of

Pooled case fatality rate (CFR) of outbreaks of Ebola disease from 1976 to 2022: **60.6%**

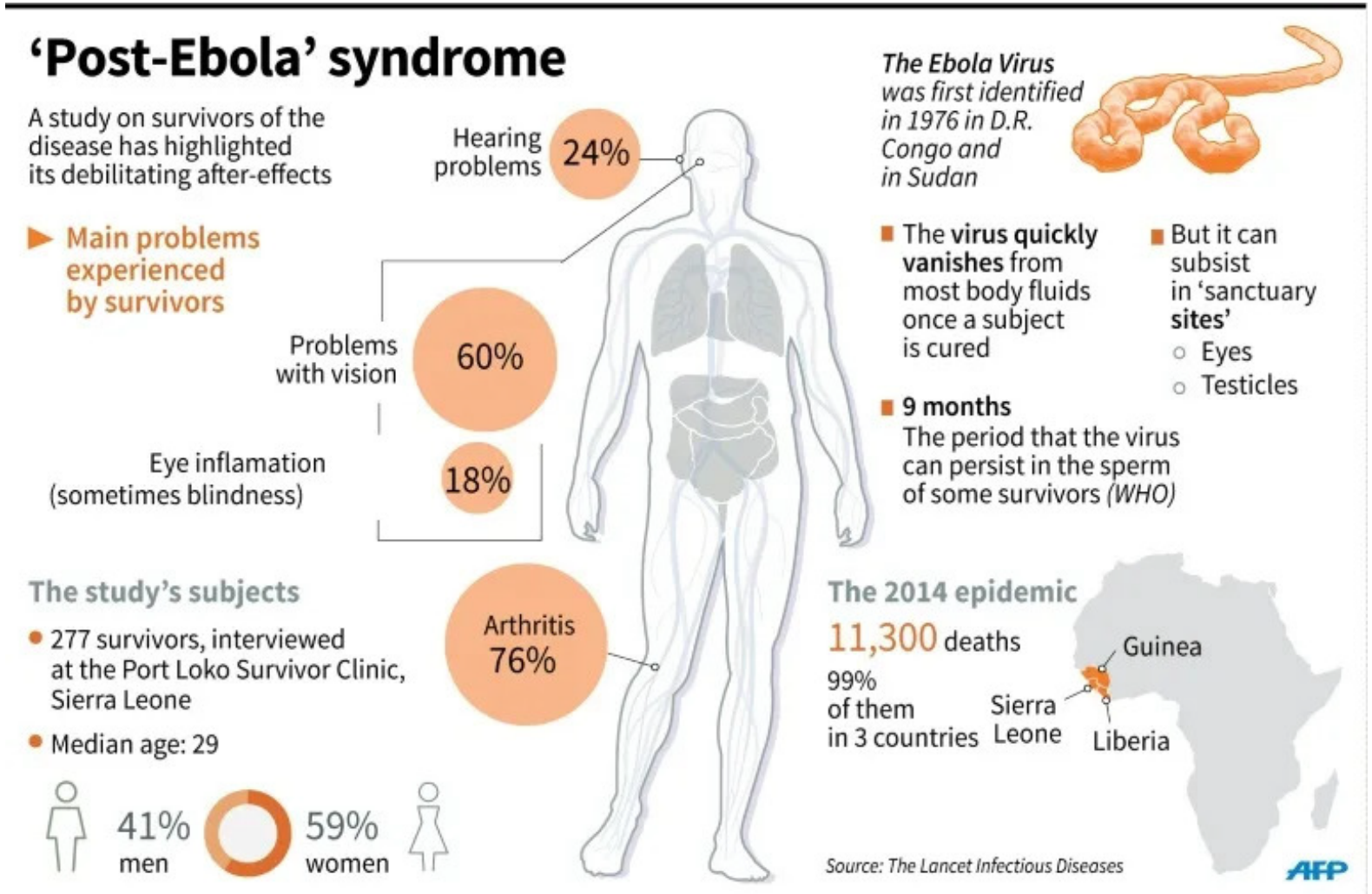
66.6% - Zaire virus

48.5% - Sudan virus

32.8% - Bundibugyo virus

The West African outbreak of Ebola in 2014

Of 277 survivors examined at a clinic in Sierra Leone, about four months after they were discharged, nearly 80% reported joint pain, 60% experienced vision problems, 18% suffered eye inflammation that could make them blind, and a quarter reported hearing difficulties.

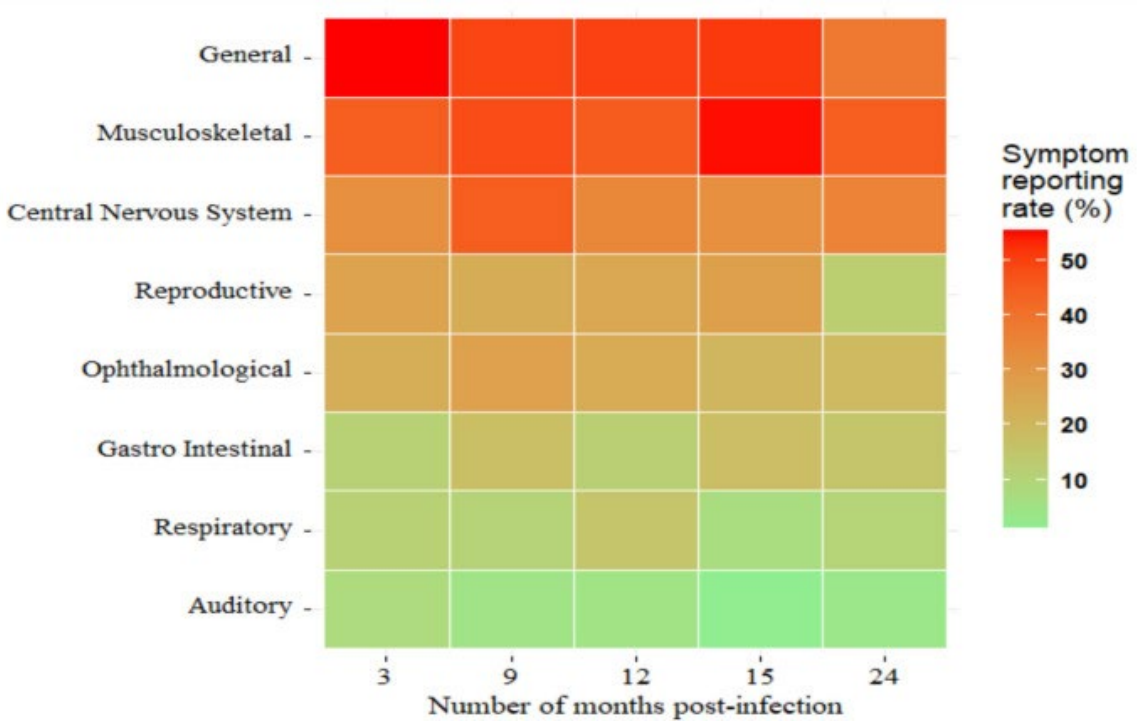


Long Term Complications

Body system	Symptoms
General	Fever, headache, fatigue, weakness, anorexia, weight loss, rash
Musculoskeletal	Joint pain, limb numbness, muscular pain, back pain, joint swelling
Gastro-intestinal	Abdominal pain, diarrhoea, vomiting, nausea, difficulty swallowing
Respiratory	Sore throat, difficulty breathing, chest pain, cough
Ophthalmological	Blurry vision, eye pain, watery eyes, vision loss, dry eyes
Reproductive	Reduced libido, testicular pain, erectile dysfunction, menstrual period change
Central nervous system (CNS)	Memory loss, depression, confusion, difficulty in sleeping
Ear, nose, throat (ENT)	Tinnitus, hearing loss

Muwonge H. et al. Long-term clinical sequelae among Sudan ebolavirus disease survivors 2 years post-infection: a matched cohort study. BMC Med 2025;23:432.

Long Term Complications



Body system	Survivors, *N* = 80 *n* (%)	Controls, *N* = 176 *n* (%)	Risk ratio	95% CI	*p*-value
Overall	46 (57.5)	57 (32.4)	1.8	1.3, 2.4	< 0.001
Musculoskeletal	36 (45.0)	25 (14.0)	3.2	2.1,4.9	< 0.001
General	31 (38.8)	34 (19.0)	2.0	1.3,3.0	0.002
CNS	29 (36.3)	12 (6.8)	5.3	2.9,9.9	< 0.001
Eye	16 (20.0)	6 (3.4)	5.9	2.4,14.4	< 0.001
Reproductive	11 (13.8)	15 (8.5)	1.6	0.8,3.4	0.026
Chest	8 (10.0)	4 (2.3)	4.4	1.4,14.2	< 0.001
GI	12 (15.0)	7 (4.0)	3.8	1.5,9.2	0.011
Auditory	3 (3.8)	1 (0.6)	6.6	0.7,62.5	0.092

Muwonge H. et al. Long-term clinical sequelae among Sudan ebolavirus disease survivors 2 years post-infection: a matched cohort study. BMC Med 2025;23:432.

Laboratory Diagnosis

1. Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR)

- **The Gold Standard:** RT-PCR is the definitive diagnostic method used globally to confirm an active infection.
- **Window of Efficacy:** It typically detects the virus within **3 days** of symptom onset, which aligns with the start of the "dry phase" (fever, headache, myalgia).
- **Clinical Protocol:** If a highly suspicious patient tests negative within the first 72 hours of symptoms, they must remain isolated and undergo a repeat RT-PCR test **48 hours later** to account for low initial viremia.
- **Strain Specificity:** Assays must utilize primers that match the specific species causing the outbreak (e.g., *Zaire*, *Sudan*, or *Bundibugyo*).

2. Antibody-capture enzyme-linked immunosorbent assay (ELISA)

3. Antigen-capture detection tests

4. Virus isolation by cell culture

⚠ Critical Sample Handling and Safety Warning

Ebola virus specimens carry an extreme risk of laboratory-acquired infection. Blood samples must only be drawn by personnel trained in full personal protective equipment (PPE) and processed in a Biosafety Level 4 (BSL-4) facility, or via strictly validated, field-deployable containment gloveboxes using automated, closed molecular platforms.

Management – Supportive

- Monitor vital signs and organ functions, and recognize complication(s) early
- Fluid and electrolyte replacement
- Respiratory support
- Blood products
- Inotropic support

- Liaise with ICU early for intensive case if anticipate clinical deterioration and need end organ support (e.g. mechanical ventilation, renal replacement therapy)

- Continue isolation and IC measures till asymptotic and two specimens, at least 48 hours apart, are tested negative by RT-PCR for Ebola virus

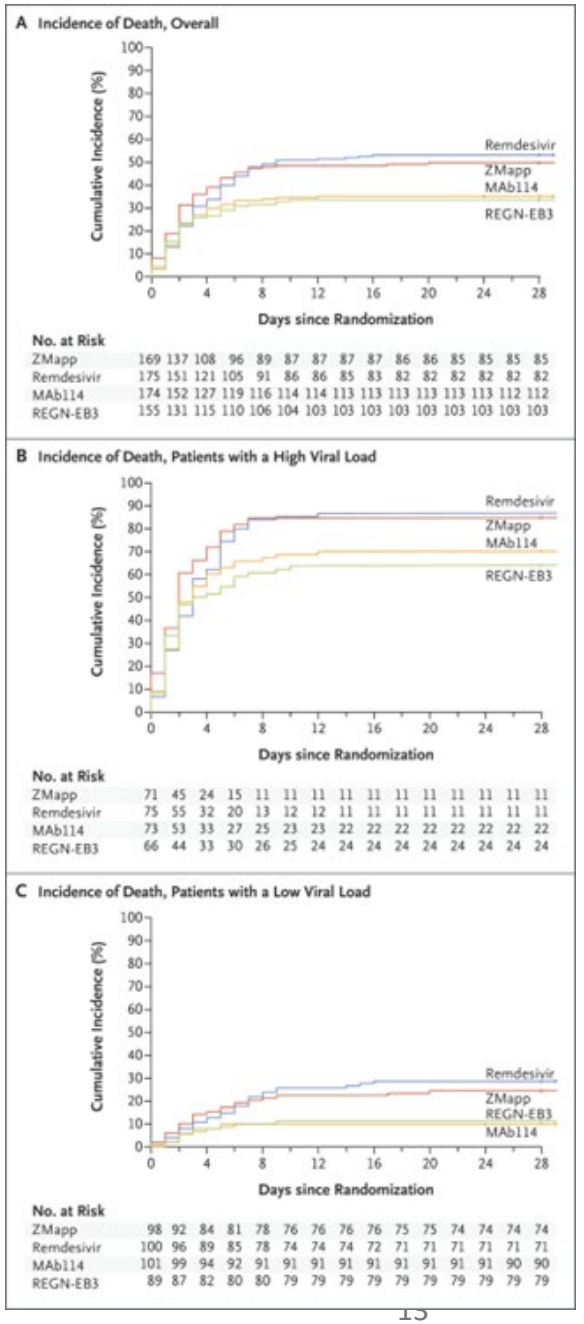
Monoclonal Antibodies – Approved by US FDA in 2020

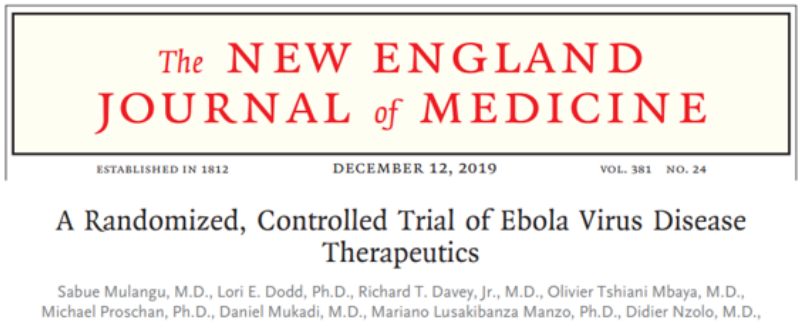
1. **Atoltivimab, maftivimab and odesivimab (Inmazeb)** is a combination of three monoclonal antibodies targeting three nonoverlapping epitopes on the Zaire ebolavirus surface glycoprotein, providing potent virus neutralization.

2. **Ansuvimab (Ebanga)** is a monoclonal antibody which is isolated from a survivor of EBOD and neutralizes the virus.

- Both monoclonal antibodies were evaluated in a randomized controlled trial during the 2018-2020 Ebola outbreak in the DRC. Overall survival is much higher for patients receiving either of the two treatments.

- Neither of the two treatments have been evaluated for efficacy against species other than **Zaire ebolavirus**, like currently circulating Bundibugyo virus. Early and aggressive supportive care is the only management option.





Vaccine – currently no registered vaccine for EBOD in HK

- The single-dose rVSV-EBOV (Ervebo) vaccine is approved for use in individuals aged 1 year and older in Europe, the United States, and several countries in Africa for protection against EBOD caused by Zaire ebolavirus.

- The two-dose Ad26.ZEBOV/MVA-BN-Filo vaccine (Zabdeno-and-Mvabea) is a two-component vaccine approved in 2020 by the European Union for use in individuals aged 1 year and older for protection against EBOD caused by Zaire ebolavirus. It requires an initial dose and a booster dose 56 days later.

- The approved Ervebo and Zabdeno-and-Mvabea vaccines are **strictly for the Zaire strain** and **provide no protection against the Bundibugyo variant.**

New Hope

Bundibugyo Ebola vaccines and treatments in development

By **Mariam E Sunny** and **Jennifer Rigby**

May 22, 2026 1:49 AM GMT+8 · Updated 9 hours ago

Red Cross workers walk in a formation as they disinfect Rwampara general hospital before handling the body of a person who died of Ebola, as aid agencies intensify efforts to contain a new Ebola outbreak involving the Bundibugyo strain, in Rwampara outside Bunia, Ituri province, Democratic Republic of Congo, May 21, 2026.... Purchase Licensing Rights **Read more**

1. A Bundibugyo-specific vaccine, rVSVΔG/BDBV-GP, which uses the same technology as Merck's approved vaccine Ervebo for the Ebola Zaire strain, has shown survival benefit in non-human primates in a 2023 proof-of-concept study.
   - A spokesperson for the University of Texas Medical Branch, whose researchers were involved in the study, said discussions are ongoing to advance the vaccine, but nothing has been finalized. The WHO has indicated a potential six-to-nine-month timeline to manufacture an rVSV Bundibugyo vaccine.

2. Another potential vaccine candidate based on ChAdOx1 technology, which was used in the Oxford/AstraZeneca COVID-19 vaccine, is being manufactured by the Serum Institute of India.
   - The company started production under its "emergency response framework", alongside partners Coalition for Epidemic Preparedness Innovations and the University of Oxford, as soon as it got word of the outbreak this month, a spokesperson said.
   - Doses could be ready within two to three months, the WHO said, though animal studies have yet to be conducted, so more testing is needed.

Take home messages

- Incubation period 2 to 21 days
- Exclude malaria for returning travelers!!
- Nonspecific symptoms and signs, as the illness progresses, vomiting and diarrhoea may develop leading to significant fluid loss
- No approved therapies exist for Bundibugyo, supportive care remains the clinical priority
- Currently no registered vaccine for EBOD in HK

Thank You