DATA DRIVEN INFECTIOUS DISEASE MODELLING FOR PUBLIC HEALTH:

USING EMPIRICAL DATA IN MALARIA MODELS

Nov 29th, 2023

Workshop on Infectious disease modelling- Malaria

National Disease Modelling Consortium | IIT Mumbai

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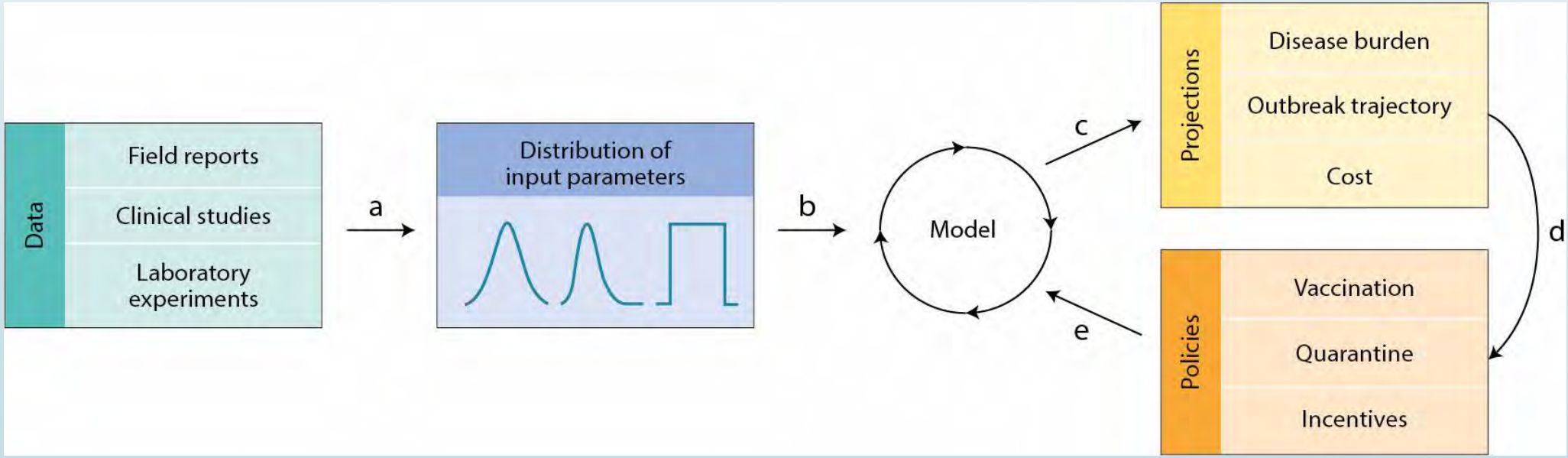
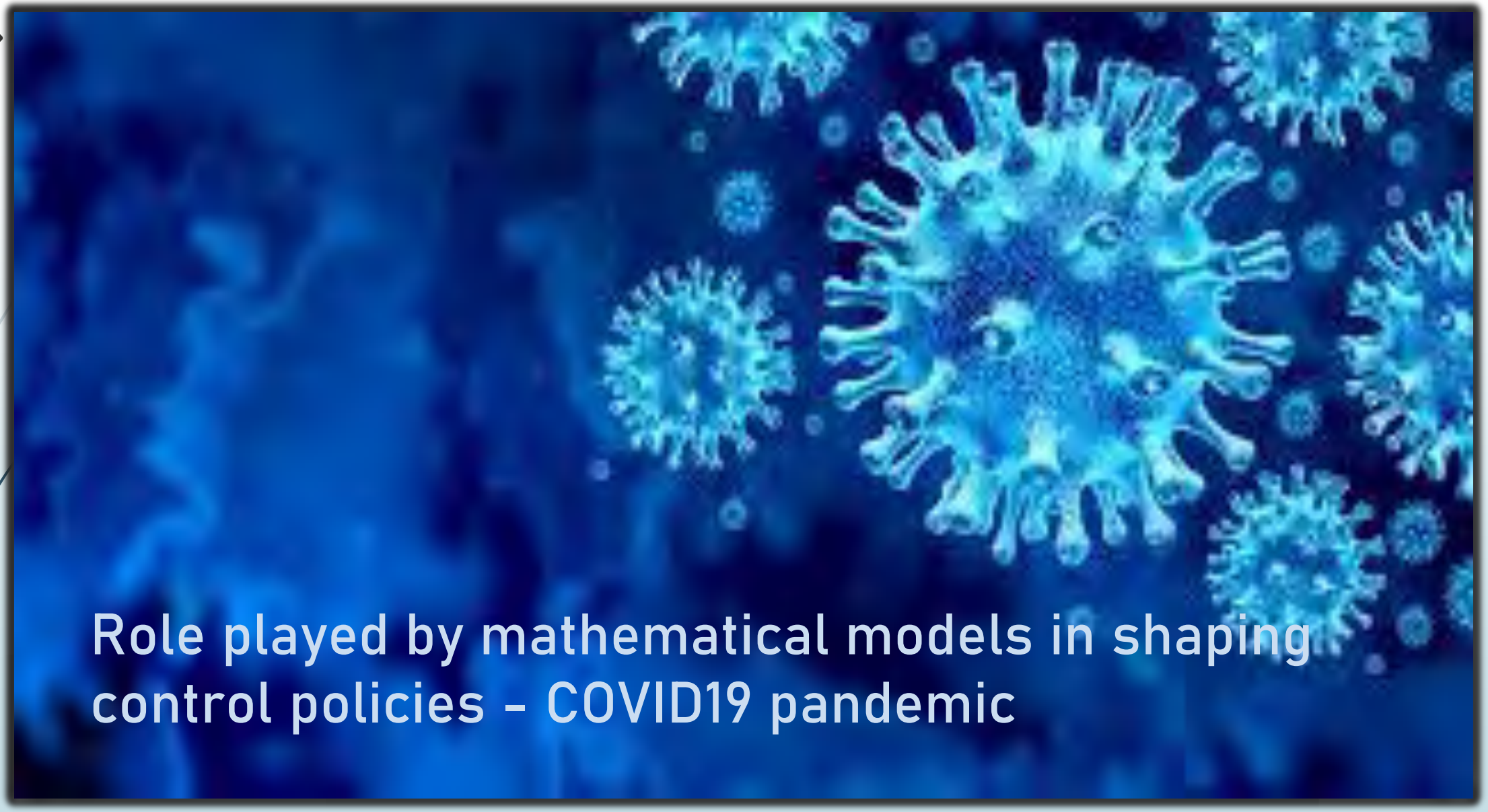
Outline

- Role played by mathematical models :
  - Some examples from *COVID19* pandemic.
- Using empirical data in mathematical models : Examples from *Malaria* Model

Core modeling opportunities (priority questions)

- Where is the pandemic/epidemic going (baseline)?
- What is driving transmission?
- What is the potential of existing/expected delivery interventions to reduce transmission and accelerate reduction in epidemic?
- What combinations of tools, strategies in real-world implementation will be most cost-effective at accelerating reduction?





Role played by mathematical models in shaping control policies – COVID19 pandemic

Example 1

16 March 2020 Imperial College COVID-19 Response Team

Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand

Neil M Ferguson, Daniel Laydon, Gemma Nedjati-Gilani, Natsuko Imai, Kylie Ainslie, Marc Baguelin, Sangeeta Bhatia, Adhiratha Boonyasiri, Zulma Cucunubá, Gina Cuomo-Dannenburg, Amy Dighe, Ilaria Dorigatti, Han Fu, Katy Gaythorpe, Will Green, Arran Hamlet, Wes Hinsley, Lucy C Okell, Sabine van Elsland, Hayley Thompson, Robert Verity, Erik Volz, Haowei Wang, Yuanrong Wang, Patrick GT Walker, Caroline Walters, Peter Winskill, Charles Whittaker, Christl A Donnelly, Steven Riley, Azra C Ghani.

On behalf of the Imperial College COVID-19 Response Team

WHO Collaborating Centre for Infectious Disease Modelling
MRC Centre for Global Infectious Disease Analysis
Abdul Latif Jameel Institute for Disease and Emergency Analytics
Imperial College London

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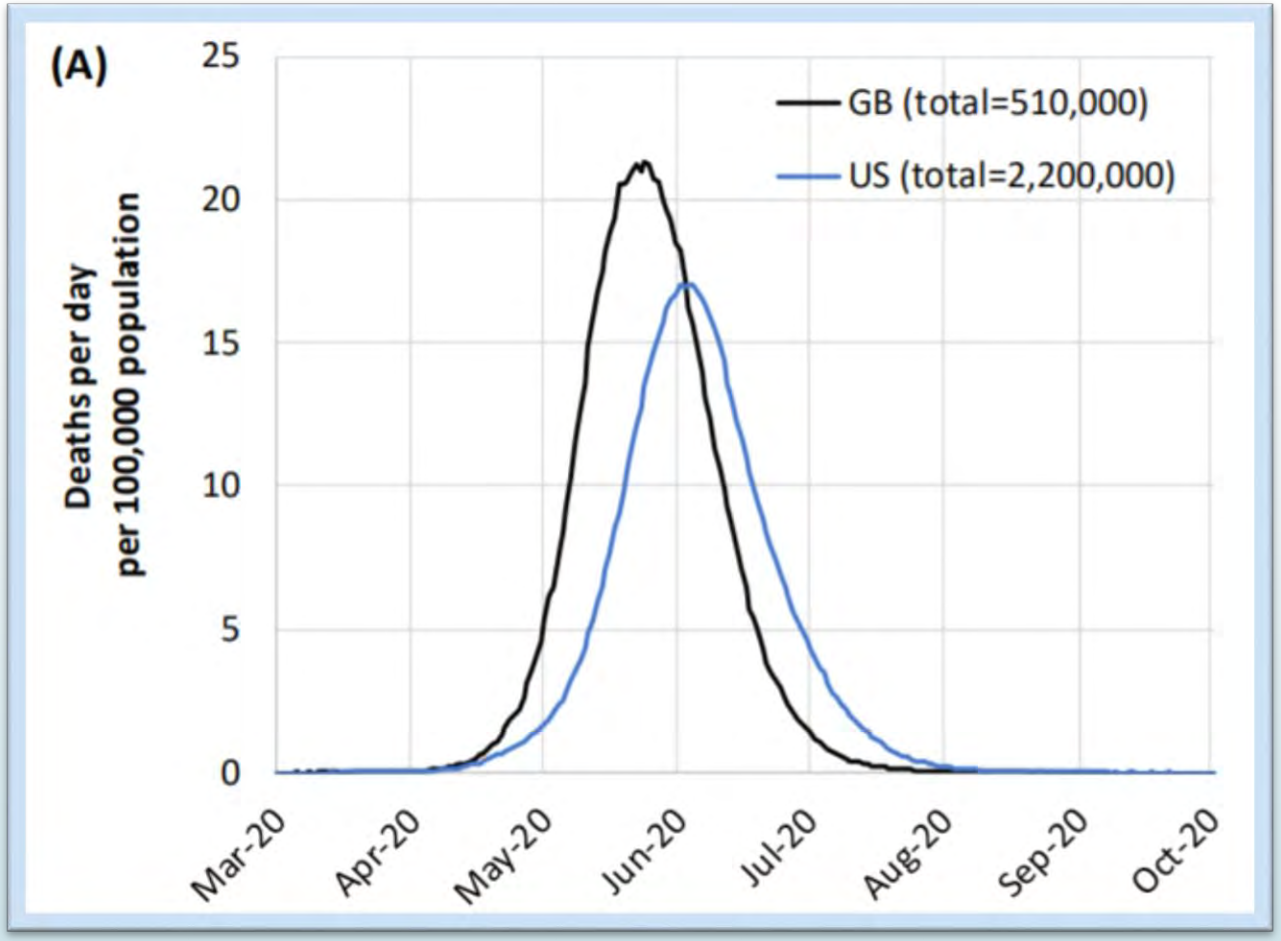
- Results of epidemiological modelling which has informed policymaking in the UK and other countries.
- Assessed the potential role of a number of public health measures – non-pharmaceutical interventions (NPIs)



Baseline Reproduction number: $R_0 = 2.4$

Figure 1: Unmitigated epidemic scenarios for GB and the US. (A) Projected deaths per day per 100,000 population in GB and US.

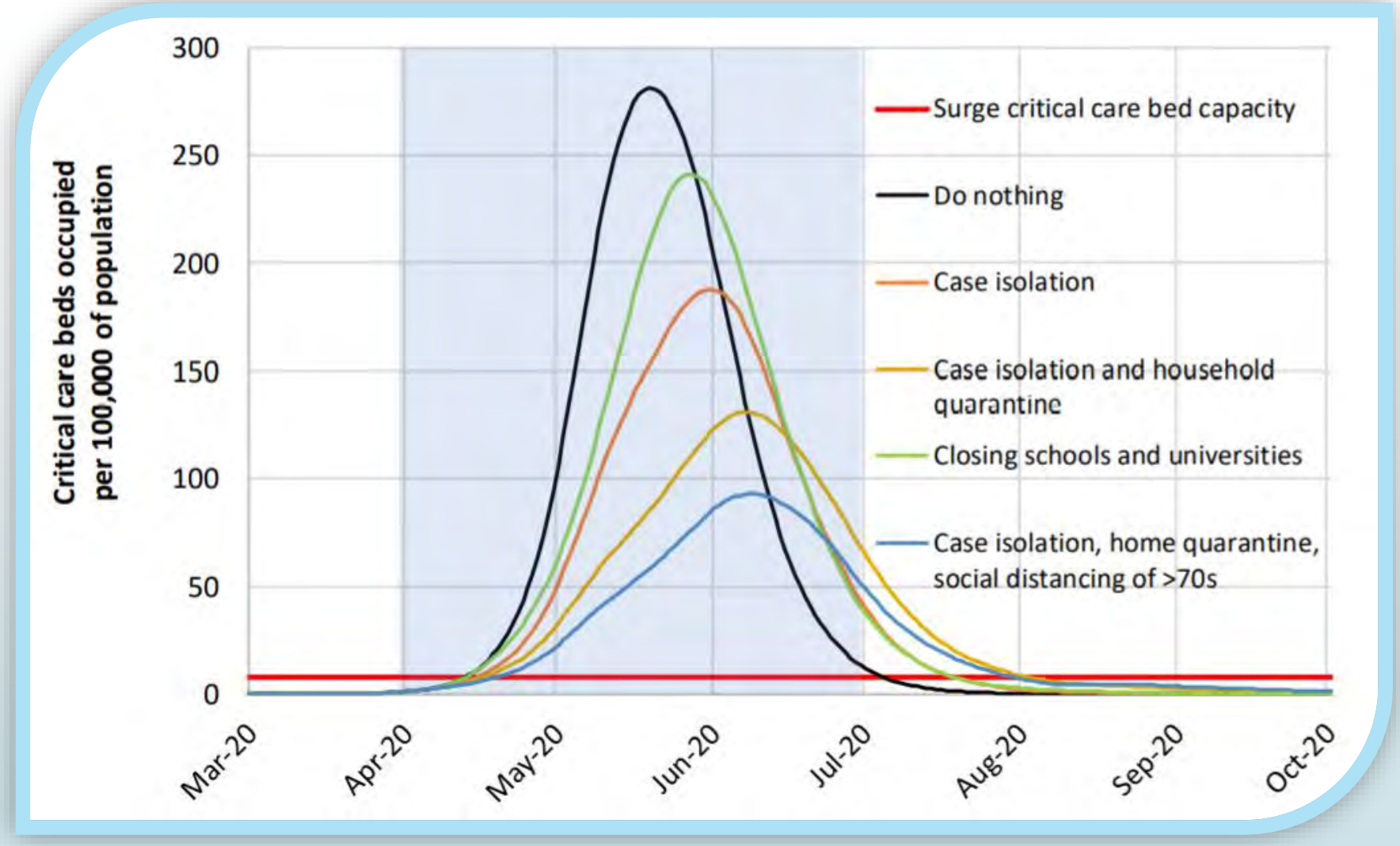
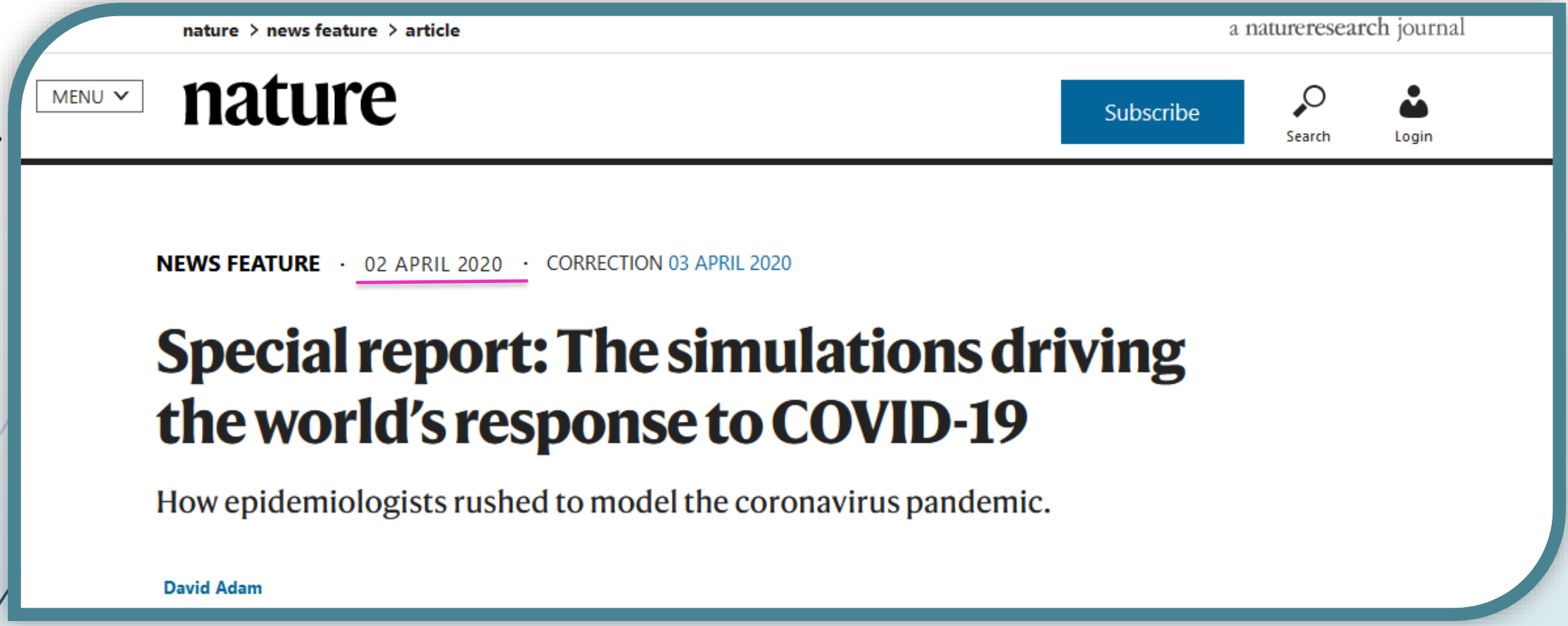


Figure 2: **Mitigation strategy scenarios for GB showing critical care (ICU) bed requirements.**



Research does not get much more policy-relevant than this. When updated data in the Imperial team's model indicated that the United Kingdom's health service would soon be overwhelmed with severe cases of COVID-19, and might face more than 500,000 deaths if the government took no action, Prime Minister Boris Johnson almost immediately announced stringent new restrictions on people's movements.*

*Ferguson, N. M. *et al.* Preprint at Spiral https://doi.org/10.25561/77482 (2020).

Example 2

Media Briefing On COVID-19

Summary of various estimates:

Cases and deaths averted

	Cases averted	Deaths averted
Estimate 1 (BCG)	**36-70 lakhs**	**1.2-2.1 lakh**
Estimate 2 (PHFI)	-	**78,000**
Estimate 3 (MK & SR)	**23 lakhs**	**68,000**
Estimate 4 (AP, RMM, SM, PN)	**15.9 lakh**	**51,000**
Estimate 5 (MoSPI/ISI)	**20 lakh** (Range 14 – 29 lakh)	**54,000** (Range 37,000 – 78,000)

https://www.youtube.com/watch?v=QI28aIqlApprx DrU

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Use of empirical data in mathematical models : Examples from Malaria model

- Using simple models to generate proxy estimation for a parameter in the complex model:
  - Discussing field data from Kenya on Mosquito density in presence and absence of Biolarvicides
  - Estimating parameters from field survey data by plugging into sub-models (Example from Malaria model)
- Using time series data to estimate transmission parameters via nonlinear inverse problem
  - Discussing Malaria incidence data from Kokrajhar Assam
  - Estimating parameters from complex models (Example from Malaria model)
- Using mathematical expressions like R0 and Endemic state to estimate parameter

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Journal of Theoretical Biology

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

Modeling the impact of biolarvicides on malaria transmission

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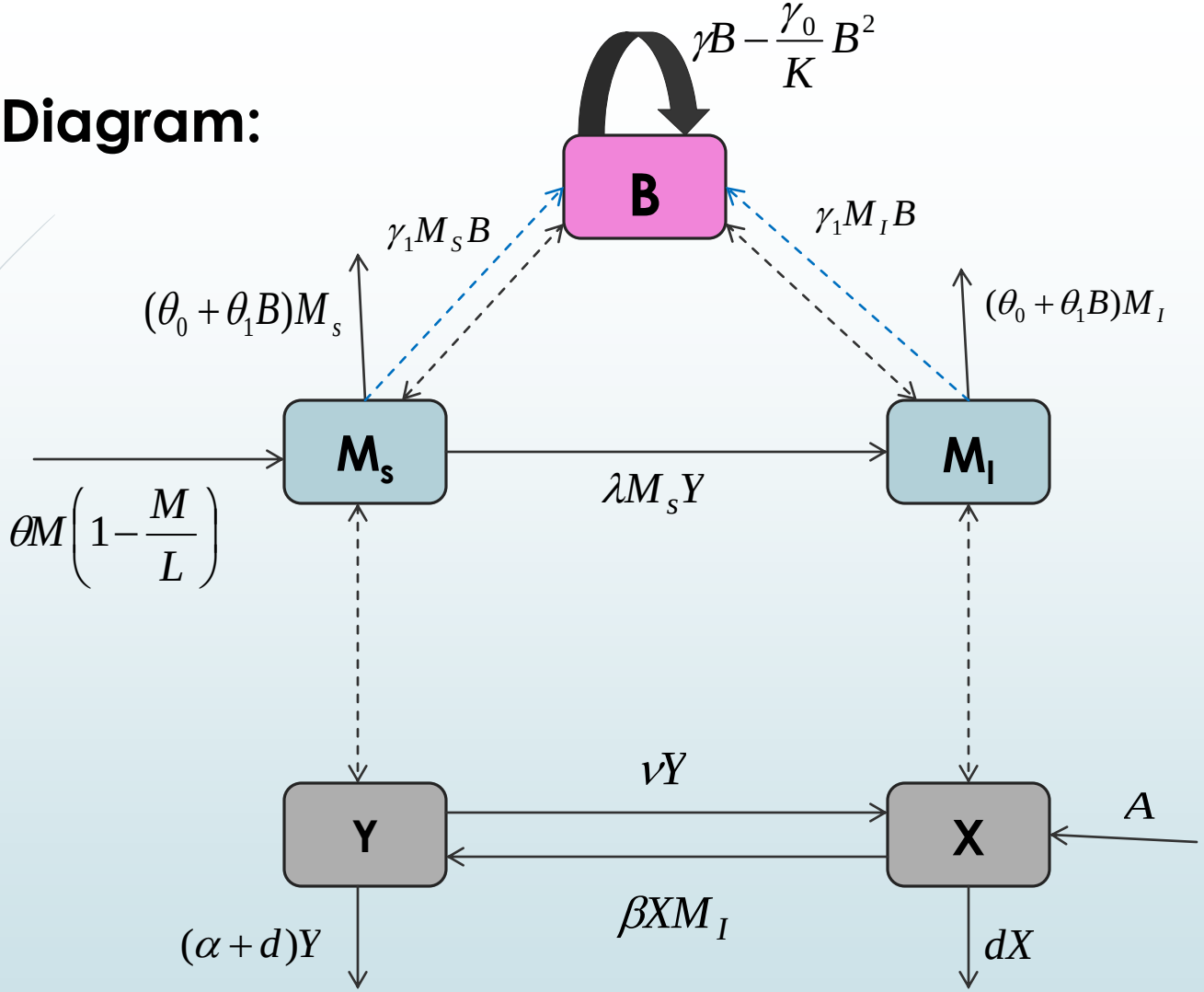
[b] Dartmouth College, Hanover, NH, USA
[c] International Centre for Theoretical Sciences, Bangalore 560089, India
[d] Harcourt Butler Technological Institute, Kanpur, India

Goal –

- To study the impact of biolarvicides on malaria prevalence.
- Estimate parameter values which were not available or measureable.

Block Diagram:



Mathematical Model

$$\frac{dX}{dt} = A - \beta X M_I - dX + \nu Y$$

$$\frac{dY}{dt} = \beta X M_I - (\nu + \alpha + d)Y$$

$$\frac{dN}{dt} = A - dN - \alpha Y$$

$$\frac{dM_s}{dt} = \theta M\left(1 - \frac{M}{L}\right) - (\theta_0 + \theta_1 B)M_s - \lambda M_s Y$$

$$\frac{dM_I}{dt} = \lambda M_s Y - (\theta_0 + \theta_1 B)M_I$$

$$\frac{dM}{dt} = \theta M\left(1 - \frac{M}{L}\right) - (\theta_0 + \theta_1 B)M$$

$$\frac{dB}{dt} = \gamma B - \frac{\gamma_0}{K} B^2 + \gamma_1 MB$$

$$X + Y = N,\ M_s + M_I = M$$

$$X(0) > 0, Y(0) \geq 0, N(0) > 0,\ B(0) \geq 0, M_s(0) \geq 0, M_I(0) > 0,\ M(0) \geq 0$$

Parameters directly obtained from literature and are fixed **(A, d, alpha - 3 parameters)**

Census/ demographic/ epidemiological data

Afrane et al. Malar J (2016) 15:577
DOI 10.1186/s12936-016-1626-6

Malaria Journal

RESEARCH Open Access

Evaluation of long-lasting microbial larvicide for malaria vector control in Kenya

Yaw A. Afrane[1,2], Nixon G. Mweresa[2], Christine L. Wanjala[4], Thomas M. Gilbreath III[3], Guofa Zhou[3], Ming-Chieh Lee[3], Andrew K. Githeko[2] and Guiyun Yan[3*]

- This was a controlled study of biolarvicide (specifically *Bti* and *Bs*) use in highland regions of Kenya that are prone to epidemic malarial outbreaks.

- Mosquito populations from trials in the presence, as well as in the absence of biolarvicides during an eight week period were used to calibrate parameters in the *M*, *B* subsystem.

- Since Kenya data was on per-household basis; the M-B subsystem was scaled down : the *M equation was factored by 30* (representing average number of households in the region).

- Setting $M_h = M/30$ and sub-system was calibrated.

$$\frac{dM_h}{dt} = M_h\left(\theta(1 - 30\frac{M_h}{L}) - (\theta_0 + \theta_1 B)\right)$$

$$\frac{dB}{dt} = B\left(\gamma(1 - \frac{B}{K}) + 30\gamma_1 M_h\right)$$

Parameters indirectly estimated from entomological data and submodel ***(7 parameters)***

1. Sub-model calibration (*M-B* system) - ***mosquito abundance timeseries data*** in the ***absence of biolarvicides***, by setting initial bacteria population $B_0 = 0$ and *estimated* the *mosquito growth* and *death rates*: θ and θ_0 and *carrying capacity L*.

2. Fixing the parameters obtained above and calibrating sub-model to intervention data (setting B_0 to *biolarvicide* population at the beginning of the field study) – *estimated* values for the *bacterial growth rates* γ, *mosquito death rate by biolarvicides* θ_1, the *interaction rate* γ_1 *of bacteria* and *mosquito*; and *carrying capacity K*.

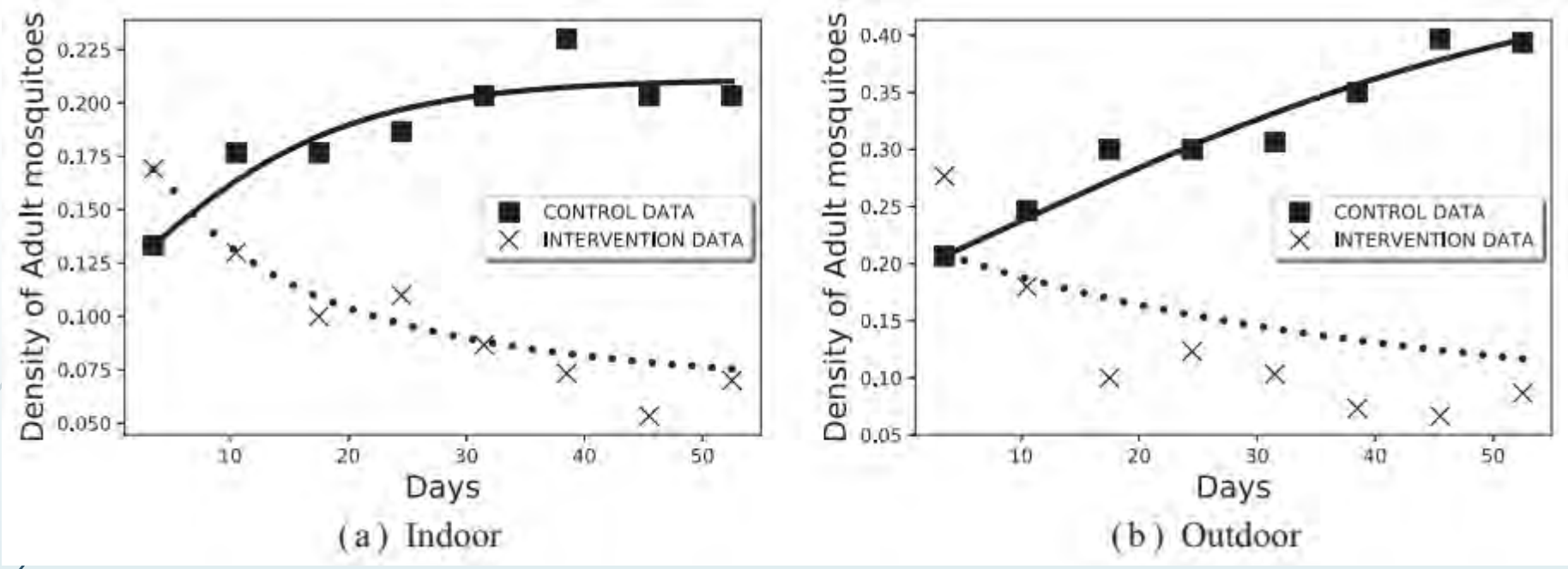


Fig. The control data corresponds to mosquito population with no biolarvicide use. The intervention data corresponds to malaria population in presence of biolarvicide in *Afrane et. al.* (2016).
Solid and dotted lines are obtained from fitting. Values obtained from fitting are
(a) Indoor: $\theta = 2.516$, $\theta 0 = 2.416$, $\theta 1 = 2.3 \times 10\text{-}7$;
(b) Outdoor: $\theta = 0.4751$, $\theta 0 = 0.4340$, $\theta 1 = 1.31 \times 10\text{-}7$.

Common parameters values obtained for both indoor and outdoor settings are $\gamma 1 = .001$, $\gamma = 39$, $L = 160$, $K = 300,000$.

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Association between Climatic Variables and Malaria Incidence: A Study in Kokrajhar District of Assam, India

Climatic Variables and Malaria Incidence in Kokrajhar District

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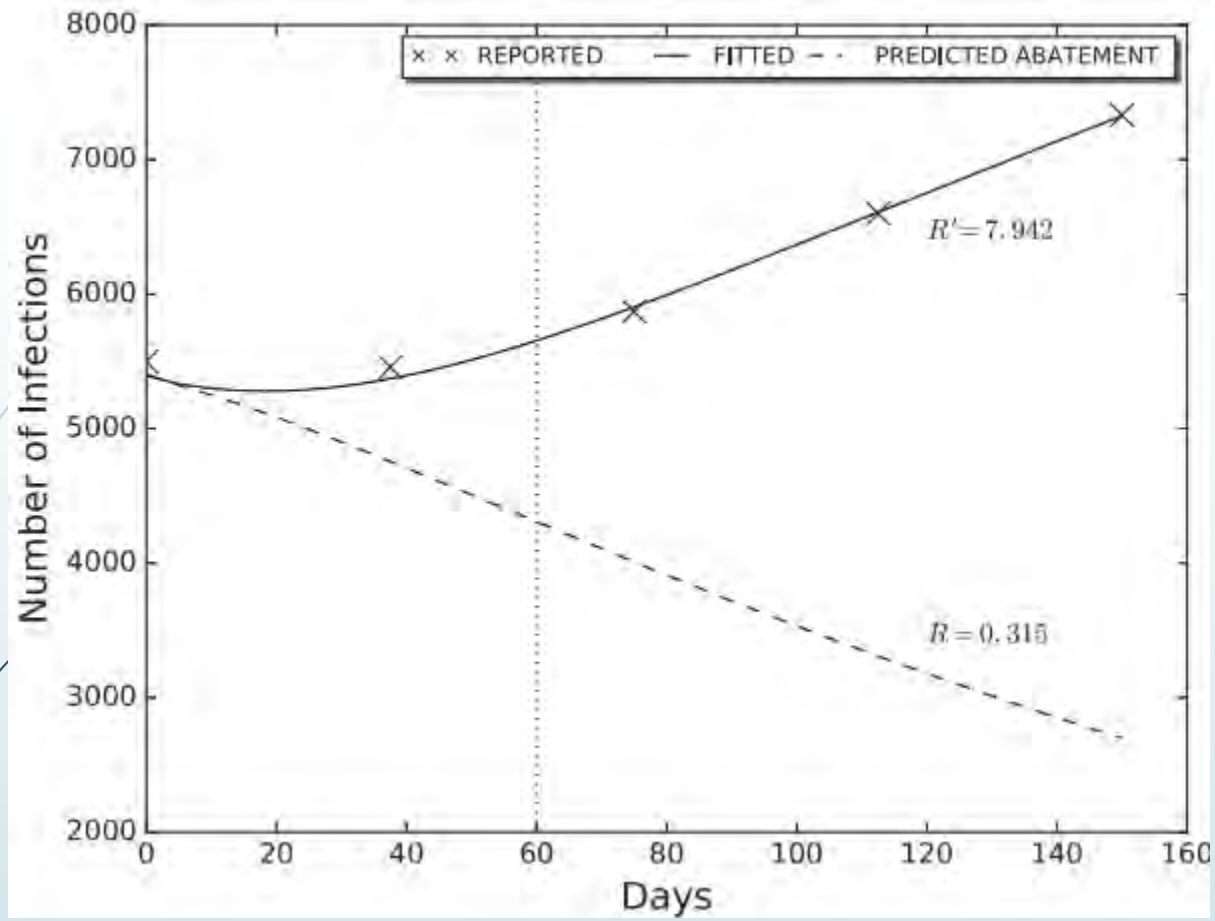
Kokrajhar district of Assam, India, a region that suffers regularly from malaria.

Considered mean *District malaria incidence rates* (DMIR) for the months of August to December (2001 to 2010), during which the district experiences a spike in malaria infections for calibration.

- While calibrating full model system to *Kokrajhar* data – parameters for the *M*, *B* system were fixed at values obtained for the outdoor region calibration above.

- Starting with no initial bacteria (in order to account for the lack of biolarvicide use), full model was calibrated to estimate transmission rates β and λ using averaged malaria incidences over a 10 year period from 2001 to 2010 from Kokrajhar.

- As a final step, using the same malaria incidence data from Kokrajhar, model was calibrated with non-zero value for B_0 ensuring presence of biolarvicide.



In absence of Biolarvicides

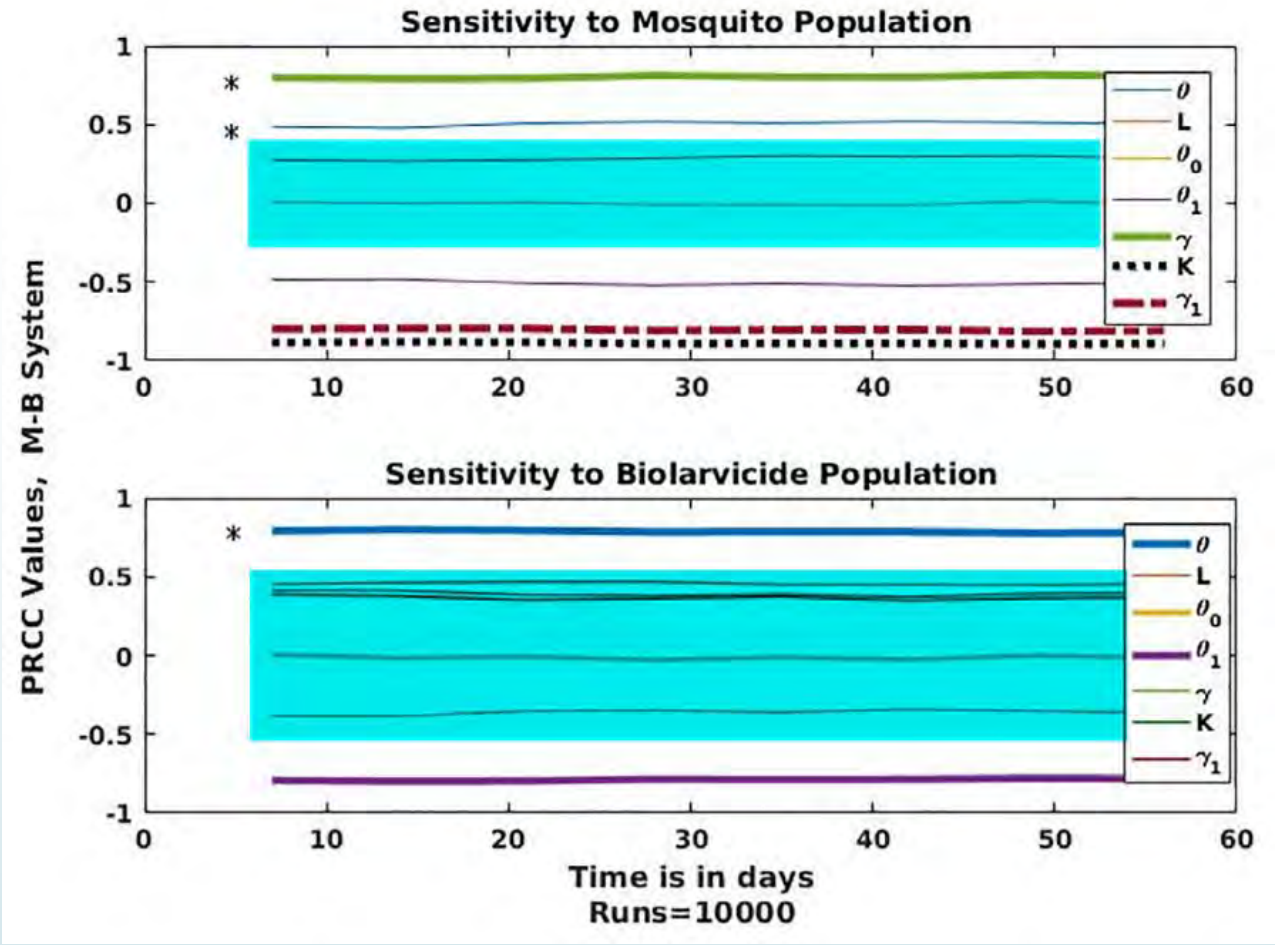
$$R' = \frac{\beta\lambda A\tilde{M}}{d\theta_0(\nu+\alpha+d)}$$

$$R = \frac{\beta\lambda A\tilde{M}}{d(\nu+\alpha+d)(\theta_0+\theta_1\tilde{B})}$$

Fig. Reported values are of total malaria infection. Fitting the full model system to malaria incidence data from Kokrajhar district of Assam, India. **Values obtained for transmission rates: $\beta = 5.227 \times 10^{-6}$** and **$\lambda = 4.117 \times 10^{-5}$**.

The dashed line shows the predicted reduction in malaria incidence – <u>if biolarvicides are used starting at initial time. The vertical dotted line captures the reduction in malaria infection at 60 days.</u>

Sensitivity Analysis



Almost *constant PRCC values indicates* the particular parameter as having a *constant influence on the outcome, over the eight week period*. The parameters were sampled from a uniform distribution with mean of the intervals. Significant parameters with $p < 0.001$ are marked with $*$. *For the mosquito population,* **γ , θ** *are the two* ***most significant*** *parameters*. θ *is the* ***most significant*** *parameter for the* ***biolarvicide population***. The *highlighted PRCC values belong* to those parameters *whose uncertainty contributes little to uncertainty of outcomes*.

Conclusion:

- Comprehending empirical studies is crucial for utilizing data within mathematical models.
- Mathematical models, crafted with insights into disease epidemiology and informed by field data, have the potential to generate evidence for policymaking.

Thank You!