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# Preliminary results for the effectiveness of typhoid vaccination strategies

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# What is mathematical modeling?

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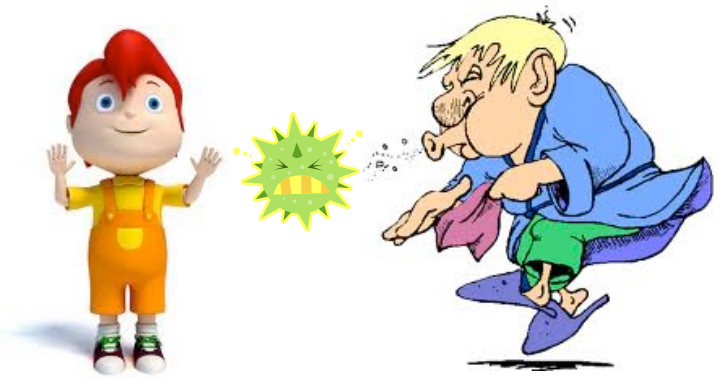
- Description of a system using mathematical concepts and equations
- Differs from traditional statistical modeling methods which assume independent observations
- Takes into account NON-LINEAR effects that result from the interaction of infectious and susceptible individuals



# Why model?

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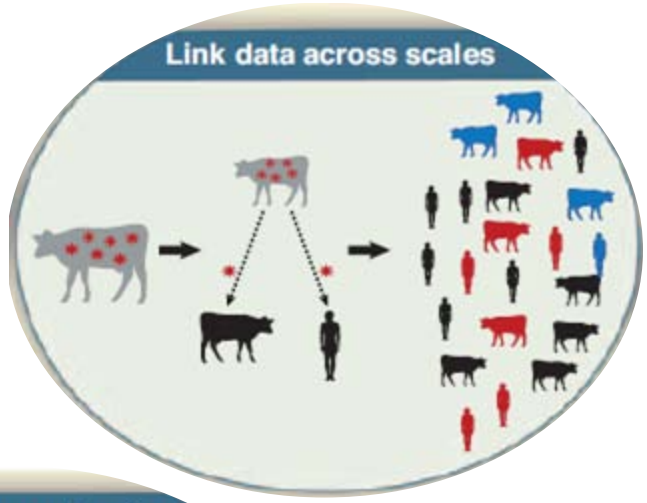


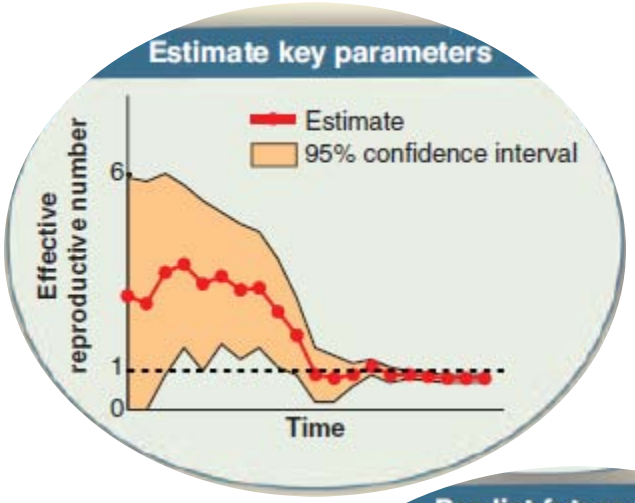


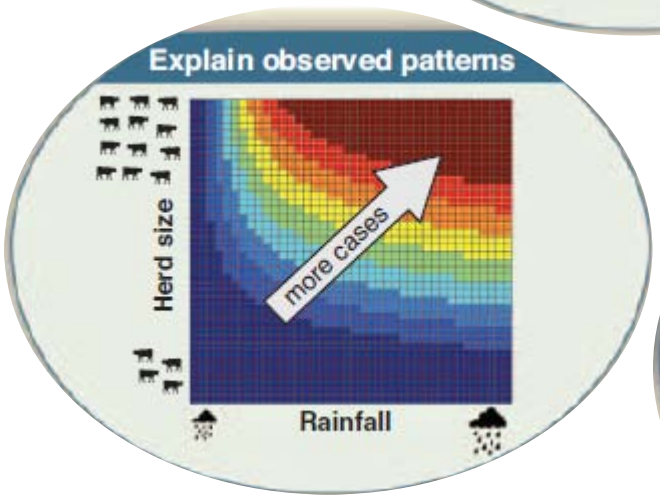


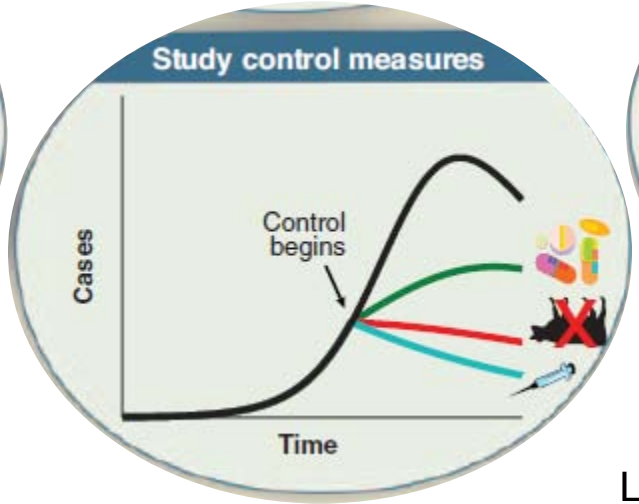


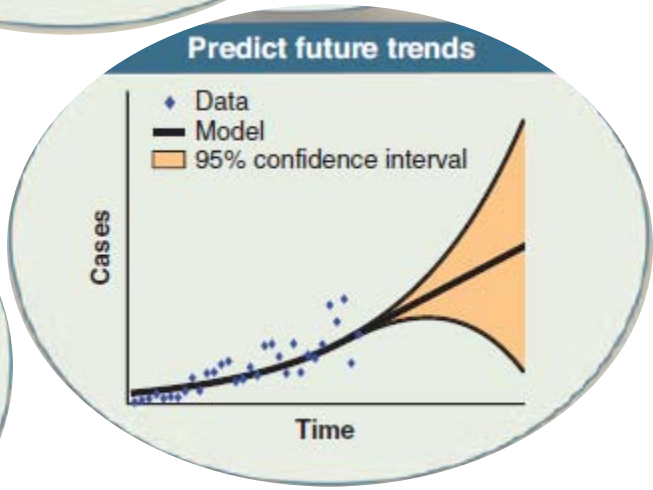


Lloyd-Smith et al, Science (2009)

# Direct vs indirect protection

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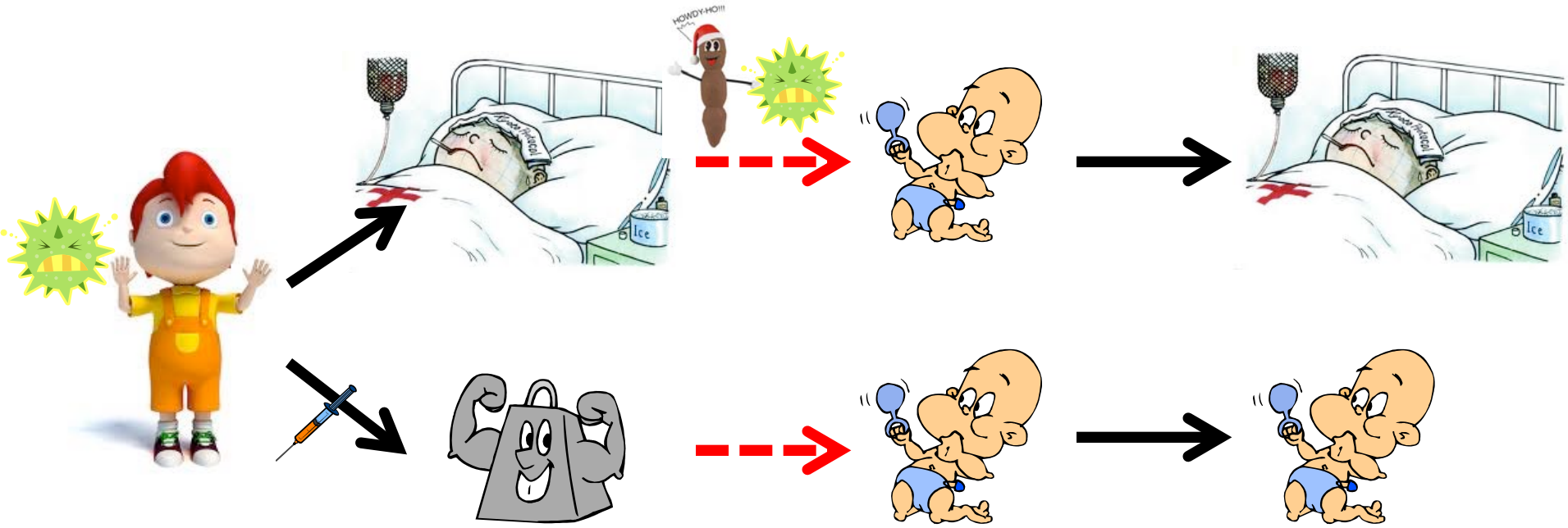
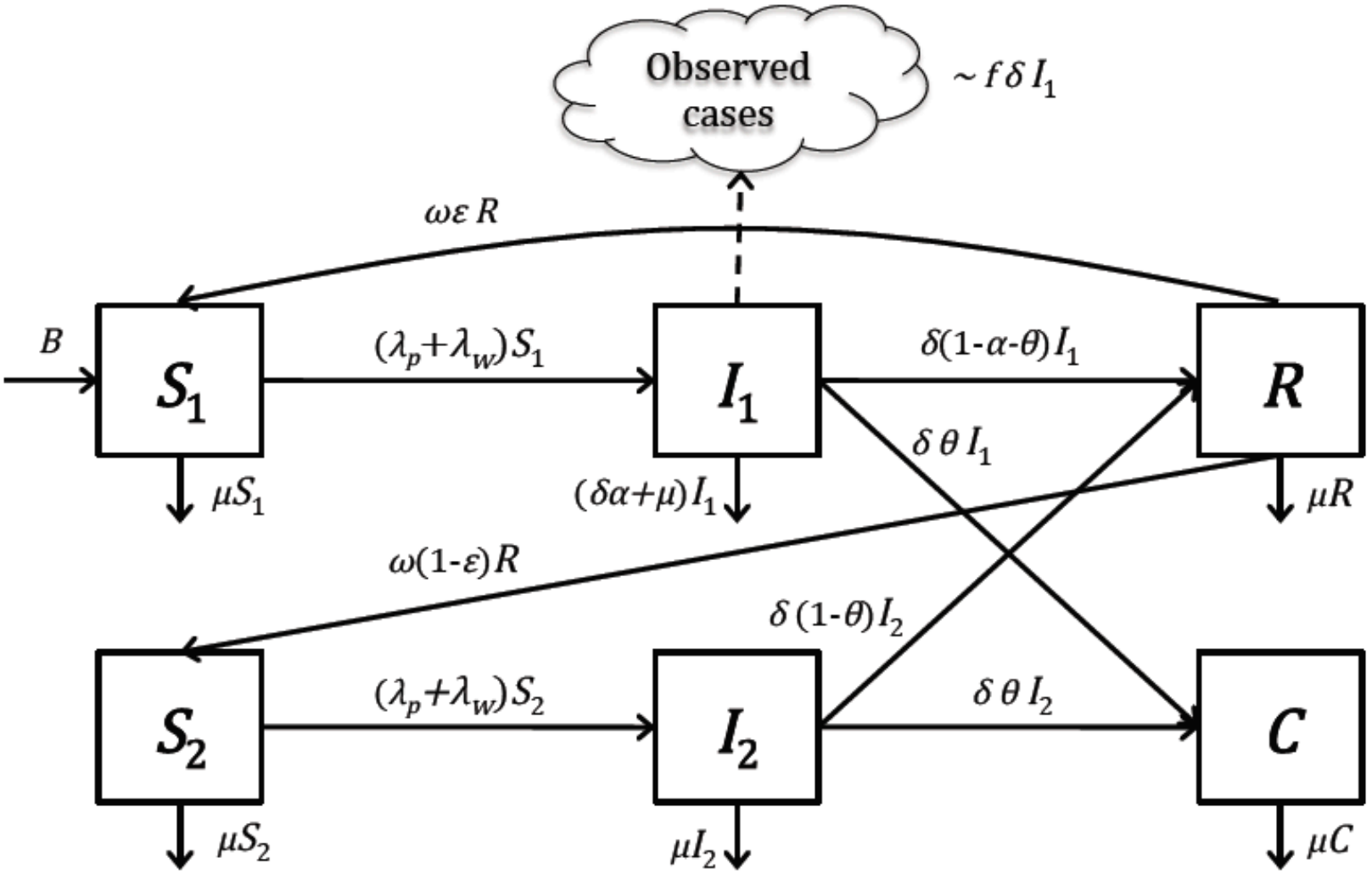
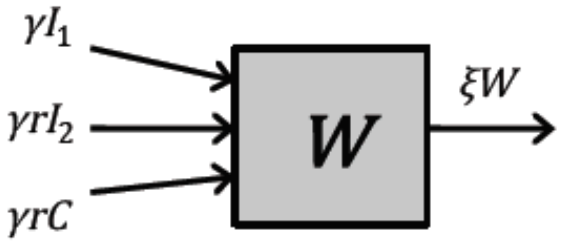
- Direct protection
  - Estimate from clinical trials
- Indirect protection (aka “herd immunity”)
  - Estimate from cluster RCT AND using models






$$\lambda_p = \beta_p(I_1 + rI_2 + rC)$$
$$\lambda_w = \beta_w(t)\ \mathrm{W}\ (1+q\cos((2\pi t-\phi)/52))$$



# Essential model features

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

# Basic Reproductive Number ($R_0$)

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"Short cycle" transmission

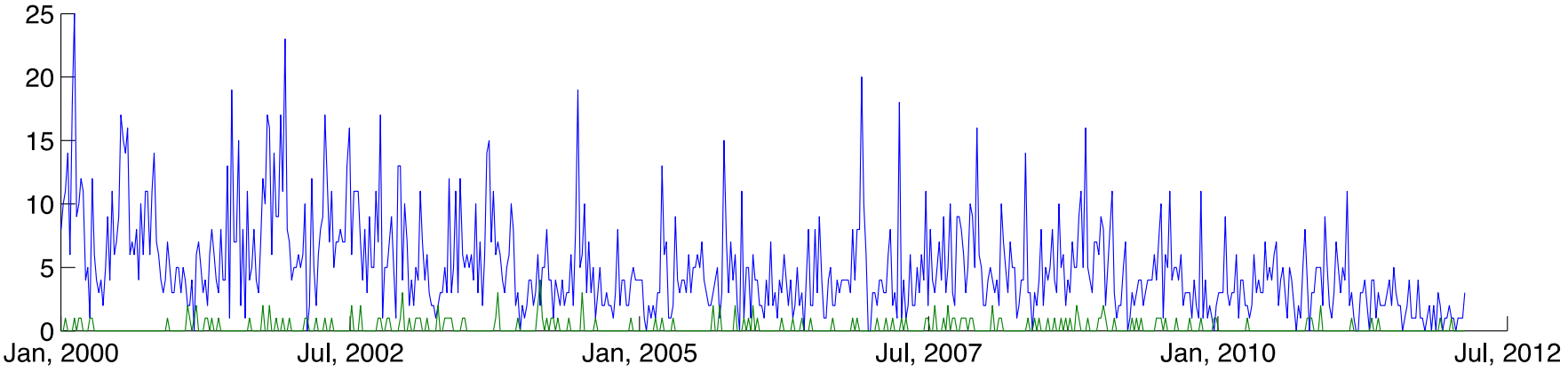
"Long cycle" transmission

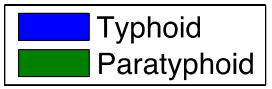
$$R_0 = \frac{1}{\mu + \delta}\left(\beta_p + \frac{\beta_w \gamma}{\xi}\right)\left(\frac{\delta\theta r_1}{\mu} + 1\right)$$

Carriers

Primary infections

# Enteric fever in Vellore, India

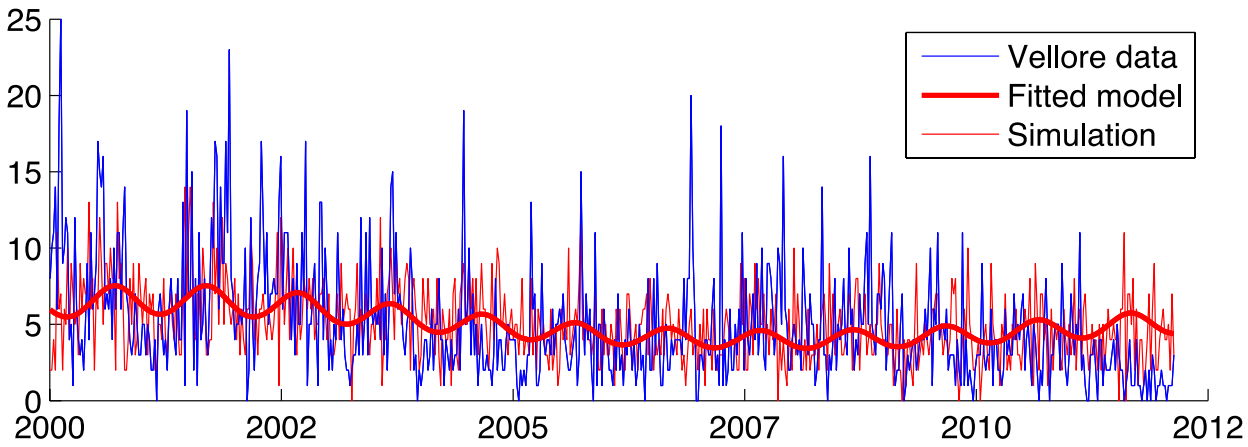



f cases

Age group (yrs)

# Fit of model to Vellore typhoid data




Captures most of the variability in incidence

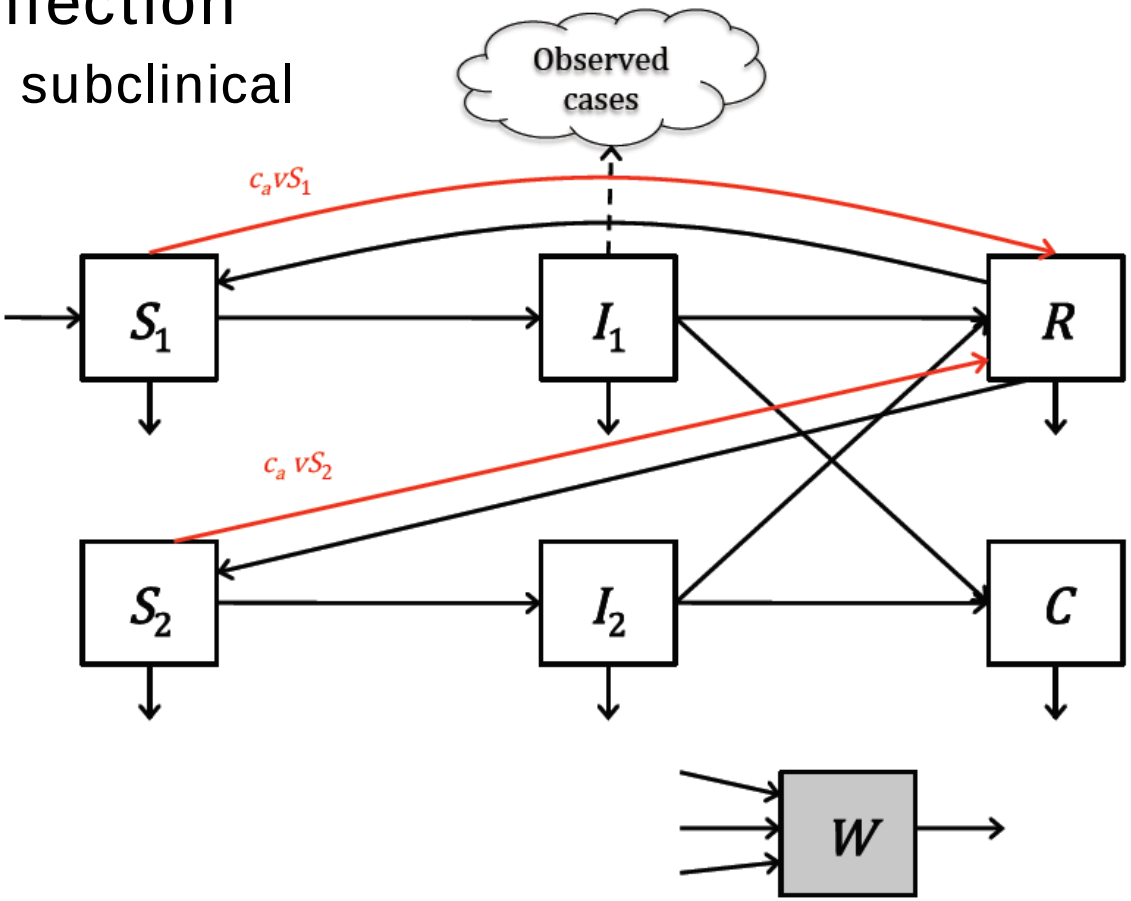

Good fit to age distribution of cases

$R_0 = 2.4 – 2.7$

)

# Modeling vaccination – Ty21a

- Vaccine efficacy = 48% (based on Cochrane review)
- Waning of immunity comparable to that from natural infection
  - Loss of immunity to subclinical infection but long-lasting immunity to clinical infection



# Modeling vaccination – ViPS and ViCV

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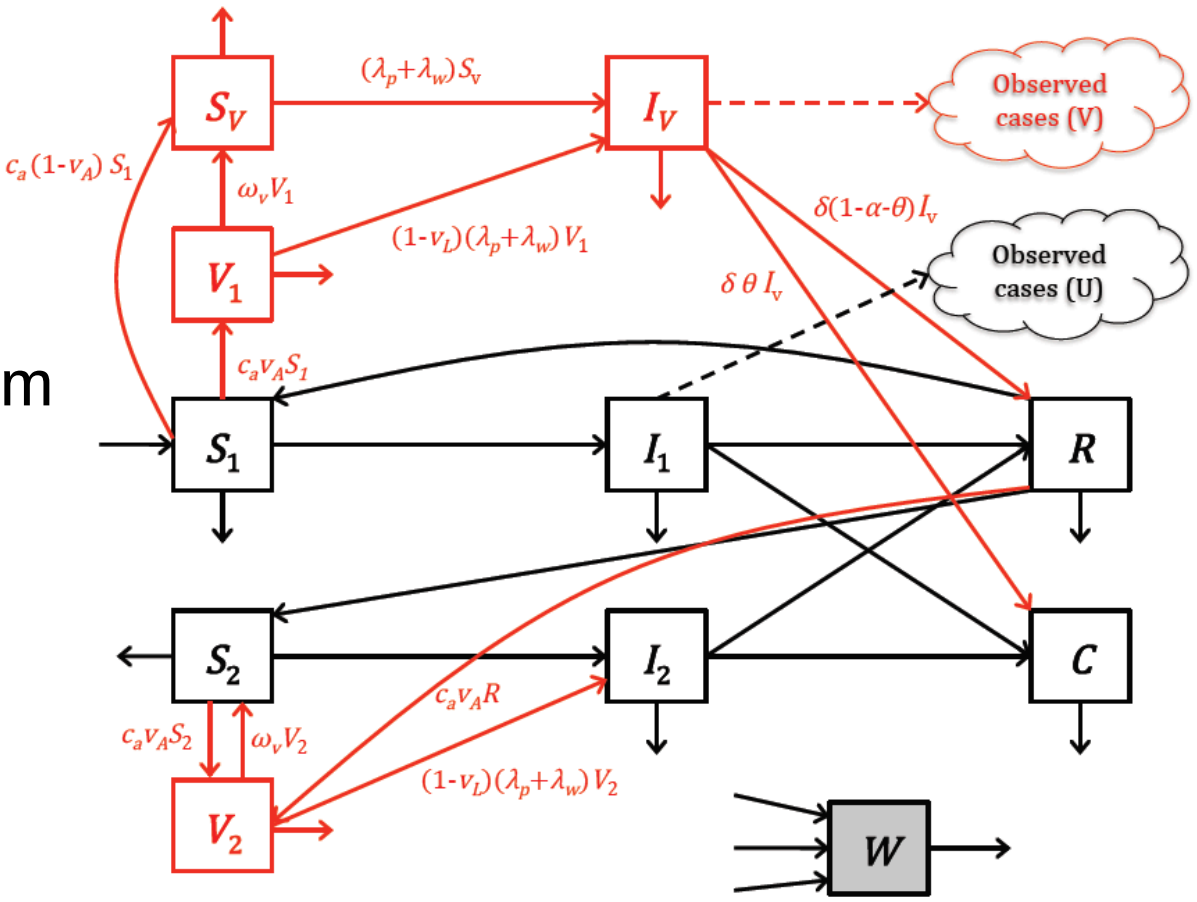
- Vaccine efficacy = 68% during first year for ViPS,
  = 94% during first year for ViCV
- Duration of immunity
  = 3 years for ViPS
  = 19 years for ViCV
  (estimated from Vi-rEPA data)



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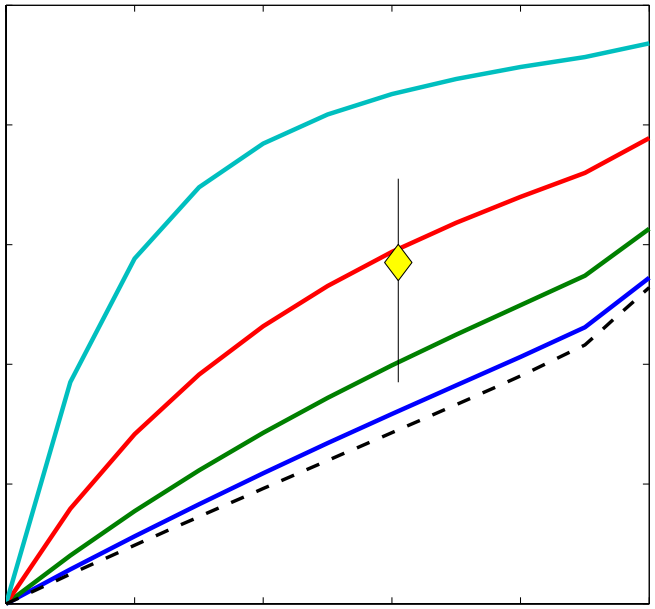
# Role of carriers and impact of vaccination



- The more important carriers are to transmission, the less indirect protection is expected from vaccination

# Dynamics of typhoid following vaccination

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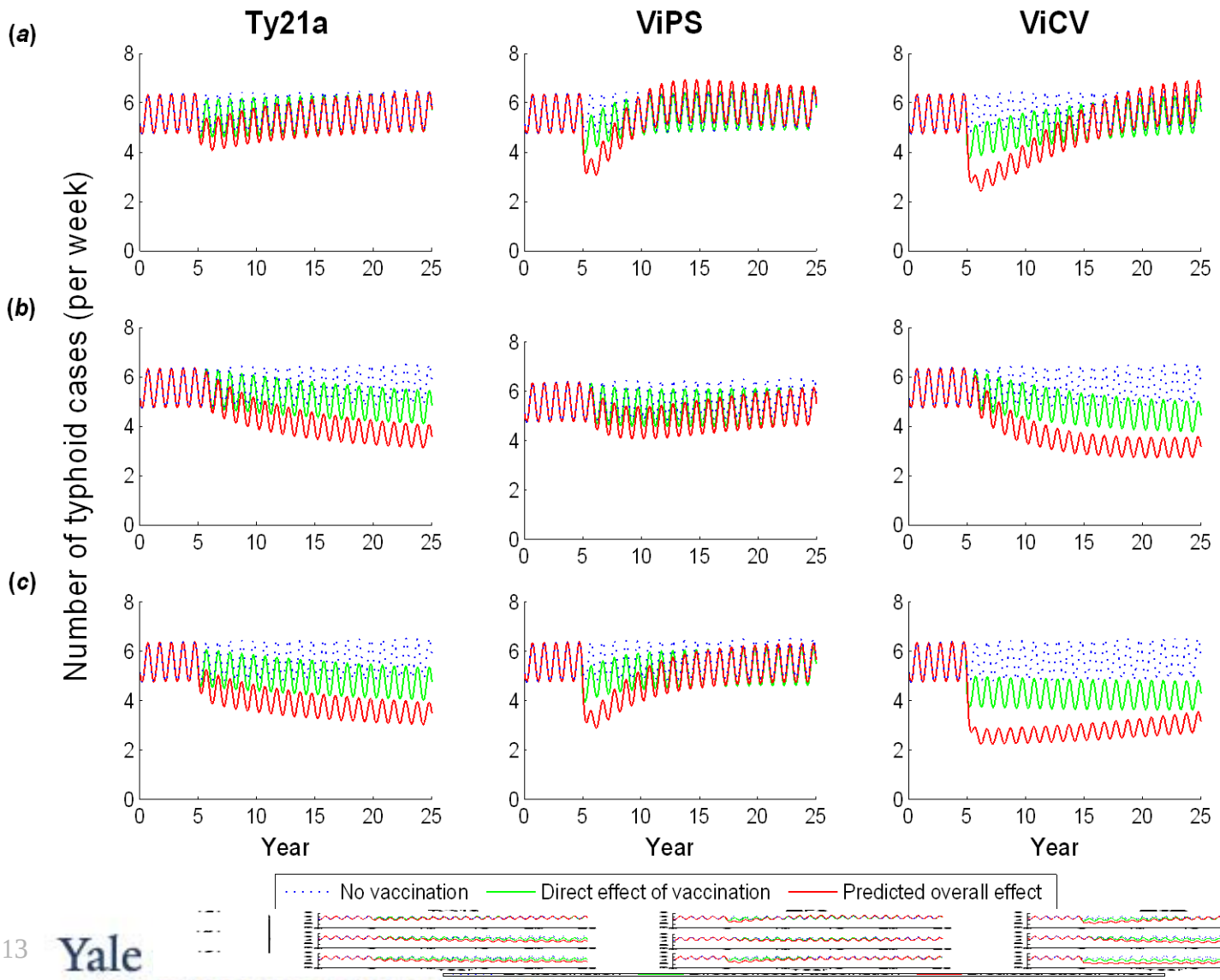
*80% coverage beginning in year 5




One-time campaign among 6-15 year olds

Routine vaccination at 6 years of age

Routine vaccination + catch-up campaign among 6-15 year olds



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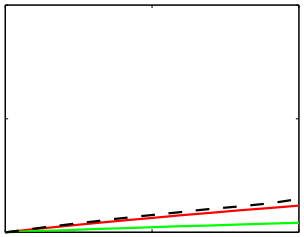


# Vaccine impact vs coverage (1-10 y post-introduction)

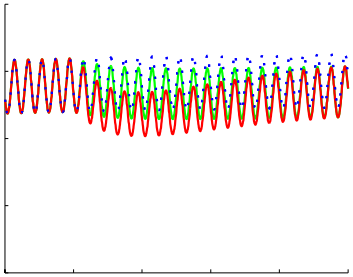
Ty21a

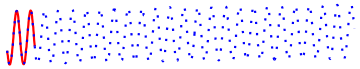
ViPS

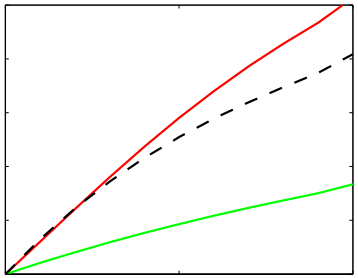
ViCV

ViCV (1 yr olds)

# Effect of revaccination with ViPS

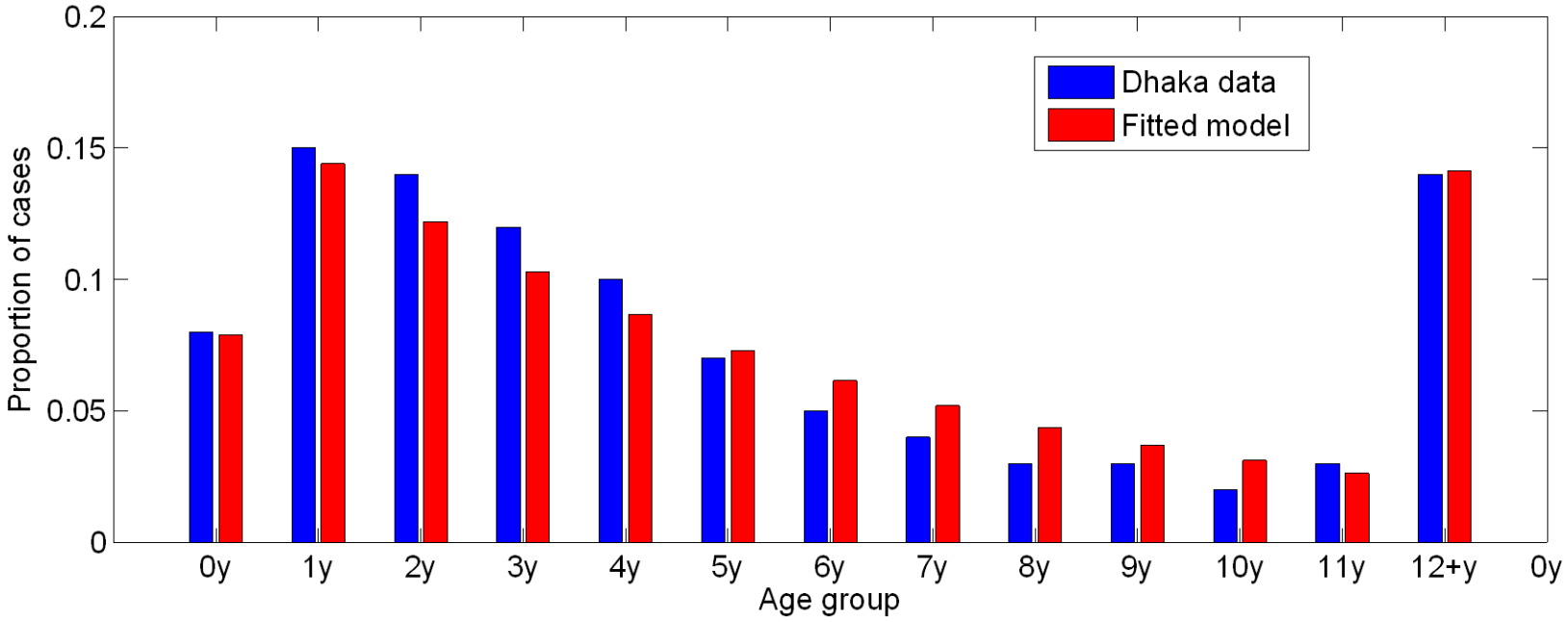






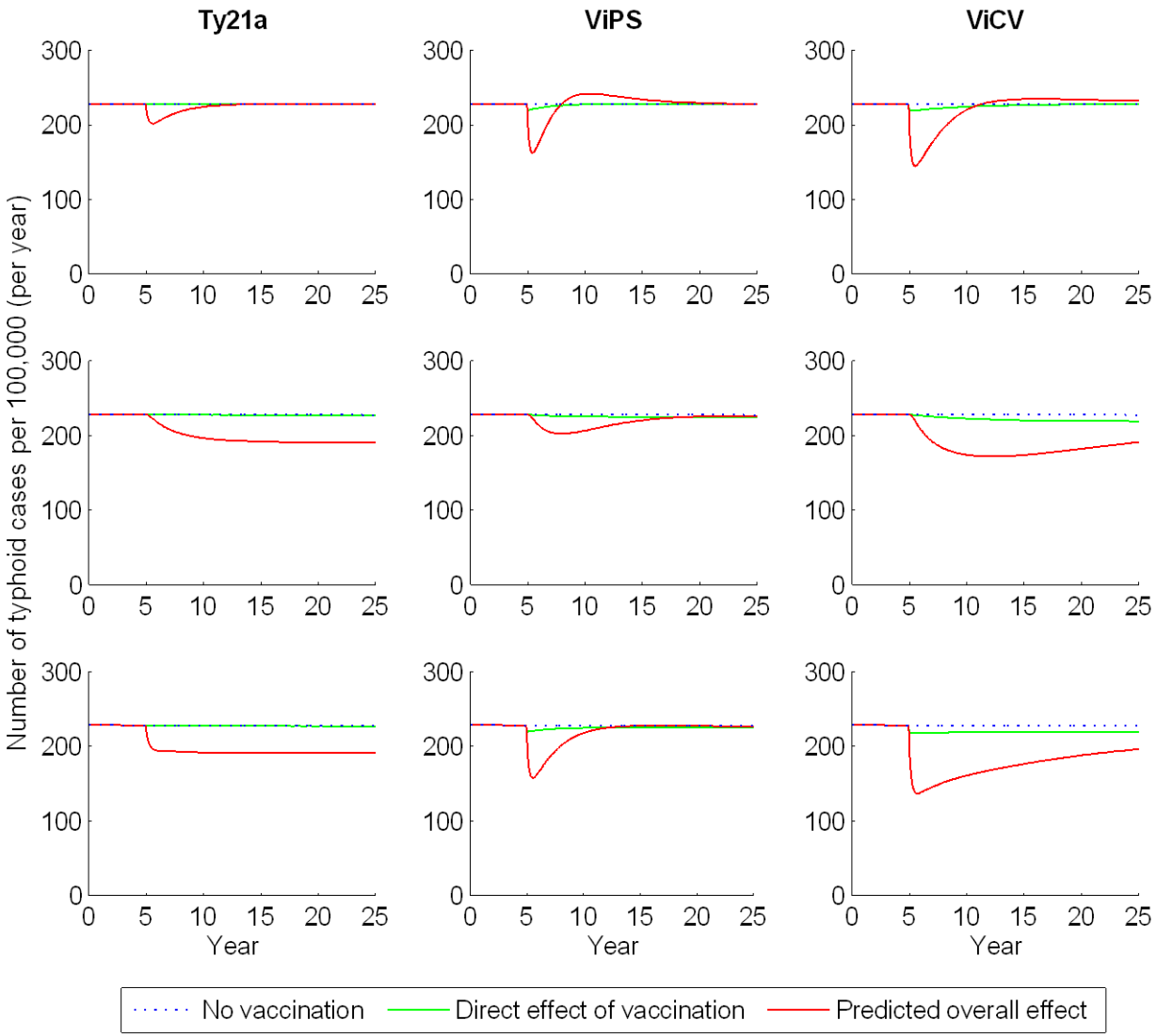
- Re-vaccinating with ViPS every 3 years during school-aged period provides added benefit and prevents typhoid incidence from rebounding

# Typhoid in Dhaka



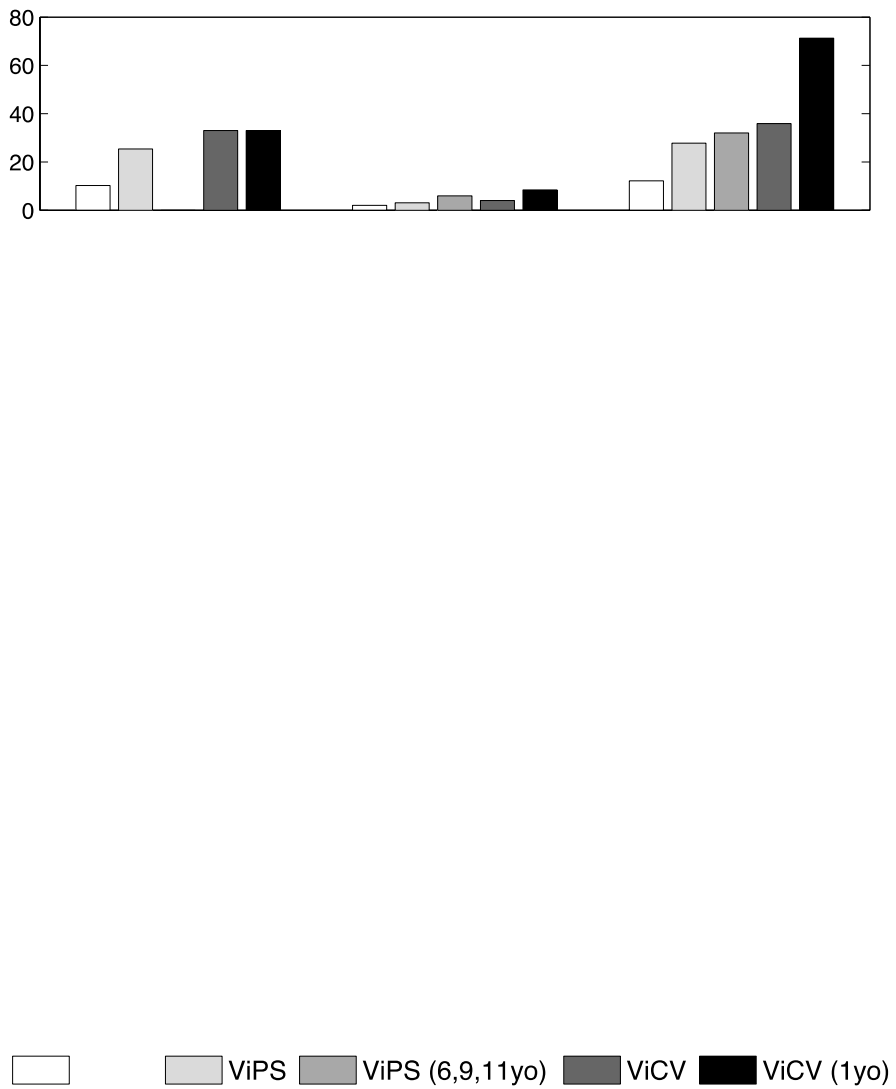

- Age distribution of typhoid cases in Dhaka is much younger than in Vellore
- Incidence rate in the population is likely higher
- Can reproduce the age distribution of cases in Dhaka by increasing $R_0$ in the model to ~7

# Typhoid in Dhaka




- Overall effectiveness is similar, but rebound in incidence happens sooner

# Summary of vaccine effectiveness




- Best strategy is routine vaccination of 9 months with ViCV
  - Especially in Dhaka, where there is a young average age of cases
- Overall effectiveness decreases over time
  - Even with continuing routine vaccination
- Vaccination should be considered as part of a more comprehensive suite of interventions
  - e.g. improved water and sanitation

# Acknowledgements


- Bryan Grenfell
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