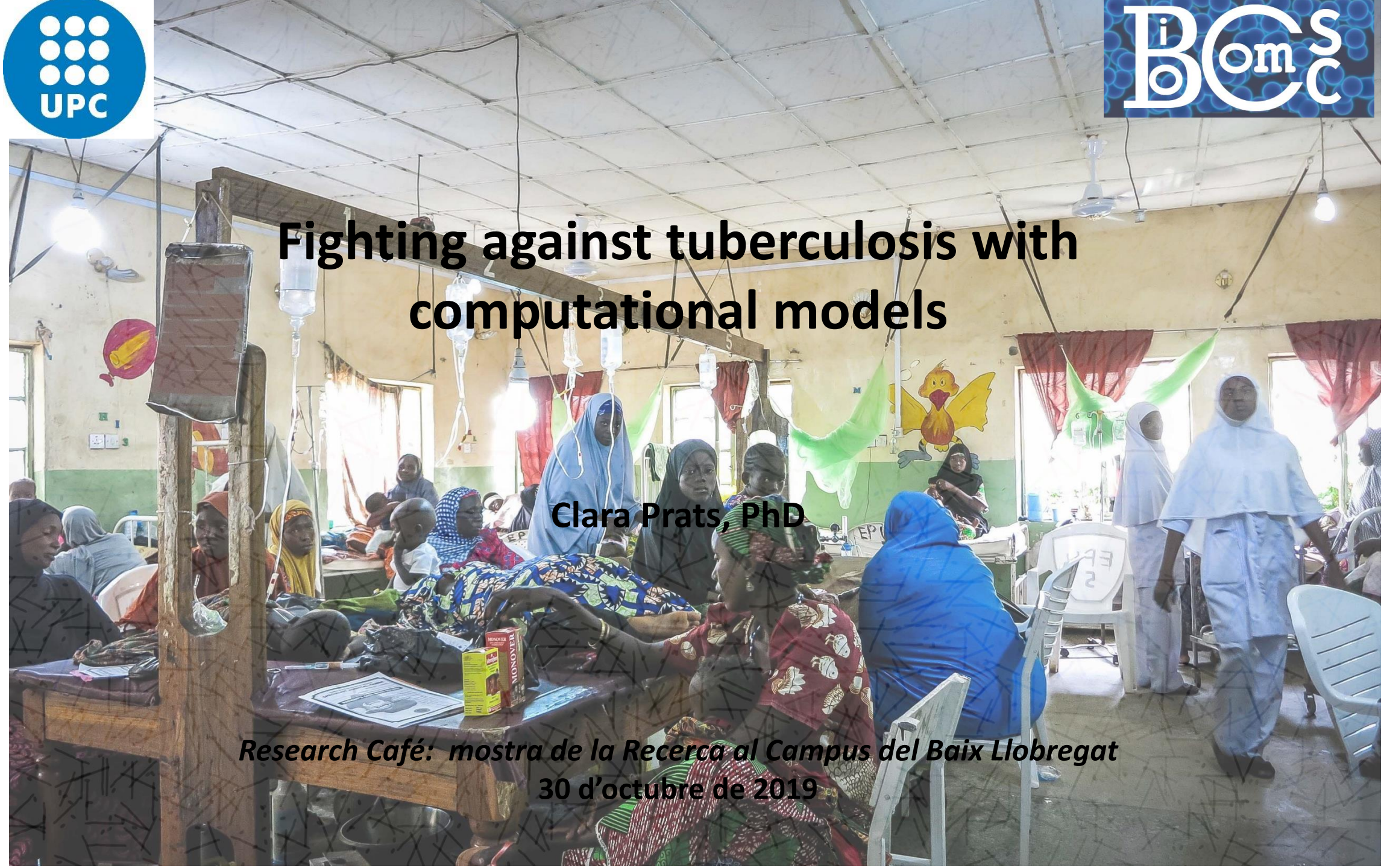
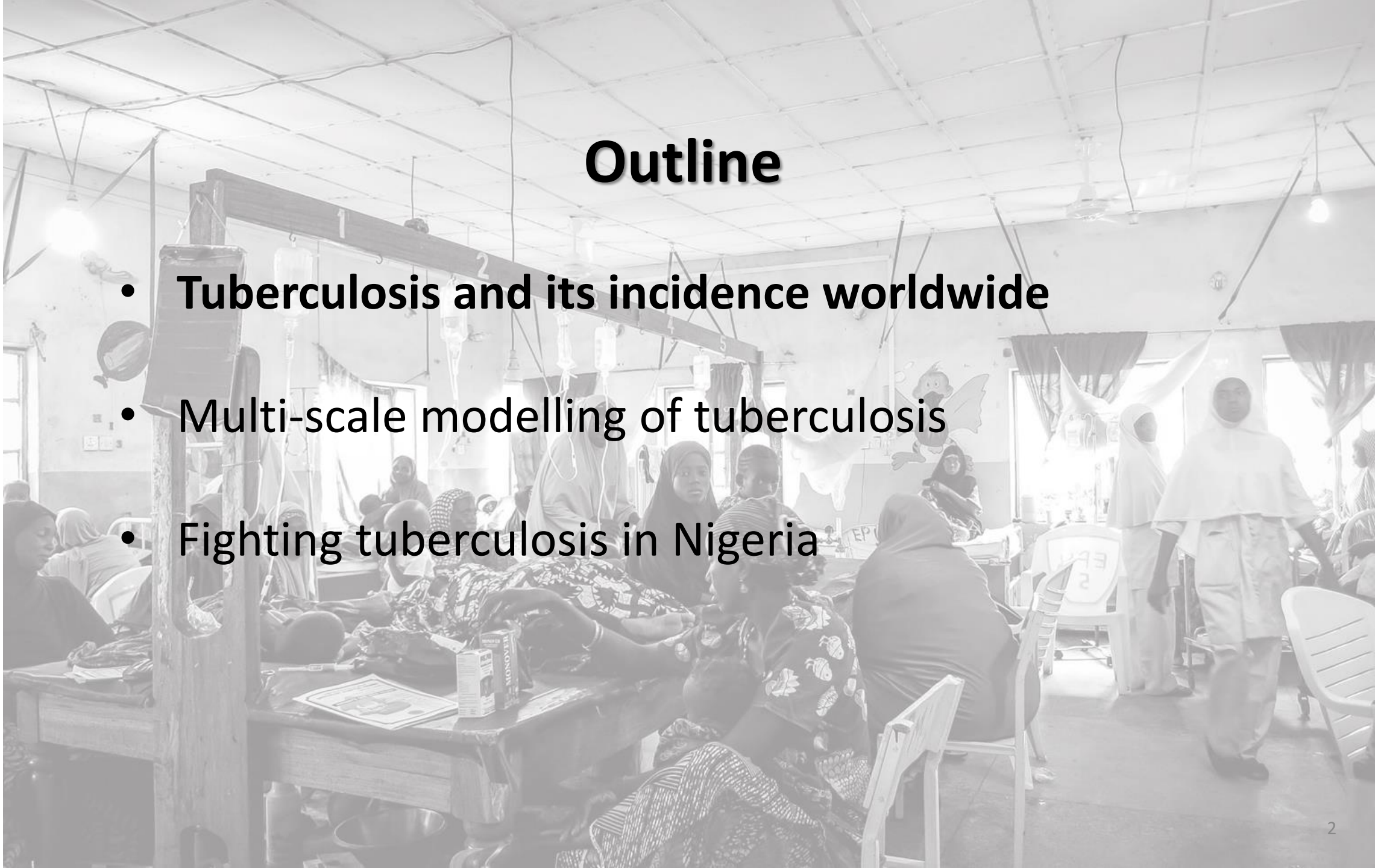


Fighting against tuberculosis with computational models

Clara Prats, PhD

Research Café: mostra de la Recerca al Campus del Baix Llobregat

30 d'octubre de 2019



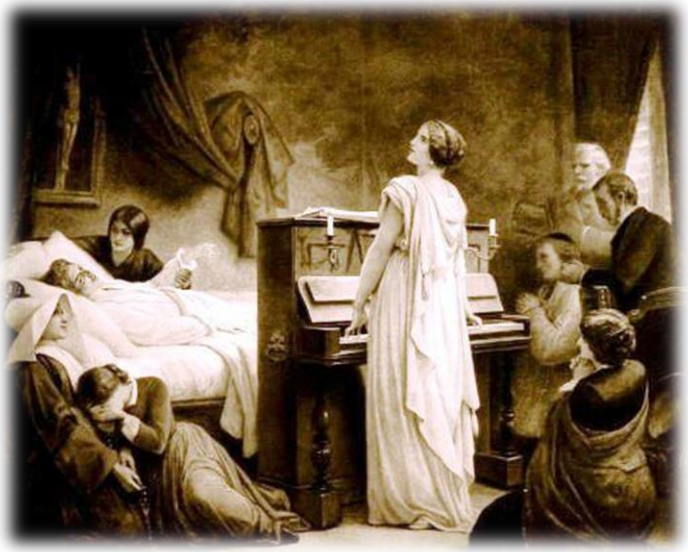
Outline

- **Tuberculosis and its incidence worldwide**
- Multi-scale modelling of tuberculosis
- Fighting tuberculosis in Nigeria

Tuberculosis: a disease with long history…

Prehistory

XIXth century

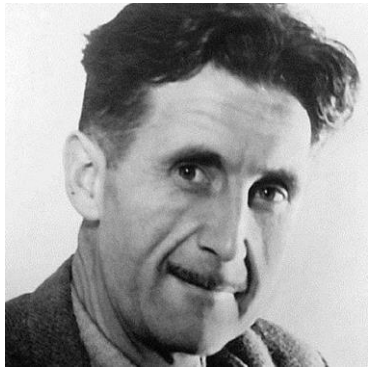


Chopin, 1849

Vivien Leigh, 1967

Cardenal Richelieu, 1642

Eleanor Roosvelt, 1962



George Orwell, 1950

Bécquer, 1870

Kafka, 1924

Pergolesi, 1736

Molière, 1673

Schrödinger, 1961

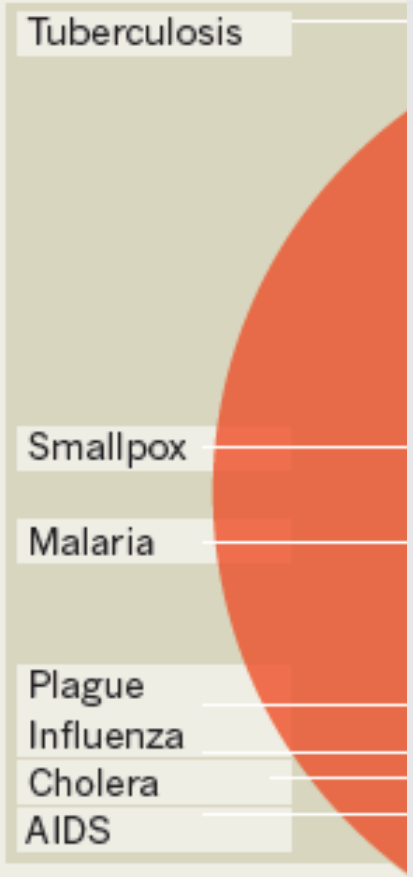
Tuberculosis: a disease with long history…

… and a topical issue!

XXI century

THE BIGGEST KILLER

Tuberculosis has killed more than any other infectious disease in history. Over a billion lives in the past two hundred years.



EVERY 15 SECONDS
1 DIES FROM TUBERCULOSIS

MDR-TB remains a crisis

WITH ONLY ONE IN FOUR MDR-TB CASES DETECTED AND ONLY ONE IN TWO CURED

GLOBAL BURDEN

TB is one of the **world's top health challenges:**

MORE THAN 2 BILLION PEOPLE, equal to a **QUARTER** of the world's population are **infected with TB**

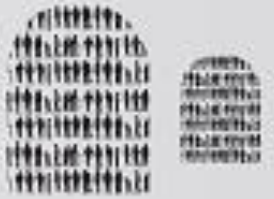
Despite our best efforts...

...there is an **unacceptable low rate** of decline in incidence each year

EACH YEAR

9 MILLION NEW CASES

1.5 MILLION DEATHS



EACH DAY

24,000 NEW CASES

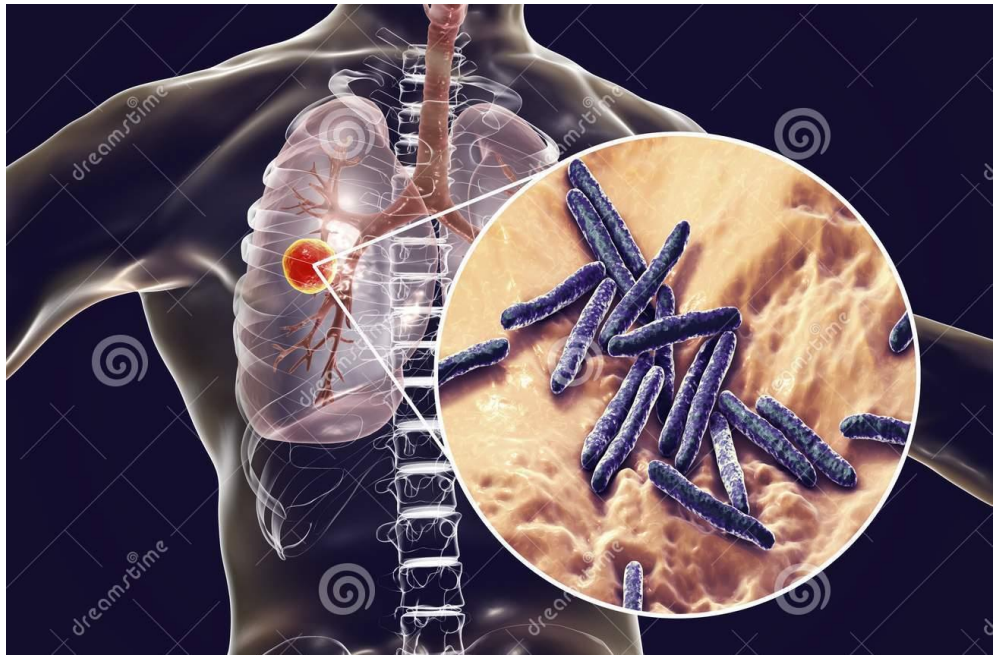
4,000 DEATHS

8,000 MISSED

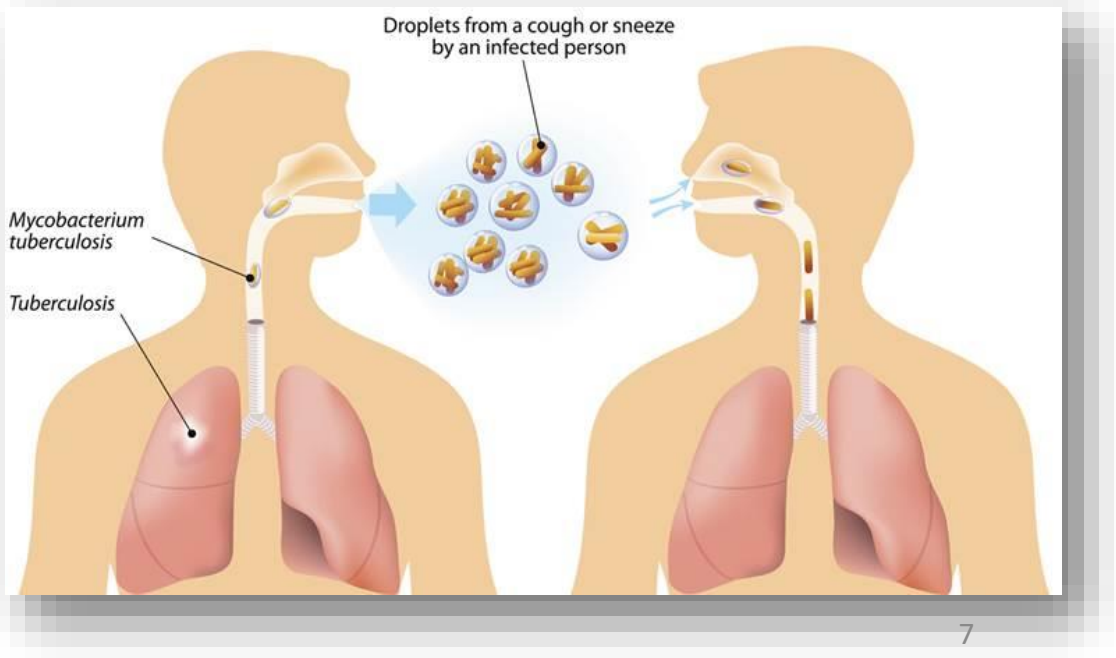
Source: StopTB Partnership

Tuberculosis is…

- ✓ Infectious disease caused by *Mycobacterium tuberculosis*

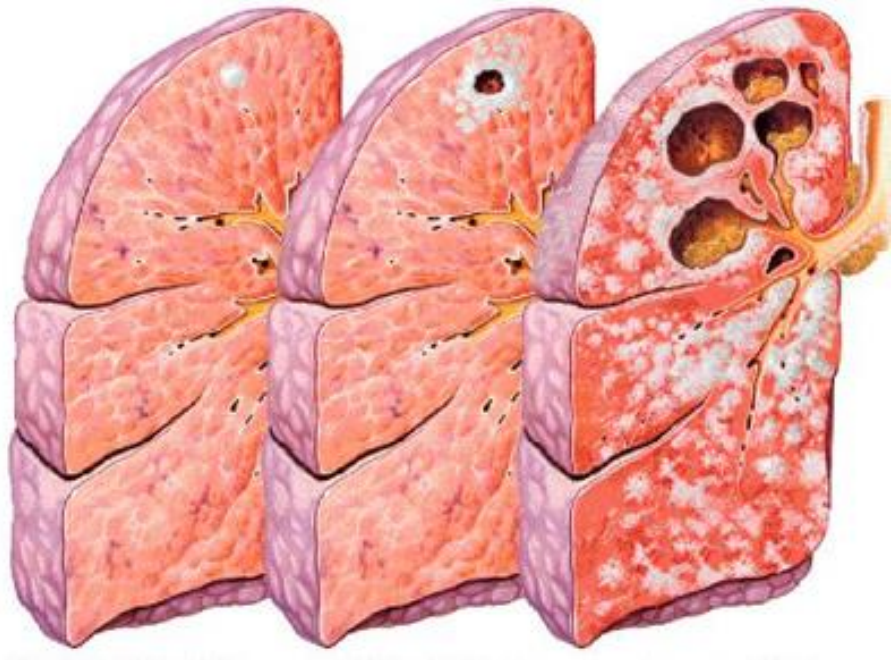


- ✓ Transmitted by small **droplets** airborne particles.
- ✓ Infectious droplet nuclei are generated when persons who have **pulmonary TB disease** cough, sneeze, shout, or sing.



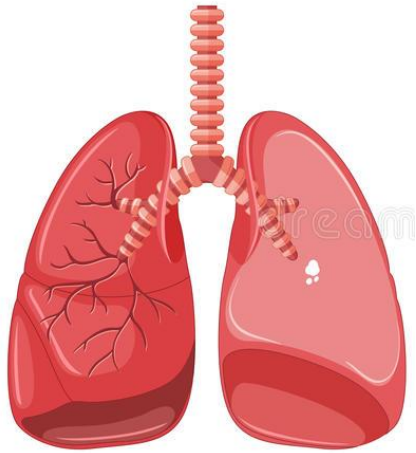
Tuberculosis…

- ✓ Affect the lungs, mainly, but can also disseminate to other organs in the body

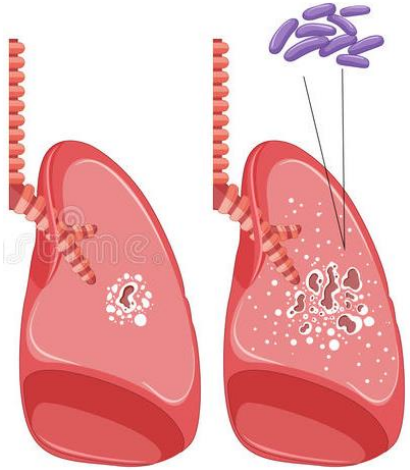


- ✓ Only a 5-10 % of infected (asymptomatic) people develop the active infectious disease.

Latent Tuberculosis Infection (LTBI)



Active Tuberculosis Disease (ATB)

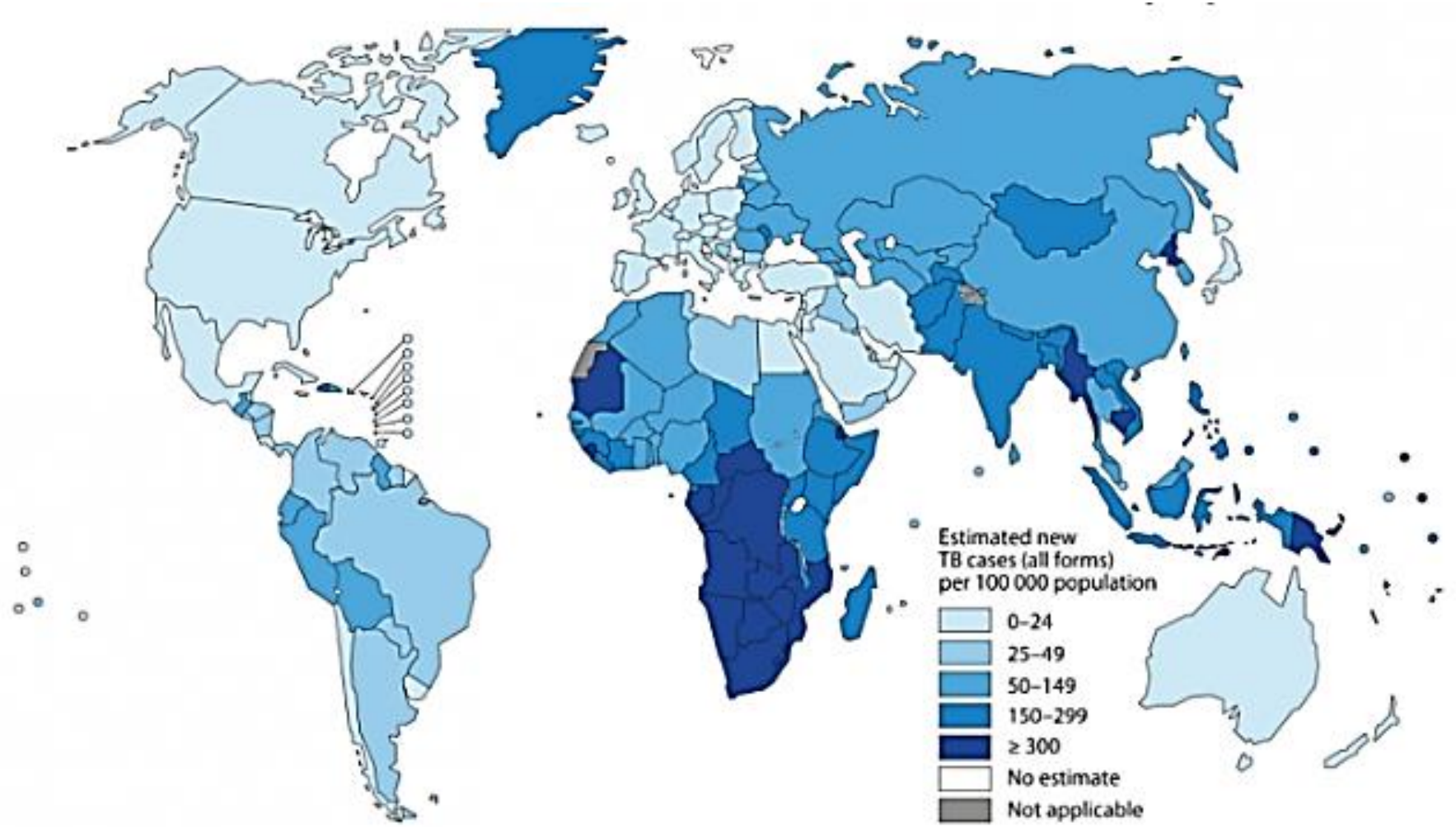


Tuberculosis in world

1/4 of world's population already infected (non infectious LTBI)

10.7 million new ATB cases in 2017

1.7 milions deaths caused by TB in 2017



Sustainable Development Goals (SDG)

United Nations
2015-2030
“The Sustainable Development Agenda: 17 Goals to Transform Our World”

The Sustainable Development Goals

Goal 1. End poverty in all its forms everywhere

Goal 2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture

Goal 3. Ensure healthy lives and promote well-being for all at all ages

Goal 4. Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all

Goal 5. Achieve gender equality and empower all women and girls

Goal 6. Ensure avai

Goal 7. Ensure acce

Goal 8. Promote su all

Goal 9. Build resilie

Goal 10. Reduce in

Goal 11. Make citie

Goal 12. Ensure su

Goal 13. Take urgent action to combat climate change and its impacts

Goal 14. Conserve and sustainably use the oceans, seas and marine resources for sustainable development

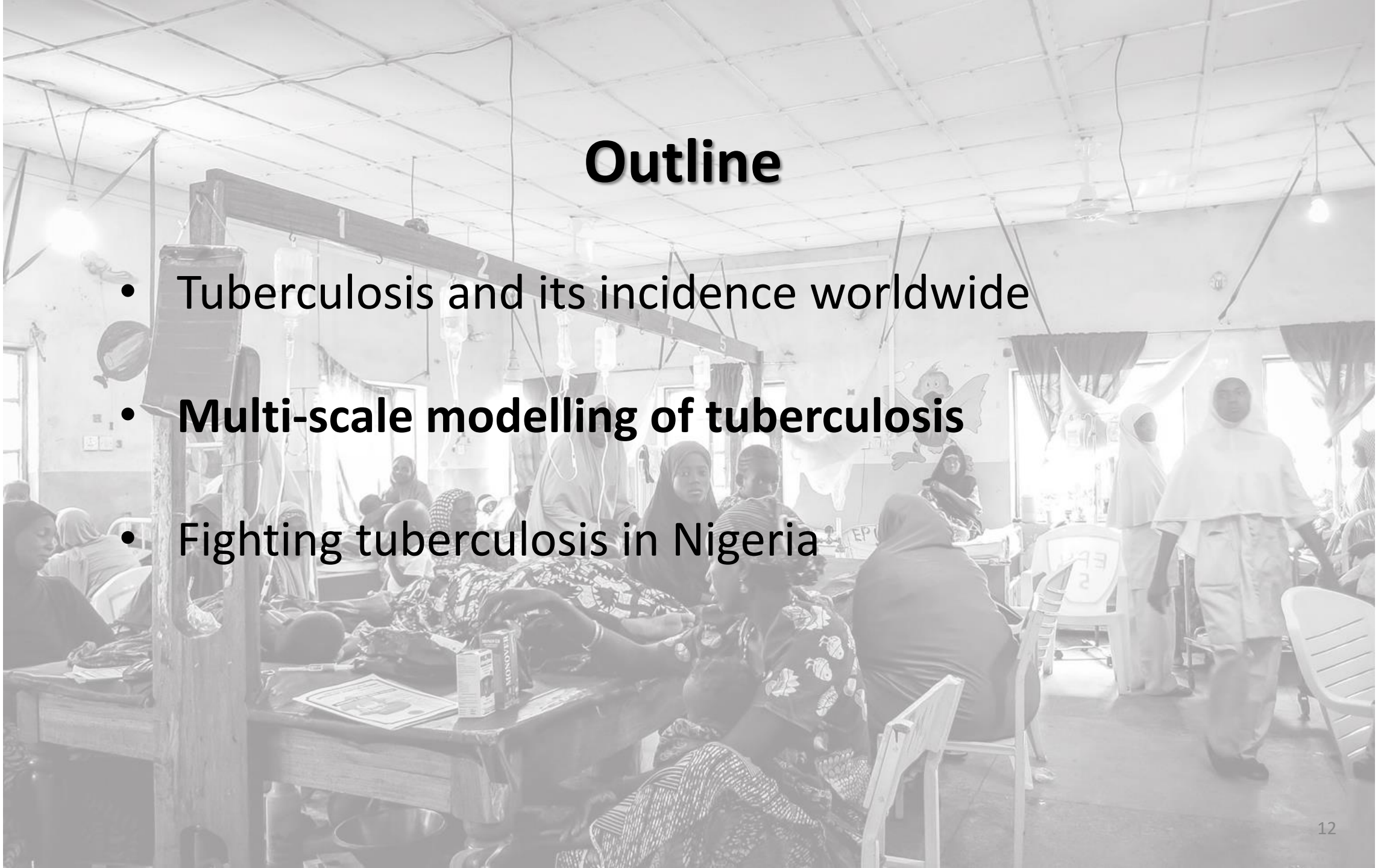
Goal 15. Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss

Goal 16. Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels

Goal 17. Strengthen the means of implementation and revitalize the Global Partnership for Sustainable Development

Goal 3: "Ensure **healthy** lives and promote **well-being** for all at all ages".

Target 3.3 : "By 2030, end the epidemics of AIDS, **tuberculosis**, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases."



Outline

- Tuberculosis and its incidence worldwide
- **Multi-scale modelling of tuberculosis**
- Fighting tuberculosis in Nigeria

The research team…

Sergio Alonso, PhD
Physicist

UNIVERSITAT POLITÈCNICA DE CATALUNYA
BARCELONATECH

Computational biophysicists

Daniel López, PhD
Physicist

Quim Valls, PhD
Physicist

Nura MR Ahmad
Mathematician

Martí Català
Physics Engineer

We are **computational biophysicists** in **interdisciplinary** research **teams**:

Dr. Cardona

Dr. Vilaplana

Dr. Orcau

Dr. Millet

IGTP Germans Trias i Pujol Research Institute

Medical Doctors, specialists in Microbiology

Germans Trias i Pujol Hospital

Medical Doctors, specialists in Radiology

Dr. Bechini
Dr. Tenesa
Dr. Pérez
Dr. Nogueira

UNIVERSITAT POLITÈCNICA DE CATALUNYA BARCELONATECH

UPC

BIOMSC

Computational biophysicists

Agència de Salut Pública

Medical Doctors, specialists in Epidemiology

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

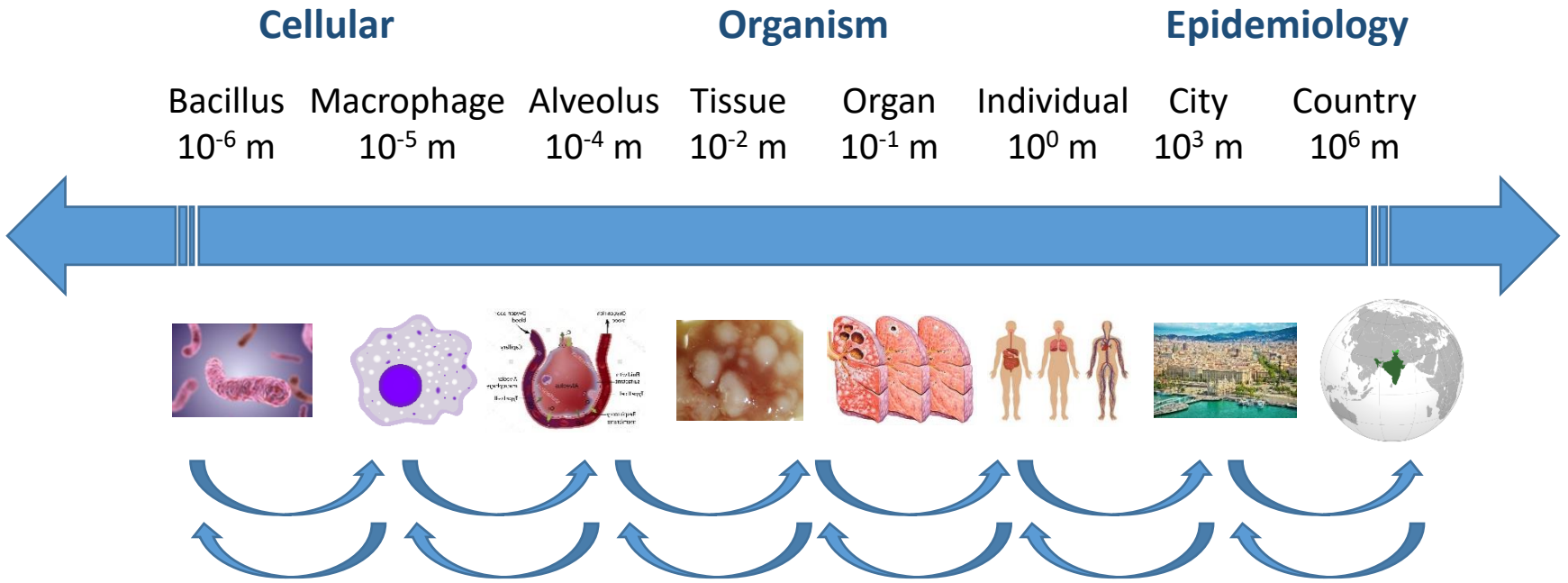
BSC

Computer Engineers

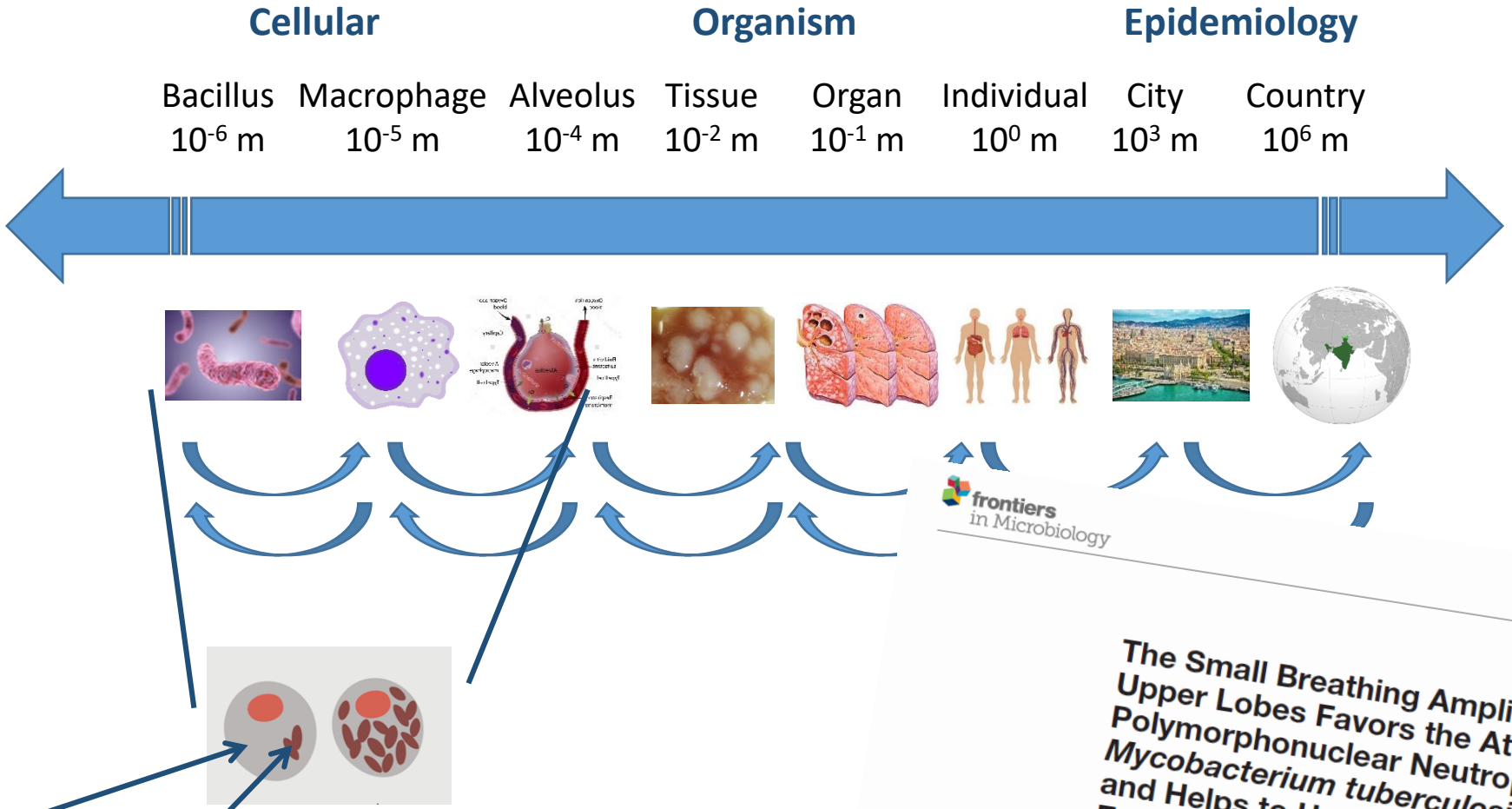
Dr. Montañola

Dr. Casanovas

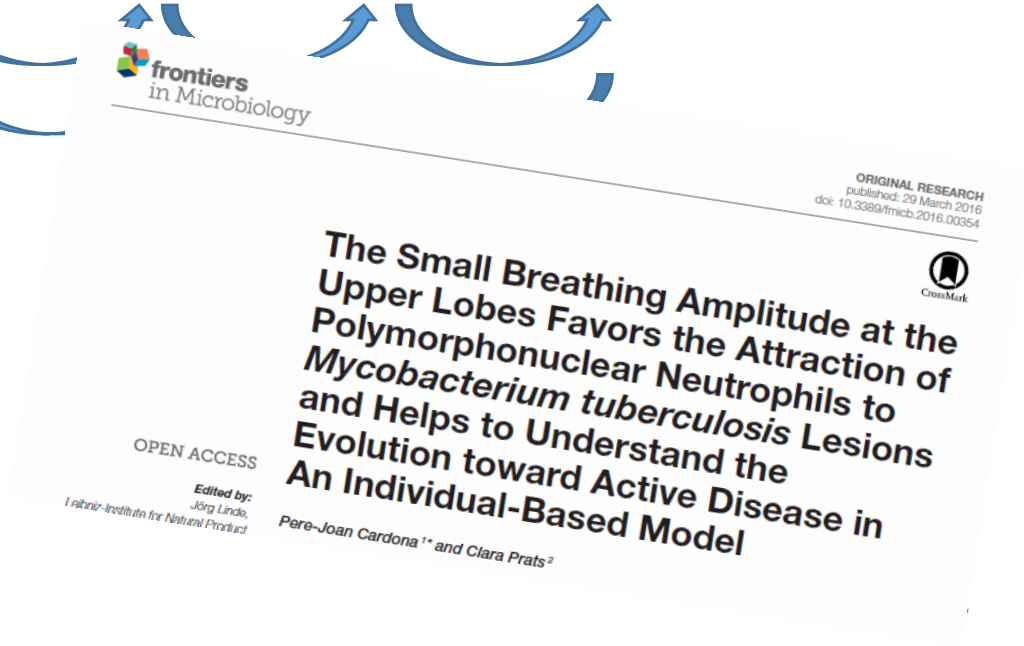
Mathematical modelling in tuberculosis: a **multiscale** and **translational** approach



Mathematical modelling in tuberculosis: a **multiscale** and **translational** approach



Cardona and Prats, Frontiers in Microbiology, 2016


frontiers in Microbiology

ORIGINAL RESEARCH
published: 29 March 2016
doi: 10.3389/fmicb.2016.00354

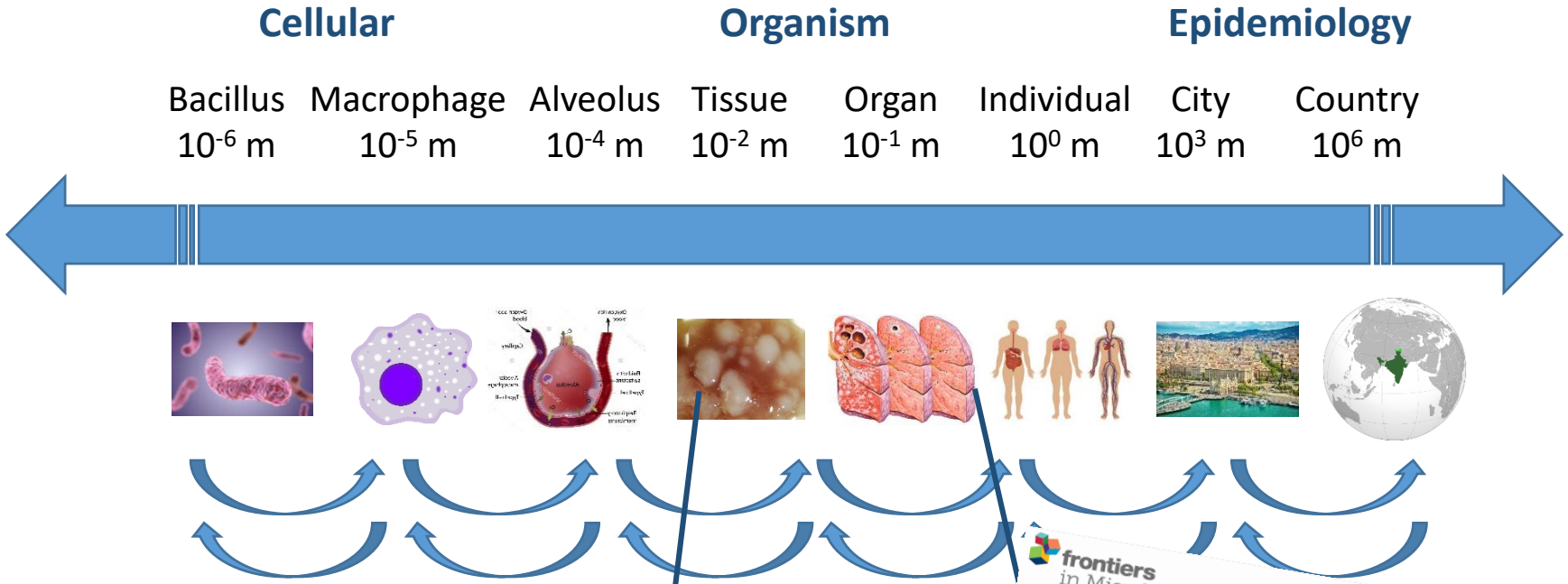
The Small Breathing Amplitude at the Upper Lobes Favors the Attraction of Polymorphonuclear Neutrophils to *Mycobacterium tuberculosis* Lesions and Helps to Understand the Evolution toward Active Disease in An Individual-Based Model

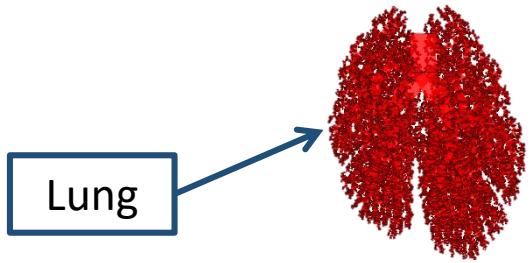
OPEN ACCESS

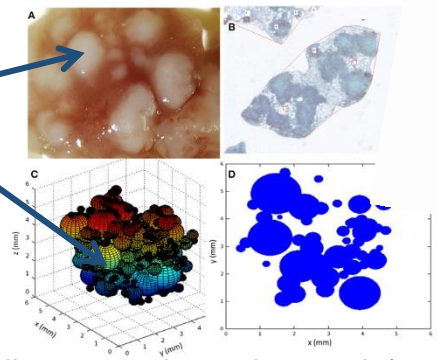
Edited by:
Jörg Linde,
Leibniz-Institute for Natural Product

Pere-Joan Cardona [1]* and Clara Prats [2]

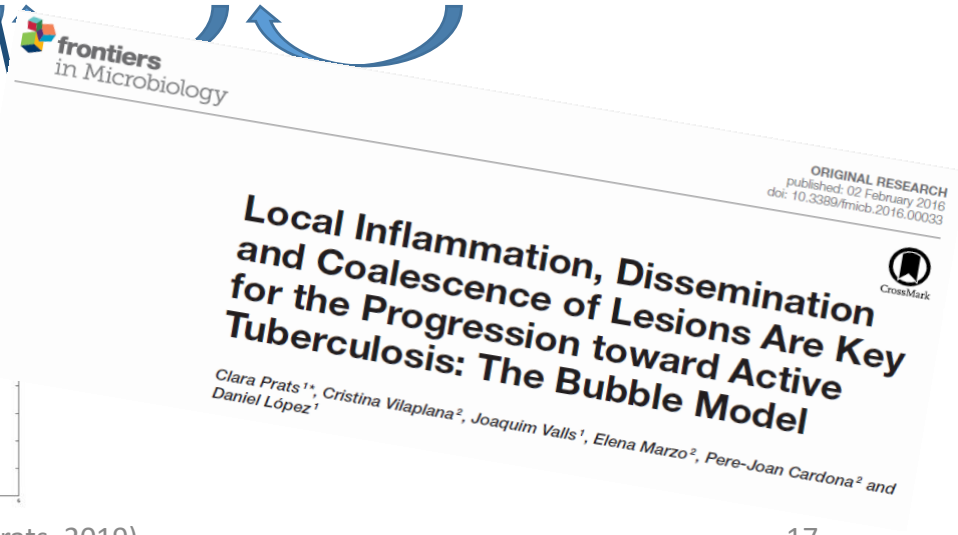
Mathematical modelling in tuberculosis: a **multiscale** and **translational** approach



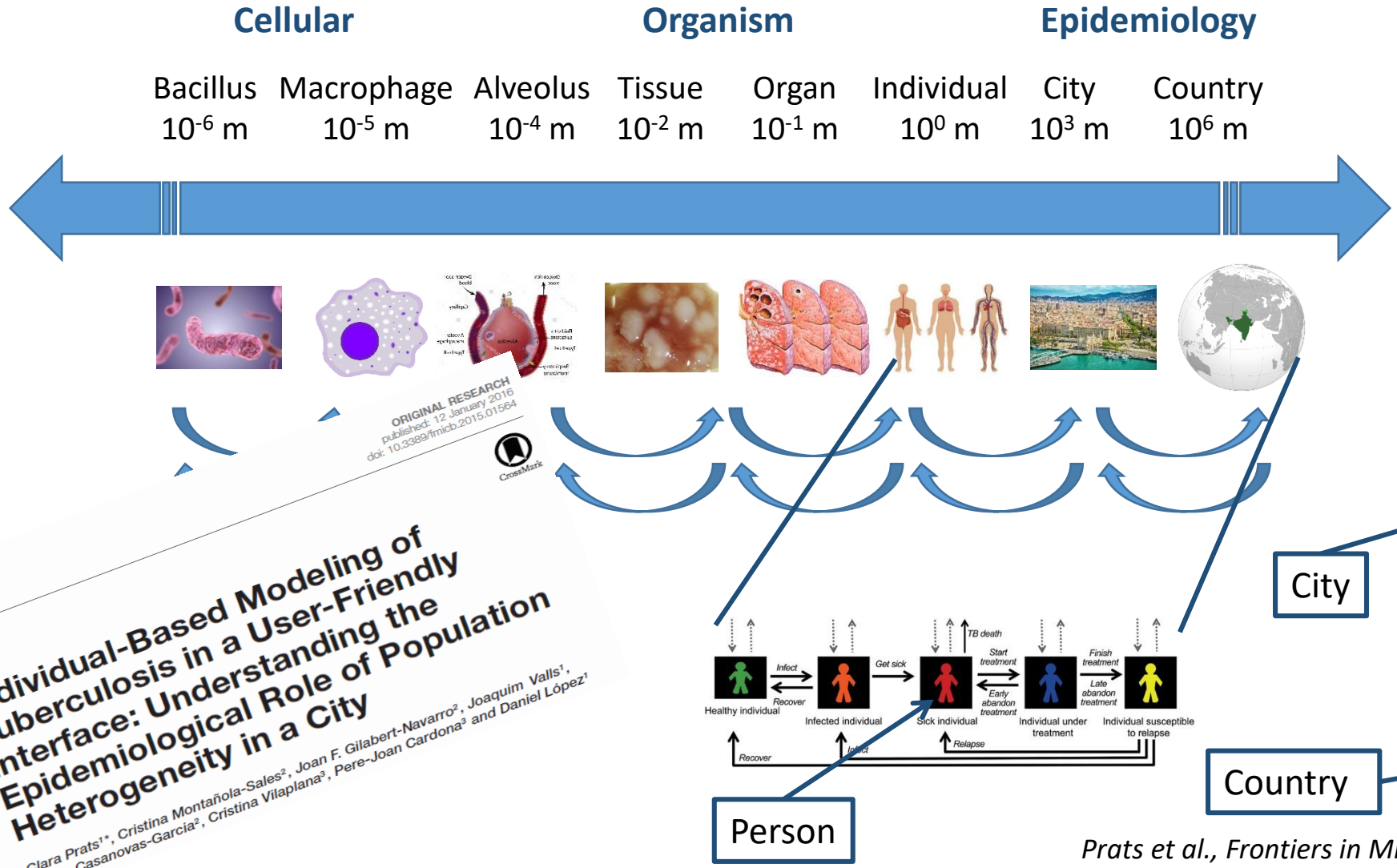




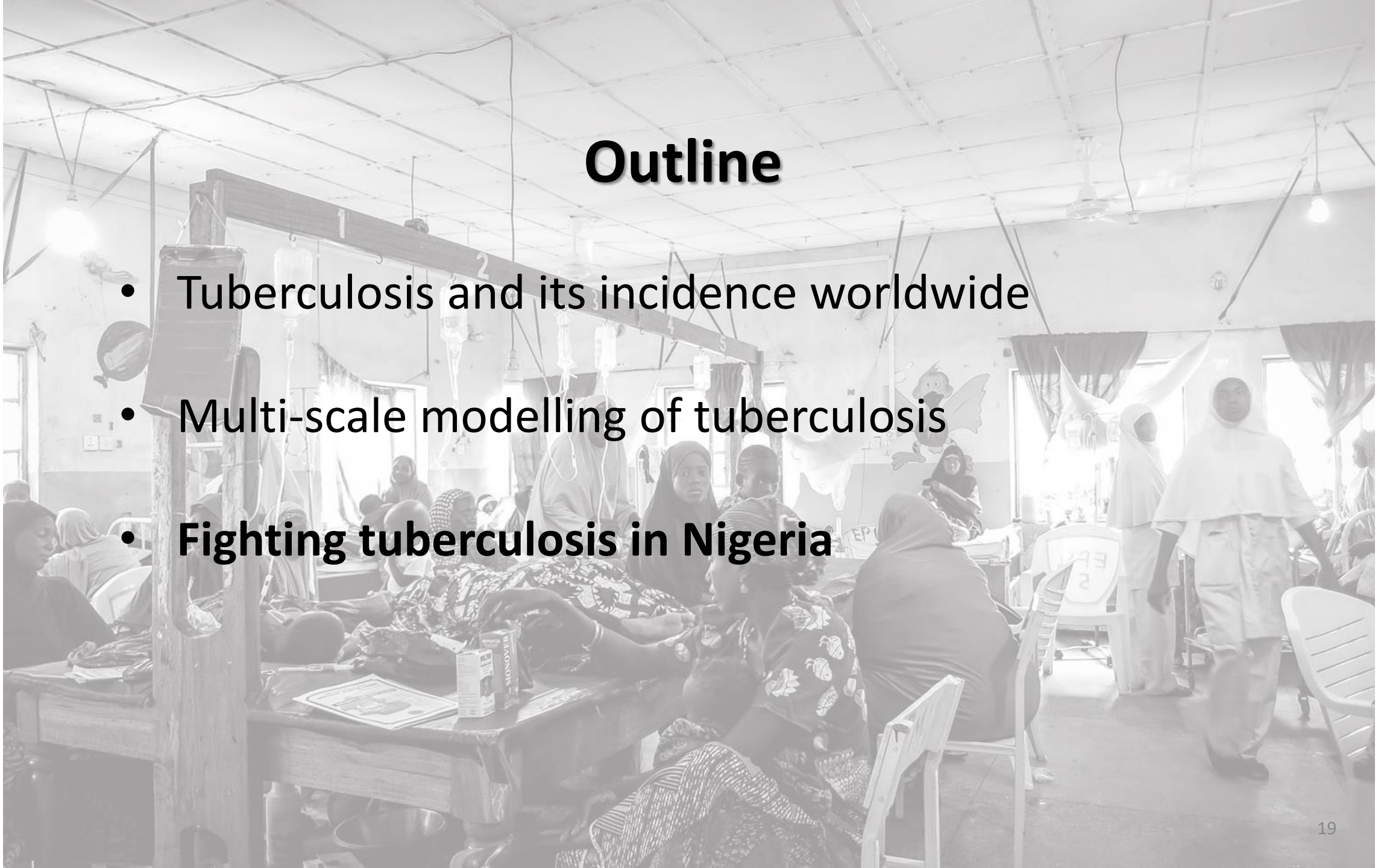
Prats et al., Frontiers in Microbiology, 2016



Mathematical modelling in tuberculosis: a **multiscale** and **translational** approach



Prats et al., Frontiers in Microbiology, 2016

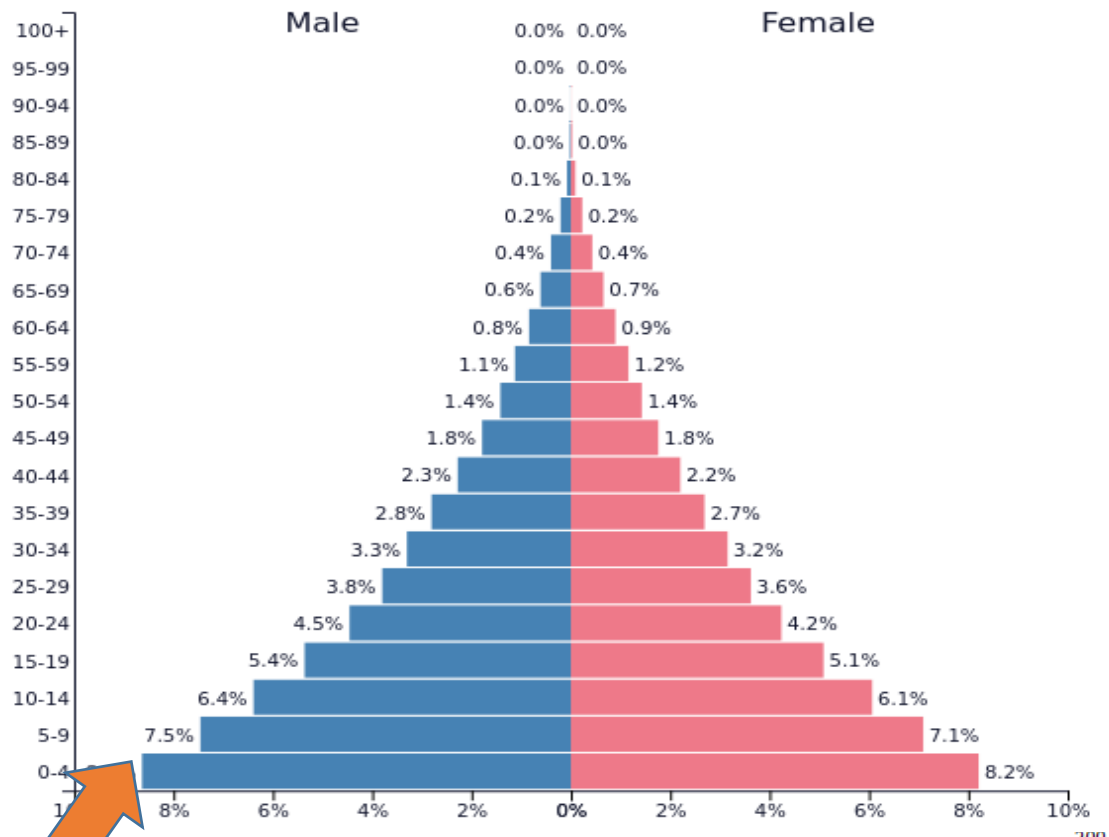


Outline

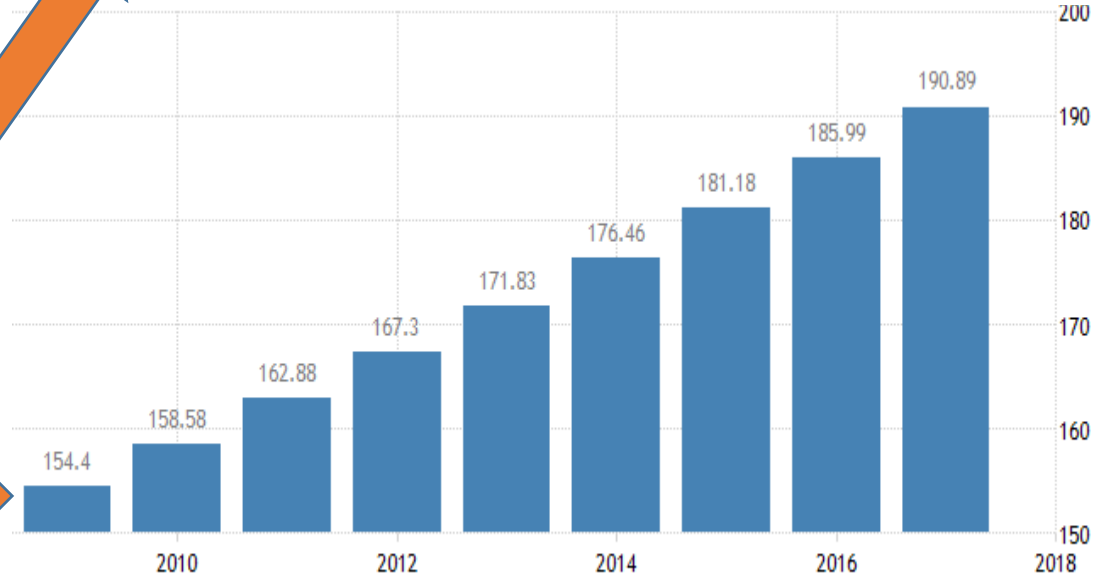
- Tuberculosis and its incidence worldwide
- Multi-scale modelling of tuberculosis
- **Fighting tuberculosis in Nigeria**

Connecting computational models with reality…

Nigeria



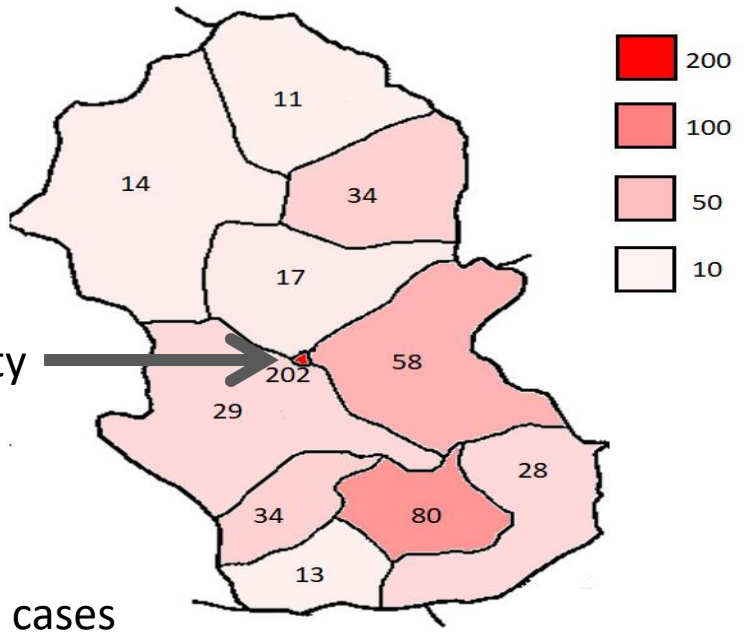
1. **Subsaharian** Africa
2. Population over **200 million inhabitants**
3. **44% of population is younger than 15; 64% younger than 20**
4. **Annual growth of 2.6%**



Nigeria

Gombe state

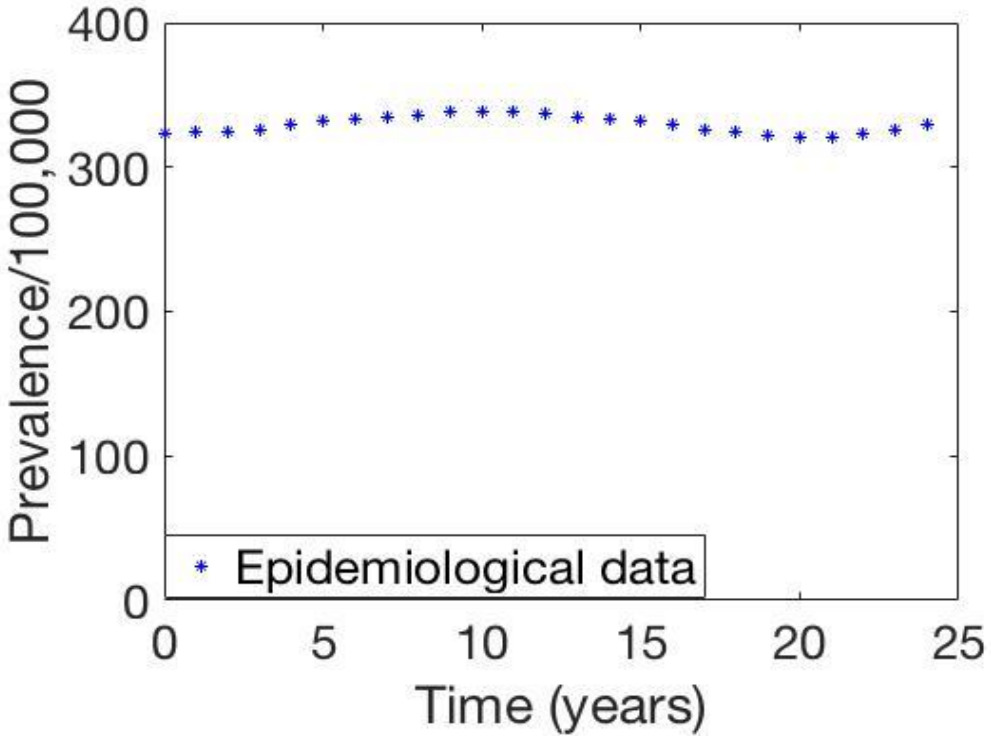
11 districts of Gombe



Gombe city

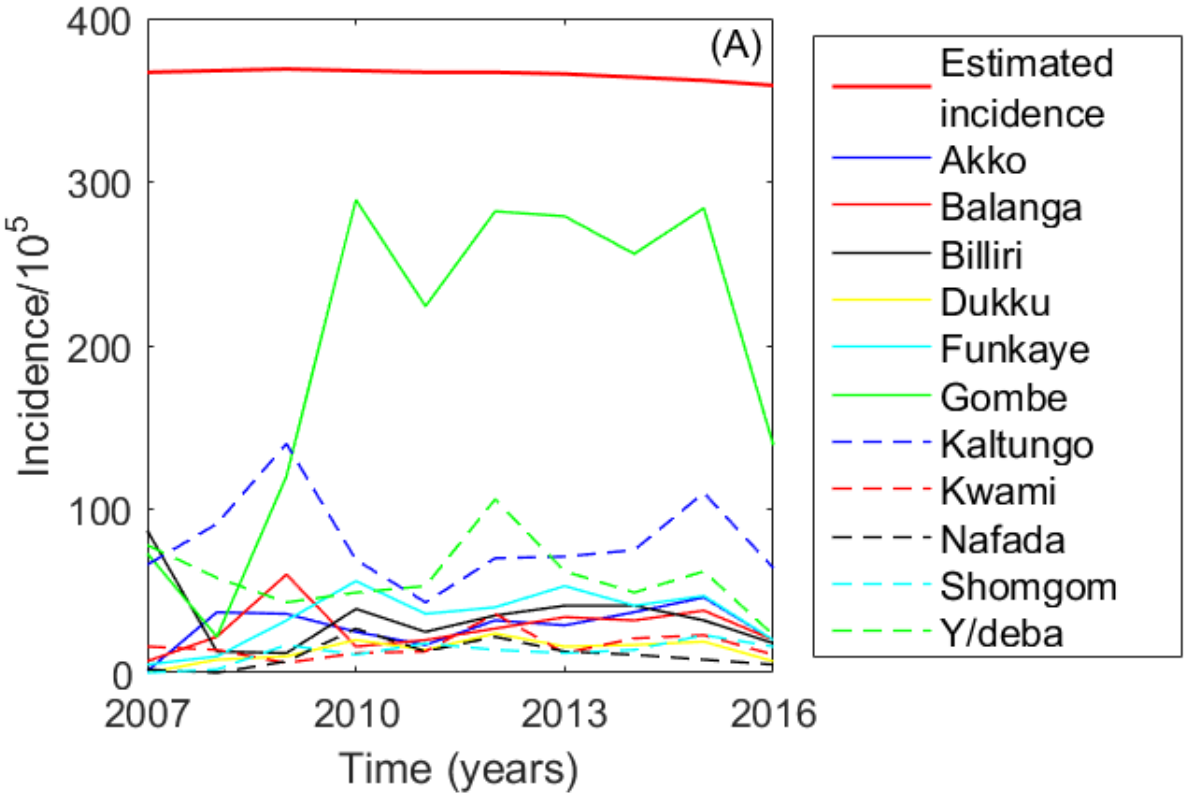
TB diagnosed cases per 10^5 inhabitants

Tuberculosis in Nigeria



Persistence of **TB prevalence** in Nigeria last 25 years

Tuberculosis in Gombe



Estimated TB incidence and **diagnosed cases/10^5 inhabitants** in Gombe's districts

A model in compartments

Compartments:

S: Susceptible

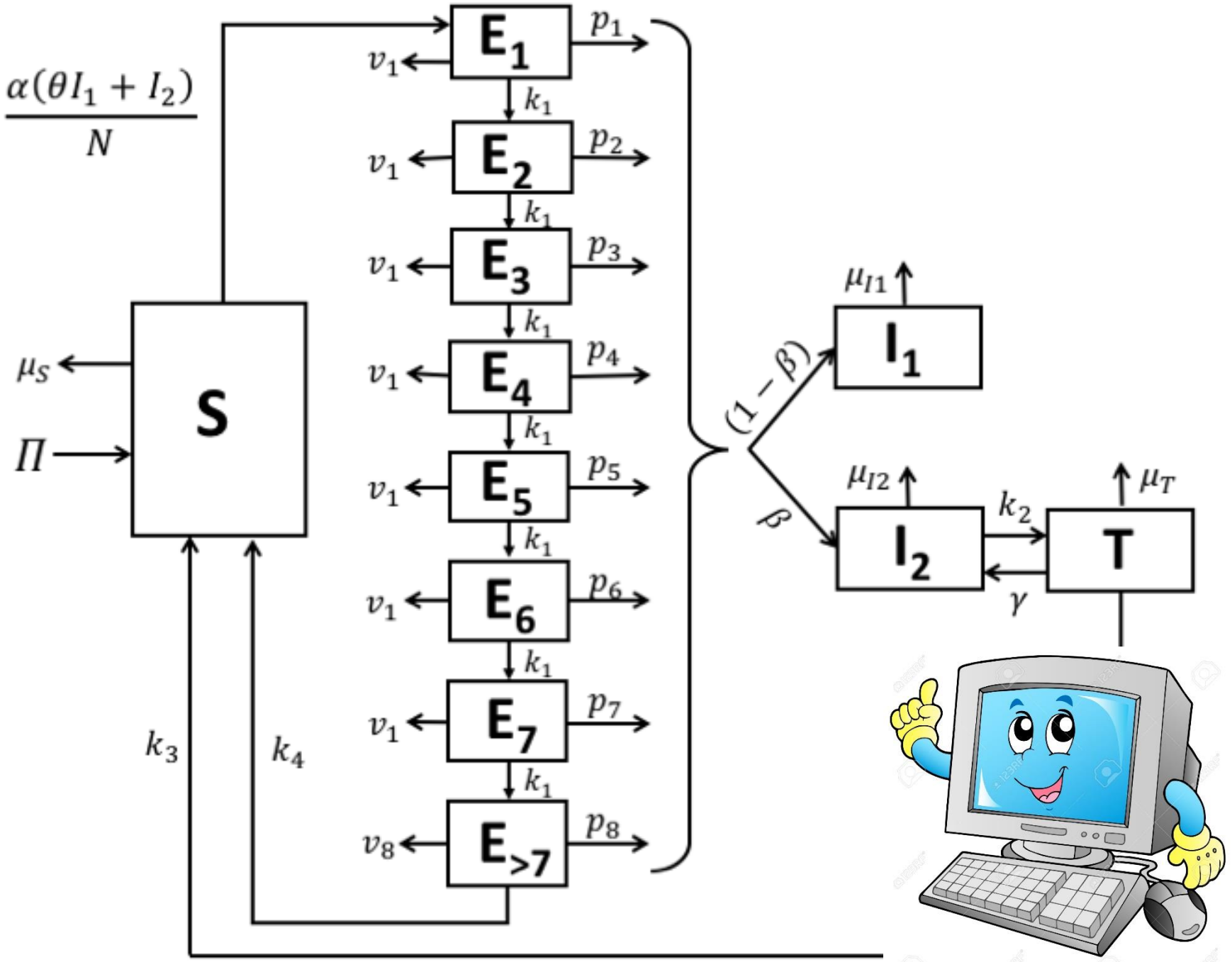
E: Exposed (LTBI)

I: Infectious (ATB)

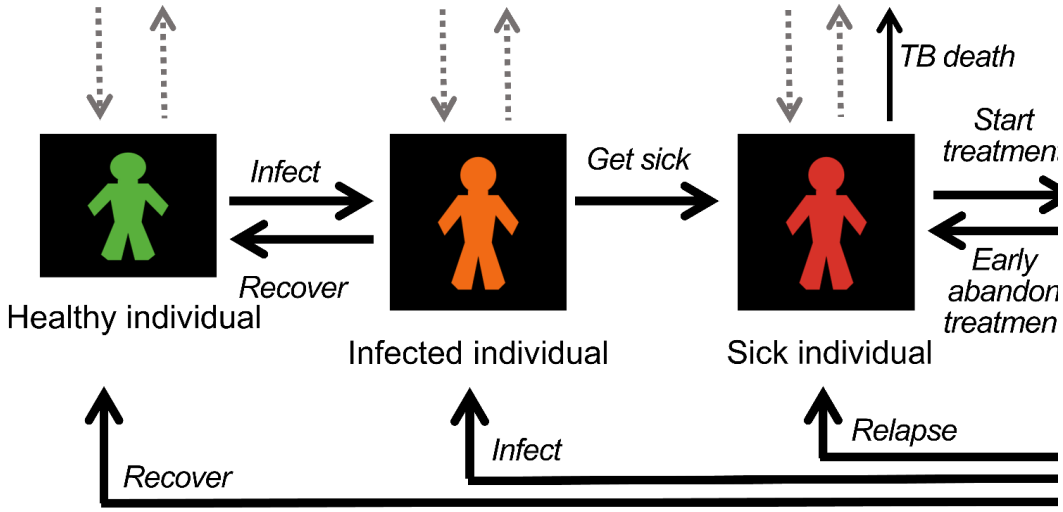
I_1: non diagnosed

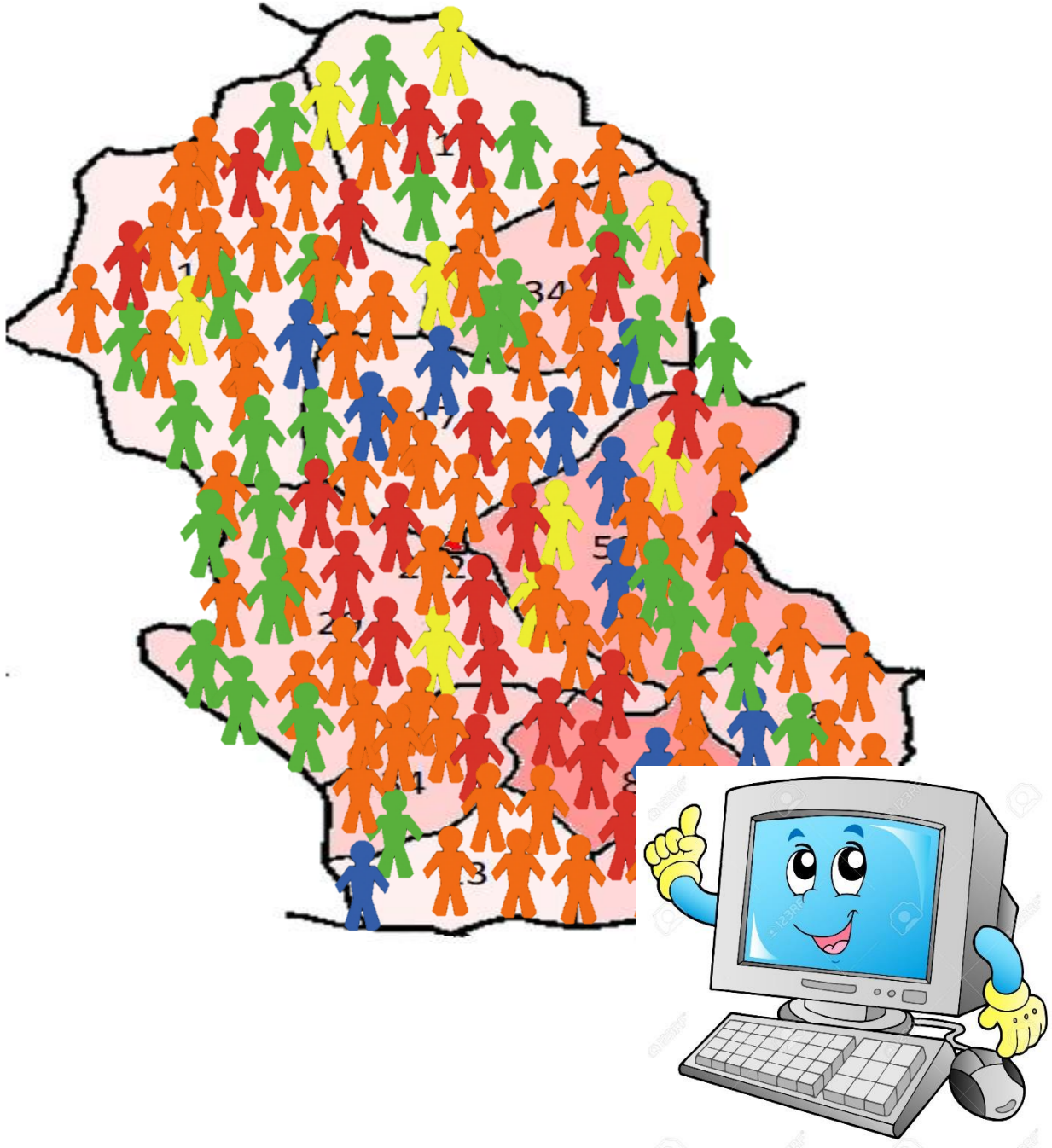
I_2: to be diagnosed

T: under Treatment

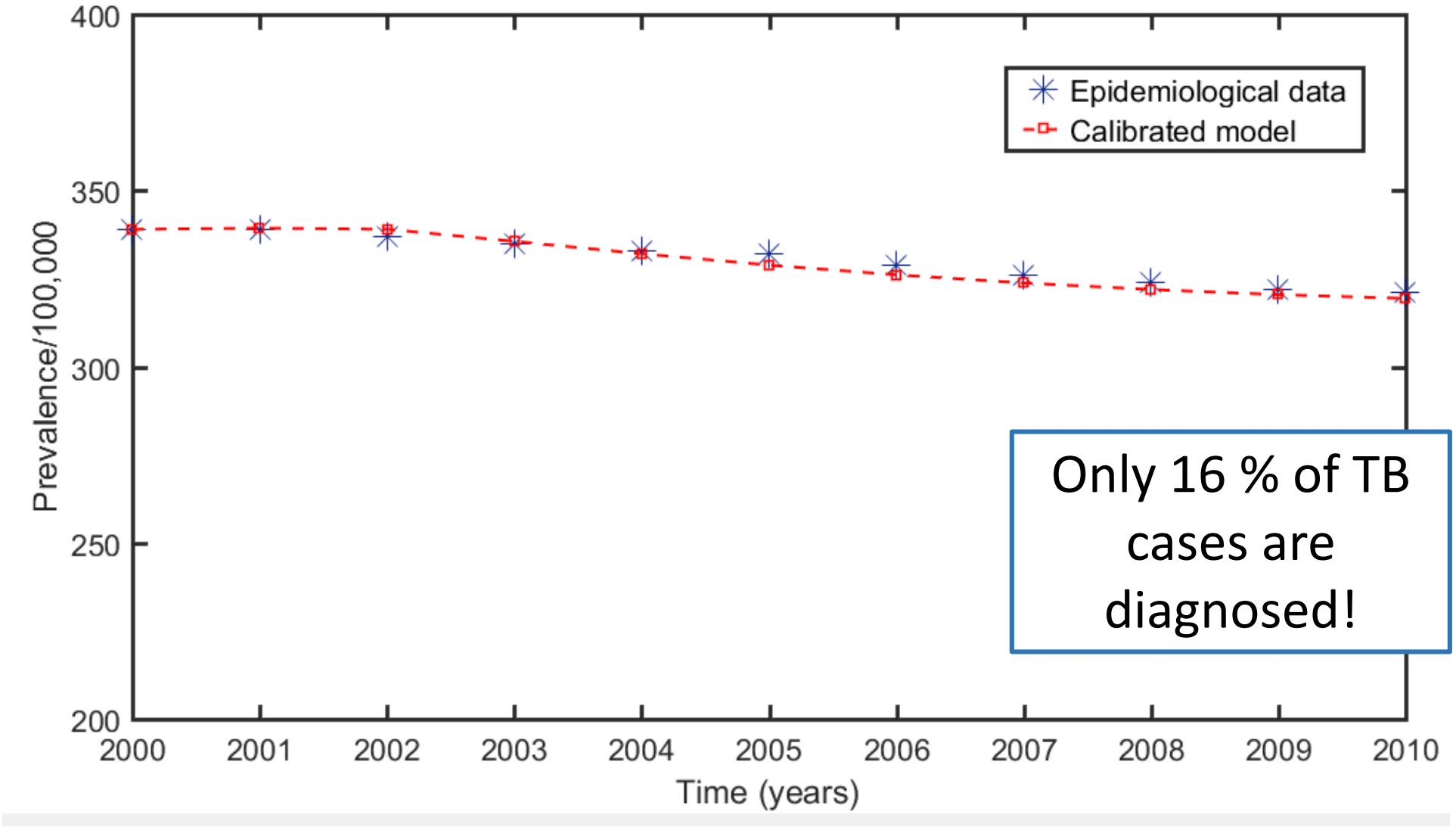


An Agent-based model

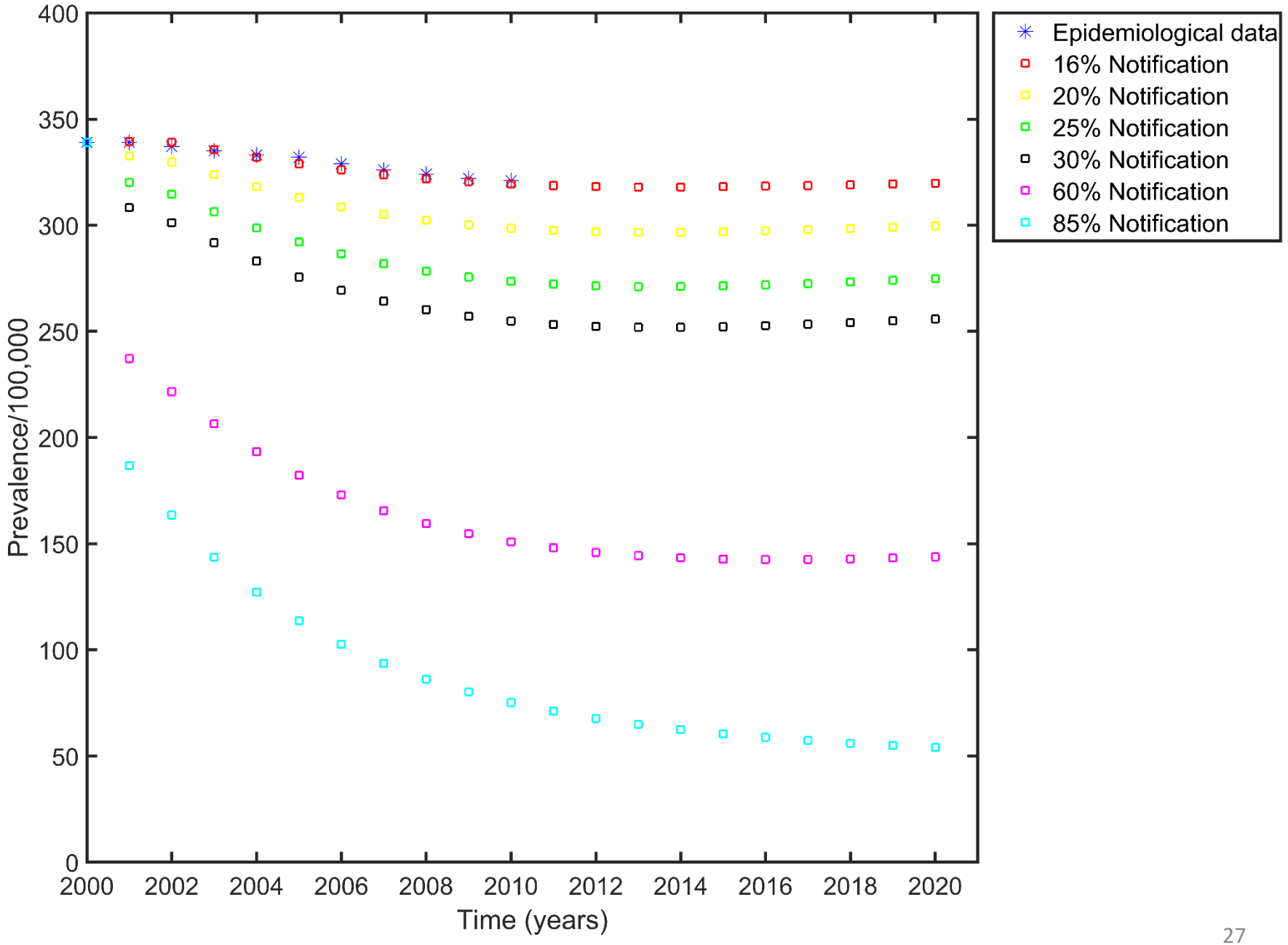




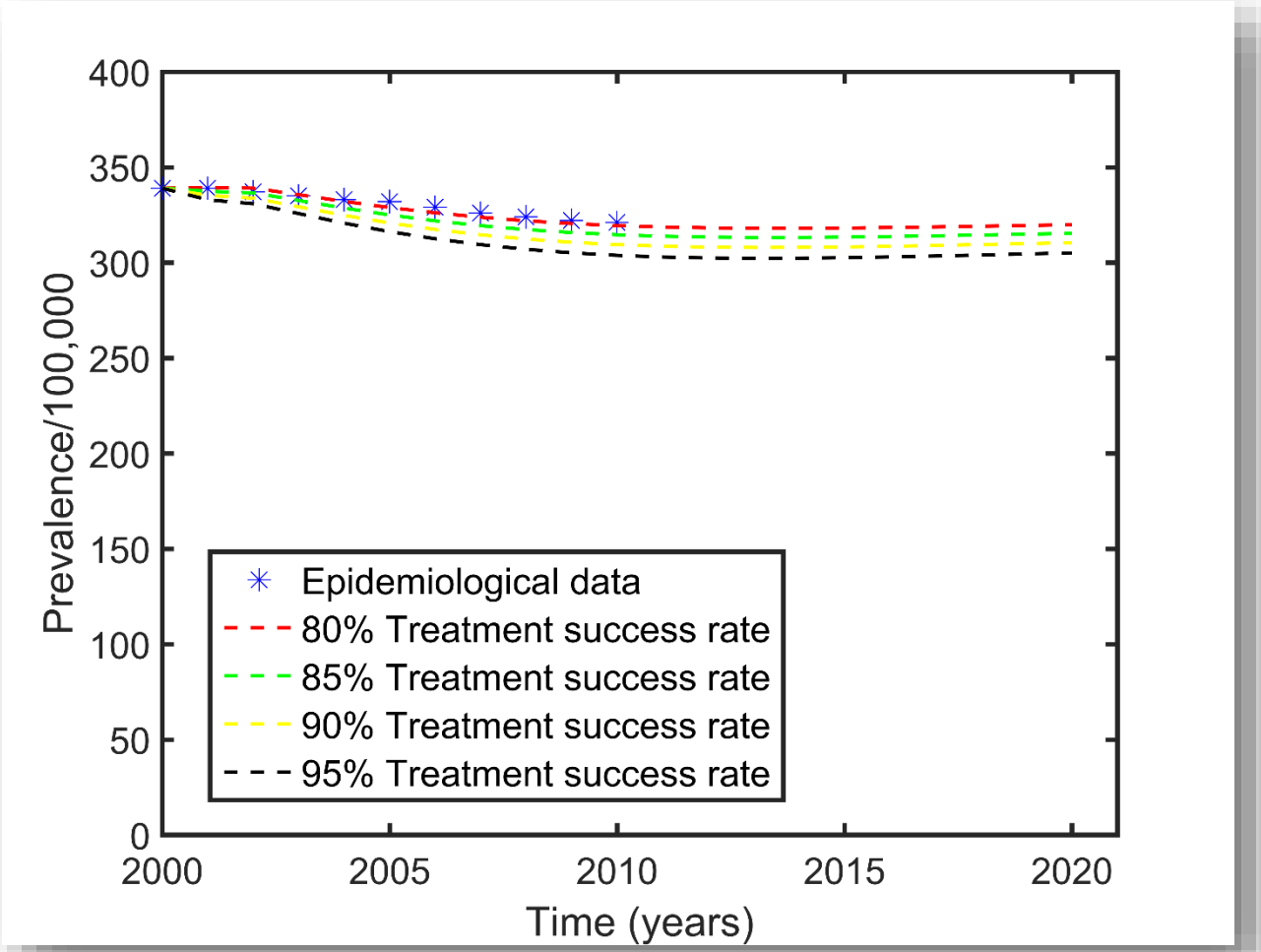
Estimating diagnosis rate with models:



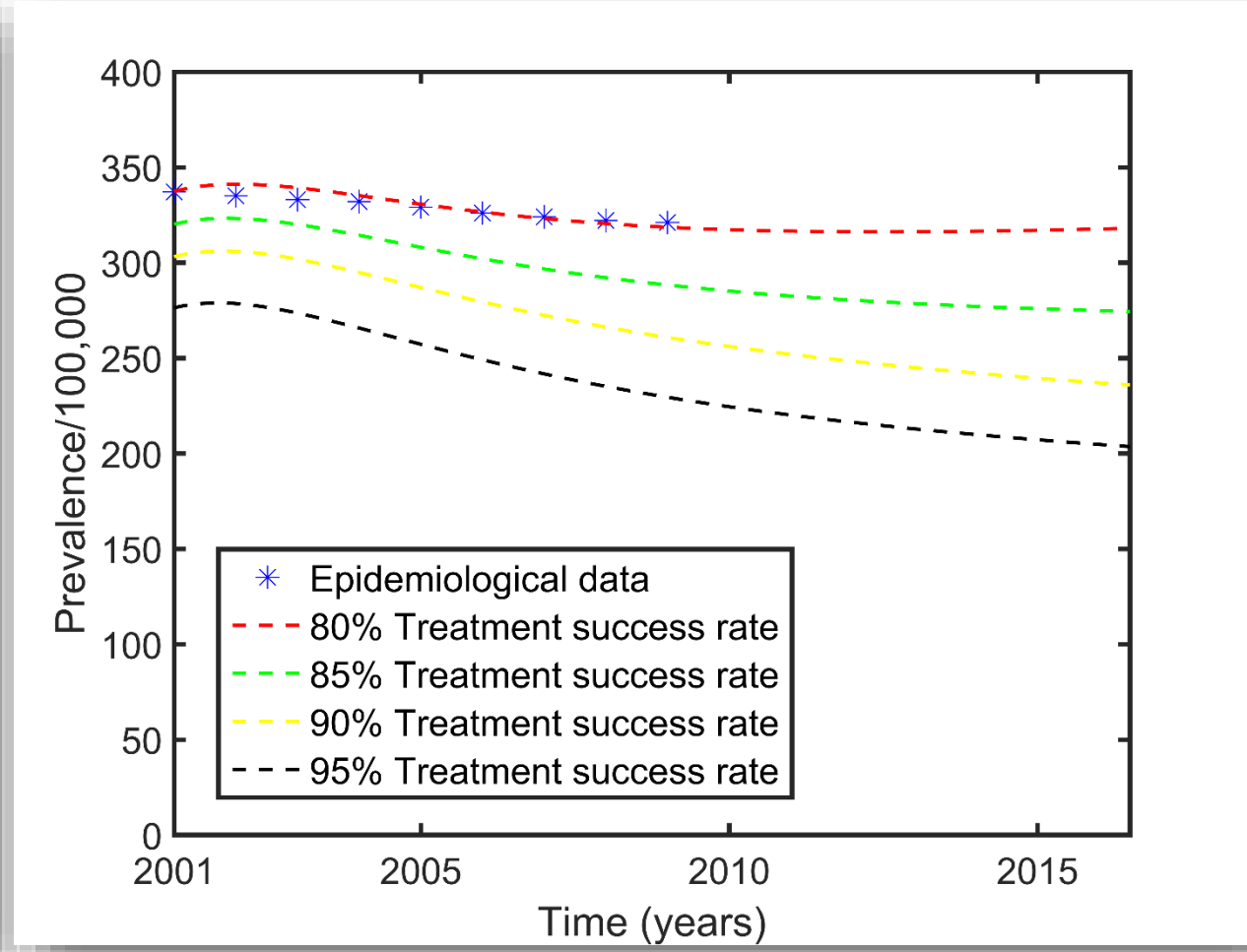
Simulation I: studying the effect of an **increase in the diagnosis rate**:



Simulation II: studying the effect of an increase in treatment success rate together **without** or **with** an increase in notification rate:

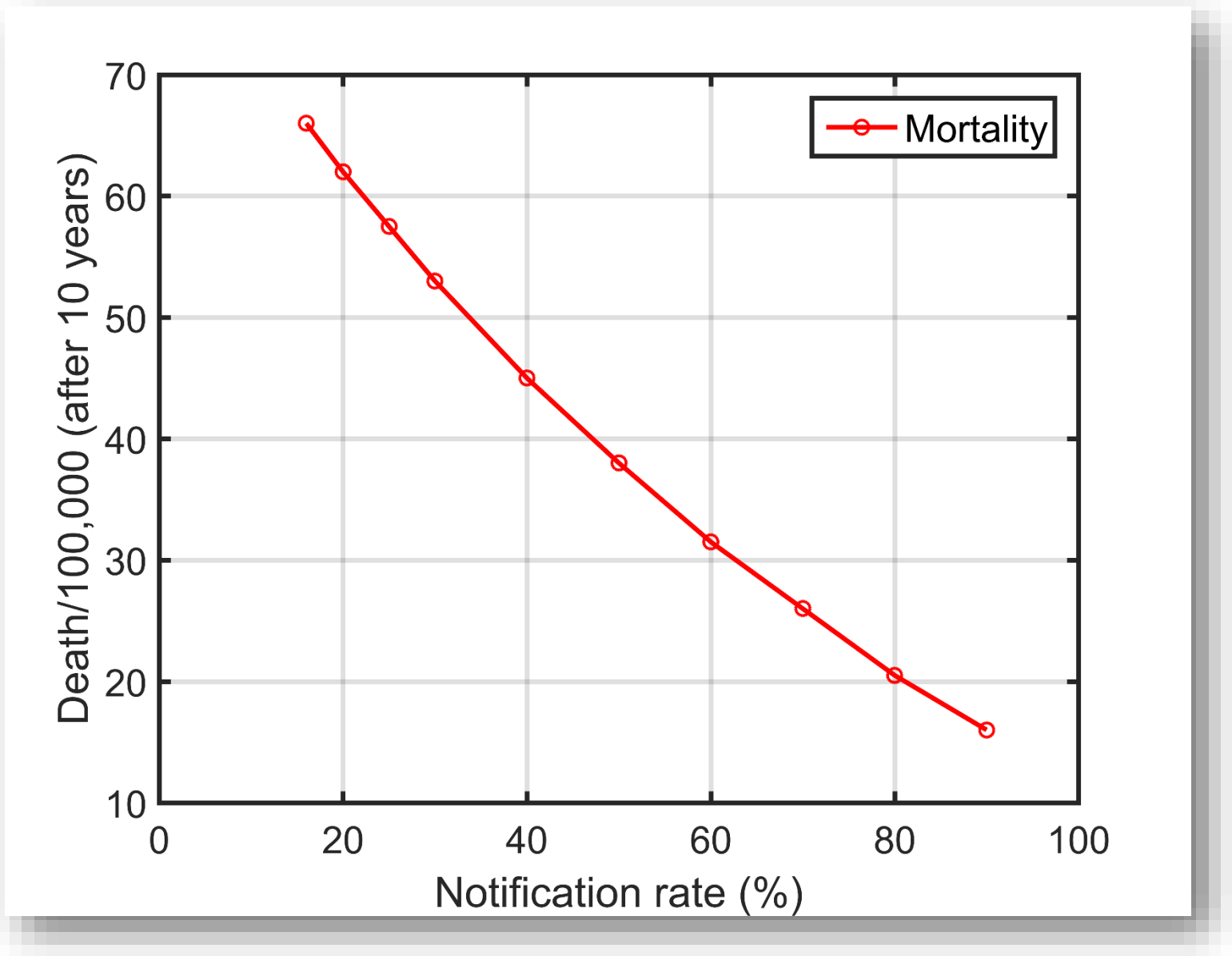


(A) Notification rate: 16 %



(B) Notification rate: 80 %

Simulation III: studying the effect of an increase in diagnosis rate on **TB-deaths**

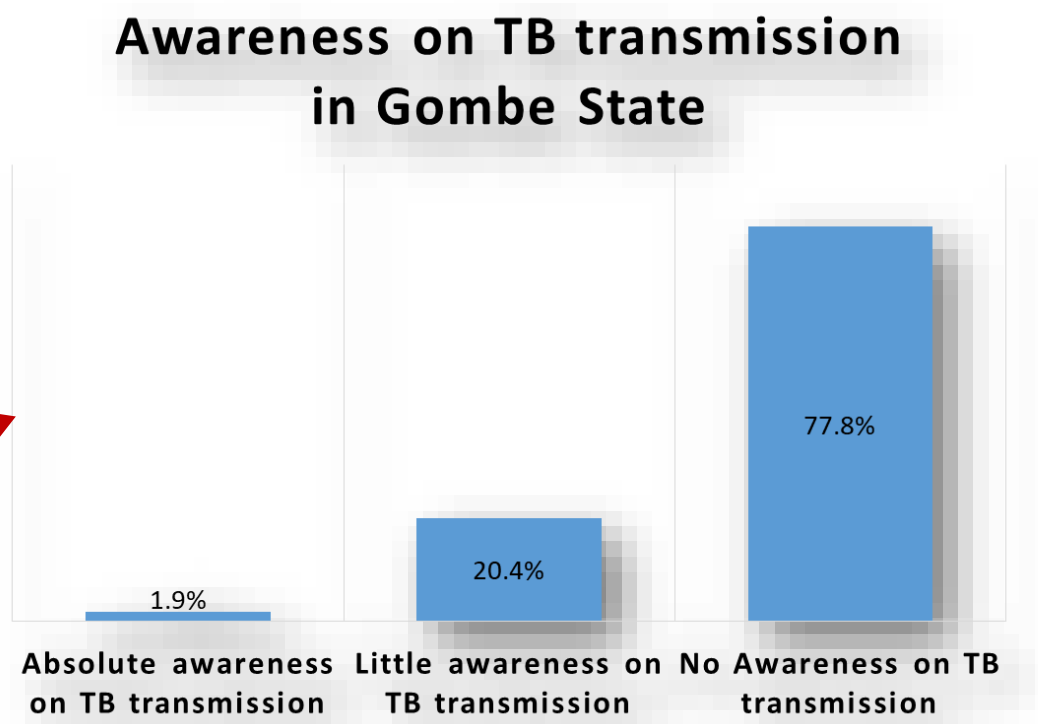


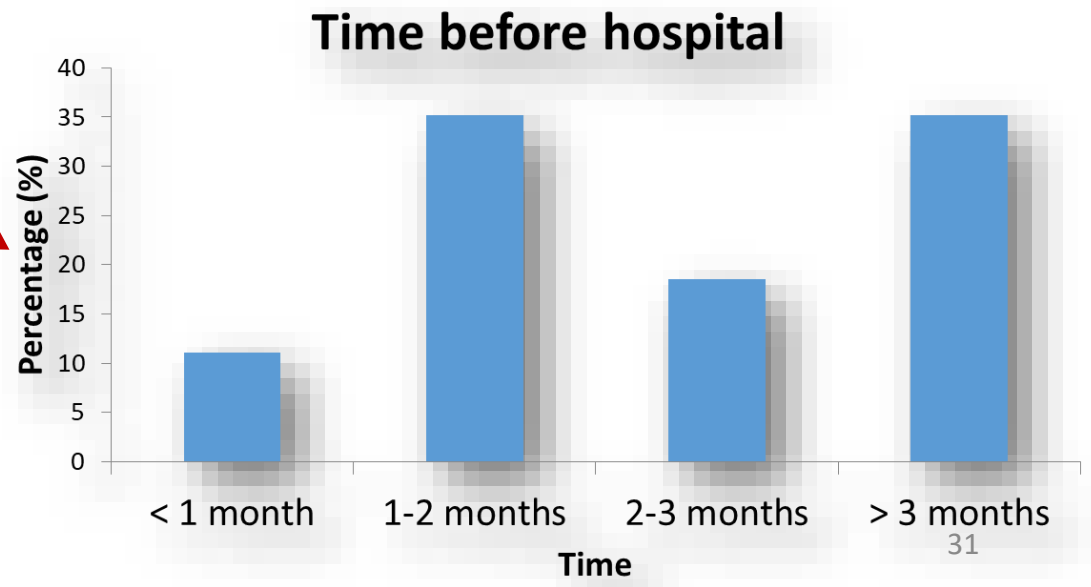
Exploring reality: field's work

Results of field's work

Major findings:

1. **0% patients** have **knowledge** of TB **symptoms after visiting the doctor**
2. 80% patients has **no knowledge on TB control and transmission** after visiting doctor
3. About 70% of patients were not informed by healthcare workers
4. **Mean delay before hospital: 25 weeks**
5. Mean delay at the hospital: 8 days
6. **Delay before hospital is associated with surface area of the respective district**

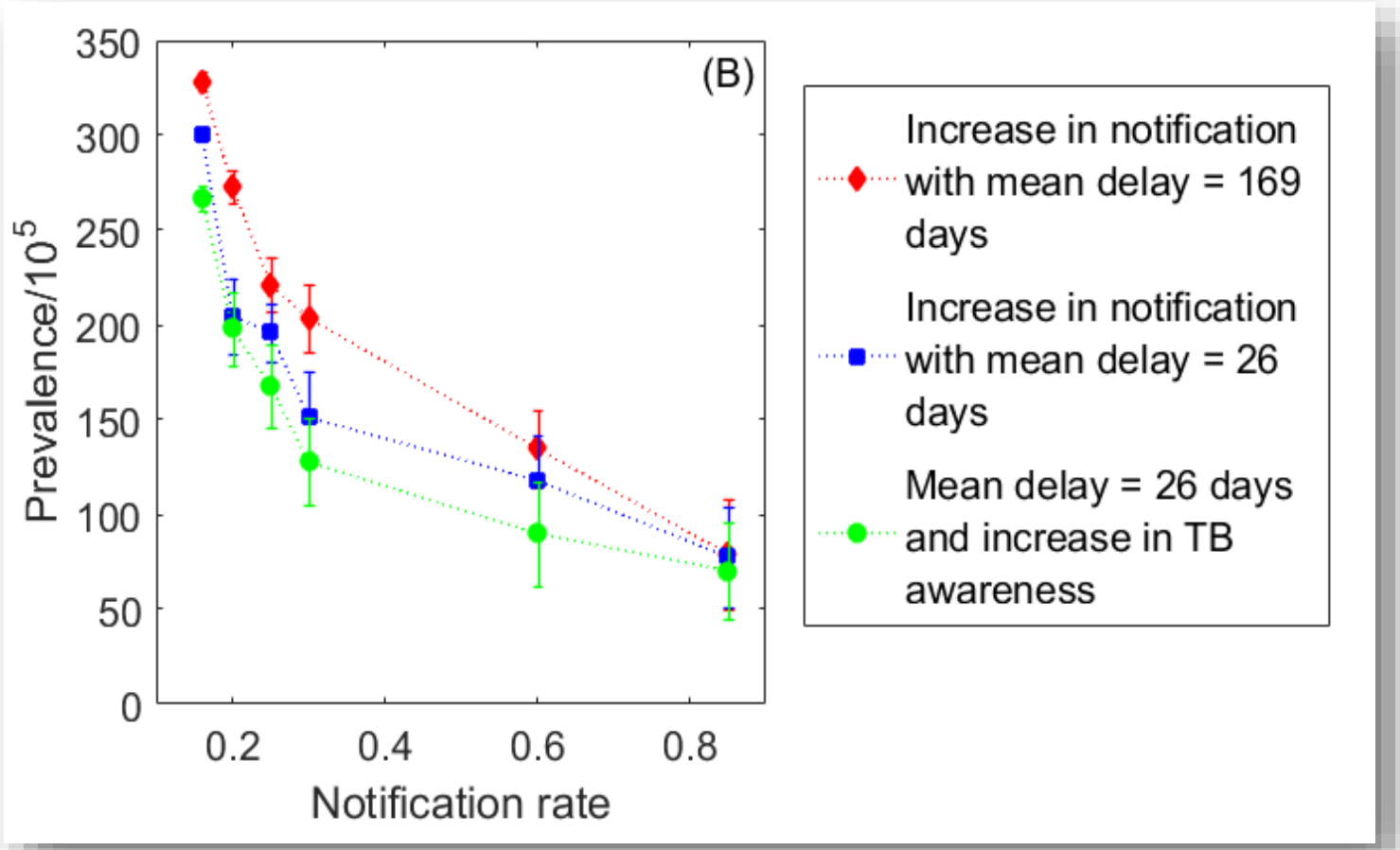




- ✓ **Awareness**
- ✓ **Accessibility/Availability**

Simulation IV: combining **three** different control strategies. TB prevalence after after 10 years…

1) Increasing notification rate
2) Increase in notification rate + decrease in diagnosis delay
3) Increase in notification rate + decrease in diagnosis delay + increase in TB awareness




NATIONAL TUBERCULOSIS & LEPROSY
CONTROL PROGRAMME (NTBLCP)
Federal Ministry of Health
Thanks for your attention!
XXVII CONVOCATÒRIA D'AJUTS DEL CCD 2019
AJUTS a projectes de cooperació local
Activitats EpD i Sensibilització
del 6 al 22 de maig
ADREÇAT a la comunitat universitària