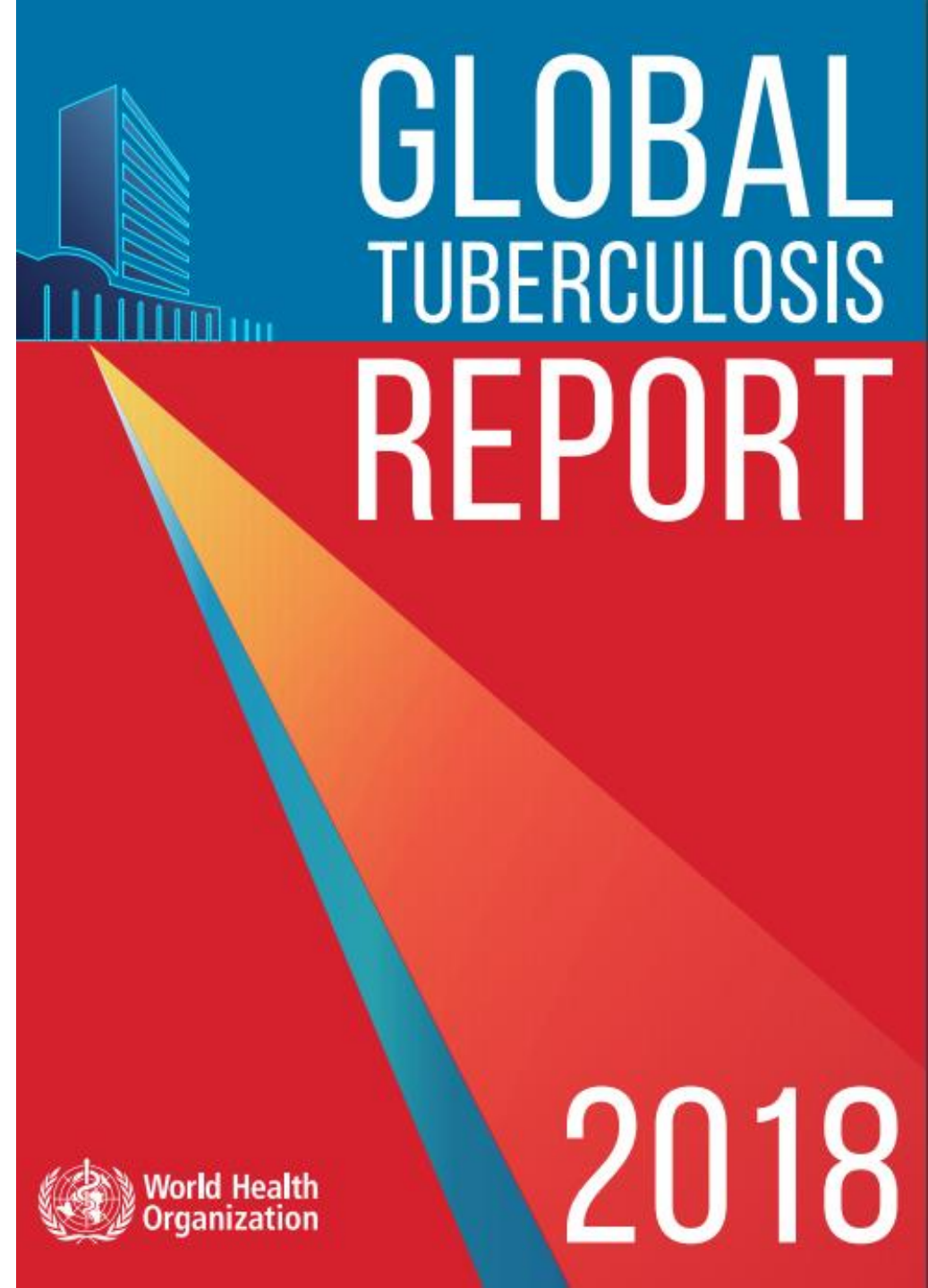# Tuberculosis

OBJECTIVES

- Understand the epidemiology and global burden of TB

- List the sign and symptoms and risk factors of different types of TB, with particular emphasis on pulmonary TB

- Describe trends and state reasons for resurgence of pulmonary TB

- List population subgroups at risk for pulmonary TB

- Draw the cycle of infection of pulmonary TB

- Describe measures for prevention and control for pulmonary TB

- Describe the role of WHO to address the global burden of TB, particularly directly observed therapy short course (DOTS) for pulmonary TB

Epidemiology And Global Burden
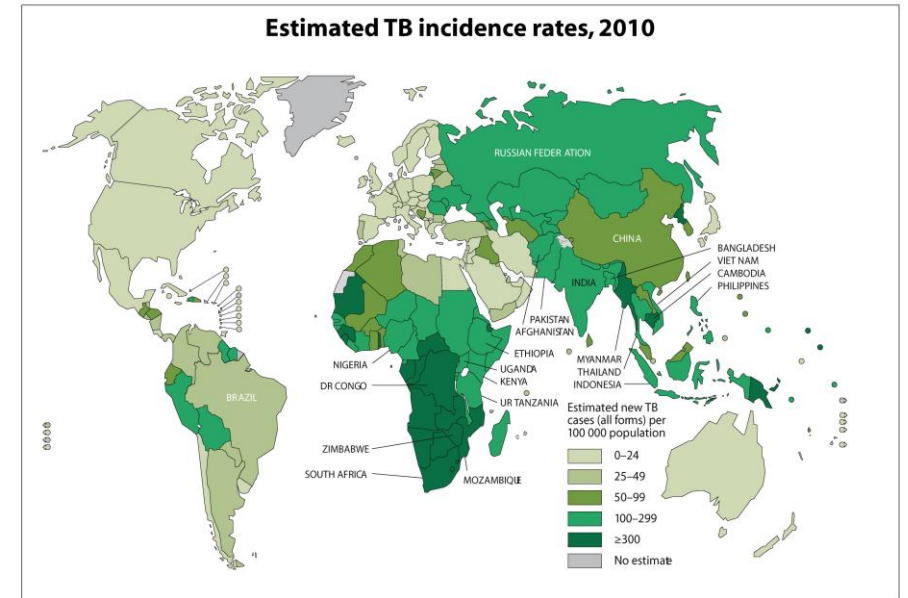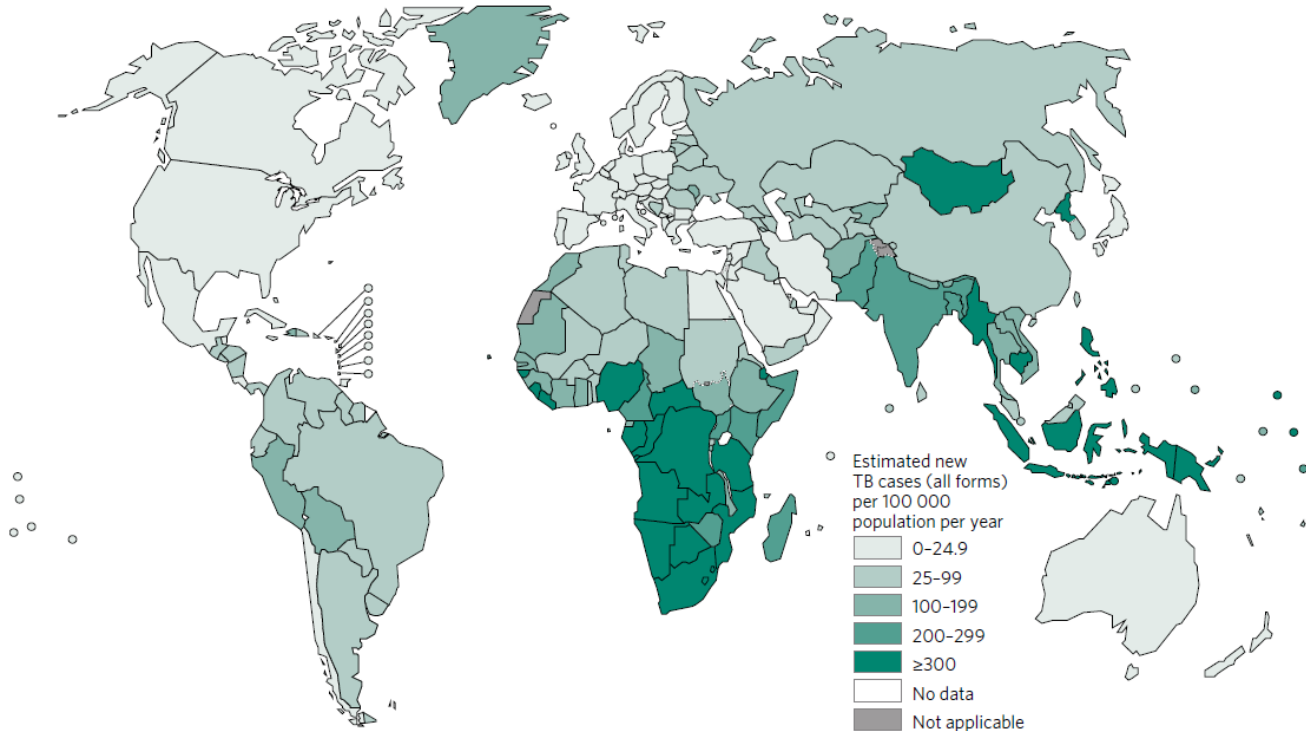
Global Impact Of Tuberculosis

- About 2 billion people, are infected by TB bacteria
- 1.8 million will die each year, making TB the leading infectious disease killer in the world.
- 10.4 million individuals who become ill with TB each year
  - approximately four million are "missed" each year by health systems
  - do not get the care they need
  - allowing the disease to continue to be transmitted

Global Impact Of Tuberculosis

- Resistance to anti-TB drugs can occur when these drugs are misused or mismanaged
  - Patients do not complete their full course of treatment
  - Wrong treatment
  - Wrong dose
  - Wrong length of time for taking the drugs
  - Drugs is not always available
  - Drugs are of poor quality

Global burden of TB disease

Estimated TB incidence rates, 2015

Estimated new
TB cases (all forms)
per 100 000
population per year
- 0–24.9
- 25–99
- 100–199
- 200–299
- ≥300
- No data
- Not applicable

Estimated TB incidence rates, 2010

Estimated new TB
cases (all forms) per
100 000 population
- 0–24
- 25–49
- 50–99
- 100–299
- ≥300
- No estimate

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

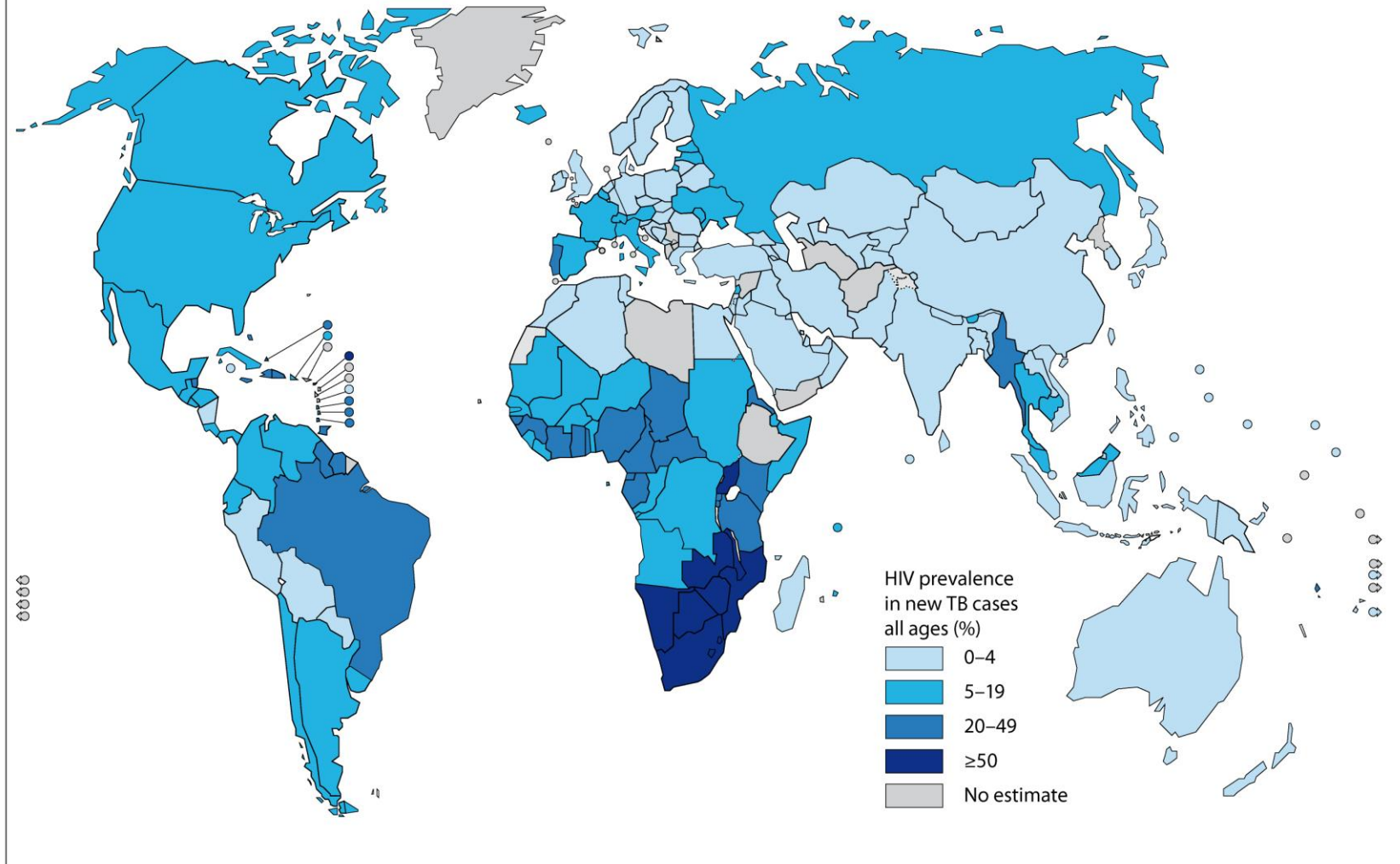Source: *Global Tuberculosis Control 2011*. WHO, 2011.

© WHO 2011. All rights reserved.

World Health Organization

In 2014, TB surpassed HIV as the **#1 infectious disease killer worldwide**

In 2015, 10.4M cases

WHO Global Tuberculosis Report 2016: http://www.who.int/tb/publications/global_report/en/

Estimated HIV prevalence in new TB cases, 2010

HIV prevalence
in new TB cases
all ages (%)

- 0–4
- 5–19
- 20–49
- ≥50
- No estimate

Source: *Global Tuberculosis Control 2011*. WHO, 2011.

World Health Organization
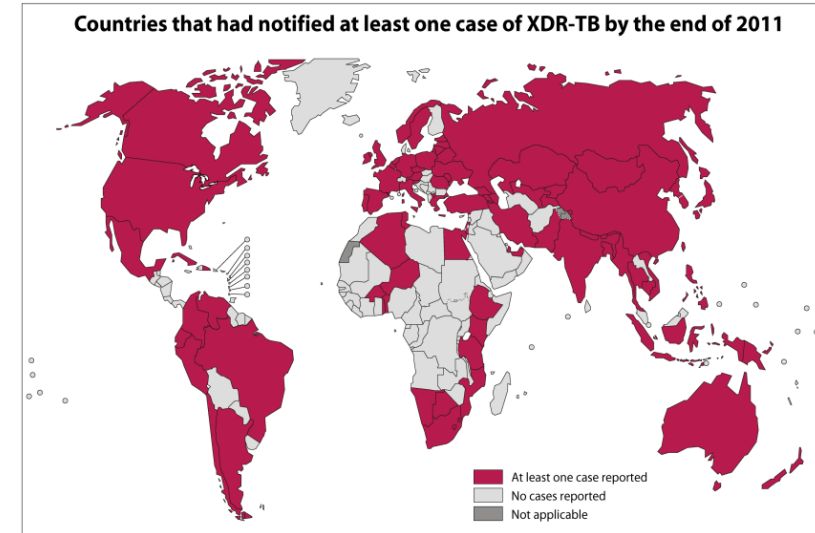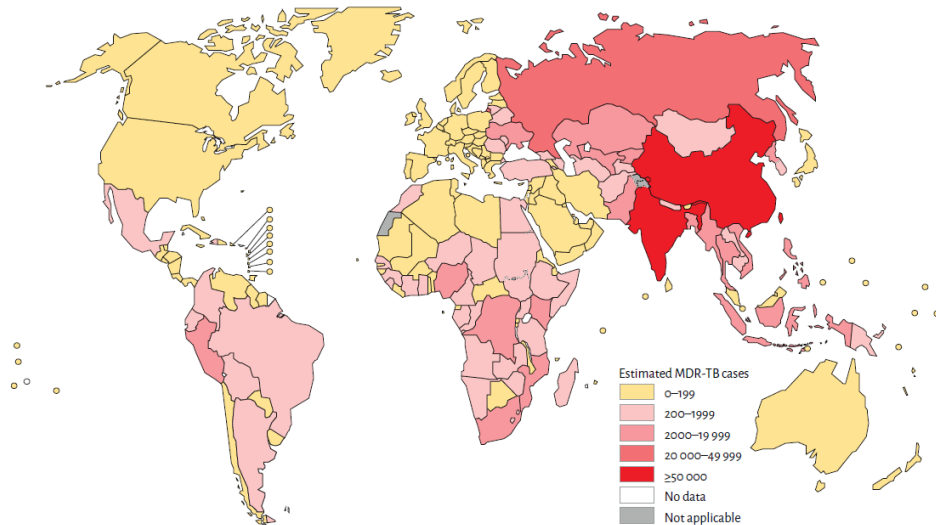
Global Impact Of Tuberculosis

- Multidrug resistant tuberculosis (MDR-TB)
    - TB resistant to two of the most important drugs used to treat TB: Isoniazid (INH) and Rifampin (RIF)
- Extensively drug resistant TB (XDR-TB)
    - A rare type of MDR-TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin)
    - Because XDR-TB is resistant to the most potent TB drugs, patients are left with treatment options that are much less effective.
    - special concern for persons with HIV infection or other conditions that can weaken the immune system
        - More likely to develop TB disease once they are infected
        - Higher risk of death once they develop TB

MDR- and XDR-TB: Global Health Emergencies

■ FIGURE 4.6

Number of MDR–TB cases estimated to occur among notified pulmonary TB cases, 2014

Estimated MDR-TB cases
- 0–199
- 200–1999
- 2000–19 999
- 20 000–49 999
- ≥50 000
- No data
- Not applicable

Countries that had notified at least one case of XDR-TB by the end of 2011

- At least one case reported
- No cases reported
- Not applicable

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Source: *Global Tuberculosis Report 2012*. WHO, 2012.

World Health Organization

Multidrug-resistant TB:
Mycobacterium tuberculosis resistant to isoniazid and rifampin: 480,000 incident cases in 2015

Extensively drug-resistant TB:
M. tuberculosis resistant to isoniazid, rifampin, fluoroquinolones, and injectable agents

The proportion of multidrug-resistant TB (MDR-TB) cases

Table 1. Estimated proportion of MDR-TB cases among new and previously-treated TB cases in countries of the Eastern Mediterranean Region, 2010

Country	% estimated in new	% estimated in retreatement	Source
Afghanistan	6.1	8.3	DRS
Djibouti	0.9	–	model
Egypt	2.2	13.9	DRS
Iran, Islamic Republic of	5	38.3	DRS
Iraq	3.4	48.2	model
Jordan	6.3	28.6	DRS
Kuwait	1.1	–	DRS
Lebanon	1.1	35.7	DRS
Morocco	0.5	12.2	DRS
Oman	0	12.5	DRS
Pakistan	3.4	20.6	model
Qatar	1.2	-	DRS
Saudi Arabia	1.2	9	model
Somalia	0.9	13.9	model
Sudan	0.9	13.9	model
Syrian Arab Republic	6.2	25.9	DRS
Tunisia	3.4	20.6	model
United Arab Emirates	1.2	9	model
Occupied Palestinian territory	3.4	20.6	model
Yemen	2.9	11.3	DRS

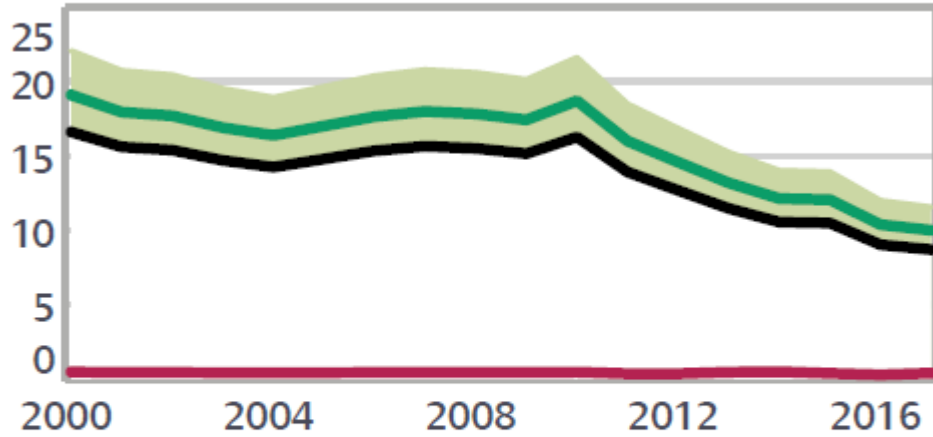# TB re-emerges

1990s   TB re-emerges as a threat
   TB-HIV co-infection
   Drug-resistant TB
   Globalization allows TB to travel

Saudi Arabia
Tuberculosis profile

(Rate per 100 000 population per year)

- Incidence
- Notified (new and relapse)
- Incidence (HIV+TB only)

TB financing, 2018	
National TB budget (US$ millions)	20

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

Generated: 2018-10-28

Data: www.who.int/tb/data

Saudi Arabia

Population 2017   33 million

Tuberculosis profile

Estimates of TB burden*, 2017	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	1 (0.93–1.2)	3.2 (2.8–3.5)
Mortality (HIV+TB only)	0.02 (0.014–0.026)	0.06 (0.04–0.08)
Incidence (includes HIV+TB)	3.3 (2.8–3.8)	10 (8.6–12)
Incidence (HIV+TB only)	0.12 (0.1–0.14)	0.37 (0.31–0.44)
Incidence (MDR/RR-TB)**	0.12 (0.089–0.15)	0.36 (0.27–0.46)

Estimated TB incidence by age and sex (thousands)*, 2017	0-14 years	> 14 years	Total
Females	0.16 (0.16–0.17)	0.85 (0.79–0.92)	1 (0.93–1.1)
Males	0.18 (0.17–0.18)	2.1 (1.9–2.4)	2.3 (2–2.6)
Total	0.34 (0.32–0.35)	3 (2.5–3.4)	3.3 (2.8–3.8)

TB case notifications, 2017	
Total cases notified	2 925
Total new and relapse	2 865
- % tested with rapid diagnostics at time of diagnosis	40%
- % with known HIV status	76%
- % pulmonary	74%
- % bacteriologically confirmed among pulmonary	85%

Universal health coverage and social protection	
TB treatment coverage (notified/estimated incidence), 2017	87% (75–100)
TB patients facing catastrophic total costs	
TB case fatality ratio (estimated mortality/estimated incidence), 2017	0.33 (0.27–0.39)

TB/HIV care in new and relapse TB patients, 2017	Number	(%)
Patients with known HIV-status who are HIV-positive	83	4%
- on antiretroviral therapy	83	100%

Drug-resistant TB care, 2017	New cases	Previously treated cases	Total number***
Estimated MDR/RR-TB cases among notified pulmonary TB cases			84 (70–98)
Estimated % of TB cases with MDR/RR-TB	2.6% (2–3.2)	20% (16–25)	
% notified tested for rifampicin resistance	46%	53%	1 360
MDR/RR-TB cases tested for resistance to second-line drugs			0
Laboratory-confirmed cases			MDR/RR-TB: 47, XDR-TB: 0
Patients started on treatment ****			MDR/RR-TB: 15, XDR-TB: 0

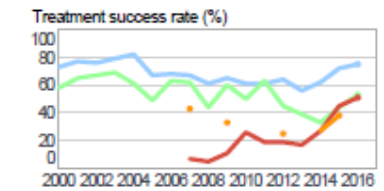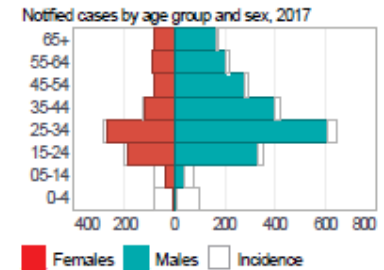| Treatment success rate and cohort size	Success	Cohort
New and relapse cases registered in 2016	75%	2 885
Previously treated cases, excluding relapse, registered in 2016	53%	85
HIV-positive TB cases registered in 2016	51%	45
MDR/RR-TB cases started on second-line treatment in 2015	38%	45
XDR-TB cases started on second-line treatment in 2015		0

TB preventive treatment, 2017	
% of HIV-positive people (newly enrolled in care) on preventive treatment	2%
% of children (aged < 5) household contacts of bacteriologically-confirmed TB cases on preventive treatment	32% (24–50)

TB financing, 2018	
National TB budget (US$ millions)	20

Mortality (excludes HIV+TB)

- Incidence
- Notified (new and relapse)
- Incidence (HIV+TB only)

Notified cases by age group and sex, 2017

- Females
- Males
- Incidence

Treatment success rate (%)
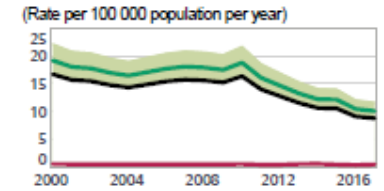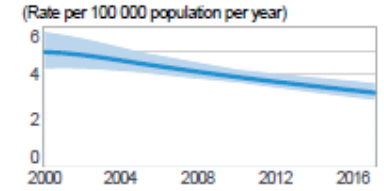
- New and relapse
- Retreatment, excluding relapse
- HIV-positive
- MDR/RR-TB
- XDR-TB

* Ranges represent uncertainty intervals
** MDR is TB resistant to rifampicin and isoniazid; RR is TB resistant to rifampicin
*** Includes cases with unknown previous TB treatment history
**** Includes patients diagnosed before 2017 and patients who were not laboratory-confirmed

Tuberculosis

- caused by
  - bacterium called *Mycobacterium tuberculosis.*
- The bacteria usually attack the lungs,
- but TB bacteria can attack any part of the body
  - such as the kidney, spine, and brain.
- Not everyone infected with TB bacteria becomes sick.
- two TB-related conditions exist:
  - latent TB infection (LTBI)
  - TB disease.

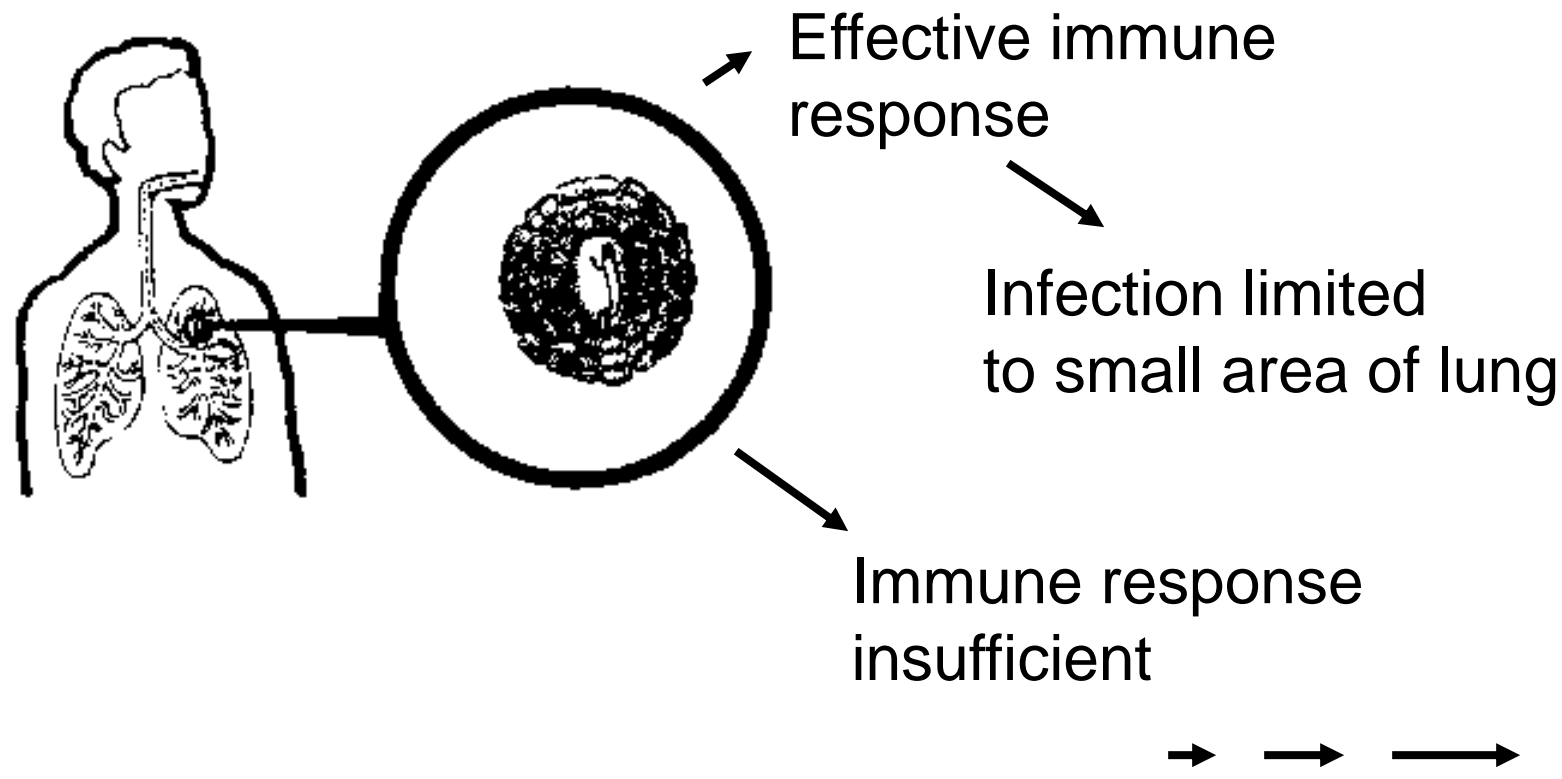# TB – A Multi-system Infection
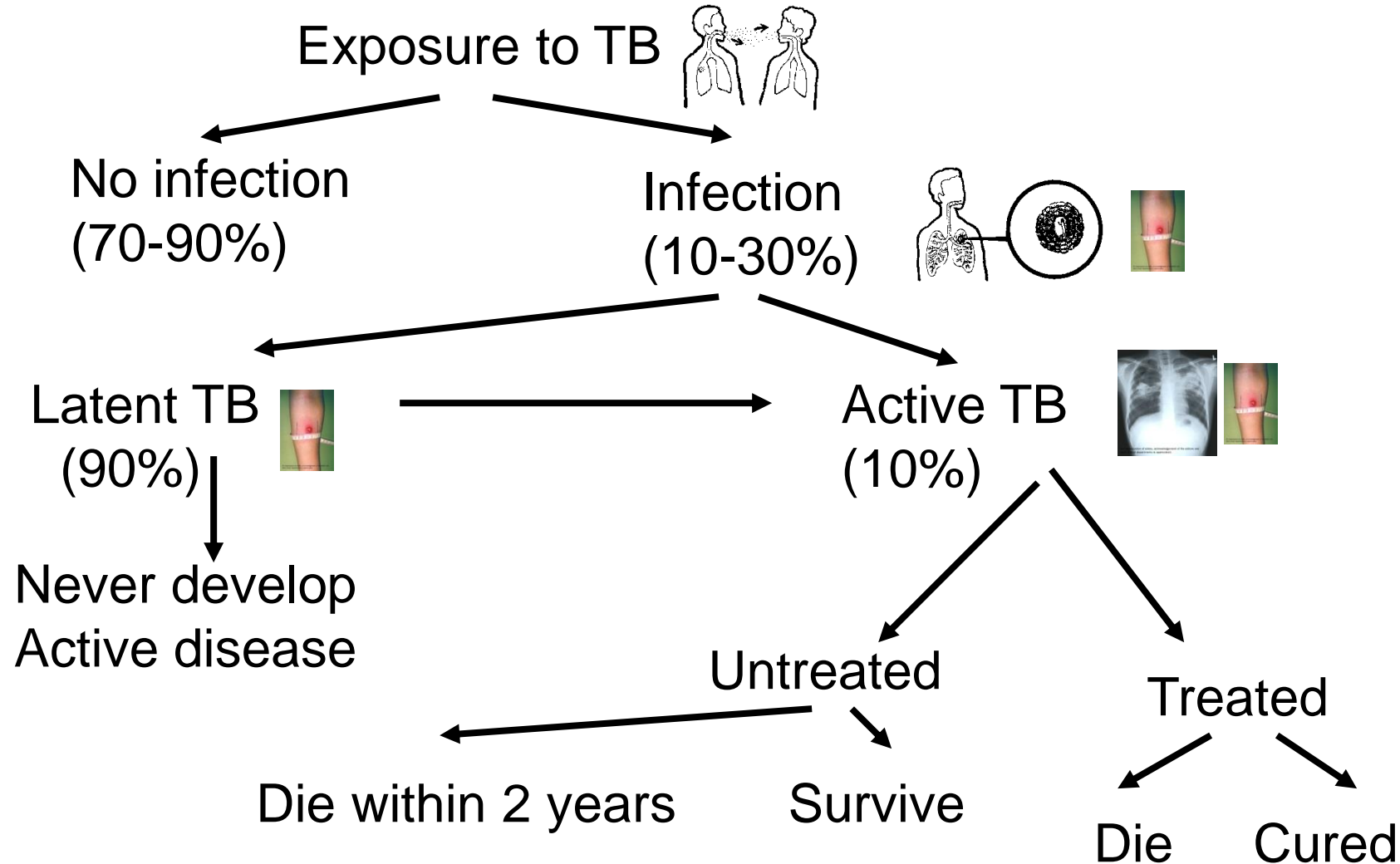
TB: Airborne Transmission
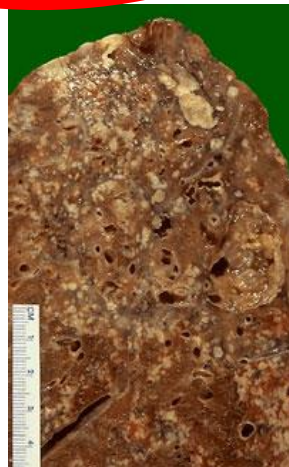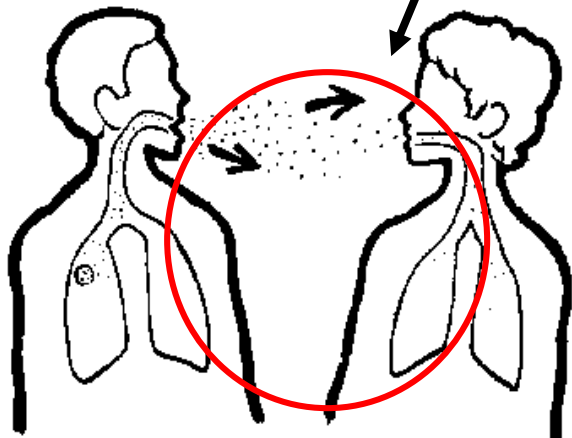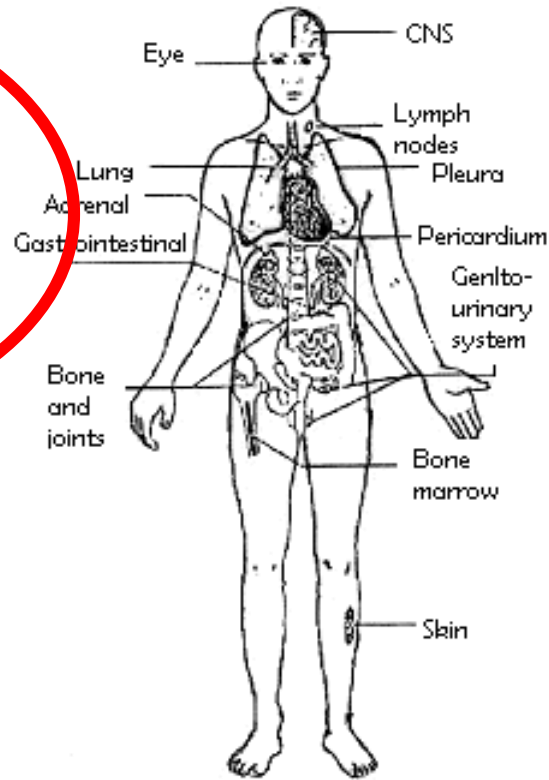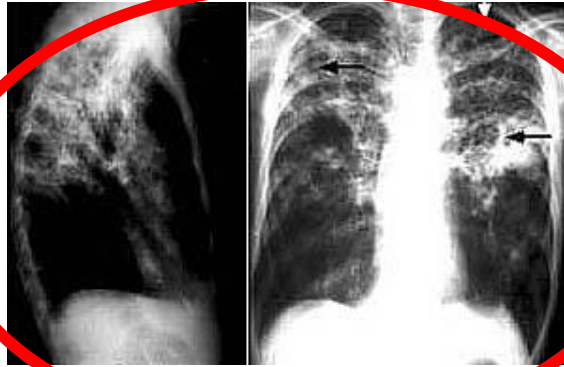
How TB Spreads

- TB bacteria are spread through the air from one person to another
- The TB bacteria are put into the air when a person with TB disease of the lungs or throat coughs, speaks, or sings
- People nearby may breathe in these bacteria and become infected.

TB Invades/Infects the Lung

Natural History of TB Infection

Latent TB vs. TB Disease

Latent TB (LTBI) (Goal = prevent future active disease)
- TB Infection
- No Disease
- NOT SICK
- NOT INFECTIOUS

- Usually positive TB skin test reaction or positive TB blood test

- May develop TB disease if they do not receive treatment for latent TB infection

- people who have a weak immune system, the bacteria become active, multiply, and cause TB disease.
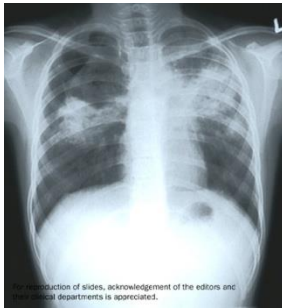
Latent TB vs. TB Disease

TB Infection

Goal ➡ treat to cure, prevent transmission

- SICK (usually)
- INFECTIOUS if PULMONARY (usually)
- NOT INFECTIOUS if not PULMONARY (usually)

Diagnosing Latent TB Infection & Disease

- Most persons, but not everyone, with TB disease have one or more symptoms of TB disease

- All persons with either symptoms or a positive TB test result should be evaluated for TB disease

- If a person has symptoms, but a negative TB test result, they should still be evaluated for TB disease

Diagnosing Latent TB Infection

Diagnosis of Latent TB Infection

person has a positive TB test result and a medical evaluation does not indicate TB disease.

Diagnosing Latent TB Infection

treatment for latent TB infection

chances of developing TB disease by considering their risk factors

Persons who have been recently infected with TB bacteria

Persons with medical conditions that weaken the immune system

Overall, about 5 to 10% of infected persons who do not receive treatment for latent TB infection will develop TB disease at some time in their live

Persons with Medical Conditions that Weaken the Immune System

- HIV infection (the virus that causes AIDS)
- Substance abuse
- Silicosis
- Diabetes mellitus
- Severe kidney disease
- Low body weight
- Organ transplants
- Head and neck cancer
- Medical treatments such as corticosteroids or organ transplant
- Specialized treatment for rheumatoid arthritis or Crohn's disease

Diagnosing TB Disease

Diagnosed by medical history, physical examination, chest x-ray, and other laboratory tests.

TB disease is treated by taking several drugs as recommended by a health care provider.

Diagnosing TB Disease

TB disease should be suspected in persons who have any of the following symptoms:
- Unexplained weight loss
- Loss of appetite
- Night sweats
- Fever
- Fatigue

Diagnosing TB Disease

- If TB disease is in other parts of the body (extrapulmonary), symptoms will depend on the area affected
- If TB disease is in the lungs (pulmonary), symptoms may include:
  - Coughing for longer than 3 weeks
  - Hemoptysis (coughing up blood)
  - Chest pain

Diagnosing TB Disease

Test for TB Infection

- The Mantoux tuberculin skin test (TST)
- TB blood test can be used to test for *M. tuberculosis* infection

Chest Radiograph

- may suggest TB, but cannot be used to definitively diagnose
- chest radiograph may be used to rule out the possibility of pulmonary TB in a person who has had a positive reaction to a TST or TB blood test and no symptoms of disease.

Diagnosing TB Disease

Diagnostic Microbiology

- The presence of acid-fast-bacilli (AFB) on a **sputum smear** or other specimen often indicates TB disease

- does not confirm a diagnosis of TB because some acid-fast-bacilli are not *M. tuberculosis*

- **culture** is done on all initial samples to confirm the diagnosis

Tuberculin skin test

0.1 ml PPD

(1)

(2)

(3)

Erythema
Edema

Induration

(4)
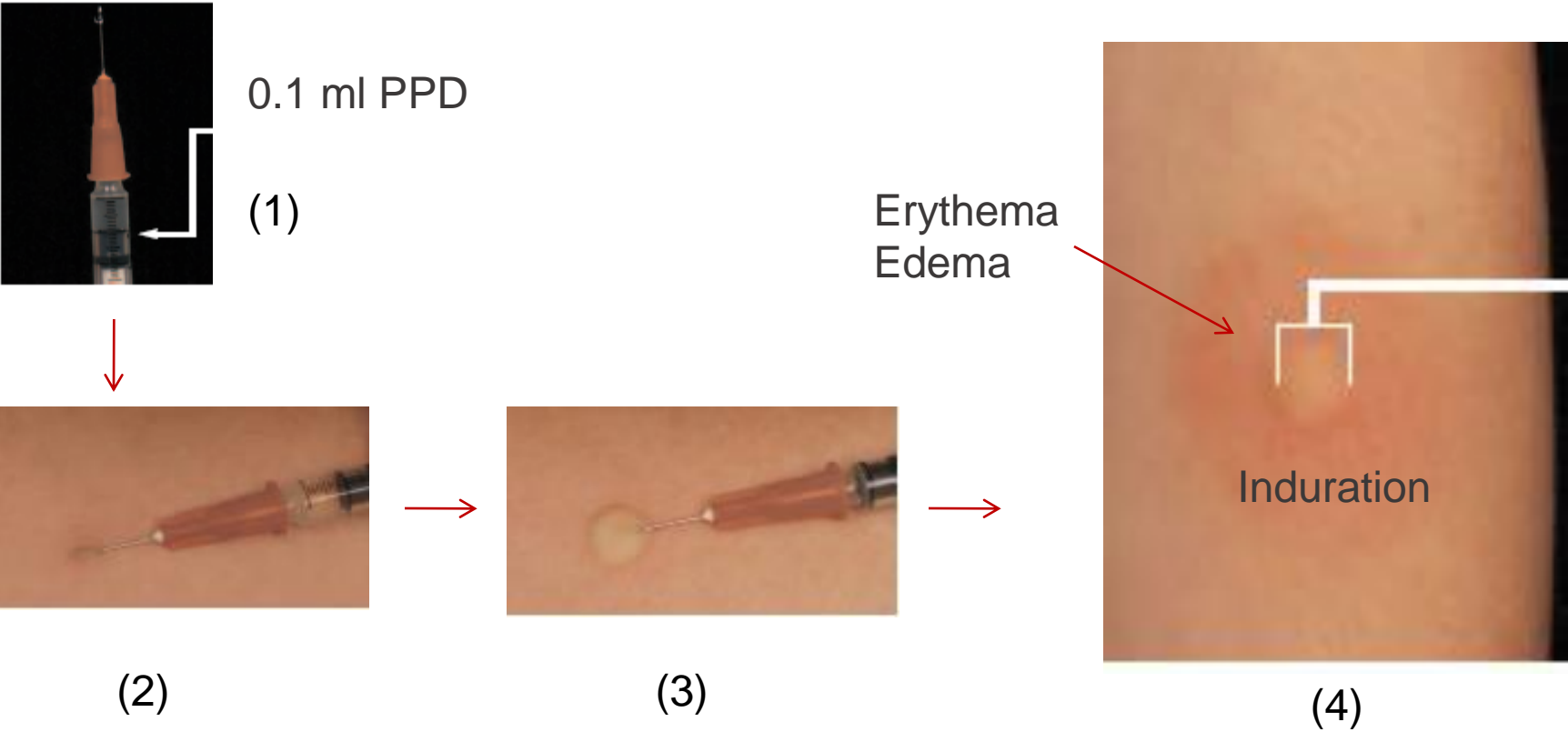
Tuberculin skin test

Induration

Report induration size in mm

Induration = Previous exposure to M. protein

Size

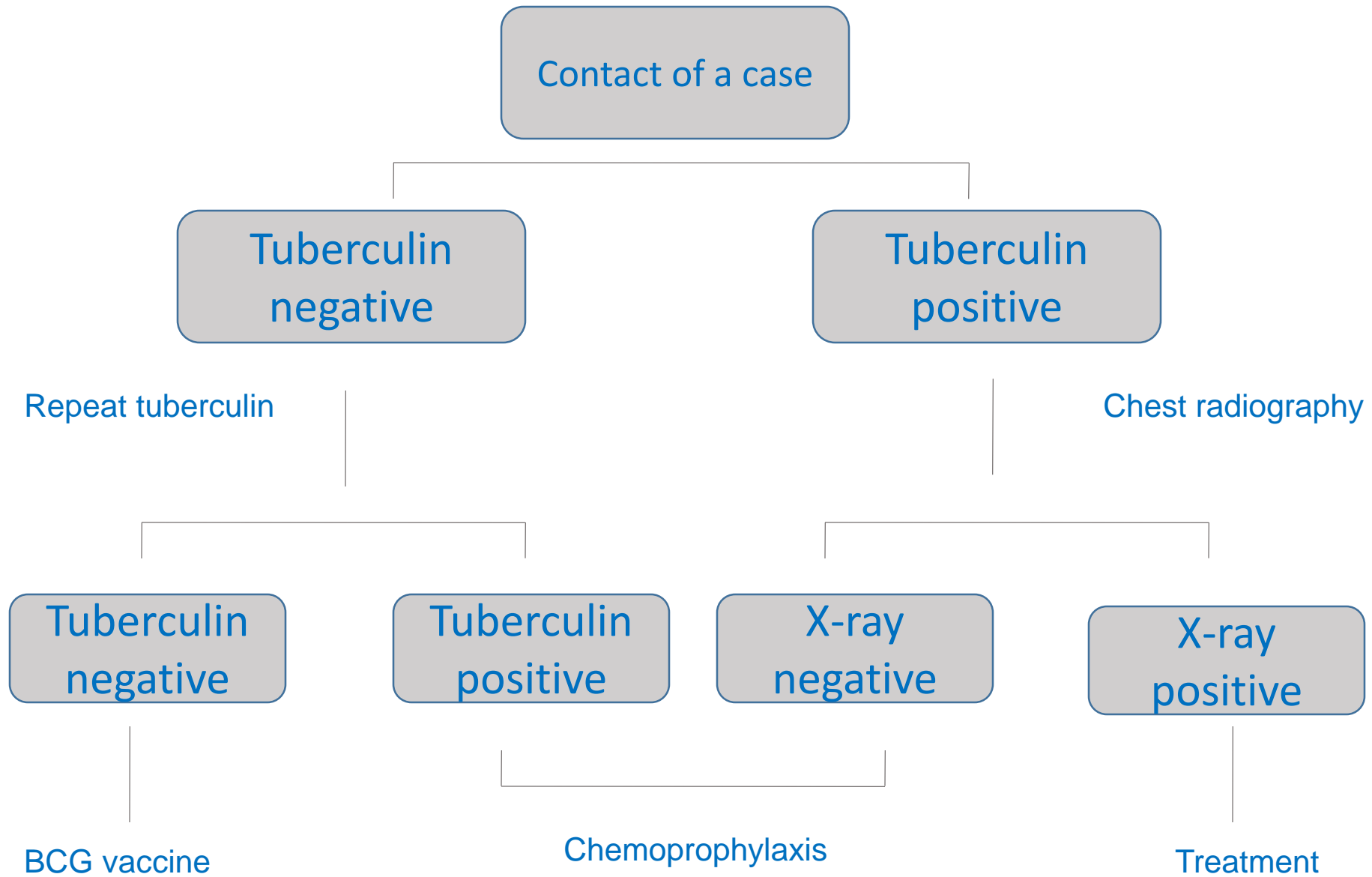10 + mm   = positive

5 - <10 mm = positive in immune compromised

≥ 15 mm   = suggestive of infection rather than BCG

Contact Investigation

- When a person is found to have TB **disease**, the health department looks for people who might have been exposed to TB germs

- If the health department thinks that you might have been exposed to TB germs, they will give you a TB test

• TUBERCULIN TESTING IN MANAGING CONTACTS

Type of Prevention	Definition	Examples
Primary prevention	Preventing the *initial development* of a disease	Immunization, reducing exposure to a risk factor
Secondary prevention	Early detection of *existing disease* to reduce severity and complications	Screening for cancer
Tertiary prevention	Reducing the *impact of the disease*	Rehabilitation for stroke

Prevention and control
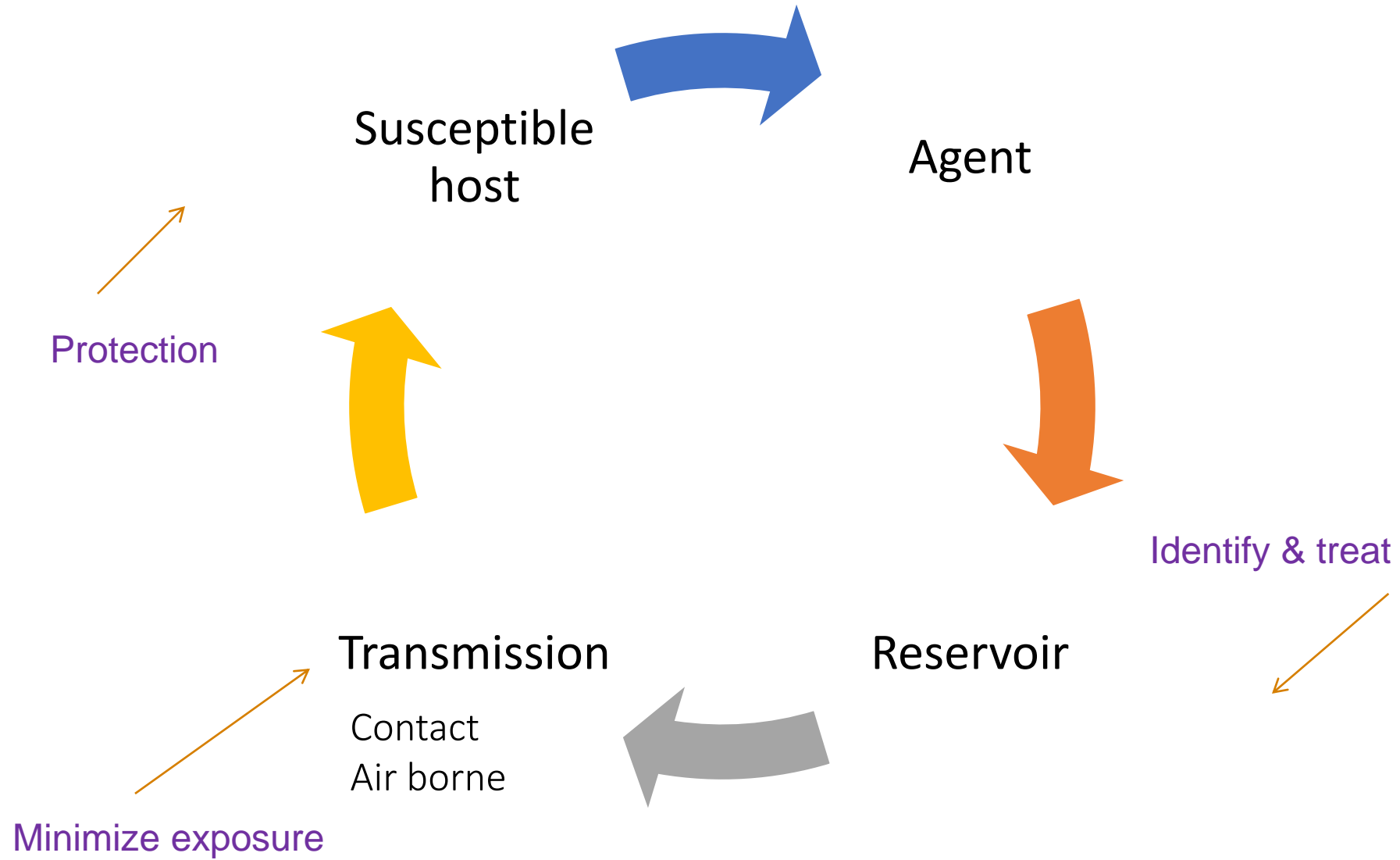
prevention & control

| **Minimize exposure** | **Protection of susceptible** | **Identification and treatment** |

- Isolation of case (respiratory precautions)
- Concurrent disinfection (patients' items)
- Ventilation exposure to sunlight
- Cleaning floor with disinfectant

- BCG vaccine: Live attenuated vaccine, 0.1ml IM injection in the left deltoid within 40 days of birth
- Improve nutrition status

Anti-tuberculosis drugs

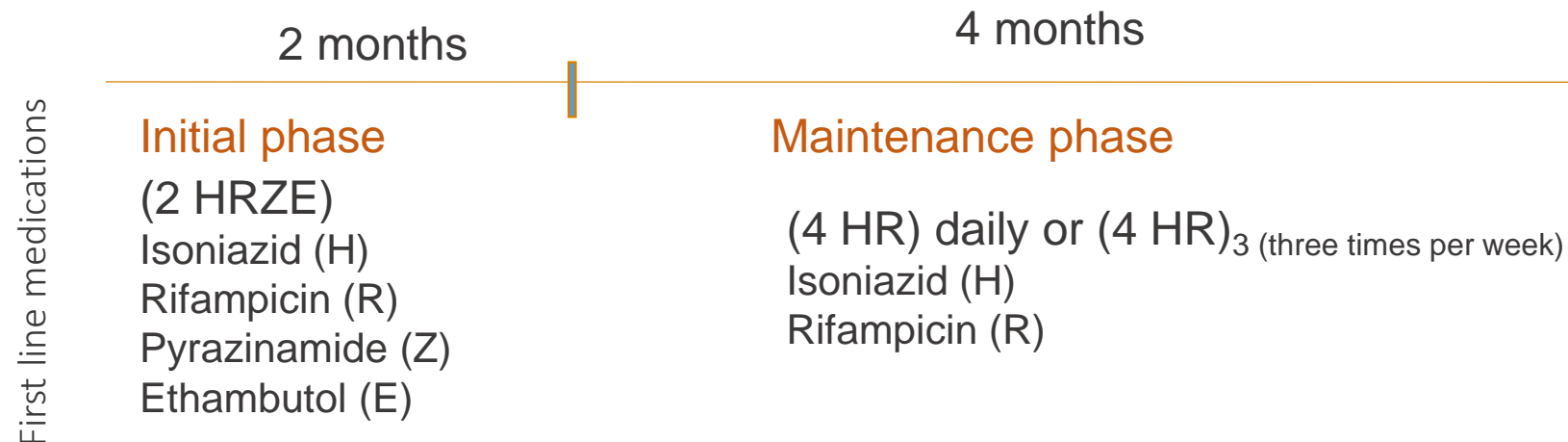| **Control transmission** | **Increase host resistance** | **Eliminate reservoir** |

DIRECTLY OBSERVED THERAPY SHORT COURSE (DOTS)

Strategy to improve compliance

Fixed Dose Combination therapy (FDC) - ALL IN ONE tablet

2 months	4 months

First line medications

Initial phase
(2 HRZE)
Isoniazid (H)
Rifampicin (R)
Pyrazinamide (Z)
Ethambutol (E)

Maintenance phase

(4 HR) daily or (4 HR)$_3$ (three times per week)
Isoniazid (H)
Rifampicin (R)

▌Stop tuberculosis

Strategy/policy

The Stop TB programme follows the WHO-developed six-point Stop TB Strategy. The Strategy builds on the successes of directly-oberserved treatment, short course (DOTS) while explicitly addressing the key challenges facing TB prevention and control.

The Strategy aims to dramatically reduce the global burden of TB by 2015 by ensuring that all TB patients, including those co-infected with HIV and those with drug-resistant TB, benefit from universal access to high-quality diagnosis and patient-centred treatment.

The Stop TB strategy also supports the development of new and effective tools to prevent, detect and treat TB. The Strategy underpins the Stop TB Partnership's Global Plan to Stop TB 2006–2015.

Stop TB Strategy has the following six components:

1.   Pursue high-quality DOTS expansion and enhancement

2.   Address TB-HIV, MDR-TB and the needs of poor and vulnerable populations

3.   Contribute to health system strengthening based on primary health care

4.   Engage all care providers

5.   Empower people with TB and communities through partnership

6.   Enable and promote research

Global Plan to Stop TB 2006–2015

Stop TB Strategy

▌Featured publications

Tuberculosis control in complex emergencies

Strategic plan for the prevention and control of multidrug-resistant and extensively drug-resistant tuberculosis in the Eastern Mediterranean Region (2010–2015) [pdf 706kb]

▌Information resources

Global tuberculosis report 2015

Fact sheet on tuberculosis

Q&A: What is multidrug-resistant tuberculosis and how do we control it?

▌Statistics and figures

DOTS Quarterly online

- https://www.cdc.gov/tb/topic/basics/tbprevention.htm