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Cost-effectiveness of typhoid conjugate vaccine strategies across five settings in Africa and Asia

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10th International Conference on Typhoid and Other Invasive Salmonelloses

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Kampala, Uganda

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Cost-effectiveness analysis

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- **Goal:** To estimate the cost-effectiveness of five TCV delivery strategies in five settings with different epidemiological and health economic characteristics

- **Delivery strategies**
  I. Routine vaccination at 9 month of age
  II. Routine vaccination at 9 mo + catch-up campaign 9m-5y
  III. Routine vaccination at 9 mo + catch-up campaign 9m-15y
  IV. Routine vaccination at 9 mo + catch-up campaign 9m-25y
  V. Routine vaccination at 9 mo + catch-up campaign all ages

- Sites were selected based on availability of both incidence data and cost-of-illness data

Settings

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Location (year)	Setting	Incidence (adjusted)	Cost of Illness (Outpatient and Inpatient)	Cost of Vaccine Delivery
Kolkata, India (2004)	Urban	**Medium** 160 (290) per 100,000	**Low/Medium** OP: $18.69 IP: $928.43	**Low** Routine: $3.55 Campaign: $1.67
Delhi, India (1996)	Urban	**High** 750 (2,200) per 100,000	**High** OP: $222.12 IP: $4,840.50	**Low** Routine: $3.55 Campaign: $1.67
Dong Thap, Vietnam (1995)	Rural	**Medium-high** 200 (550) per 100,000	**Low/High** OP: $10.70 IP: $1,241.32	**High** Routine: $8.33 Campaign: $9.02
Kibera, Kenya (2010)	Urban	**Medium-high** 250 (900) per 100,000	**Low** OP: $4.78 IP: $103.87	**Low** Routine: $3.60 Campaign: $3.60
Lwak, Kenya (2010)	Rural	**Low** 30 (100) per 100,000	**Low** OP: $4.78 IP: $103.87	**Low** Routine: $3.60 Campaign: $3.60

Typhoid transmission & treatment model

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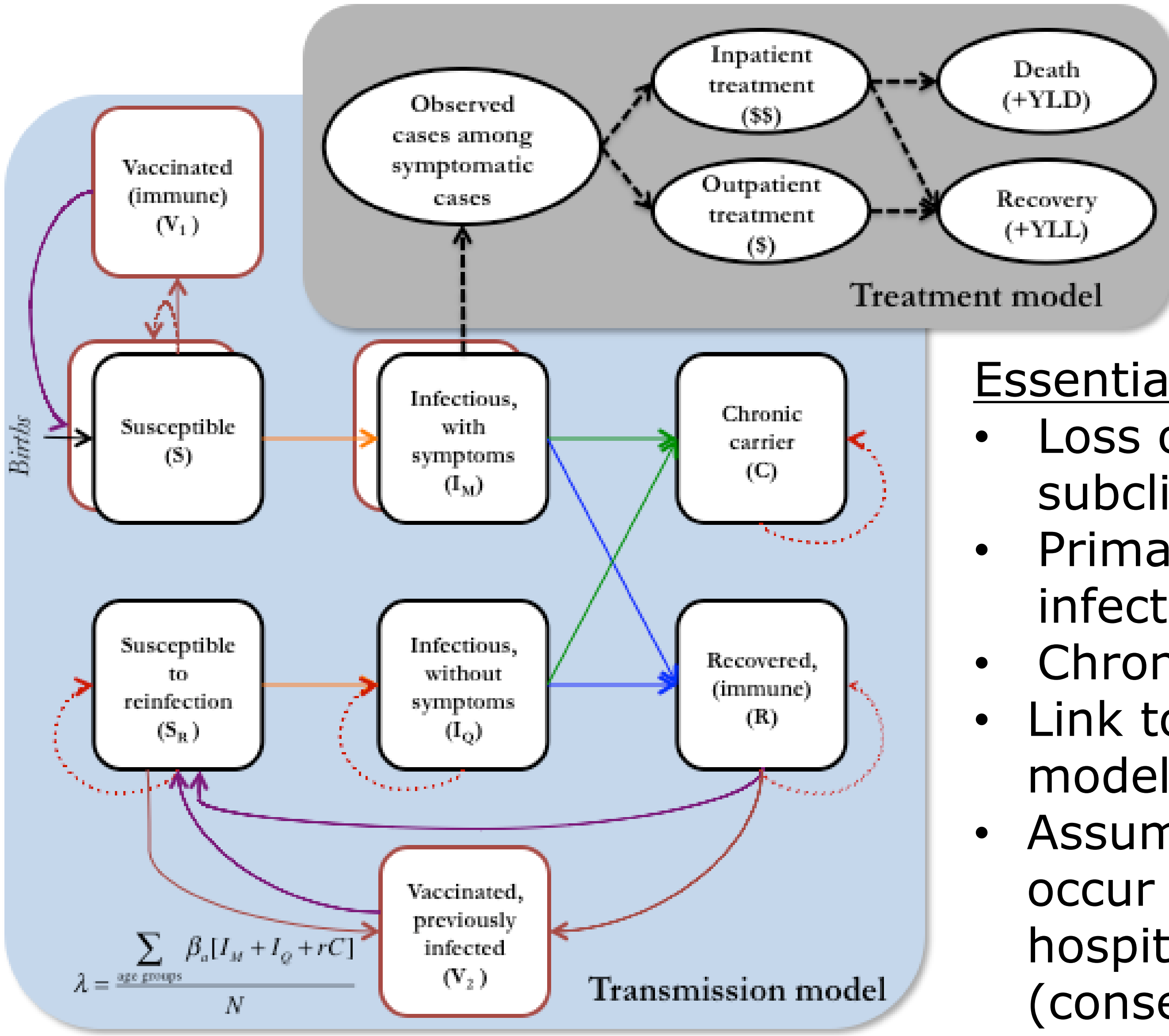

<u>Essential features</u>:

- Loss of immunity to subclinical infection
- Primary vs secondary infection
- Chronic carriers
- Link to treatment model
- Assume deaths only occur among hospitalized patients (conservative)

Fitting the model to age-specific incidence

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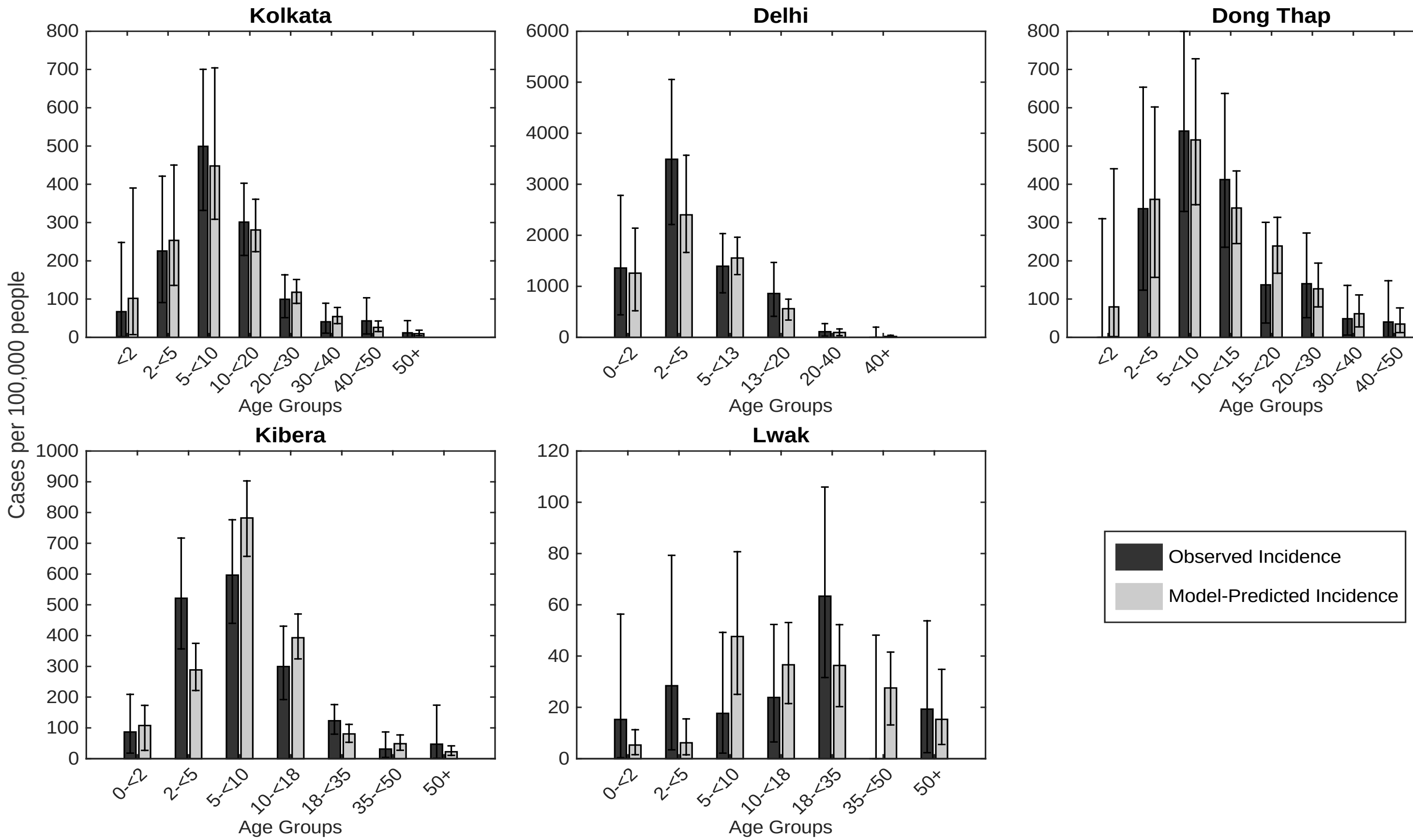

- Fit using Stan (Hamiltonian Monte Carlo)
- We drew 5,000 samples from the joint posterior distribution of model parameters

Base case assumptions

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- Vaccine price: $1/dose
- Single dose
- Efficacy = Vi-rEPA
- 80% coverage for routine vaccination
- 70% coverage for campaigns
- Null comparator: no vaccination
- Time horizon: 10 years

Scenario analyses:

- Vaccine price of $2/dose and $5/dose
- Two doses required to fully immunize children <5 years of age

Modeling vaccination with TCV

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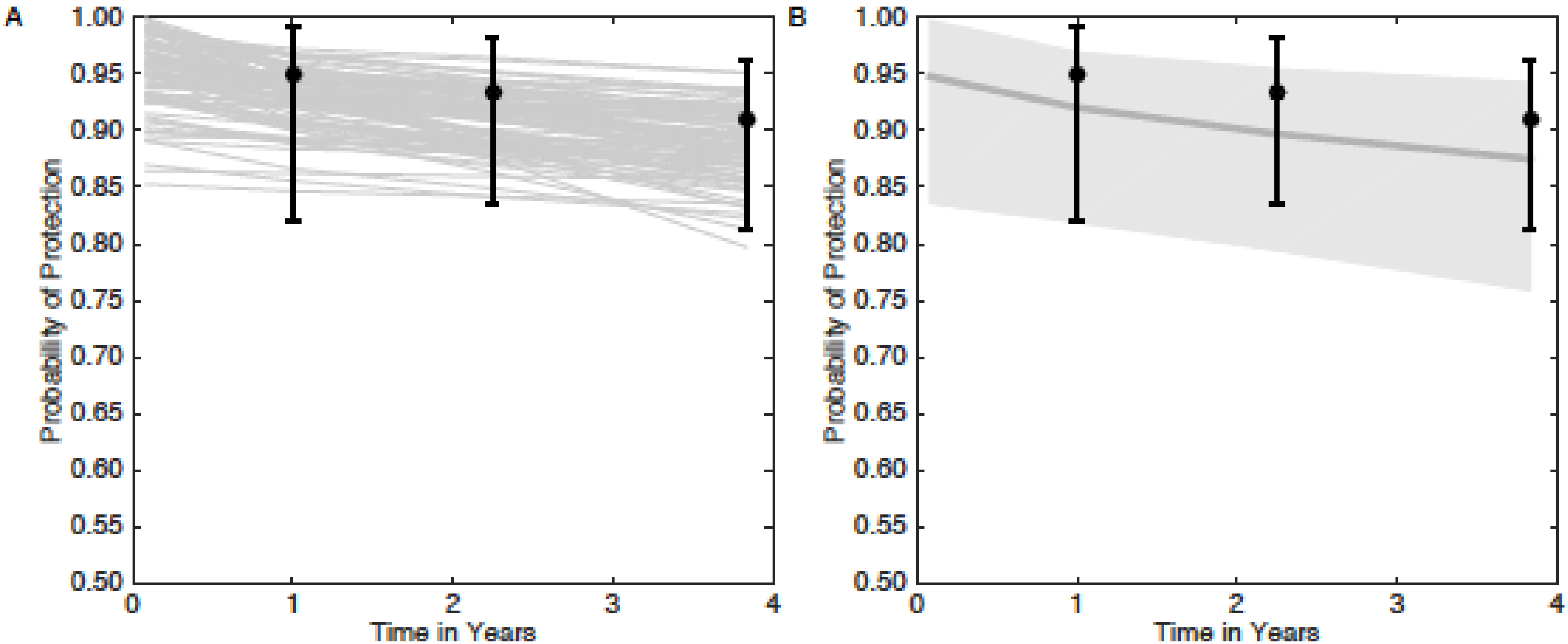

- **Vaccine efficacy**

  =95% (87.0-99.7%) during 1st year for (based on Vi-rEPA)

- **Duration of immunity**

  =19 years (6-147 yrs) (estimated based on Vi-rEPA)

Lin F et al (2001) NEJM; Lahn MN et al (2003) NEJM; Fraser A et al (2009) Cochrane Review

Cost-Effectiveness Analysis

- Healthcare provider perspective
  - Direct medical costs only

- Net benefit framework to evaluate the probability that each strategy was optimal across a range of willingness-to-pay (WTP) thresholds while accounting for parameter uncertainty
  - Low emphasis on WHO thresholds

- Sensitivity analysis to assess contribution of each parameter to uncertainty in determining the optimal strategy
  - Net monetary benefit (NMB) at WTP equal to 1xGDP

Cost-effectiveness acceptability curves

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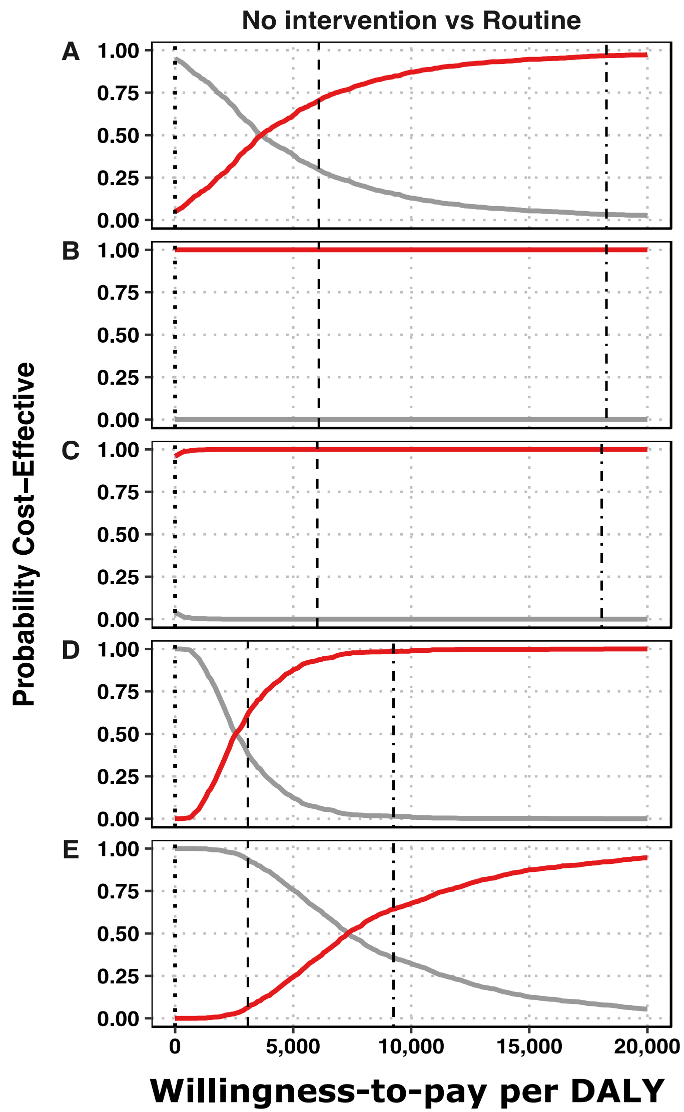
WTP=I$0
(Cost-saving)

WTP=1xGDP
(Very cost-effective)

WTP=3xGDP
(Cost-effective)



Kolkata

Delhi

Dong Thap

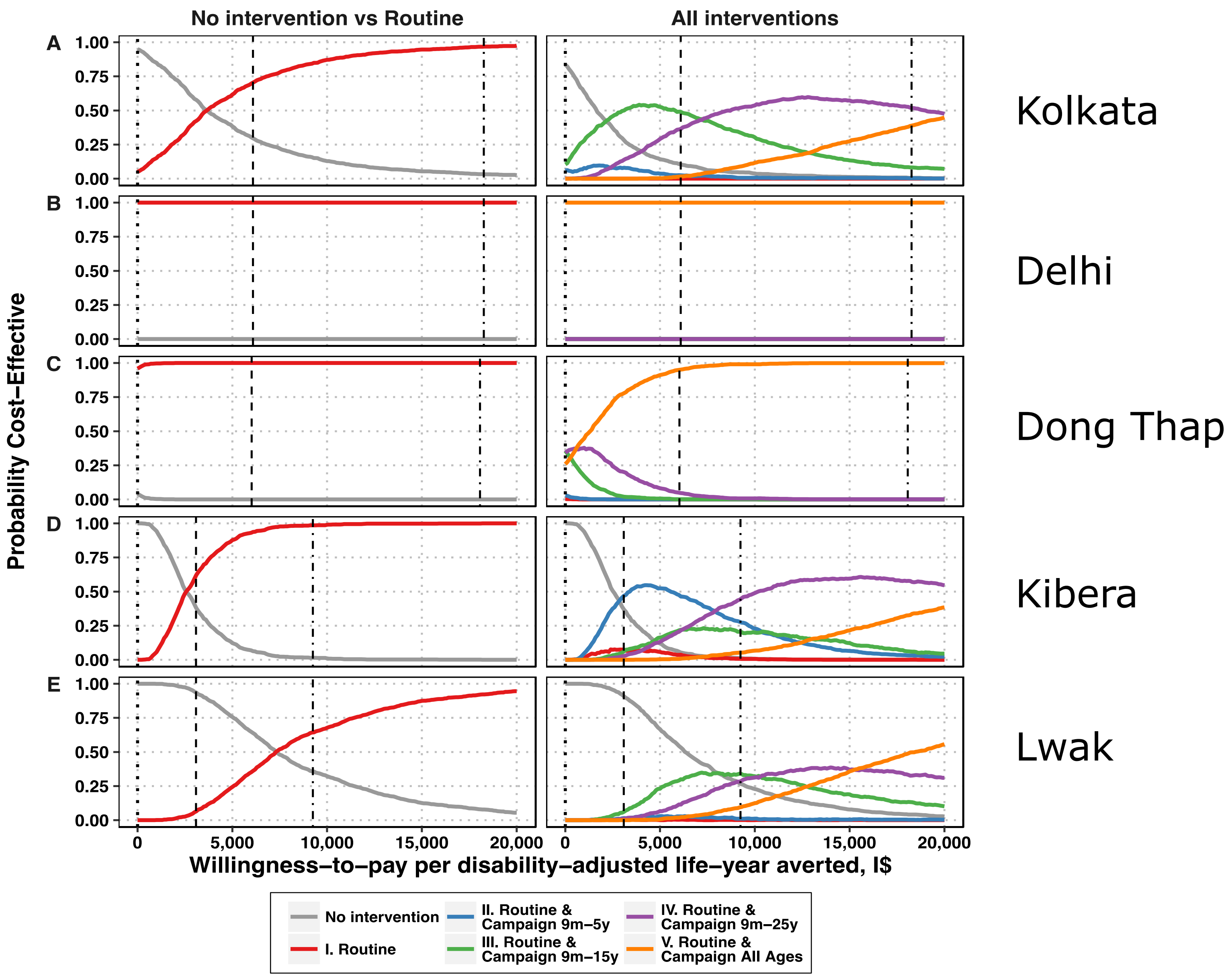
Kibera

Lwak

No intervention

I. Routine

Cost-effectiveness acceptability curves



Scenario analysis: Vaccine price

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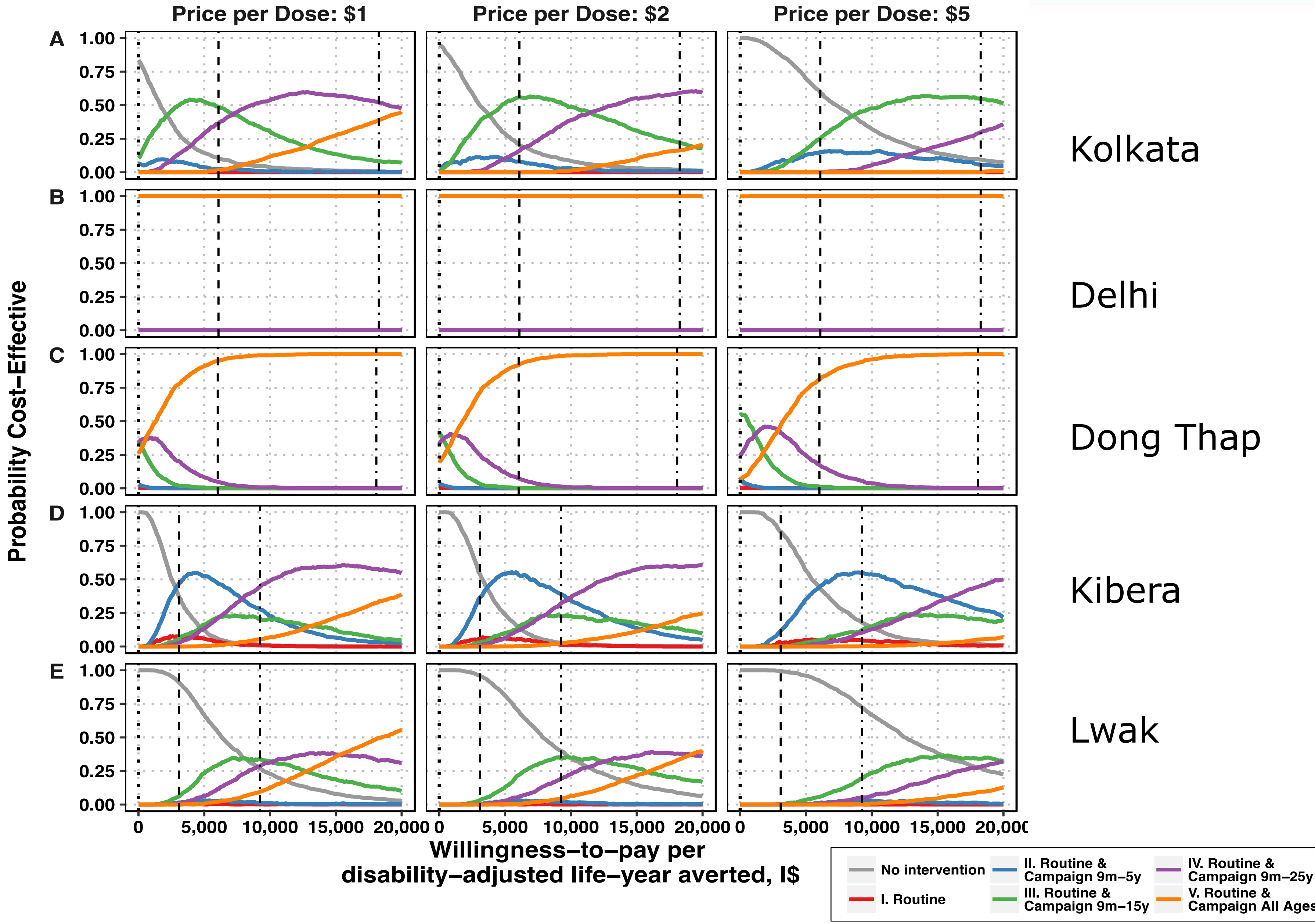

Scenario analysis: Price & number of doses

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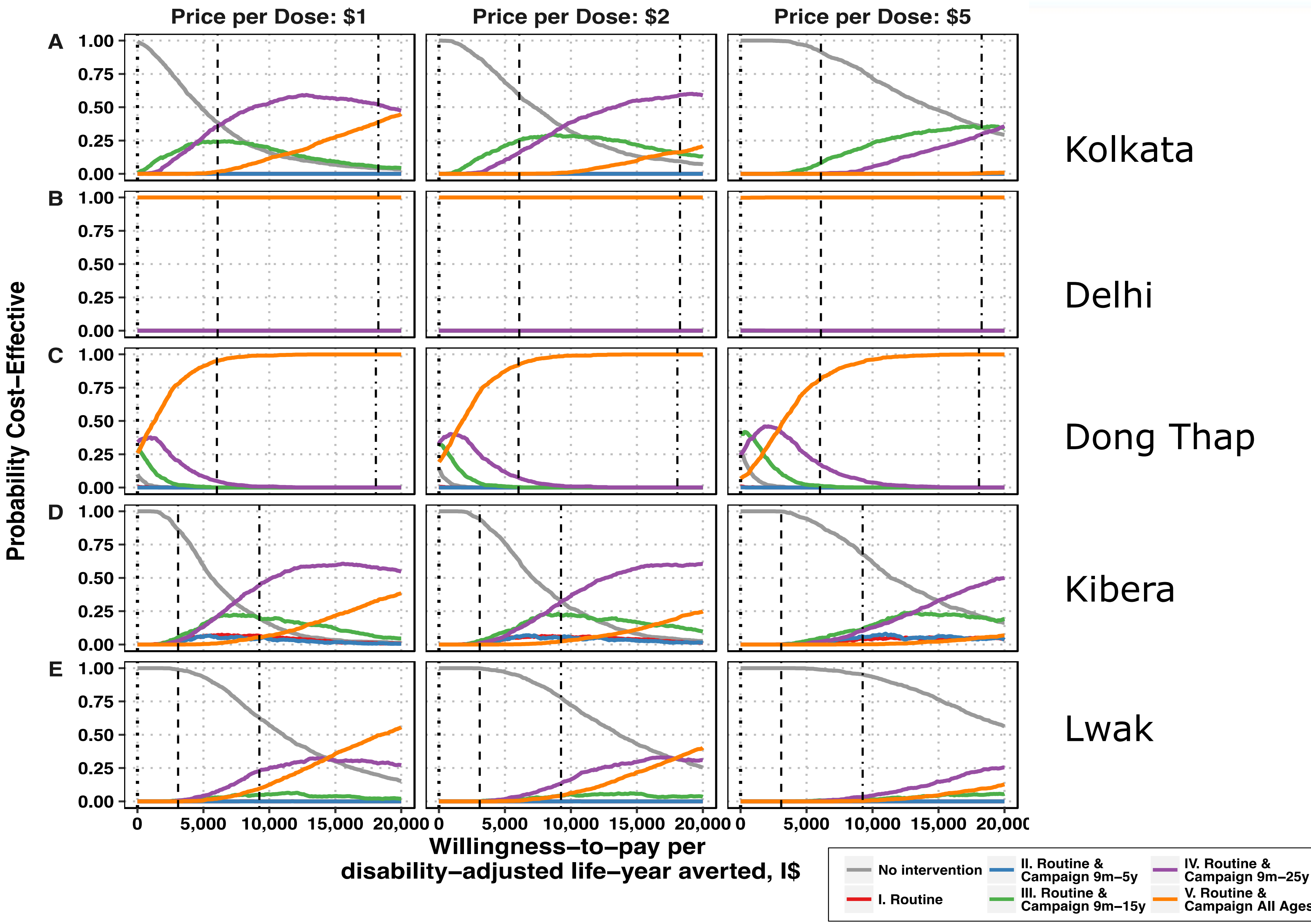
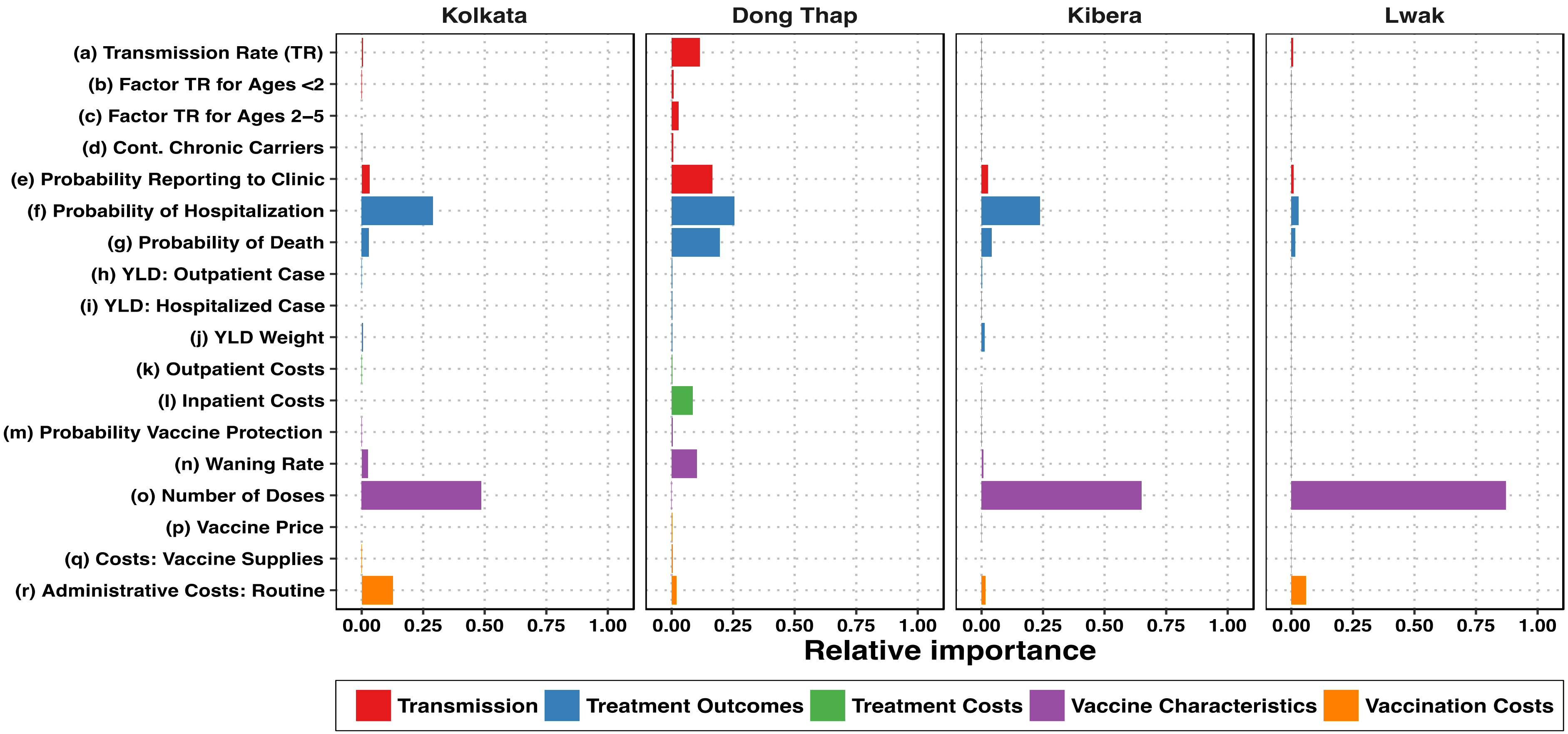


Sensitivity analysis



- Random forest analysis (robust to correlation between parameters)
- **Number of doses required** and **probability of hospitalization** were the primary sources of uncertainty in most settings

Conclusions

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- **Routine vaccination** at 9 months old would be ″cost-effective″, ″very cost-effective″, or even "cost-saving″ in most settings

- However, additional benefits gained by including **one-time catch-up campaigns** would be economically justified
  - Optimal delivery strategy varied by country and willingness to pay

Acknowledgements

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- TyVAC consortium

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- Gates Foundation (OPP1151153)—TyVAC

We're hiring! Two faculty positions available in laboratory- and field-based epidemiology

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Additional slides

ICER of routine vaccination vs status quo

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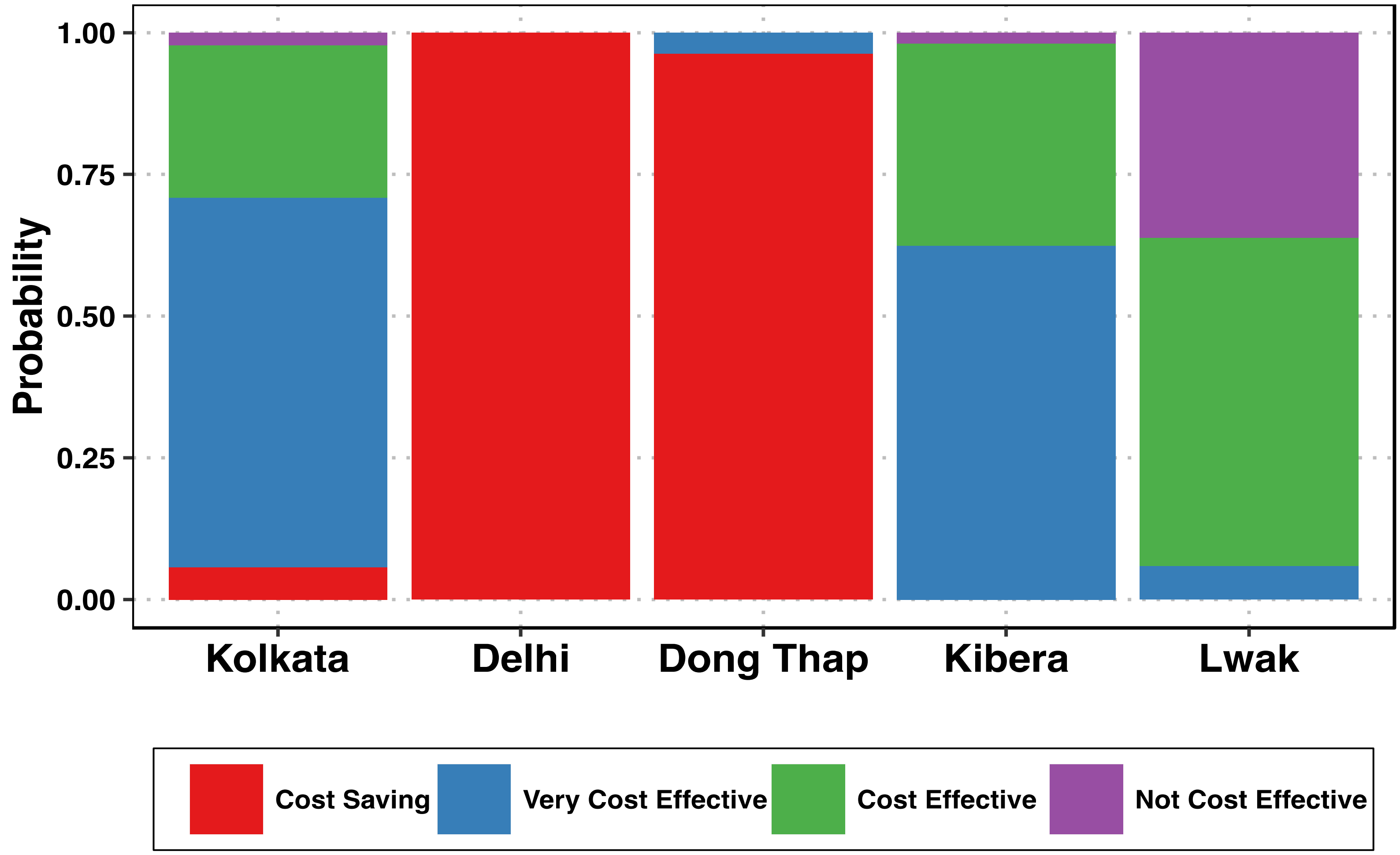

Predicted vaccine impact

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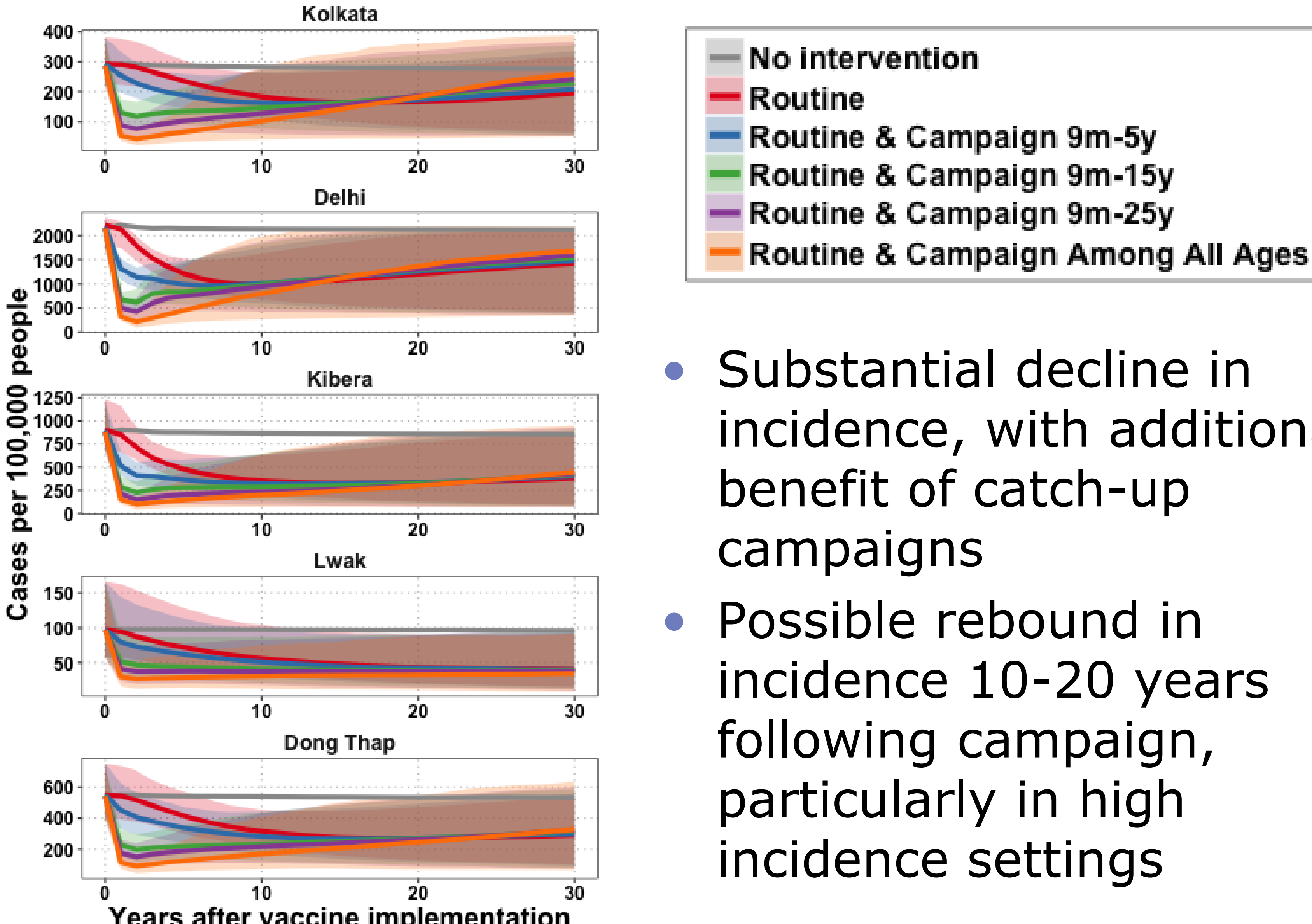

- Substantial decline in incidence, with additional benefit of catch-up campaigns
- Possible rebound in incidence 10-20 years following campaign, particularly in high incidence settings

CEACs at current market price

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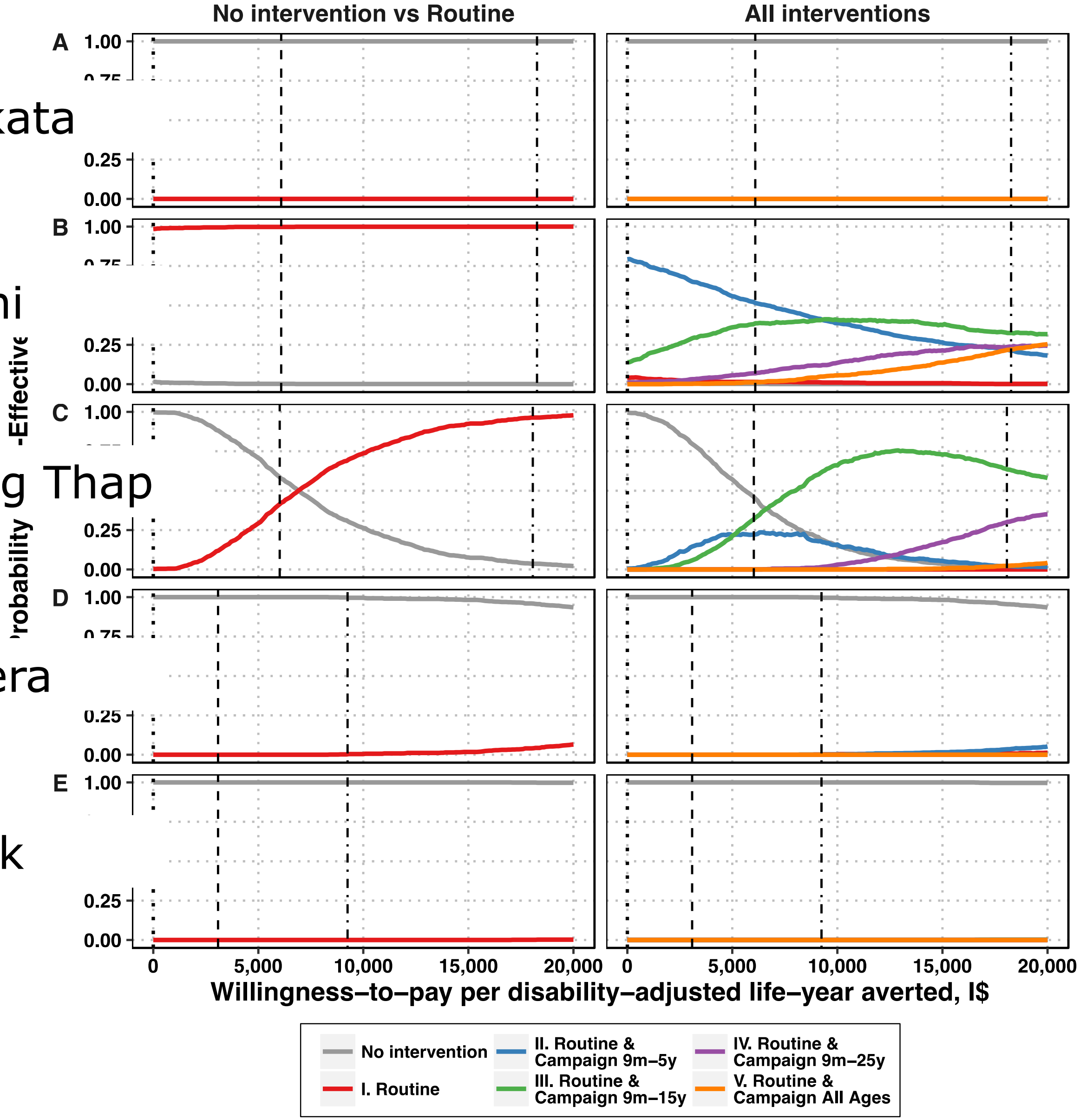
Kolkata

Delhi

Dong Thap

Kibera

Lwak



Current price = 1,800 rupees

=I$106 in India
=I$78 in VN
=I$57 in Kenya

(converted to international dollars based on PPP conversion factor for each country in 2015)

Observed vs adjusted age-specific incidence

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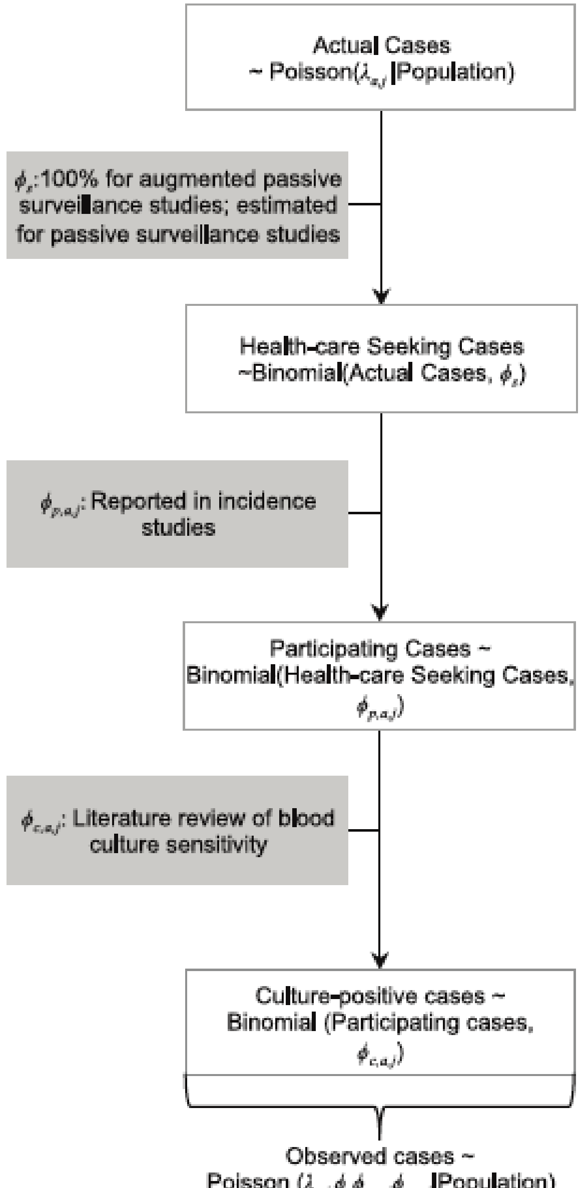

Passive surveillance estimated to detect 42% (22-58%) fewer cases on average than active surveillance

Not all individuals meeting the case definition may consent/have blood drawn for culture, and this may vary by age

Blood culture sensitivity is only ~50-70% and varies depending on the volume of blood drawn. Lower volumes of blood often drawn for children <5 years old.

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Observed vs adjusted incidence

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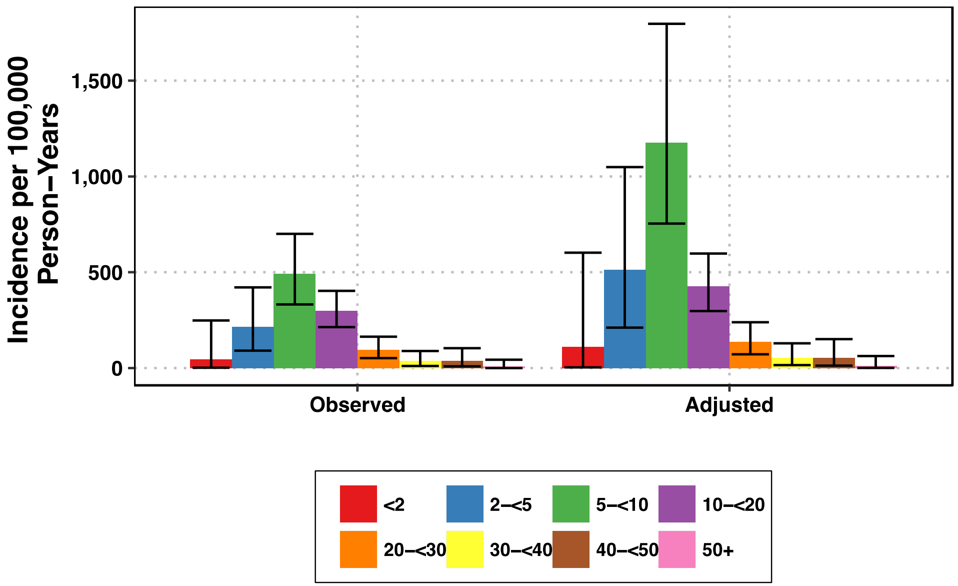
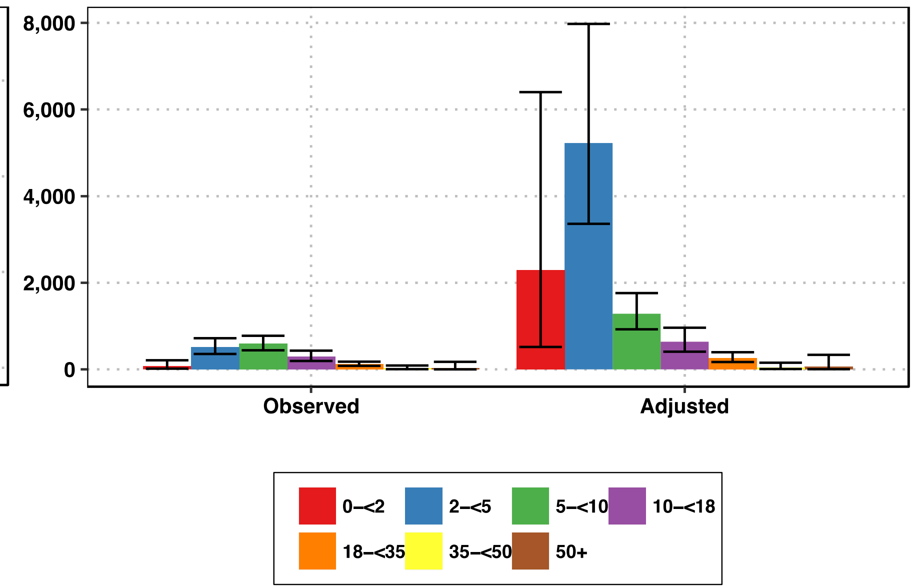
Kolkata



Kibera



- Adjusted incidence is much greater for Kibera than Kolkata (particularly in <5 yr olds) because:
  - A low percentage of those meeting the case definition had blood culture performed, particularly among children <5 yrs
  - A low volume of blood (1-3 mL) was collected from children <5 yrs old, and sensitivity was estimated to be lower

Typhoid dynamic model structure

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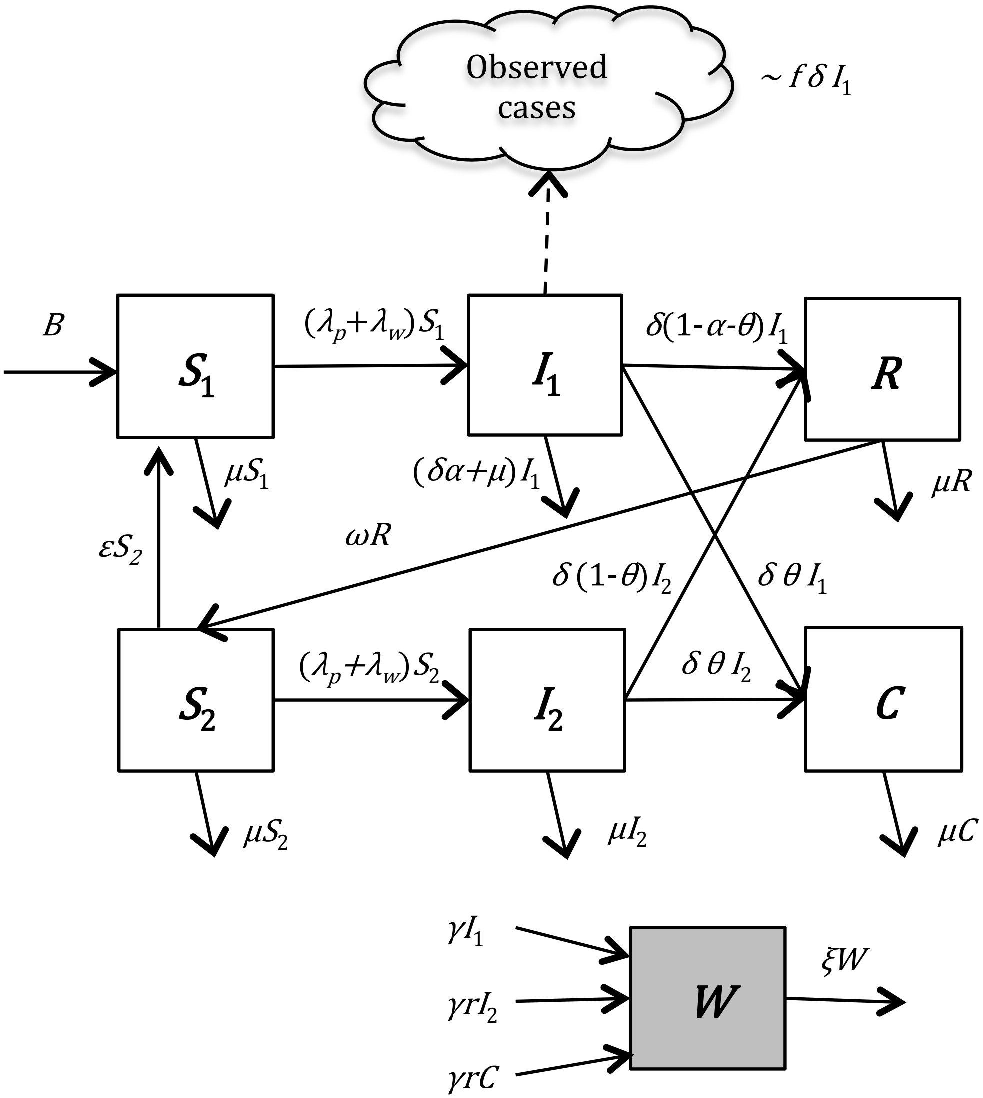

Essential features:

- Loss of immunity to subclinical infection
- Primary vs secondary infection
- Chronic carriers
- Balance between "short cycle" transmission via contamination of food, etc in the immediate environment
- …and "long cycle" transmission via contaminated water
  - May be more seasonal