Tuberculosis & COVID-19:

Risk of Delay in TB Diagnosis & Treatment

IPC Overlap

RESOLVE TO SAVE LIVES
AN INITIATIVE OF VITAL STRATEGIES

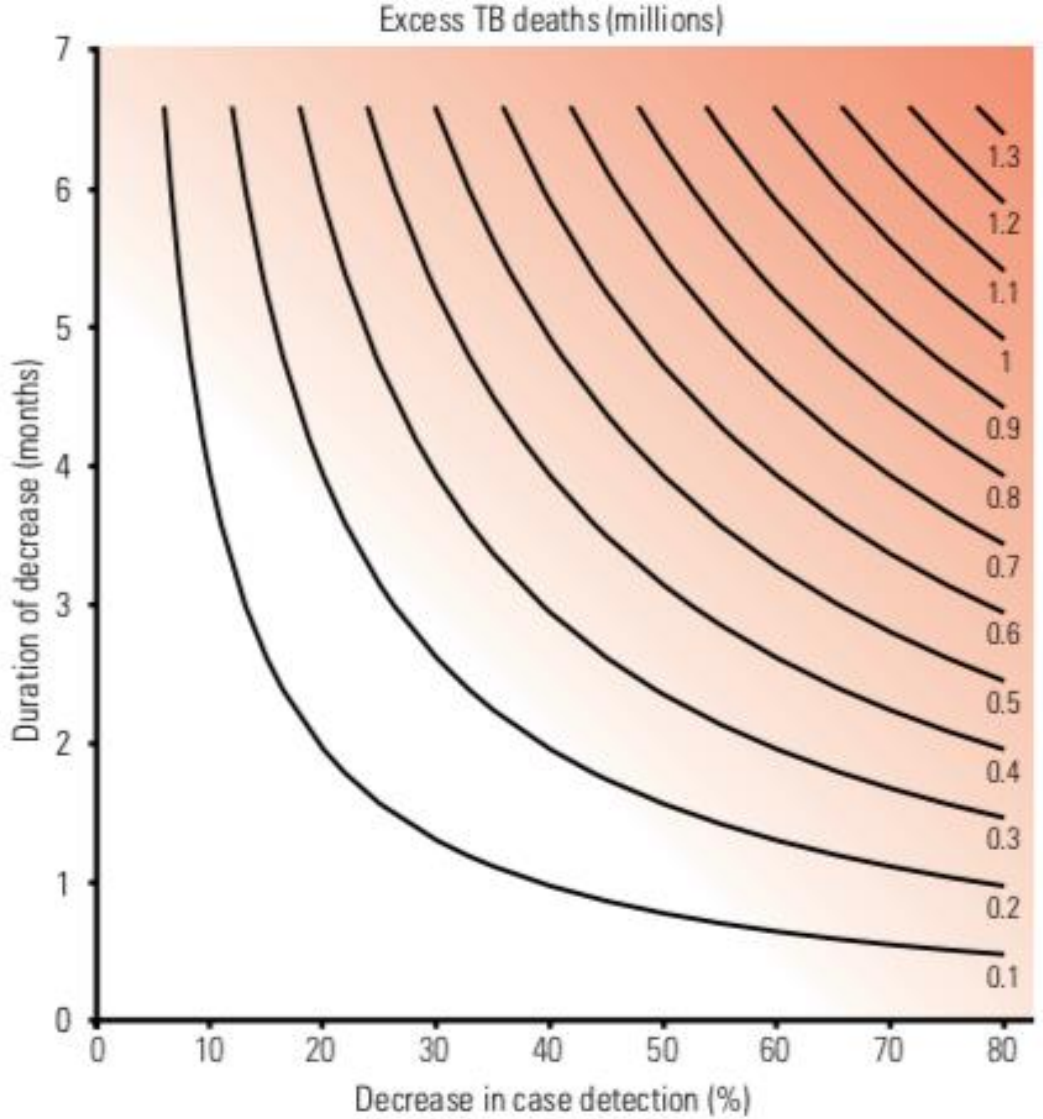
Outline of Presentation

- TB diagnostic and treatment delays during COVID-19
- TB epidemiology
- TB pathophysiology including HIV intersection
- TB IPC: Airborne Infection Control
- HCW infections

WHY ARE WE DISCUSSING TB?

- In June, a WHO modelling estimate suggested that if the COVID-19 pandemic led to a reduction of 25% in expected TB detection over a 3 month period, a 13% increase in TB deaths would be expected
- This would bring TB mortality back to levels from 5 years ago
- Estimates suggest that between 2020 and 2025, an additional 1.4 million TB deaths could be registered as a consequence of the COVID-19 pandemic

ESTIMATED IMPACT OF COVID-19 ON # OF TB DEATHS IN 2020



WHO Global TB Report 2020- https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf?ua=1

WHAT DO THESE CURVES MEAN?

- Suppose the number of people with TB detected were to fall by 25–50% over a period of 3 months (plausible based on data from several high TB burden countries)
- This could lead to 200,000–400,000 excess TB deaths in 2020
- IF THERE WERE 200,000 EXCESS TB DEATHS, THE WORLD WOULD BE BACK TO 2015; IF THERE WERE 400,000 EXCESS TB DEATHS, WE WOULD BE BACK TO 2012

Zimbabwe: Key risks for TB service delivery

- Similar clinical presentation of COVID-19 & TB increase chances of misdiagnosis
- TB testing capacity may be negatively affected as molecular testing platforms are used to test for SARS-CoV-2
- Global supply of TB Health Commodities (medicines and diagnostics) driven by activities in China & India, may be reduced during COVID-19 response
- Rapid assessment done by NTP from 23-24 April 2020

- Aim of the assessment was to identify Zimbabwe's TB service delivery gaps since the onset of the COVID-19 pandemic
- DTLCs and District Nursing Officers were contacted telephonically for information gathering
- Zimbabwe's COVID-19 taskforce conducted a review of global literature & guidance on COVID-19 response to align the NTP strategy with healthcare service delivery priorities
- Did re-assessment of TB programming strengths & weaknesses since the onset of COVID-19
- Opportunities for continuity and program integration explored for future planning

Zimbabwe Programme Area: TB Diagnosis

Challenges	Adaptation Strategies
1. Inadequate resources (human, financial and fuel) for TB activities, as available resources prioritized for COVID-19 activities 2. Delays in receipt of SARS-CoV-2 cartridges due to grounding of flights globally due to the COVID-19 pandemic 3. COVID-19 testing will be prioritized over TB testing where multiplexing is being done	1. MoHCC plans to decentralize PCR testing from 5 laboratories to 13 with GeneXpert at provincial level to increase access to COVID-19 testing for early case detection & prevention of spread 2. The COVID-19 strategy recommends use of additional testing platforms such as GeneXpert machines, Rapid Diagnostic Test Kits for screening and 2 mobile PCR testing laboratories 3. Additional GeneXpert Machines & Staff support-both additional numbers & risk allowances

Programme Area: Community TB Care

Challenges	Adaptation Strategies
1. Reduced TB screening and treatment support activities at community level by community health workers (CHWs) due to the on-going movement restrictions 2. Knowledge gaps for CHWs on COVID-19 3. Limited availability of PPE for CHWs to enable them to continue with their community TB duties 4. Limited implementation of community TB care activities by civil society/community based organizations (CBOs)	1. TB patients provided with medicines for longer periods; either do self administered therapy (SAT) or community DOT w/ family members. 2. Conduct re-orientation meetings at health facility level for community health workers on TB and COVID-19 to revamp community TB case finding 3. Provide PPE for CHWS & increase DOT & SAT through counselling patients & family to ensure treatment adherence 4. Provide guidance & support to CBOs on safe continuation of community TB care activities

Nigeria: Comparison between # of specimens collected for TB & cases diagnosed in 1st & 2nd quarters 2019 and 2020

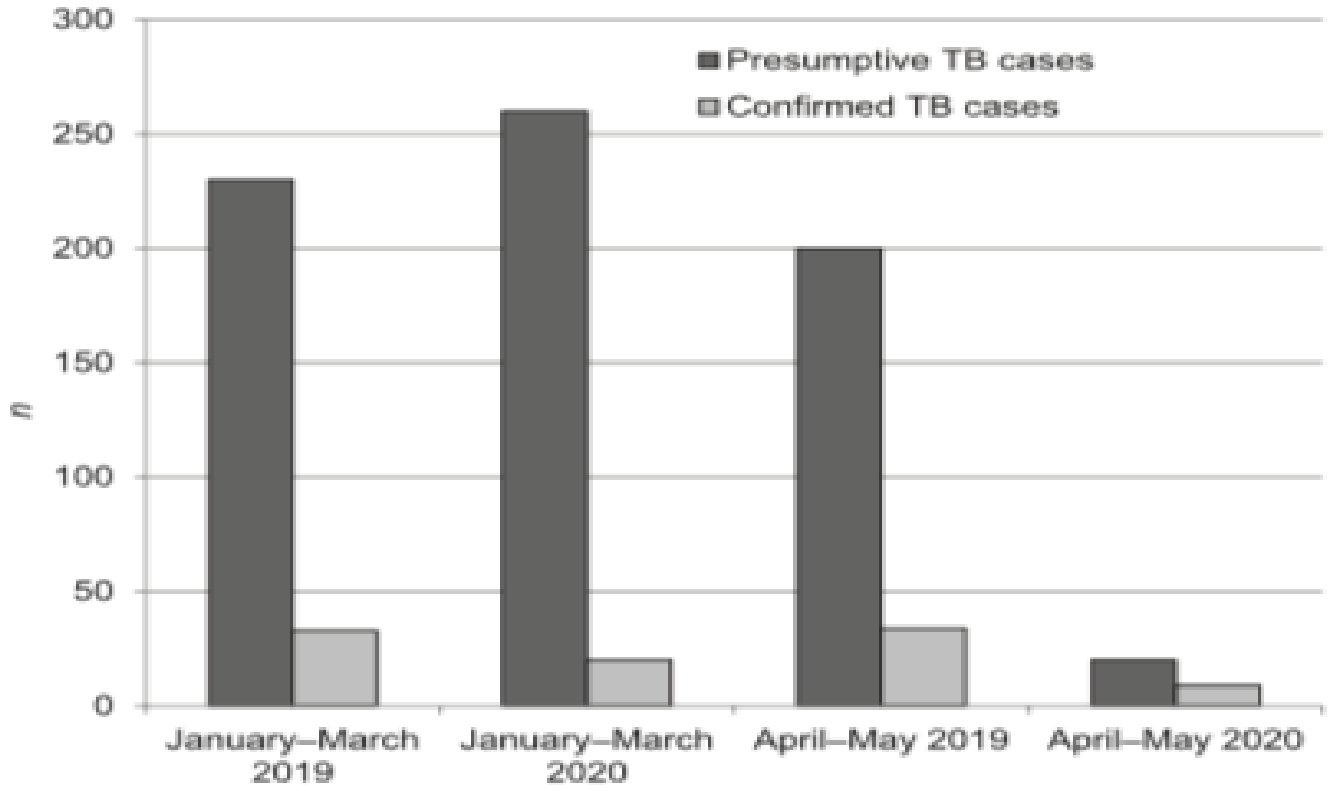
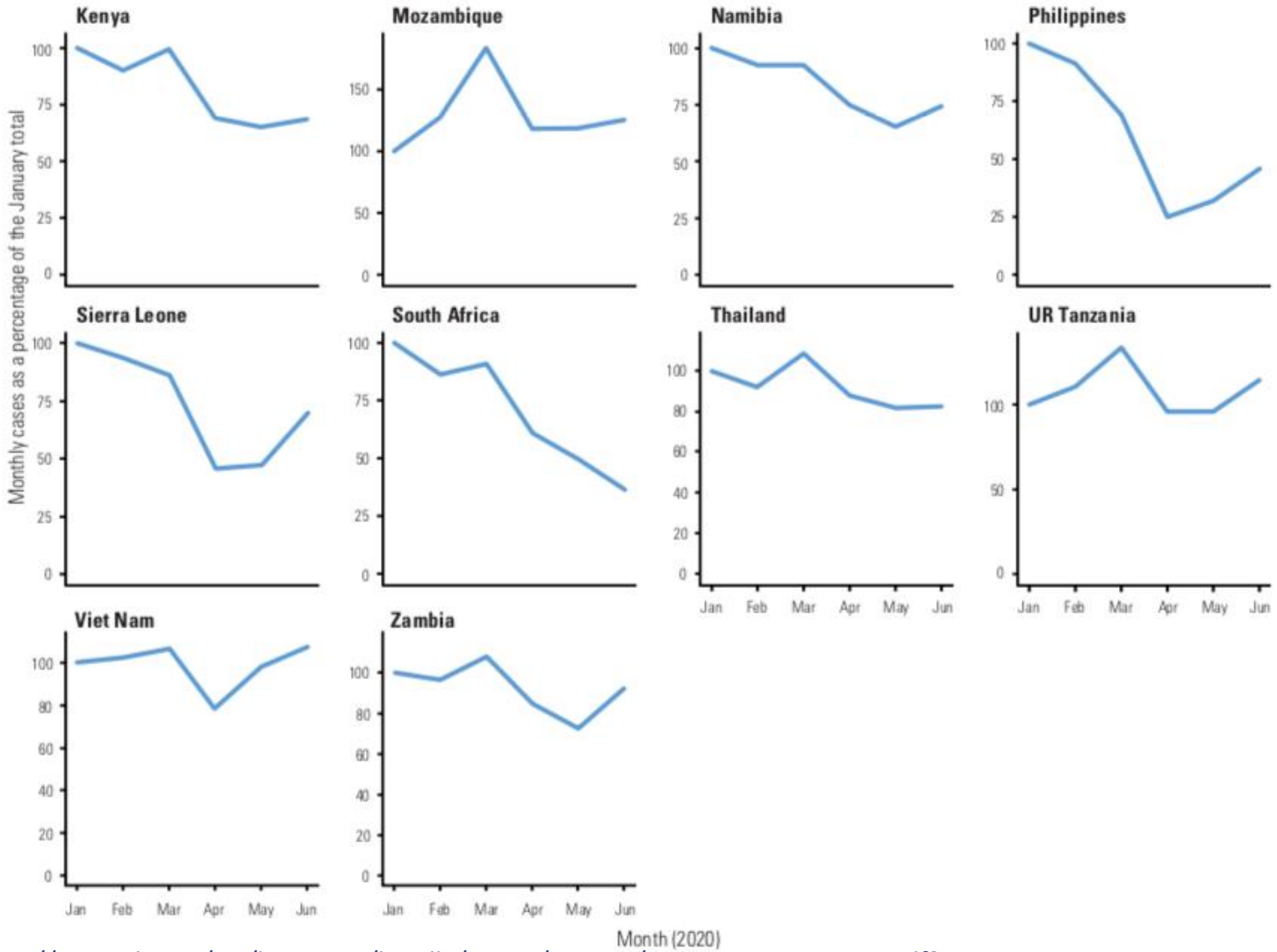


Figure Frequency distribution of presumptive and confirmed TB cases between January–May 2019 and January–May 2020 (the country was in lockdown between 30 March and 1 June 2020). TB = tuberculosis.

Trends in monthly notifications of TB 2020



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WHY IS TB DIAGNOSIS DOWN?

- People with mild symptoms or more chronic symptoms have been discouraged from seeking care to avoid crowding in HCFs
- Number of HCFs offering TB diagnostics & treatment reduced
- TB staff and molecular diagnostics (GeneXpert machines) reallocated for COVID-19 testing
- Disruption of procurement of laboratory consumables
- Restrictions of movement and loss of wages have made it harder for people to travel to health facilities
- Stigma, given the similarities in some clinical features of TB (e.g. fever and cough) with COVID-19

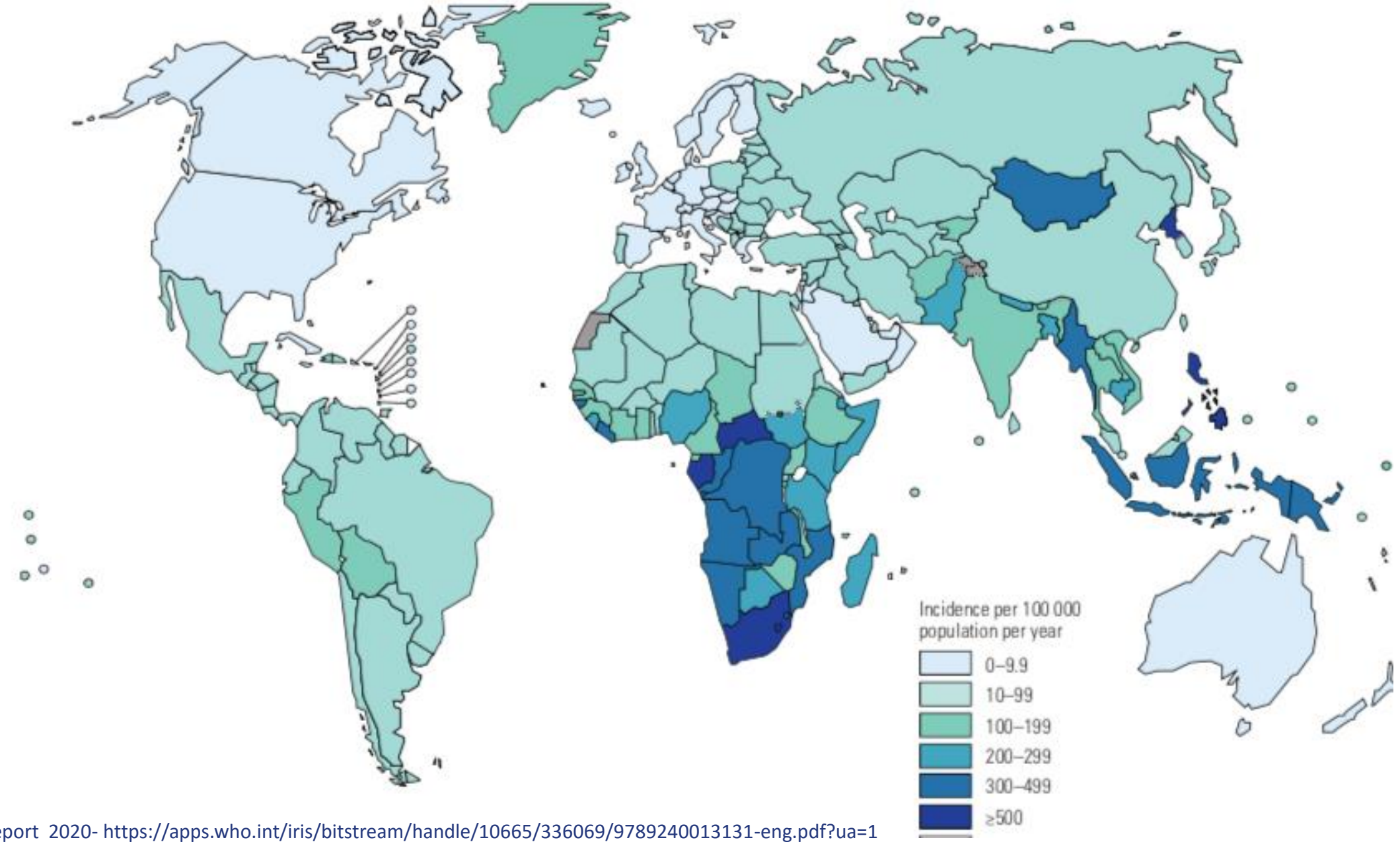
EPIDEMIOLOGY: SLOW DECREASE in TB since 2006

- *M. Tuberculosis* infects 1/4 world's population = 2 BILLION PEOPLE
- 10 MILLION TB INCIDENT CASES 2019
- BUT: ONLY 7.1 MILLION NOTIFIED TO WHO in 2019
- 1.2 MILLION TB DEATHS IN HIV-NEGATIVE people in 2019 = a 27% decline since 2000 from 1.7 million
- 208,000 TB DEATHS IN HIV-POSITIVE people in 2019 = a 60% decline since 2000 from 620,000

HIV/TB ARE A DEADLY COMBINATION

- TB IS A LEADING CAUSE OF DEATH IN PEOPLE WITH HIV IN AFRICA
- 1 IN 4 PEOPLE WITH HIV DIE DUE TO TB
- 862,000 HIV POSITIVE TB PATIENTS GLOBALLY IN 2019 OF WHOM 72% LIVED IN SUB-SAHARAN AFRICA
- THE RISK OF DEVELOPING TB FOR THE 38 MILLION PEOPLE INFECTED WITH HIV IS 18 TIMES HIGHER THAN THE RISK FOR THE GENERAL POPUATION

Estimated TB incidence rates, 2019



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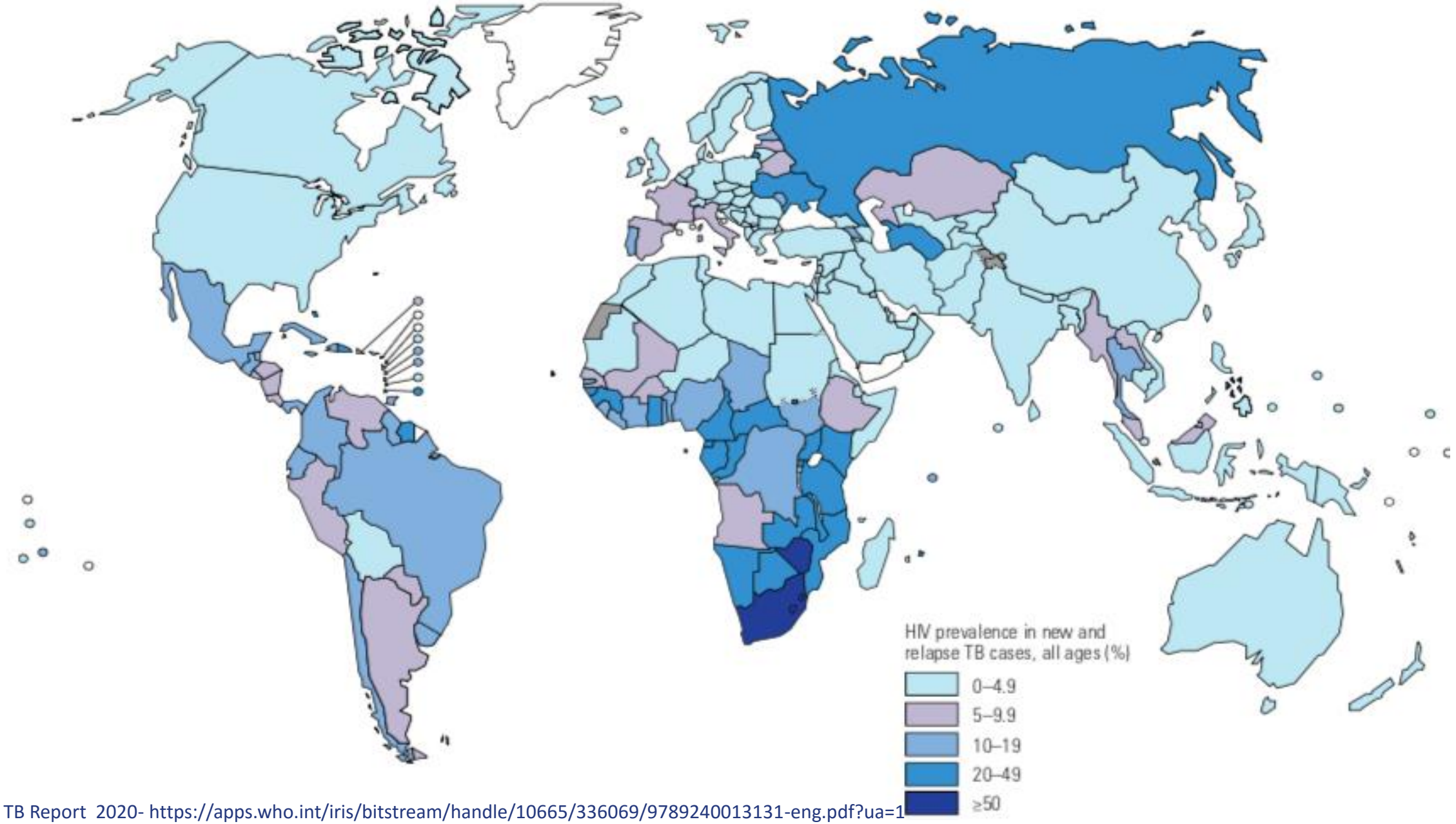
Estimated HIV prevalence in new and relapse TB cases, 2019



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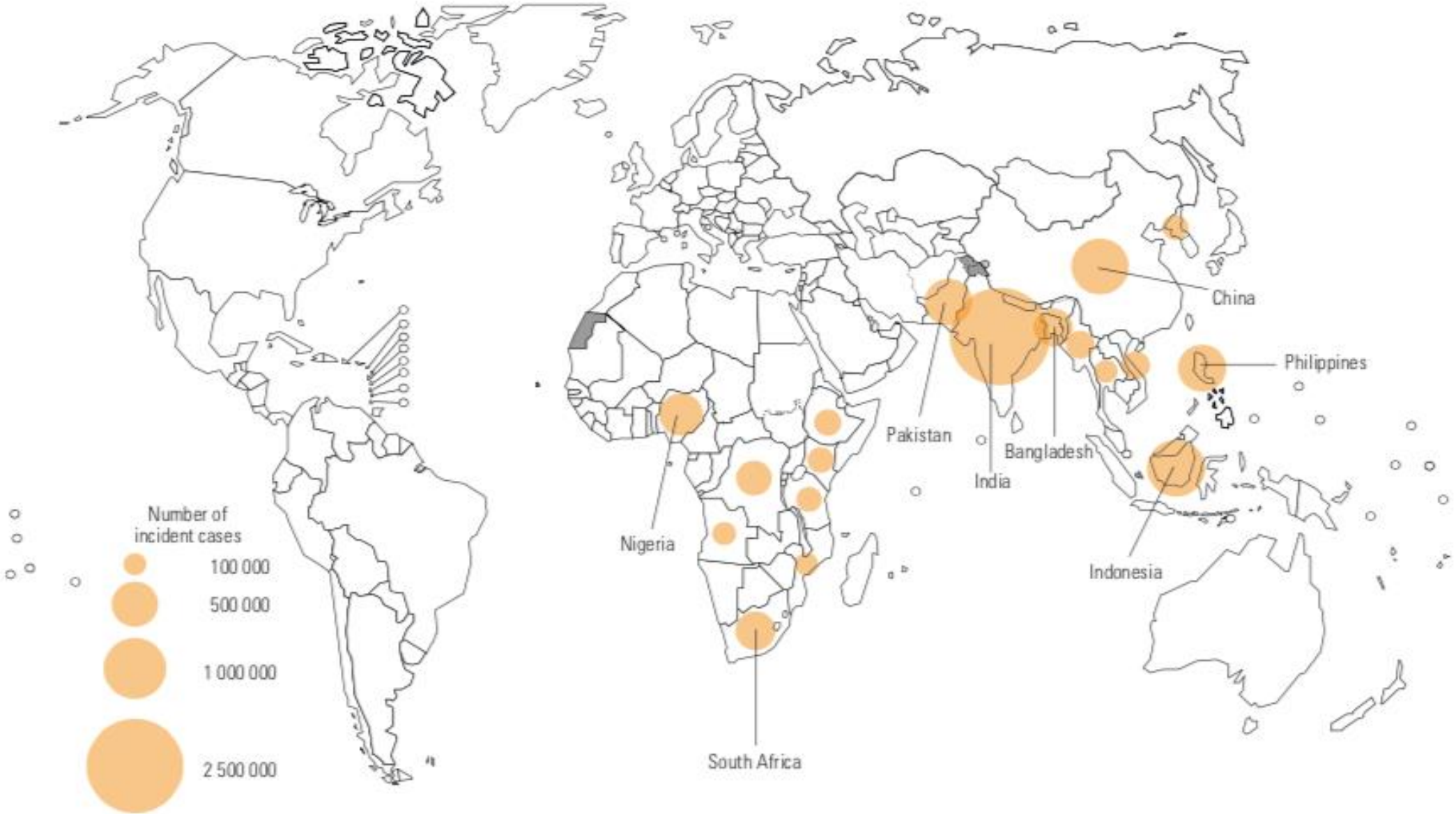
Countries that had at least 100 000 incident cases of TB in 2019

The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2019, are labelled.



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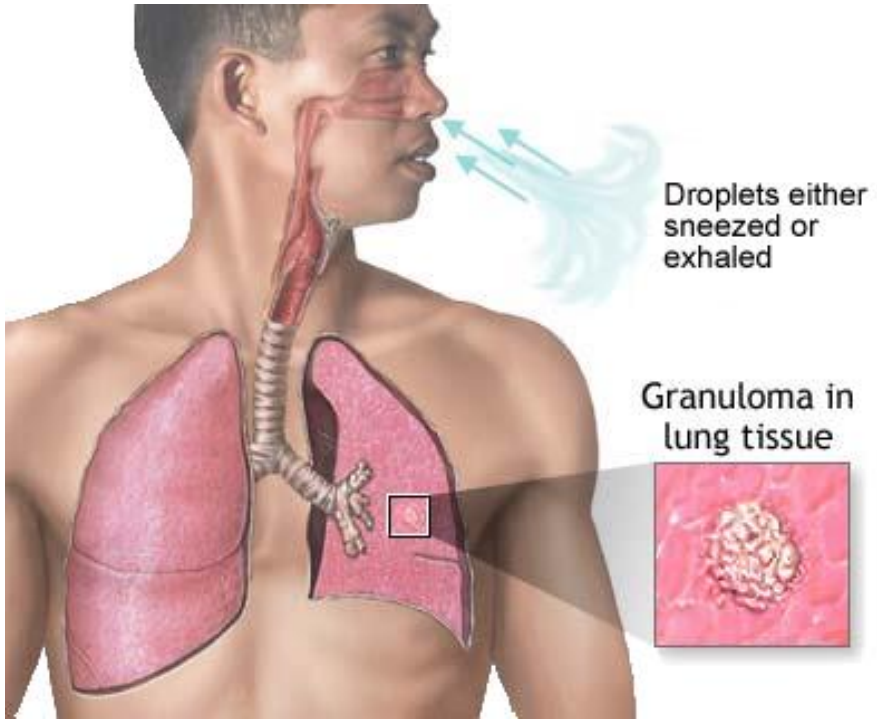
TRANSMISSION

- Lungs=entry portal
- Inhalation of droplet nuclei
- Coughing: 3000 droplet nuclei/cough
- Talking: 5 minutes
- Sneezing: BEST



TRANSMISSION ENHANCERS

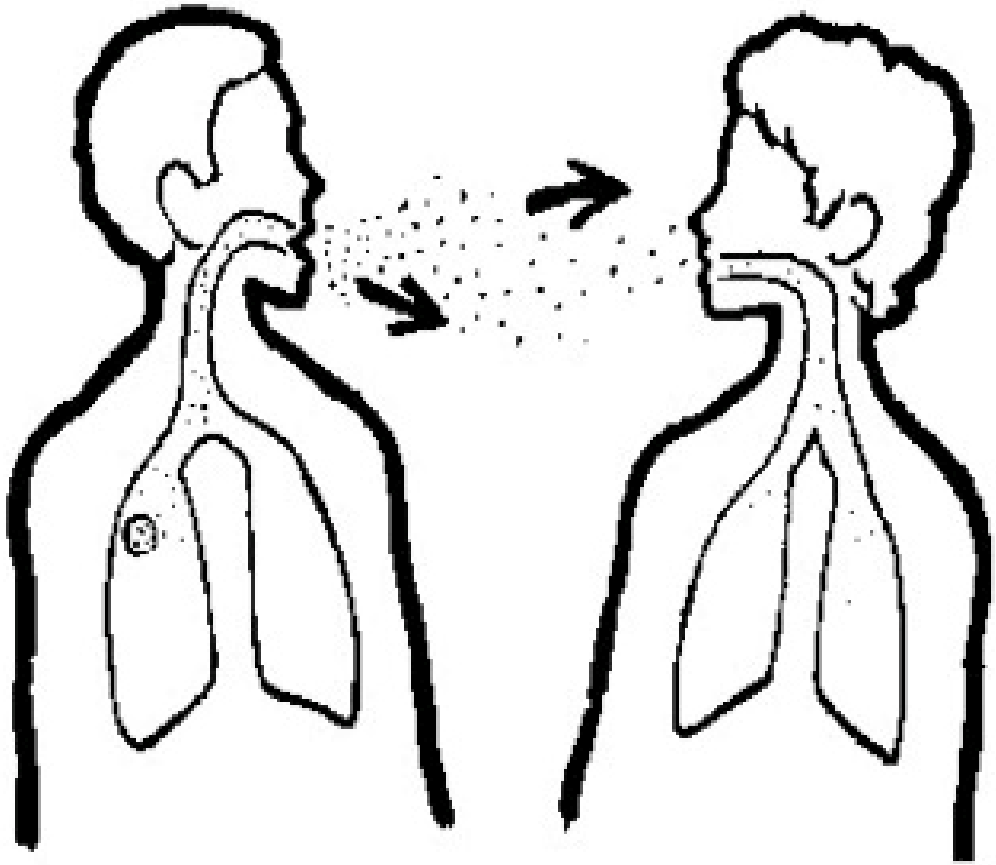
- INOCULUM SIZE: Cavitary lesions in coughing patient
- STRAIN VARIABILITY/VIRULENCE: Outbreaks from one known index case in non-HIV setting
- SUPER EFFECTIVE AEROSOLIZATION: Autopsy suite transmission
- VENTILATION (LACK OF): BACILLUS LONGEVITY & INFECTIVITY IN AIR

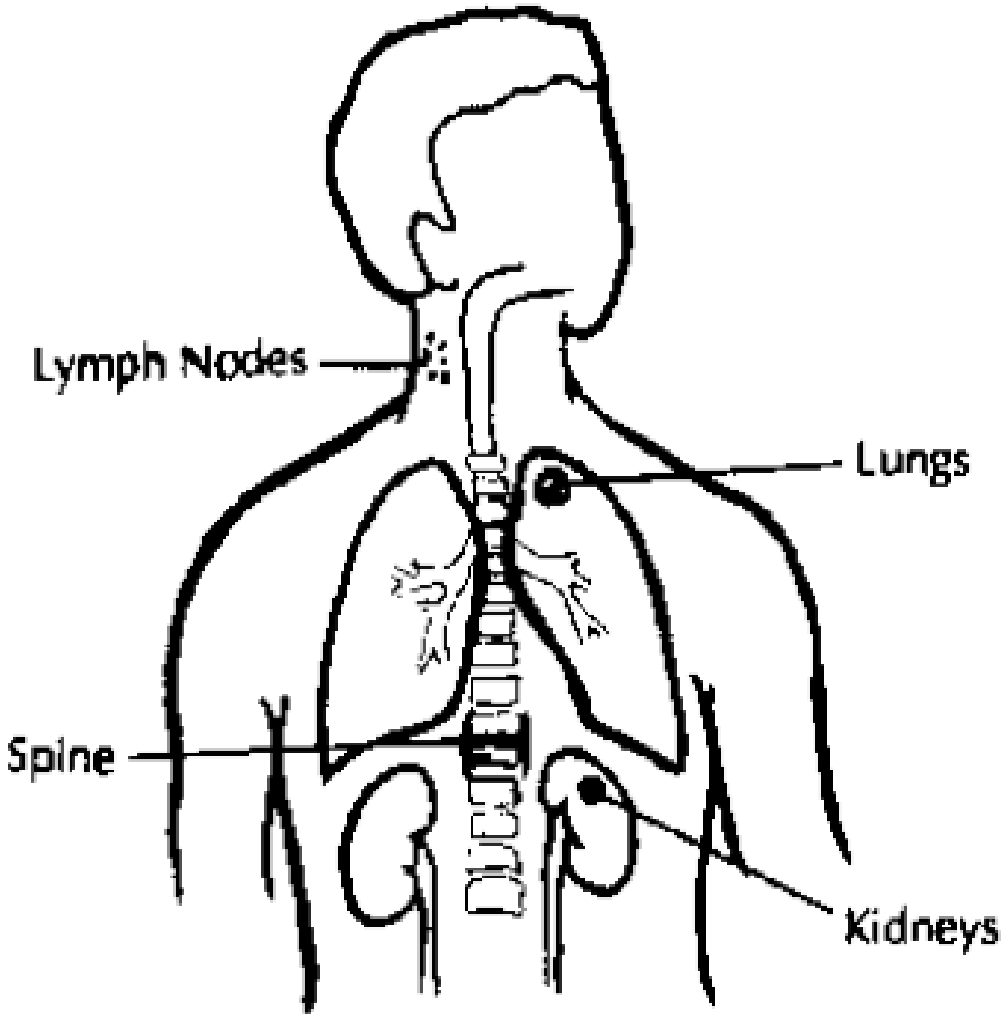
VARIATIONS IN RISK FOR TRANSMISSION

- SETTING
- OCCUPATIONAL GROUP
- LOCAL PREVALENCE OF TB
- PATIENT POPULATION
- EFFECTIVENESS OF TB INFECTION CONTROL MEASURES

BEFORE IMMUNE RESPONSE

- TB reaches alveoli
- Replicates intracellularly within alveolar macrophages
- Prevents acidification of phagosome w/in macrophage
- Lack of immediate host immune response





- Metastatic foci established in regional nodes
- Seed blood
- Travel to tissues favoring multiplication
- Alveolar macrophage infected with TB secretes Interleukins 12 & 18
- These attract CD4 cells
- CD4 cells meet TB antigen macrophage presents to them
- Transformation of CD4 cells

TRANSFORMED

- **PROLIFERATE:** PRODUCTION OF CLONES OF SIMILARLY REACTIVE CD4 CELLS
- **CUTANEOUS HYPERSENSITIVITY AND/OR POSITIVE BLOOD TEST**:

  BIG ENOUGH POPULATION OF TRANSFORMED CD4 ALLOWS DELAYED RXN TO TUBERCULIN SKIN TEST OR RXN TO ANTIGEN IN INTERFERON GAMMA RELEASE ASSAY (IGRA) WHICH IS T-CELL BASED ASSAY AND DEPENDS ON PATIENT HAVING ADEQUATE CD4

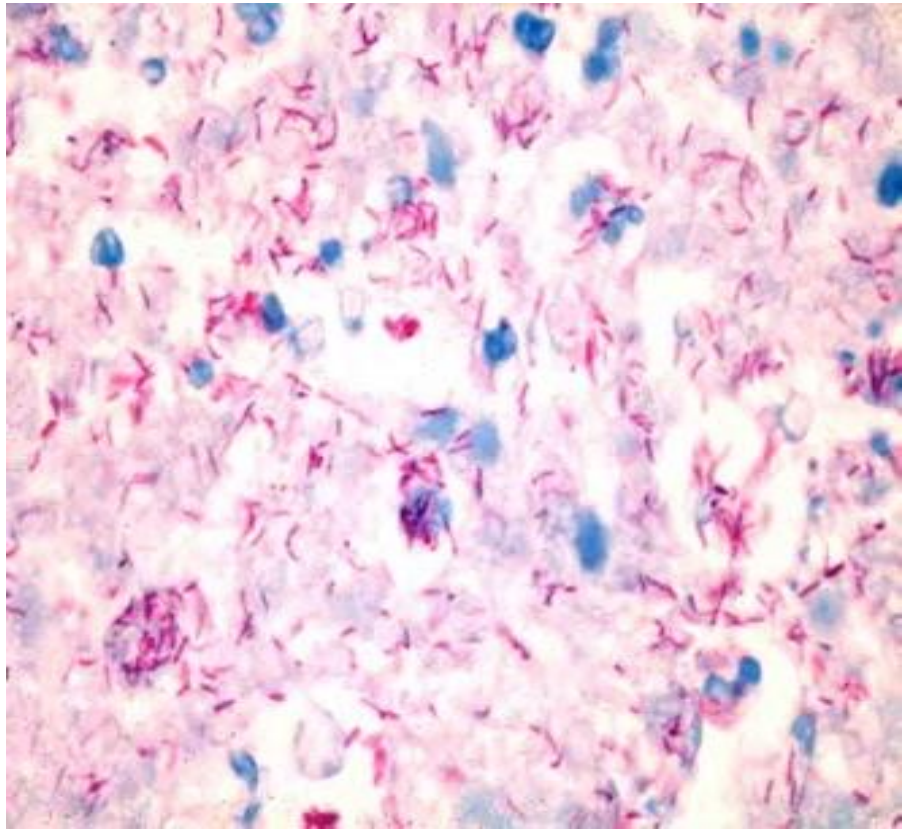
  (Neither of these tests for the presence of TB Infection (LTBI) is reliable in patients with advanced AIDS)

PRIMARY TB: RAPID PROGRESSION FROM INFECTION TO DISEASE IN ADULTS

- IMMUNO-COMPROMISED ADULTS
- MULTIPLE NOSOMIAL OUTBREAKS OF TB in AIDS WARDS, HOMELESS SHELTERS & PRISONS IN USA: 1980S & 1990S
- Nosocomial outbreak in HIV clinic in South Africa 2006; Tugela Ferry
- ATYPICAL CHEST X-RAY: HILAR ADENOPATHY; HARD TO DX
- TIME FROM EXPOSURE TO DISEASE ONLY 3–6 WEEKS

OVERWHELMING TB

- NO IMMUNOLOGIC CONTROL of bacillus: No CD4 to mobilize
- No interferon gamma: Rapid dissemination in each patient
- MDR strains killed scores in NYC AIDS wards & in multiple outbreaks in South Africa in HIV clinics



Diagnosis: Take a history, but…

- Symptoms: Systemic symptoms for TB are non-specific: fever, night sweats, weight loss suggesting chronic illness; COVID-19 symptoms more acute and shorter Pulmonary symptoms: cough, productive or dry; Most patients cough but may not have noticed (denial); COVID-19 cough not necessarily different
- Caveat: Patients cannot always accurately recall duration/degree of symptoms
  - Fear of diagnosis
  - Stigma of diagnosis of EITHER TB or COVID-19
  - Denial
  - Other activities of daily living more important: Obtaining food, getting to work, child care etc.

DIAGNOSIS OF COVID-19 vs TUBERCULOSIS

- In addition to cough and fever, loss of taste or smell, sore throat, aches and fatigue are more characteristic of COVID-19, not of TB
- BUT TB can cause fatigue and patients may have difficulty describing symptoms clearly
- Shortness of breath and/or rapid respiratory rate points to COVID-19 rather than TB
- Abnormal O2 saturation (pO2<93) points to COVID-19 if facility has access to pulse oximeter

Diagnosis of TB: Chest X-Ray

- Chest x-ray more sensitive than sputum for detecting TB
- Chest x-ray findings in TB differ from COVID
- BUT Chest x-ray often not available especially at PHC level
- CAVEATS: Immunocompromised hosts with active TB have atypical chest x-rays or even normal chest x-rays: Chest x-ray abnormalities are CD4 dependent
- COVID-19 patients may have normal chest x-ray

MICROBIOLOGIC TESTING: TB vs COVID-19: WHO recommendations, June 2020

- Many countries may be sharing molecular platforms for COVID-19 testing or diverting Xpert machines completely: Mozambique
- Maintaining current molecular diagnostic services for TB is crucial
- Do not move equipment from currently designated TB laboratories to respond to the demand for COVID-19 testing.
- In areas with high TB incidence, test those with cough for BOTH COVID and TB

Airborne Infection Control (AIC)

"Infection prevention and control measures aim to ensure the protection of those who might be vulnerable to acquiring an infection both in the general community and while receiving care due to health problems, in a range of settings."

World Health Organization (WHO)

Administrative Controls

- Early screening of patients
- Separate coughers from non-coughers
- Promote cough etiquette and cough signage
- Fast-track patients to a care provider
- Ensure health facility design, construction or renovation is conducive for TB infection control – as well as COVID, Influenza and all respiratory pathogens
- Promote occupational health measures for staff: screening
- Ensure monitoring and evaluation

Early Screening at Registration

Waiting Room

- Do not allow waiting room crowding: Too many people, too close together, indoors with no ventilation; dropped ceiling

Separation of Coughers

Fast-Tracking to a Care Provider

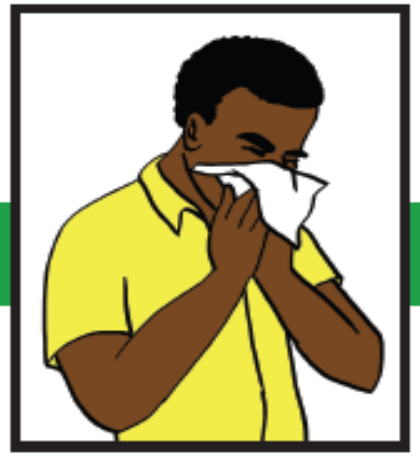
Cough Etiquette for All Staff and Patients

Protect Others. Protect Yourself.

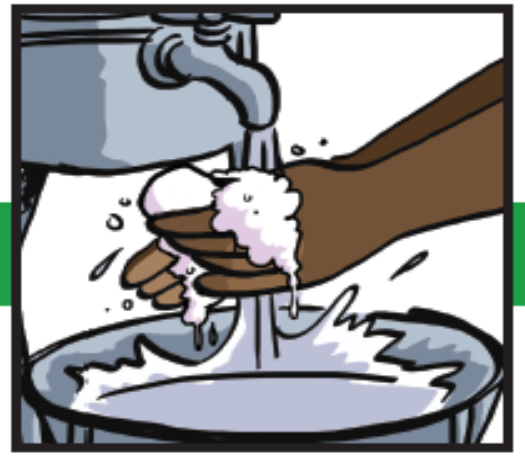
Cover your cough or sneeze.

Cough or sneeze into your arm.

or



Use a tissue and then throw away...



...then wash your hands.

Stop the spread of TB, colds, and influenza.

C5221395-A

Ensure that Training is Conducted for All Staff

Environmental Controls: TB and COVID-19

Use of Open Air Spaces

Natural Ventilation

Environmental Controls

- Promotion of natural ventilation
- Use of mixed ventilation systems (mechanical and natural)
- Mechanical: Remember that air conditioning is NOT ventilation
- Avoid dropped ceilings: they cut down on volume for airflow and cannot be ventilated by roof placed whirlybirds
- Avoid windows that open sideways or up and down, thereby cutting 50% of the airflow

Whirlybird

“Whirly Bird” Wind Turbine

Wind speed	=	15 km/h (9.3 mph)
Diameter	=	30 cm (12 in)
Airflow rate	=	1 500 m^3/h (876 cfm)
Wind speed	=	25 km/h (15.5 mph)
Diameter	=	30 cm (12 in)
Airflow rate	=	2 200 m^3/h (1 285 cfm)

PA Jensen

Environmental Control Issues

- Design
- Operational
- Maintainable
- Sustainable

General Guidelines

- Building location and orientation
- Building form and dimensions
- Window types and operation
- Other openings (doors, chimneys, etc.)
- Construction methods and detailing (infiltration)
- External elements (walls, screens, etc.)
- Urban planning conditions

Personal Protective Equipment (PPE)
Surgical Masks

- Can be worn by **patients** if cough cannot be contained with cloth or tissue
- Can be worn by HCWs in most situations for COVID-19

N95 or FFP2 Respirators

- Should be worn by healthcare workers in high risk settings (such as MDR-TB wards)
- Must be fit-tested

Occupational Health: Responsibility of Administrative Controls

- Staff receive annual evaluations for TB: Should be mandatory
- For COVID-19, consider staff screening for symptoms daily
- Staff are offered a confidential HIV test
- Staff offered treatment for TB and/or HIV and reassignment if HIV-infected
- A CONFIDENTIAL log of staff diagnosed with TB is maintained in locked cabinet

Global Evidence on Risk of TB in HCWs

- Increased rates of TB disease
  - 2.4 X rate of disease in low- and medium- burden countries
  - 3.7 x rate of disease in high-burden countries
- Increased rate of MDR-TB
  - 5.5 x rate of MDR-TB admission in HCWs compared to general population
- Increased rates of Latent TB Infection (LTBI)
  - 10 x risk in high-income countries
  - 6 x risk in low-income countries
  - 4-8% annual risk of TB Skin Test (TST) conversion

Nosocomial TB Outbreaks

- MDR-TB outbreaks, U.S. Hospitals, 1989-1992
  - ~240 cases, majority HIV-infected
  - Mortality ~ 80%; mean interval dx to death = weeks
  - HCWs infected and died
  - Inadequate TB IC measures identified; TB IC interventions associated with decrease or cessation of cases/transmission
- XDR-TB outbreak, Tugela Ferry, S Africa, 2006
  - ~ 53 initial cases, majority HIV-infected
  - Mortality ~98%, median interval dx to death=16 days
  - HCWs infected and died
  - Inadequate TB IC measures identified; TB IC interventions modeled/associated with decreased cases/transmission

HCWs & COVID-19

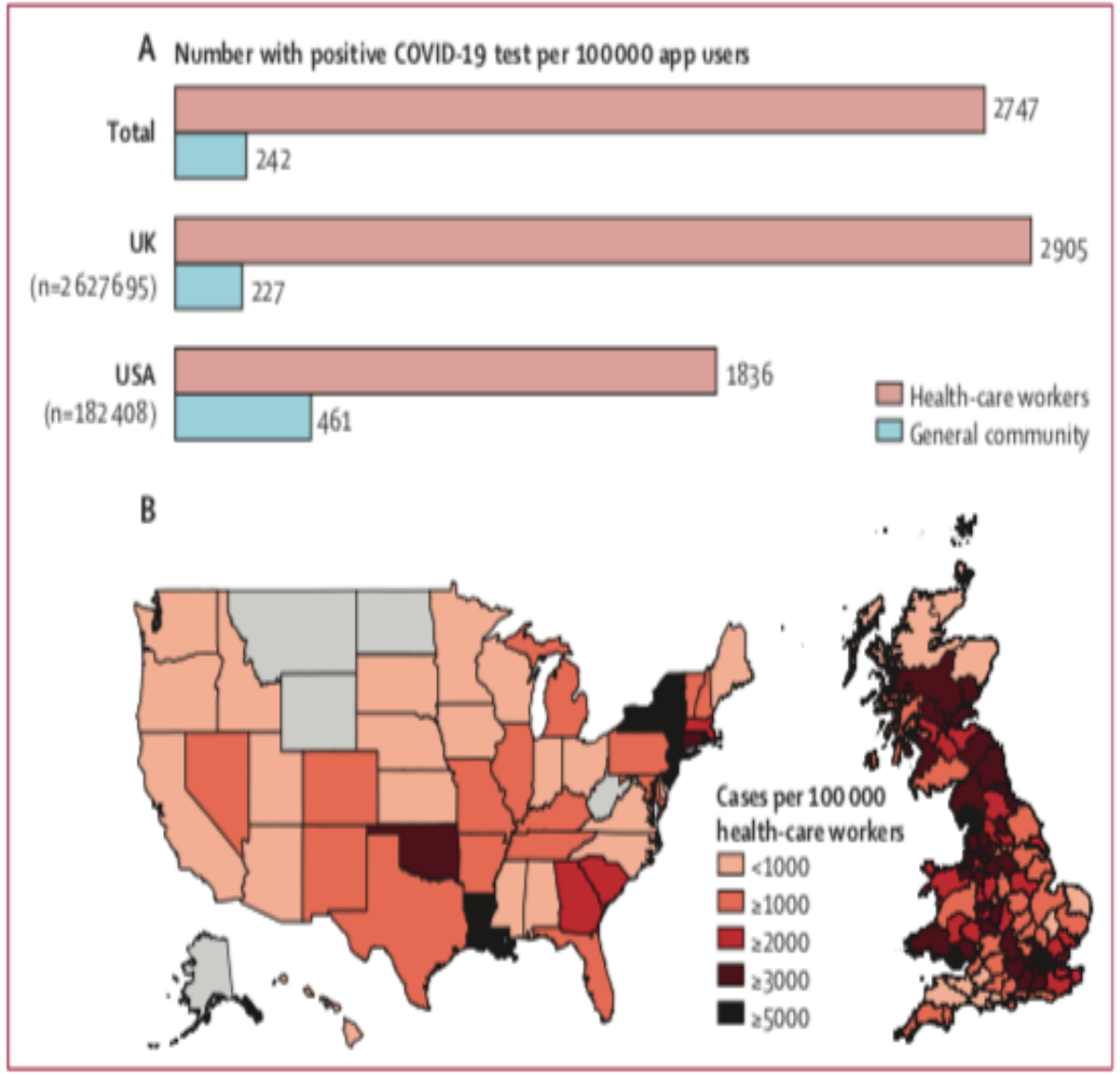


Figure: Risk of testing positive for COVID-19 among front-line health-care workers

- Amnesty International reported that at least 7,000 health workers have died around the world after contracting COVID-19
- HCW deaths in the USA (1,077), Brazil (634), South Africa (240) and India (573)
- >1,300 health workers have died in Mexico alone, the highest known figure for any country
- HCWs account for 1 in 7 covid-19 cases (WHO)
- Globally, 14 percent of COVID-19 cases are among HCWs (WHO-September)
- Figures are disproportionate: WHO data suggests HCWs represent <3% of the population in the majority of countries & <2% in almost all LMICs

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