The potential impact of different vaccination policies

Rosalind Eggo, John Edmunds, Anton Camacho, Adam Kucharski, Sebastian Funk, Alexis Robert, Conall Watson, Stefan Flasche

London School of Hygiene & Tropical Medicine

r.eggo@lshtm.ac.uk
Summary & key questions

1. Vaccination of health care workers
   – What is impact of prophylactic vaccination?

2. Ring vaccination
   – Clearly effective (clinical trial)
   – Are there conditions when it might fail to control an outbreak?

3. Mass vaccination (district level)
   – What effect if vaccines had been available during the current outbreak?
HCW: questions

- Do HCW play an active role in driving the transmission during the increasing phase of the epidemic?
- What are the benefits (direct and indirect) of vaccinating HCW before an epidemic?

<table>
<thead>
<tr>
<th>Location</th>
<th>Population size</th>
<th>Confirmed &amp; probable cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Community</td>
<td>HCW</td>
</tr>
<tr>
<td>Kikwit (1995)</td>
<td>200,000</td>
<td>900</td>
</tr>
<tr>
<td>Liberia (2014)</td>
<td>4.3 m</td>
<td>11.7 k</td>
</tr>
<tr>
<td>Sierra Leone (2014)</td>
<td>6.3 m</td>
<td>6.2 k</td>
</tr>
<tr>
<td>Guinea (2014)</td>
<td>10.5 m</td>
<td>1.7 k</td>
</tr>
</tbody>
</table>
Outbreak in Kikwit (1995)

76 of 317 cases (24%) were HCW

6 April, 1st case at Kikwit General Hospital

Undetected outbreak

4 & 10 May, control measures start
Transmission tree (Kikwit)

1 HCW
39 secondary cases
25 (69%) are HCW

1 COM
21 secondary cases
100% are COM

262/317 (83%) known index cases
Model fit

Fit the model to the second part of the outbreak, from 6 April 1995

Community incidence

HCW incidence

Level
- 50%
- 95%
Vaccination characteristics

- Single dose vaccine
- 80% efficacy
- Protective 1 week post-vaccination
- All-or-nothing immunity
- 1 year protection
- 100,000 doses deployed per week in community

1. HCW prophylaxis +/- reactive community vaccination
2. Reactive HCW + community vaccination

- **Base scenario:** vaccinate all HCW before the epidemic only
- **Reactive vaccination:**
  - 20 April: 2 weeks after first case in Kikwit General Hospital
  - 10 May: arrival of international response team
Reactive community vaccination: cases averted

- Vaccination of HCW can prevent cases in both HCW and community
- Rapid community vaccination can avert a large fraction of cases
- Late start to the community campaign results in little additional benefit
- Number of doses very different (900 in HCW vs 150,000 in community)
Without early start to HCW campaign, protection of HCW is lower.

Even ~1 month delay from 1st case to vaccination of HCW diminishes effect.

Both in HCW and community.
Limitations of HCW model

• Definition of HCW may vary
  – Both geographically and through time
• Depletion of HCW
  – Due to morbidity/mortality
  – Leaving posts
• Homogeneous mixing of HCW and community members
• Duration of protection of vaccine is key
Ring vaccination

- Randomised clinical trial gives clearest evidence of effectiveness of ring vaccination policy
- Are there conditions when it might fail to control an outbreak?

80% efficacy
70% of individuals in rings are vaccinated
2 days from case identification to vaccination of contacts
7 days to onset of immunity
Ring vaccination model

Vaccine:
- 80% efficacy
- 70% of individuals in rings are vaccinated
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Ring vaccination model

Vaccine:
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Input data

- Initial (i.e. missed) cases have $R=7$
- Other cases have $R=0.66$
- With funeral and hospital transmission omitted, initial cases have $R=2.5$

Faye et al (2015) *The Lancet Infectious Diseases*
Model can generate realistic epidemics

- Each colour is a transmission chain
- Distribution comparable to observed data
Proportion of cases not in known chain

Guinea, 2015. Weekly proportion not in known chain. Data from Situation Reports
If missed cases associated with superspreading, ring vaccination might fail to stop large outbreak (i.e. >500 clusters) even if small proportion of cases missed

- No vaccination
- Ring vaccination

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1 index case

5 index cases
If missed cases associated with superspreading, ring vaccination might fail to stop large outbreak (i.e., >500 clusters) even if small proportion of cases missed.

- No vaccination
- Ring vaccination

If no funeral or hospital superspreading events, ring vaccination can prevent large outbreaks even if ~40-50% cases missed.
Limitations of ring vaccination model

• Reliance on data from early part of the epidemic
• Clustering of cases and contacts is not included
• No depletion of susceptibles
Model for mass vaccination

- Mass vaccination at the regional level
  - Liberia: county
  - Sierra Leone: district
- Meta-population model
  - Importations from neighbouring regions
  - Rate dependent on size & proportional to cases
Base case results

Vaccination (base case)
80% efficacy
Protection for 10 years
Trigger: 10 cases per region
2 week delay to start
100,000 doses per region per week
70% coverage
Delay in vaccine availability

Liberia
- no vaccination immediate from 1 Aug 2014 from 1 Oct 2014

Sierra Leone
- no vaccination immediate from 1 Aug 2014 from 1 Oct 2014

Cases Averted
- Liberia
- Sierra Leone

Doses Deployed
- Liberia
- Sierra Leone
Limitations of mass vaccination model

• Doses
  – Reactive vaccination ends only when coverage is reached, or the end of the simulation (1 year)

• Importation of cases
  – number of importations proportional to the local simulated epidemic
  – do not account for the region that imported cases are from

• Homogeneous mixing
  – widely used in epidemiology due to their tractability and accuracy in large populations

• Guinea
  – More spatial heterogeneity
Summary

General approach
- Impossible to tell what next epidemic will be like
- What if vaccine had been available in past outbreaks

Ring vaccination
- Trial demonstrates the effectiveness of this strategy
- Least effective if cases who “escape detection” have high reproduction number
- May need to widen ring &/or supplement with more widespread vaccination
  - Stockpile implications

Mass vaccination (district, country, etc)
- Effectiveness of vaccination depends on timing
  - Late vaccination has little impact

HCW vaccination (prophylactic)
- HCW at very high risk, particularly at the outset of Ebola epidemics
- May also play a role in amplifying initial spread
  - Vaccination of HCW has potential population-level effects, i.e. limiting spread to the community
Acknowledgements & further details

More detailed weekly assessments and district-level forecasts at: http://cmmid.lshtm.ac.uk/research/ebola/

For further details on models, email: r.reggo@lshtm.ac.uk

Data:
• MoHs
• WHO
• MSF
Extra slides
Ring vaccination

- Randomised clinical trial gives clearest evidence of effectiveness of ring vaccination policy

All individuals

Transmission model

Ring vaccination model

Vaccination delays

80% efficacy and 70% vaccinated means:

\[ R_v = (1 - 0.7 \times 0.8) R_w = 0.44 R_w \]
Transmission trajectories

- 3 examples showing distribution of Reproduction number in fitted model
- Use 100 trajectories to simulate epidemics
- Captures public health responses & behavioural changes
Model for mass vaccination

- Model fitted to region-specific data
- Reproduction number (in each region) allowed to vary over time
  - Captures public health responses & behavioural changes
- Simulations: allow model to run with and without vaccination
If missed cases associated with superspreading, ring vaccination might fail to stop large outbreak (i.e. >500 clusters) even if small proportion of cases missed

- No vaccination
- Ring vaccination
- Mass vaccination

1 index case

5 index cases
If no funeral or hospital superspreading events, ring vaccination can prevent large outbreaks even if ~40-50% cases missed.

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