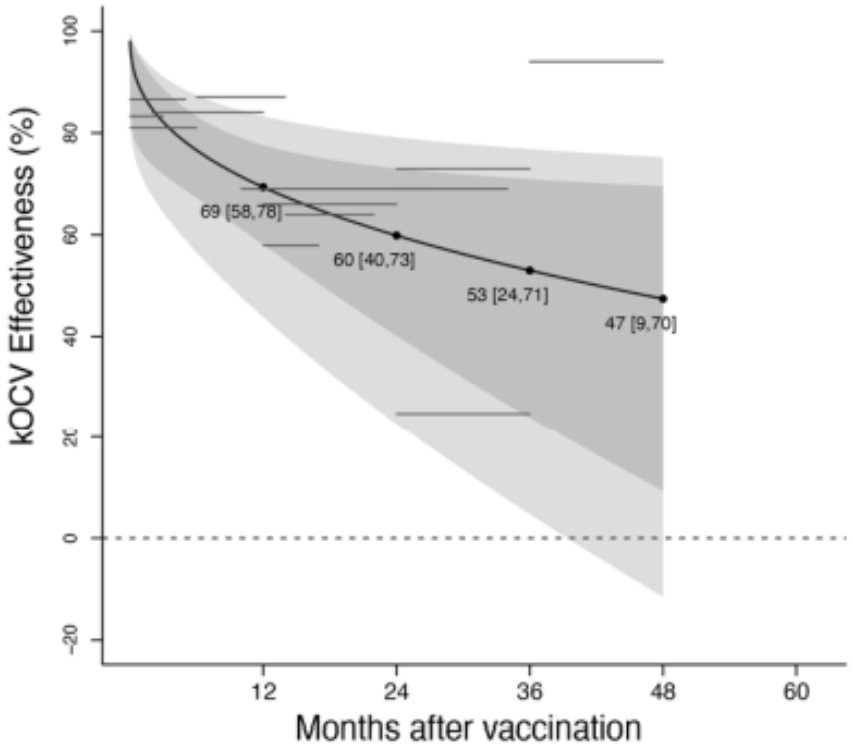
Understanding the population-level impact of mass vaccination campaigns against cholera in Uvira, DRC

Dr. Judith Bouman, University of Bern, Switzerland, Judith.bouman@unibe.ch

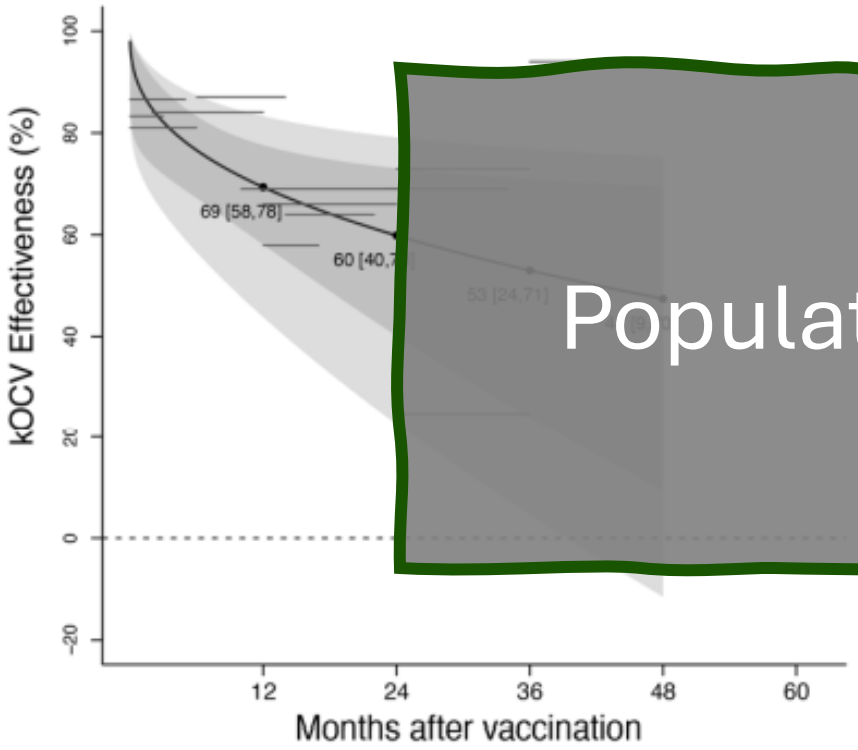
Direct effectiveness Oral Cholera Vaccine (OCV)



Xu et al. (2024). MedRxiv

- Effective, but effect wanes in time
- Increasingly used in outbreaks and as preventive measure, but supply does not meet demand

Direct effectiveness Oral Cholera Vaccine (OCV)

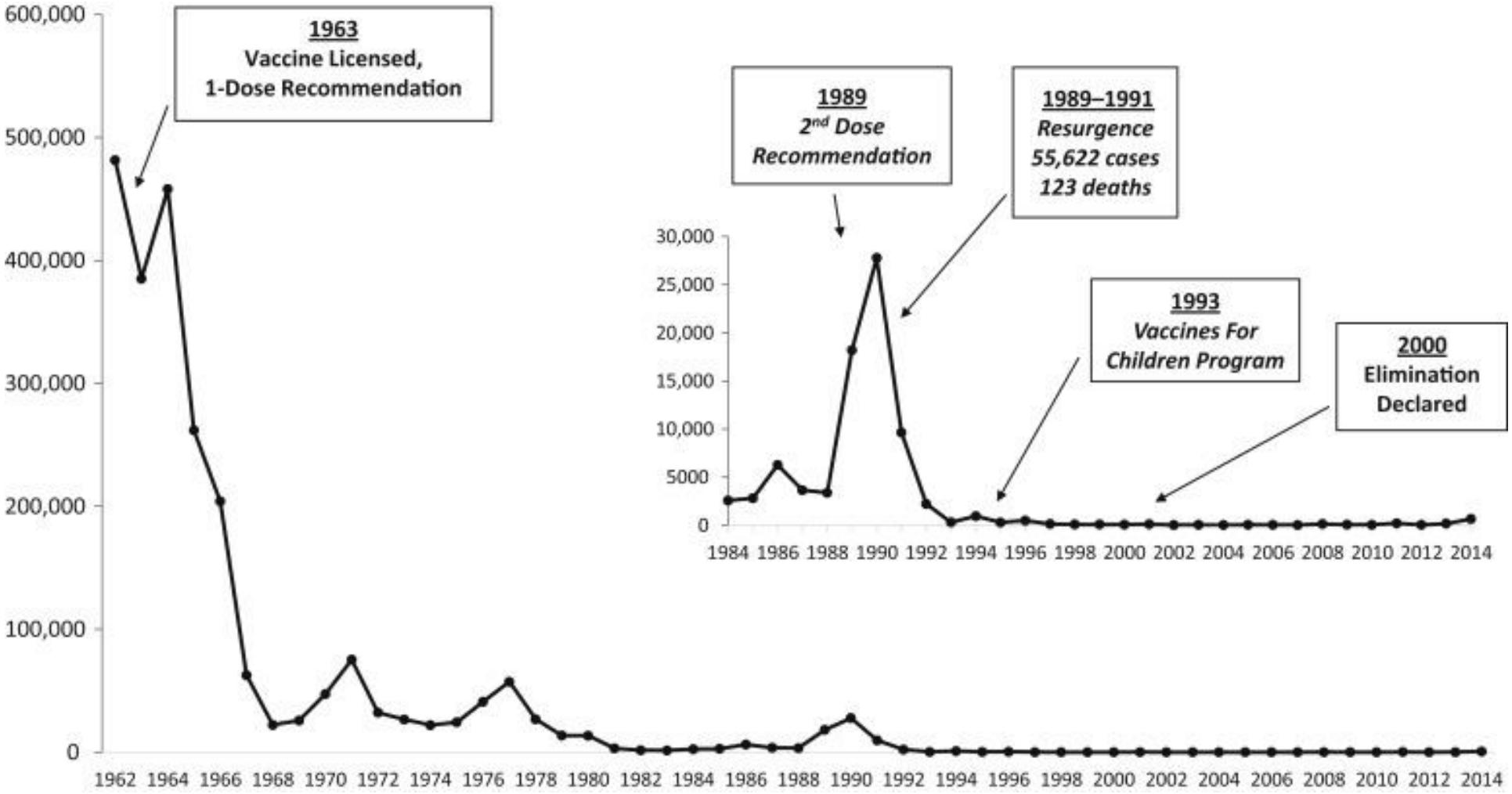


Xu et al. (2024). MedRxiv

- Effective, but effect wanes in time
- Increasingly used in outbreaks and as preventive measure, but supply does not always meet demand

Population level impact?

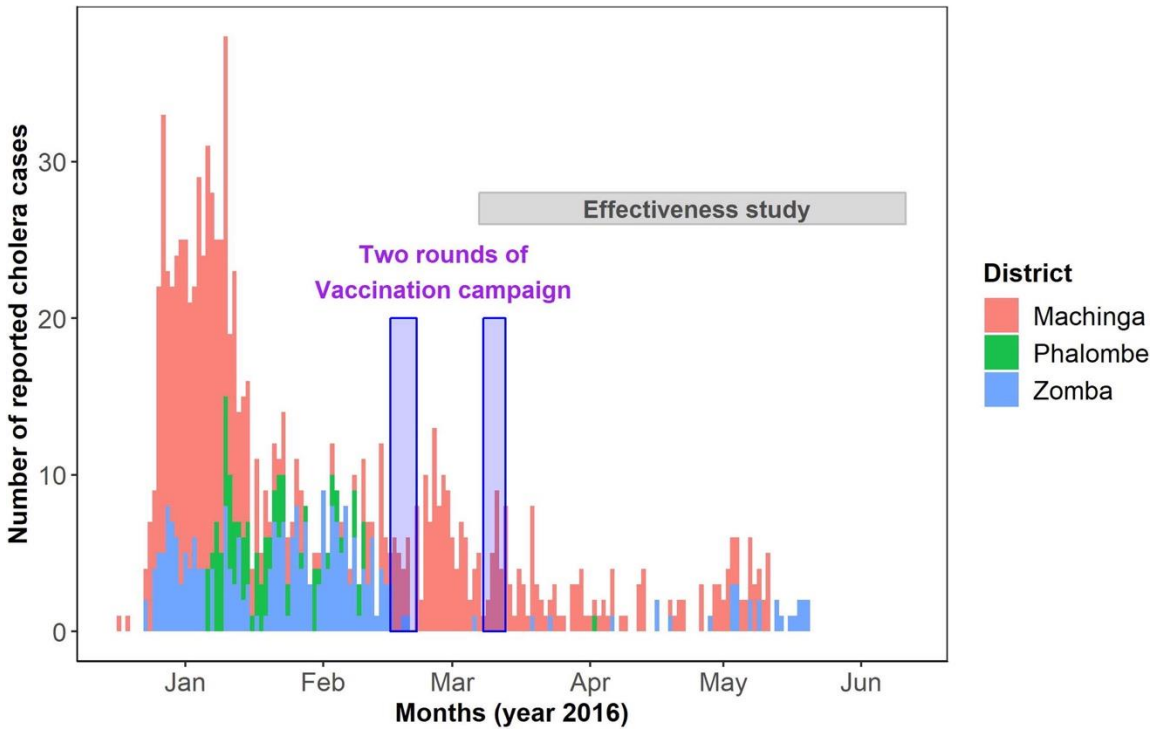
Vaccine impact: Measles in the USA



Goodson & Seward (2015). *Infectious Disease Clinics*

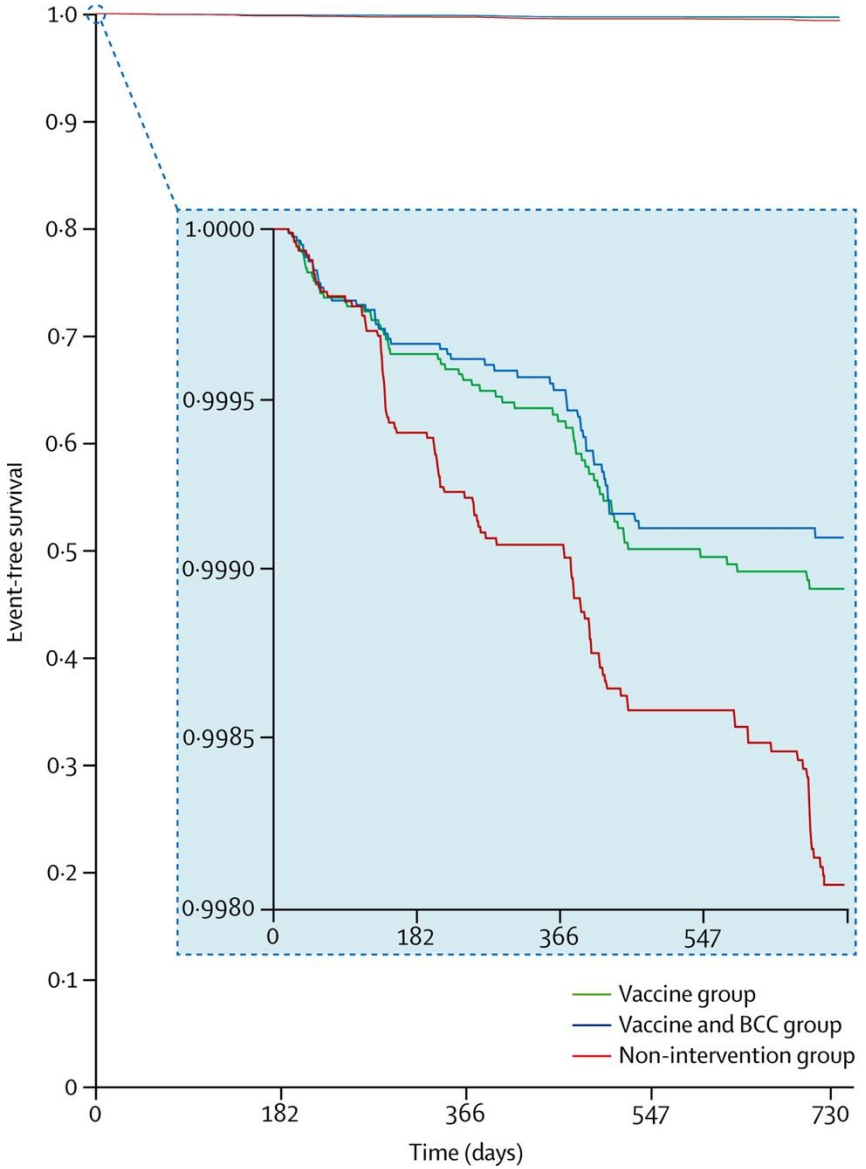
Population level impact?

Malawi



Grandesso et al. (2019). *Vaccine*

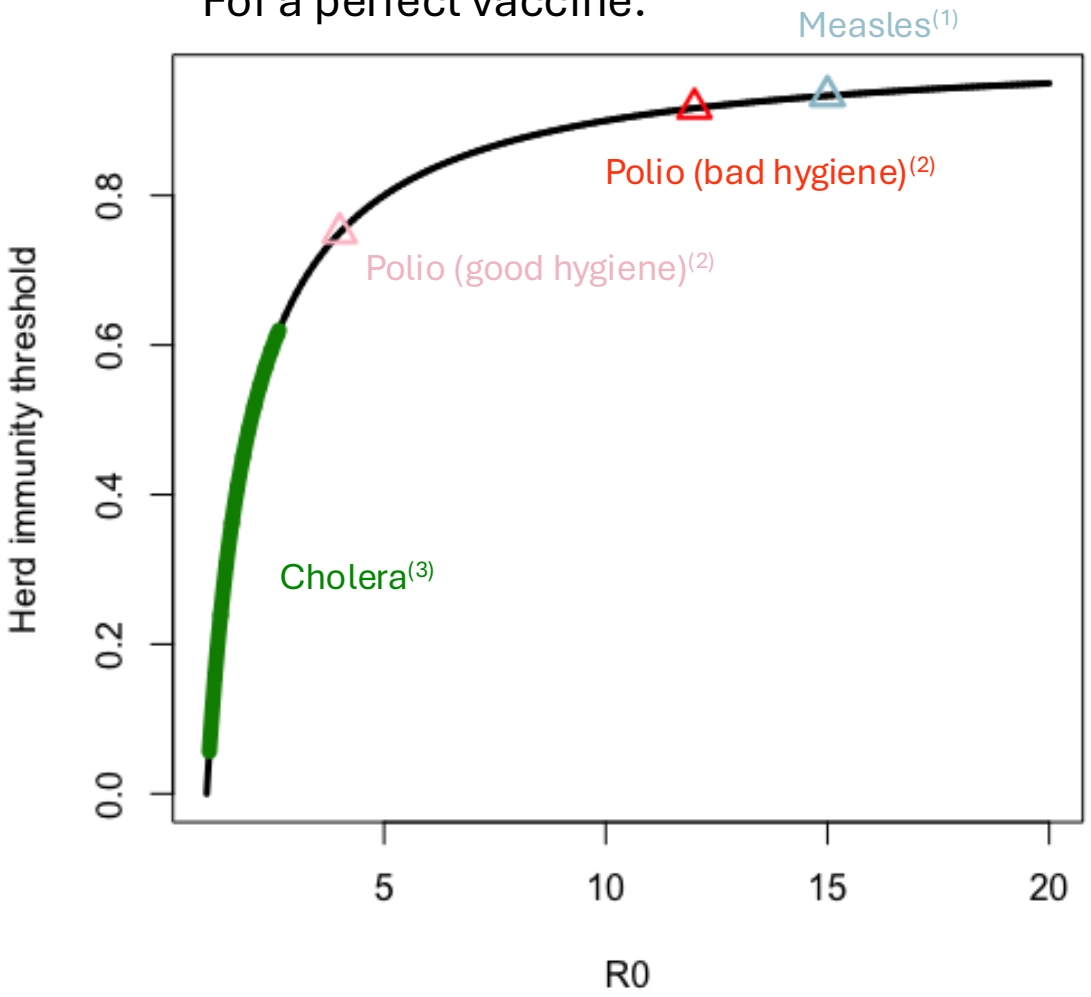
Bangladesh



Qadri et al. (2015). *The Lancet*

Expected vaccine impact based on R_0

For a perfect vaccine:

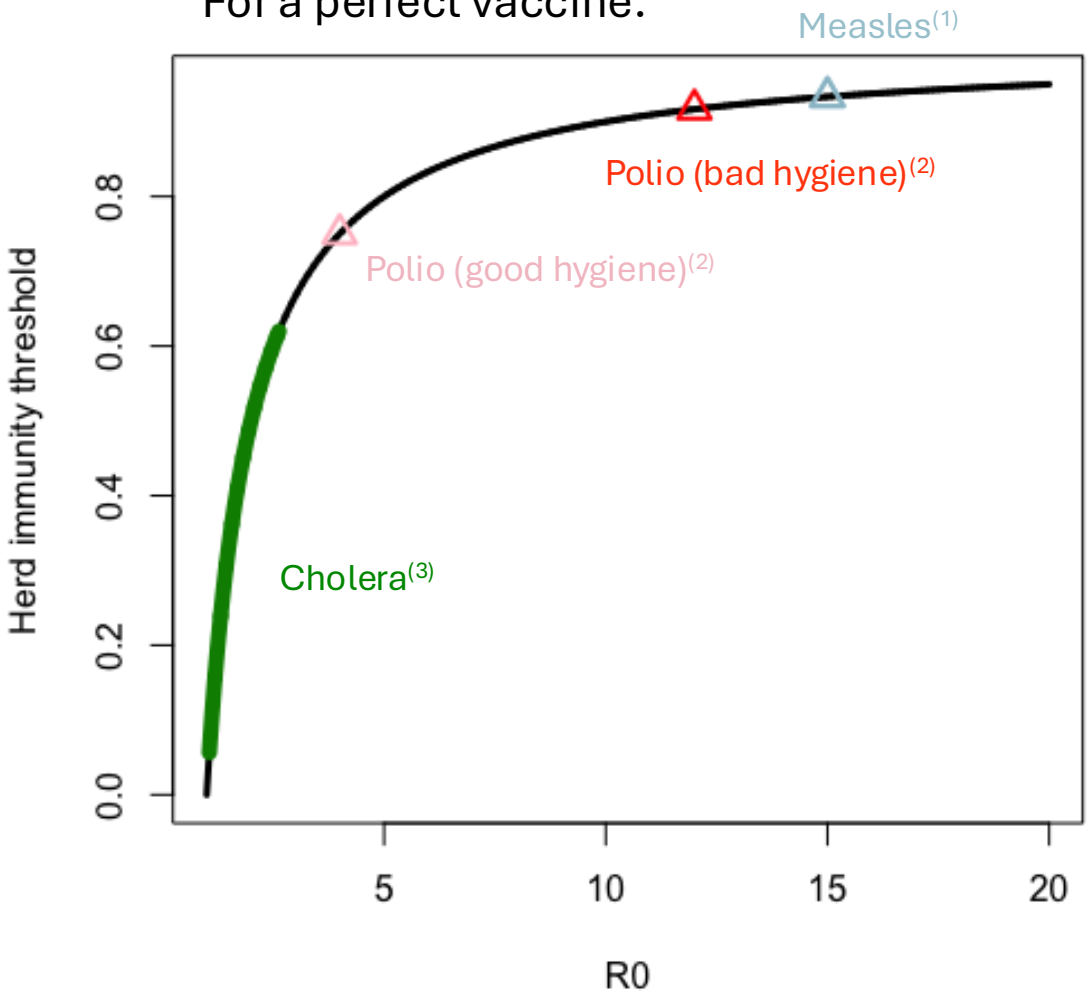


Herd immunity threshold = 1 - $\frac{1}{R_0}$ (4)

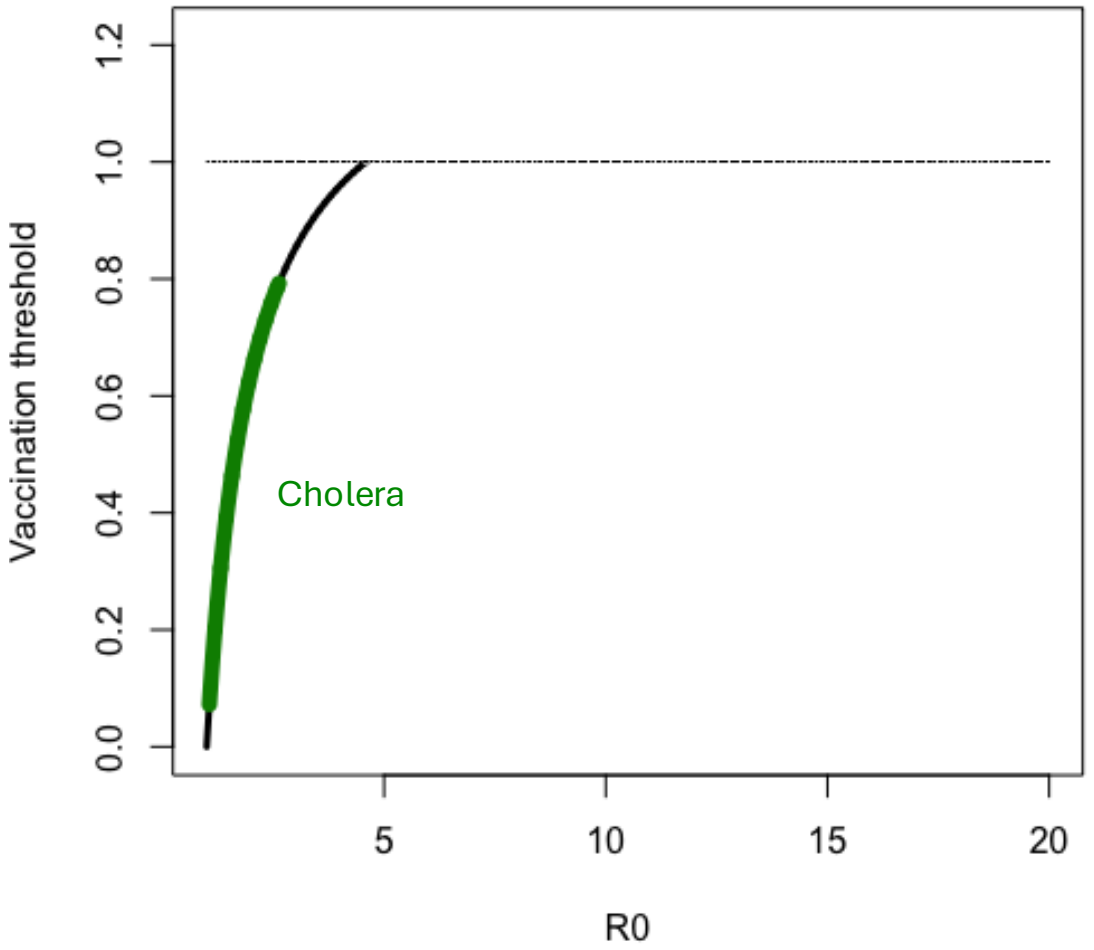
(1) Guerra et al. (2017). *The Lancet Infectious Diseases*
(2) Fine and Carneiro (1999). *American journal of epidemiology*
(3) Zindoga et al. (2013). *Scientific reports*
(4) Diekmann, Heesterbeek & Britton (2013). *Princeton series in theoretical and computational biology*

Expected vaccine impact based on R_0

For a perfect vaccine:



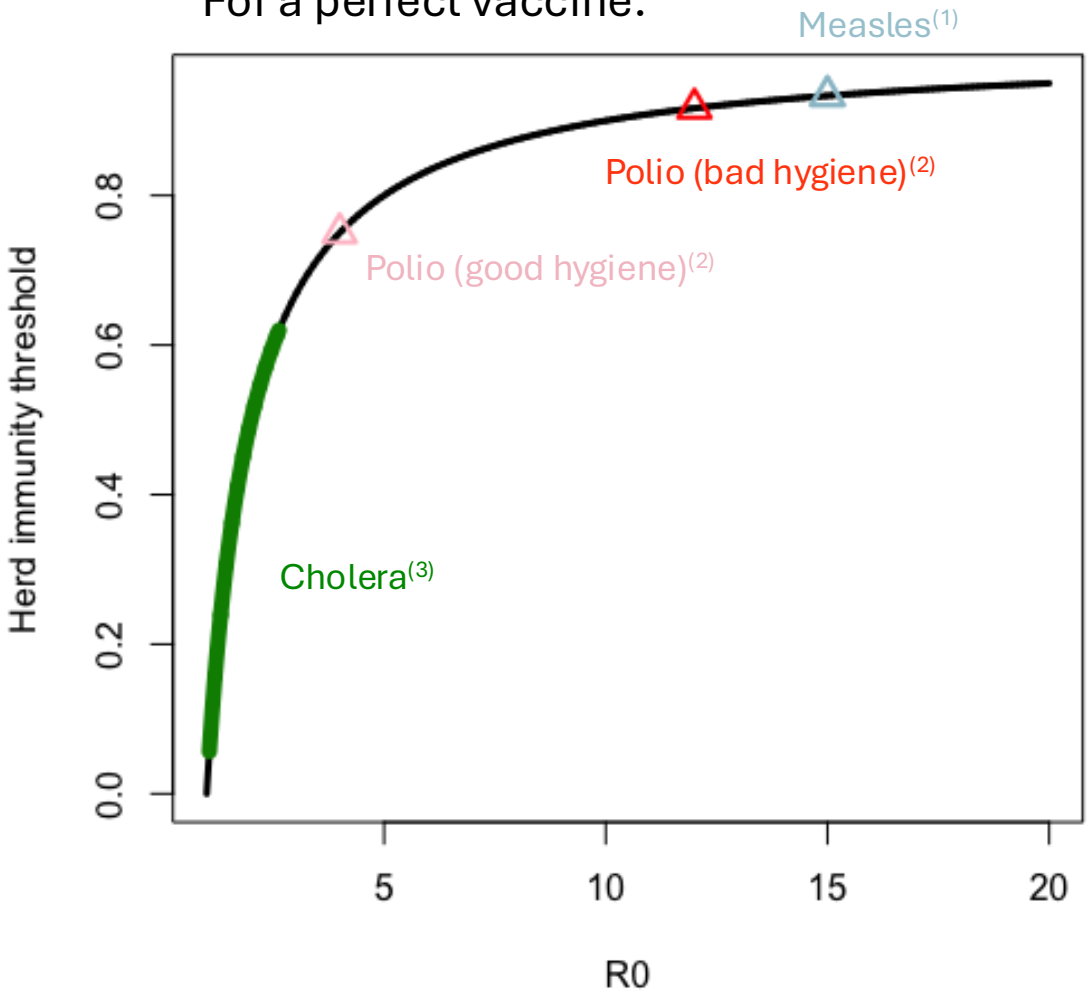
Corrected for estimated vaccine effectiveness:



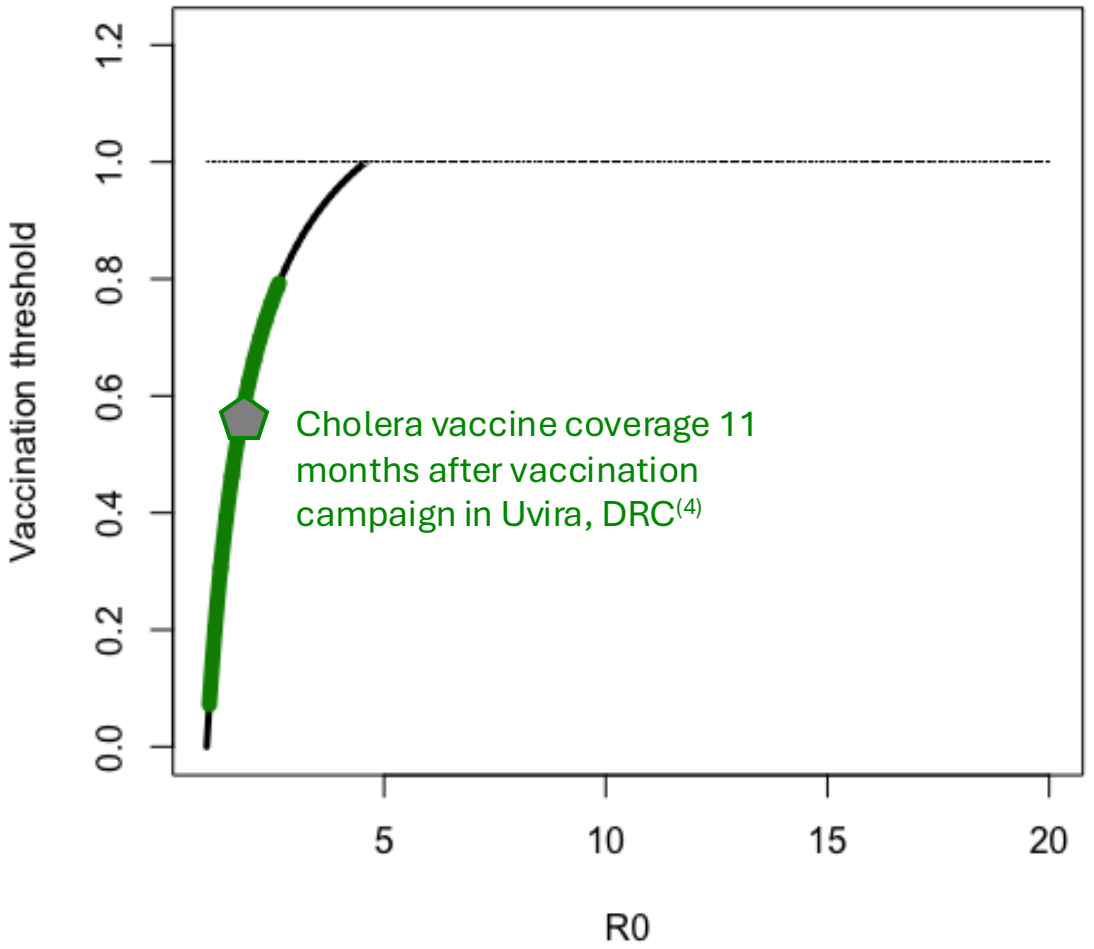
(1) Guerra et al. (2017). *The Lancet Infectious Diseases*
(2) Fine and Carneiro (1999). *American journal of epidemiology*
(3) Zindoga et al. (2013). *Scientific reports*

Expected vaccine impact based on R_0

For a perfect vaccine:

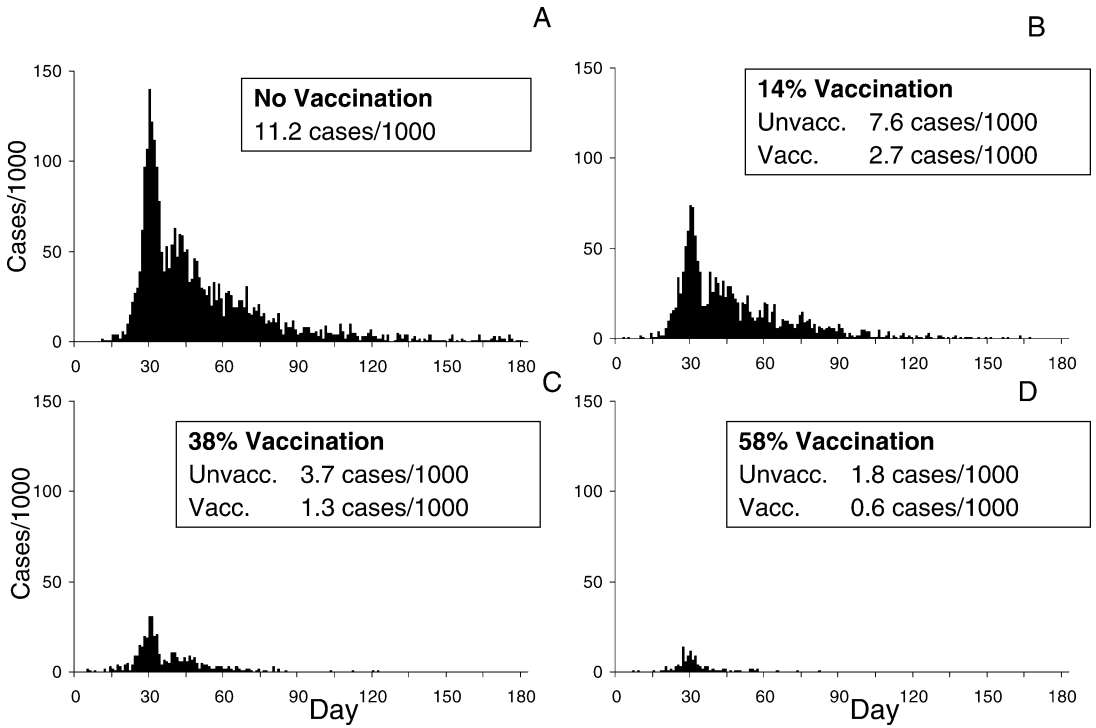


Corrected for estimated vaccine effectiveness:



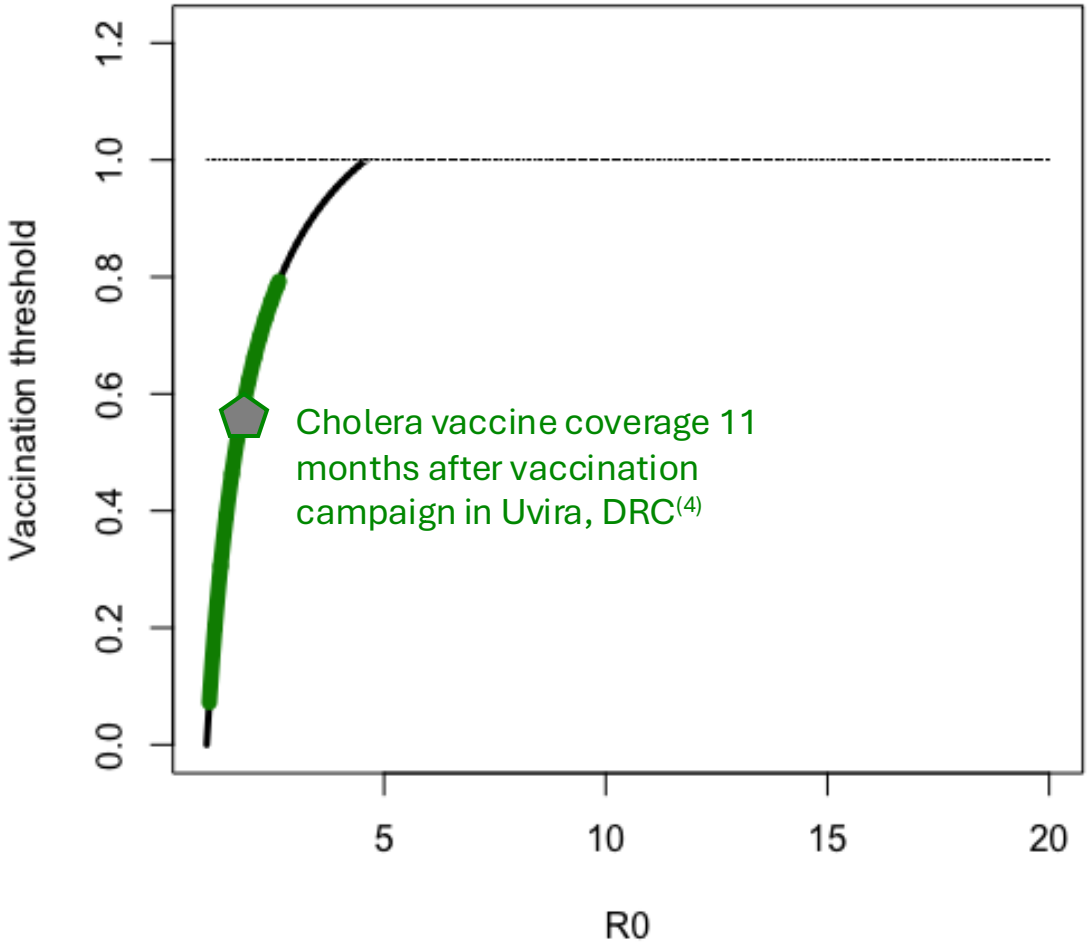
(1) Guerra et al. (2017). *The Lancet Infectious Diseases*
(2) Fine and Carneiro (1999). *American journal of epidemiology*
(3) Zindoga et al. (2013). *Scientific reports*
(4) Koyuncu et al. (2024). *OSF preprints*

Expected vaccine impact based on R_0



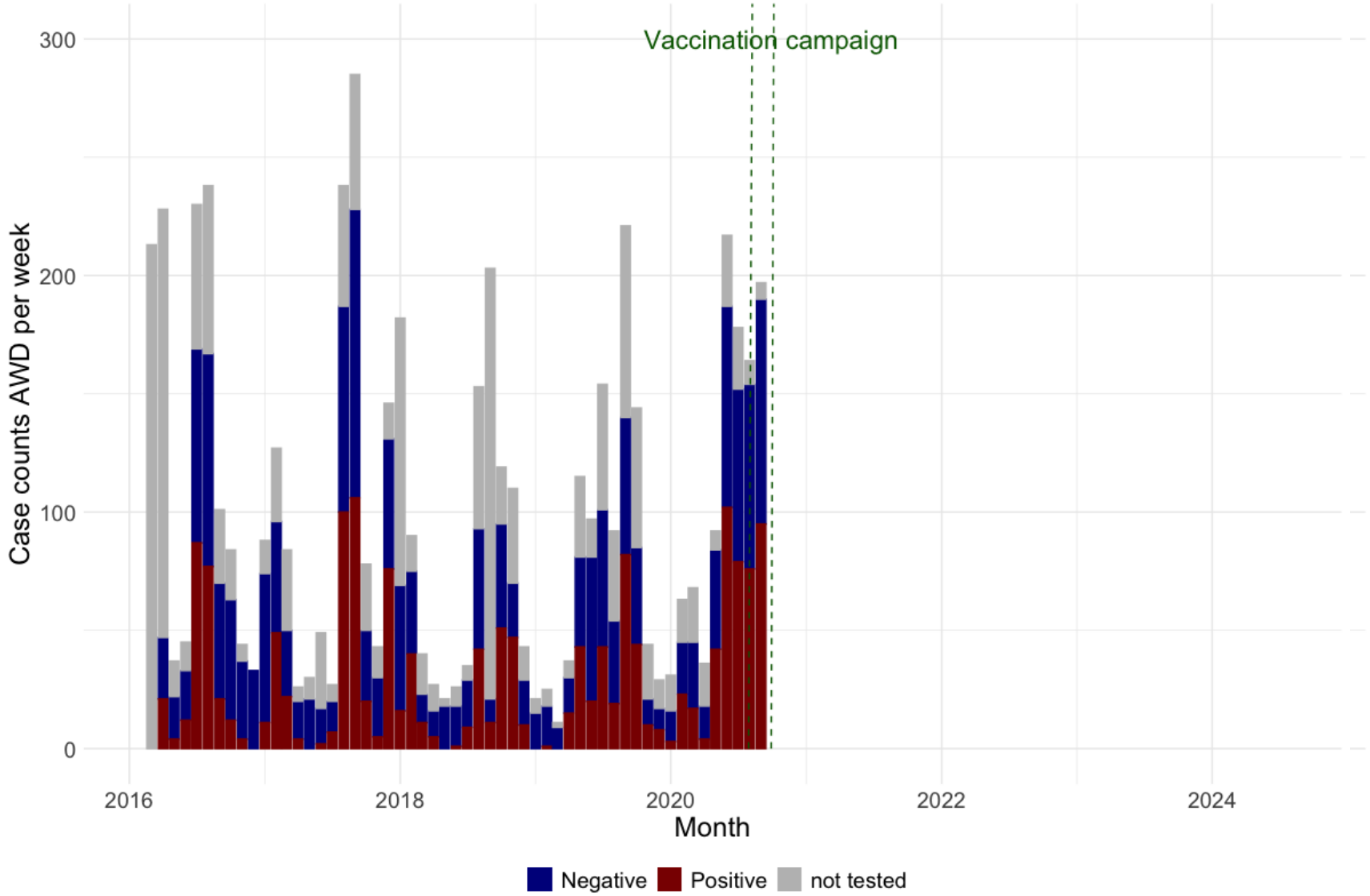
(1) Longini et al. (2007). *PLOS medicine*

Corrected for estimated vaccine effectiveness:

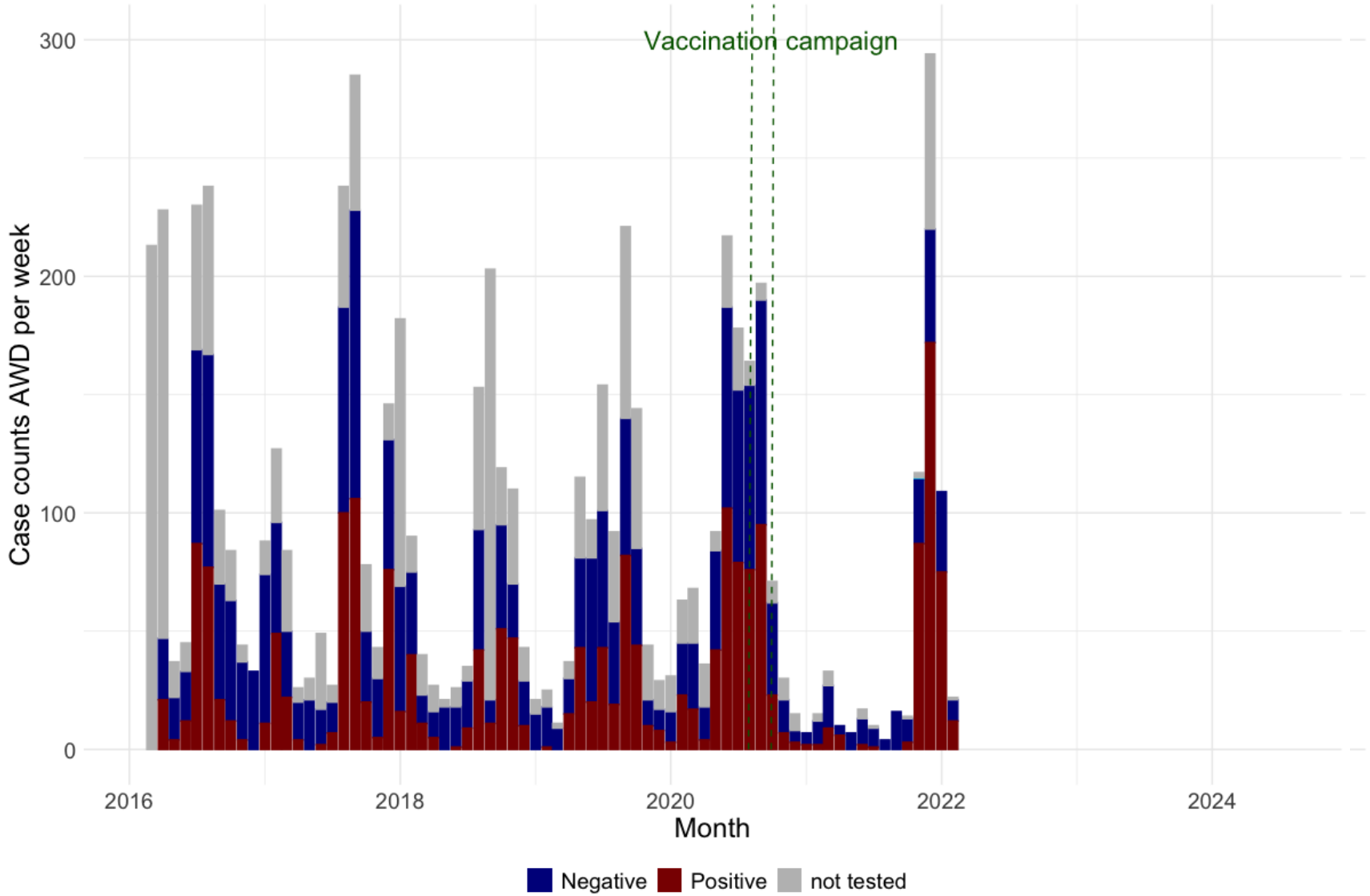


(2) Koyuncu et al. (2024). *OSF preprints*

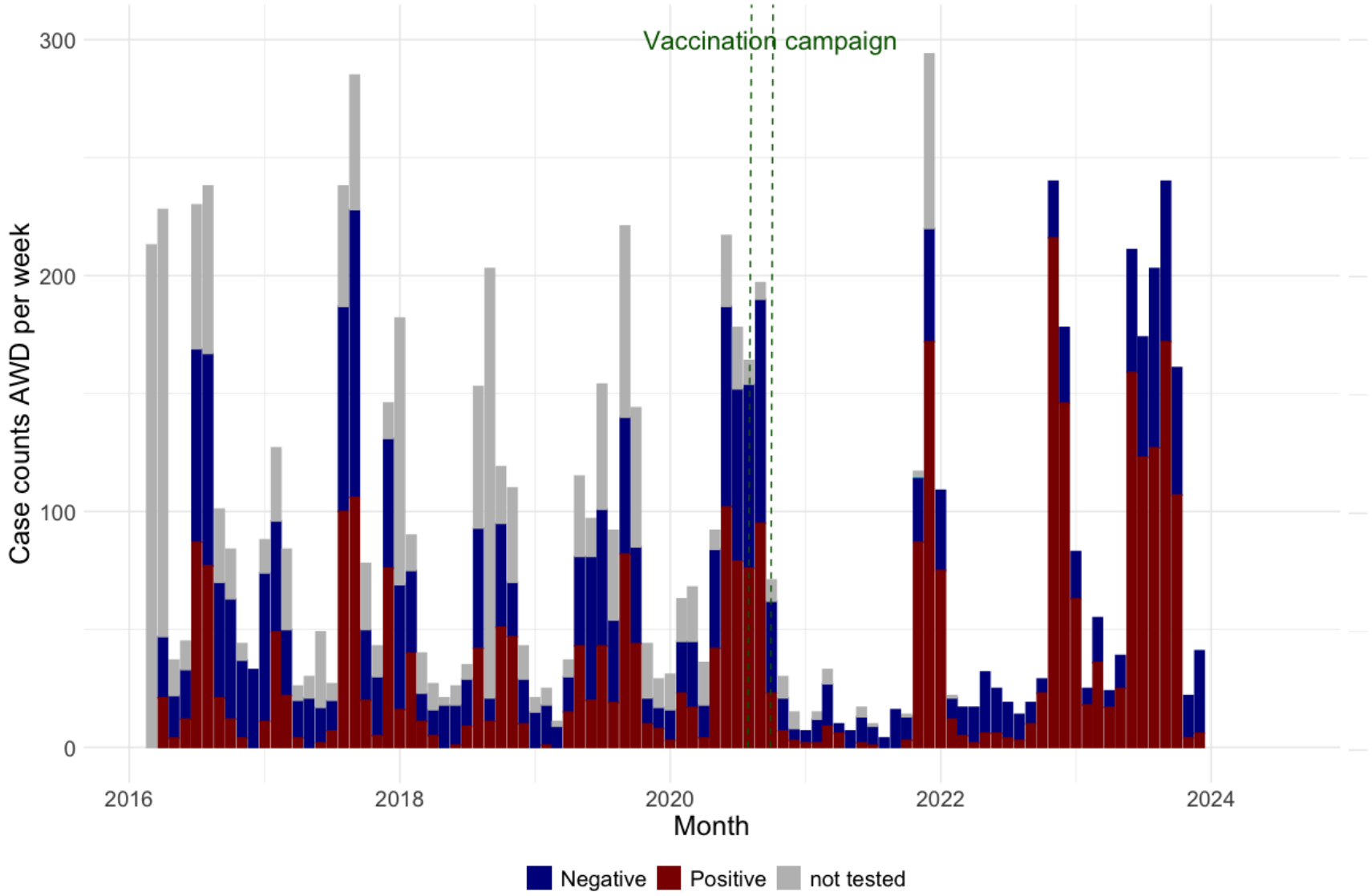
Initial reduction after vaccination



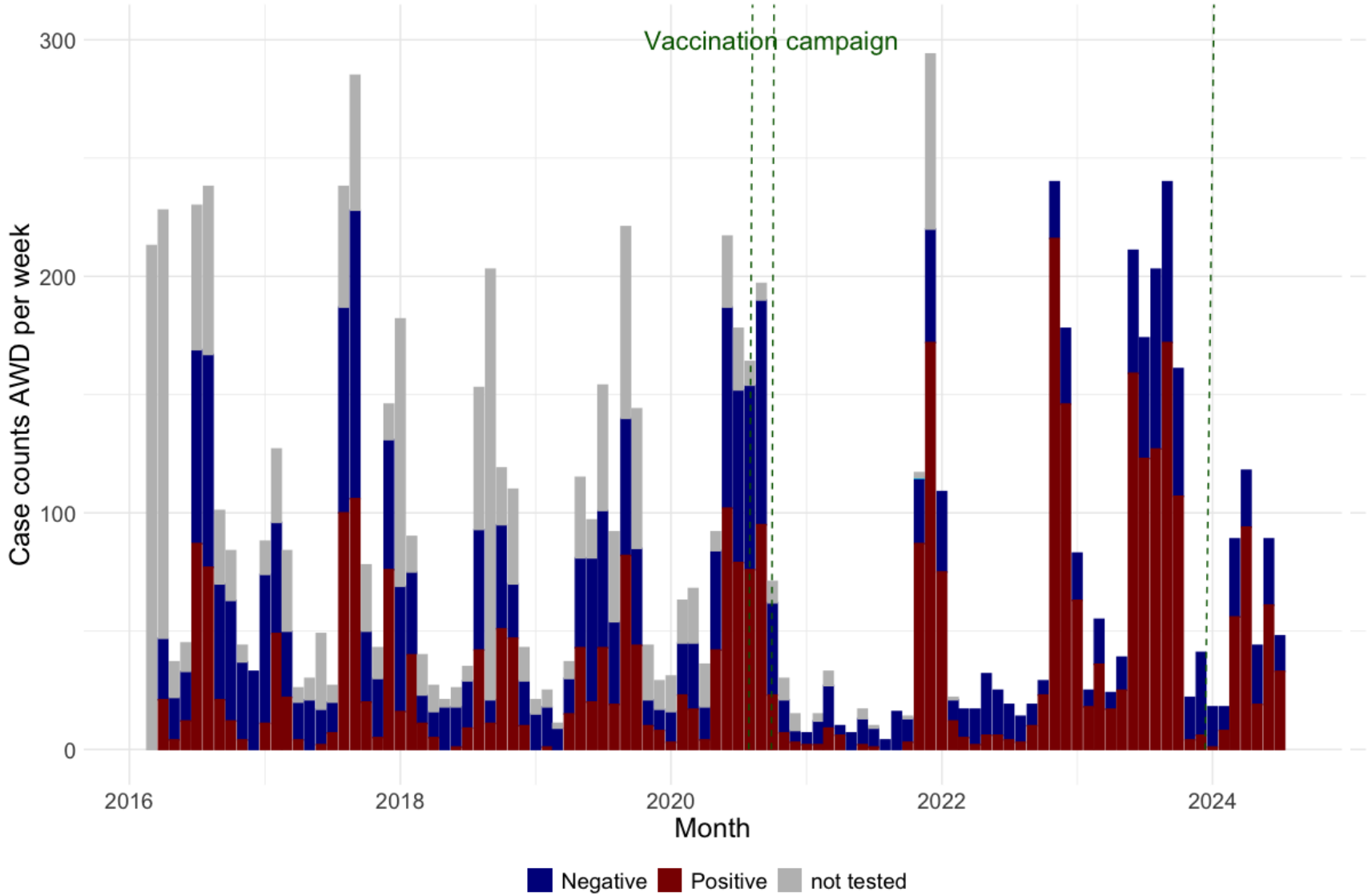
Large outbreak



Persistent transmission



Additional vaccination end of 2023



Main objectives

- **To estimate the number of symptomatic cases and infections prevented by the 2020 mass vaccination campaign**

- To describe changes in transmission dynamics of pandemic *V. cholerae* O1 in Uvira after the vaccination

Main objectives

- **To estimate the number of symptomatic cases and infections prevented by the 2021 vaccination campaign**

Requires modelling

- To describe changes in transmission dynamics of pandemic *V. cholerae* O1 in Uvira after the vaccination

Main objectives

- **To estimate the number of symptomatic cases and infections prevented by the 2021 vaccination campaign**

- To describe changes in transmission dynamics of pandemic *V. cholerae* O1 in Uvira after the vaccination

Requires modelling

Models need adequate data

Main objectives

- **To estimate the number of symptomatic cases and infections prevented by the 2021 vaccination campaign**
- To describe changes in transmission dynamics of pandemic *V. cholerae* O1 in Uvira after the vaccination

Requires modelling

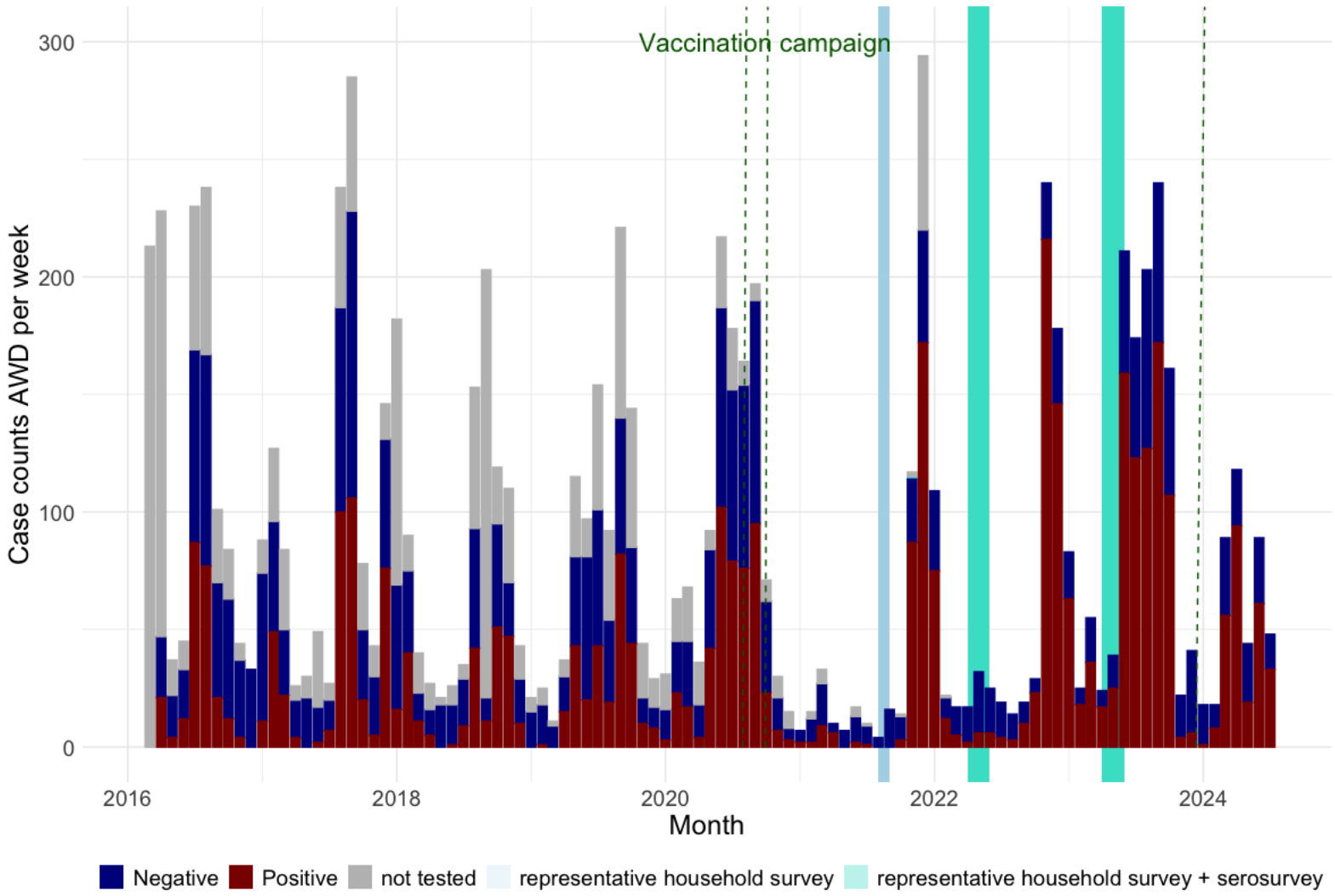
Models need adequate data

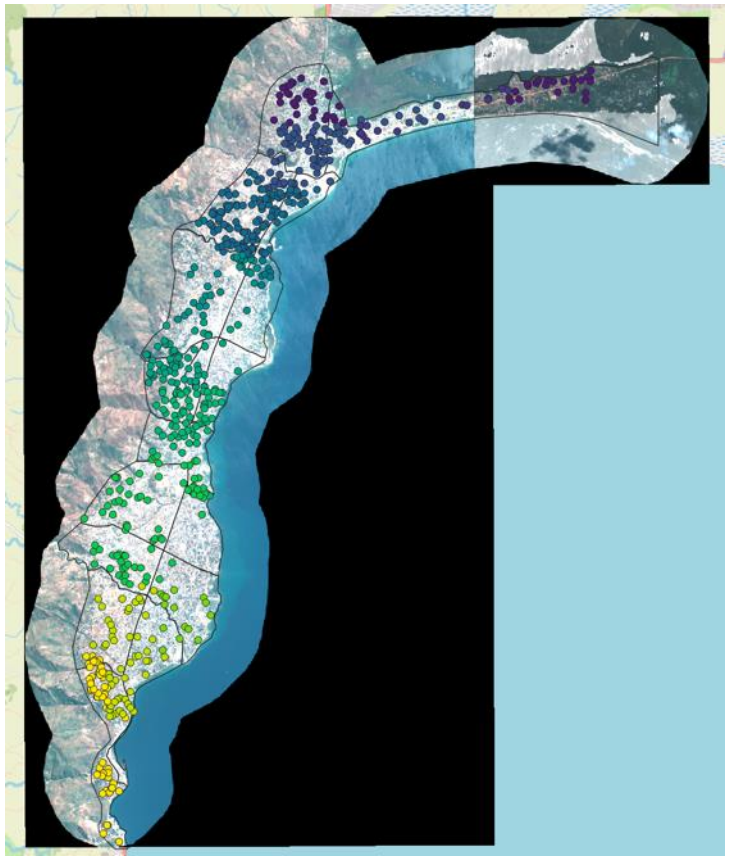
Unique setting in Uvira provides these data

Data from Uvira provides unique opportunity

Build testing capacity in Uvira for systematic AWD testing

Data from Uvira provides unique opportunity





Selection of households for serosurvey

Data from Uvira provides unique opportunity

Systematic testing

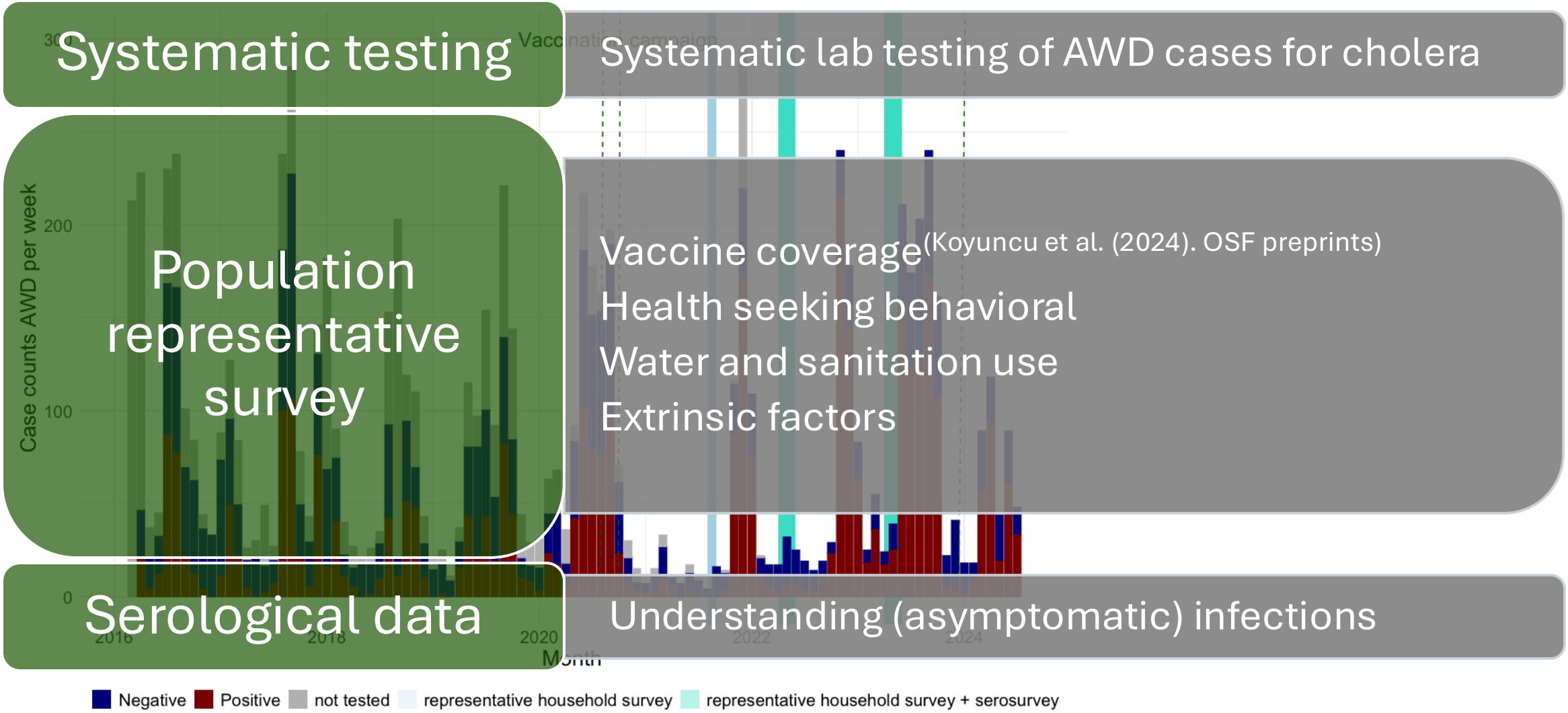
Systematic lab testing of AWD cases for cholera

Population representative survey

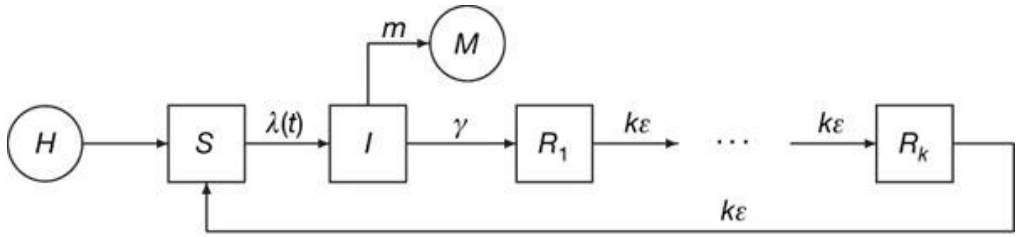
Vaccine coverage (Koyuncu et al. (2024). OSF preprints)
Health seeking behavioral
Water and sanitation use
Extrinsic factors

Serological data

Understanding (asymptomatic) infections



Past cholera modelling

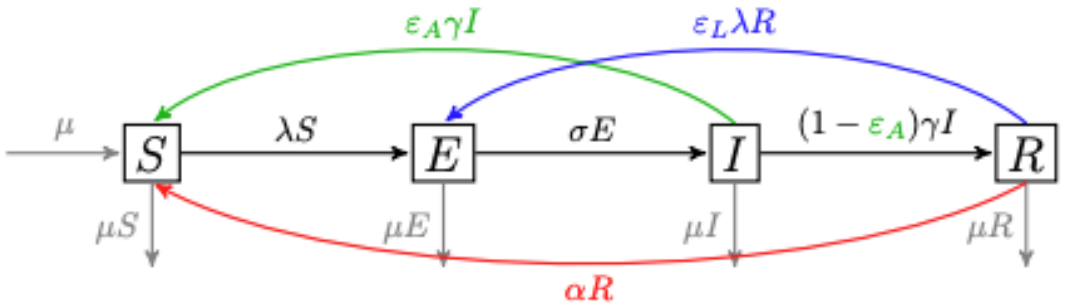


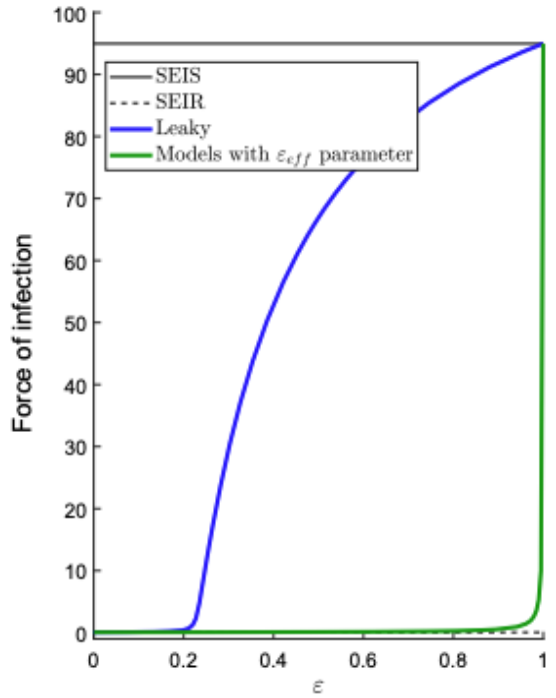
King et al. (2008). *Nature*

—Exponential waning

—All-or-nothing

—Leaky





Force of infection for $R_0 \approx 4.4$

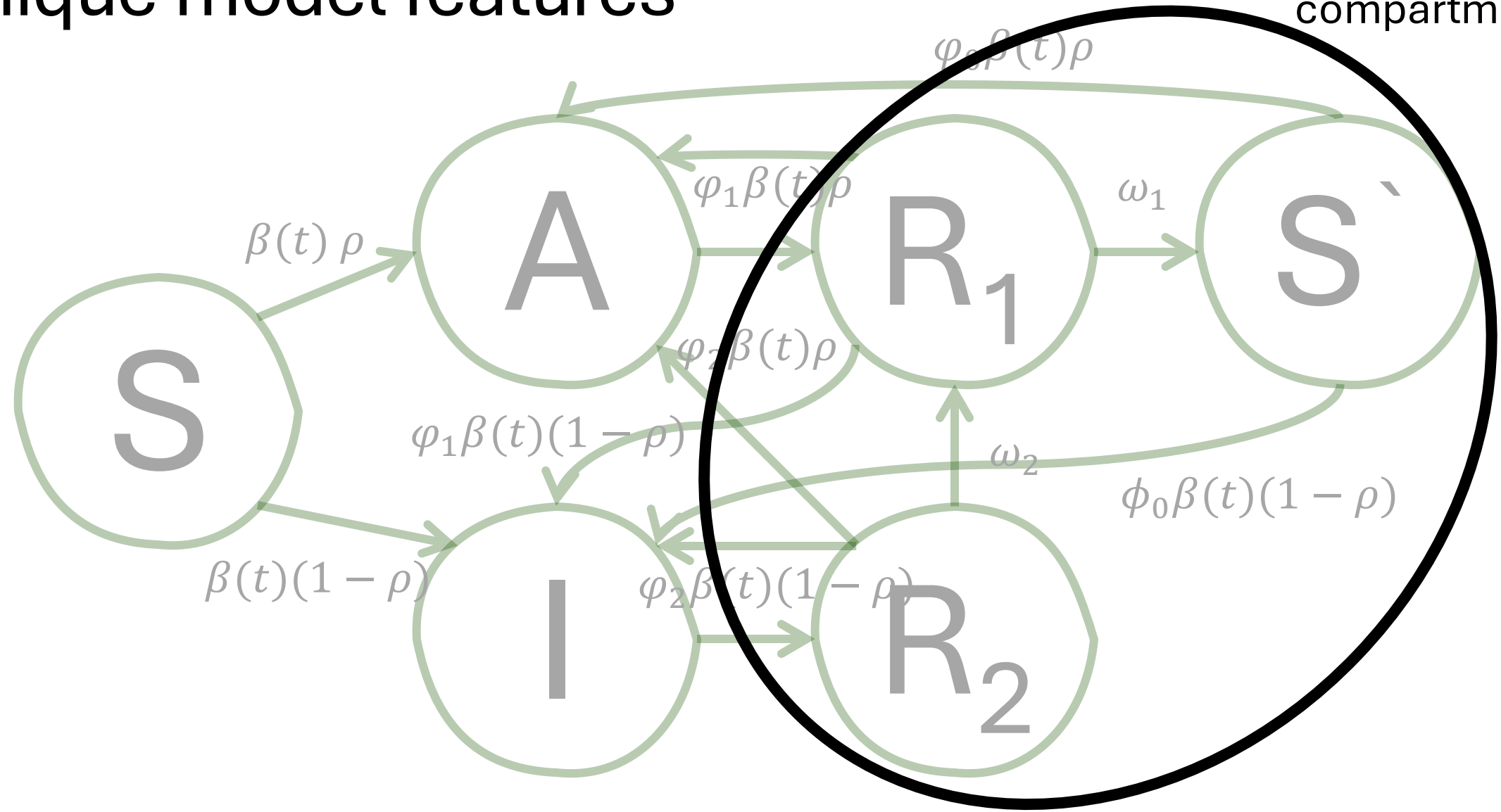
Le et al. (2021). *Journal of Mathematical Biology*

Key model features

Time-varying transmission	Incorporating all transmission dynamics: seasonality, rainfall, flooding, drought, etc.
Multiple immune compartments	King et al. (2008). *Nature*
Leaky immunity	Le et al. (2021). *Journal of Mathematical Biology*
Observation process	Correction for imperfect testing & care seeking behavior

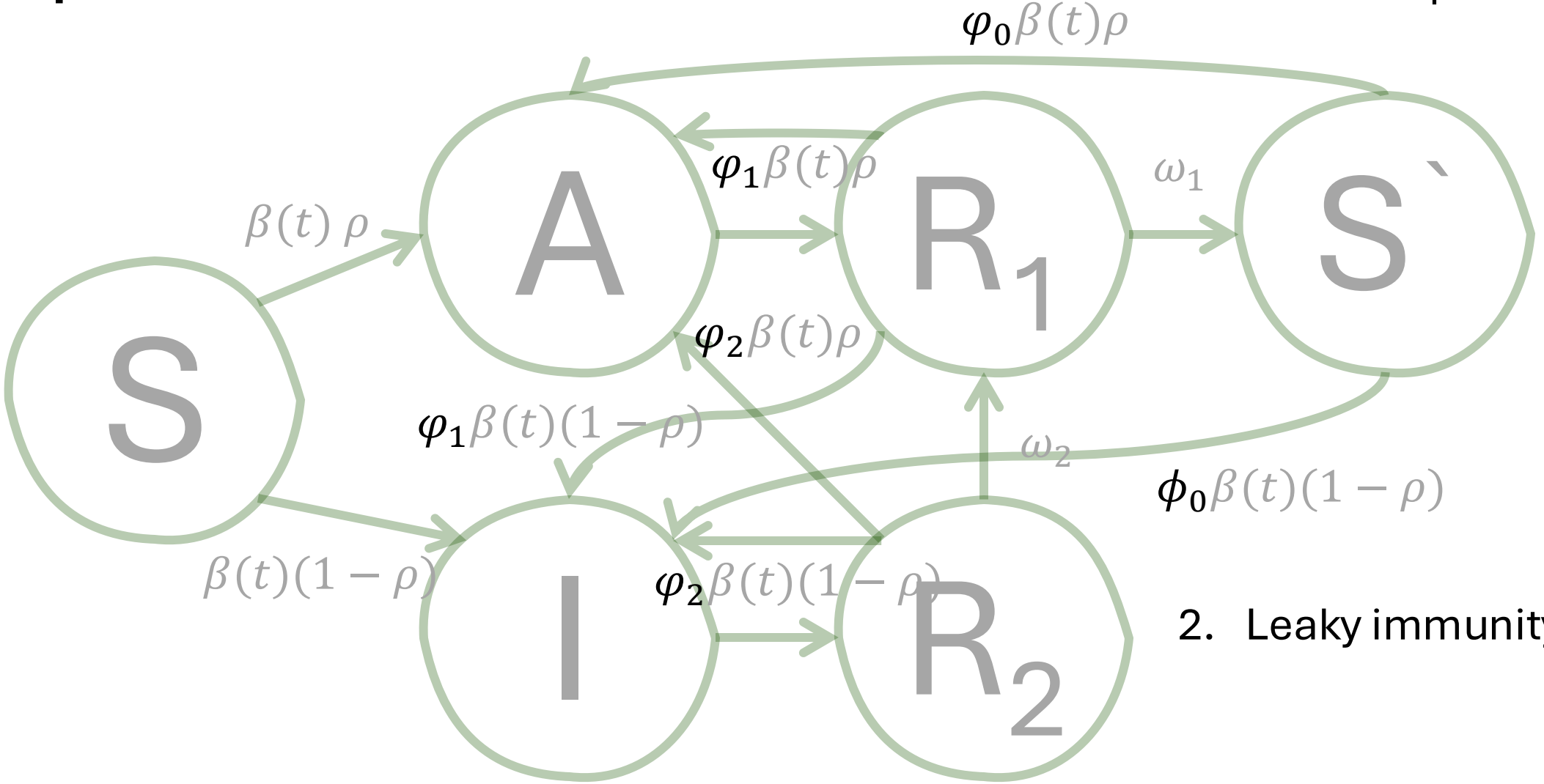
Unique model features

1. Different immune compartments



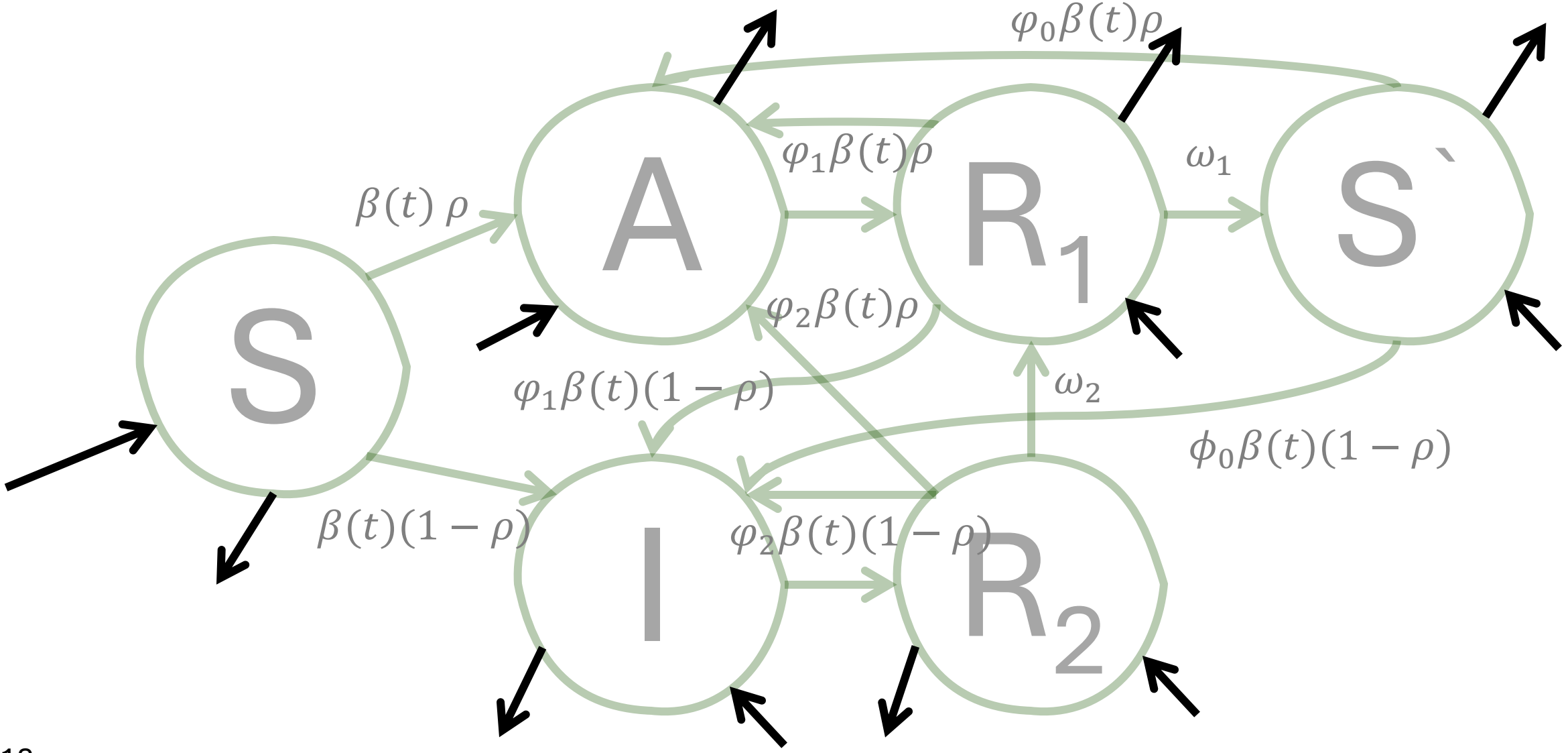
Unique model features

1. Different immune compartments

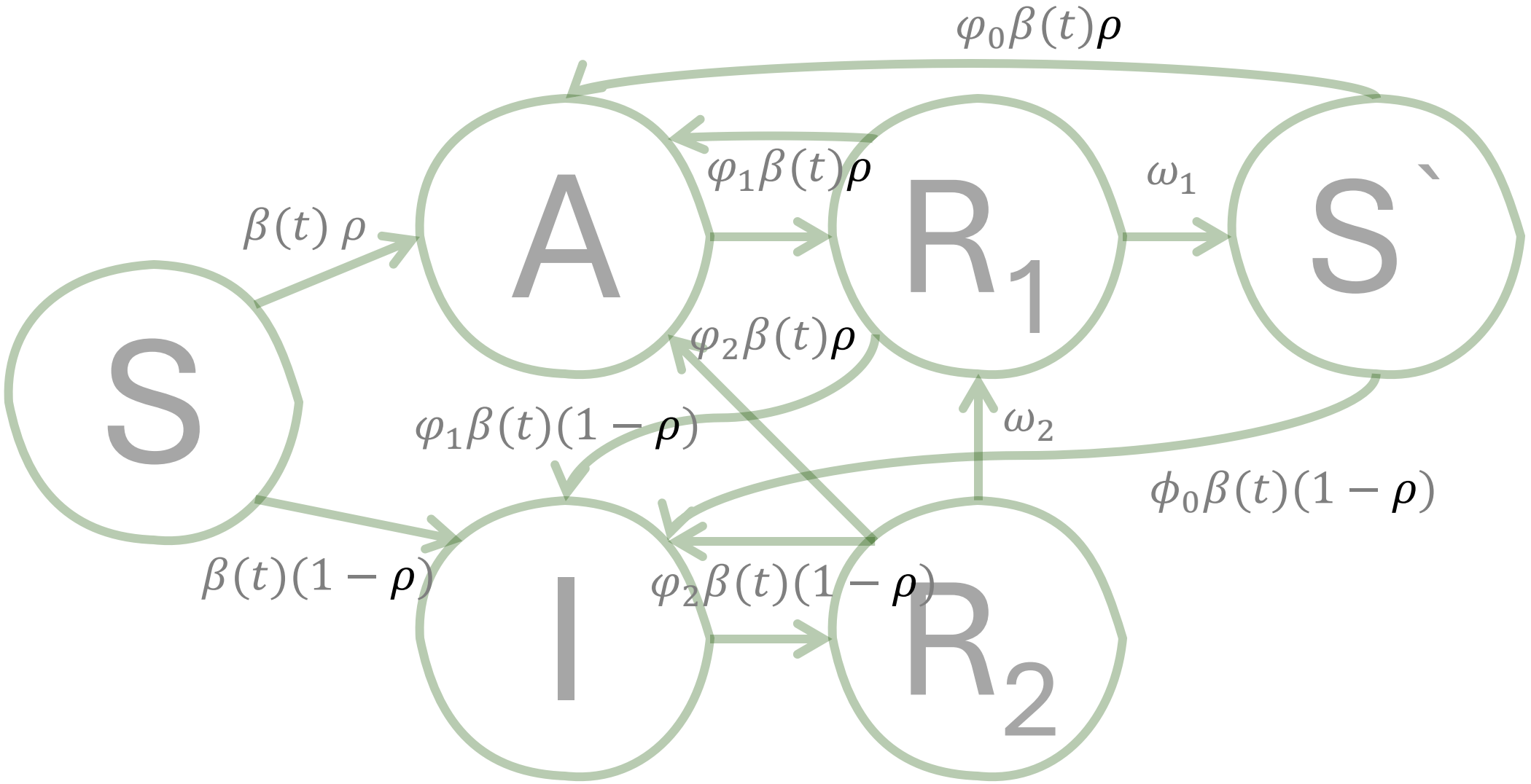


2. Leaky immunity

Vaccine coverage data – population dynamics

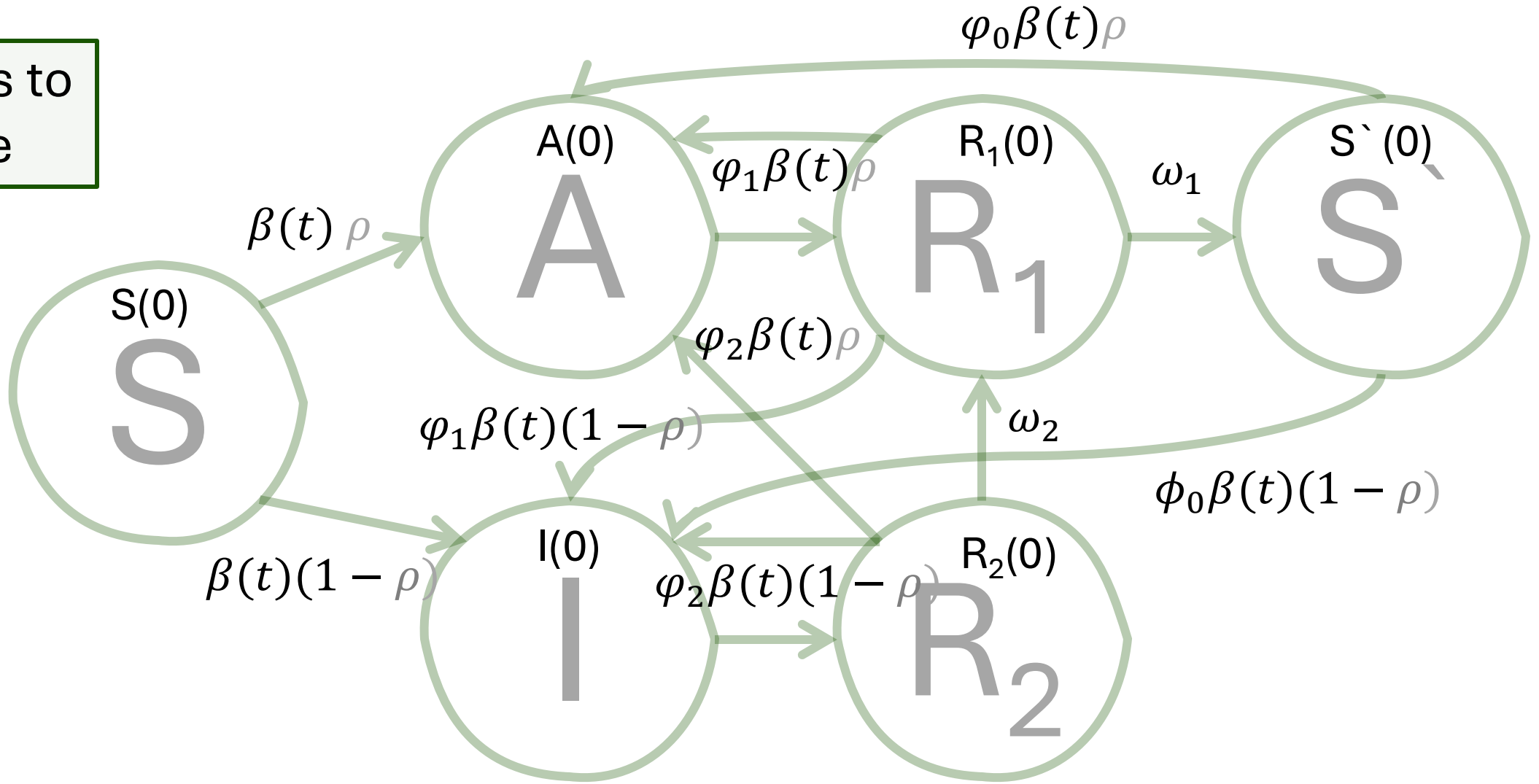


Seroprevalence data – fraction asymptomatic



Fitting model in Bayesian language STAN

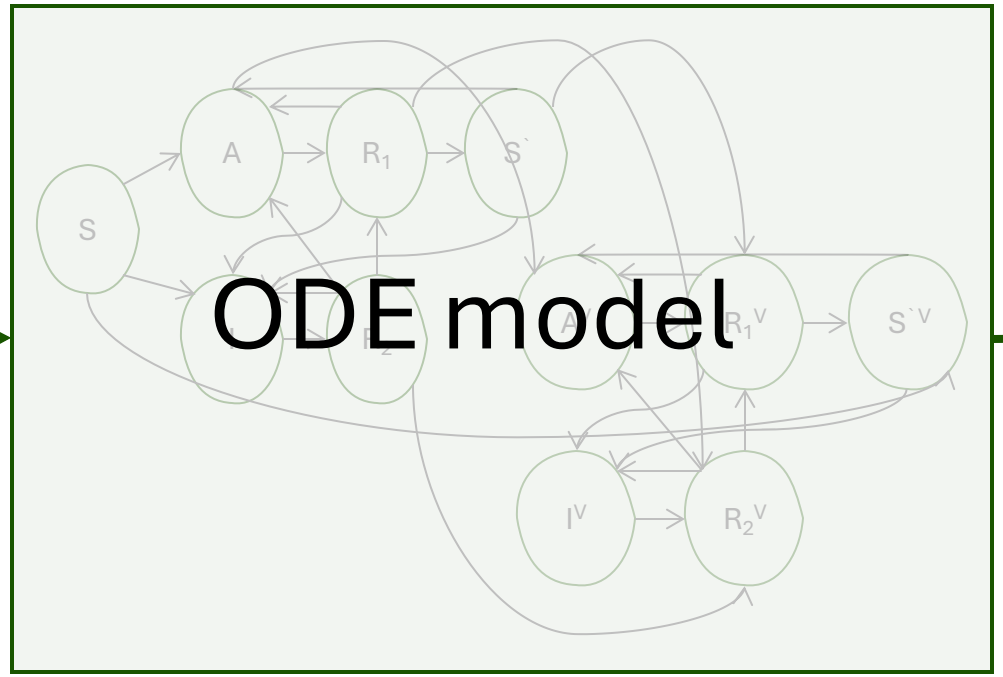
Parameters to estimate



Fitting model in Bayesian language STAN

Parameters to estimate

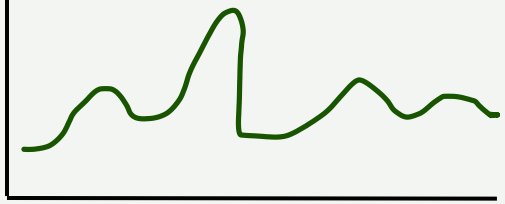
Value for fixed parameters



ODE model

Solving the ODE-system

Incidence curve observed **cholera cases**



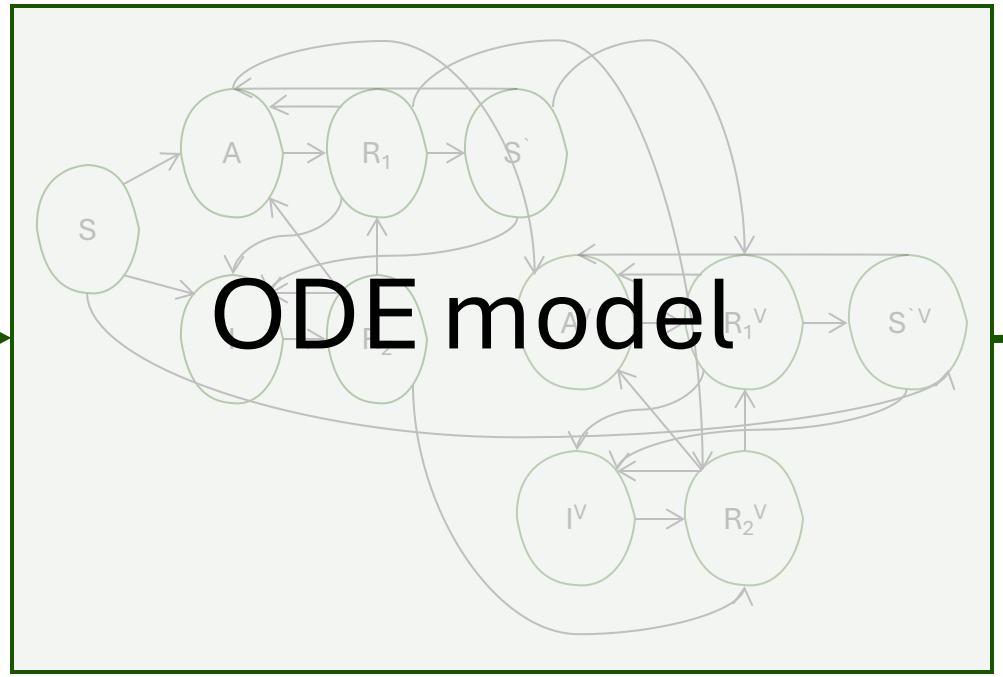
Observation process

- Health seeking behavior
- Correction for imperfect testing

Fitting model in Bayesian language STAN

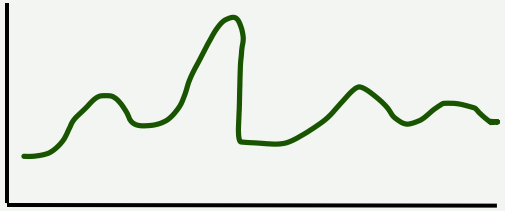
Parameters to estimate

Value for fixed parameters

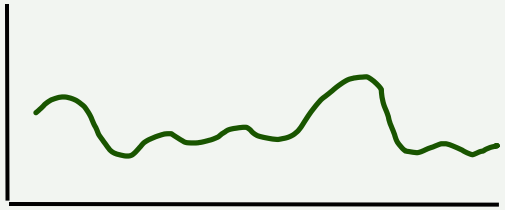


Solving the ODE-system

Incidence curve observed **Cholera cases**



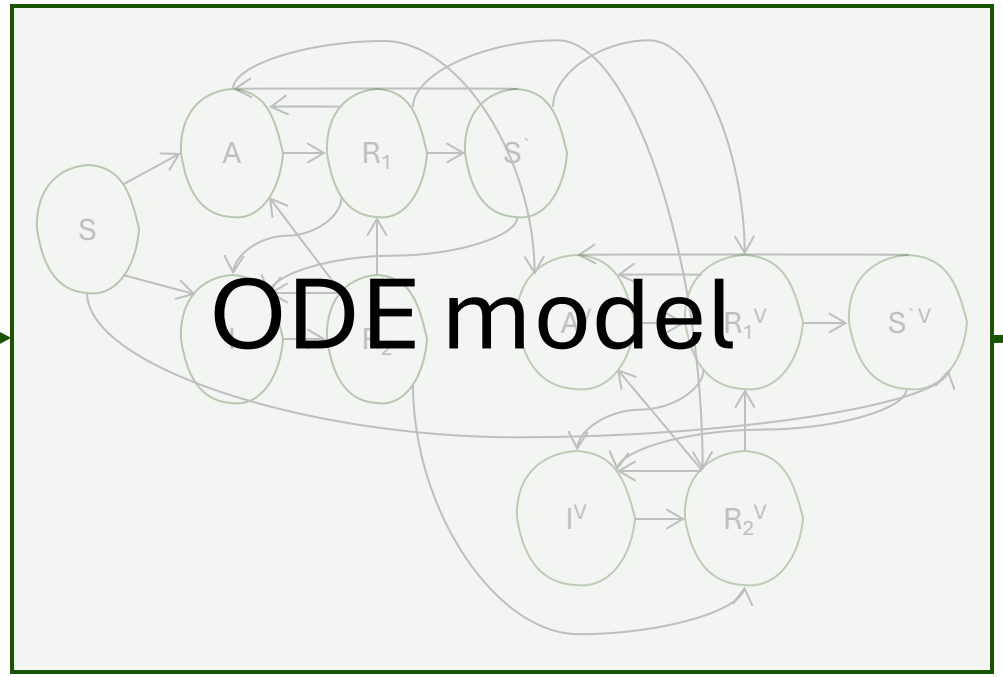
Independent **incidence** curve **non-cholera cases**



Fitting model in Bayesian language STAN

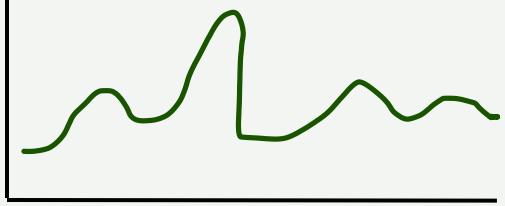
Parameters to estimate

Value for fixed parameters

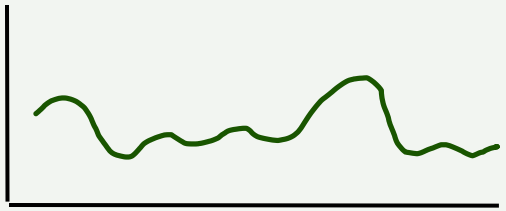


Solving the ODE-system

Incidence curve observed **cholera cases**



Independent **incidence** curve **non-cholera cases**



Calculate likelihood

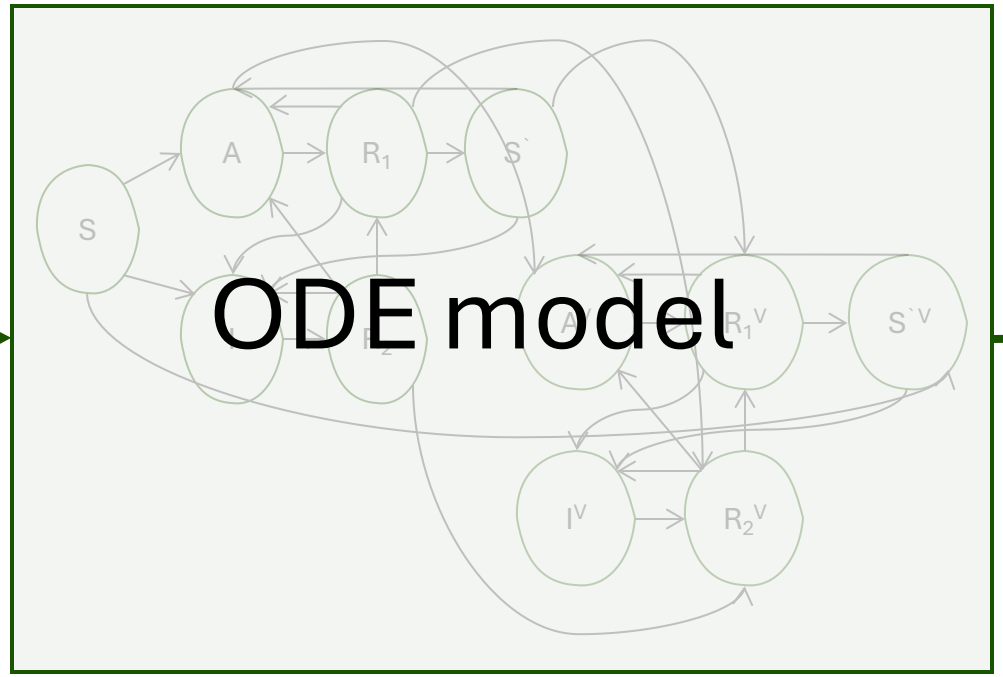
observed AWD incidence ~ Poisson(incidence cholera cases + incidence non cholera cases)

number of positive tests ~ binomial(number of tests performed, probability of positive RDT if AWD)

Fitting model in Bayesian language STAN

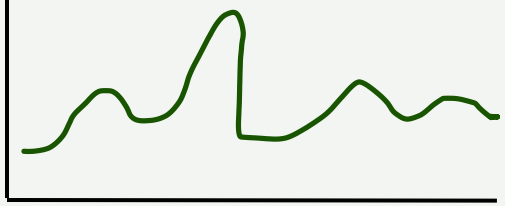
Parameters to estimate

Value for fixed parameters

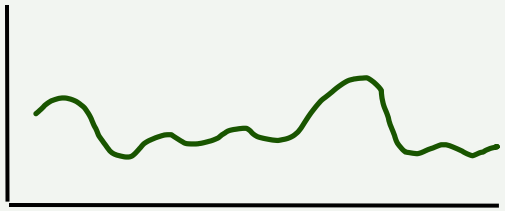


Solving the ODE-system

Incidence curve observed **cholera cases**



Independent **incidence** curve **non-cholera cases**



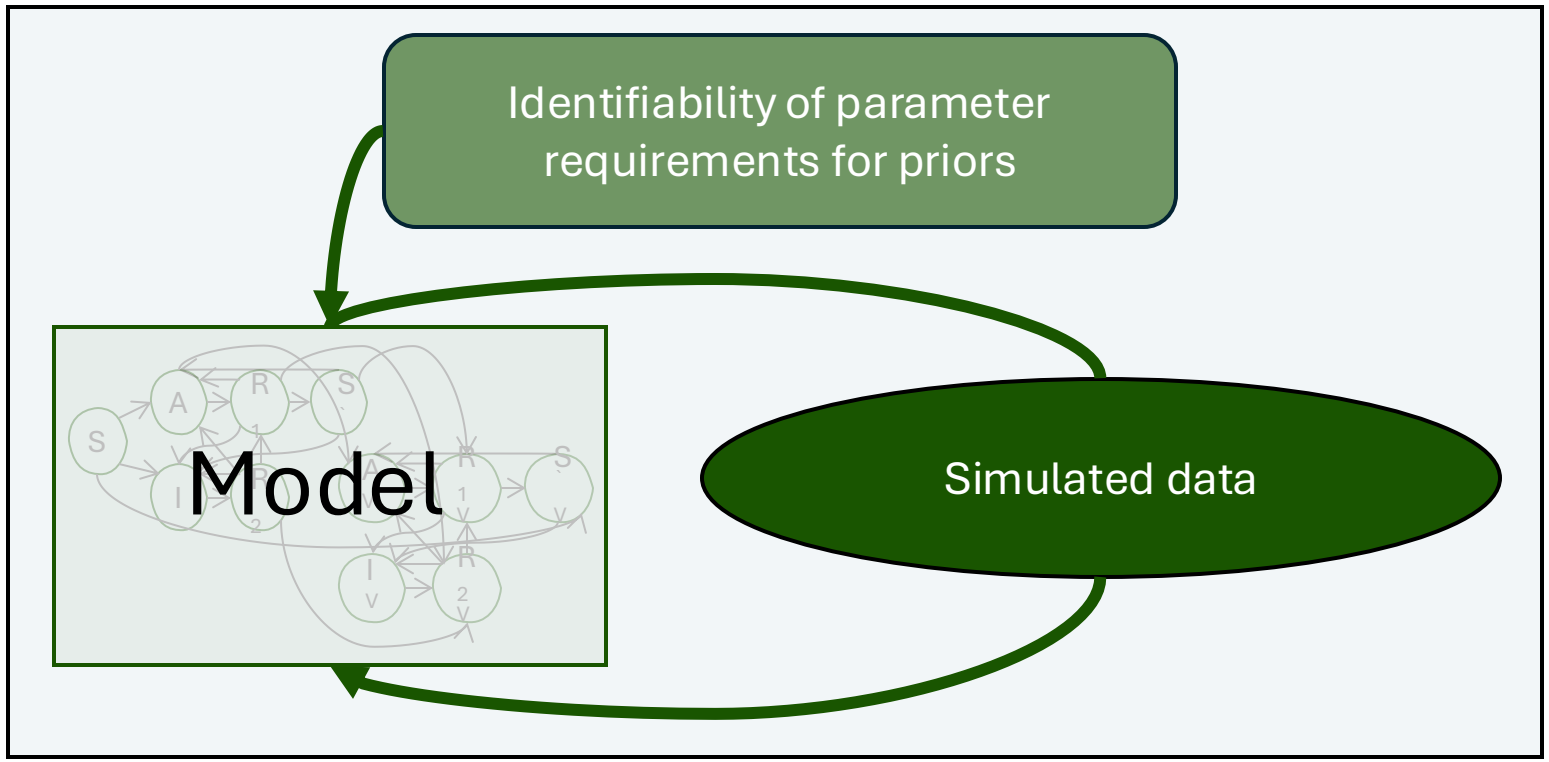
Calculate likelihood

observed AWD incidence ~ Poisson(incidence cholera cases + incidence non cholera cases)

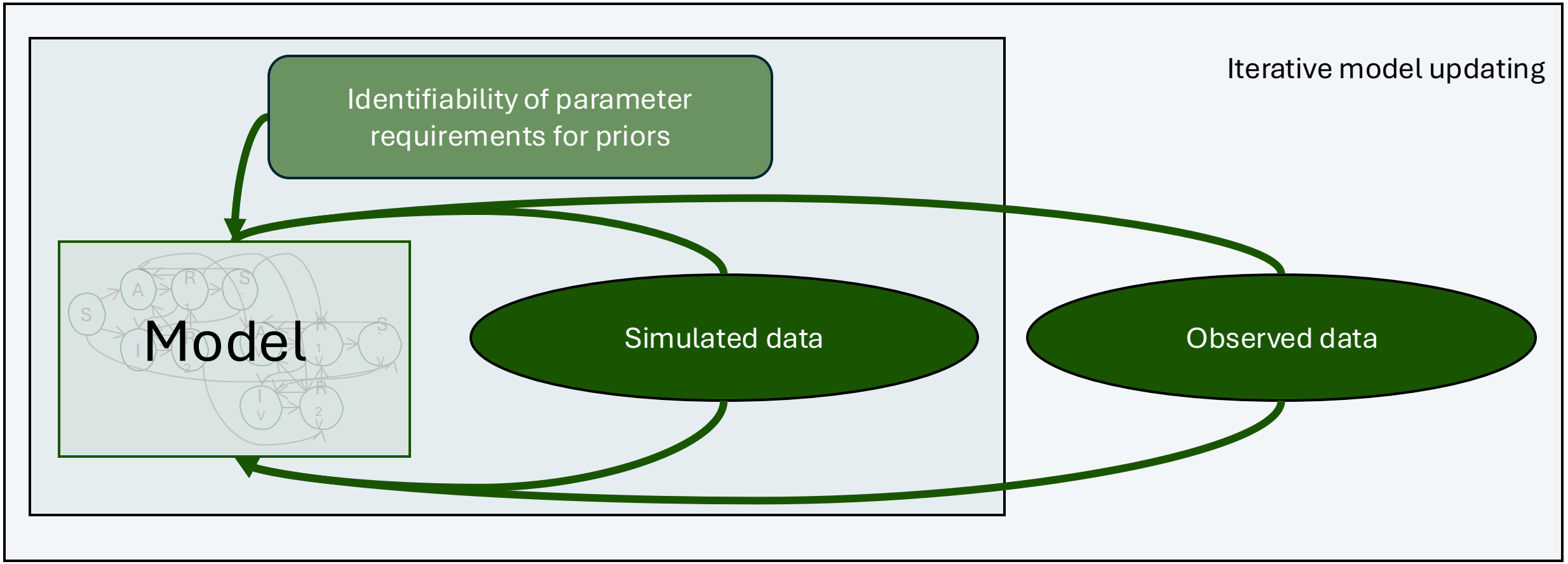
number of positive tests ~ binomial(number of tests performed, probability of positive RDT if AWD)

Updating parameter values (MCMC)

Bayesian workflow



Bayesian workflow



Bayesian workflow

Iterative model updating

Identifiability of parameter requirements for priors

Model

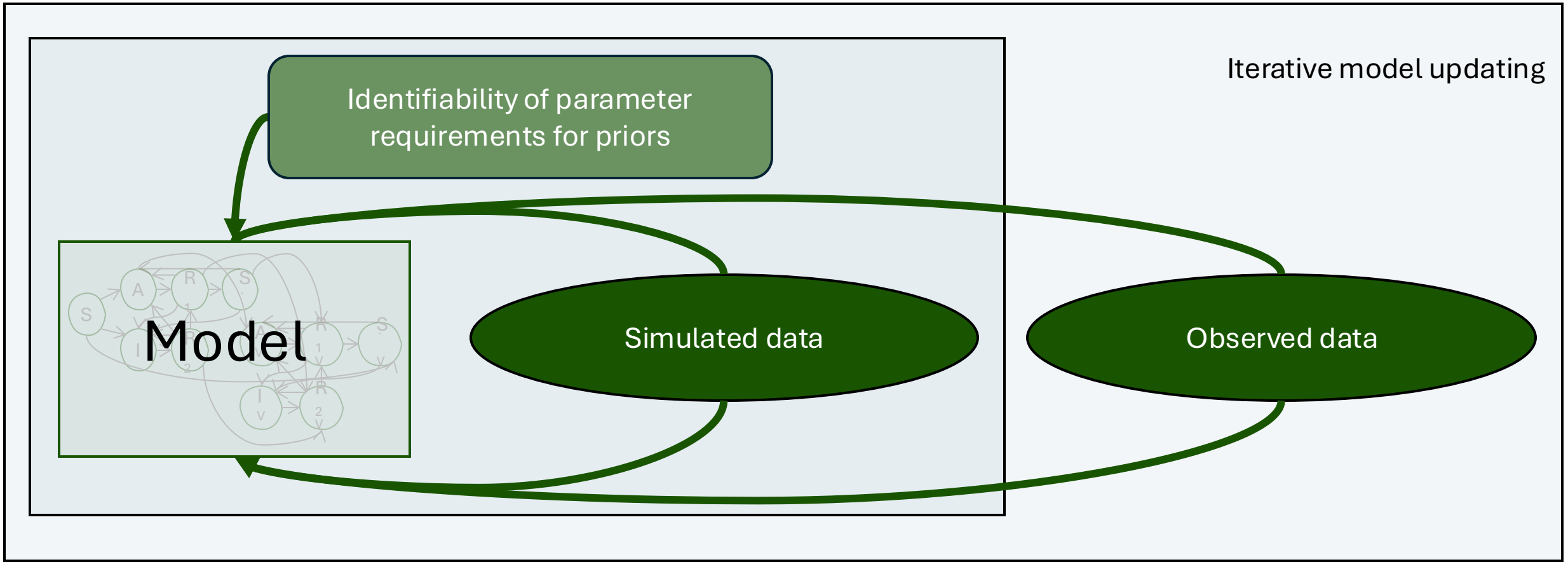
Simulated data

Observed data

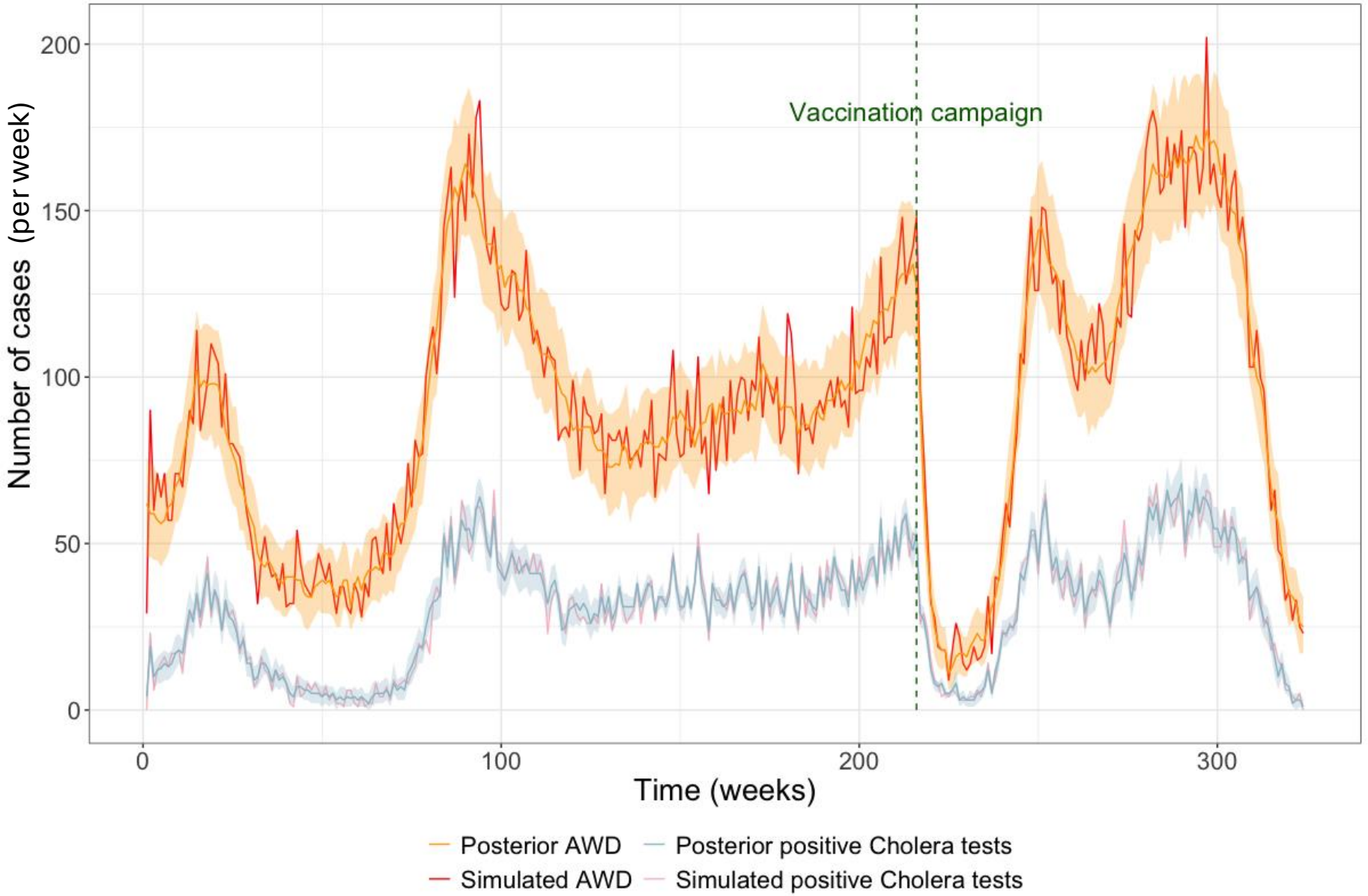
Impact estimate

Generated counterfactual scenario

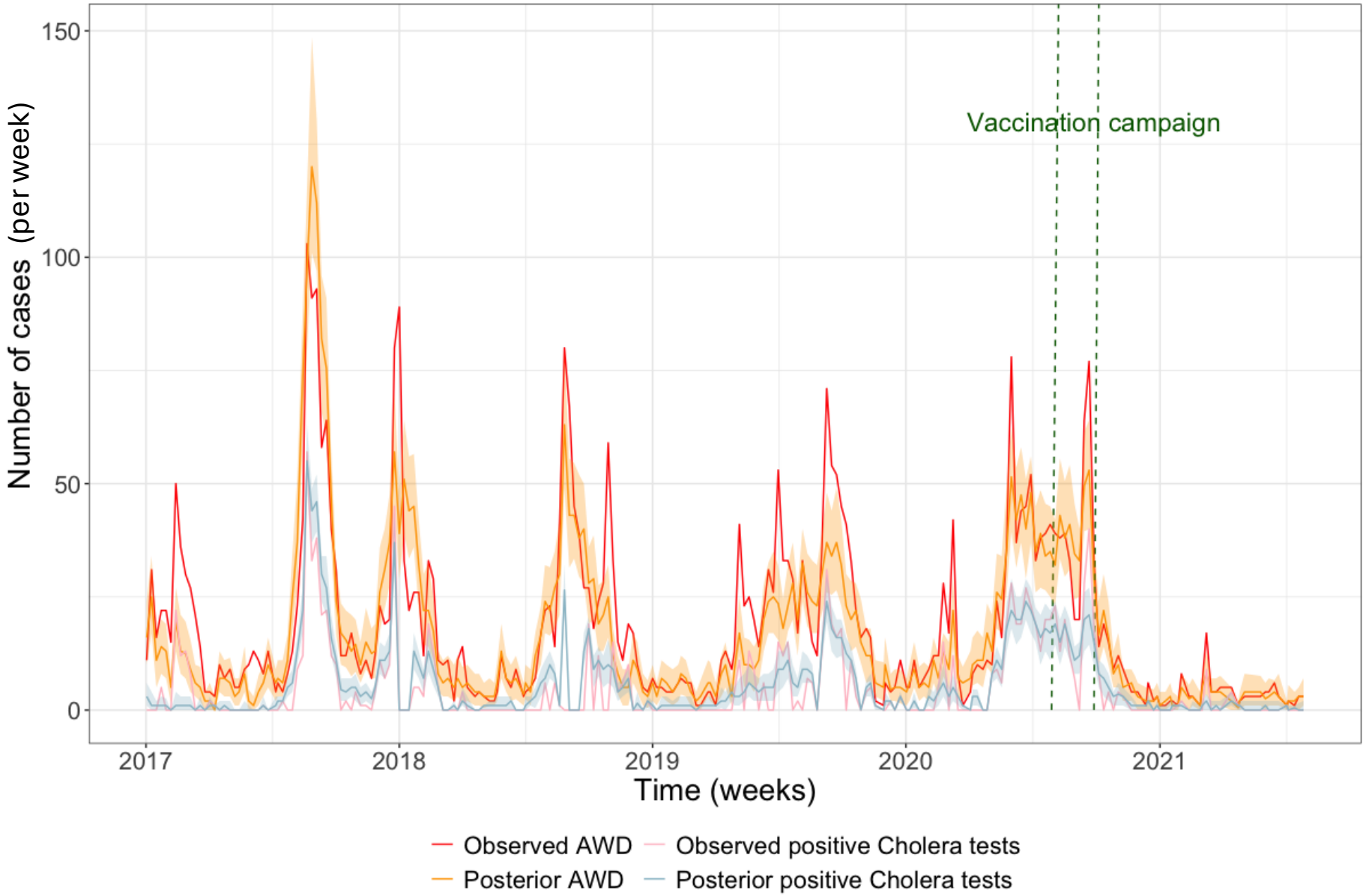
Bayesian workflow



Validation with simulated data



Preliminary model fit observed data



Take home messages

- Predicting the population level impact of oral cholera vaccination campaigns is complex, especially in endemic settings
- Rich data collected in Uvira, DRC, offers unique opportunity to estimate the actual impact of a mass cholera vaccination campaign & provides a framework to improve impact in the future
- Relatively complex models seem necessary, including various leaky immune compartments

Ministère de la Santé
République Démocratique du Congo

Programme National d'Elimination du Choléra et de lutte contre les autres Maladies Diarrhéiques
(PNECHOL-MD)

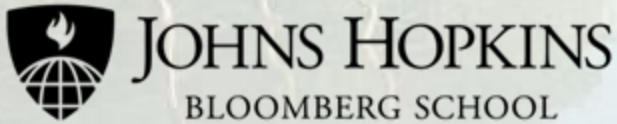
Placide Welo
Okitayemba
Bodiongo Landu

Daniel Lung
Christy Clutter

Javier Perez-Saez

<u>Uvira Health Zone</u>
Jaime Saidi Mufitini
Panzu Nimi

Thank you!

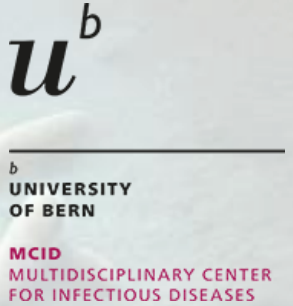


Espoir B Malembaka
Patrick Musole Bugeme
Juan Dent Hulse
Baron Bashige Rumedeka
Maya Demby
Jules Jackson
Hanmeng Xu
Elizabeth Lee
Andrew Azman

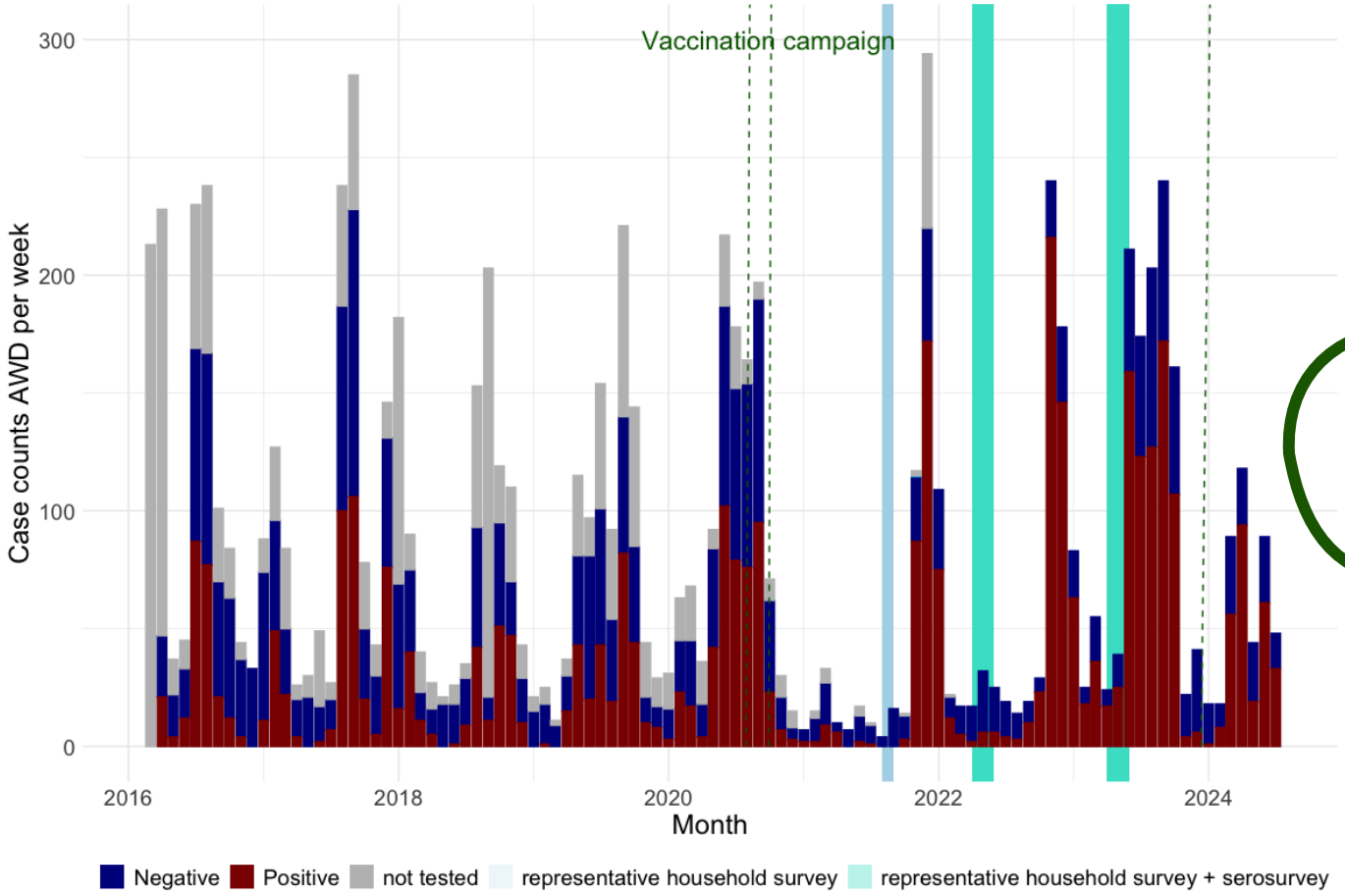
Jackie Knee
Karin Gallandat
Chloe Hutchins
Oliver Cummungs

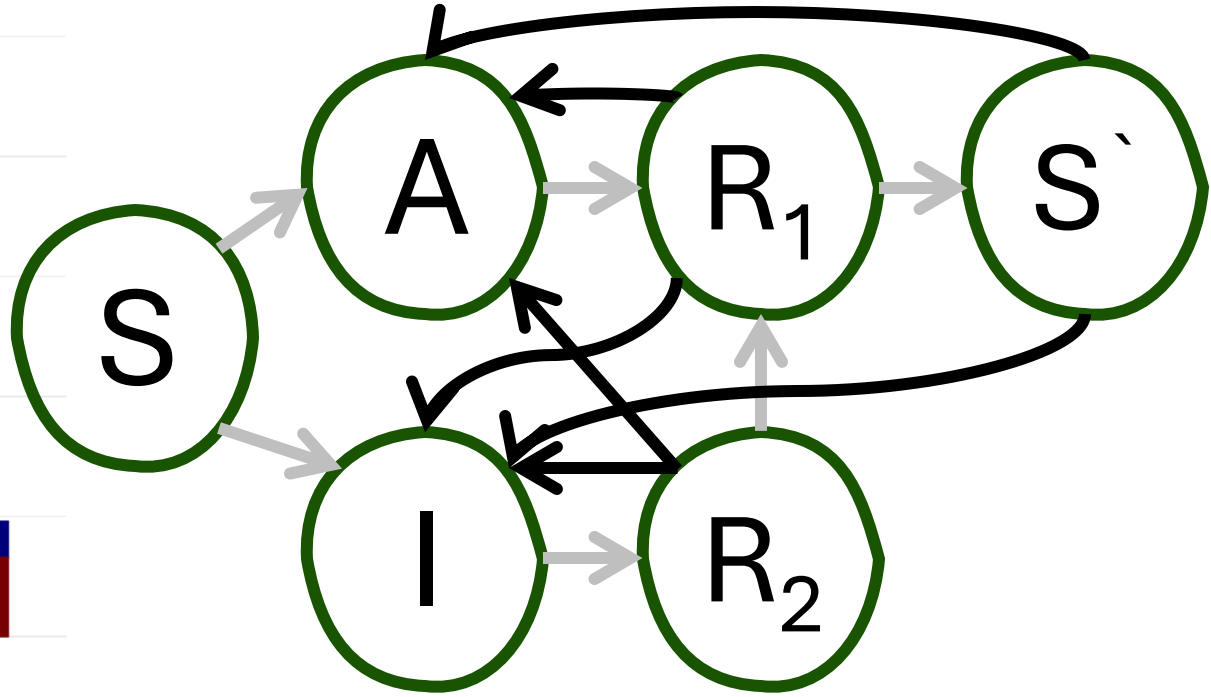
Jean-Marie Cirhonda
Emmanuel Nzenze
Moise Itongwa
Faraja Masembe
Joël Zigashane
Belinda Byamungu

Daniel Mukadi
Espérance Tshiwedi
Faida Kitoga
Tavia Bodisa
Hugo Kavunga



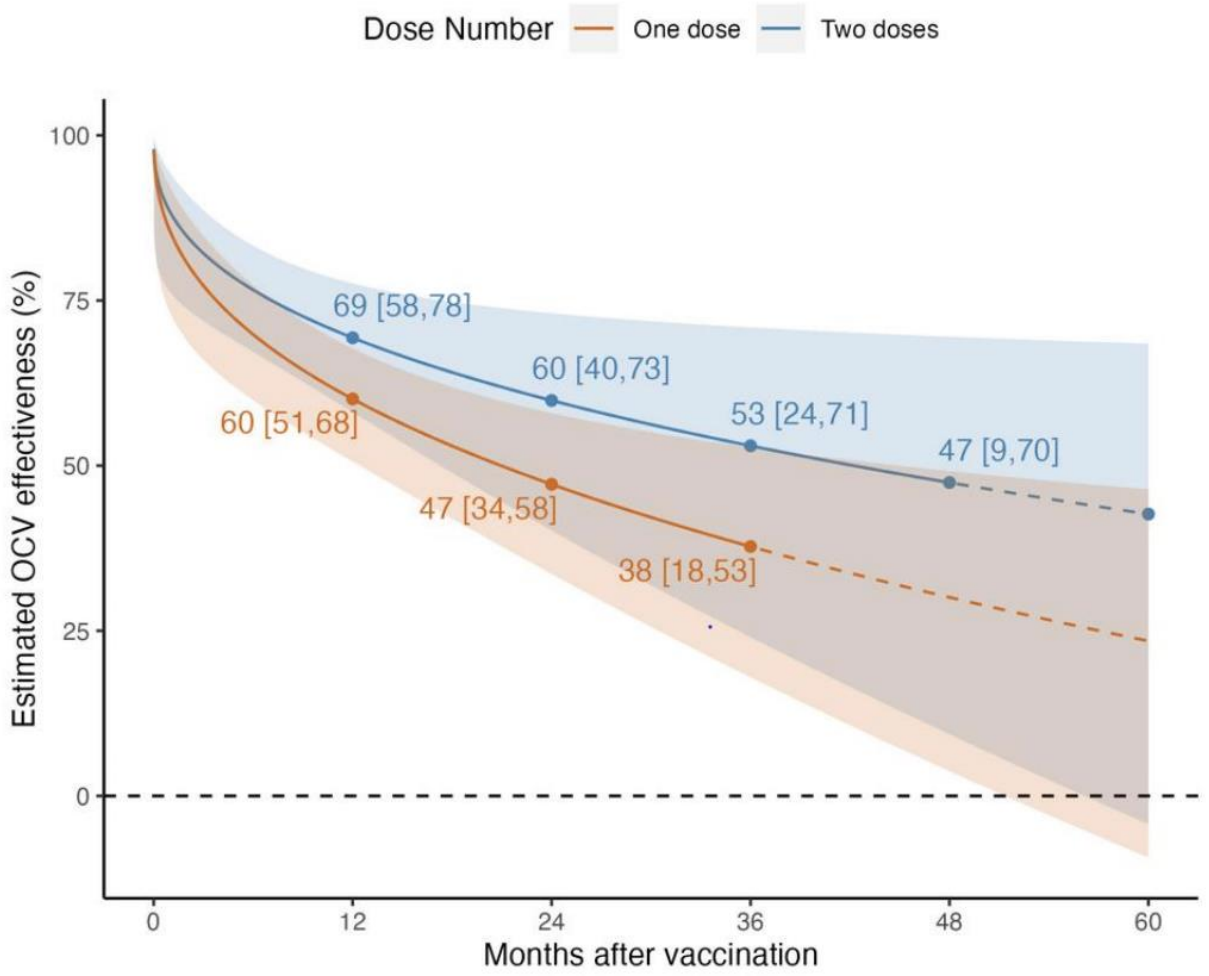
Understanding the population-level impact of mass vaccination campaigns against cholera in Uvira, DRC





Dr. Judith Bouman, University of Bern, Switzerland, Judith.bouman@unibe.ch

One vs. two dose OCV



Xu et al. (2024). MedRxiv