

Vaccination Strategies for Filoviruses in the Context of the Current BDBV Outbreak



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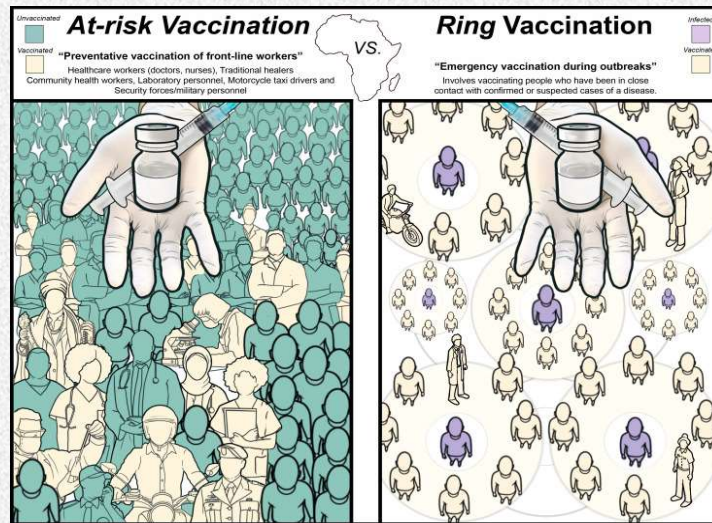
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Vaccination strategies overview

- During outbreaks vaccination has 2 main goals:
 - Interrupt transmission
 - Protect those at the highest risk of infection
 - *Reduce disease severity?*
- Broadly there are 4 strategies:
 1. Ring Vaccination
 2. At-Risk (Targeted Preventive) Vaccination
 3. Geographic or Community Vaccination
 4. Mass Vaccination
 5. Vaccination in the context of clinical trials

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At-risk vaccination vs. ring-vaccination.



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Ring Vaccination

- Most used strategy in Ebola outbreaks
- In ring vaccination vaccines are administered to contacts & contacts-of-contacts of identified disease cases (cluster), creating a protective "ring" of immunity around infected individuals
- This approach breaks transmission chains by immunizing those at highest risk of exposure, rather than vaccinating entire populations
- This strategy was instrumental in smallpox eradication (1967-1980) & has been adapted for modern vaccine efficacy trials

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Advantages and challenges

- **Advantages**

- Efficient use of limited vaccine supplies
- Rapid outbreak containment
- Targets highest transmission risk

- **Challenges**

- Requires strong contact tracing systems
- Difficult in insecure or mobile populations
- Delays reduce effectiveness



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At-Risk (Targeted Preventive) Vaccination

In this strategy high risk persons are vaccinated. The strategy reduces nosocomial transmission, maintains response teams capacity. Can be implemented in no affected areas

At risk persons include:

- Healthcare workers
- Laboratory personnel
- Burial teams
- Surveillance officers
- Communities in endemic zone

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Targeted Geographic and Expanded Ring Vaccination

- Strategy involves vaccinating entire localized communities or neighborhoods in the immediate geographic vicinity of an outbreak cluster, alongside strictly traced contacts
- it is considered in situations when ring vaccination is not possible such as in:
 - Densely populated or highly mobile communities
 - Areas of intense and endemic transmission/High-transmission zones.
 - When need of creating an **immune boarder** may be needed such in boarder communities
- May also be considered in when the aim is to reduce broader community transmission and outbreaks expansion



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Mass Vaccination

- Rarely used in outbreaks
- May be considered when the outbreak is small and localised and sporadic



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Vaccination in the context of clinical trials

- This probably the most applicable to the current outbreak because there no approved vaccines are available.
- In the context of clinical trials
- The following designs can be considered:
 - **Randomised**
 - Individually randomized controlled trial
 - Cluster randomised trials
 - Ring vaccination trial
 - Parallel cluster randomized controlled trials
 - Stepped wedge cluster randomized trial
 - Two-stage designs: individual randomization within cluster randomized trials
 - Trials with multiple vaccine candidates and a control comparator arm
 - Factorial trials
 - **Non randomized approaches**
 - Cohorts and case controls trials
 - Effectiveness trials- Test Negative designs



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Vaccine trials approaches in the context of the current BDBV outbreak

- Since there are no approved vaccines for this BDBV, the ring vaccination trial approach may be the best choice.
- Step wedge may be considered where rings in the highest risk areas are vaccinated while those in low risk are delayed to provide control, a form of targeted geographic approach
- A roll out approach could also be considered where candidate vaccines are offered to at risk contacts to the extent possible and post hoc analysis comparing those who received the vaccines to those who did not in a matched analysis



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The Ring Vaccine Trials

- Ring Vaccine trials are the best example of cluster randomized trials used in public health emergencies
- In ring vaccination vaccines are administered to contacts & contacts-of-contacts of **identified disease cases (cluster)**, creating a protective "ring" of immunity around infected individuals
- This approach breaks transmission chains by immunizing those at highest risk of exposure, rather than vaccinating entire populations
- This strategy was instrumental in smallpox eradication (1967-1980) & has been adapted for modern vaccine efficacy trials
- *By defining eligibility around a confirmed cases ring vaccine trials borrow principles from [case-ascertained study designs](#)*



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Prerequisites for success of a ring vaccination strategy

- **Fast-acting vaccines**
 - The vaccine must provide protection quickly, ideally within days of a single dose.
- **Robust surveillance**
 - Requires the ability to find & test cases rapidly to trigger the "ring" before the virus spreads further
- **Effective contact tracing**
 - Must have the logistics & community trust to identify all contacts
- **Containable pathogen**
 - Works best for diseases that spread relatively slowly through close contact (e.g., Smallpox, Ebola) rather than highly airborne or vector-borne diseases



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Advantages 2

• Operational Flexibility

- Mobile teams can follow epidemic progression—moving into new hotspots as they emerge and scaling down where incidence wanes

• Cost-Effectiveness

- Lower per-dose delivery costs through targeted administration & reduced logistics burden compared to population-wide campaigns

• Operational Flexibility

- Mobile teams can follow epidemic progression—moving into new hotspots as they emerge & scaling down where incidence wanes



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Field experiences with Ring Vaccine trials in Public Health Emergencies

- The best example of modern day ring vaccine trial is the **Ebola ça Suffit Ring Vaccination Trial** in Guinea (Henao-Restrepo et al. 2015, 2017).
- This cRCT was used to rapidly evaluate one of the most effective EVD vaccines ever

Design

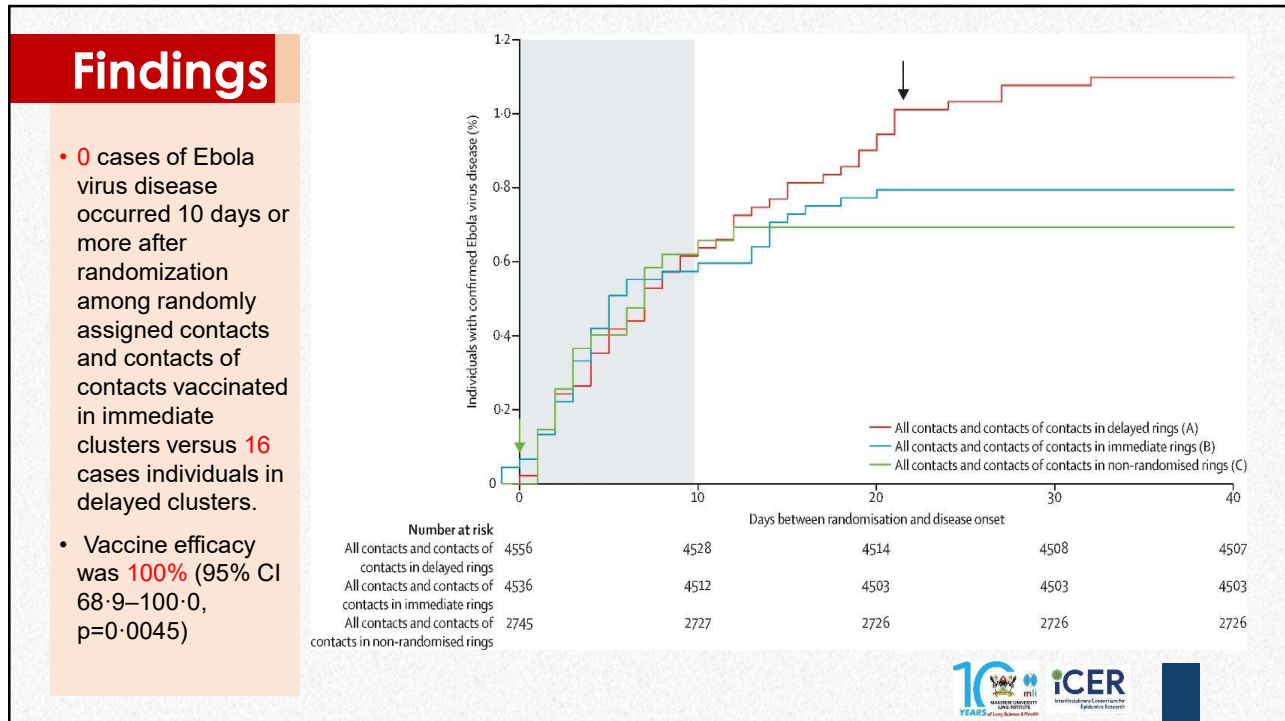
- *Open-label, cluster-randomised ring vaccination trial (Ebola ça Suffit!) in the communities of Conakry and eight surrounding prefectures in the Basse-Guinée region of Guinea, and in Tomkolili and Bombali in Sierra Leone*

Intervention

- *rVSV-ZEBOV; a recombinant, replication competent vesicular stomatitis virus-based candidate vaccine expressing a surface glycoprotein of Zaire Ebolavirus*
- *Single intramuscular dose of rVSV-ZEBOV (2×10^7 plaque-forming units administered in the deltoid muscle*



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Uganda Solidarity trial 2025 (TOKOMEZA EBOLA trial)

- Is a Ring vaccination trial to evaluate the efficacy and safety of a Sudan ebolavirus vaccine in Uganda

AIM:
to assess the effect of candidate vaccines in protecting against laboratory-confirmed SUDV.

PRIMARY OBJECTIVE:
Primary analysis is laboratory-confirmed SUDV (from samples taken either while the person is living, or within 48 hours of their death).

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Thank you

