Measuring the "burden" of TB

Measures of TB burden

- Case notifications
- Disease Incidence
  - By smear status
- Disease Prevalence
- Case Fatality Rate
- TB mortality
- Prevalence of infection
- Annual risk of TB infection

Some definitions

- Incidence
  - Number of new cases diagnosed over a specified time period – usually a year.

- Prevalence
  - Number of cases in the population at a specified time point.

- Case detection rate
  - Number of cases notified divided by number of cases that happened (incidence).

Case notifications

Bangladesh

Tuberculosis profile

Population 2017 — 165 million

Estimates of TB burden*, 2017	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	59 (38–85)	36 (23–52)
Mortality (HIV+TB only)	0.17 (0.085–0.29)	0.11 (0.05–0.18)
Incidence (includes HIV+TB)	364 (265–479)	221 (161–291)
Incidence (HIV+TB only)	0.55 (0.27–0.92)	0.33 (0.17–0.56)
Incidence (MDR/RR-TB)**	8.4 (3.8–15)	5.1 (2.3–9)

Estimated TB incidence by age and sex (thousands)*, 2017	0-14 years	> 14 years	Total
Females	17 (16–18)	118 (98–137)	134 (110–158)
Males	18 (17–19)	212 (164–259)	230 (176–284)
Total	35 (32–38)	329 (237–421)	364 (265–479)

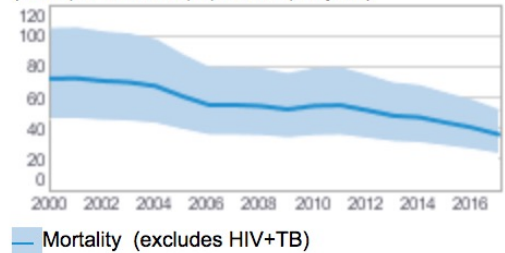| TB case notifications, 2017	
Total cases notified	244 201
Total new and relapse	242 639
- % tested with rapid diagnostics at time of diagnosis	<1%
- % with known HIV status	2%
- % pulmonary	81%
- % bacteriologically confirmed among pulmonary	74%

Universal health coverage and social protection	
TB treatment coverage (notified/estimated incidence), 2017	67% (51–92)
TB patients facing catastrophic total costs	
TB case fatality ratio (estimated mortality/estimated incidence), 2017	0.17 (0.1–0.26)

TB/HIV care in new and relapse TB patients, 2017	Number	(%)
Patients with known HIV-status who are HIV-positive	89	2%
- on antiretroviral therapy	84	94%

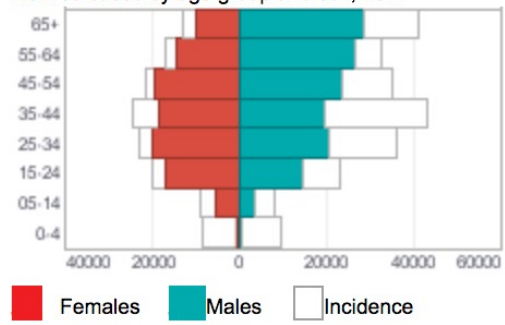| Drug-resistant TB care, 2017	New cases	Previously treated cases	Total number***
Estimated MDR/RR-TB cases among notified pulmonary TB cases			5 800 (3 800–7 800)
Estimated % of TB cases with MDR/RR-TB	1.6% (0.74–2.8)	29% (24–35)	
% notified tested for rifampicin resistance	18%	63%	49 943
MDR/RR-TB cases tested for resistance to second-line drugs			362
Laboratory-confirmed cases			MDR/RR-TB: 944, XDR-TB: 6

(Rate per 100 000 population per year)

— Mortality (excludes HIV+TB)

(Rate per 100 000 population per year)
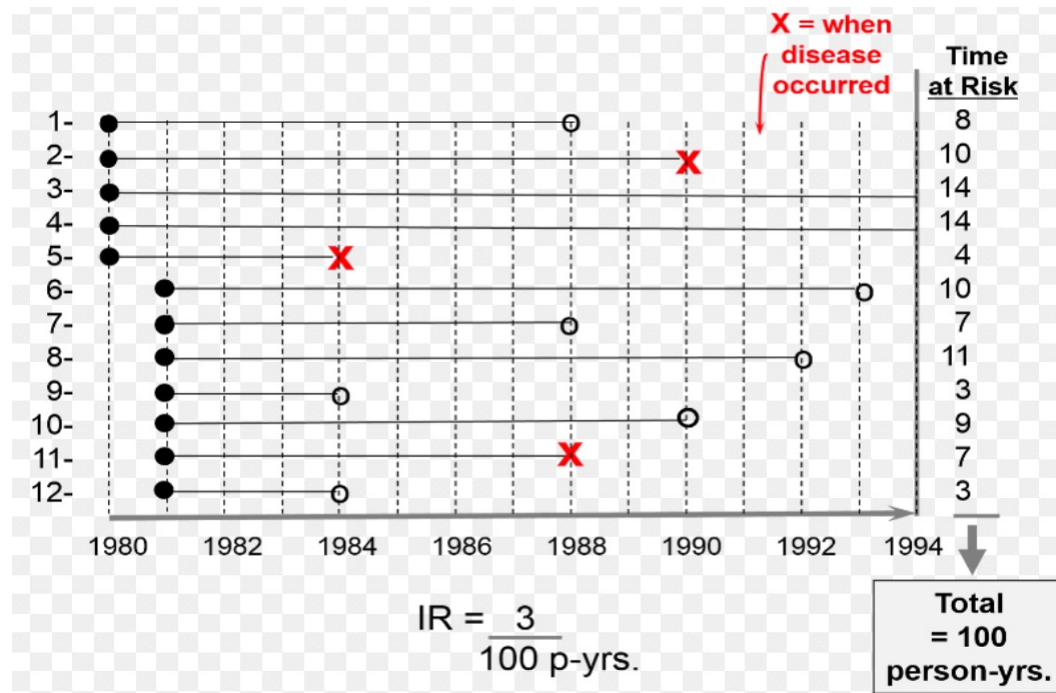
— Incidence
— Notified (new and relapse)
— Incidence (HIV+TB only)
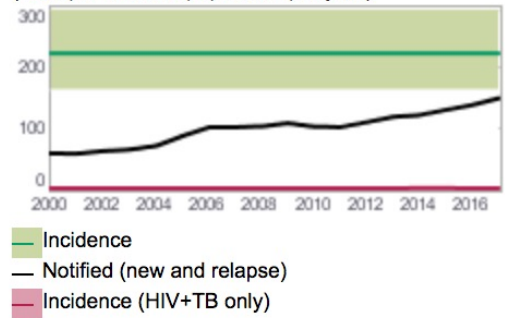
Notified cases by age group and sex, 2017

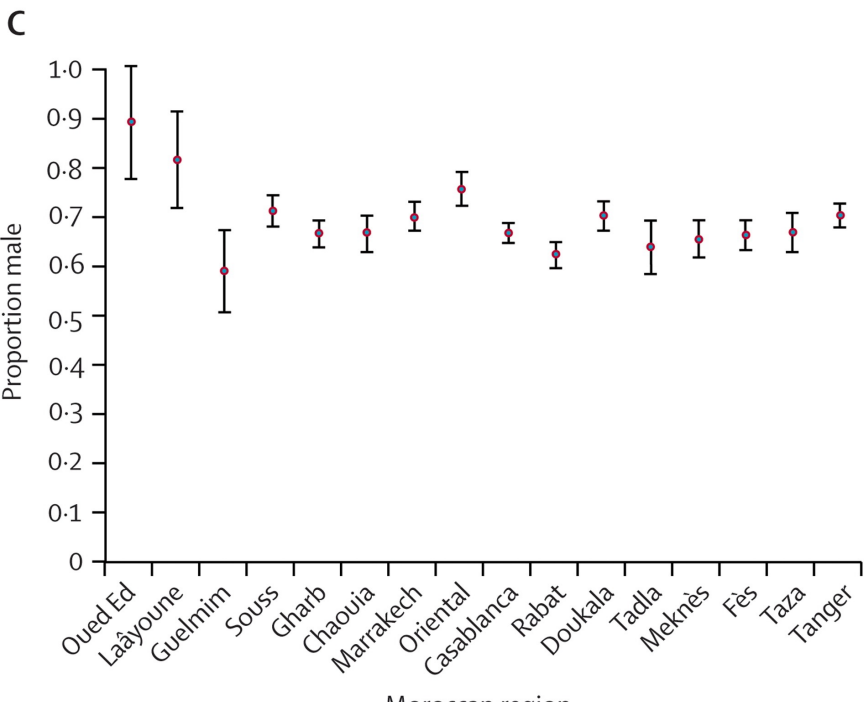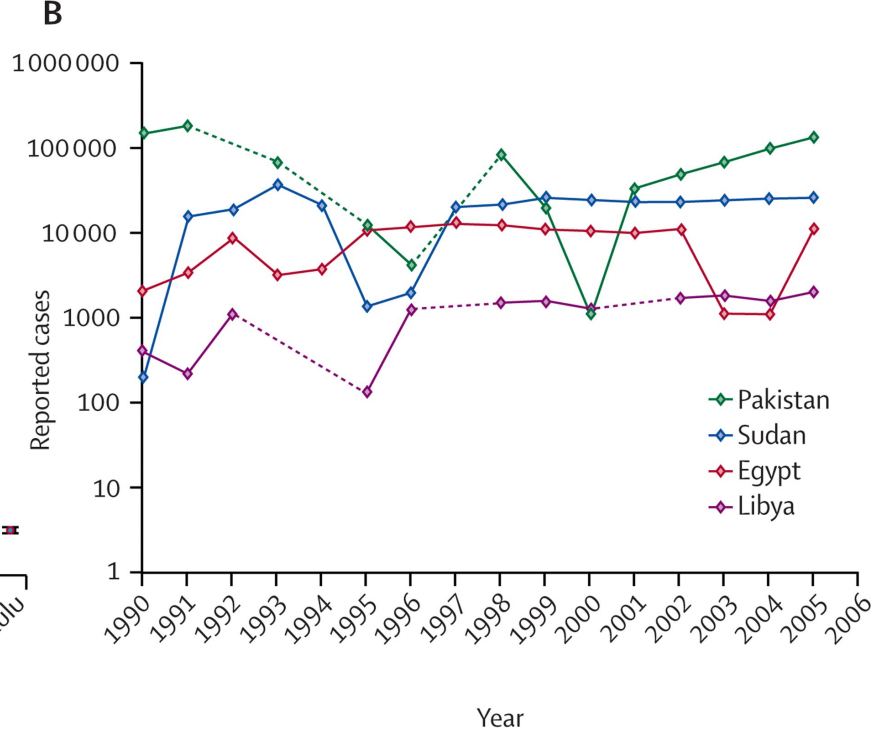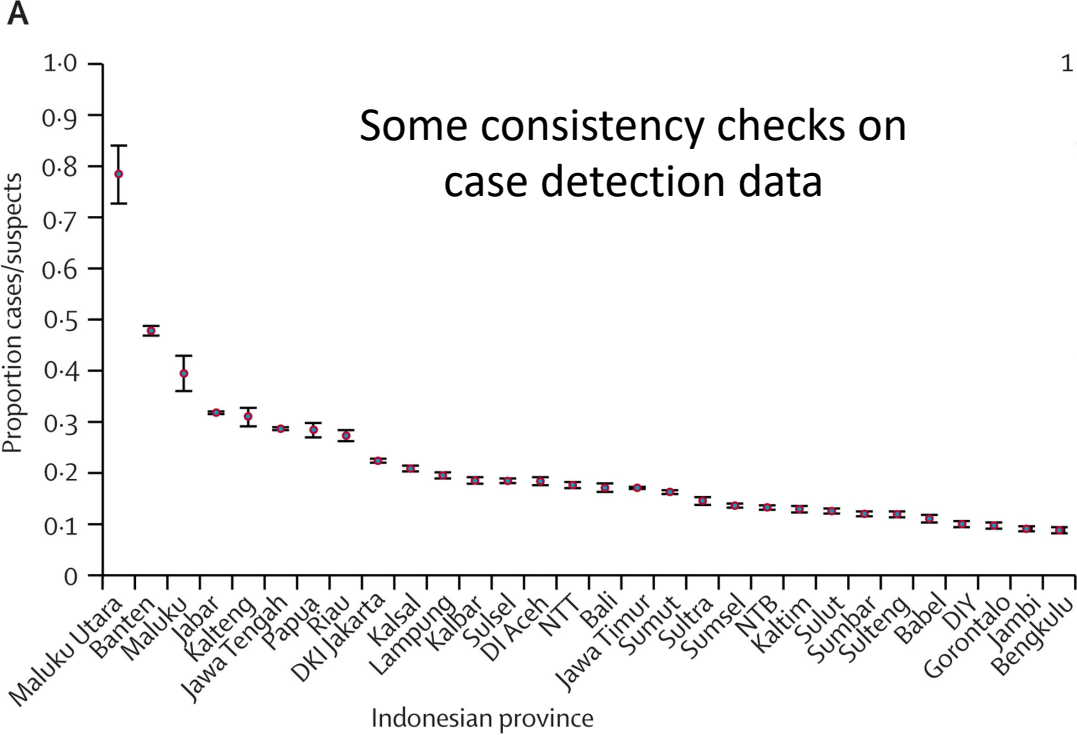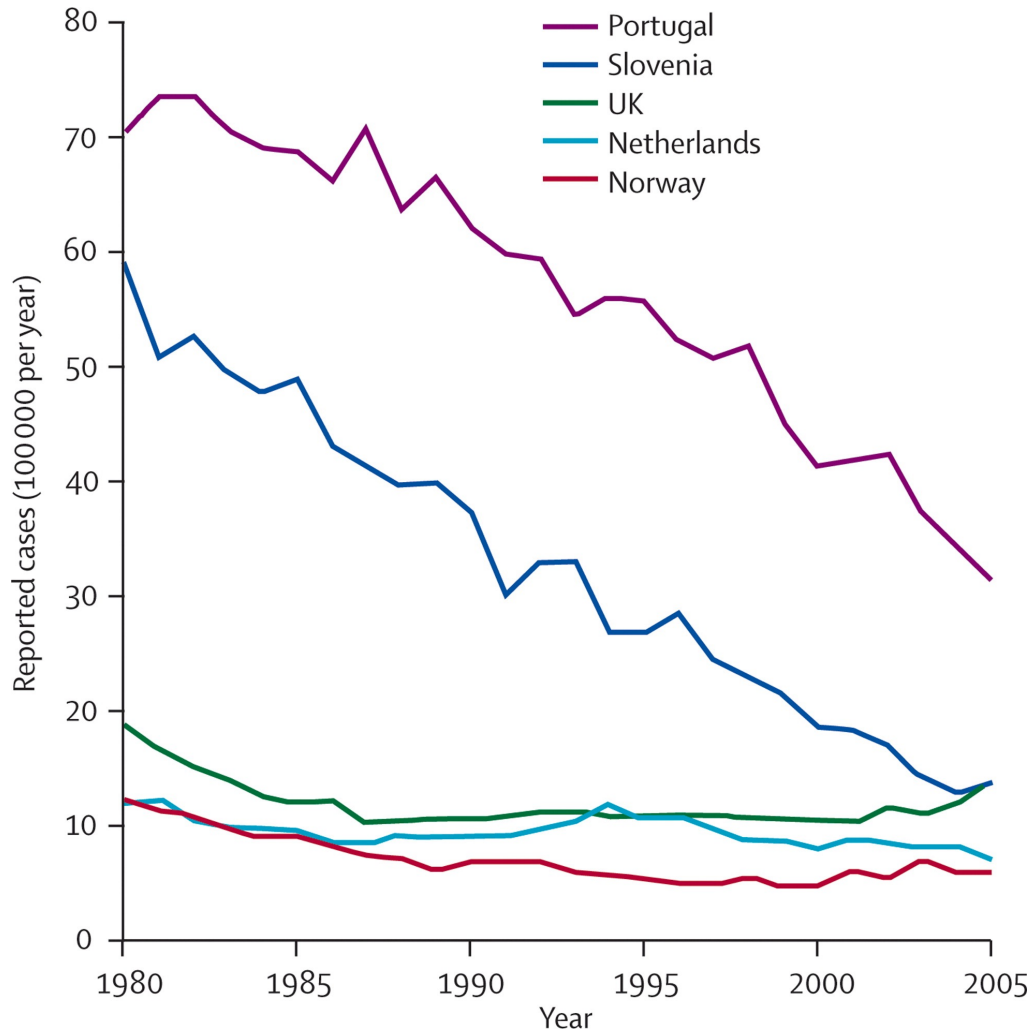Females   Males   Incidence

Incidence

- Could be measured in a longitudinal cohort study.

- Usually indirectly measured from case notification rate adjusted for case detection rate.

A

Proportion cases/suspects (y-axis) vs Indonesian province (x-axis):
Maluku Utara, Banten, Maluku, Jabar, Kalteng, Jawa Tengah, Papua, Riau, DKI Jakarta, Kalsal, Lampung, Kalbar, Sulsel, DI Aceh, NTT, Bali, Jawa Timur, Sumut, Sultra, Sumsel, NTB, Kaltim, Sulut, Sumbar, Sulteng, Babel, DIY, Gorontalo, Jambi, Bengkulu

Some consistency checks on case detection data

B

Reported cases (y-axis) vs Year (x-axis): 1990–2006

- Pakistan
- Sudan
- Egypt
- Libya

C

Proportion male (y-axis) vs Moroccan region (x-axis):
Oued Ed, Laâyoune, Guelmim, Souss, Gharb, Chaouia, Marrakech, Oriental, Casablanca, Rabat, Doukala, Tadla, Meknès, Fès, Taza, Tanger

D

Proportion smear-positive (y-axis) vs Moroccan region (x-axis):
Oued Ed, Laâyoune, Guelmim, Souss, Gharb, Chaouia, Marrakech, Oriental, Casablanca, Rabat, Doukala, Tadla, Meknès, Fès, Taza, Tanger

Issues: assumptions

Case notification series that are assumed by WHO to represent the true underlying trends in incidence.

Issues: missed cases

- Private sector TB care

- Smear negative TB rates vary

- Children not usually counted

So, how does one measure the case detection rate?

Prevalence surveys

- Cross sectional studies of sampled population requiring well-designed sampling strategy, sensitive and specific means of detection.
- Most use symptom screen, CXR and sputum processing.

Laos Prevalence Survey
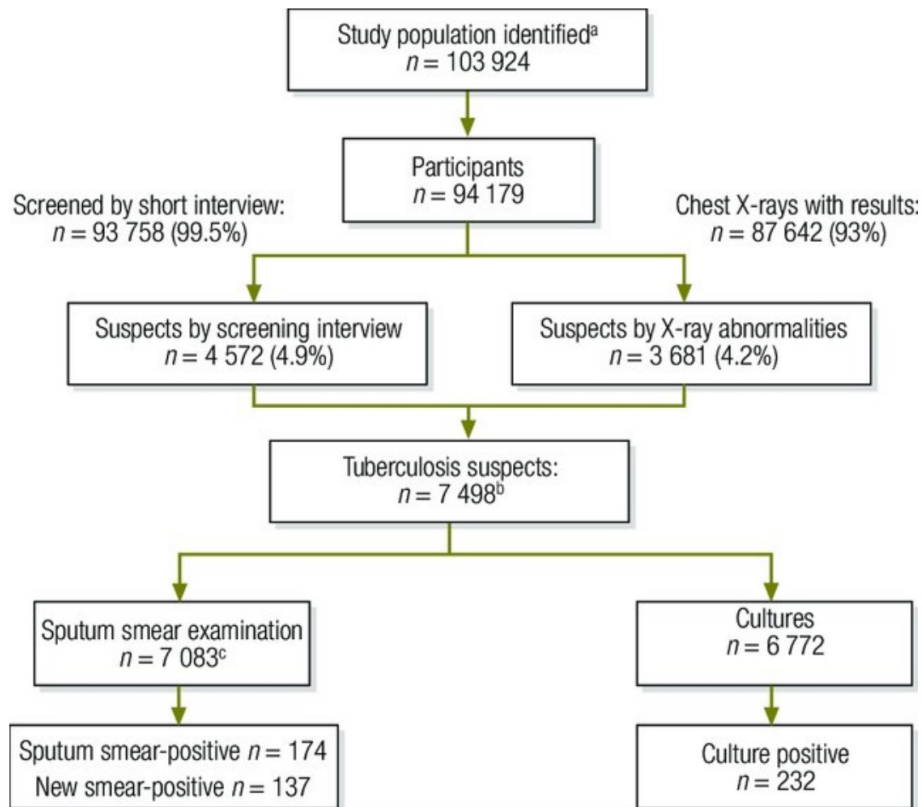
1. Census collection

2. Interview

Field Activities

3. Chest X-Ray

4. Specimen collection

Issues

- Labor intensive

- Costly

- Case detection depends on method of diagnosis
  - Symptoms only present in 50% of people with smear positive TB

- Unclear how long people have had TB

Indonesia

Population 2017   **264 million**

Estimates of TB burden*, 2017	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	110 (100–110)	40 (38–43)
Mortality (HIV+TB only)	9.4 (5–15)	3.6 (1.9–5.8)
Incidence (includes HIV+TB)	842 (767–919)	319 (291–348)
Incidence (HIV+TB only)	36 (20–57)	14 (7.7–21)
Incidence (MDR/RR-TB)**	23 (16–31)	8.8 (6.2–12)

Estimated TB incidence by age and sex (thousands)*, 2017			
	0-14 years	> 14 years	Total
Females	23 (23–23)	326 (308–345)	349 (329–370)
Males	26 (26–27)	466 (435–497)	492 (458–526)
Total	49 (48–50)	792 (723–862)	842 (767–919)

TB case notifications, 2017	
Total cases notified	446 732
Total new and relapse	442 172
- % tested with rapid diagnostics at time of diagnosis	2%
- % with known HIV status	29%
- % pulmonary	90%
- % bacteriologically confirmed among pulmonary	54%

Revised up to 1.2 after prevalence survey

Translating prevalence to incidence

- Prevalence = incidence X duration

- BUT
  - This assumes that there is a disease is in steady state with the same number of people leaving the state as arriving in it.
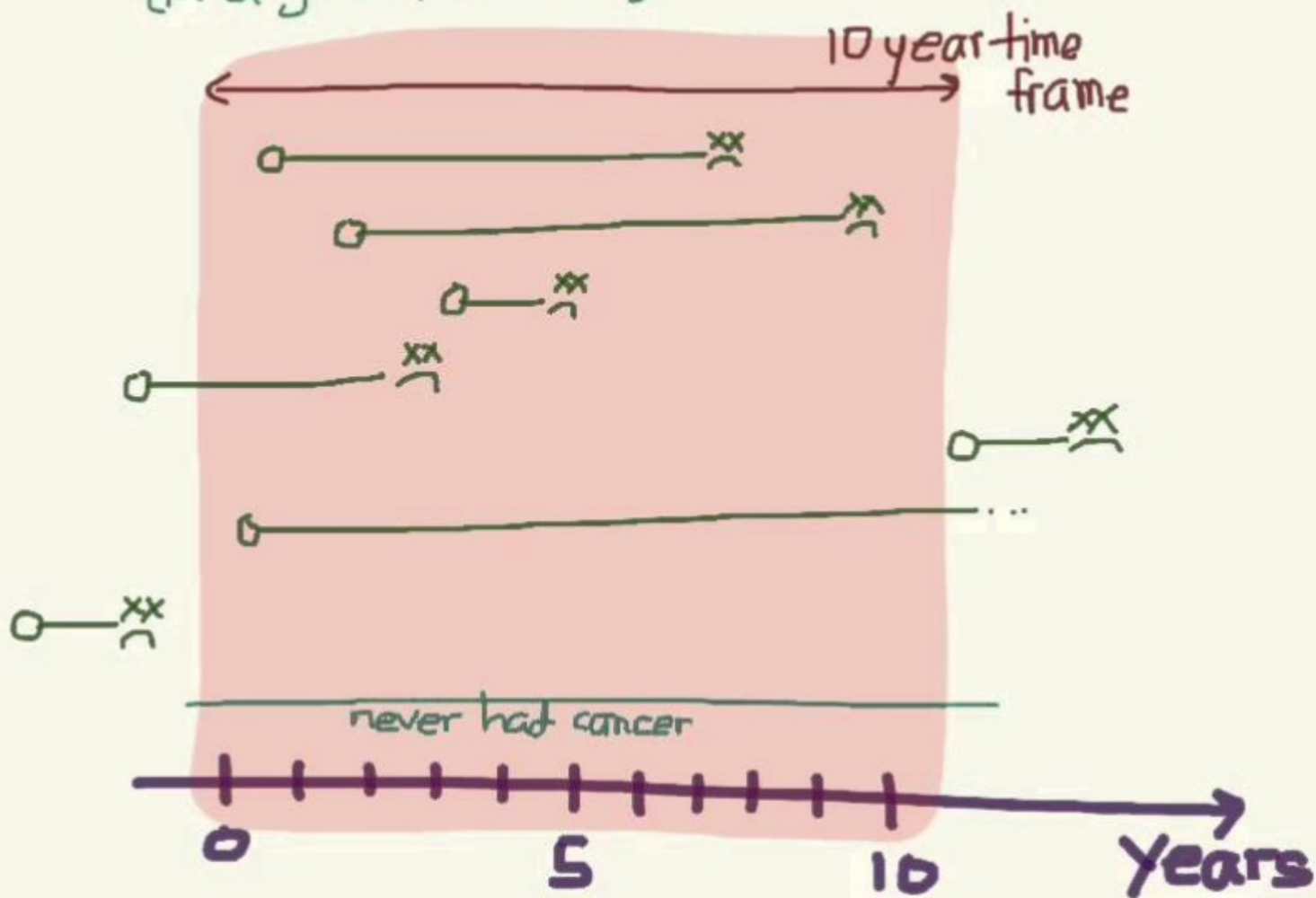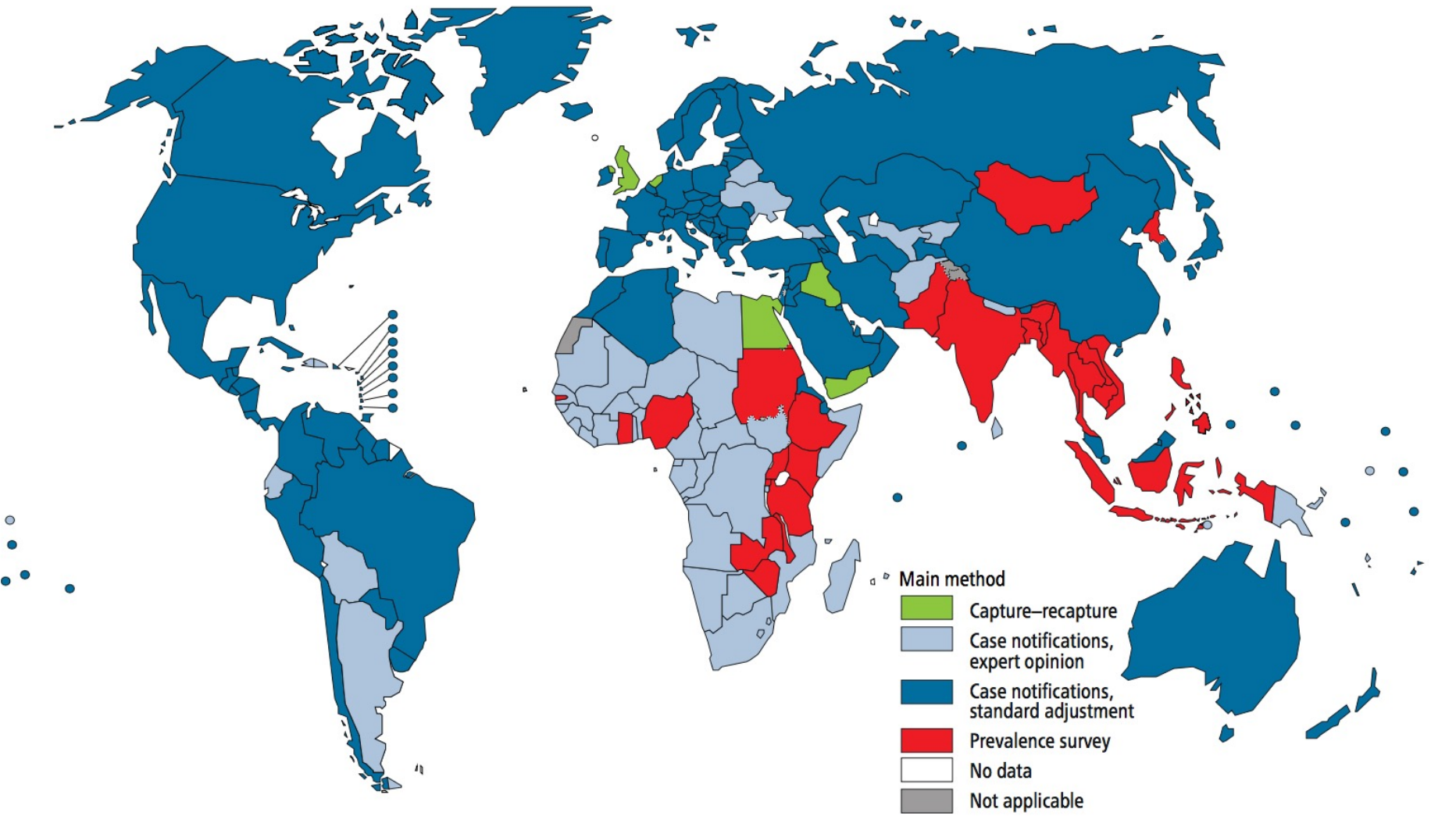 - So not true in general for TB.

incidence = #new cases / #people @ risk (in a given time frame)

prevalence = #cases / #total people

10 year time frame

never had cancer

Years

Main methods used to estimate TB incidence

Main method

- Capture–recapture
- Case notifications, expert opinion
- Case notifications, standard adjustment
- Prevalence survey
- No data
- Not applicable

TB mortality

- Reflects both incidence and success of case finding and treatment.

- Good proxy for programmatic success but not necessarily incidence.

- Multiple ways to measure:
  - Vital status
 - Using case fatality rate measured in treatment cohorts
 - Verbal (or real) autopsy

Issues

- Autopsy studies show much TB missed during life.

- Verbal autopsies poorly differentiate TB from other chronic diseases.

- Vital registration data only available for 1/3 of deaths globally.

- Patients with TB die from other causes than TB even during TB treatment.

Measuring TB infection

- Two tools
  - TST
    - Overlap with BCG and other mycobacteria
    - Unclear if TST positivity correlates with presence of viable mycobacteria

  - IGRA
    - Measures interferon-gamma response to stimulation with Mtb specific antigen.
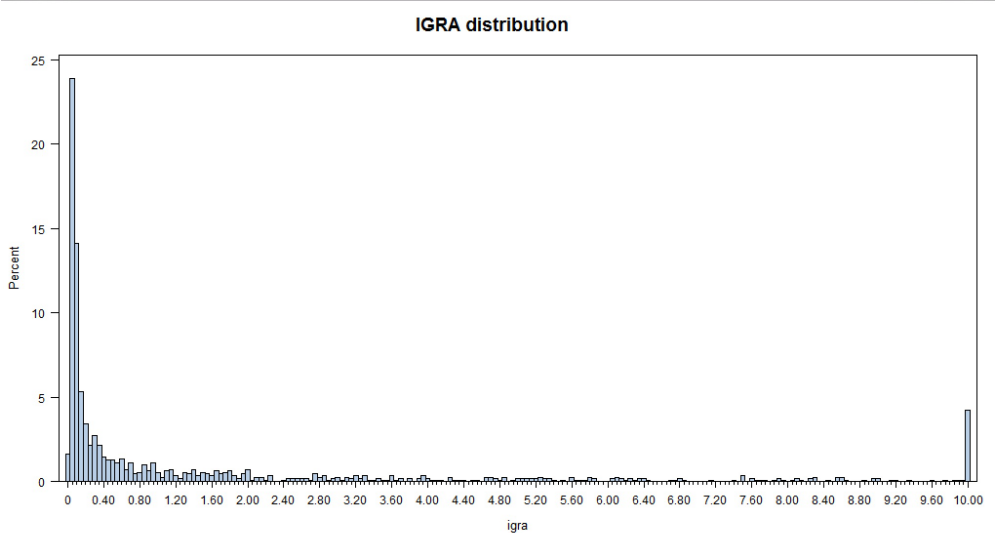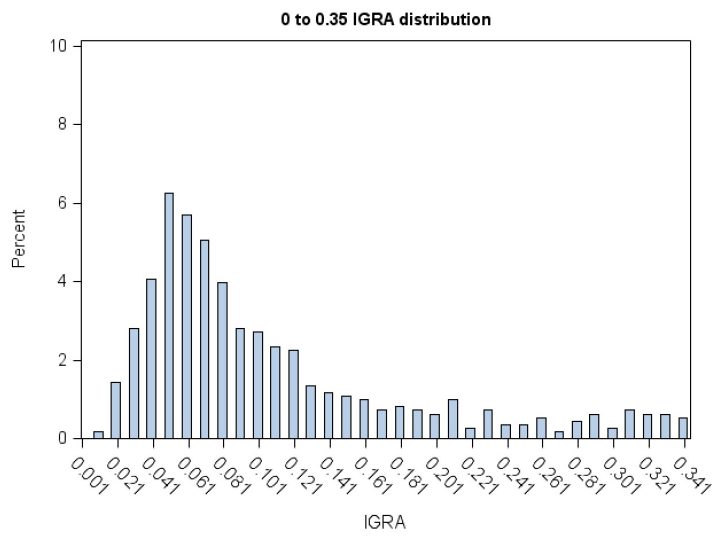
Population distribution of TST induration sizes
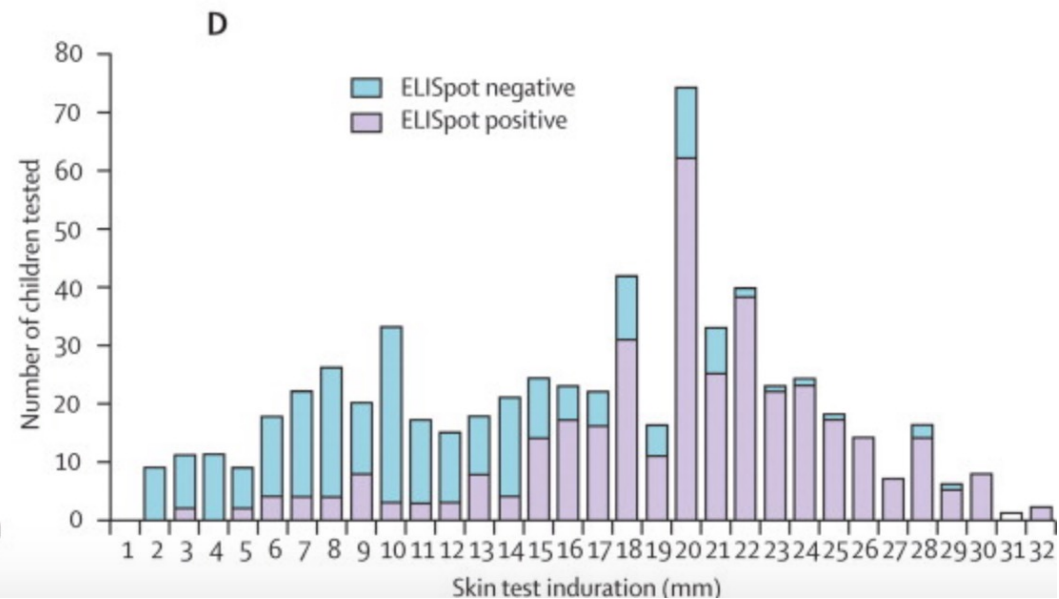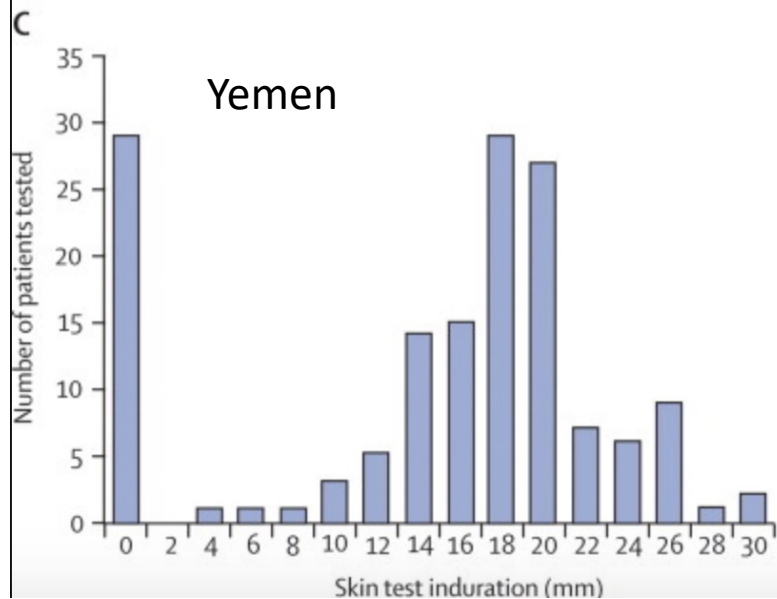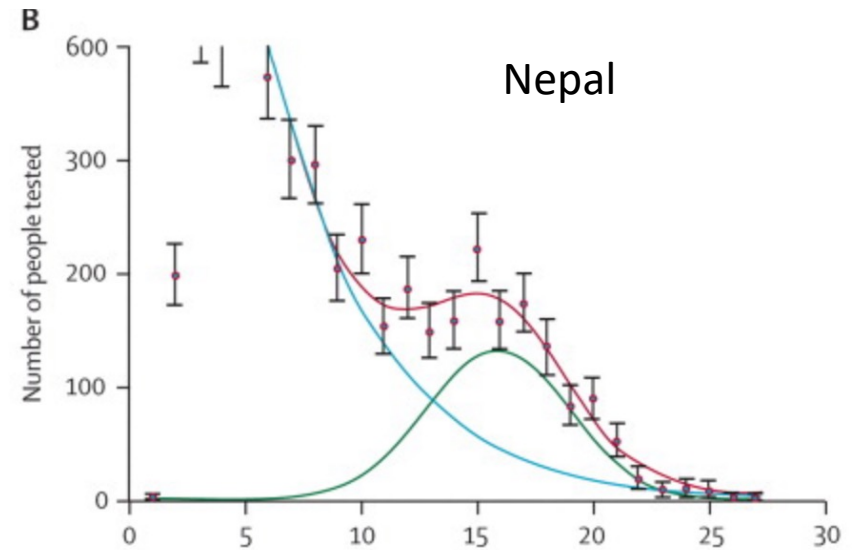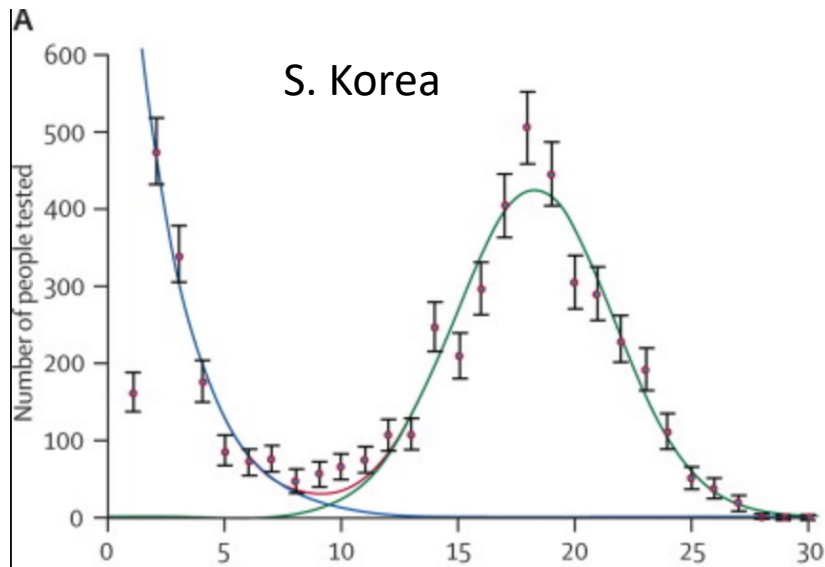
Why different curves?

- Different types of BCG

- Different age groups

- Different endemic mycobacteria
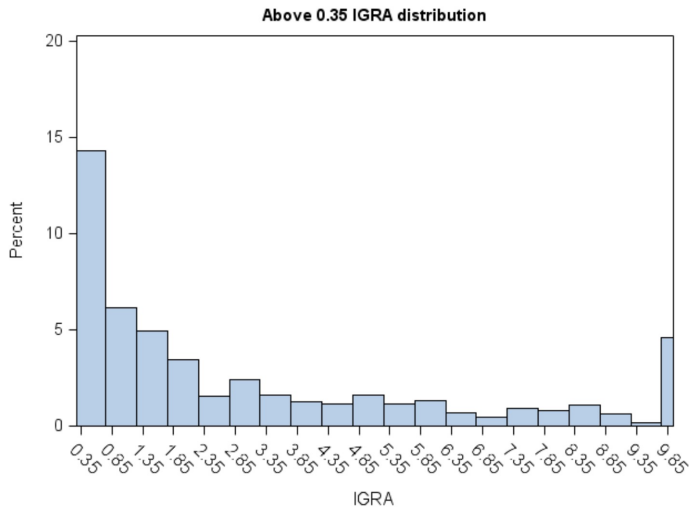
- Others?

  – Genetics?

  – Helminth infection?

How about IGRA?

IGRA distribution

Distribution in people who are negative on binary outcome.

0 to 0.35 IGRA distribution

Distribution in people who are positive on binary outcome.

Above 0.35 IGRA distribution

Estimating yearly incidence of infection - ARTI

- Binomial model for infection each year.

- Focus on young age group

- Assume that incidence does not change over the time period equivalent to participants age.

- PR = $1-(1-p\text{^age})$
- Where p is yearly risk or ARI
- PR is prevalence of infection.

How is ARI associated with incidence?

- Styblo's ratio
  - Every increase of 50 smear positive cases per 100,000 leads to a 1% increase in the ARI.

- Incidence (of infection) = beta*(prevalence of source cases)
  - Where beta reflects
    - Probably of transmission event given contact (b)
    - Contact rate (K)

Assumptions

- Source cases are smear positive?

- Homogeneous mixing

- Duration of infectiousness stable.

Breaking a law: tuberculosis disobeys Styblo's rule

Christopher Dye[a]

GLOBAL TUBERCULOSIS REPORT

2017

World Health Organization
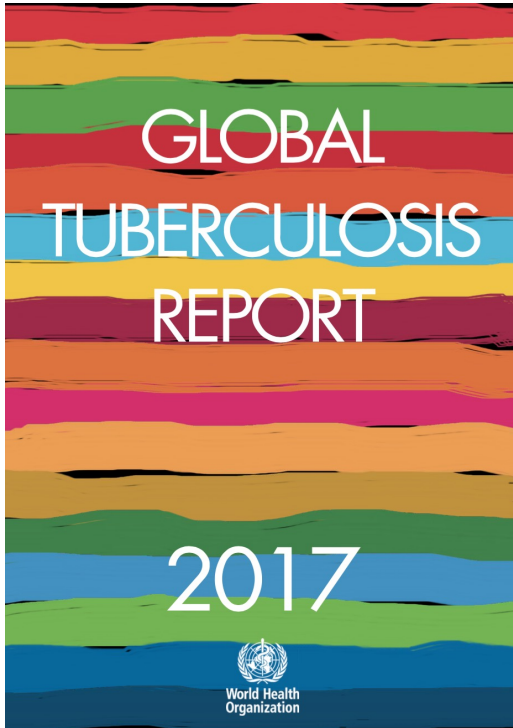
FIG. 3.3
Estimated TB incidence in 2016, for countries with at least 100 000 incident cases

Number of incident cases
- 100 000
- 500 000
- 1 000 000
- 2 500 000

China, Philippines, Pakistan, Nigeria, India, Indonesia, South Africa

Estimated TB incidence rates, 2016

Incidence per 100 000 population per year
- 0–24
- 25–99
- 100–199
- 200–299
- ≥300
- No data
- Not applicable
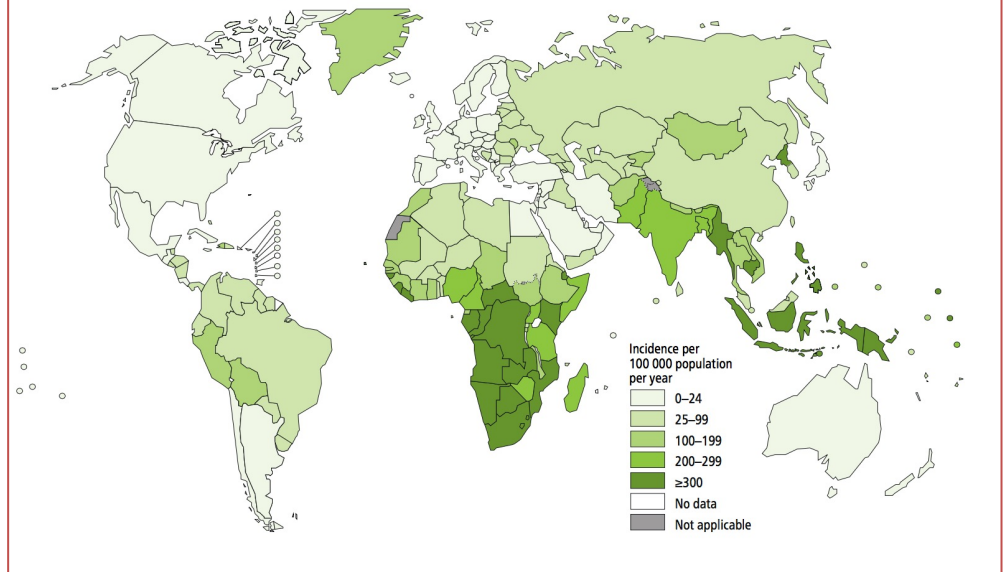
Global trends in estimated TB incidence and mortality rates, 2000–2016. Shaded areas represent uncertainty intervals.
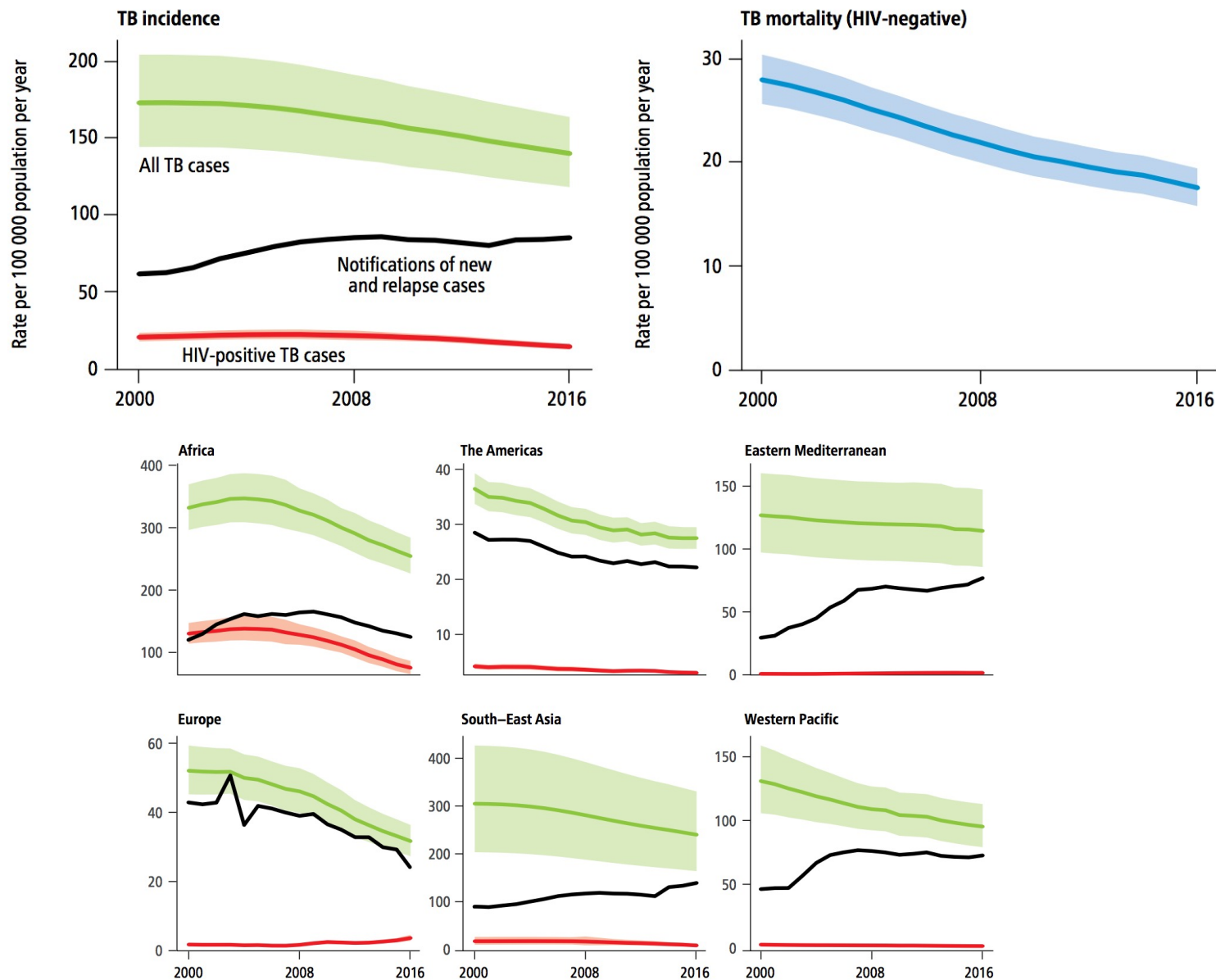
FIG. 3.15

Regional trends in estimated TB mortality rates by WHO region, 2000–2016. Estimated TB mortality rates in HIV-negative people are shown in **blue**, and estimated mortality rates of HIV-positive TB are shown in **red**. Shaded areas represent uncertainty intervals.