DH301: Basic Epidemiology

Dr Kalyani Addya

&

Dr Sandip Mandal

Indian Institute of Technology - Bombay

31 July 2024

Epidemiology

- Epidemiology is a branch of science that focuses on studying the distribution, patterns, and determinants of health and disease conditions within specific populations.
- It explores how diseases spread, why certain groups are more affected than others, and what factors contribute to the occurrence and outcomes of diseases.
- Epidemiologists collect and analyze data to identify the causes and risk factors for diseases, understand how diseases are transmitted, and assess the impact of interventions or preventive measures.
- By studying large groups or populations, epidemiologists can uncover trends, make predictions, and develop strategies to prevent or control diseases, ultimately improving public health.

Main content

- Basic Epidemiology
- Mathematical Epidemiology

Course content (Basic Epidemiology)

- Introduction to Epidemiology – Definition & 0bjectives of epidemiology, principles and methods of epidemiology to investigate disease distribution.
- Using epidemiology methods to study the cause, extent and prevention of various infectious and non-infectious diseases.
- Dynamics of disease transmission: modes of transmission, attack rate, disease outbreak investigation
- Disease surveillance and measures of morbidity and mortality: Active and passive surveillance, emergency warning systems.
- Stages of a disease, incidence and prevalence of disease, mortality rates, case fatality
- Assessing screening tests: Validity of tests, Tests with binary and continuous outcomes, sequential testing, sensitivity and specificity measures.
- Different types of study design, including randomized trials, case-control and cohort studies, risk estimation and causal inferences

Course content (Mathematical Epidemiology)

- Model development
  - Rates, proportion, average duration, competing hazards
  - Model building
  - Force of infection, reproduction number
- Model calibration
  - Fitting with data
- Modelling interventions
  - Treatment
  - Prevention

Examination pattern and marks division

- Basic Epidemiology – 60 Marks
- Mathematical Epidemiology – 40 Marks

No re-examination

DH301: Basic Epidemiology

Mathematical Epidemiology

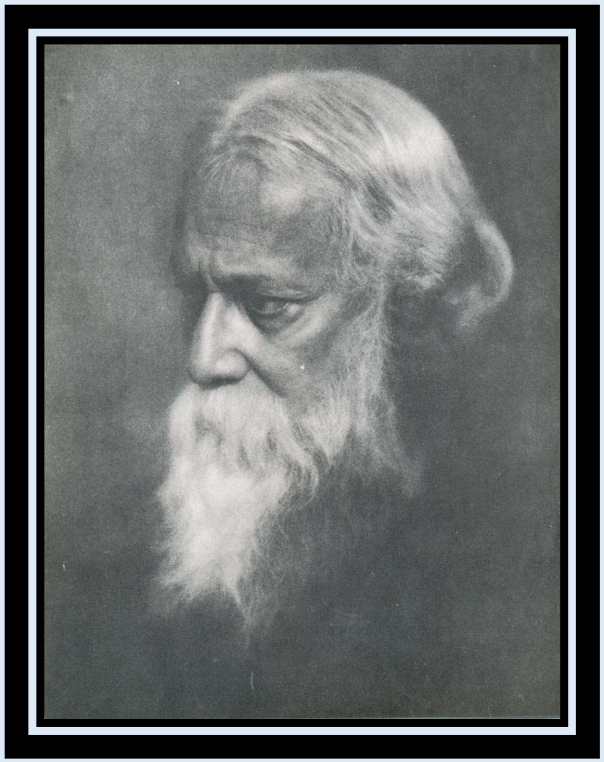
Sandip Mandal

Email: mandal.iitb@gmail.com

Indian Institute of Technology - Bombay

31 July 2024

Model
A simplified abstract view of the complex reality



Reality and Abstraction

What is epidemic modelling?

- A way of capturing natural history and transmission of disease
- A way of capturing how interventions shape transmission
- A framework for quantifying *costs* and *epidemiological impact*

Caution:

- A model is no substitute for surveillance and primary data!
- Offers a framework for
  - **making sense** of this data, and
  - Simulating **potential control policies**

Outline

- Story Ronald Ross and the first useful mathematical model
- McKendric and Kermack
- Story of Covid-19 modelling at ICMR-HQ
- Types of mathematical models
- Content to be covered in this section of the course (DH301)
- Concept of compartmental models
    - Understanding of data
    - Model development
    - Calibration
    - Intervention
- Reference books

Story of Ronald Ross

Sir Ronald Ross

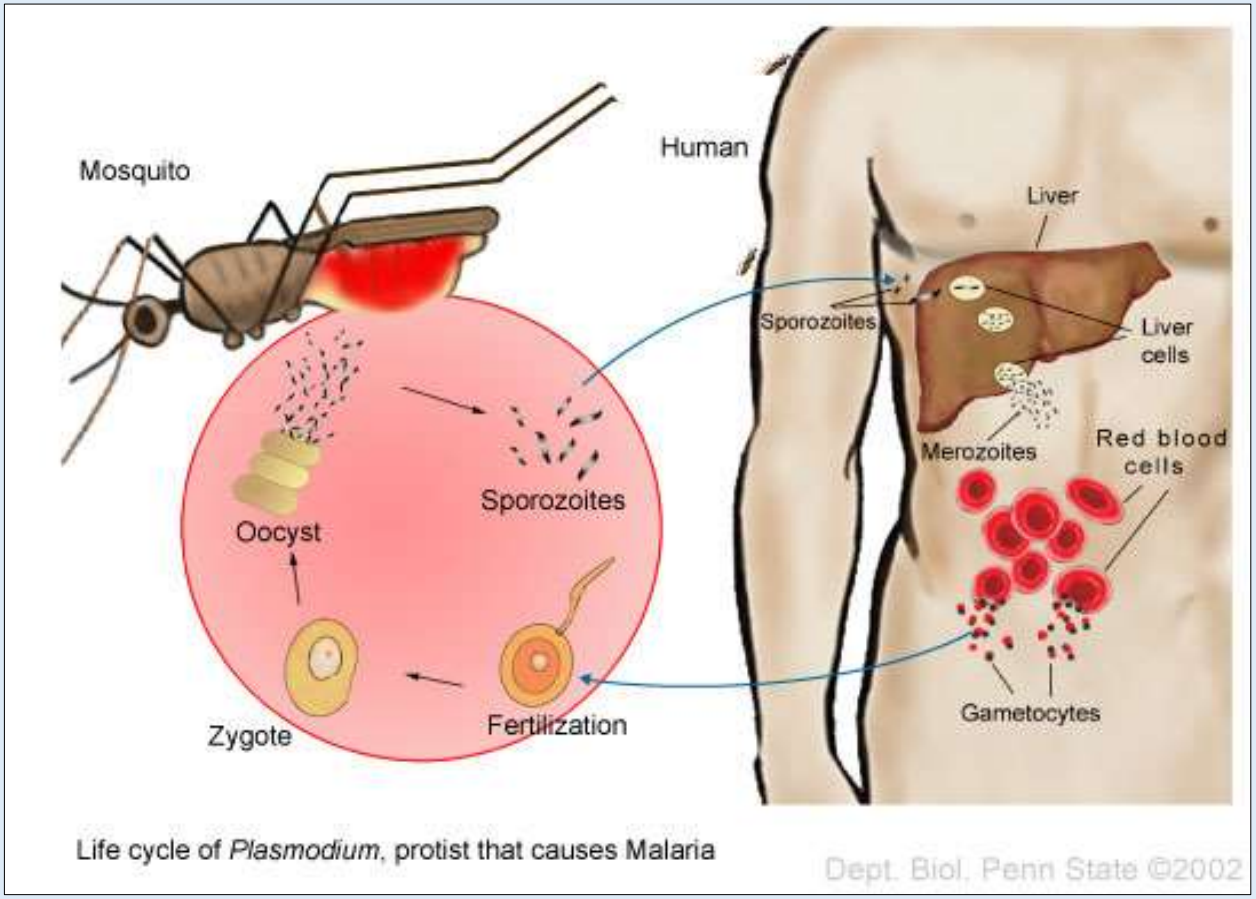
1857 - 1932

India chapter

- Indian Medical Service (1881)
- Bangalore life (1883)
- First experiment with mosquitoes
- ‘Mosquitoes carry malaria just as they carry *filariae*’ - Patrick Manson.
- Second experiment in Bangalore
- Third experiment (on birds)
- Nobel Prize (1902)

MALARIA: Life cycle of Plasmodium parasite

Human host, Mosquito vector, Malaria parasite



The latency period of the malaria parasite within the mosquito [extrinsic incubation period (EIP)]: 10-21 days

The latency period of the malaria parasite within humans, also known as the incubation period, is the time between the mosquito bite (infection) and the appearance of symptoms: 9 – 40 days

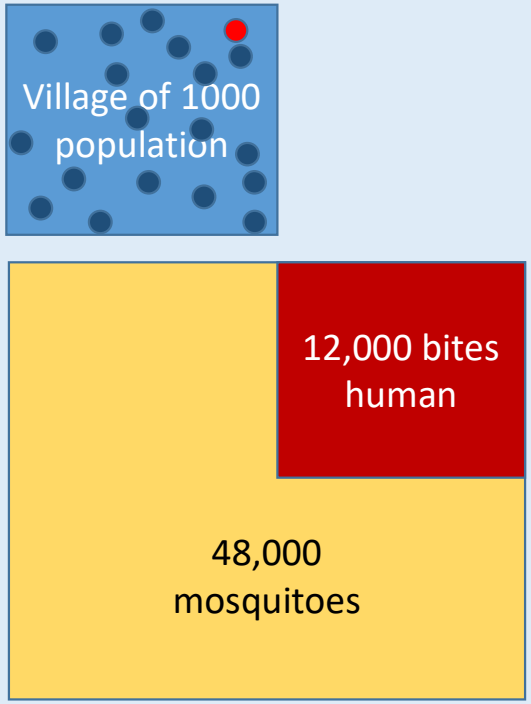
The average longevity of Anopheles mosquito: 10- 21 days

Female mosquitoes usually live longer than males, as males typically die shortly after mating.

Link between insects and infections

- Ross's hypothesis - Removing mosquitoes was the key to controlling malaria
  - Practical experience – Sierra Leone (a country in West Africa), 1901
  - Experience during Suez Canal Project –Ismailia (Egypt)
- This was against popular wisdom – It was impossible to get rid of every last mosquito, which meant there would always be some insects left, and hence potential for malaria to spread.
- Need a stronger argument to persuade Ross's idea of mosquito control

Was it really possible to control malaria without removing every mosquito?



Assumptions:

- 1 in 4 mosquitoes would manage to bite someone
  - 1 of 3 mosquitoes survived to be infectious

12

Among all bites only 12 bites would be such that they can pick up the parasite

4

Survives to be infectious

1

Bites another human

Even if there were 48,000 mosquitoes in the area, on average they would generate only one new human infection.

Concluding analyses

- More mosquitoes/more infected human → more new infections per month
- Process to counteracts the number → Estimated around 20% of humans infected with malaria would recover each month
- Condition for malaria to remain endemic in the population:

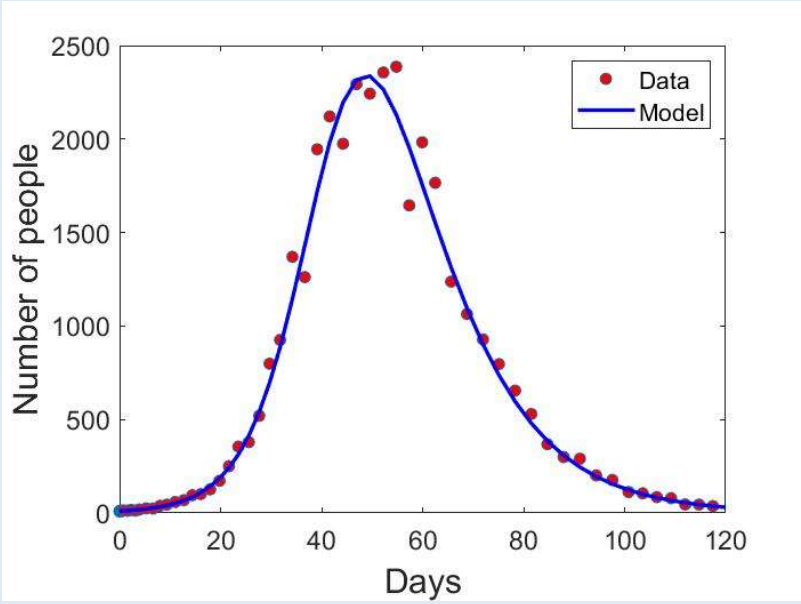
  Infection and recovery would need to balance each other
- If the recoveries outpaced the rate of new infections, the level of disease eventually would decline to zero.

"Malaria cannot persist in a community unless the *Anopheles* are so numerous that the number of new infections compensates for the number of recoveries." – *The Prevention of Malaria* (1910)

Two ways to approach disease analysis

Descriptive methods

- This involved starting with real life data and working backwards to identify predictable patterns.
- Example: William Farr's analysis of London smallpox outbreak, in 1830 and in 1840.
- Farr's method focused what shape epidemics take, not why they take the shape.

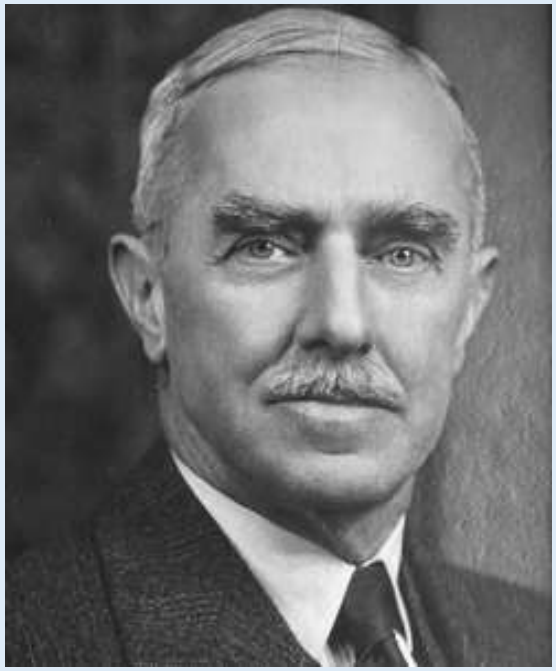


Mechanistic methods

- This started outlining the main processes that influenced transmission.
- Example: Ross's analysis by applying the knowledge of malaria transmission.
- Ross's conceptual model of transmission using mathematical equations, to make conclusions about likely outbreak patterns. It can answer 'what if' without doing real experiments.

McKendrick and Kermack: Mathematics of disease

Anderson Gray McKendrick



1876 - 1943

William Kermack

1898 - 1970

Extended Ross's ideas to look at epidemics in general

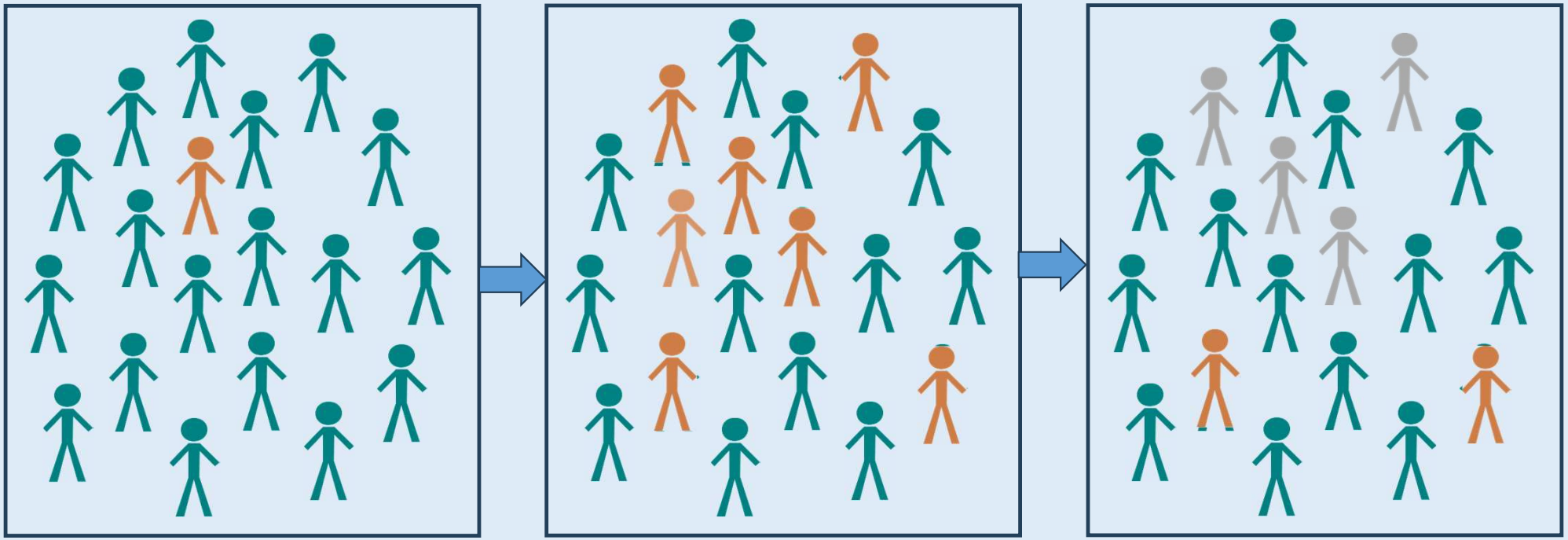
Mathematical model of disease transmission

What causes epidemics to end?

Two popular explanations:

- Transmission ceased because there were no susceptible people left to infect
- Pathogen itself became less infectious as the epidemic progressed

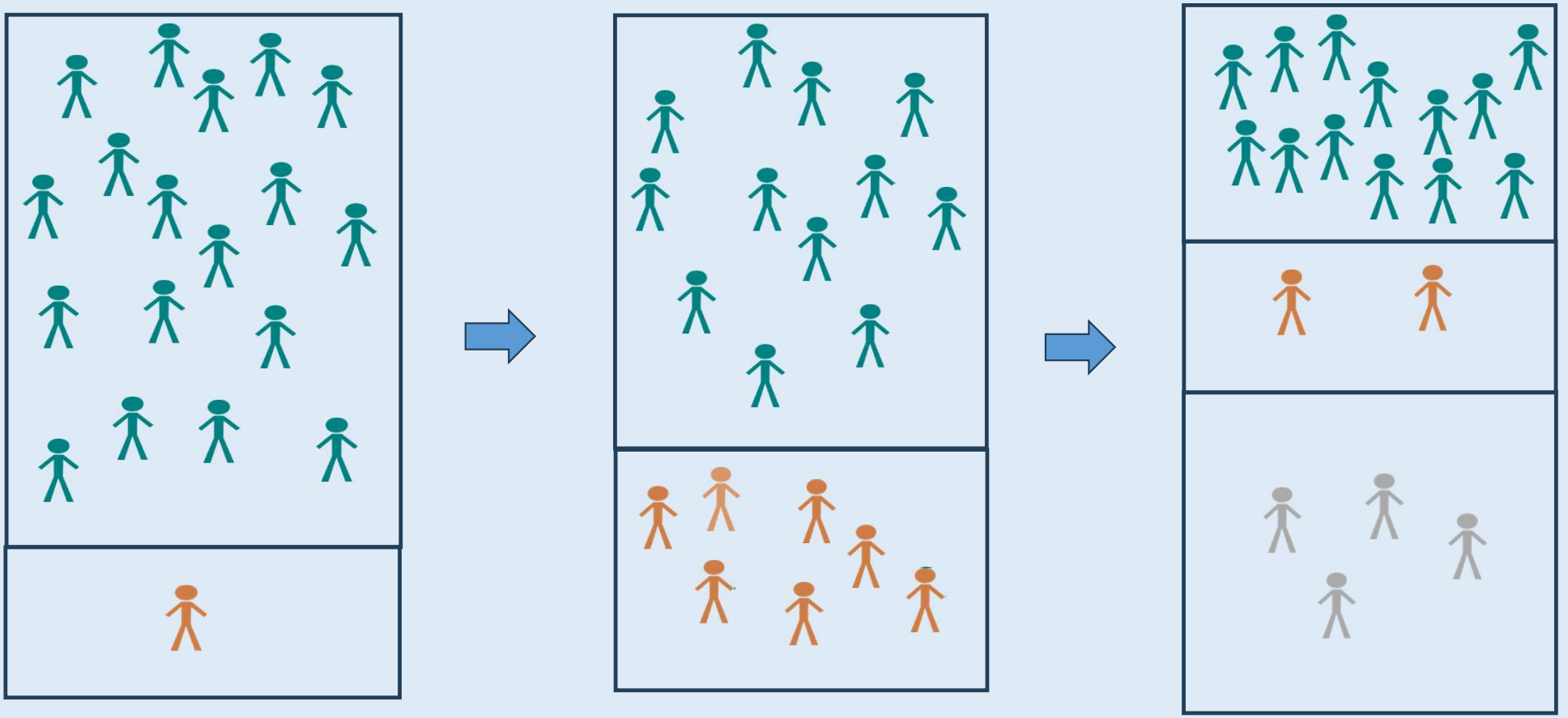
Neither explanation was correct



Day 1

After one week

After one month



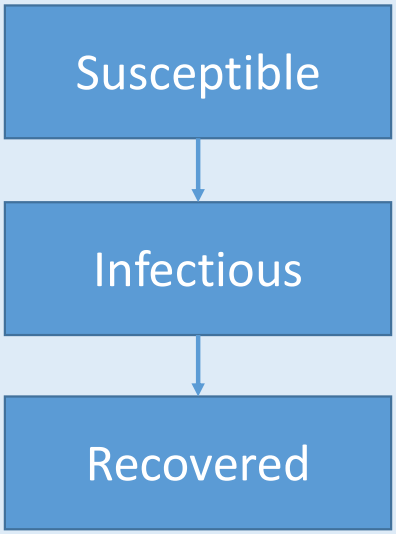
Day 1

After one week

After one month

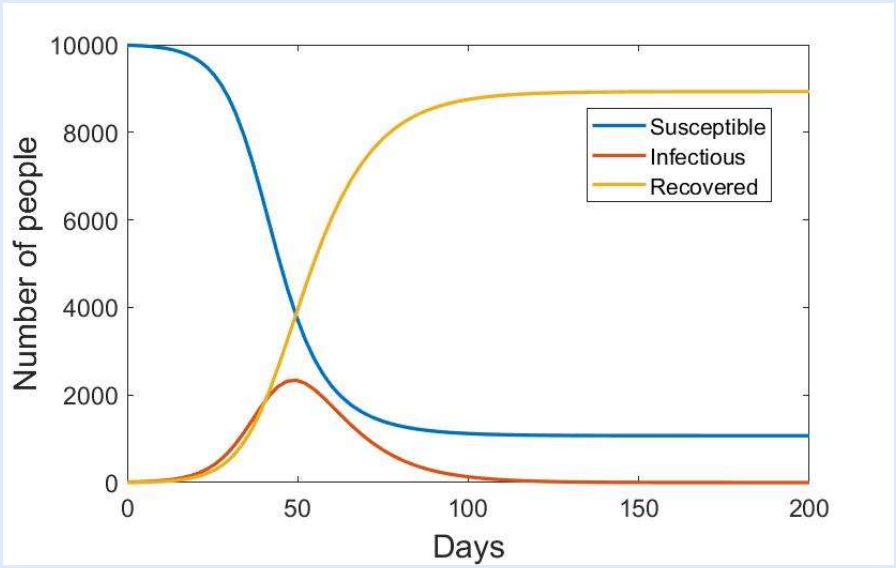
Mathematical model of disease transmission

Compartments according to disease status



SIR Model

Simulated outbreak using SIR model



"An epidemic, in general comes to an end before the susceptible population has been exhausted" – Kermack and McKendrick

COVID-19 modelling

Some practical application

Novel Coronavirus (COVID-19)

- The first known cases were identified in Wuhan, China, in December 2019.
- This was spreading rapidly in various European countries and USA
- Many unknowns - transmissibility (R0), infectiousness

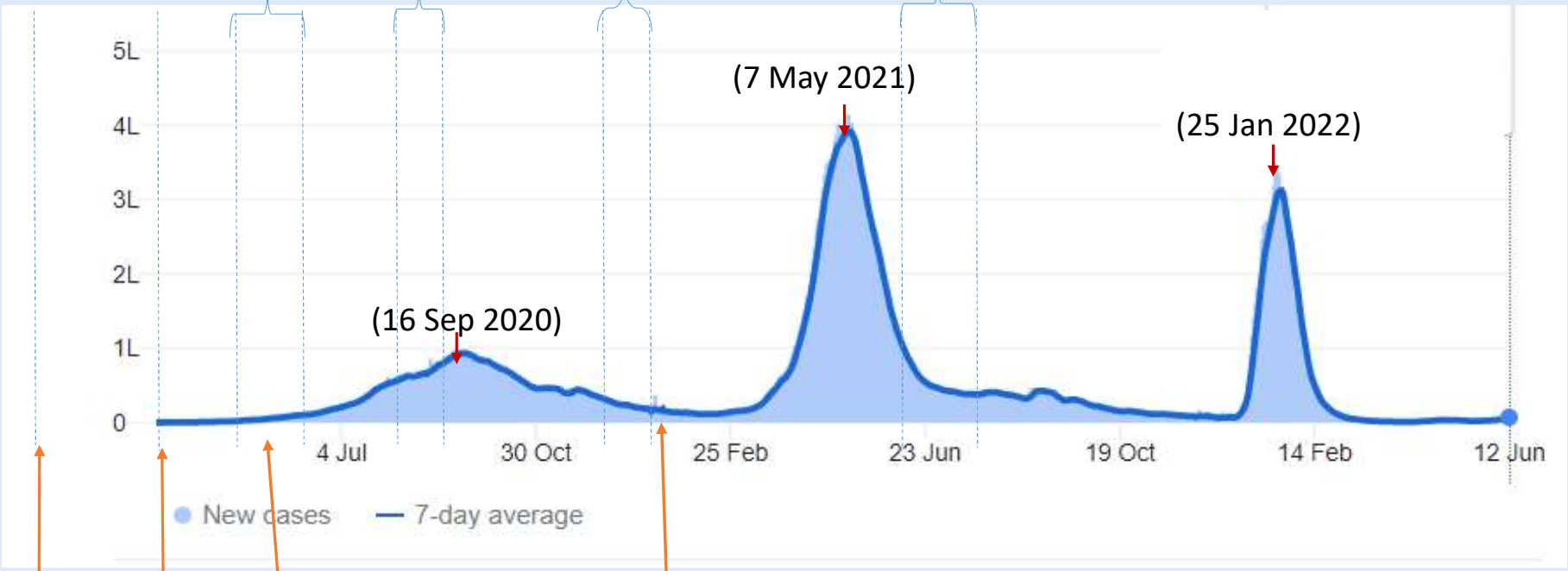
TIME LINE

1st National sero survey (May-Jun 2020)

2nd (Aug-Sep 2020)

3rd (Dec 2020-Jan 2021)

4th (Jun-July 2021)



First report (30 Jan 2020)

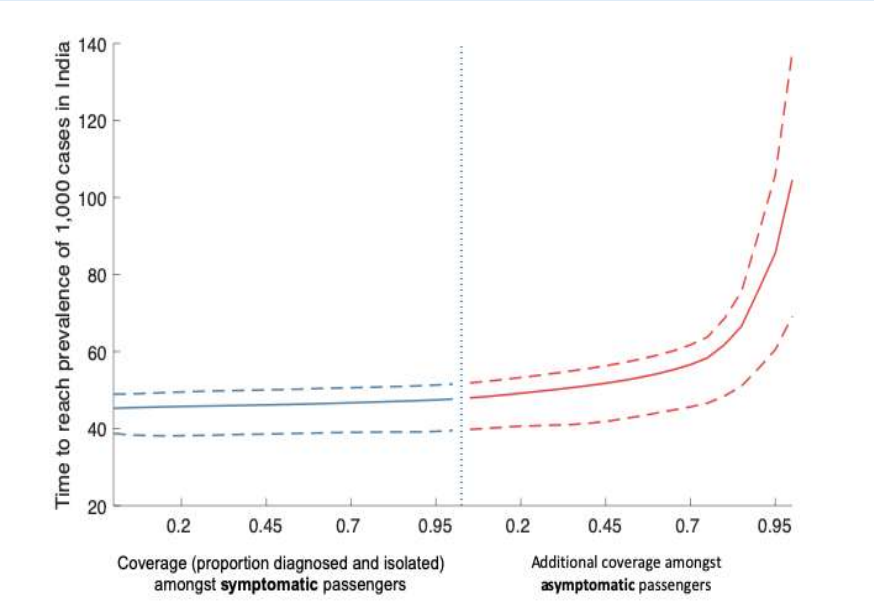
Lockdown start (25 Mar 2020)

Unlock start (1 June 2020)

Vaccination began (16 Jan 2021)

With limited data (Early February, 2020)

- Would the thermal screening be effective?



Ref: Mandal el al. Indian Journal of Medical Research, 2020

- How much reduction is possible by isolating infected persons?

Table I. Model parameters for optimistic and pessimistic scenarios of coronavirus disease-19 transmission in India

Parameters	Optimistic scenario	Pessimistic scenario
Basic reproduction number (R_0)	1.5	4
Infectiousness of asymptomatic cases, relative to symptomatic case (k)	0	0.5

Reduction of	Optimistic scenario	Pessimistic scenario
Peak prevalence	89%	8%
Cumulative incidence	62%	2%

Intervention: 50% of symptomatic cases are isolated within 3 days

Need to add new test & quarantine plan to lockdown: ICMR research | India News,The Indian Express

ENGLISH தமிழ் বাংলা മലയാളം हिंदी मराठी

The Indian EXPRESS

Friday, April 03, 2020

Need to add new test & quarantine plan to lockdown: ICMR research

The study, led by Sandip Mandal of the ICMR's Department of Health Research, estimates that the current 21-day lockdown will reduce epidemic peak by 43 per cent and total mortality by 19 per cent.

In the previous ICMR model, completed in February and publicly released on March 23, the researchers had made a case for post-travel tracking rather than border containment. The paper's mathematical model had showed that spending resources on quarantining symptomatic cases can achieve a meaningful impact on the disease burden rather than attempting to achieve infeasible levels of containment at the borders. The paper had also proposed "symptomatic surveillance" rather than indiscriminate testing — a position the government eventually adopted.

NDTV FULL COVERAGE CORONAVIRUS LATEST INFOGRAPHICS VIDEO FAQs HELPLINE DONATE COMMENT ...
READ IN OTHER LANGUAGES

How Rapidly Can COVID-19 Spread In India? Government Did The Math

In the optimistic scenario, symptomatic cases would be about 1.5 million in Delhi, with roughly 500,000 each in Mumbai, Kolkata and Bengaluru.

All India | Reported by Chetan Bhattacharji and Sukirti Dwivedi, Edited by Deepshikha Ghosh | Updated: March 24, 2020 12:33 pm IST

MENU #Covid-19 Jagran English

Latest News | India | Entertainment | World | Politics | Business | Lifestyle | Education | Technology | Cricket | Vishvas News | Photos

News / India

Coronavirus Outbreak: ICMR's math on how COVID-19 may spread in India shows some alarming projections

In the pessimistic scenario, the symptomatic cases would be about 10 million in Delhi and 4 million in Mumbai, which will peak in just 50 days starting February.

Updated: Wed, 25 Mar 2020 08:52 AM IST

NEWS • LIVE TV INDIA TODAY APP MAG

HOME | MY FEED | INDIA | WORLD | BUSINESS | TECH | MOVIES | SPORTS | SCIENCE | HEALTH | VIDEOS | CORONA

News / SCIENCE / Coronavirus in India: Social distancing can reduce India's cases by up to 62%, says ICMR study

Coronavirus in India: Social distancing can reduce India's cases by up to 62%, says ICMR study

Using mathematical modeling, a study by experts at ICMR has estimated that India may be able to reduce its Covid-19 cases by up to 62 per cent if social distancing and quarantines are strictly observed.

Hindustan Times

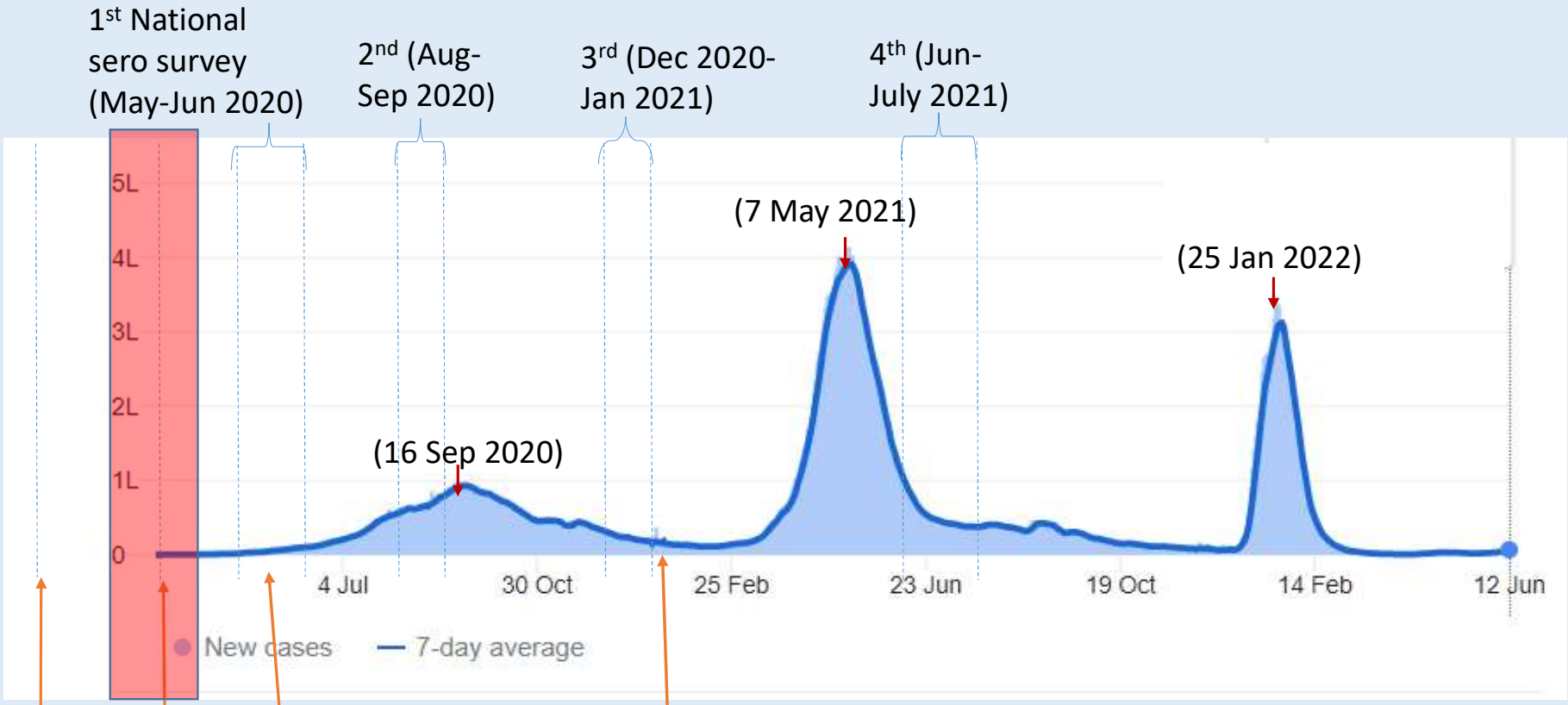
INDIA NEWS

Each new coronavirus infected Indian could spread it to 4 others, finds ICMR study

Covid-19: The Indian Council of Medical Research mathematical modeling is based on data of coronavirus patients till late February before the second wave of the outbreak.

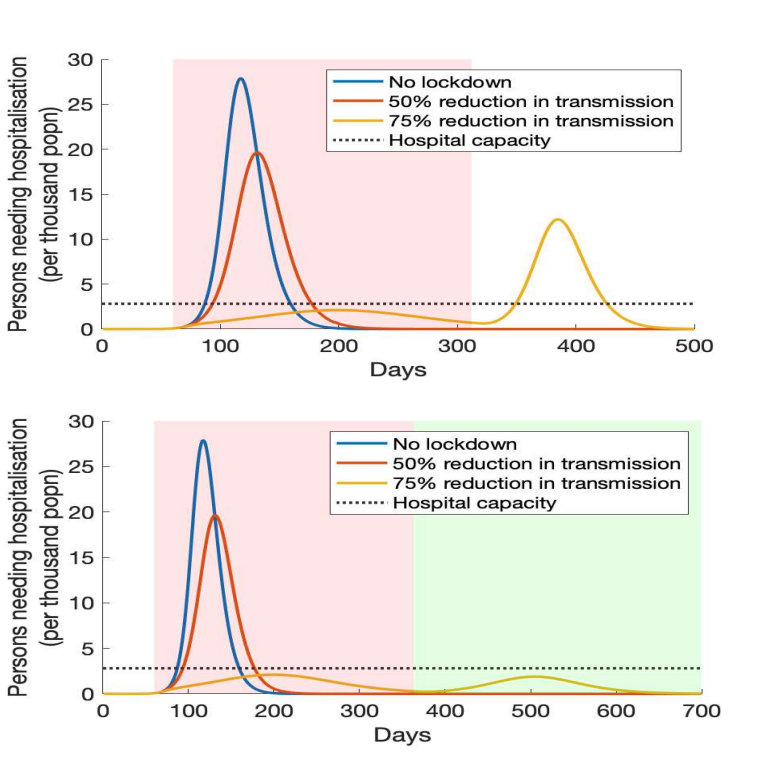
Hindustan Times, New Delhi | By Rhythma Kaul
UPDATED ON MAR 24, 2020 12:44 PM IST

TIME LINE


1st National sero survey (May-Jun 2020)
2nd (Aug-Sep 2020)
3rd (Dec 2020-Jan 2021)
4th (Jun-July 2021)
(7 May 2021)
(25 Jan 2022)
(16 Sep 2020)
5L
4L
3L
2L
1L
0
4 Jul
30 Oct
25 Feb
23 Jun
19 Oct
14 Feb
12 Jun
New cases
7-day average
First report (30 Jan 2020)
Lockdown start (25 Mar 2020)
Unlock start (1 June 2020)
Vaccination began (16 Jan 2021)

With seroprevalence data

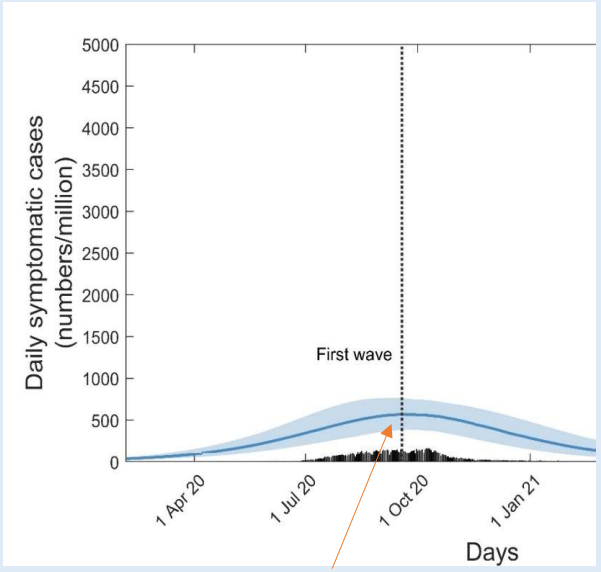
- Strategy for removing lockdown



Ref: Mandal el al. Scientific Reports, 2021

- Model calibration with seroprevalence: estimation of number of cases

Aligning the data with reality:



8% seroprevalence in mid-September 2020

MOST READ Kirron Kher, battling cancer, makes appearance in son Sikandar Kher's video, asks him to get married

Testing needed for 'unlock' would cost 2% of lockdown economic losses, says study, encourages antibody tests

In another metric, the study found that "a resource-intensive (testing) strategy ... corresponds to less than half of the lockdown-caused loss in goods and services tax (GST) revenue."

Written by **Karishma Mehrotra** | New Delhi |
Updated: June 4, 2020 7:25:48 am

November- December 2020

Vaccination strategies: priority groups

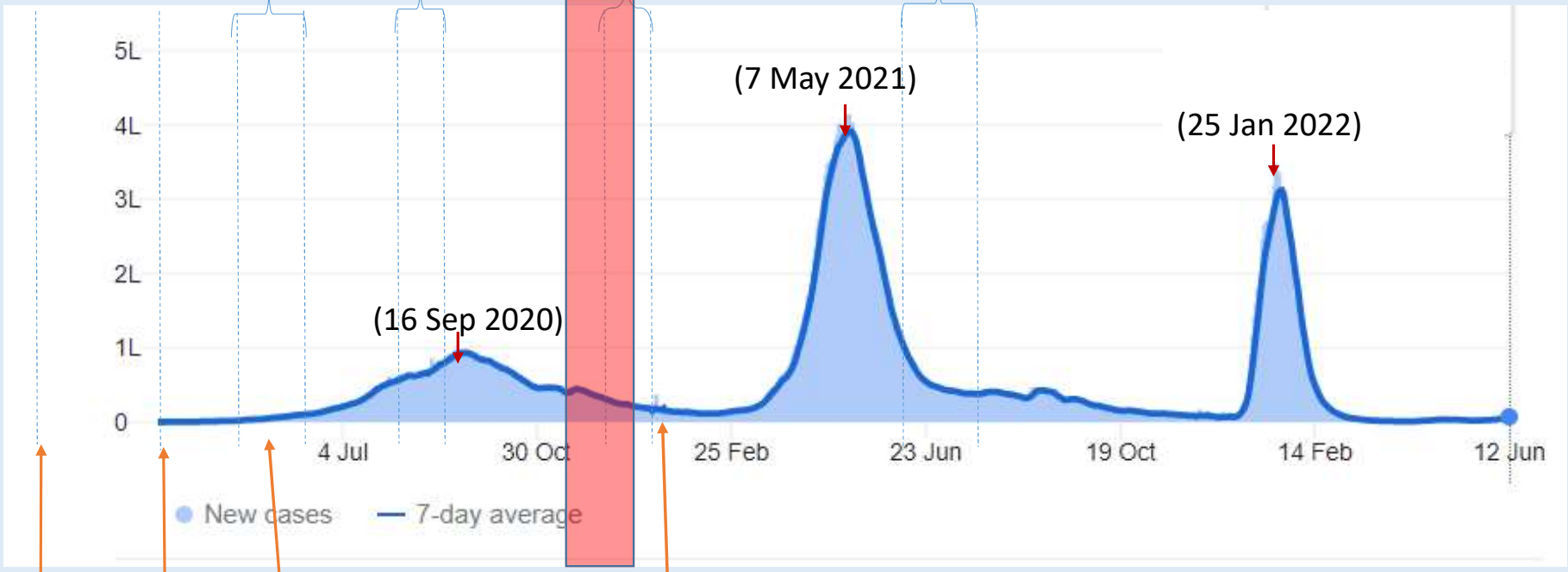
TIME LINE

1st National sero survey (May-Jun 2020)

2nd (Aug-Sep 2020)

3rd (Dec 2020-Jan 2021)

4th (Jun-July 2021)



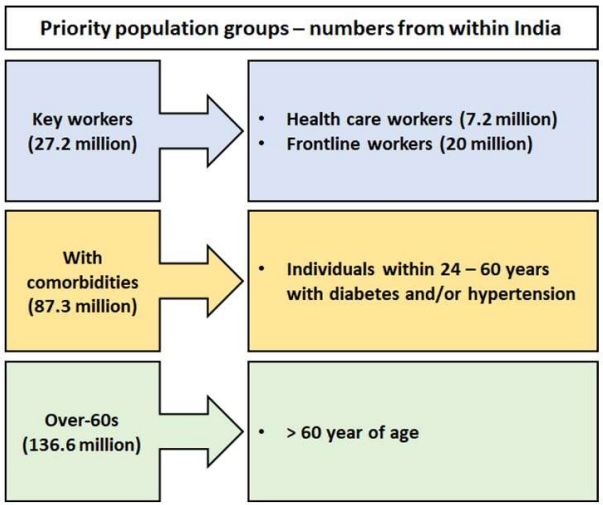
First report (30 Jan 2020)

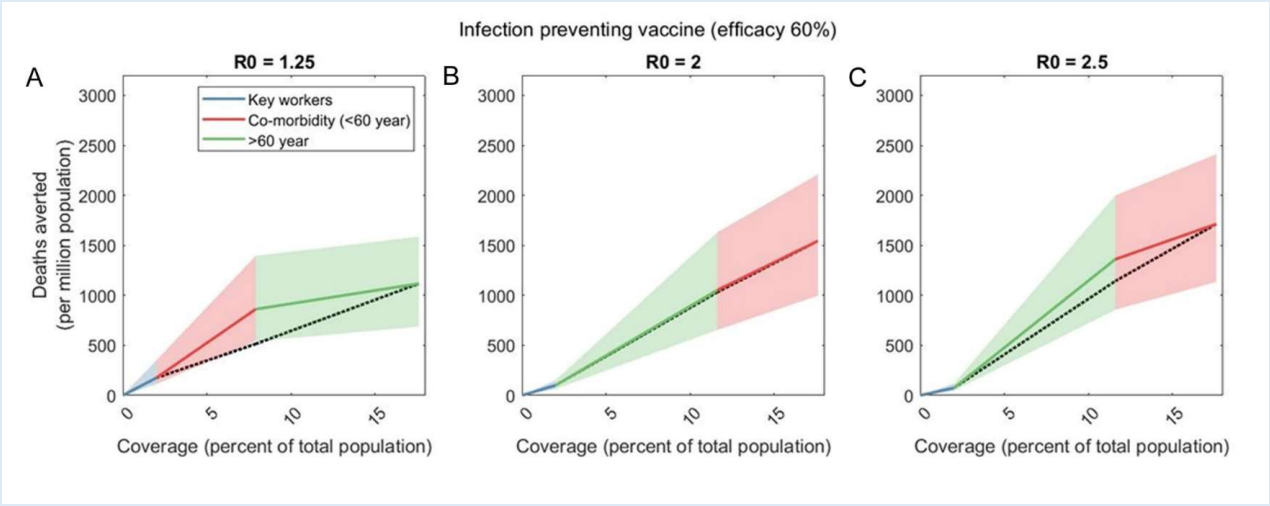
Lockdown start (25 Mar 2020)

Unlock start (1 June 2020)

Vaccination began (16 Jan 2021)

Vaccination strategy against COVID-19 amongst different priority groups





Model findings

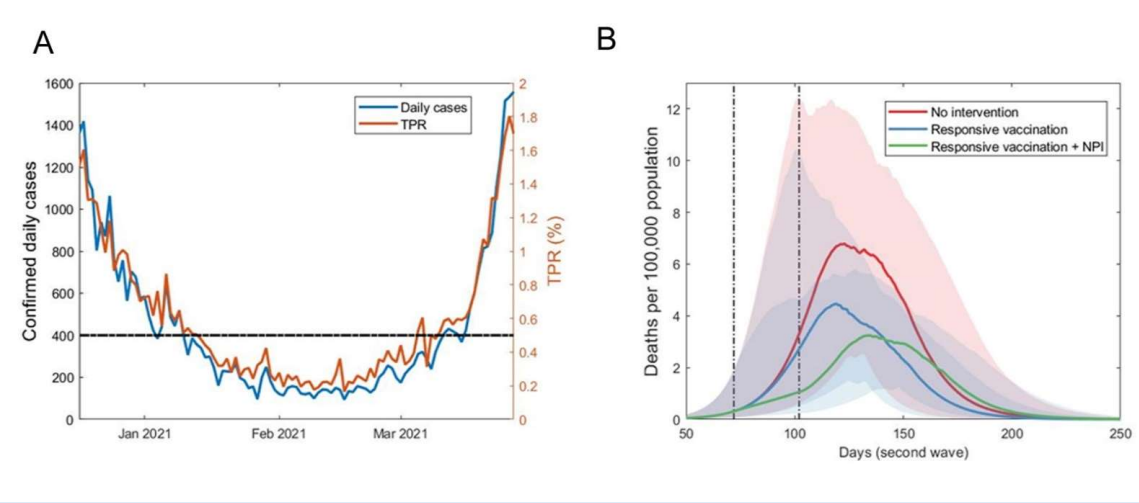
- Keyworkers → Over- 60s → with comorbidities (relatively high transmission setting)
- Keyworkers → with comorbidities → Over- 60s (In settings with weakest transmission, e.g. sparsely-populated rural areas)

Ref: Mandal el al. BMJ Open, 2021

March- April 2021

Vaccination strategies: area prioritisation

How can vaccination efforts be best prioritised in order to help those areas of the country that need it most?



(A) Time course of test positivity rate between the first and second epidemic waves in Delhi

(B) Model projections for mortality during the second wave in a hypothetical district in India, where 25% of the population has prior immunity, with R_0 = 2, and under three different scenarios

Model findings

Flexible, agile vaccination strategies could play an important role in protecting lives and livelihoods as the COVID-19 pandemic continues to unfold.

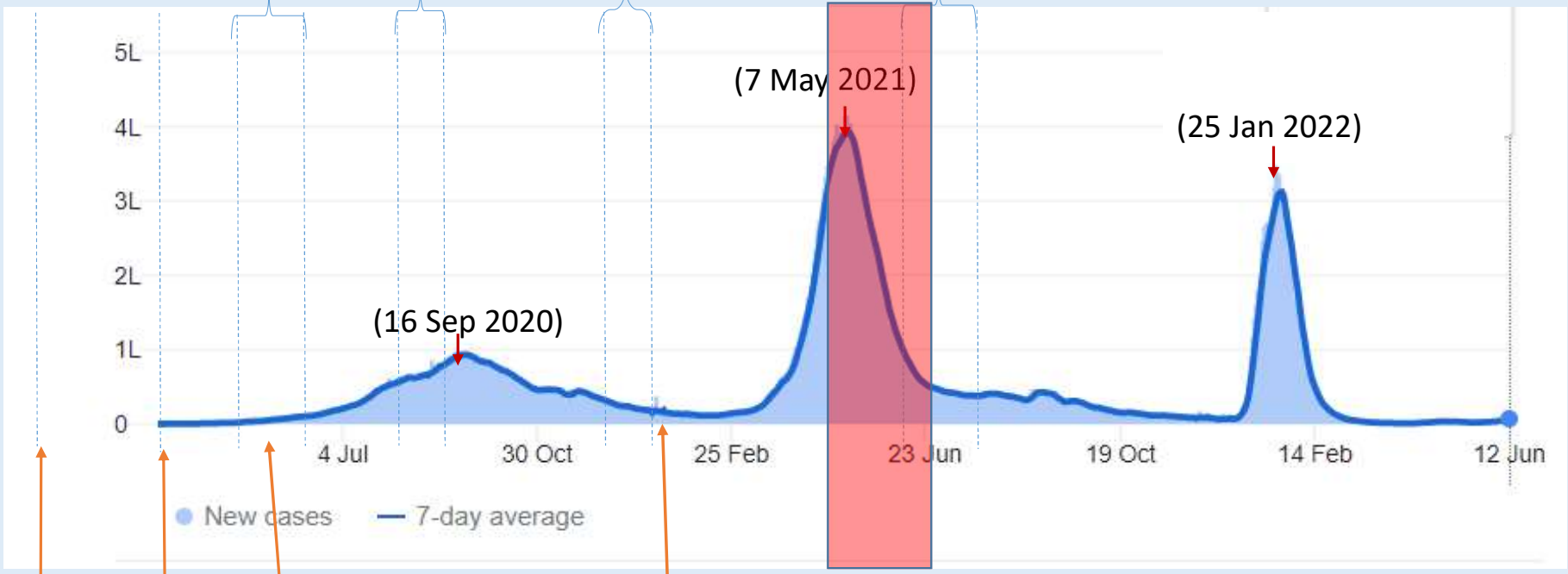
Ref: Mandal el al. The Lancet Global Health, 2021

April - June 2021

Plausibility of third wave

Third wave concerns

TIME LINE



First report
(30 Jan 2020)

Lockdown start
(25 Mar 2020)

Unlock start
(1 June 2020)

Vaccination began
(16 Jan 2021)

Some hypotheses for a severe third wave

1. Restrictive measures/release

If restrictions have been successful at reducing transmission, releasing them may afford new opportunities for transmission

3. Viral evolution for **increased transmission**

Emergence of a new virus with a higher R_0 than previously

2. Full **waning** of immunity

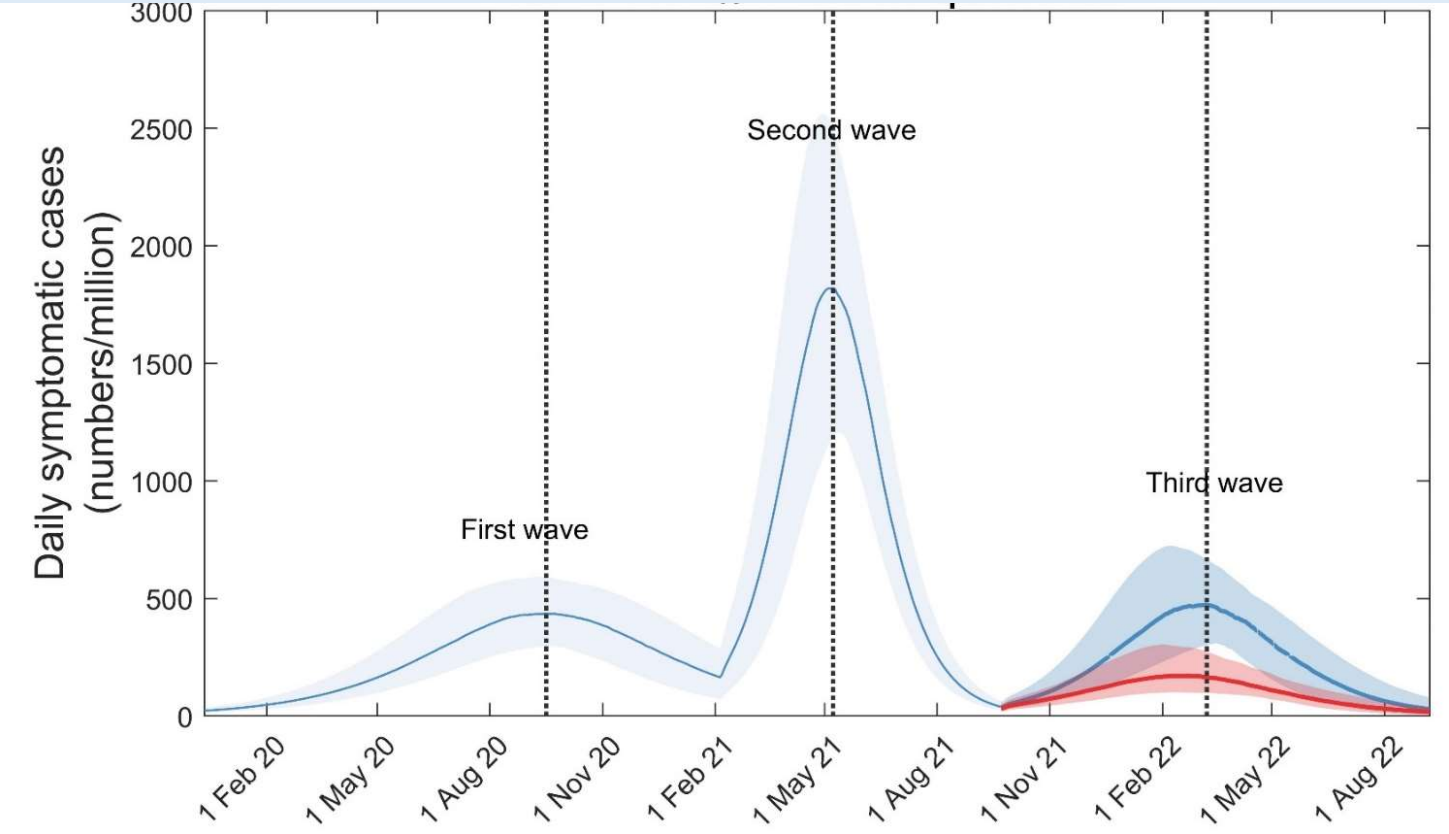
Independent of the virus, any acquired immunity in the population so far decays over time

4. Viral evolution for **immune escape**

Emergence of a new virus that can fully escape prior immunity

One example scenario of third wave of COVID-19 in India

R0 = 3 and 25% immune escape



Assumptions:

1. **Date of emergence of variant (mid September 2021)**
2. **R0 = 3 and 25% immune escape**
3. **Proportion symptomatic among all cases (33%-66%)**
4. **Vaccine efficacy on reducing severity (60%)**

Ref: Mandal el al. Indian Journal of Medical Research, 2021

Conclusions

June-July 2021

Local projection with local data

covidwaveapp.duredemos.com/advanced-dashboard/#

CHROMIC SIMULATOR *for* COVID 19

About | Simulator | Print | Log out

Type State/District Name: India

Natural History & Demographic Parameters

Enter First Wave Details

Date - first wave peak: 17-09-2020

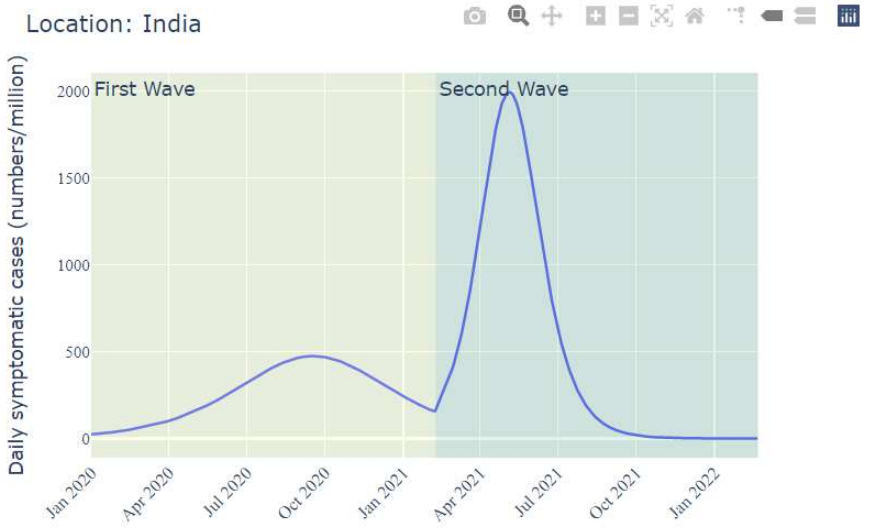
Seroprevalence at peak (%): 8.1

Absolute number of symptomatic cases reported on the first wave peak date: 93180

Enter Second Wave Details

Simulate | Reset

Simulated multi-wave dynamics of COVID-19



Seroprevalence 8.1% as of 17-09-2020

Peak Healthcare demand for 3rd wave scenarios (per million population)

Among Symptomatic Cases	Age Groups (Years)			Total
	0-17	18-59	>59	
Needing Hospitalization	0	0	0	0
Needing Oxygen	0	0	0	0
Needing Ventilator	0	0	0	0

Third Wave is not predicted

Dure Technologies

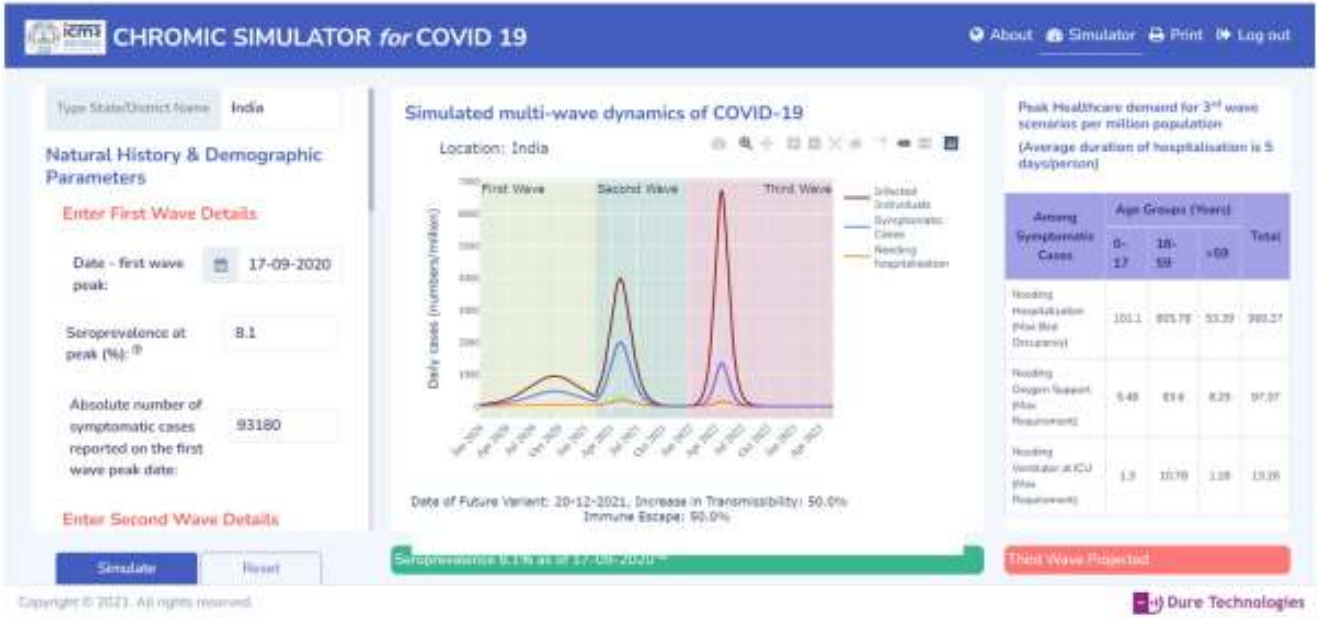


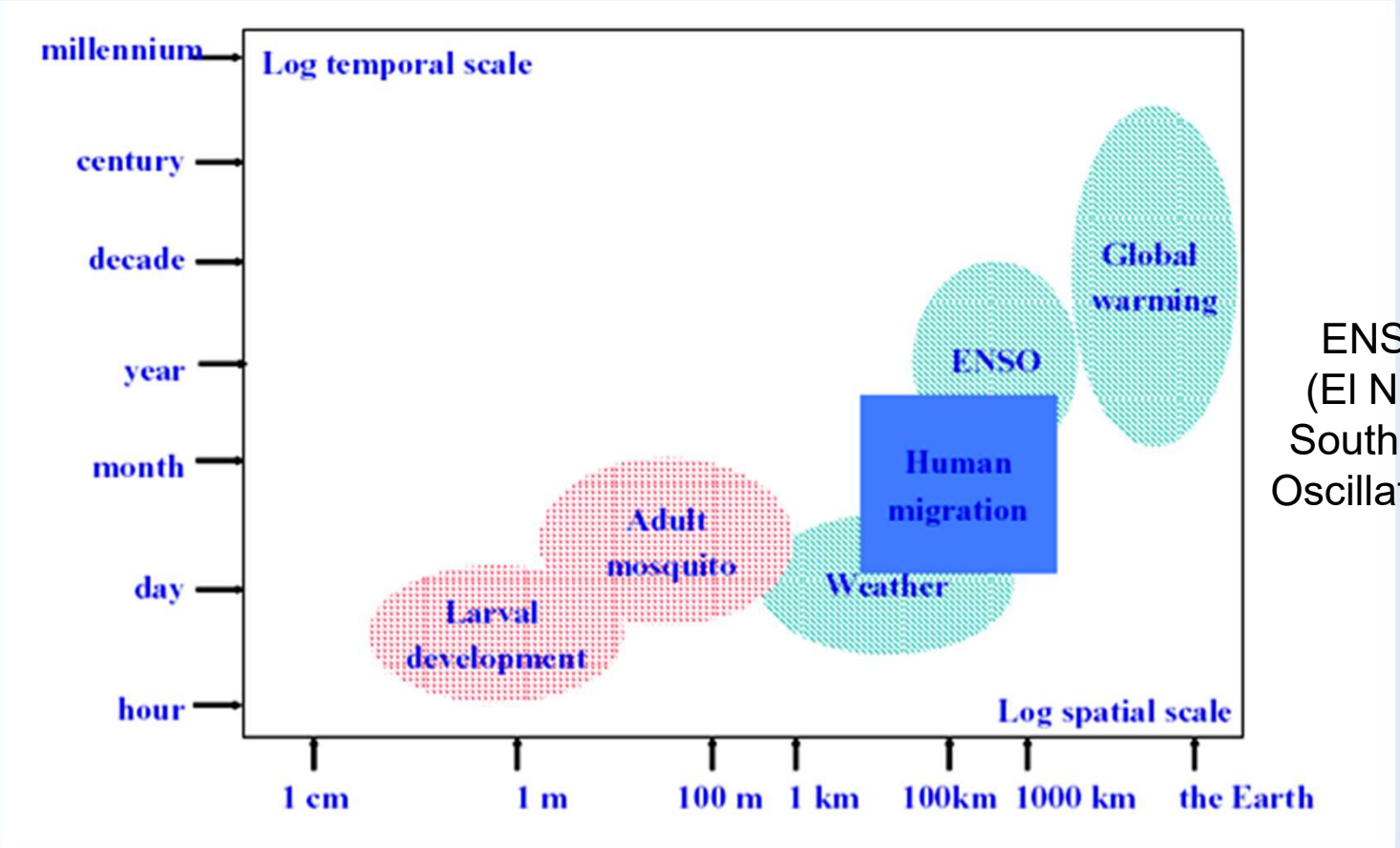
Figure 1 Illustrative screenshot of the simulator. The left-hand panel includes all user-specified scenario specifications. The central panel shows model projections, including the first two waves, while the right-hand panel shows model projections for required hospital capacity in the third wave.

Mandal S, *et al. BMJ Global Health* 2022;**7**:e008710. doi:10.1136/bmjgh-2022-008710

Lesson learned

- Modelling is an useful tool if used properly
- Model outcomes depend on assumptions
- Always important to know why a model suggests certain conclusions
- Better to think of a model as *bringing together* our best understanding of an epidemic and *Projecting* their implications under given future scenarios
- ‘Project’ rather than ‘predict’

Spatial and temporal scales of disease dynamics



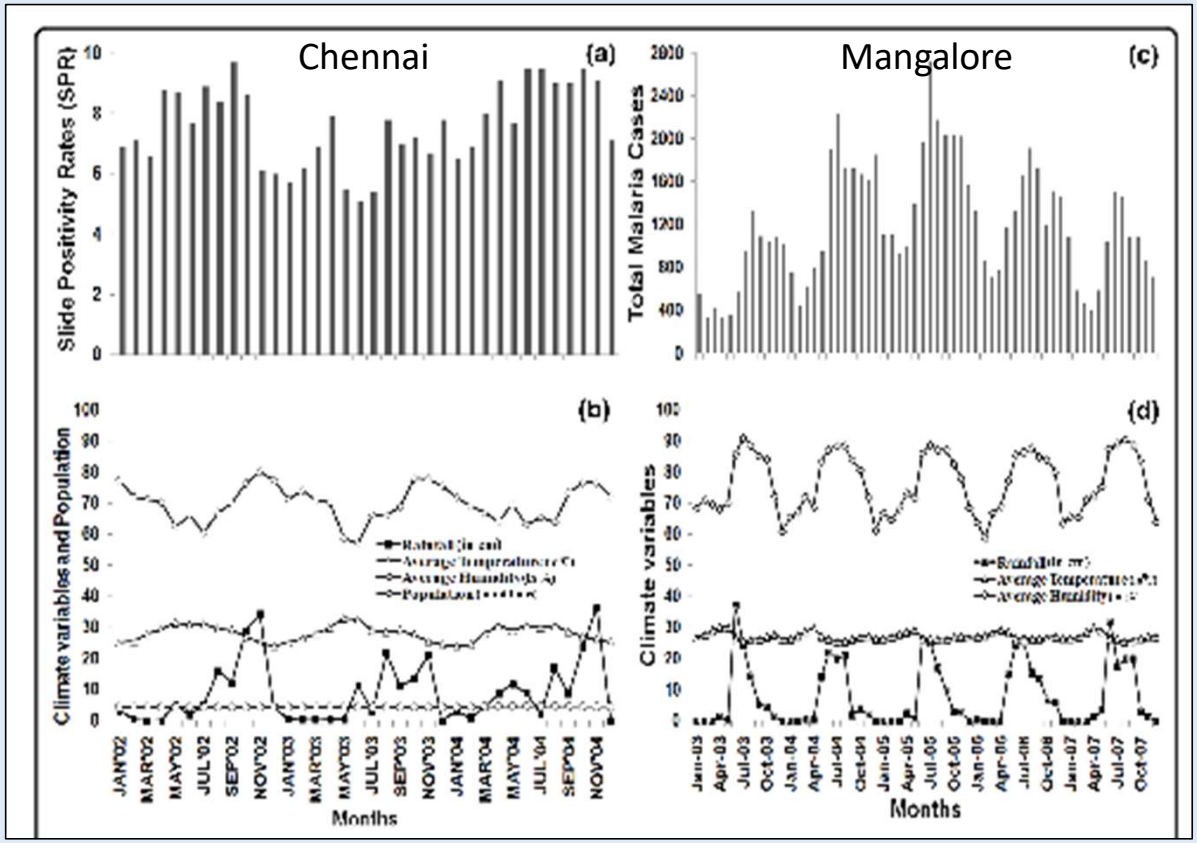
ENSO (El Niño Southern Oscillation)

Modelling disease prevalence

Mechanistic way of modelling Mathematical & Computational Modelling	Data-based modelling Mathematical & Statistical Modelling
Discrete & continuous generation ecological and epidemiological models to understand general features of eco-epidemiological and demographic influences	Analyse the prevalence data of a parasitic disease to search for patterns of occurrence under the influence of environmental variables.

The final aim is to unify model studies with real observation

Example of data-based *Statistical Modelling*



Malaria incidence and climate data.

(a) SPR (%) values in Chennai, during January 2002 - December 2004, and

(c) TMC values in Mangalore, during January 2003 - December 2007. The climate variables**, Rainfall (cm), Temperature (°C), Humidity (%), and Population (in millions)** are appropriately scaled to fit in the same plot

Mechanistic approach of modelling

Different types of theoretical approaches are used in epidemiological modelling

1) Standard differential equation based SIR models
2) Discrete models using generic host parasite population growth models
3) Agent-based models
4) Network-based models – SIR or individuals
5) Lattice based models – continuous or discrete

Reference Books

Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation. By *Diekman and Heesterbeek. Wiley*

Modeling Infectious Diseases in Humans and Animals. By *Matt J. Keeling and Pejman Rohani. Princeton University Press*

Mathemtical Models in Biology. By *Leah Edelstein-Keshet. SIAM Classics in Applied Mathematics 46*

Mathematical Biology I and II. *J D Murray. Springer*

Mathematical Models in Molecular and Cellular Biology. *Lee Segel. Cambridge University Press*

Thank you for your patience