Observed and forecasted impact of different candidate Ebola vaccines immunization strategies and target populations

Anton Camacho (Epicentre & LSHTM)
On behalf of the 3 modelling teams who presented at the SAGE Working Group of March 2017

SAGE meeting, 25-27 April 2017
Objective

• Summarize existing evidence about the **population-level effectiveness** of Ebola virus disease (EVD) immunisation of different strategies and target populations, using:

  • Observational data (following a flare-up in Guinée in March 2016)
  
  • **Predictions from Mathematical Models**

• Strategies & target populations tested:

  • **Pre-emptive** and/or **Reactive** vaccination

  • **Ring vs Targeted vs Mass** vaccination

  • Health-care workers; Front-line workers; Contacts and contacts of contacts of EVD cases; General population
Content

1. Overview of the different models

2. Summary of the findings
Models overview

**Individual based**
Tracks individual status
Models overview

**Individual based**
Tracks individual status

**Compartmental**
Tracks population status
Models overview

**Individual based**
Tracks individual status

**Compartamental**
Tracks population status

**Branching process**
Tracks infected individuals

[Diagram showing different models of disease spread]
Models overview

**Individual based**
Tracks individual status

**Compartmental**
Tracks population status

**Branching process**
Tracks infected individuals
Models overview

**Individual based**
Tracks individual status

**Compartmental**
Tracks population status

**Branching process**
Tracks infected individuals

---

**DATA NEEDED FOR CALIBRATION**

**Complexity tractability**

\[ S \rightarrow I \rightarrow R \]
Models overview

**Individual based**
Tracks individual status

**Compartmental**
Tracks population status

**Branching process**
Tracks infected individuals
Models can reproduce both localised & widespread outbreaks.
Vaccination strategies

- **Pre-emptive** vaccination:
  - **Targeted**: health-care workers (HCWs). *NB: excluding front-line workers (FLWs) as they are recruited after the outbreak is declared.*
  - **Mass** vaccination: random allocation among people living in areas at risk of Ebola.
Vaccination strategies

• **Pre-emptive** vaccination:
  
  • **Targeted**: health-care workers (HCWs). *NB: excluding front-line workers (FLWs) as they are recruited after the outbreak is declared.*

  • **Mass** vaccination: random allocation among people living in areas at risk of Ebola.

• **Reactive** vaccination:

  • **Ring** vaccination: contacts and contacts of contacts (CCCs) of EVD cases. *Parameters based on Ebola ça Suffit ring trial data.*

  • **Targeted** vaccination: HCWs and/or FLWs

  • **Mass** vaccination: random allocation among people living in areas reporting EVD cases.
<table>
<thead>
<tr>
<th></th>
<th>Branching process</th>
<th>Comp. 1 Kikwit</th>
<th>Comp. 2 West-Africa</th>
<th>IBM</th>
<th>IBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-emptive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-emptive</td>
<td>HCW</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Pre-emptive</td>
<td>Mass</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Reactive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reactive</td>
<td>Ring</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Reactive</td>
<td>Targeted</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Reactive</td>
<td>Mass</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
</tr>
</tbody>
</table>
Vaccine efficacy

Single-dose:
VE = 100% (CI: 64-100%) after day 7 post-vaccination

Prime-boost:
VE = 80% after day 7 and 90% after day 28 post-vaccination
Models limitations

- Models do not explicitly account for spontaneous human behavioural changes
- **Data used for calibration** might be incomplete thus introducing potential biases
- Several **unknown parameters** are based on assumptions:
  - Efficacy of prime-boost vaccine (no phase 3 trial yet)
  - Duration of immunity (>1 year for single dose and prime-boost)
  - Capacity on the field for mass vaccination (e.g. number of doses distributed per day)
1. Overview of the different models

2. Summary of the findings
Impact of health-care workers vaccination

Effect of different vaccination strategies

Total number of cases

Effect of HCW coverage in ahead-of-time strategies

Note: this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.
Impact of health-care workers vaccination

Effect of different vaccination strategies

HCW coverage = 30%

-40%

Note: this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.
Impact of health-care workers vaccination

Effect of different vaccination strategies

- HCW coverage = 30% + reactive mass vaccination of community (140k doses) - 41%

Note: this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.
Impact of health-care workers vaccination

**Effect of different vaccination strategies**

- **HCW coverage = 30% + reactive mass vaccination of community (140k doses)**
- -41%

**Note:** this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.
Impact of health-care workers vaccination

Effect of different vaccination strategies

Total number of cases

HCW

HCW + community

HCW only (30% coverage)

HCW + reactive community vaccination

No vaccination

Ahead-of-time HCW vaccination

Reactive

Kikwit 1995

Jan 1995

Apr 1995

Jul 1995

Note: this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.
Health-care workers

- **HCWs are at high-risk of infection** during EVD outbreaks, especially at the outset of the outbreak when they can amplify the spread of the disease.

- Models suggest that pre-emptive vaccination of HCW may be an **effective strategy with both direct and indirect protective effects** to limit the spread to the community and avoid depletion of HCWs in areas with limited health-resources.

- The number of doses needed depends on the number of HCW in areas at risk of EVD outbreaks, their turnover and the **(unknown) duration of vaccine-induced immunity**.
Impact of ring vaccination + pre-emptive/reactive HCW/FLW vaccination

Seeding in rural areas

Basic reproduction number (R0)

EPP is defined as the reduction of the risk of observing a large outbreak (>300 cases).

Note: this model assumes poor or zero initial infrastructure for classical control measures.
Impact of ring vaccination + pre-emptive/reactive HCW/FLW vaccination

EPP is defined as the reduction of the risk of observing a large outbreak (>300 cases).

Note: this model assumes poor or zero initial infrastructure for classical control measures.
Impact of ring vaccination + pre-emptive/reactive HCW/FLW vaccination

Seeding in rural areas

Basic reproduction number (R0)

EPP is defined as the reduction of the risk of observing a large outbreak (>300 cases).

Note: this model assumes poor or zero initial infrastructure for classical control measures.
• **Ring vaccination may be an effective reactive strategy** to contain Ebola outbreaks because it tracks the transmission dynamics and target the CCCs who are the most at risk of being infected.

• **Effectiveness of this strategy has been demonstrated** during the *Ebola ça Suffit* ring vaccination trial in Guinea as well as during the flare-up in Guinea.

• Models suggest that ring vaccination may be **more effective in rural than in urban areas**, due to higher population density in cities.
Ring vaccination of contacts and contacts of contacts (2/2)

- Models suggest that ring vaccination should work best in conjunction with pre-emptive/reactive vaccination of HCWs/FLWs as well as with classic control measures.

- In particular, comprehensive contact tracing is essential for effective ring vaccination since missed infected contacts can seed the epidemic to new areas.

- Models results suggest that localised Ebola outbreaks can be contained with 10,000 doses whereas more widespread epidemics can be contained with 50,000 doses.
Mass vaccination

- In case of poor case detection and contact tracing, models suggest that ring vaccination should be supplemented by more geographically targeted mass vaccination.

- Targeting villages of patients would require a tenfold increase of doses to be effective (~100,000 doses).

- Targeting regions reporting cases would require a hundredfold increase of doses (~1,000,000 doses) but would have little impact in case of late vaccination.
Thank you!

Acknowledgements:

M. Ajelli
N. Dean
L. Fumanelli
M.E. Halloran
I.M. Longini
S. Merler
A. Pastore y Piontti
A. Vespignani
A. Camacho
J. Edmunds
R. Eggo
S. Funk
A. Kucharski
A. Robert
C. Watson
C. Donnelly
N. Ferguson
W. Hinsley
G. Nedjati-Gilani
S. Riley
Impact of health-care workers vaccination

Note: this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.
Impact of ring vaccination

Note: classical control measures are also implemented in this model
Impact of ring vaccination + reactive HCW vaccination

Note: this model is gauged to a baseline with poor or zero initial infrastructure for classical control measures.
Number of doses/rings after 6 months

Note: this model is gauged to a baseline with poor or zero initial infrastructure for classical control measures.
Impact of ring vaccination + pre-emptive/reactive HCW/FLW vaccination

Note: this model assumes poor or zero initial infrastructure for classical control measures.
Impact of mass vaccination (village)

Seeding in rural areas

EPP (%)

Impact of mass vaccination (village)

EPP is defined as the reduction of the risk of observing a large outbreak (>300 cases).

Note: this model is gauged to a baseline with poor or zero initial infrastructure for classical control measures.

a: mass vaccination (village of patients + random component)
b: a + reactive HCWs
c: a + pre-emptive HCWs + reactive FLWs
Impact of mass vaccination (region)

These campaigns can reduce transmission and shorten the outbreak, but use 1-3 million doses (per country) to decrease the number of cases by approximately 50%.

Note: this model reproduces the 2013-2016 EVD outbreak in Liberia and Sierra-Leone and accounts for classical control measures that were implemented at that time.