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

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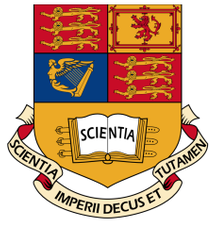

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Objective

- 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

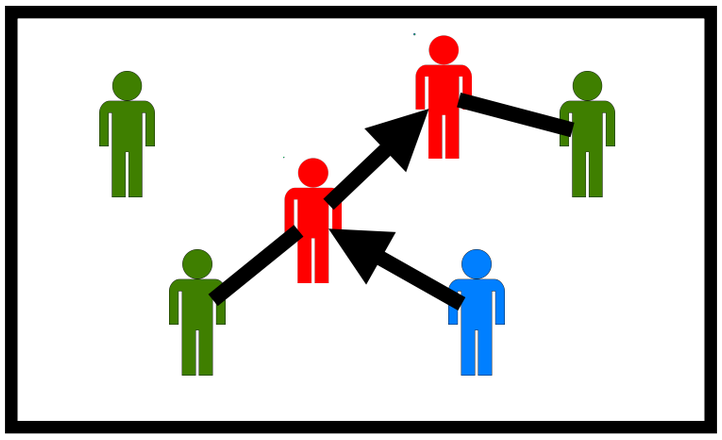
Content

1. Overview of the different models
2. Summary of the findings

Models overview

Individual based

Tracks individual status



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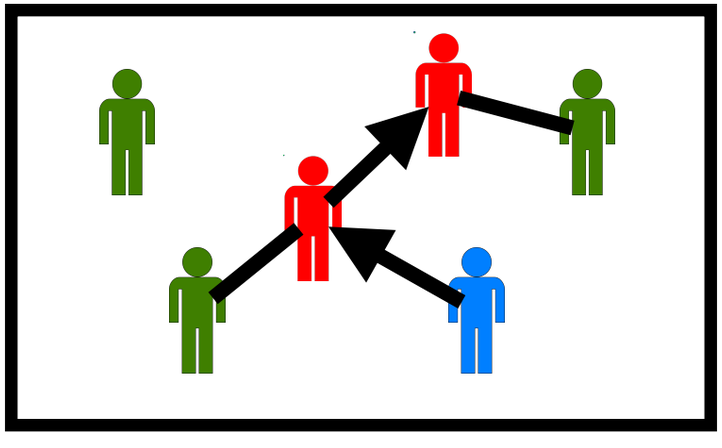
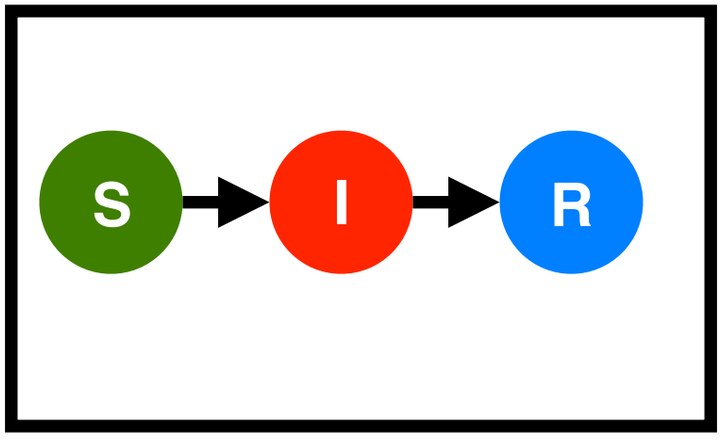


Compartmental

Tracks population status



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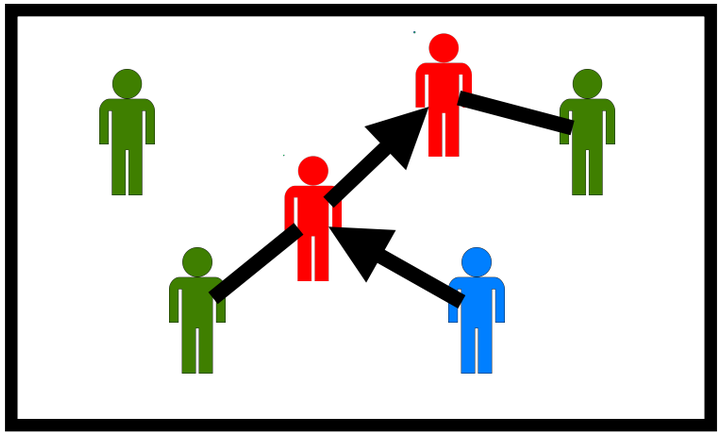

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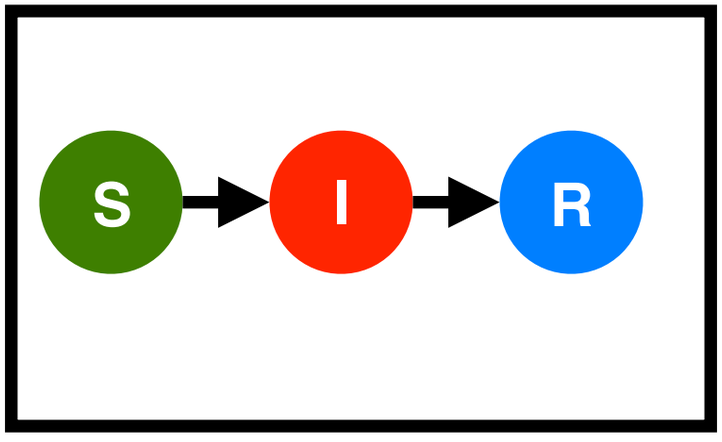
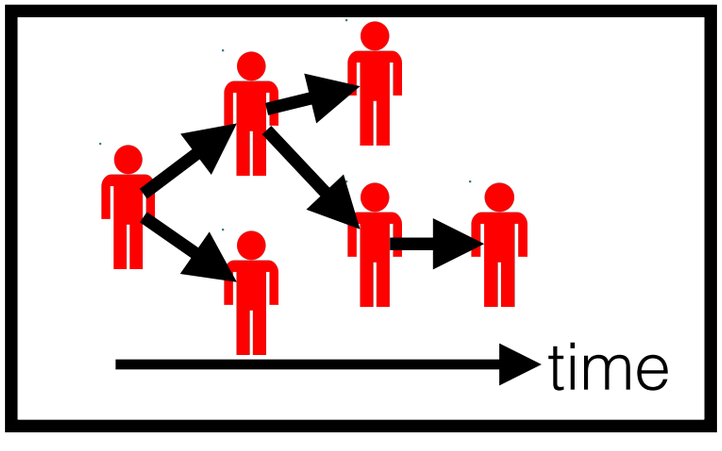


Branching process
Tracks infected individuals



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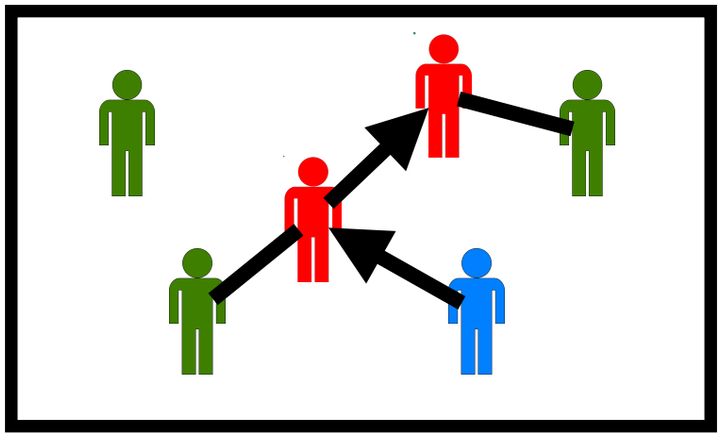

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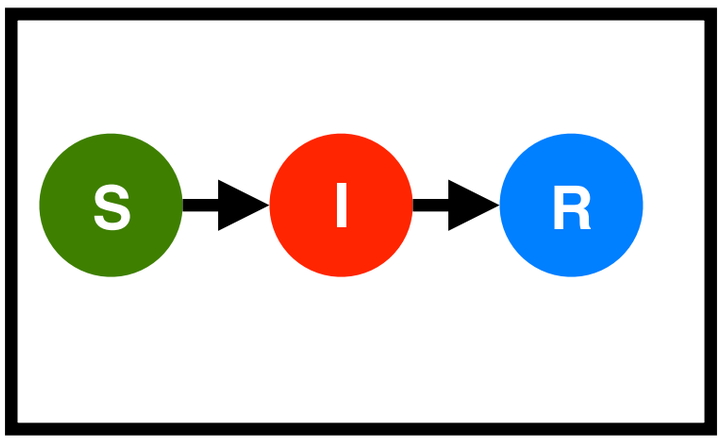

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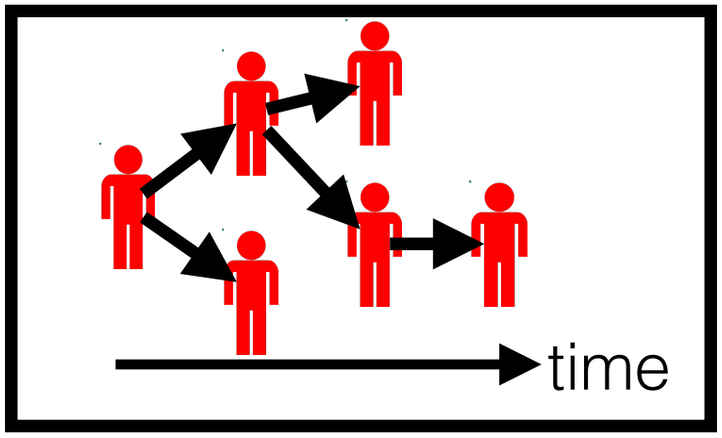

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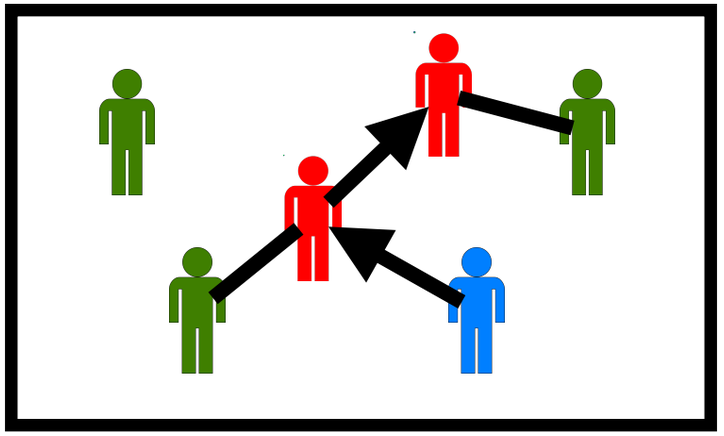

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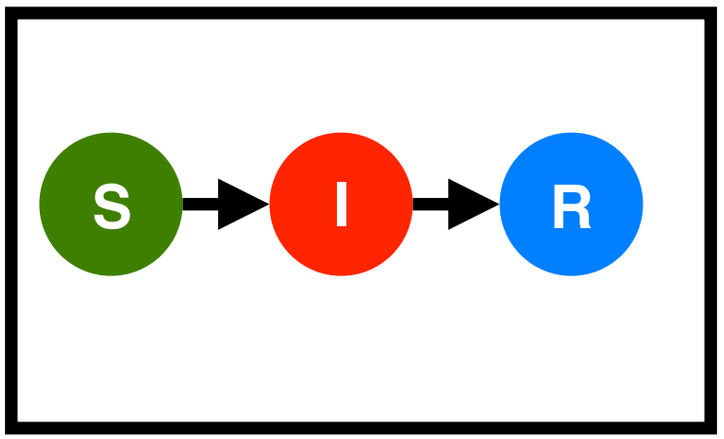

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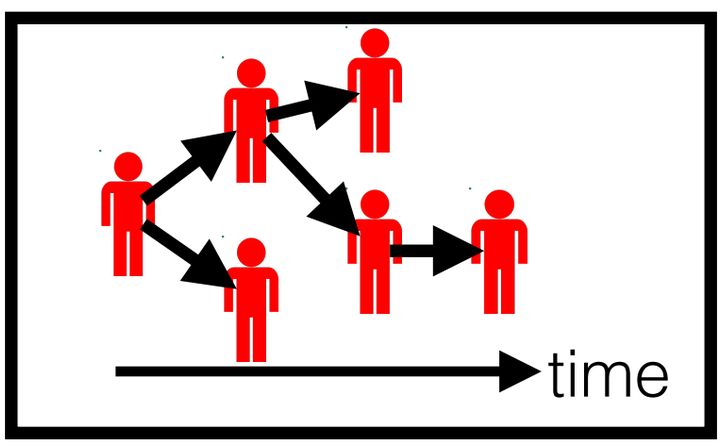

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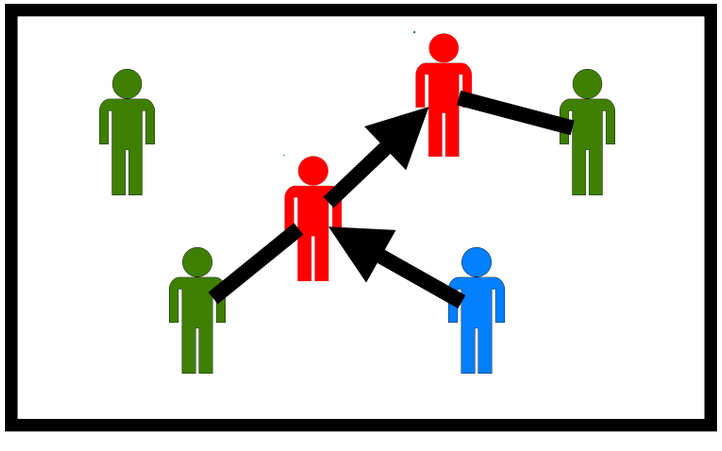

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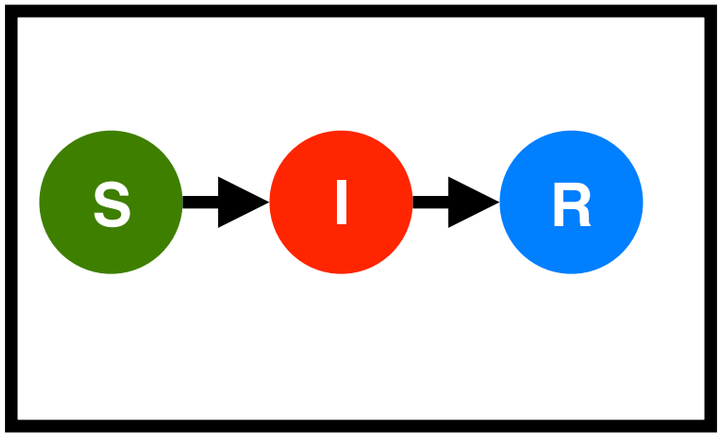

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x2

Branching process
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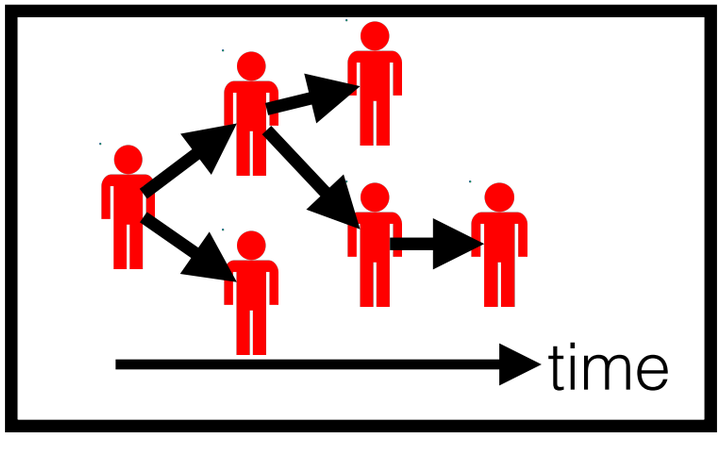

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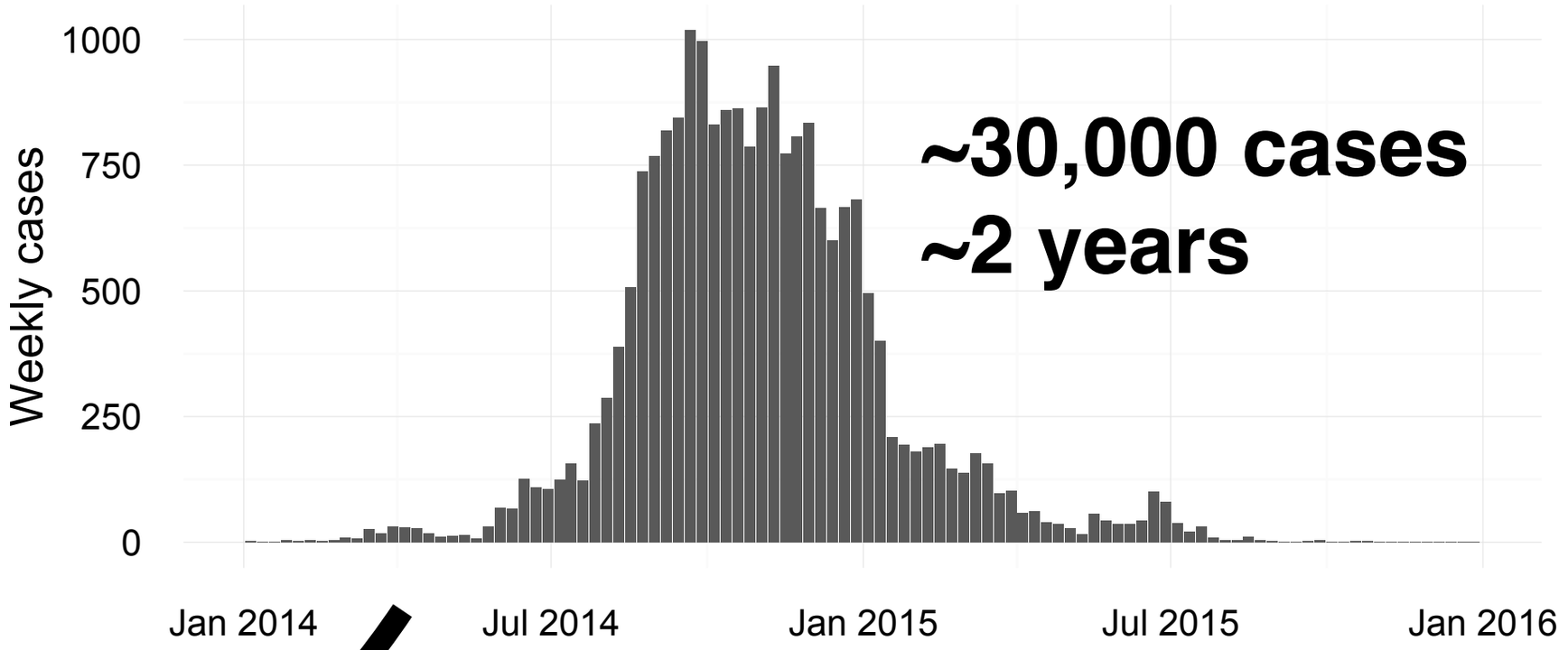
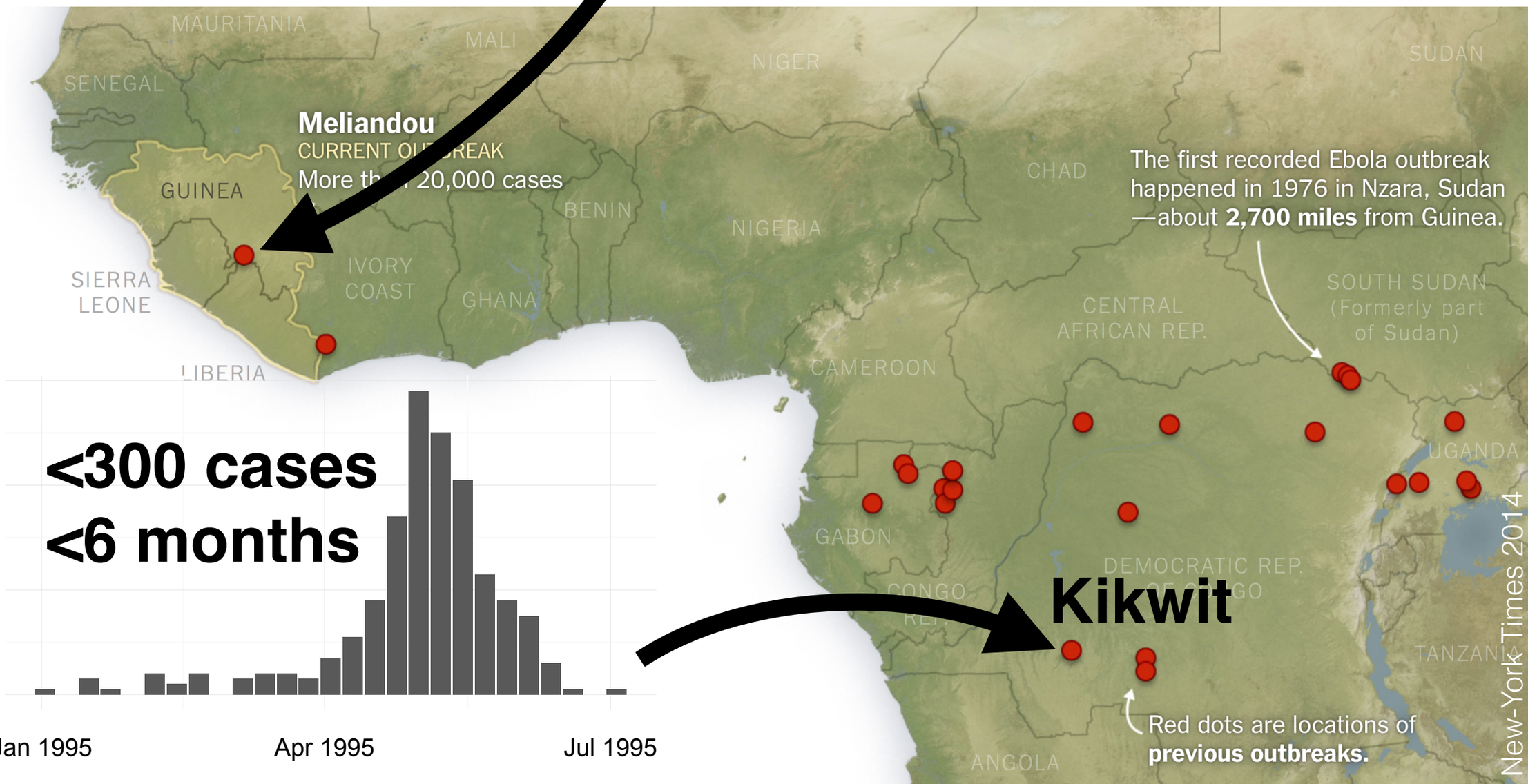
Models can reproduce both **localised** & **widespread** outbreaks





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.

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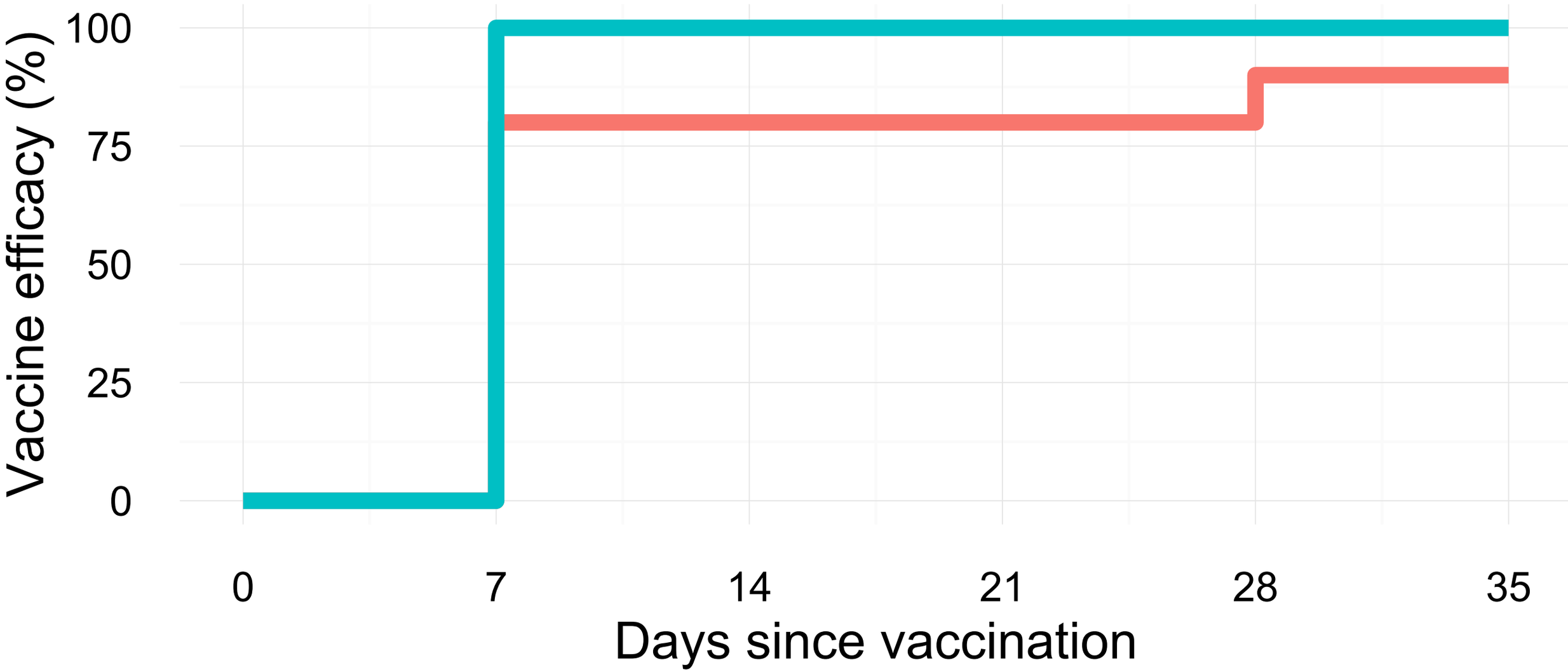
  - **Mass** vaccination: random allocation among people living in areas at risk of Ebola.
- **Reactive** vaccination:
  - **Ring** vaccination: contacts and contacts of contacts (CCCs) of EVD cases. *Parameters based on Ebola ça Suffit ring trial data.*
  - **Targeted** vaccination: HCWs and/or FLWs
  - **Mass** vaccination: random allocation among people living in areas reporting EVD cases.

		Branching process	Comp. 1 Kikwit	Comp. 2 West-Africa	IBM	IBM
Pre-emptive	HCW		✔		✔	
Pre-emptive	Mass	✔	✔	✔	✔	
Reactive	Ring	✔			✔	✔
Reactive	Targeted		✔		✔	
Reactive	Mass		✔	✔	✔	

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)

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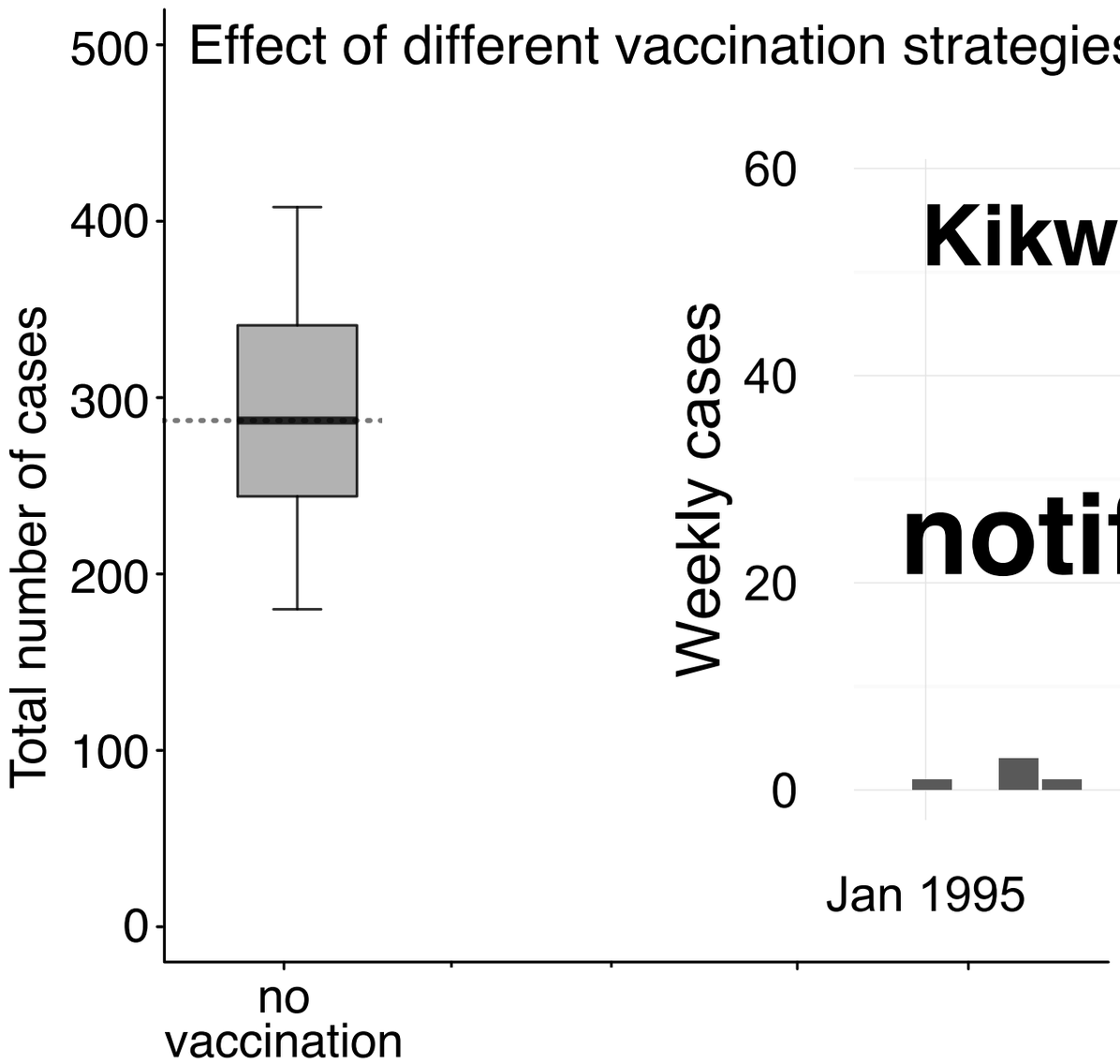
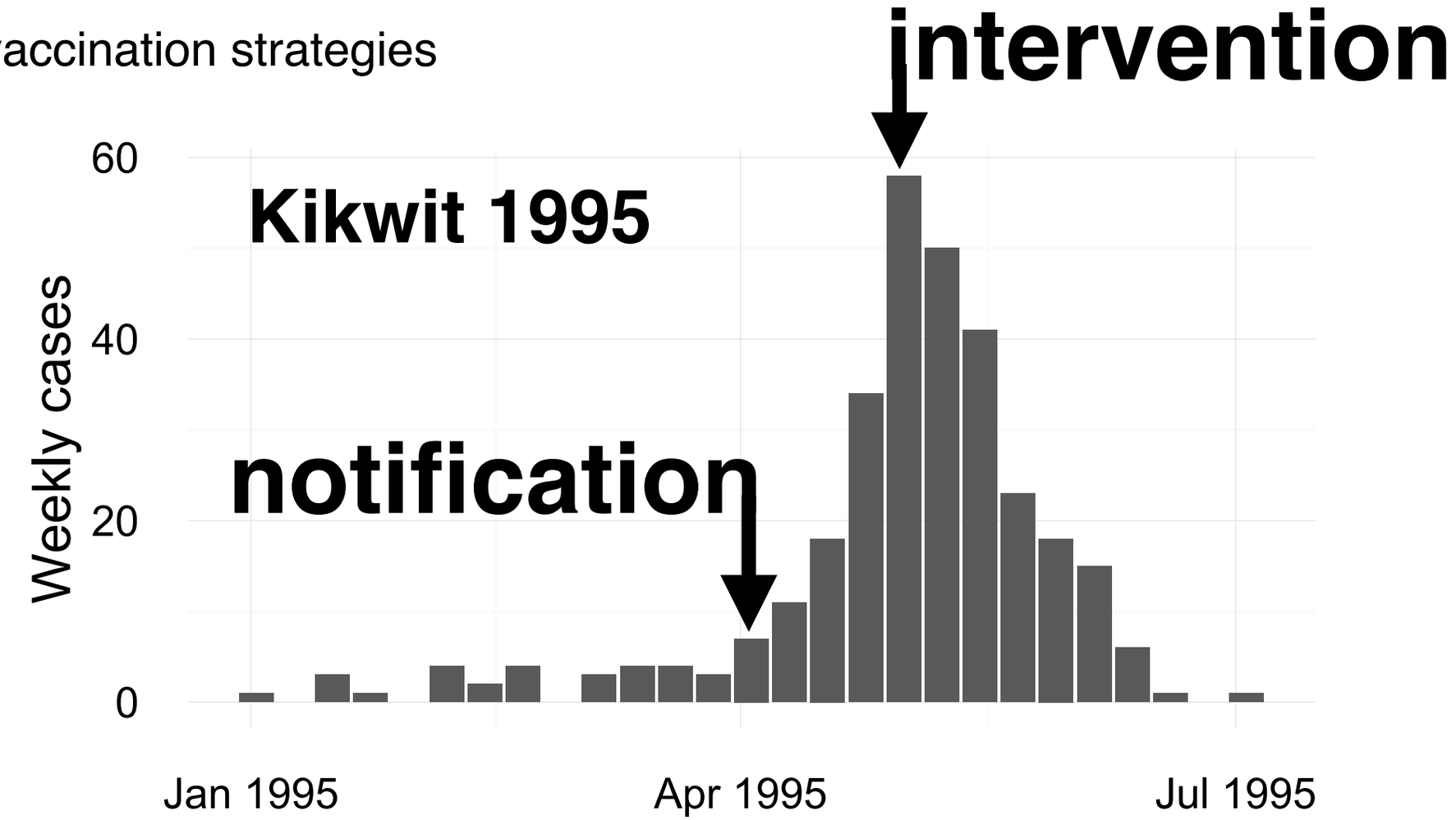
Impact of health-care workers vaccination





<u>Note:</u> this model reproduces the 1995 EVD outbreak in Kikwit and accounts for classical control measures that were implemented at that time.

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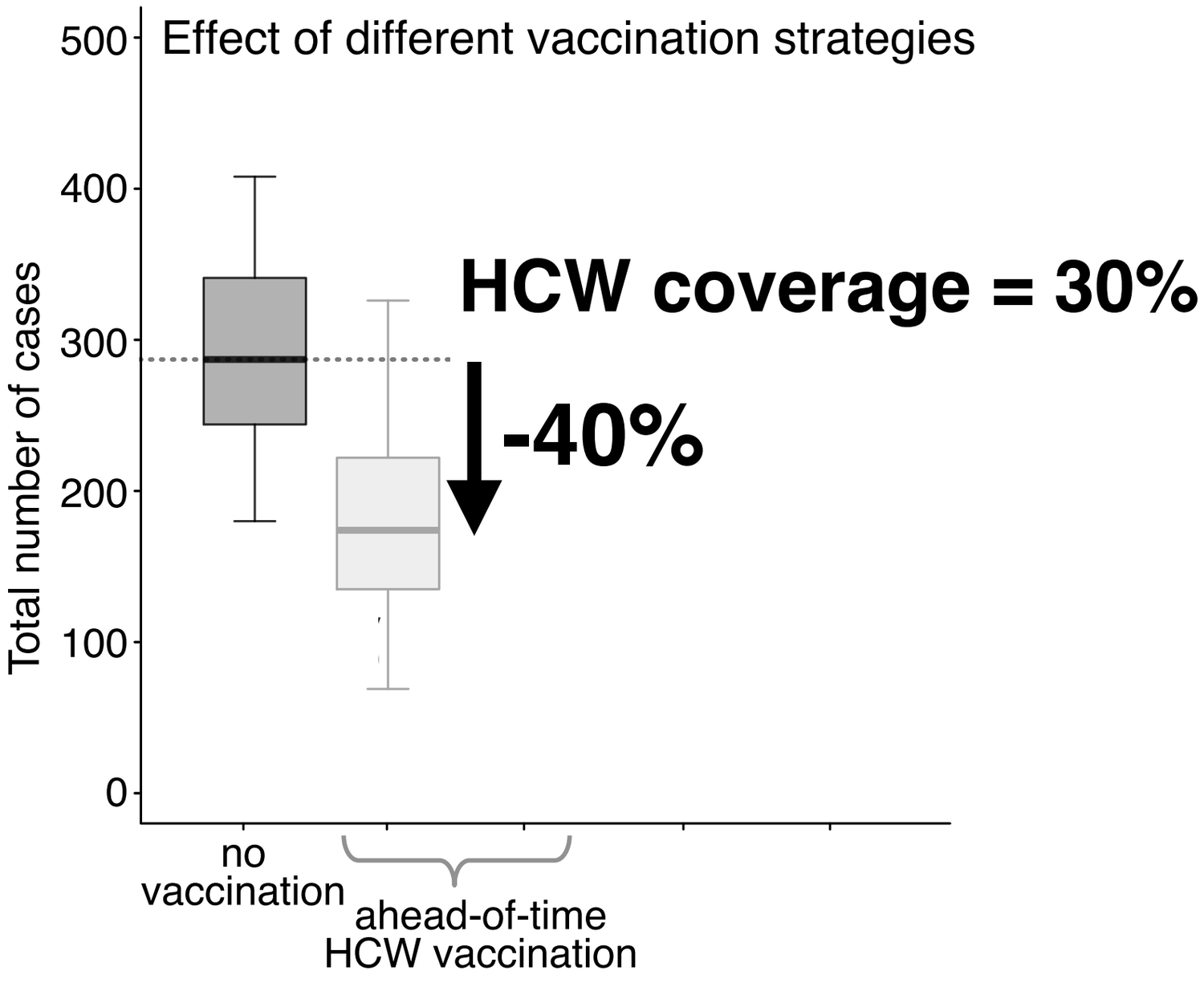

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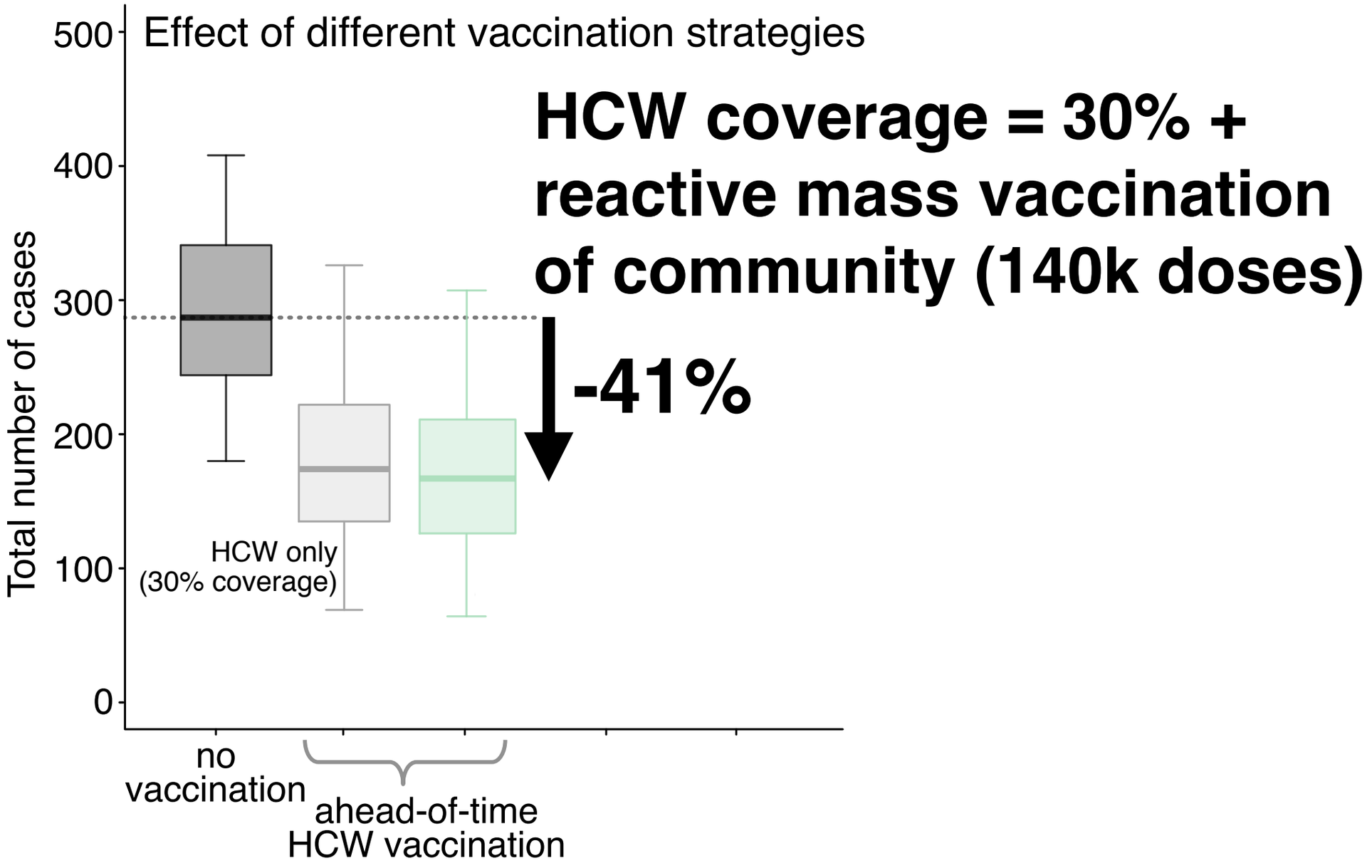

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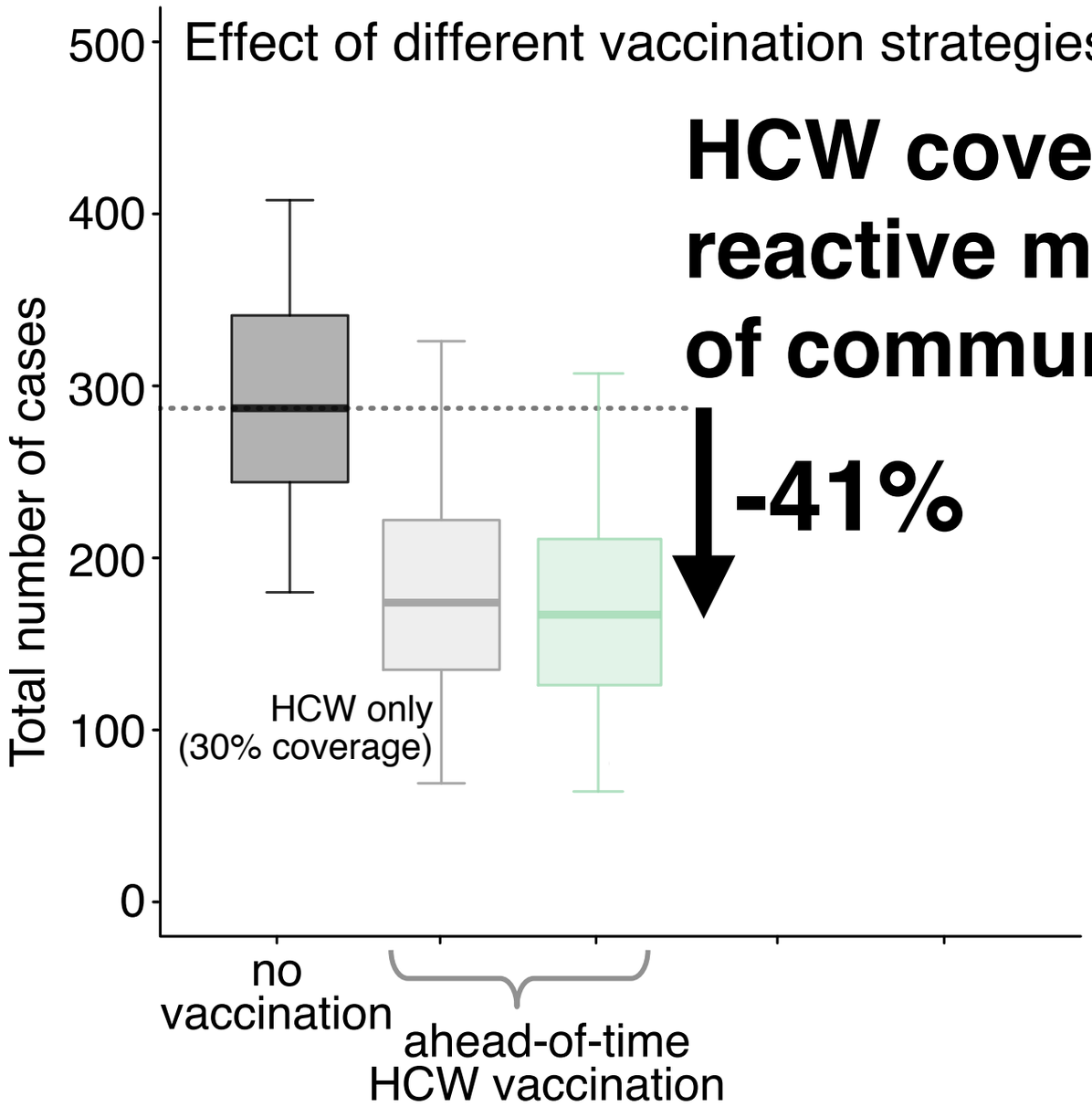

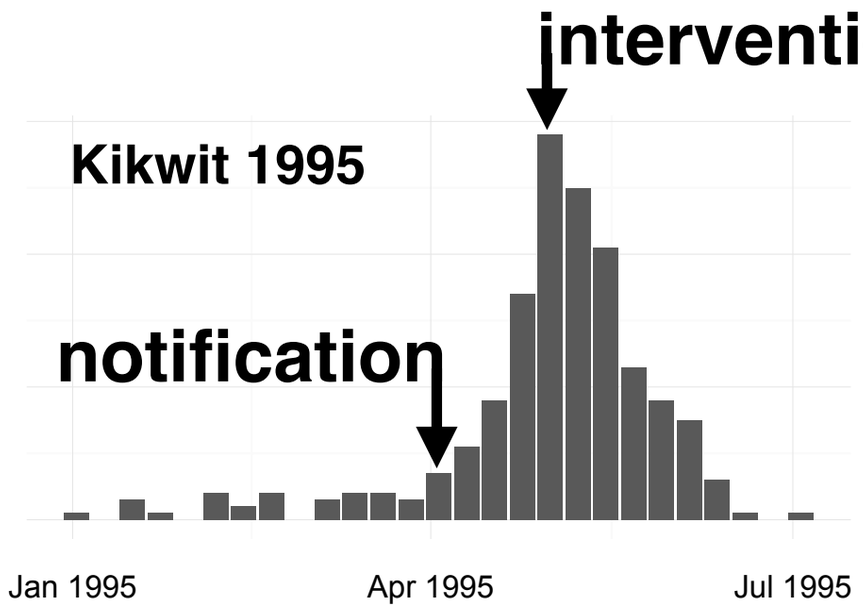

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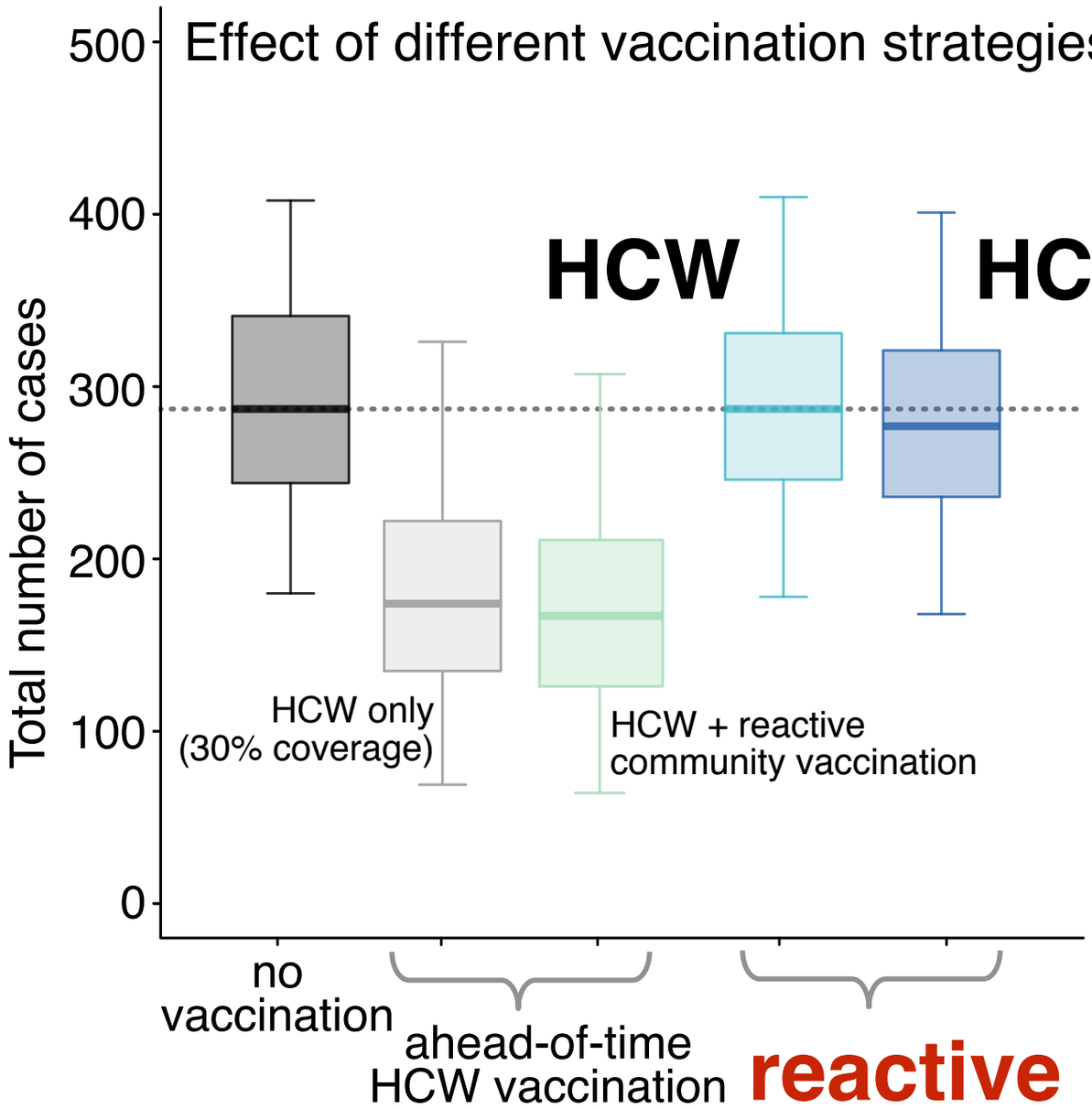

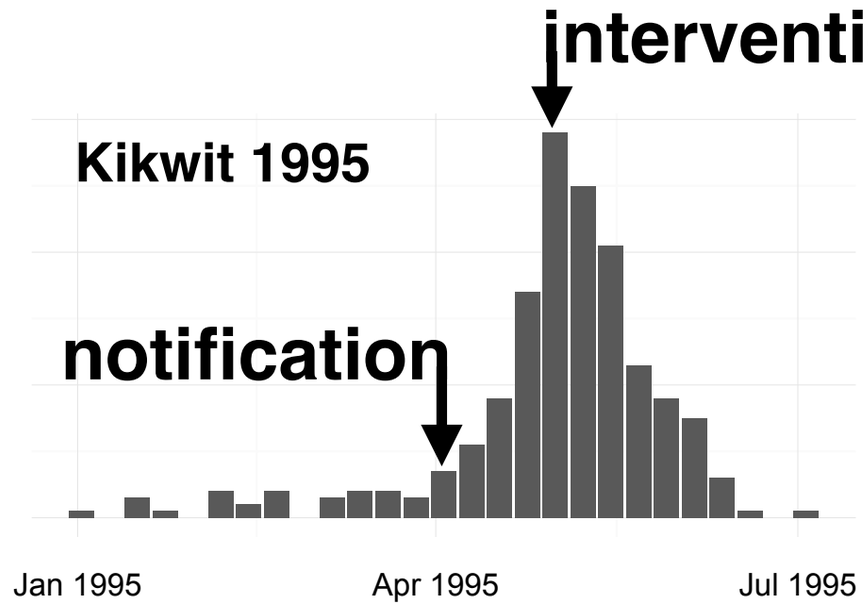

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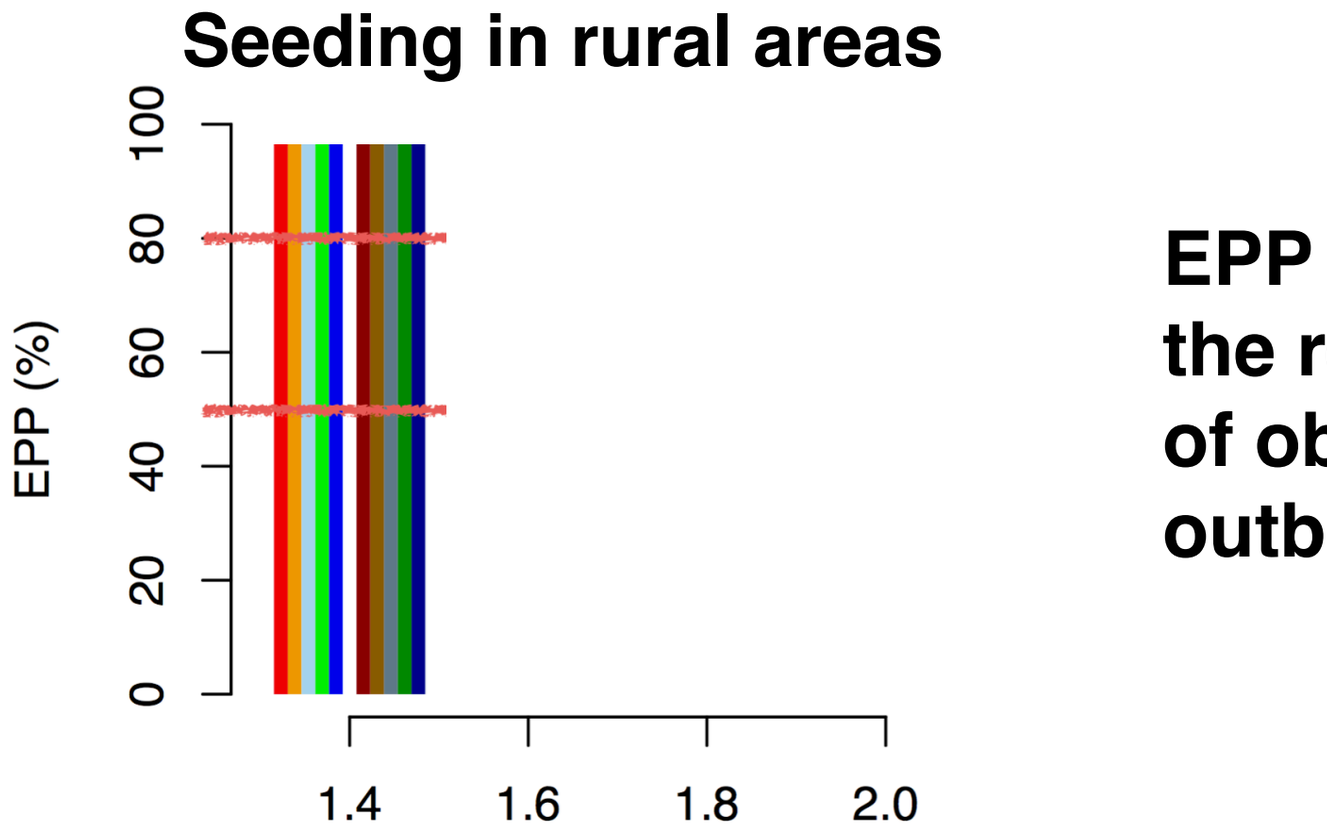
Health-care workers

- **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



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

<u>Note</u>: this model assumes poor or zero initial infrastructure for classical control measures.

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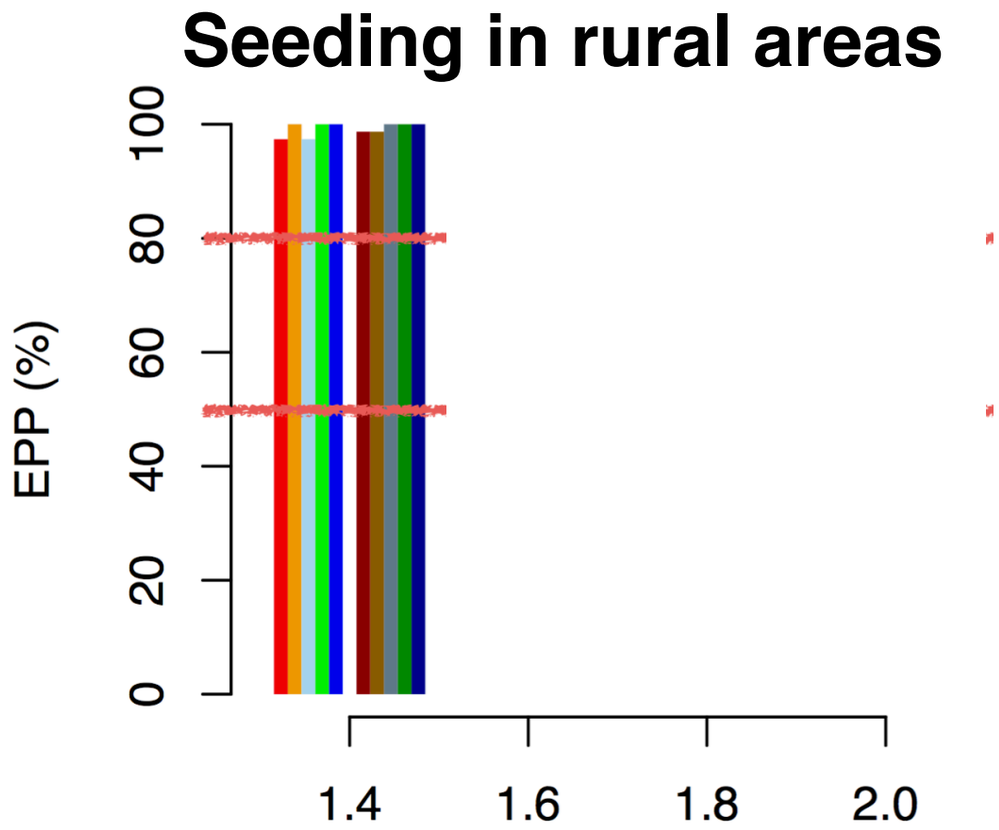

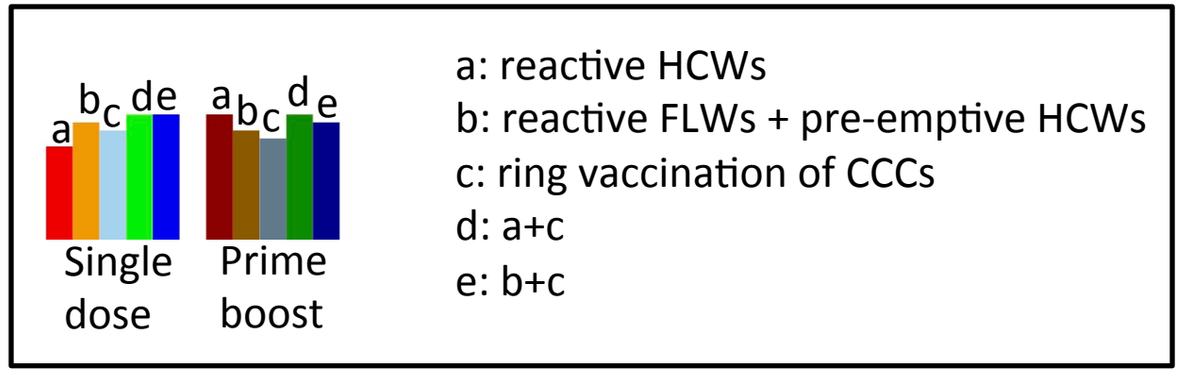

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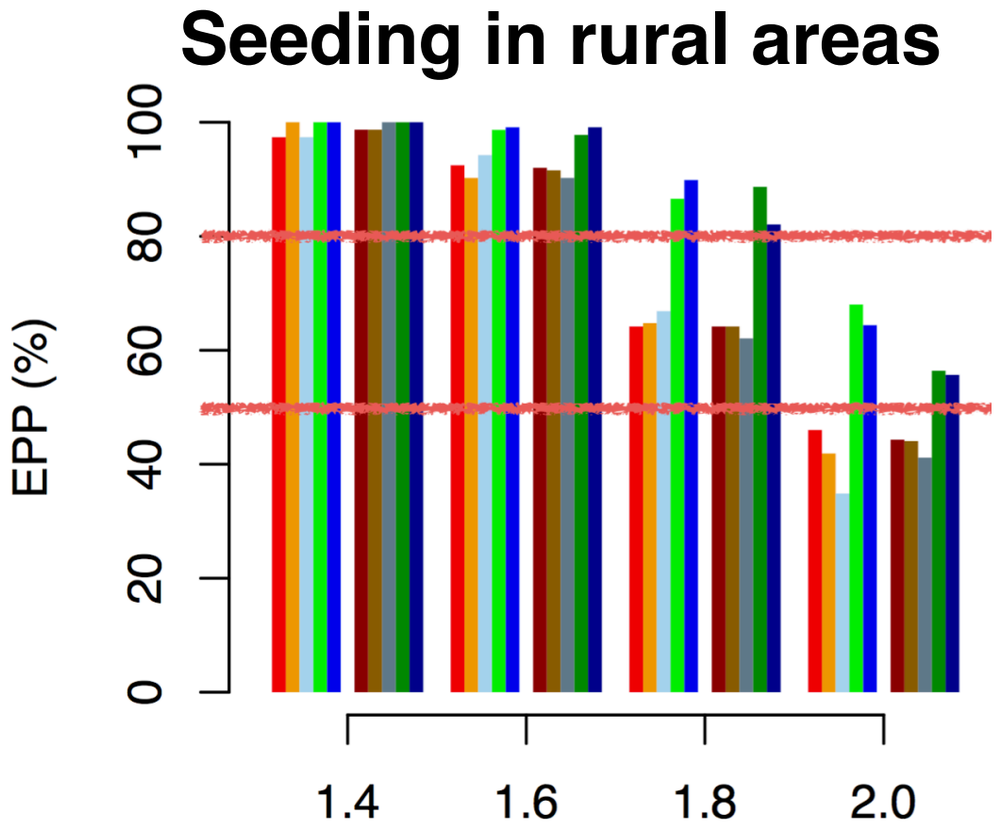

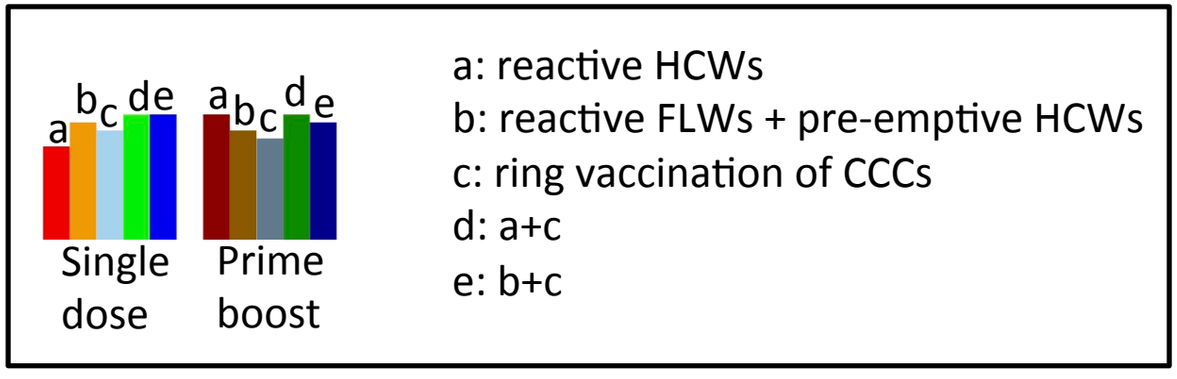

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Ring vaccination of contacts and contacts of contacts (1/2)

- **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!

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S. Riley

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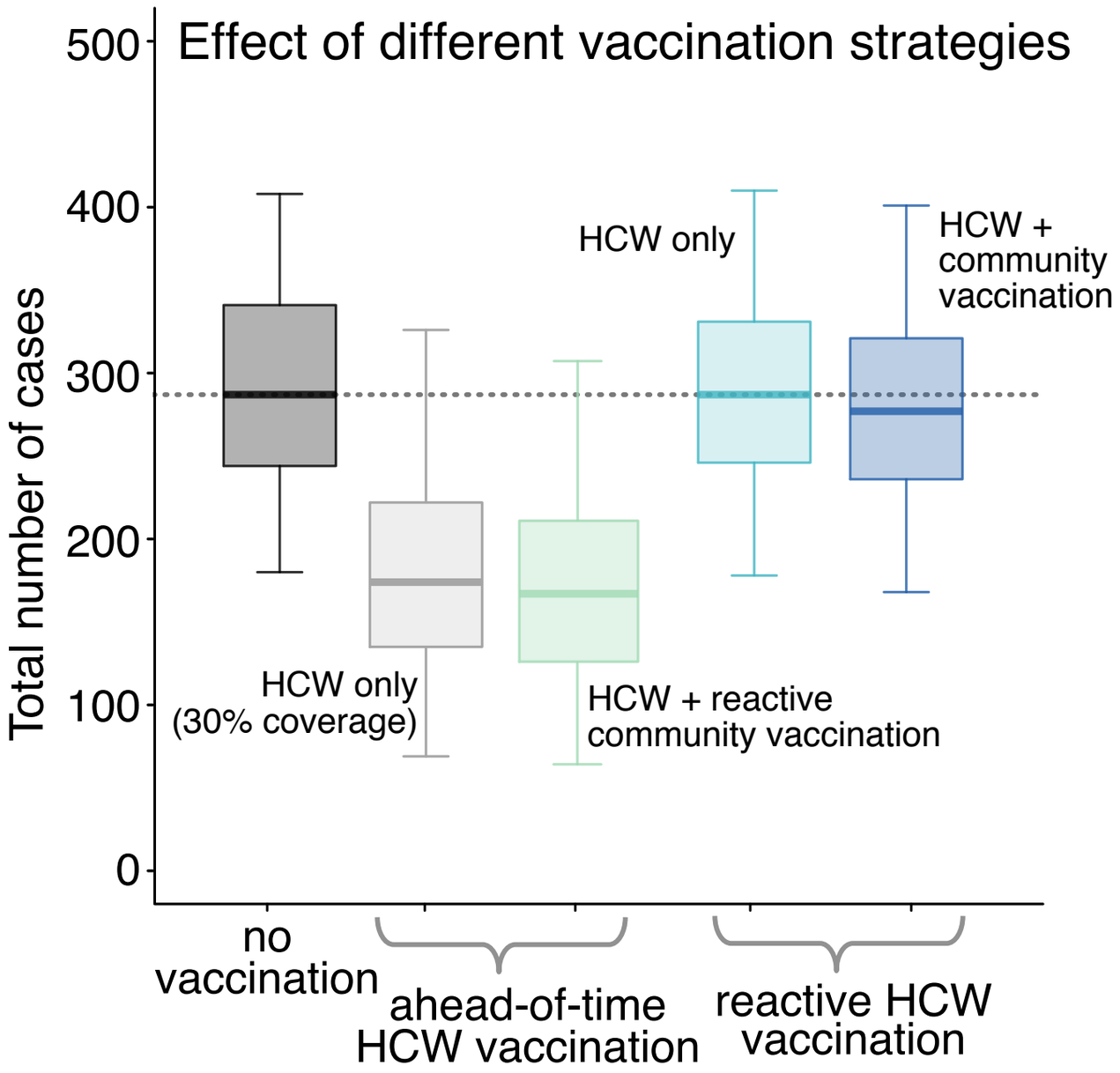

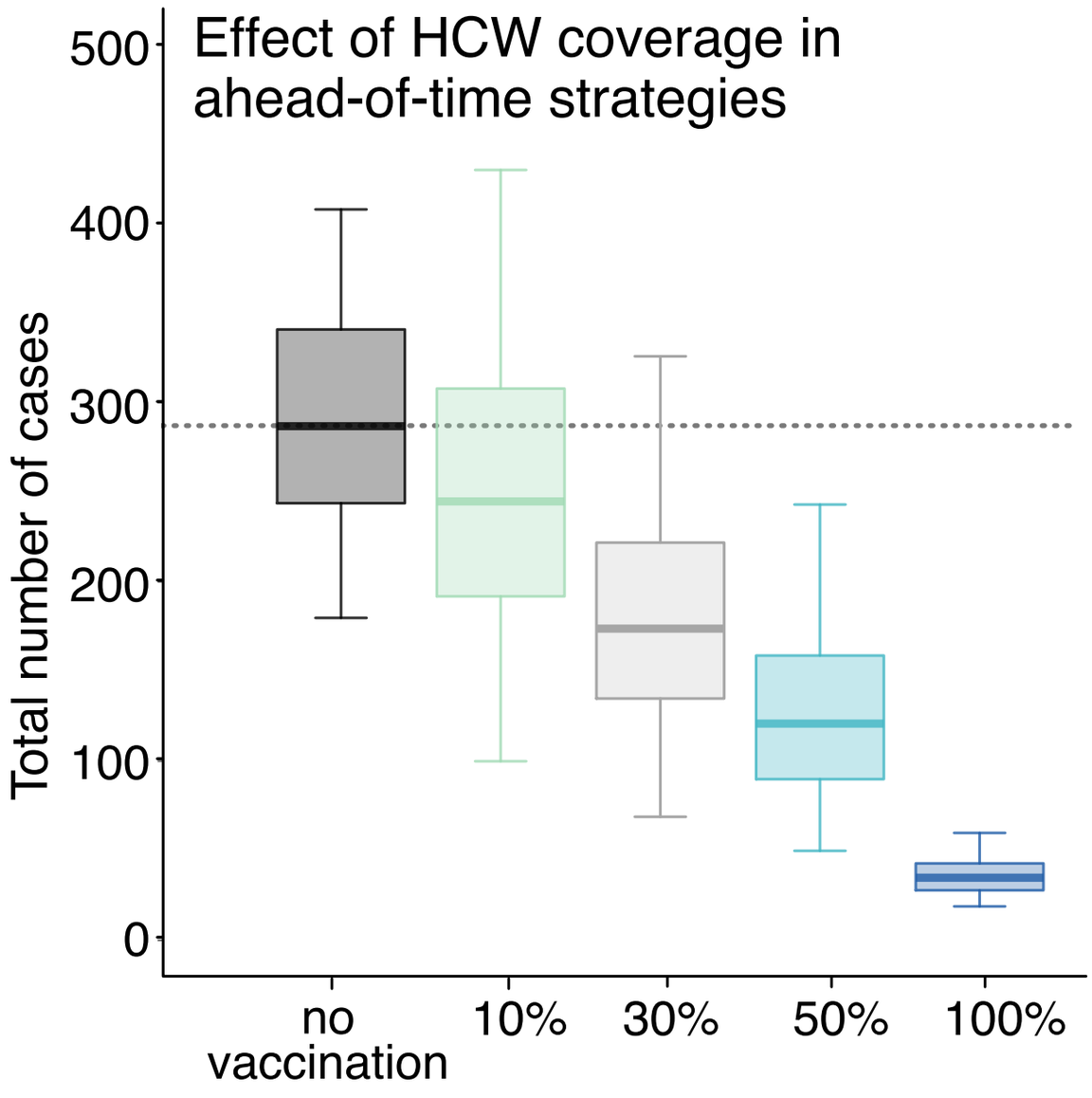

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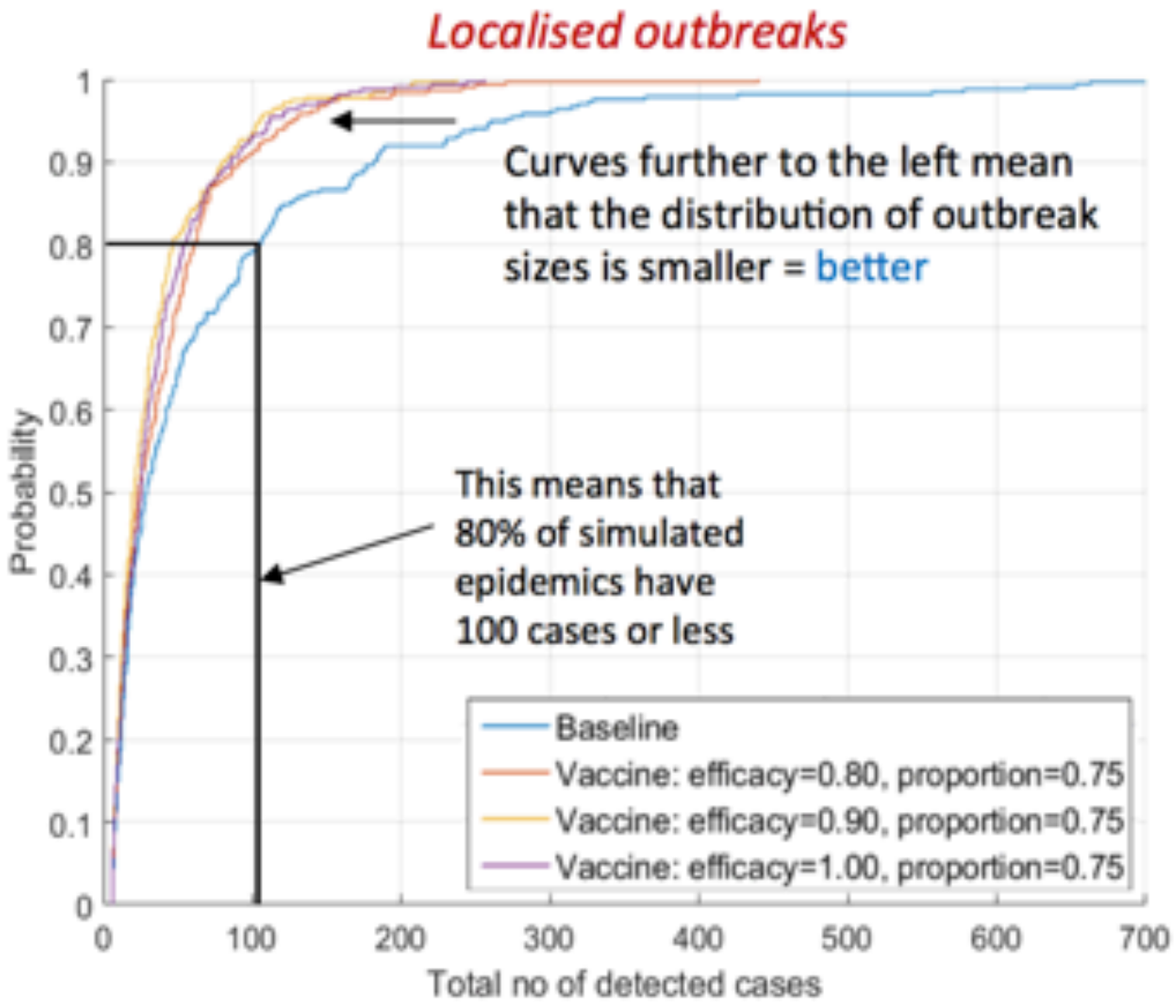
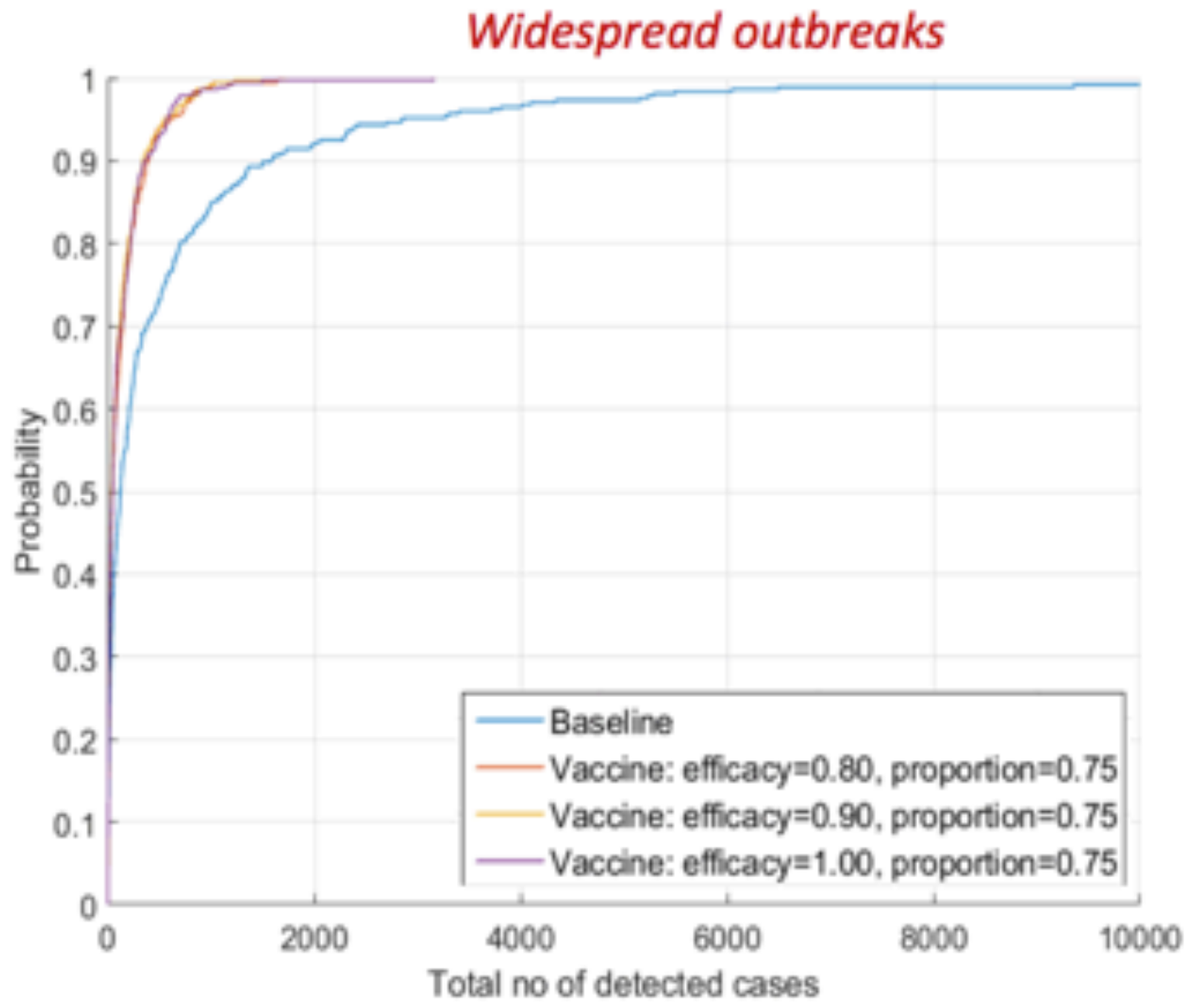
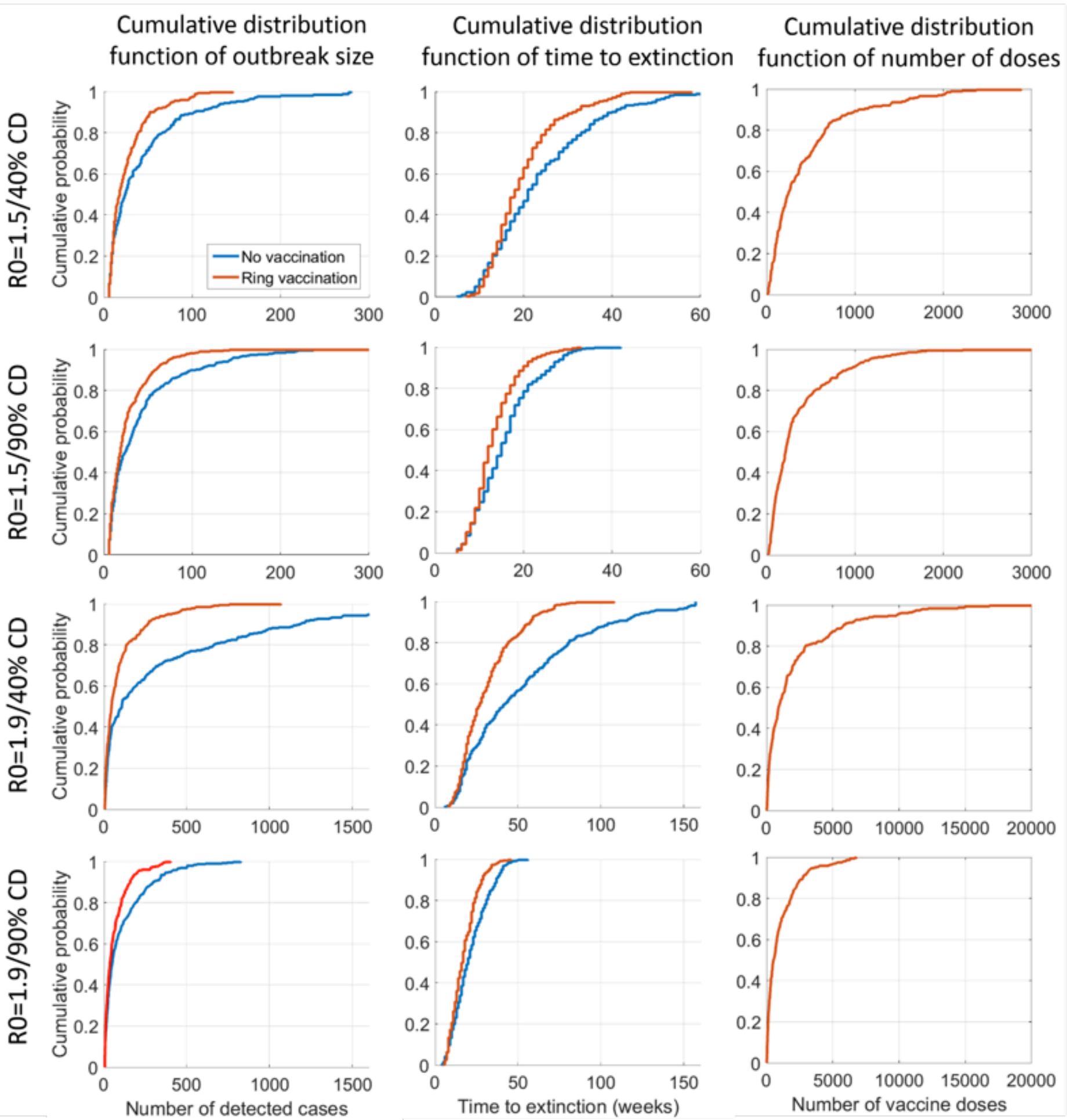
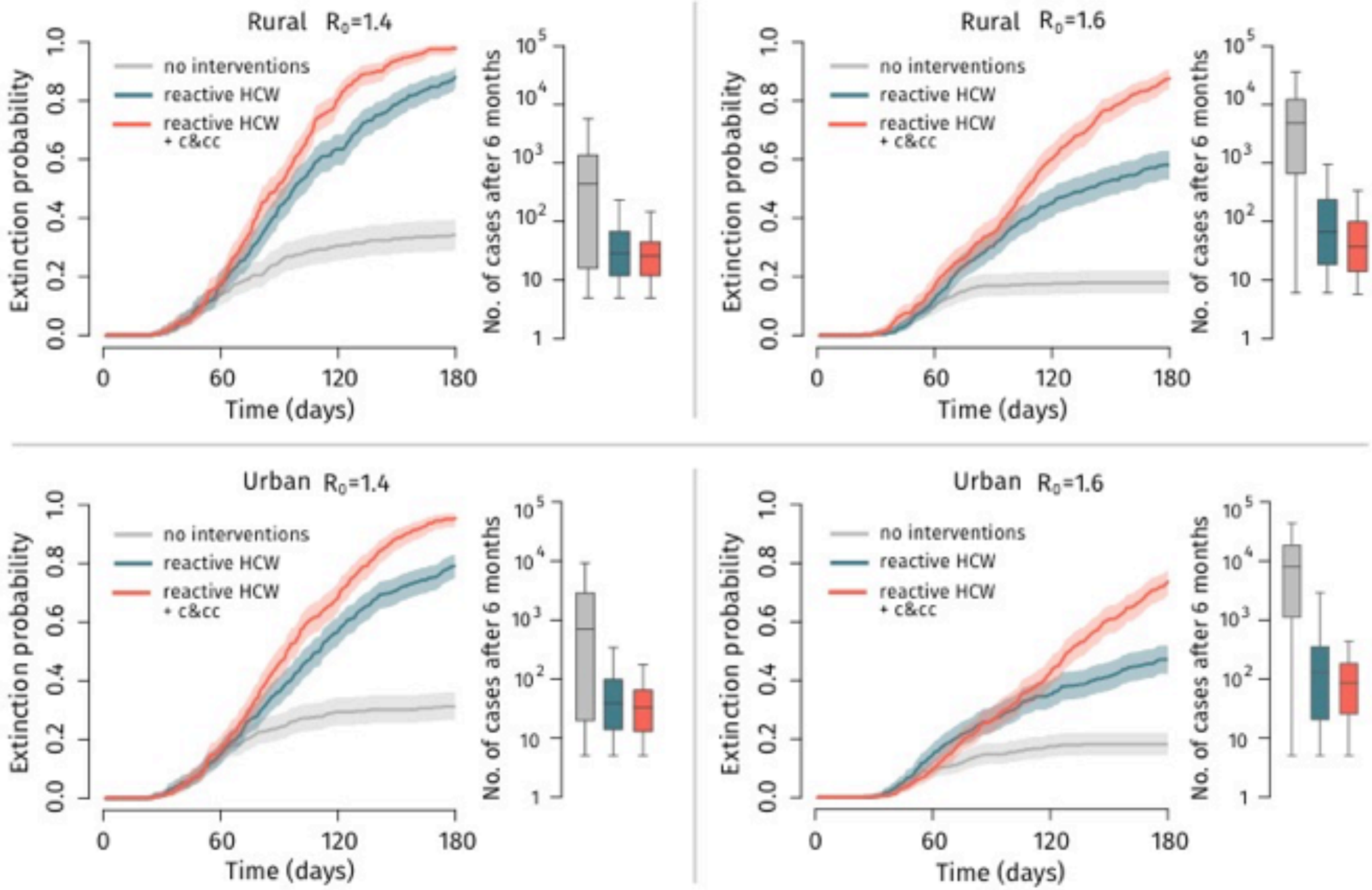




Note: classical control measures are also implemented in this model

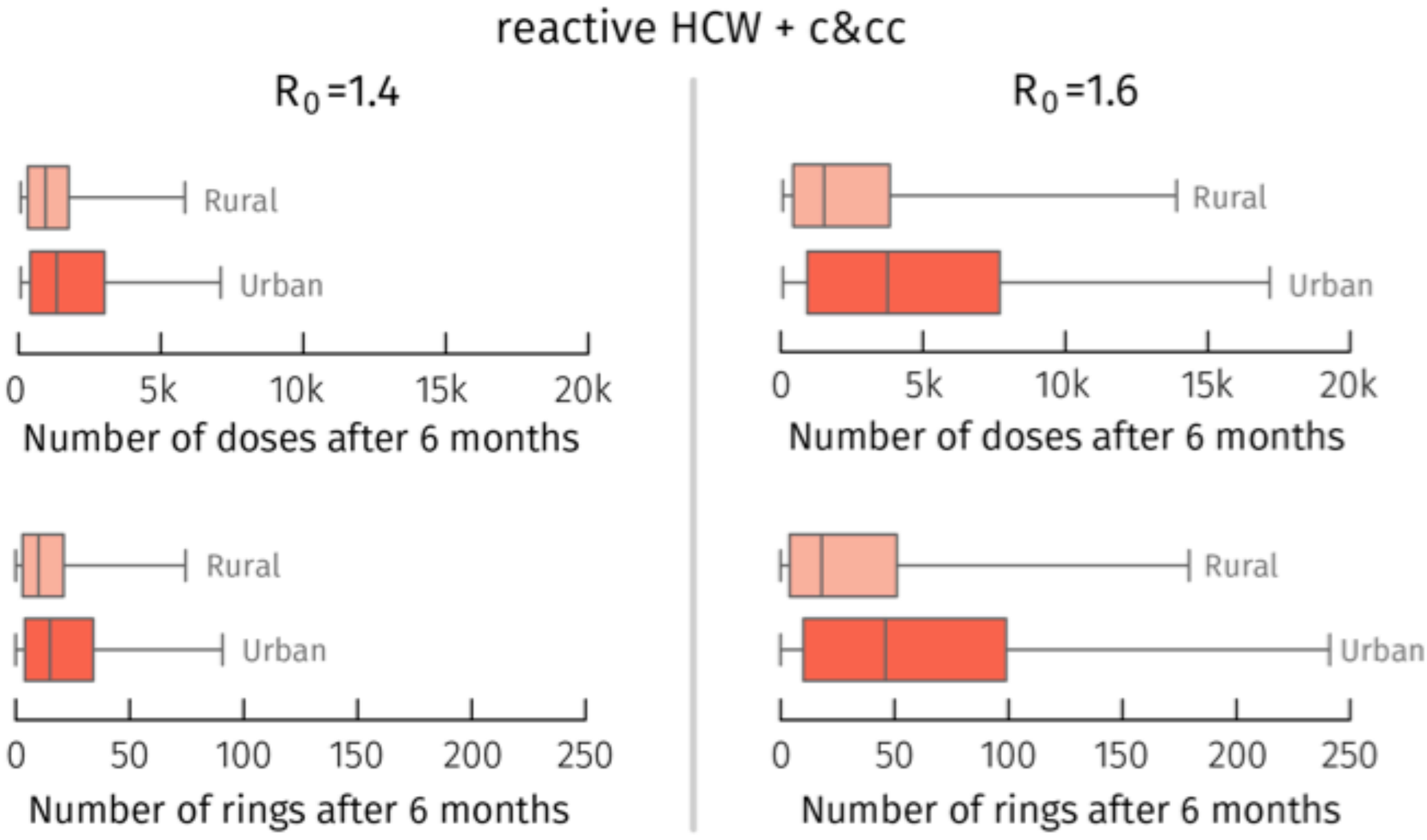

Cumulative distribution function of outbreak size
Cumulative distribution function of time to extinction
Cumulative distribution function of number of doses
R0=1.5/40% CD
R0=1.5/90% CD
R0=1.9/40% CD
R0=1.9/90% CD
Cumulative probability
No vaccination
Ring vaccination
Number of detected cases
Time to extinction (weeks)
Number of vaccine doses

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



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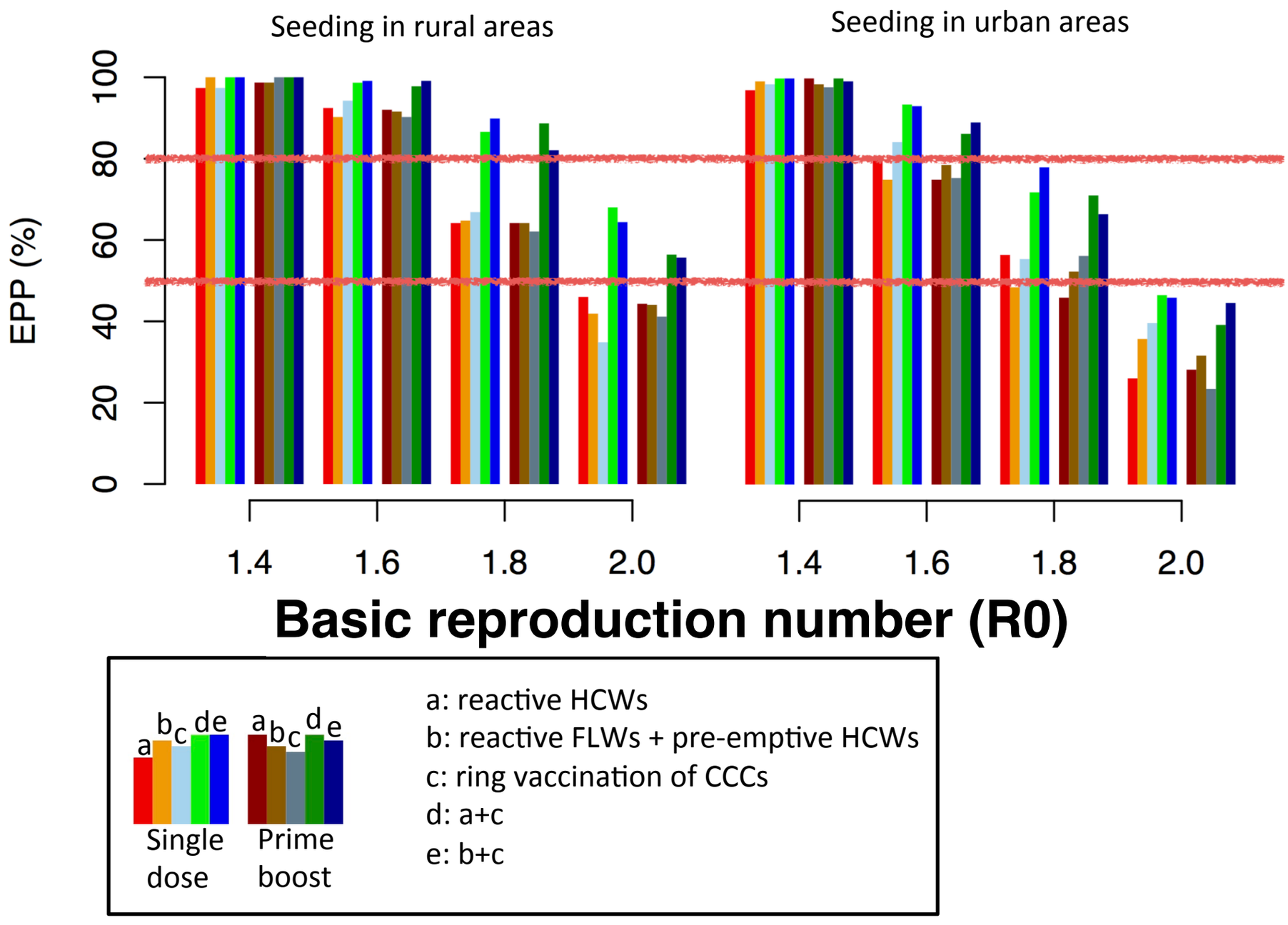
Impact of ring vaccination + pre-emptive/ reactive HCW/FLW vaccination



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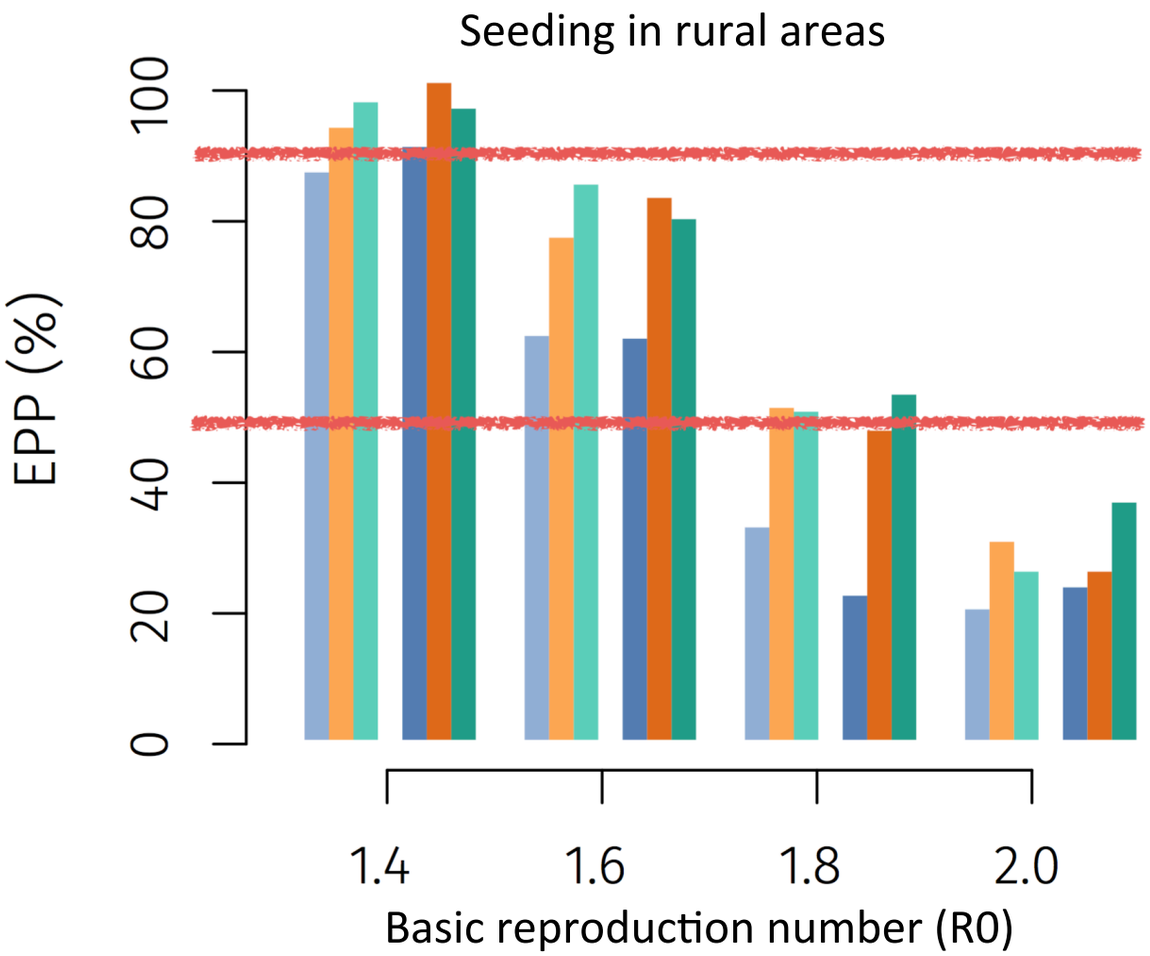
Impact of mass vaccination (village)



a b c — Single dose

a b c — Prime boost

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

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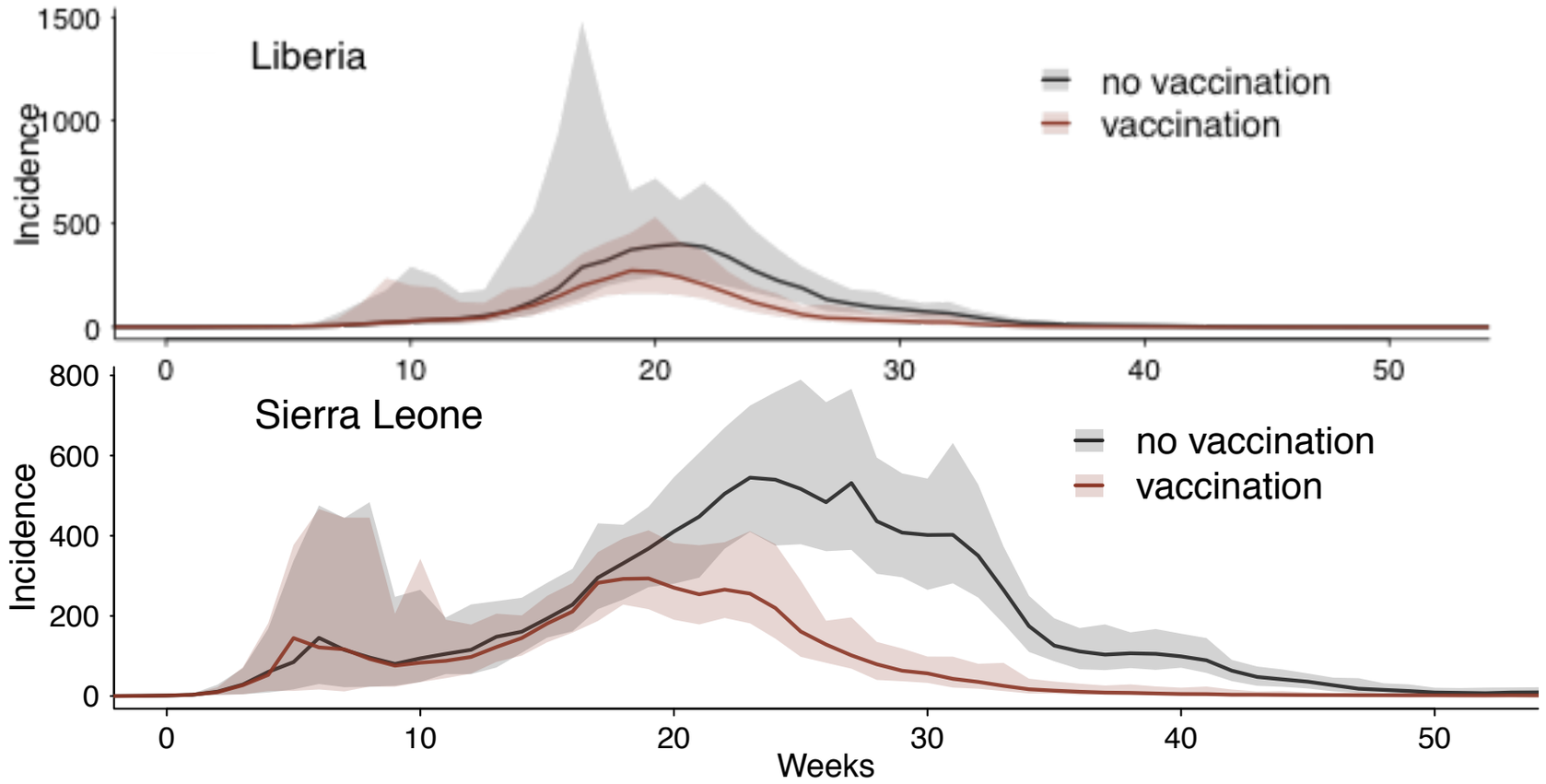
Impact of mass vaccination (region)



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.