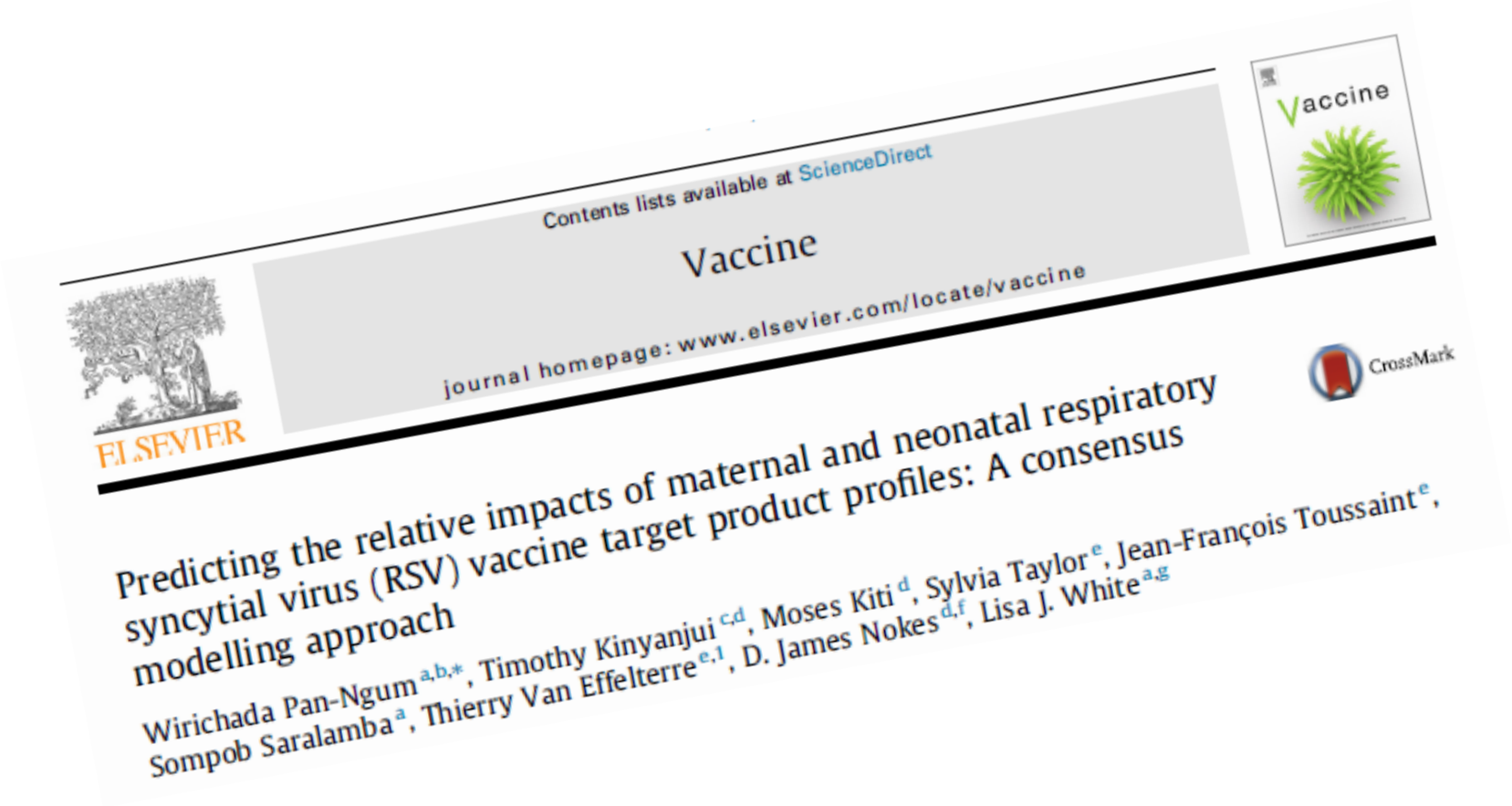
Modelling vaccination strategies in LMIC : an overview

Tim Kinyanjui
Department of Mathematics
University of Manchester

Disclosure

- One of my previous RSV modelling study has been funded by GSK



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Predicting the relative impacts of maternal and neonatal respiratory syncytial virus (RSV) vaccine target product profiles: A consensus modelling approach

Wirichada Pan-Ngum[a,b,*], Timothy Kinyanjui[c,d], Moses Kiti[d], Sylvia Taylor[e], Jean-François Toussaint[e], Sompob Saralamba[a], Thierry Van Effelterre[e,1], D. James Nokes[d,f], Lisa J. White[a,g]

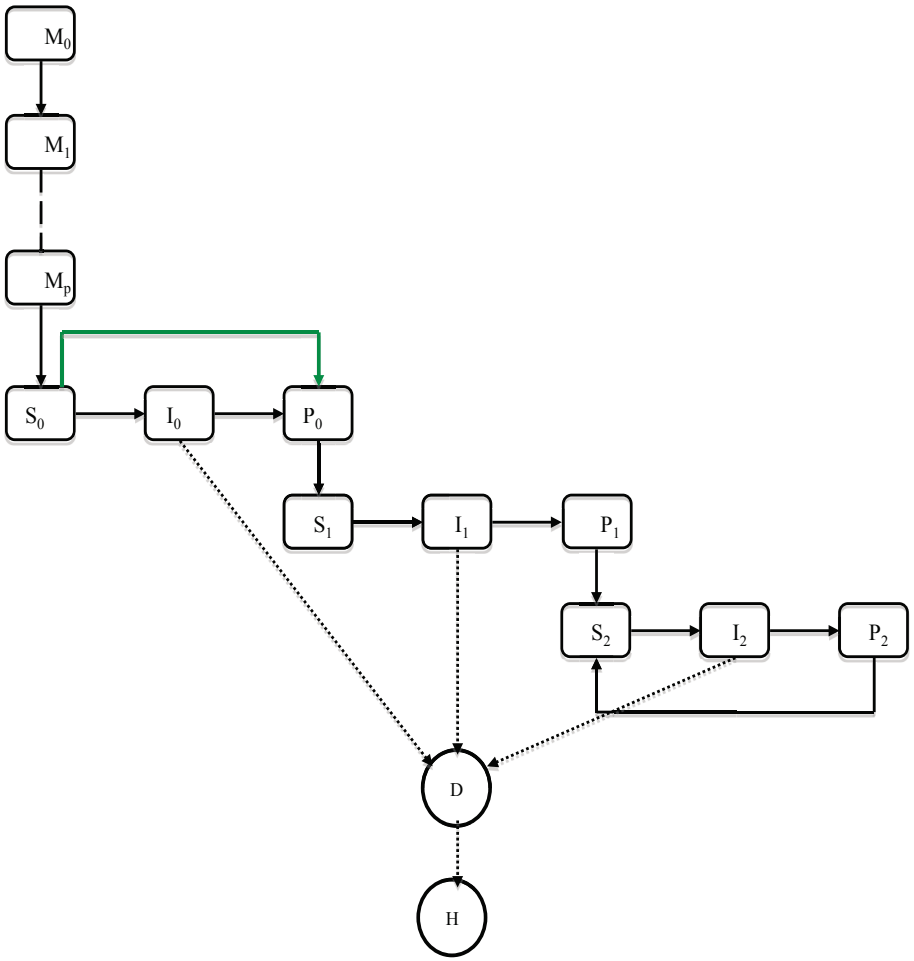
Outline

- Motivation
- An overview of the modelling studies
  - Modelling structure, data used, basic assumptions
  - Results: An overview the best vaccination strategies
- Observations
- Knowledge gaps

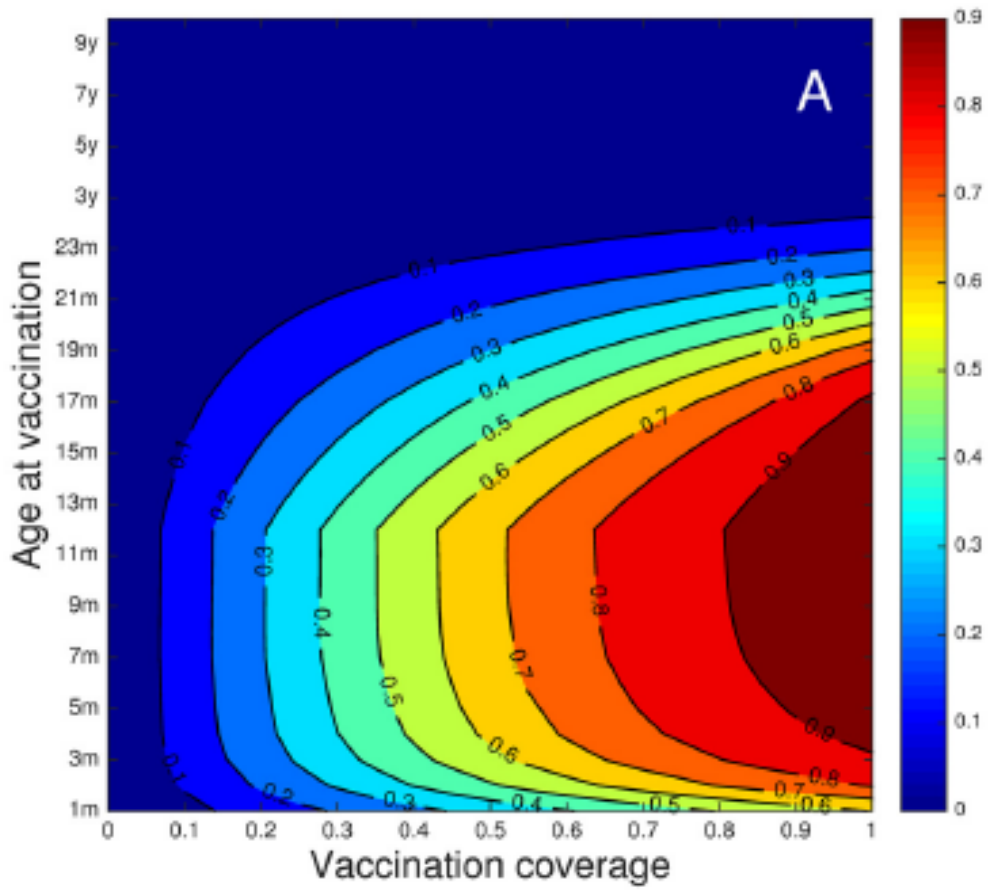
Motivation

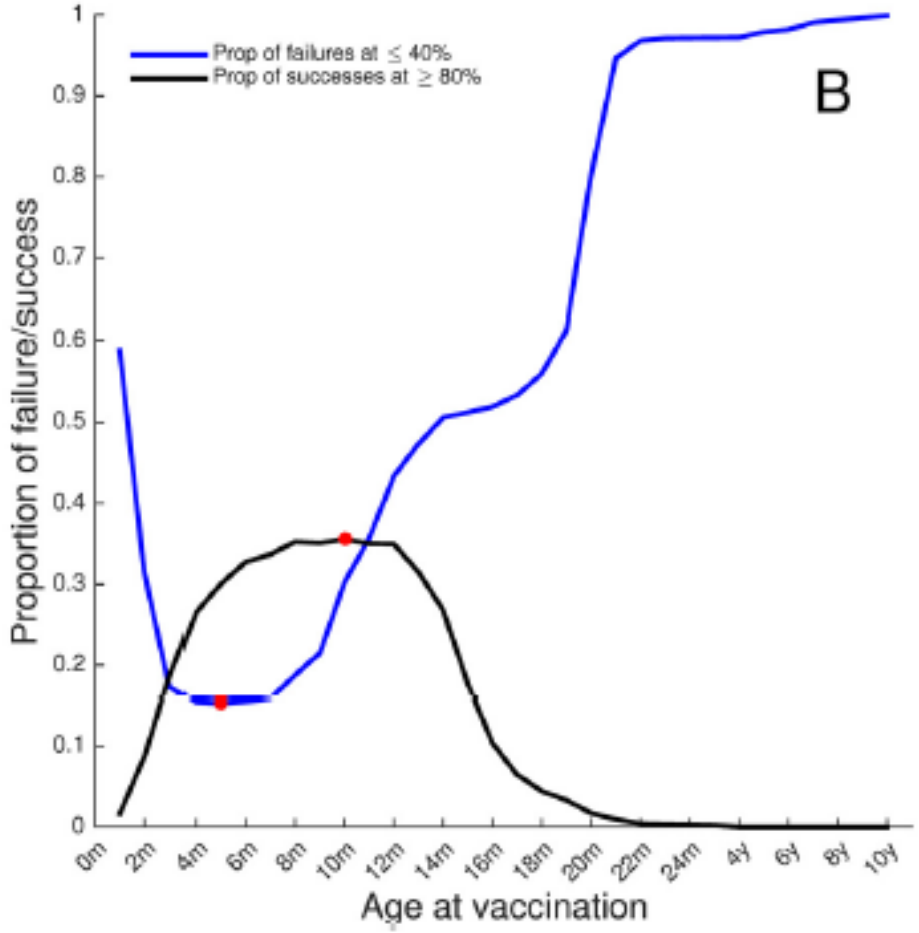
- RSV has been identified as an important human pathogen About 33m <5yr RSV-LRTI /annum global, 3m hospitalisations 96% in LDCs, 66,000-199,000 died from (99% in LCD) (Lancet 2010)
- Severe disease associated with primary infection – mostly 1-3 m key age
- No vaccine available for this target group. Immunogenicity vs safety
- Need to evaluate both **best vaccination strategies** and **vaccine characteristics**
- This objective renders itself well to mathematical modelling treatment
  - Risk free environment
- **Caveat**: This is no replacement for clinical trials, all models are wrong

Kinyanjui et al 2015



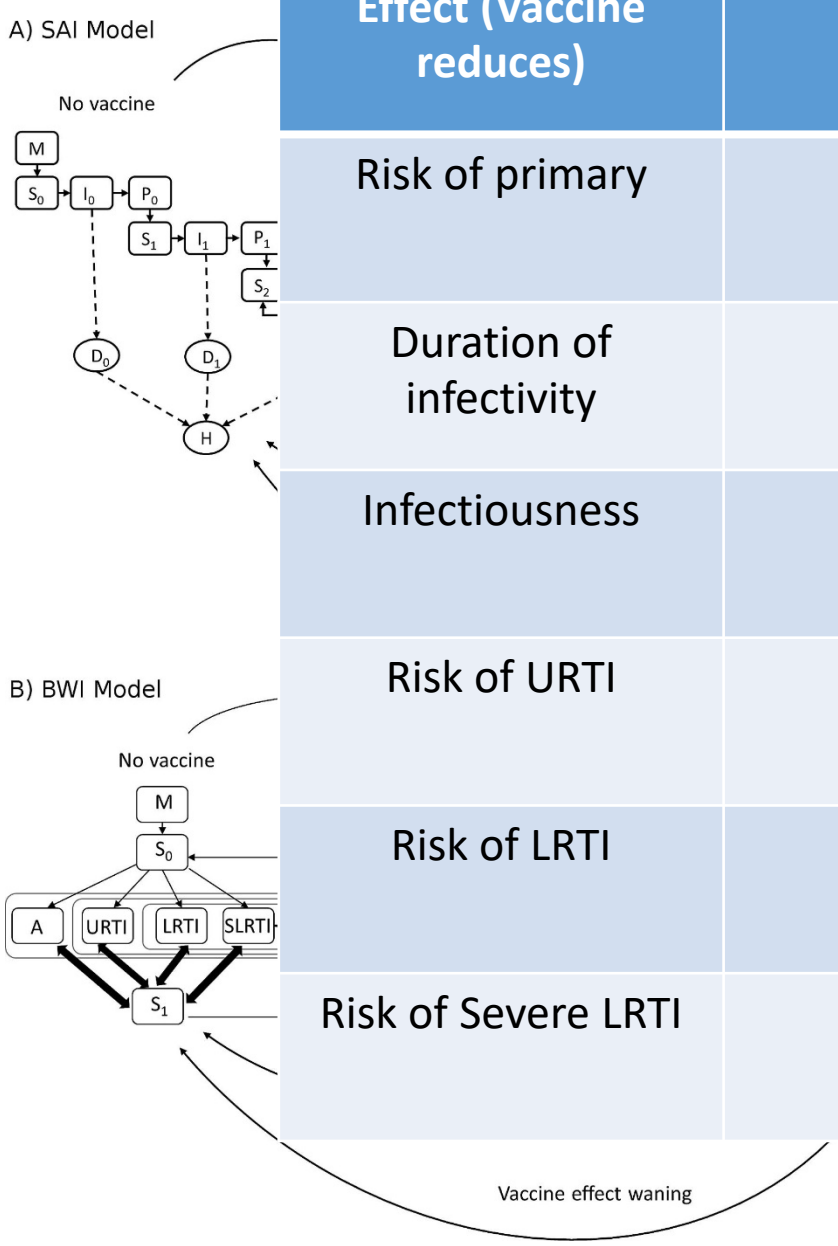
- Deterministic age structure model
- 10 distinct epidemiological classes
  - Differential infectivity, susceptibility, infectiousness, duration of infection
  - Dependent on age and number of previous infections
- Model parameterised with data from Kilifi, Kenya
- Vaccine elicits an immune response ~ to natural infection
- Hospitalisations are proportional to the number of new cases





Optimal vaccination age between 5-10 months

Pan et al 2018 – A consensus modelling approach



Effect (Vaccine reduces)	Low	Medium	High
Risk of primary	**0%**	25%	50%
Duration of infectivity	0%	**50%**	75%
Infectiousness	0%	**50%**	75%
Risk of URTI	**0%**	50%	75%
Risk of LRTI	50%	**70%**	90%
Risk of Severe LRTI	50%	**70%**	90%

odel

mpartments

ection

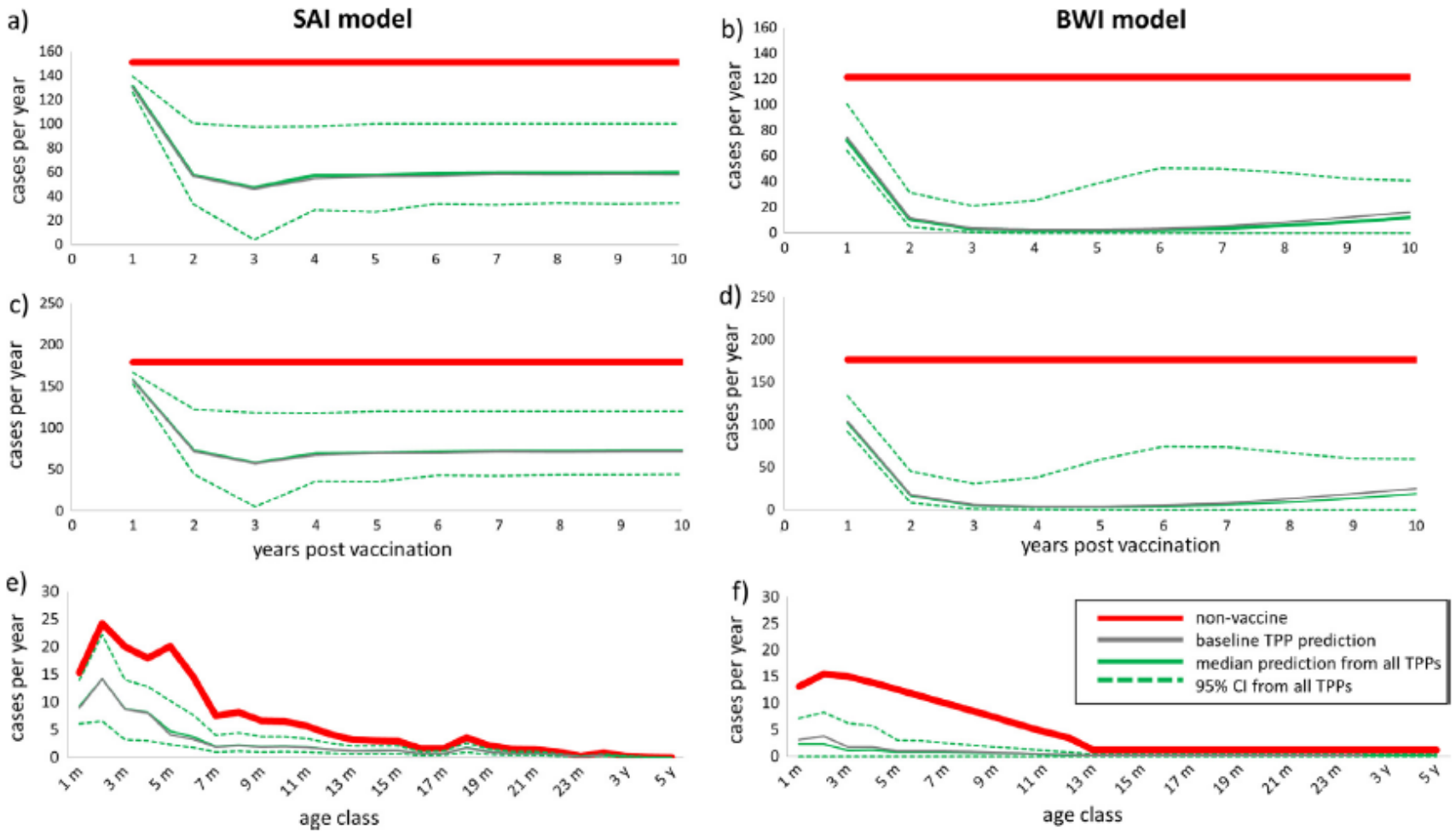
,6 months.
months

nd natural

nths duration

2 years

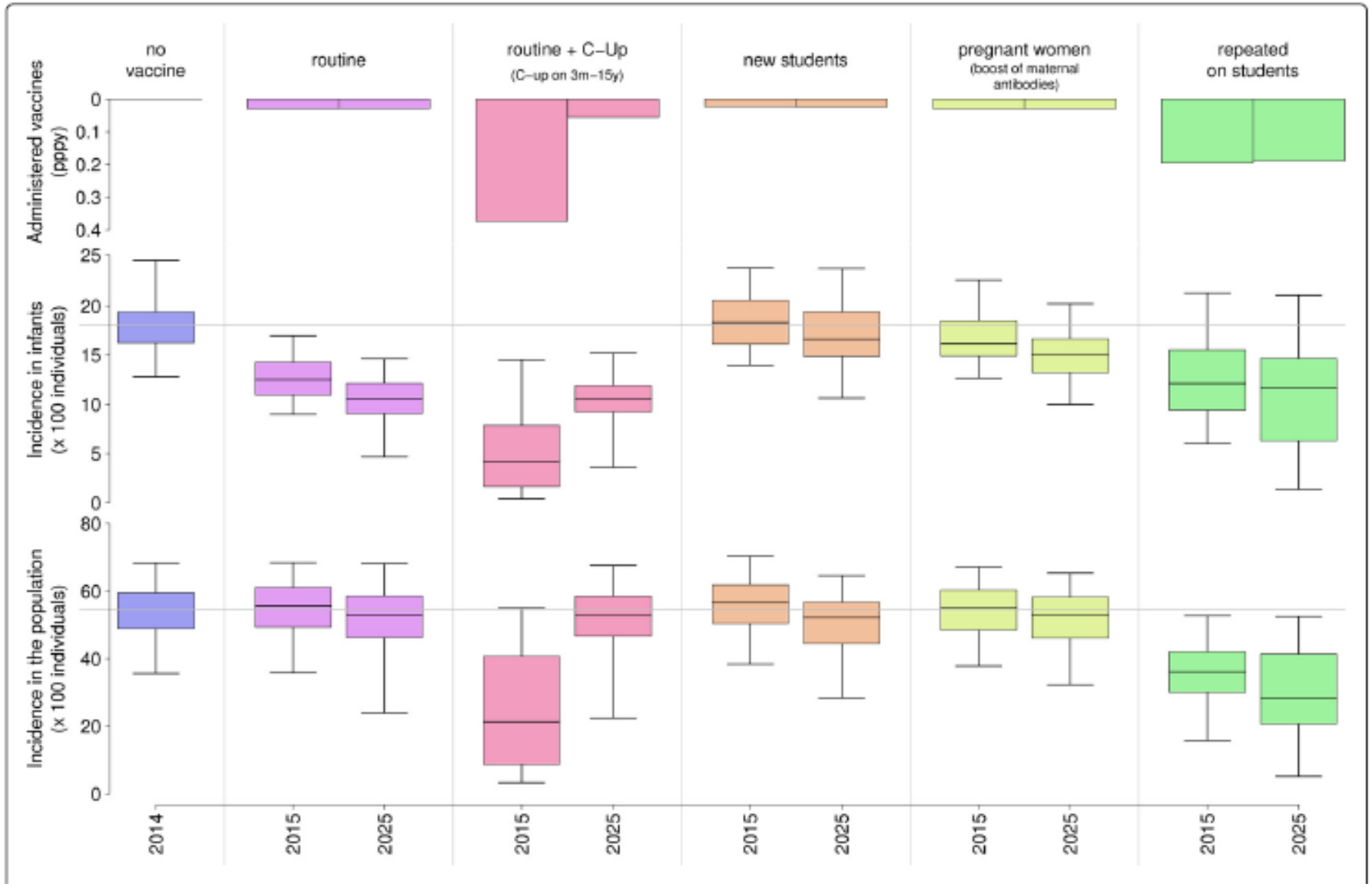
acterisitics



- Best outcome is with vaccine characteristics that impact indirect protection
  - Reduce duration of infections
  - Reduce infectiuousness
  - Reduces risk of transmission

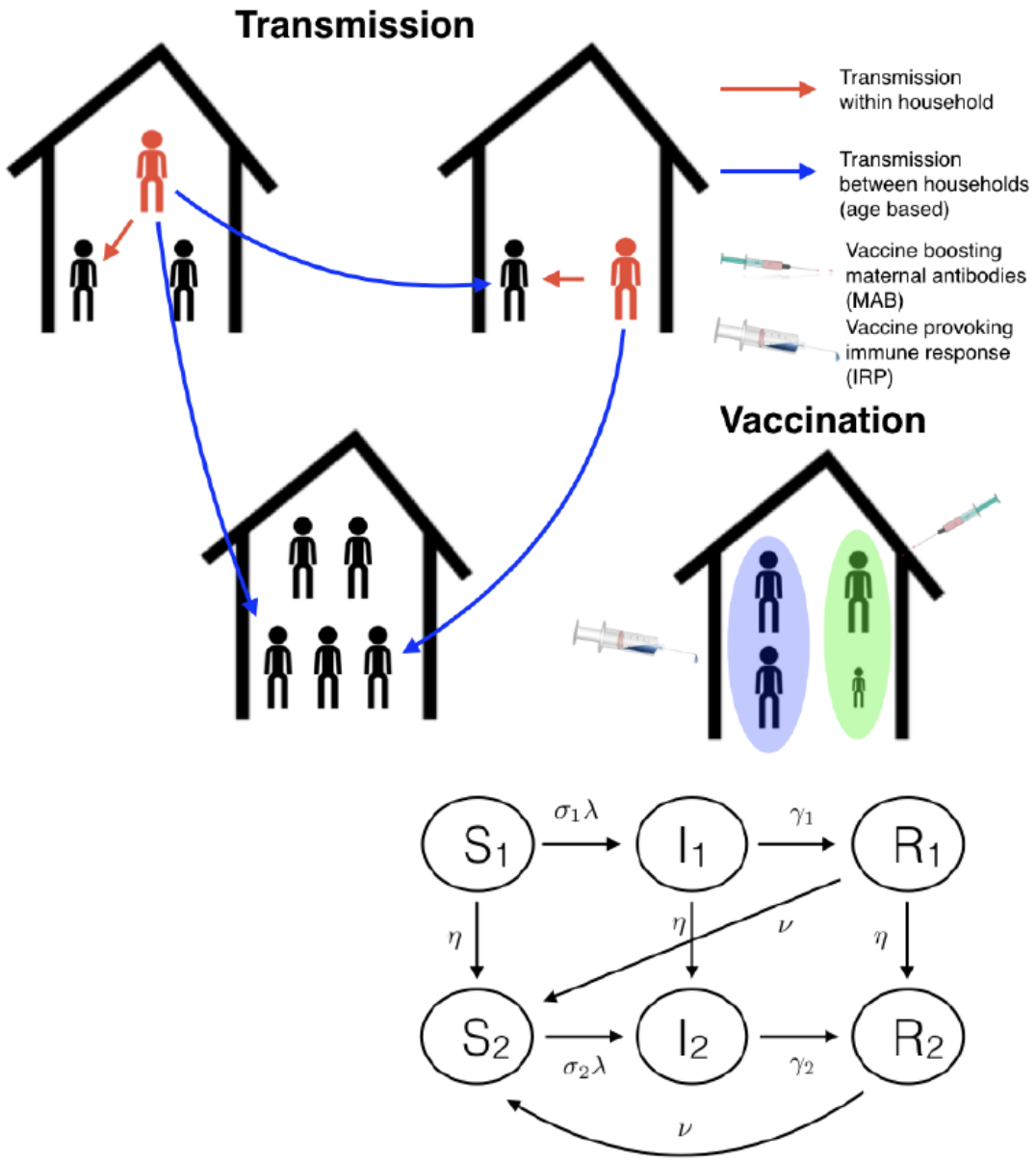
Piero et al 2015

- Individual based model (stochastic model) - data from Kenya DHS
- Simulates a synthetic population structured into
  - Households and primary schools
- Sequential acquisition of immunity with two levels
  - Lifelong reduced susceptibility
- Vaccine provides full but temporary protection against infection
  - Routine vaccination 1 at 3m with catch-up [3m – 15 years]
  - School age children vaccination with catch-up
  - Maternal vaccination – direct and indirect effects

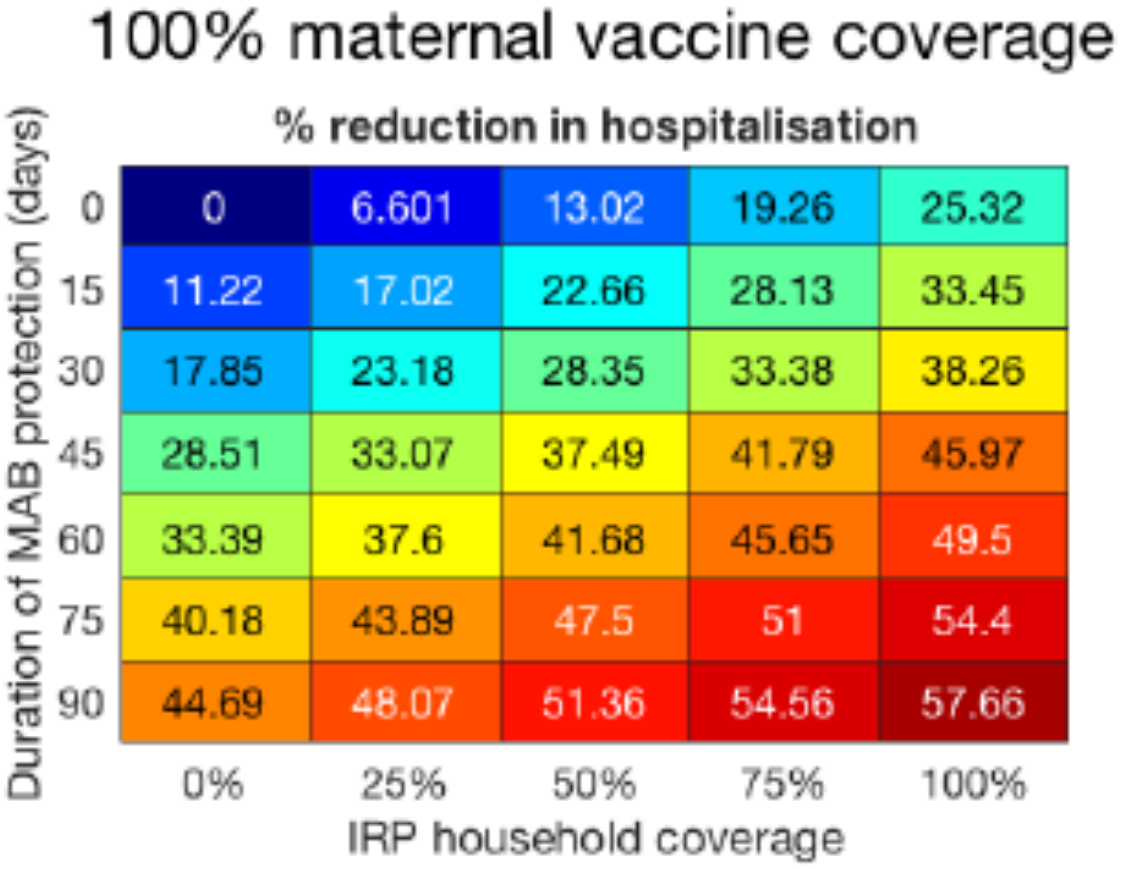


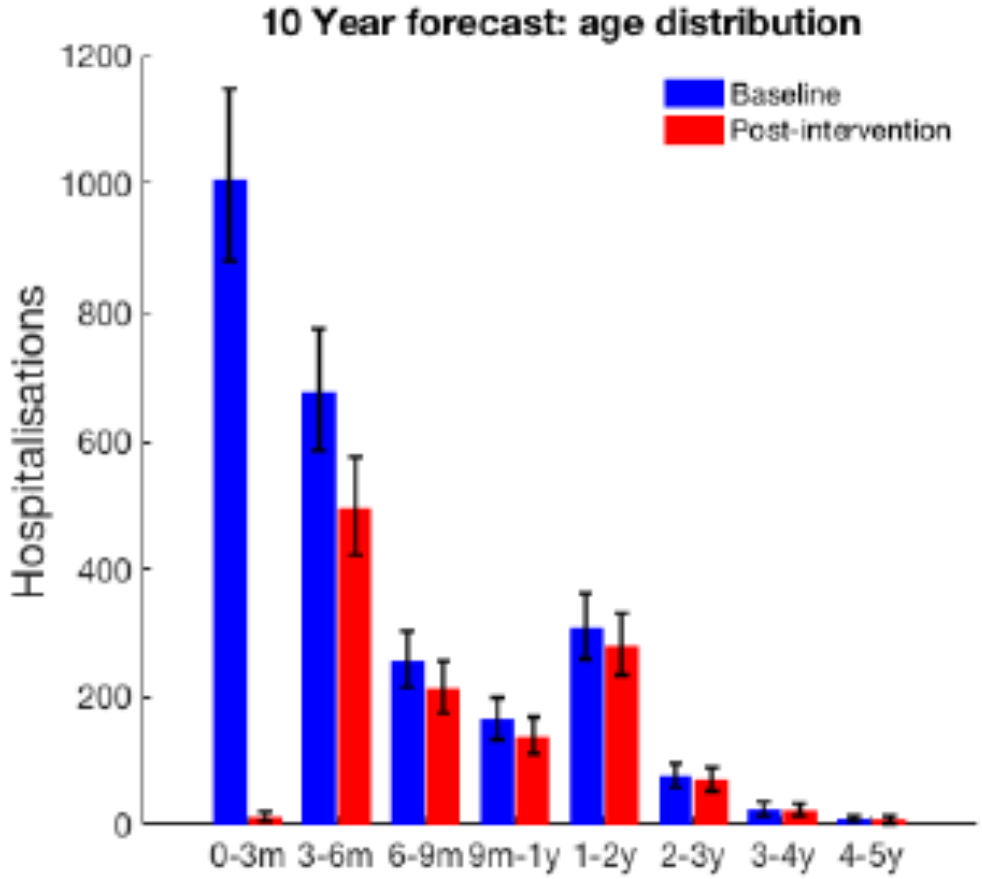
- Most effective strategies considered
  - matAB 6 months
  - 100% coverage
- Best strategies
  - Routine vaccination
  - Routine + Catch-up
  - Students

Brand et al 2019 (bioRxiv)



- IBM household model with 2 levels of mixing
  - Within household transmission
  - Between household transmission
- Epidemiology -> Modified SIR
  - M class with waning immunity
  - Temporary but solid protection
- Two age categories U1 and O1, captures demographic transition
- Combined vaccination strategies
  - Maternal vaccination, third trimester (**Joyce Nyiro poster**)
  - O1 vaccine -> immune response ≈ natural inf.





- Combined vaccination strategy can achieve over 50% reduction in hospitalisations – no huge reduction in amount of infection in population

Observations

- Focus on modelling: Most studies target disease in infants and children
  - Significant impact for a vaccine targeting this group
- Herd immunity effects: All suggest a role for both direct and indirect benefit from vaccination -
- Model structures: A wide range but qualitatively similar results
- Vaccination strategies: A wide range of immunisations strategies have been considered and some in combination
- Vaccine design: One study address the impact of vaccine characteristics on primary outcome

Knowledge gaps

- Model structures: Do we know enough about the natural history?
  - Natural history and epidemiology
- Contact structure
- Inclusion of population sub-units: Households, schools
- Antigenic diversity: No model includes diversity
- Uncertainty about drivers of seasonality
- Immunity to infection:
  - What degree does immune boosting help
  - Duration of maternal antibody protection
  - Vaccine interaction
- Cost effectiveness studies are needed – Policy makers need this