

Global Epidemiology of TB in Children, Adolescents and Pregnant Patients

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Conflicts of Interest

- I have no conflicts of interest to disclose.

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Outline

- Review Tuberculosis (TB) definitions
- Discuss limitations in estimating TB in children & pregnant patients
- Provide an overview of TB Epidemiology in children & pregnant patients
- Discuss the impact of the COVID-19 pandemic on TB
- Case Based Discussion
- Q&A

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- TB disease is > 9,000 years old
- Has killed ~ 1 billion people in the past 200 years

Alexandria, Middle of the 3rd Century B.C. Bronze wit silver inlay work. Height 6.7 cm. Inv. No. 1949.40.

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END TB

World Health Organization

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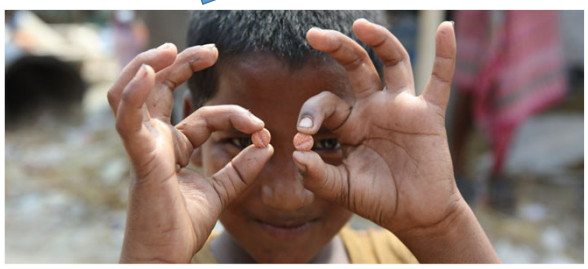
END TB

World Health Organization



https://www.tballiance.org/news/one-million-child-friendly-tuberculosis-medicines

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Clinical Case

- 14 yo F, US born
- Was living with mother in Reynosa, Mexico
- Developed TB symptoms in April 2020
  - Shortness of breath
  - Exercise intolerance
  - 3 kg weight loss
  - Cough

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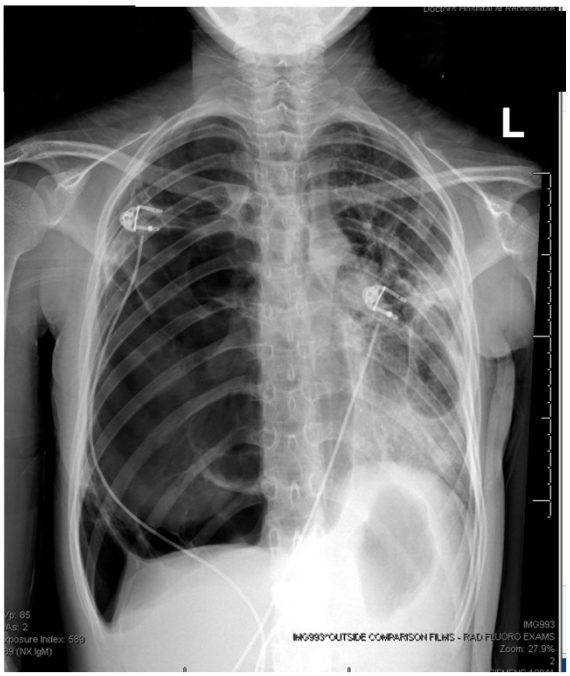
Original CXR



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- Started on RIPE therapy
- Culture confirmed pan-susceptible TB on 4/24/20, 4/25, and 4/26

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- Moved to the US in May 2020
  - Clinical symptoms improved
- Negative cultures: 3 in May, 1 in June, 1 in July
- Bi-national TB treatment program:
  - video DOT during week, self-administered on weekends
  - 13 missed doses
- Serial CXRs (8/14 with some improvement, 12/7 with blebs)

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- Complicated social setting, diagnosed with depression
- Moved to the U.S. to live with maternal grandmother

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- Jan 2021, developed shortness of breath
- Taken to OSH
  - Concern for pneumothorax
  - → chest tube placed, then removed
- Transferred to TCH

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Evaluation

- Exam
  - Weight 84 lbs (38.5kg); 0.7%
  - Thin, flat affect
  - decreased breath sounds diffusely in the right lung fields
- Labs:
  - Anemic (Hb 10.4), normal LFTs
- TSPOT:
  - 8/11 spots
- HIV negative
- Sputa collected x3
  - Smear negative

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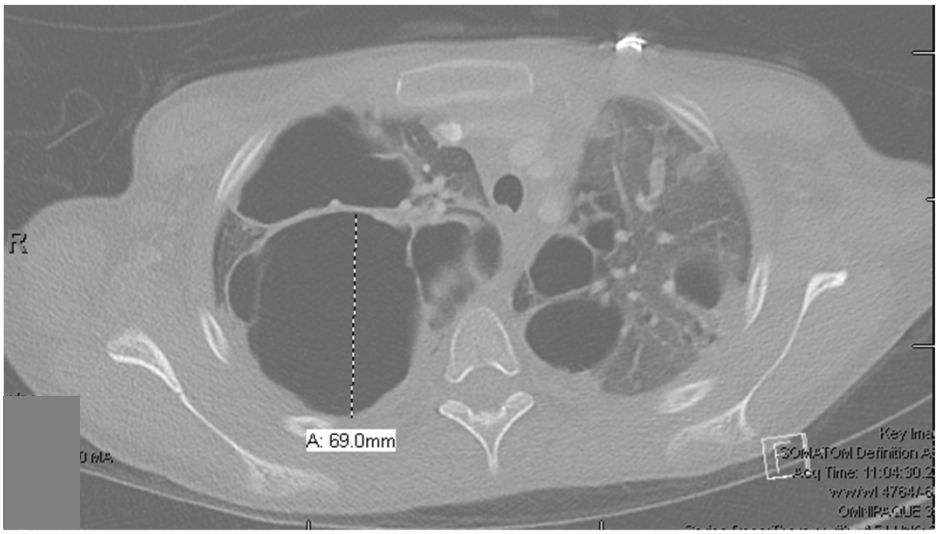
CXR

15

CT Chest (TCH)



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- Continued on RIPE therapy
  - Mycobacterial cultures negative
- Chest tube placed for acute onset SOB
- Nutritional rehabilitation

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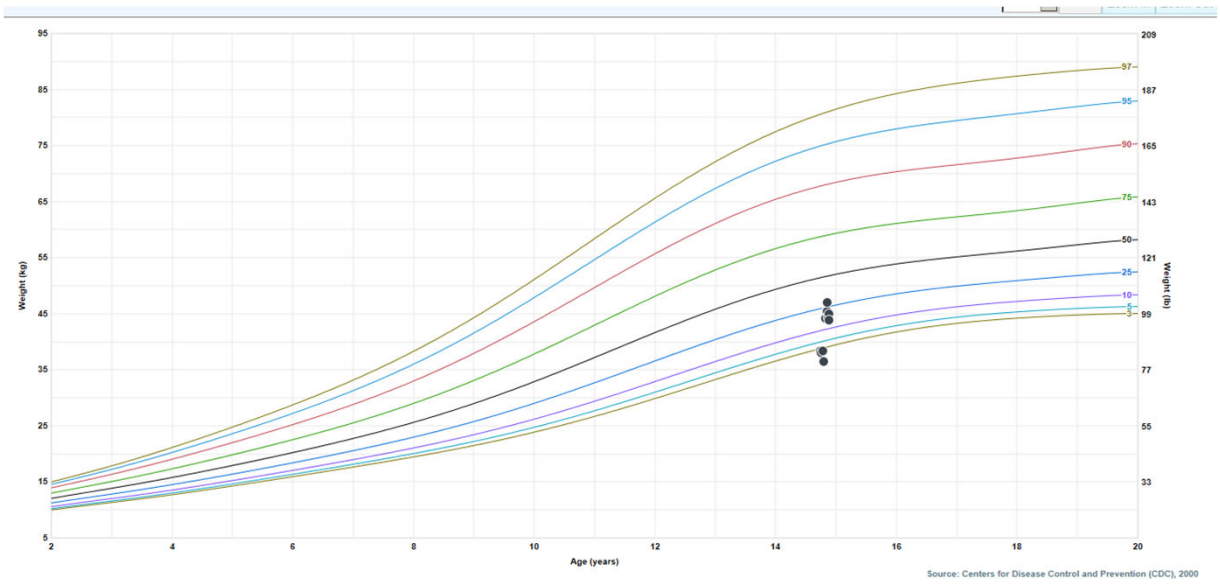

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Surgical Intervention (Feb 2020)

- Right thoracotomy
- Blebectomy
- Pleurodesis

- Findings:
  - Moderate adhesions of the RUL, RML, RLL to the chest wall and diaphragm
  - Resection of the multiloculated RLL bleb
  - A mechanical pleurodesis
  - Excellent expansion of all lobes of R lung
  - Fibrin sealant over the staple lines & surface of the lung

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Pleura Pathology & Microbiology

- Pleura, right lower lobe, blebectomy:
  - Markedly thickened pleura with adhesions, hemorrhage, granulation tissue formation and chronic (non-granulomatous) inflammation.

- Lung, right lower lobe, wedge biopsy:
  - Subpleural and pleural necrotizing and non-necrotizing granulomatous inflammation.
  - No acid fast organisms identified on Fite and AFB stains.
- ***Smear negative, cultures negative (6 weeks)***

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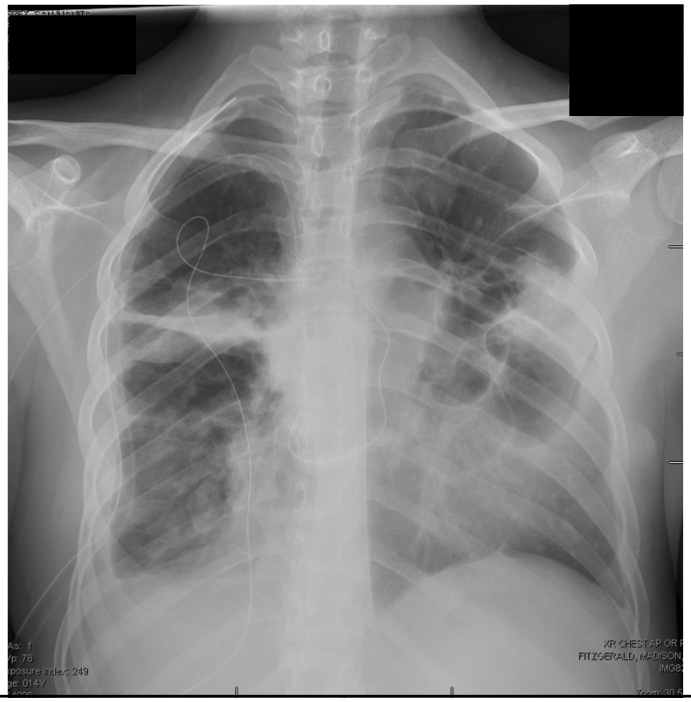

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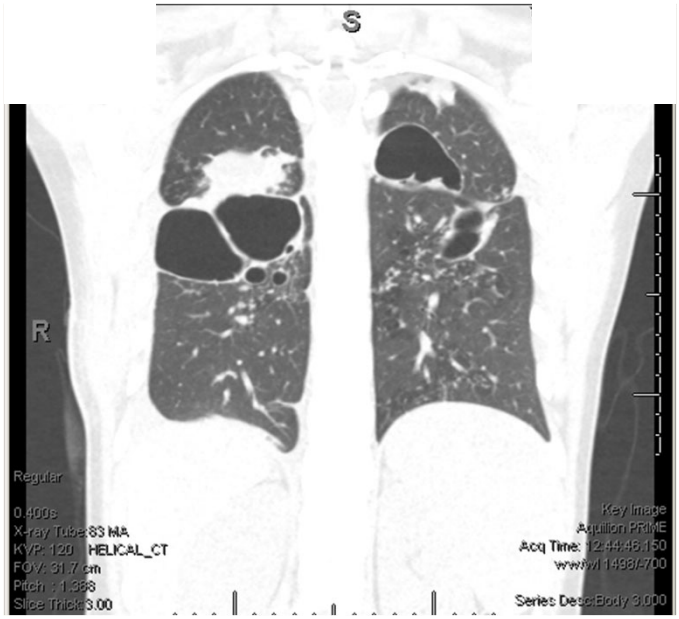
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Aquilion PRIME
Acq Time: 12:44:46.150
Series Desc: Body 3.000

22

- Continued on
  - INH, RIF and ETH
  - No optic neuropathy
- X 4 additional months
- Discharged home (Hidalgo Co. HD)

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- ***This case highlights the importance of prevention and treatment of TB Worldwide (& in children).***

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TB is a Disease of Poverty

- TB is *often* known as "a disease of the poor"
- ***"the burden of TB follows a strong socioeconomic gradient both between and within countries, and also within the poorest communities of countries with high TB incidence."***
- ***~95% of TB cases worldwide occur in low-middle income countries***

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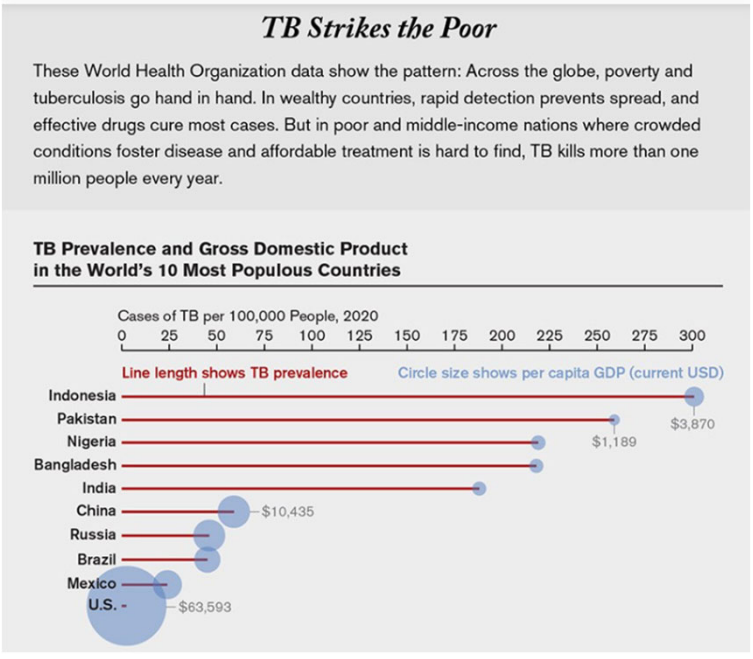

https://www.nature.com/articles/d41586-022-01348-0

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The Sityaya family in Khayelitsha, South Africa, all had tuberculosis, except for the baby, who received preventive treatment. Credit: Jonathan Torgovnik

https://www.nature.com/articles/d41586-022-01348-0

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- ***How do we identify children at risk for TB?***

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TB Definitions

TB exposure:

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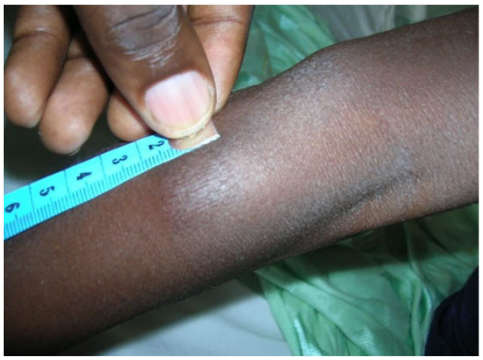
TB Definitions cont.

- **TB infection (TBI):**



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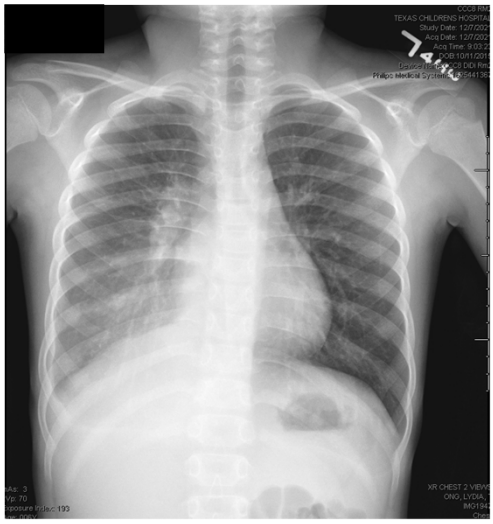
TB Definitions cont.

- **TB disease:**



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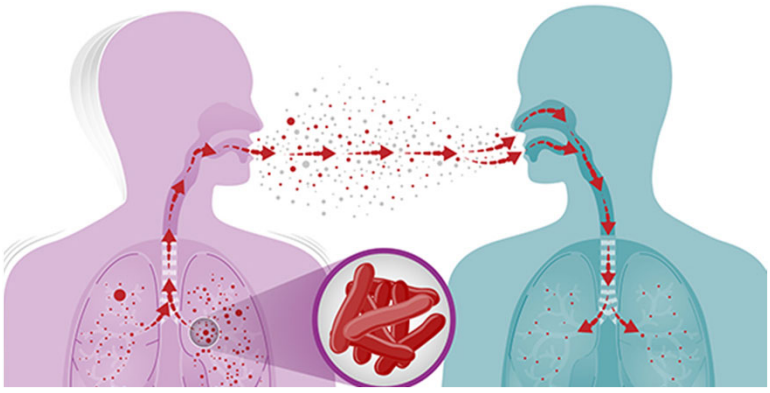
Most M.TB is transmitted <u>to</u> children <u>by</u> adults (or adolescents)



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The Sityaya family in Khayelitsha, South Africa, all had tuberculosis, except for the baby, who received preventive treatment. Credit: Jonathan Torgovnik

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A child newly diagnosed with TB is a <u>sentinel</u> event indicating recent transmission in a community.

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Children with TB infection = reservoir for disease

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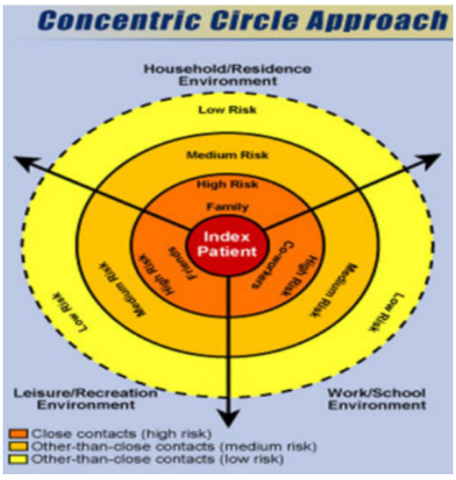
How do we identify children at risk for TB?



- Immigration based screening
- TB risk factor based screening
  - Exposure to TB contact
  - Birth or extended travel to high-prevalence TB setting
  - Regular exposure to high-risk adult/setting

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Probability of Infection

- Intimacy & duration of contact
- Infectiousness of sourse case
- Virulence of bacterial strain
- Shared environment

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INT J TUBERC LUNG DIS 8(3):278–285

STATE OF THE ART

The clinical epidemiology of childhood pulmonary tuberculosis: a critical review of literature from the pre-chemotherapy era

B. J. Marais,* R. P. Gie,* H. S. Schaaf,* A. C. Hesseling,* C. C. Obihara,* L. J. Nelson,† D. A. Enarson,‡ P. R. Donald,* N. Beyers*

* Centre for TB Research and Education and the Department of Paediatrics and Child Health, Tygerberg Children's Hospital and the Faculty of Health Sciences, Stellenbosch University, Cape Town, South Africa; † Centers for Disease Control and Prevention, Atlanta, Georgia, USA; ‡ International Union Against Tuberculosis and Lung Disease, Paris, France

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HHC, smear + → 60-80% infected
HHC, smear - → 30-40% infected

HIGH RISK

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- 60% children infected < 3 months*
  - *TST conversion
- >80% <2 years: HHC, or close caregiver
- 50-70% CXR abnormalities
  - 60-80% <2 years

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LESS RISK*

- *complicated by poverty

Markcarolan.com

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Table 3 The calculated risk of developing primary tuberculosis (TB) infection, compared to the calculated risk of being notified with TB-related disease or death following primary TB infection, within specific age groups

Age group, years	Calculated risk to develop primary TB infection* %	Calculated risk to be notified with TB-related disease, following primary TB infection† %	Calculated risk to be notified with TB-related death, following primary TB infection‡ %	Relative TB-related mortality§ %
<1	<1	11.9	6	0.6
1–4	10	5.6	1	12.1
5–9	20	3.8	0.3	9.1
10–14	10	6.4	0.5	9.1
15–24	30	10 (males) 13 (females)	1.5 (males) 2.6 (females)	16.7 (males) 39.4 (females)

* Indicates the calculated percentage of children who develop primary infection (tuberculin conversion) within a specific age group.
† Indicates the number of children notified with TB, as a percentage of the total number expected to have developed primary TB infection, within a specific age group.
‡ Indicates the number of children notified with death due to TB, as a percentage of the total number expected to have developed primary TB infection within a specific age group.
§ Indicates the percentage of TB-related mortality compared to all-cause mortality within a specific age group.
Data on primary TB infection were collected from the British MRC tuberculin skin test survey for London (1949–1950).[5] This was converted into the number of children expected to develop primary infection within a specific age group, using national census data for London (1951). Data on TB-related disease and death were collected from TB notifications and death certificates for London (1945–1949).[5] Absolute notification numbers were converted into percentages, using the number expected to develop primary infection within a specific age group as denominator and accepting that all notifications result from recent primary infection. Relative TB-related mortality was calculated from death certificates for England and Wales (1950), comparing TB-related mortality with all-cause mortality.[5]

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Risk of Infection → Disease

- **Infants – *HIGHEST RISK***
  - 30-40% develop TB meningitis
  - 10-20% miliary disease
- **Children <5 years**
  - **10-20% (highest risk <2 years)**
- 5-10 years "GOLDEN PERIOD"
- **Adolescents → 10-20%**
- **Other risk groups:**
  - primary or secondary immunodeficiency, malnutrition, renal disease, diabetes

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TB in Adolescents vs. Children

Adolescents
Reactivation of infection
Adult type disease
Often infectious
Smear/culture/PCR +

Children
Paucibacillary
Most non-infectious
Smear/culture/PCR negative
Intrathoracic adenopathy
Diagnosed clinically

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TB Epidemiology Worldwide

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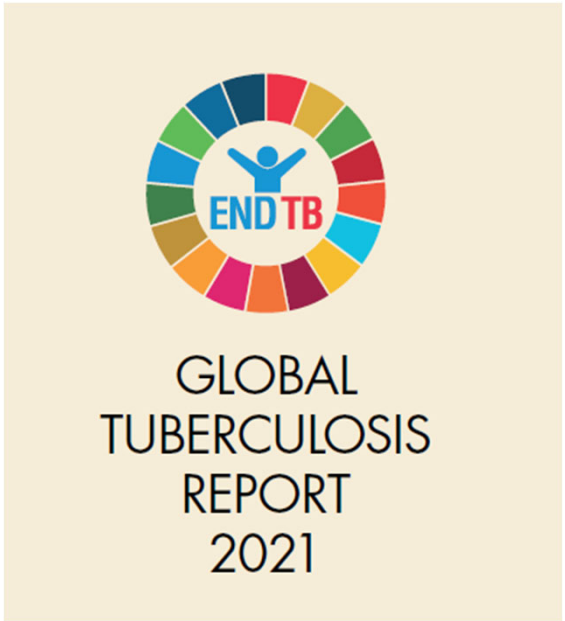

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WHO Global Report

- Reports annual estimates of Global TB:
  - Incidence, prevalence & mortality
  - Regional & country levels
    - 22 countries [195], 10 in Africa [54]
  - Age & gender
  - ***No specific statistics in pregnant patients***

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TB Incidence/Prevalence Worldwide

- Disaggregation by age (2012)
  - Adolescents/adults, ≥ 15 years
  - Children (0-14 years)
  - Inclusion of child cases is limited

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Prior Challenges, New Goals

- Limited focus on non-infectious TB
- New focus on child/maternal health (2012)
  - Increased surveillance, identification and reporting
  - Focus on development of enhanced diagnostics

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Enhancing Childhood TB Estimates

- Improved health infrastructure
  - Integration of child/maternal health services
- Funding for contact investigations
  - *all infants & children living with a TB case
- Promotion of case-based recording
  - Age-specific data

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ALL OF THIS "PROGRESS" ***WAS*** MADE… *then*…

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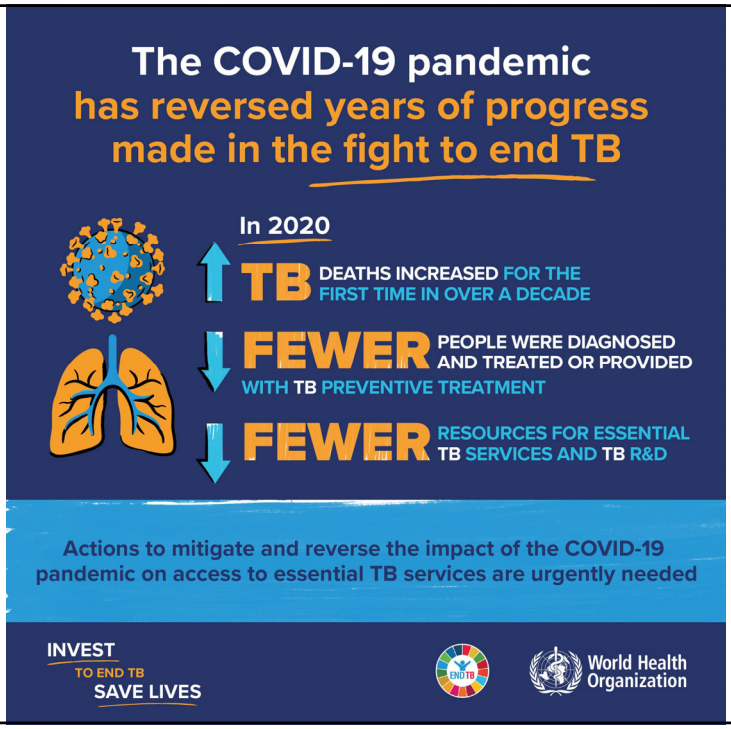

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COVID Pandemic, Impact on Global TB

Dr Tedros Adhanom Ghebreyesus
Director-General
World Health Organization

"Ending this debilitating disease remains a priority for WHO, and in recent years, we have made encouraging progress globally. But the COVID-19 pandemic has put these gains at risk. Not only does the virus pose an increased risk to people with TB, it has also caused severe disruption to services.

I want to remind you that the struggle to end TB is not just a struggle against a single disease. It's also the struggle to end poverty, inequity, unsafe housing, discrimination and stigma, and to extend social protection and universal health coverage. If the pandemic has taught us anything, it's that health is a human right, not a luxury for those who can afford it.

With solidarity, determination and the equitable use of tools, we will defeat COVID-19. And with the same solidarity, determination and equitable use of tools, we can end TB."

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- TB funding ↓ from 5.8 billion → 5.3 billion
  - (<50% of need)
- Monetary & HR shortages
  - Reduction in TB case detection & reporting
  - Supply- and demand-side disruptions
    - Affected both diagnostic & treatment services

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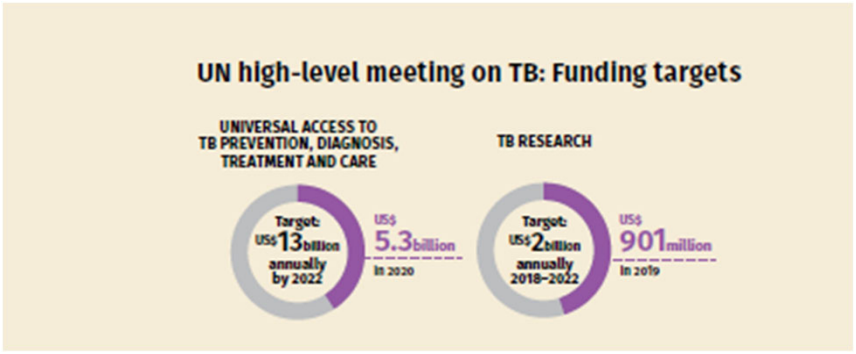
UN high-level meeting on TB: Funding targets
UNIVERSAL ACCESS TO TB PREVENTION, DIAGNOSIS, TREATMENT AND CARE
Target: US$13billion annually by 2022
US$ 5.3billion in 2020
TB RESEARCH
Target: US$2billion annually 2018–2022
US$ 901million in 2019

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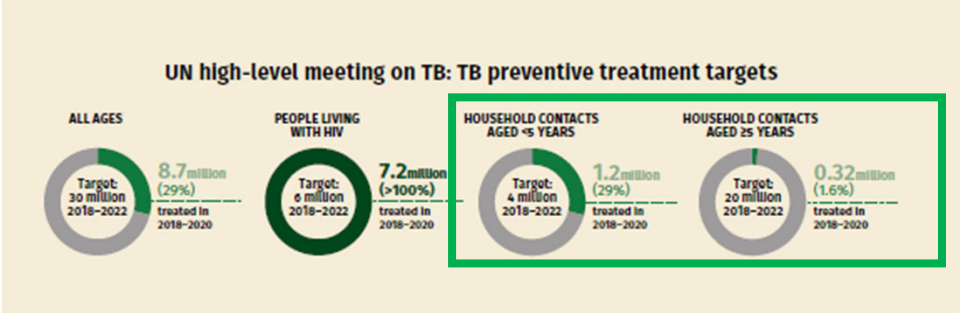
UN high-level meeting on TB: TB preventive treatment targets
ALL AGES
Target: 30 million 2018–2022
8.7million (29%) treated in 2018–2020
PEOPLE LIVING WITH HIV
Target: 6 million 2018–2022
7.2million (>100%) treated in 2018–2020
HOUSEHOLD CONTACTS AGED <5 YEARS
Target: 4 million 2018–2022
1.2million (29%) treated in 2018–2020
HOUSEHOLD CONTACTS AGED ≥5 YEARS
Target: 20 million 2018–2022
0.32million (1.6%) treated in 2018–2020

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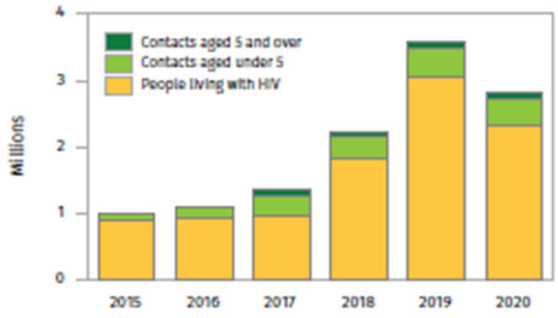
FIG. 26

The global number of people provided with TB preventive treatment, 2015–2020[a]



[a] The number of people living with HIV who were provided with TB preventive treatment in 2019 is lower than published in the *Global tuberculosis report 2020*. This is due to an update of the data reported by India.

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BCG Vaccination Worldwide

- Provided by 154 countries
  - 53 ≥ 95%
  - 31 reported > 5% reduction in coverage (due to funding)

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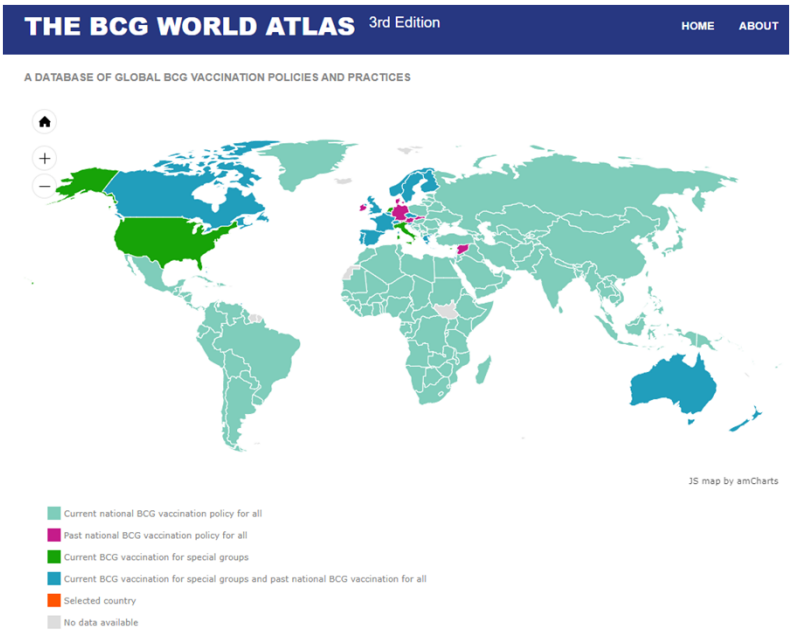

http://www.bcgatlas.org/index.php

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TB Incidence

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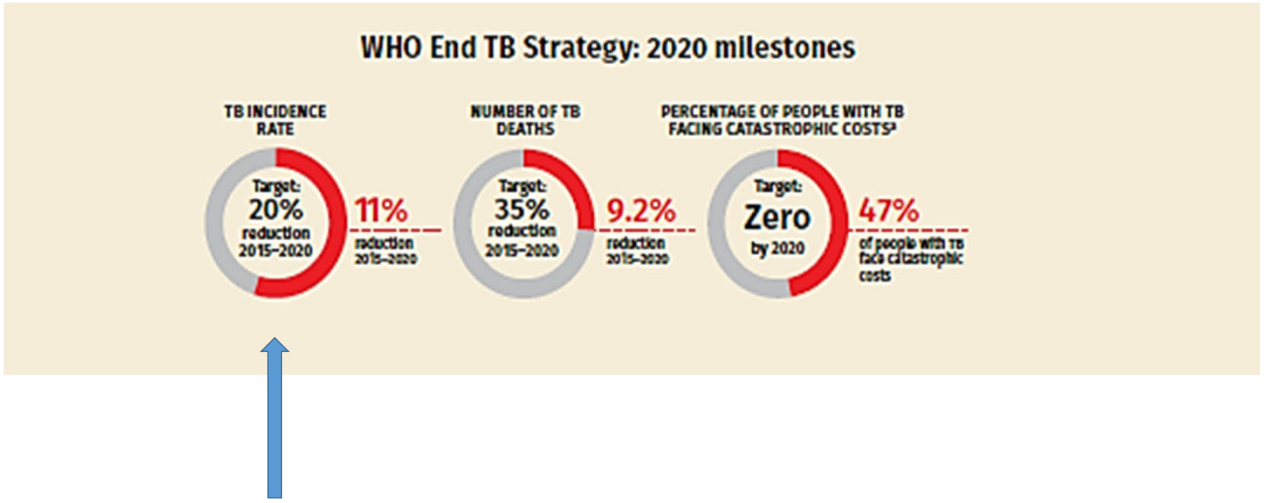

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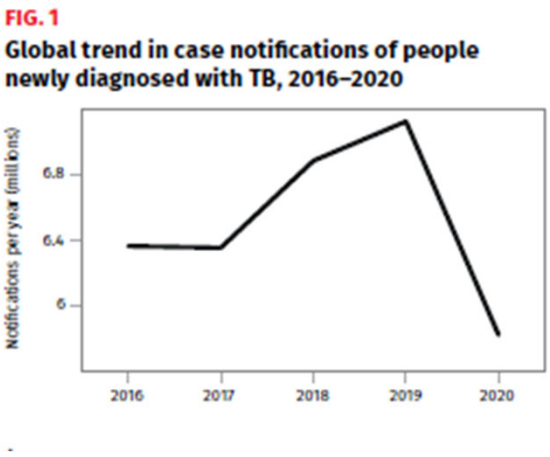
18% Reduction in TB reporting



7.1 million (2019) → 5.8 million (2020)

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FIG. 3
The 16 countries with the largest contributions to the global shortfall in TB notifications in 2020 compared with 2019

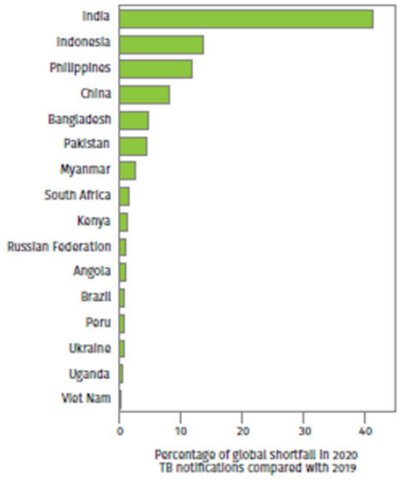

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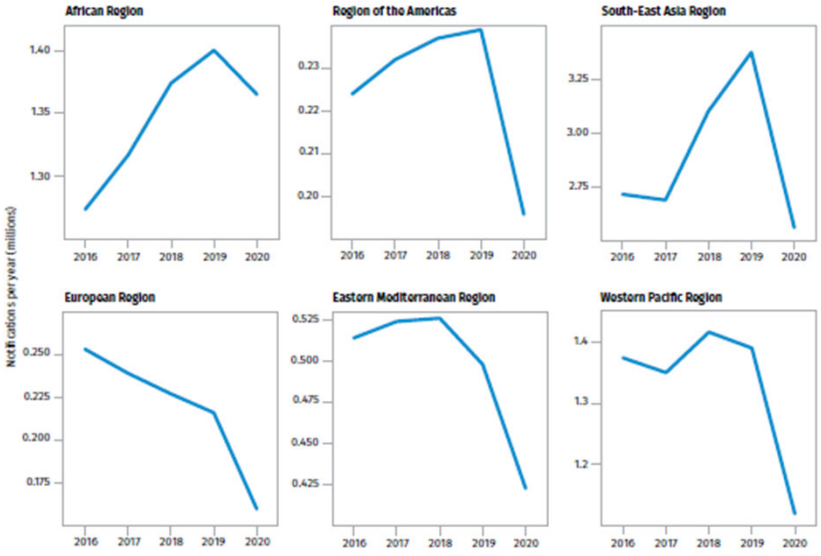
FIG. 2
Trends in case notifications of people newly diagnosed with TB by WHO region, 2016–2020



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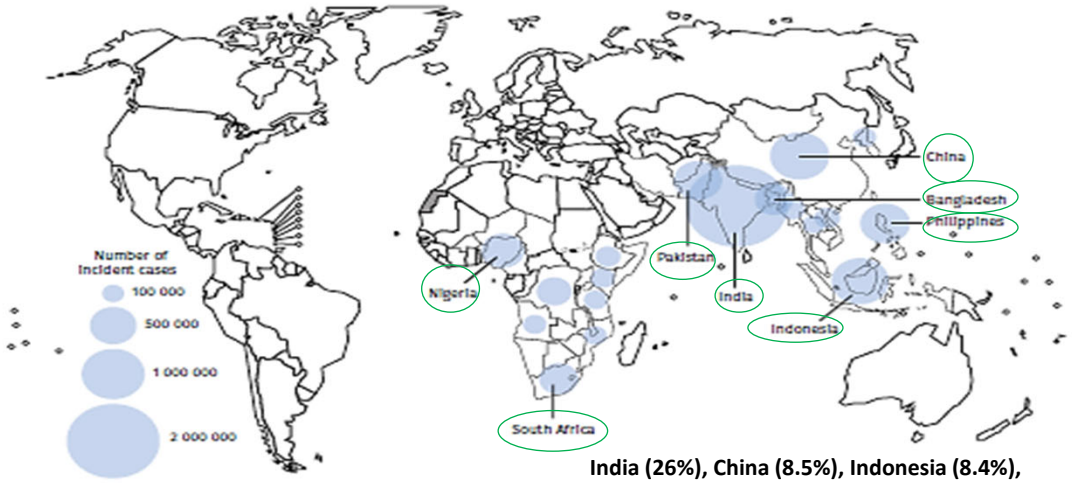
- 9.9 million new cases ***(2020)***
  - 30 HB countries → 86% of estimated incident cases
  - 127/100K
- Most new cases reported in:
  - SE Asia (43%)
  - Africa (25%)
  - Western Pacific (18%)

65

FIG. 11

Estimated TB incidence in 2020, for countries with at least 100 000 incident cases

The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2020, are labelled.



India (26%), China (8.5%), Indonesia (8.4%), Philippines (6.0%), Pakistan (5.8%), Nigeria (4.6%), Bangladesh (3.6%), South Africa (3.3%)

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FIG. 18
The relationship between GDP per capita and the prevalence of undernutrition, and TB incidence per 100 000 population

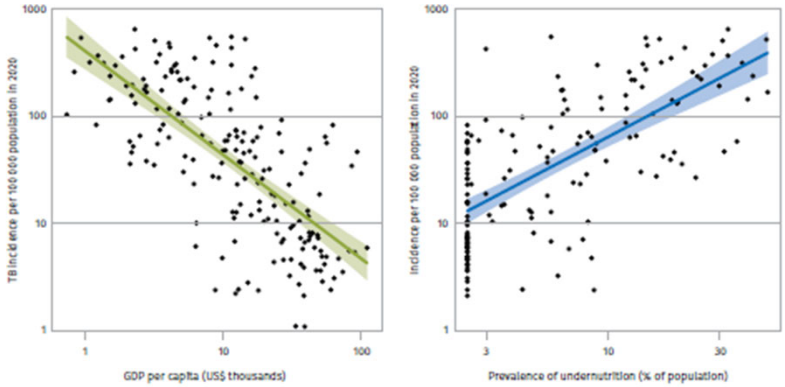

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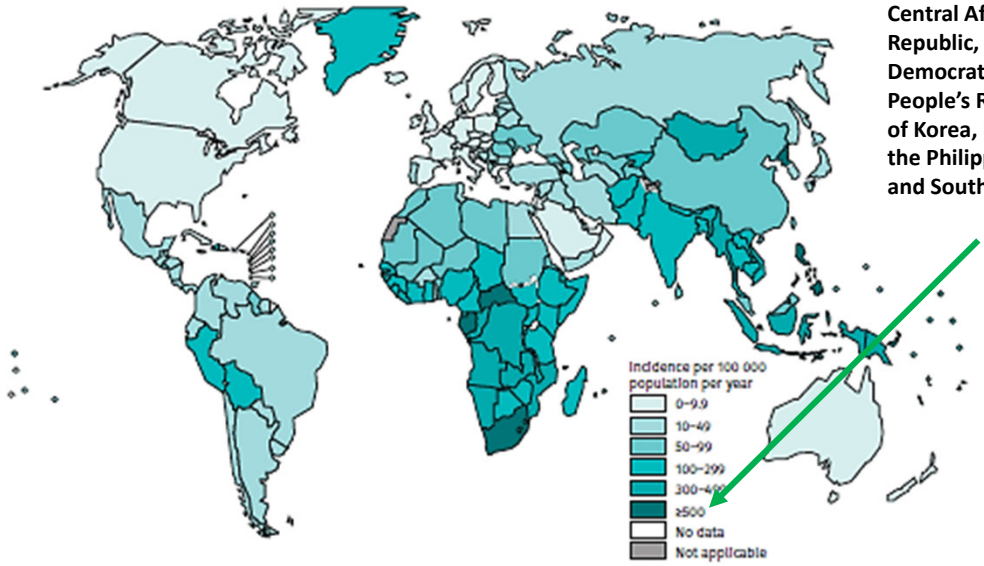
FIG. 13
Estimated TB incidence rates, 2020



Central African Republic, Democratic People's Republic of Korea, Lesotho, the Philippines and South Africa

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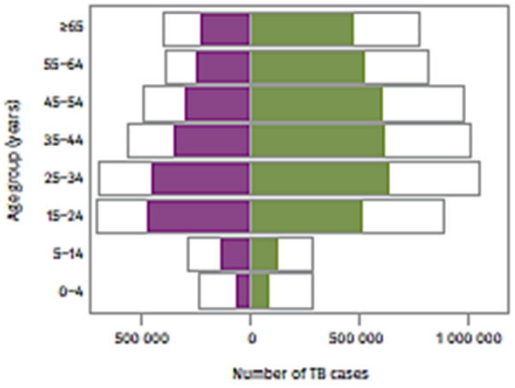
Women 33%

FIG. 1.2
Global estimates of TB incidence (black outline) and case notifications of people newly diagnosed with TB disaggregated by age and sex (female in purple; male in green), 2020



Children 11% (1.1 million)

Highest burden of new TB cases – in adult males (56%)

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TB Incidence in Children

- Mathematic model, estimate (2014)
  - ~1,000,000 (range: 900,000 – 1,100,000) TB cases
  - 10% of the cases
- ~32,000 with MDR-TB
- ~53 million TB infection cases
  - (in the 22 HB countries)

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MDR/RR-TB Incidence Worldwide

- Incidence is stable
  - 3-4% new infections
  - 18-21% previously treated
- Highest proportion of cases (>50%)
  - Countries of the former Soviet Union

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Global burden of drug-resistant tuberculosis in children: a mathematical modelling study

Peter J Dodd, Charalambos Sismanidis, James A Seddon

WHO Global Project DR Surveillance 1988-2014

Lancet Infect Dis 2016; 16: 1193-1201
Published Online June 21, 2016
http://dx.doi.org/10.1016/S1473-3099(16)30132-3

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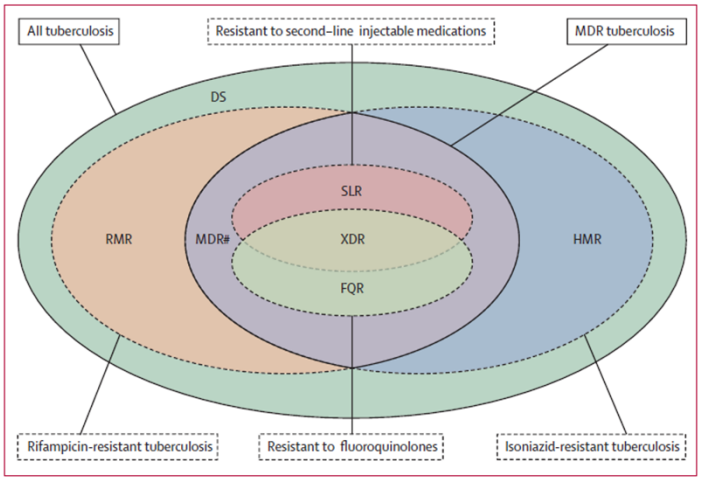

Figure 1: **Definitions of drug-resistance types used in our analysis**
DS=drug-susceptible (susceptible to isoniazid and rifampicin). HMR=isoniazid monoresistant. RMR=rifampicin monoresistant. MDR=multidrug resistant. MDR#=multidrug resistant only to isoniazid and rifampicin. FQR=multidrug resistant to isoniazid and rifampicin plus resistant to a fluoroquinolone but not any second-line injectable. SLR=multidrug resistant to isoniazid and rifampicin, plus resistant to a second-line injectable but not to any fluoroquinolone. XDR=extensively drug resistant (multidrug resistant to isoniazid and rifampicin plus resistant to at least one fluoroquinolone and at least one second-line injectable). We did not consider resistance to other antituberculosis drugs.

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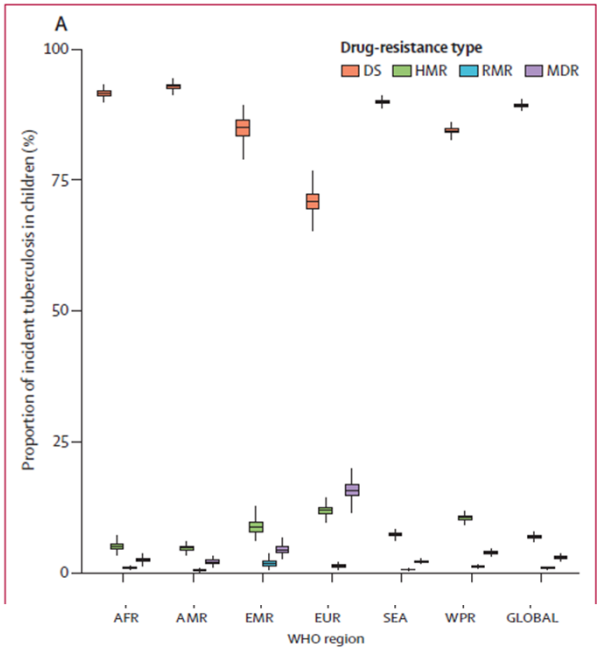
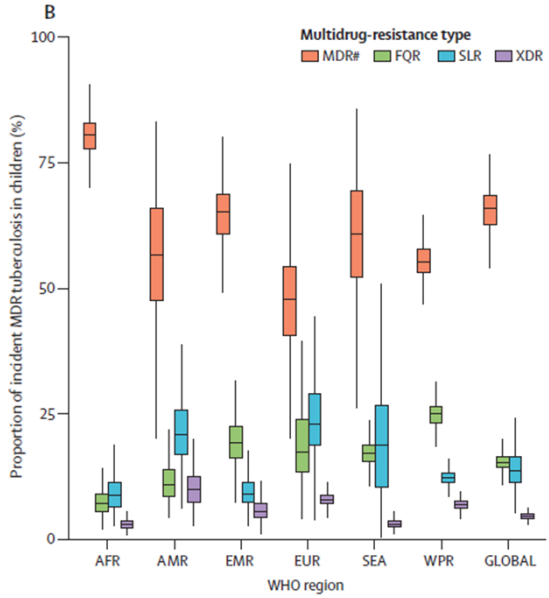


- 2014
  - 6.9% INH R
  - 2.9% MDR
    - 4.7% XDR

74



- Estimated incidence
- 847K R cases
  - 25K MDR

75

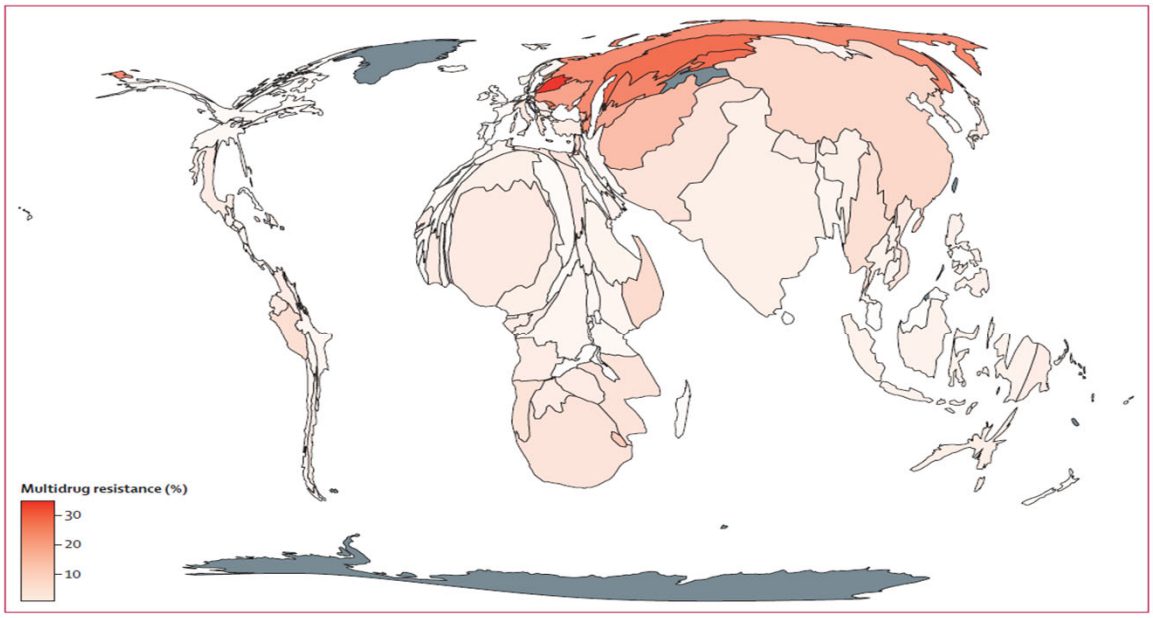


Figure 3: **Cartogram showing total incidence of MDR tuberculosis in children in 2014 by area**
We used the Gastner-Newman method[19] to calculate incidences and depict the proportion of incidences in children with multidrug resistant (MDR) tuberculosis by colour (grey shading indicates no estimate).

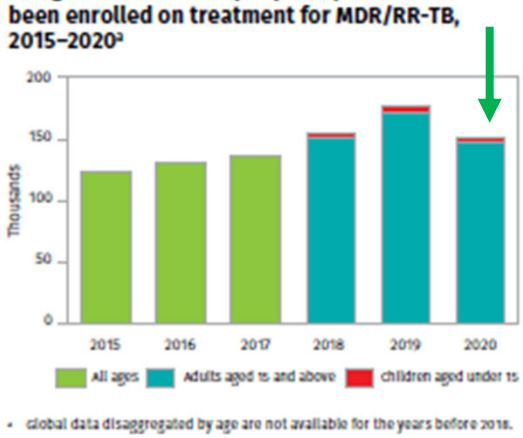
76

- ~67 million children infected
  - 2 million MDR
  - 101,000 XDR
- Many children undiagnosed
  - At risk of developing DR disease
    - In childhood
    - In adulthood

77

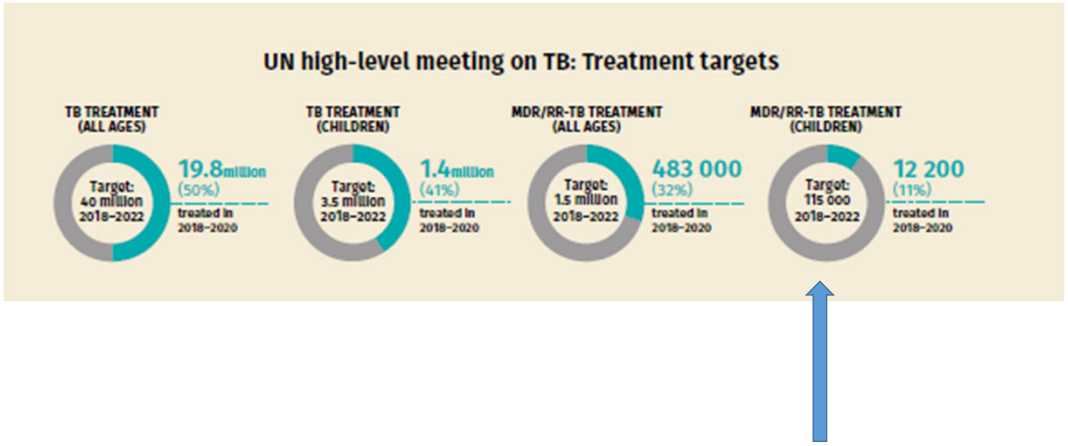
FIG. 25

The global number of people reported to have been enrolled on treatment for MDR/RR-TB, 2015–2020[a]



[a] Global data disaggregated by age are not available for the years before 2018.

78



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Tuberculosis Epidemiology in Children in the U.S.

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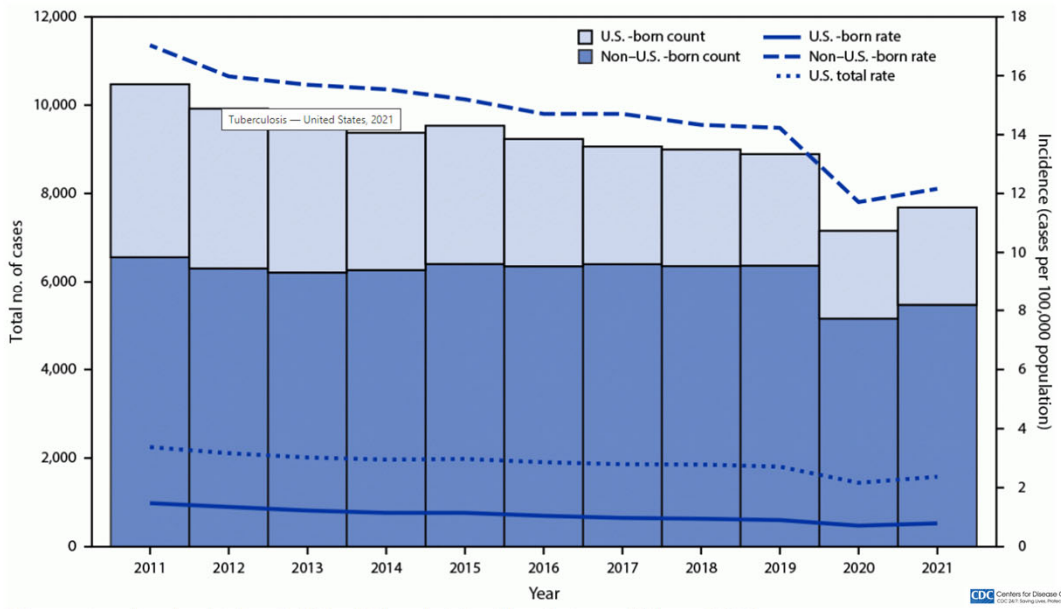
FIGURE. Tuberculosis disease case counts* and incidence,† by patient birth origin§ — United States, 2011–2021



* Case counts are based on data from the National Tuberculosis Surveillance System as of February 9, 2022.

CDC Centers for Disease Control and Prevention

Morbidity and Mortality Weekly Report (*MMWR*)

81

Epidemiology of tuberculosis among children and adolescents in the USA, 2007–17: an analysis of national surveillance data

Tori L Cowger, Jonathan M Wortham, Deron C Burton

Lancet Public Health 2019; 4: e506–16

82

	Reported in US states*				Reported in US-affiliated islands† (n=897)	Total reported to the NTSS (n=6072)
	US born‡ (n=3520)	Non-US born (n=1655)	Total (n=5175)	p value§		
Age, years						
<15	2977 (85%)	919 (56%)	3896 (75%)	<0·0001	754 (84%)	4650 (77%)
<1	448 (13%)	26 (2%)	474 (9%)	<0·0001	55 (6%)	529 (9%)
1–4	1503 (43%)	253 (15%)	1756 (34%)	<0·0001	293 (33%)	2049 (34%)
5–14	1026 (29%)	640 (39%)	1666 (32%)	<0·0001	406 (45%)	2072 (34%)
15–17	543 (15%)	736 (45%)	1279 (25%)	<0·0001	143 (16%)	1422 (23%)

68% overall

8% of total (adults + children)

83

	Reported in US states*				Reported in US-affiliated islands† (n=897)	Total reported to the NTSS (n=6072)
	US born‡ (n=3520)	Non-US born (n=1655)	Total (n=5175)	p value§		
Race or ethnicity¶						
Asian	468 (13%)	591 (36%)	1059 (20%)	<0·0001	46 (5%)	1105 (18%)
Black	861 (25%)	489 (30%)	1350 (26%)	<0·0001	0	1350 (22%)
Hispanic	1659 (47%)	444 (27%)	2103 (41%)	<0·0001	7 (1%)	2110 (35%)
Native American or Alaska Native	107 (3%)	0	107 (2%)	<0·0001	0	107 (2%)
Native Hawaiian or other Pacific Islander	100 (3%)	47 (3%)	147 (3%)	0·9896	834 (93%)	981 (16%)
Two or more races	36 (1%)	9 (1%)	45 (1%)	0·0849	1 (<1%)	46 (1%)
White	277 (8%)	65 (4%)	342 (7%)	<0·0001	0	342 (6%)

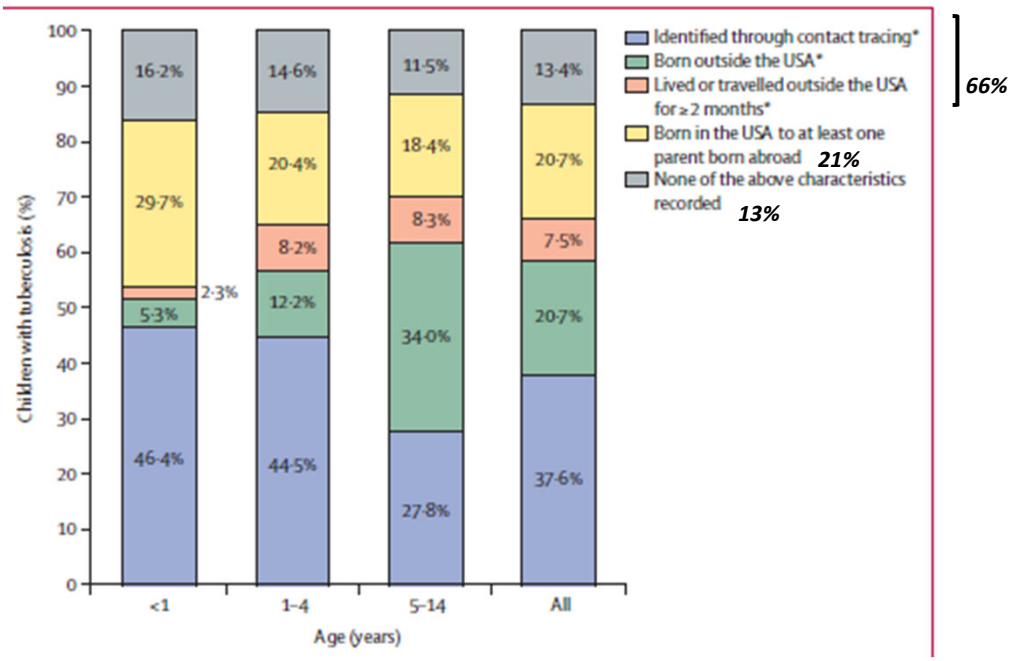
84

	Reported in US states*				Reported in US-affiliated islands† (n=897)	Total reported to the NTSS (n=6072)
	US born‡ (n=3520)	Non-US born (n=1655)	Total (n=5175)	p value§		
Nativity of parents or primary guardians‖						
Both US born	604 (20%)	40 (4%)	644 (17%)	<0·0001	25 (3%)	669 (14%)
Both non-US born	1205 (41%)	526 (57%)	1731 (44%)	<0·0001	372 (49%)	2103 (45%)
Non-US born and US born	284 (10%)	19 (2%)	303 (8%)	<0·0001	9 (1%)	312 (7%)
US born and unknown	280 (9%)	15 (2%)	295 (8%)	<0·0001	3 (<1%)	298 (6%)
Non-US born and unknown	355 (12%)	224 (24%)	579 (15%)	<0·0001	137 (18%)	716 (15%)
Both unknown	249 (8%)	95 (10%)	344 (9%)	0·0654	208 (28%)	552 (12%)

85

	Reported in US states*				Reported in US-affiliated islands† (n=897)	Total reported to the NTSS (n=6072)
	US born‡ (n=3520)	Non-US born (n=1655)	Total (n=5175)	p value§		
Primary reason evaluated for tuberculosis**						
Tuberculosis symptoms	1220 (35%)	698 (42%)	1918 (37%)	<0·0001	457 (51%)	2375 (39%)
Contact investigation	1456 (41%)	159 (10%)	1615 (31%)	<0·0001	306 (34%)	1921 (32%)
Abnormal chest x-ray	550 (16%)	360 (22%)	910 (18%)	<0·0001	108 (12%)	1018 (17%)
Immigration medical exam	0	208 (13%)	208 (4%)	<0·0001	6 (1%)	214 (4%)
Incidental laboratory result	152 (4%)	72 (4%)	224 (4%)	0·9576	14 (2%)	238 (4%)
Targeted testing	95 (3%)	104 (6%)	199 (4%)	<0·0001	2 (<1%)	201 (3%)
Other††	16 (1%)	22 (1%)	38 (1%)	0·0006	0	38 (1%)

86



87

	Nativity of parents or primary guardians†	Number with tuberculosis	Population aged <15 years‡	Incidence rate (95% CI)§	Incidence rate ratio (95% CI)
Non-US-born child	All nativities	919	1765819	6·5 (6·1–6·9)	23·1 (20·9–25·6)
US-born child	Both non-US born	1205	6310790	2·4 (2·3–2·5)	8·5 (7·7–9·3)
US-born child	One US born, one non-US born	284	3629607	1·0 (0·9–1·1)	3·5 (3·0–4·0)
US-born child	Both US born	604	26819512	0·3 (0·3–0·3)	1 (ref)

*The nativity of parents or primary guardians variable was introduced in 2009 and only collected for children with tuberculosis aged younger than 15 years. Data are shown for children aged younger than 15 years from 2010 to 2017 when the variable was collected regularly. †Only children with known nativity for two parents or guardians are shown. Children with at least one unknown or missing nativity for parent or guardian not shown to prevent misclassification between National Tuberculosis Surveillance System numerators and US Census Bureau population estimates. ‡Annualised (average) population estimate, 2010–17. §Tuberculosis incidence rate per 100 000 person-years.

Table 4: **Incidence rates of tuberculosis by nativity of child and nativity of parents for children with tuberculosis aged younger than 15 years in US states, 2010–17***

88

- 68% pulmonary TB
  - 22% extra-pulmonary
- 39%, culture confirmed
  - 8% mono INH R
  - 1% RIF R
  - 1% MDR
- 80%, abnormal CXR
- <1% HIV+
- 91% completed treatment
- <1% mortality (n = 32)

89

Incidence

- Overall incidence, 1.0/100,000 person years
- Highest in < 1yr olds (1.9)
- Followed by adolescents (1.4)
- Age-specific incidence (10X) non-US born (9.0)
- Highest in Native Hawaiian/Pacific Islander (114.0)
  - High rates in Marshall Islands & Federated States of Micronesia

90

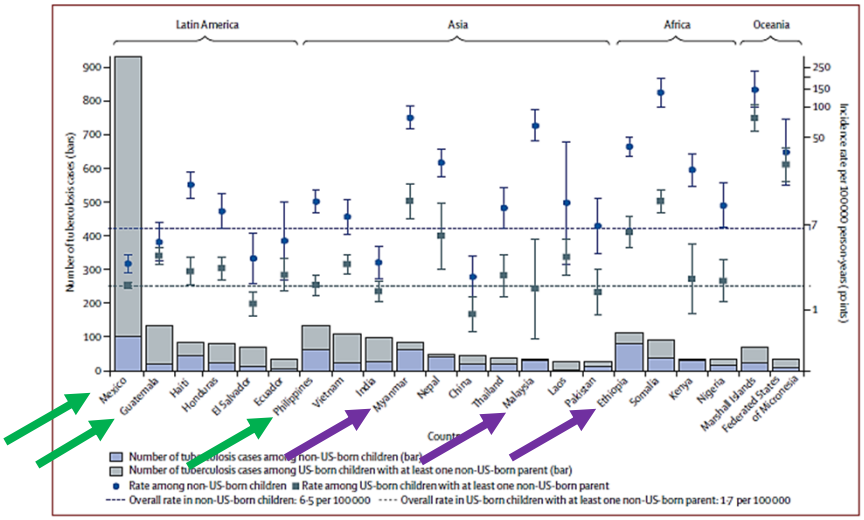


Figure 2: **Number of tuberculosis cases and tuberculosis incidence rates by country of birth among non-US-born children aged younger than 15 years and by parental country of birth among US-born children with at least one non-US-born parent in US states, 2010–17**

Countries are shown by descending case count (bars) within US Census Bureau world regions (Latin America, Asia, Africa, and Oceania). All countries with at least 25 children who were non-US born or had non-US-born parents from that country (total bar height) are shown. For US-born children with at least one non-US-born parent, includes children who have two non-US-born parents, children with one non-US-born and one US-born parent, and children with one non-US-born parent and one parent with unknown nativity. For the 100 children with two non-US-born parents from different countries, children are counted twice for each country of birth for their parents (eg, for a child with one parent born in El Salvador and one parent born in Ecuador, the child will appear in the calculations and totals for both El Salvador and Ecuador).

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TB Mortality Worldwide

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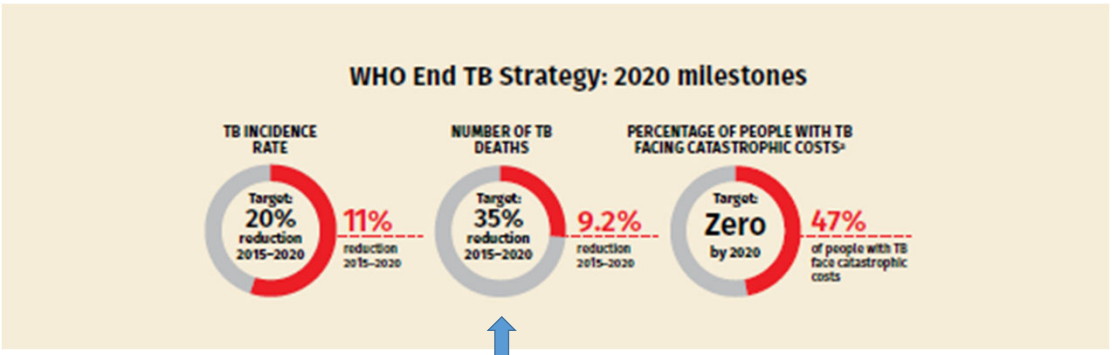


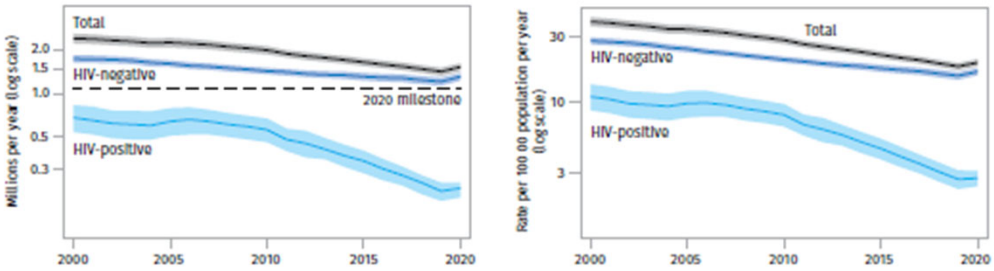
93

1st time >10 years, TB deaths have increased

FIG. 5

Global trends in the estimated number of TB deaths (left) and the mortality rate (right), 2000–2020

Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone of the End TB Strategy.



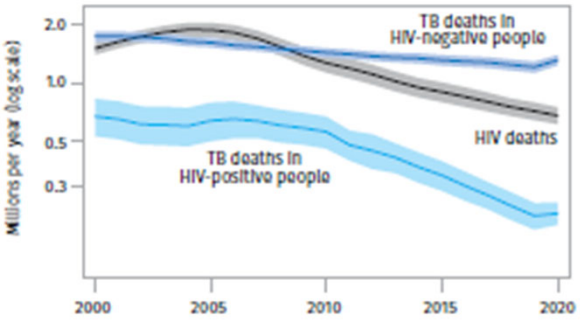
Includes data from 197 countries & territories

94

FIG. 6

Global trends in the estimated number of deaths caused by TB and HIV, 2000–2020[a,b]

Shaded areas represent uncertainty intervals.



[a] For HIV/AIDS, the latest estimates of the number of deaths in 2020 that have been published by UNAIDS are available at http://www.unaids.org/en/. For TB, the estimates for 2020 are those published in this report.

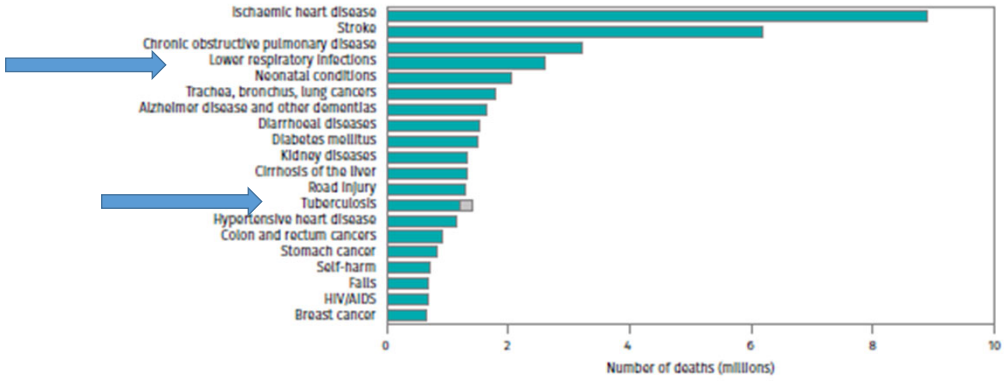
[b] Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.

95

FIG. 7

Top causes of death worldwide in 2019[a,b]

Deaths from TB among HIV-positive people are shown in grey.



[a] This is the latest year for which estimates for all causes are currently available. See WHO estimates, available at https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death

[b] Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.

TB 2nd → leading infectious cause of death

96

- 1.3 million TB deaths (HIV-) ***(2020)***
  - 1.2 million ***(2019)***
- 214K (HIV +) ***(2020)***
  - 209K ***(2019)***
- TB deaths ↑ in most 30 HB countries

97

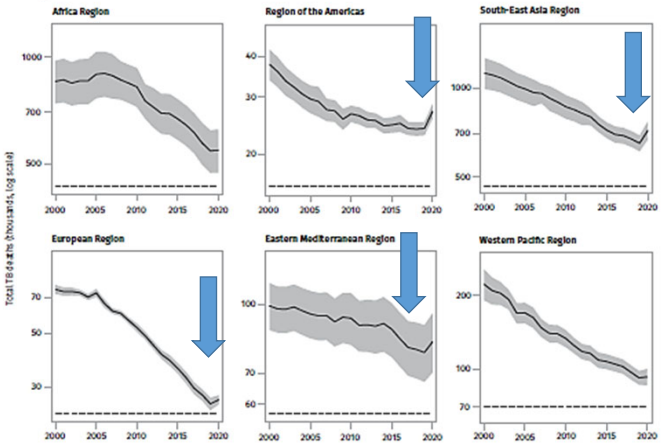
- 85% of TB associated deaths: African and SE Asia
  - India: 38% of global TB deaths (HIV negative)
- Among the HIV negative (1.3 million)
  - 32% women
  - **16% children (<15 years)**
- HIV positive (214K)
  - 40% women
  - **9.8% children**

98

FIG. 8

Trends in the estimated absolute number of TB deaths (HIV-positive and HIV-negative) by WHO region, 2000–2020

Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone of the End TB Strategy.

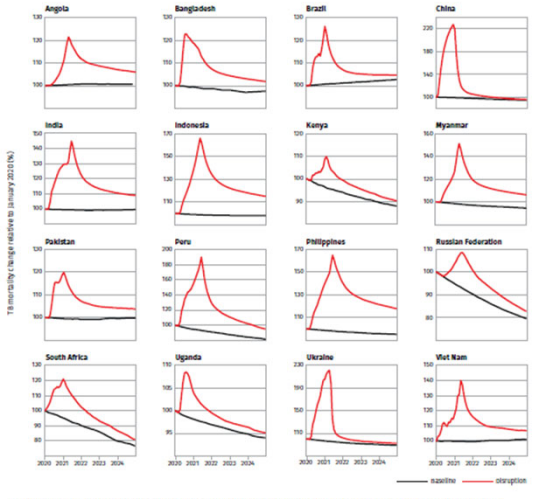


99

FIG. 16

Estimated impact of the COVID-19 pandemic on TB mortality for 16 selected countries, up to 2025

Standardized TB mortality rate (including HIV)*



* These estimates are standardized so that rates in January 2020 equal 100 and all subsequent rates are relative to January 2020. For example, a reading of 115 translates into a 15% increase relative to January 2020. Baseline is a scenario of no COVID-19 disruptions based on pre-2020 trends. The impact of COVID-19 related disruptions on estimated mortality is noticeable from 2020 onwards.

100

TB Mortality in Children

- Mathematic model, estimate (2014)
- Total deaths: 136,000 (range: 115,000-157,000)
  - 81,000 (range: 69,000-93,000) (HIV negative children)
  - 7% of total deaths
  - 55,000 (range: 50,000-60,000) (HIV positive children)
- Case fatality rate: 13.6%

101

Tuberculosis Epidemiology in Pregnancy

102

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Risk of TB during Pregnancy

- Increased maternal mortality
- 2x increase in:
  - premature birth
  - LBW infant
  - IUGR
- 6x risk
  - Perinatal death (*especially in HIV-co-infection)
- Risk of transmission to infant
  - Early post-partum, vulnerable time → 2x risk of TB
  - South African study:
    - Pregnant patients, active TB
    - 15% of infants infected w/in 3 weeks

104

- ***True burden of TB in pregnant patients worldwide is unknown***

105

Tuberculosis in pregnancy: an estimate of the global burden of disease

Jordan Sugarman, Charlotte Colvin, Allisyn C Moran, Olivia Oxlade

Lancet Glob Health 2014;
2: e710–16

106

$$\text{Case notification rate women (age 15–44 years) smear positive} = \frac{\text{Total N new smear positive cases notified woman (15–44 years)}}{\text{Full country population} \times \text{proportion of population women age 15–44 years}}$$

Formula 1·2:

$$\text{Estimated tuberculosis prevalence rate women (age 15–44 years)} = \frac{\text{Case notification rate woman (age 15–44 years) smear positive}}{\text{Full country case notification rate smear positive}} \times \text{Full country tuberculosis prevalence rate}$$

Formula 1·3:

$$\text{Estimated number of tuberculosis cases in pregnant women} = \text{Total population} \times \text{crude birth rate} \times \frac{\text{280 days per pregnancy}}{\text{365 days per year}} \times \text{Estimated tuberculosis prevalence rate women (age 15–44 years)}$$

107

- 216,500 pregnant patients with TB ***(2011)***

108

	Mean (95% uncertainty range)	Rate per 1000 pregnant women (95% uncertainty range)	Percentage of global burden
All countries combined	216 500 (192 100–247 000)	2·1 (1·8–2·4)	--
African Region	89 400 (74 200–110 500)	3·6 (3·0–4·5)	41%
Region of the Americas	4800 (3900–6000)	0·4 (0·3–0·5)	2%
Eastern Mediterranean Region	28 500 (19 700–41 900)	2·3 (1·6–3·4)	13%
European Region	4900 (3800–6300)	0·6 (0·5–0·8)	2%
South-East Asia Region	67 500 (52 000–87 100)	2·4 (1·9–3·1)	31%
Western Pacific Region	21 400 (19 400–23 700)	1·1 (1·0–1·2)	10%

Table 2: Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden by WHO region and combined

109

	Mean (95% uncertainty range)	Rate per 1000 pregnant women (95% uncertainty range)	Percentage of global burden among pregnant women*
Afghanistan	6100 (3200-11 000)	7·2 (3·7-12·8)	2·8%
Bangladesh	8100 (4100-14 300)	3·5 (1·8-6·1)	3·8%
Brazil	800 (400-1600)	0·4 (0·2-0·7)	0·4%
Cambodia	1700 (1400-2000)	5·9 (5·0-7·0)	0·8%
China	9500 (8100-11 100)	0·7 (0·6-0·8)	4·4%
DR Congo	16 200 (8700-26 900)	7·2 (3·9-12·1)	7·5%
Ethiopia	8000 (6500-9600)	3·7 (3·0-4·4)	3·7%
India	44 500 (30 600-62 000)	2·3 (1·6-3·1)	20·6%
Indonesia	9500 (4700-16 400)	2·7 (1·3-4·6)	4·4%
Kenya	4300 (2200-7100)	3·8 (2·0-6·4)	2·0%
Mozambique	4300 (2300-7400)	5·9 (3·2-10·4)	2·0%
Myanmar	2500 (2000-3200)	3·9 (3·1-5·0)	1·2%
Nigeria	10 900 (3000-27 700)	2·1 (0·6-5·4)	5·0%
Pakistan	14 800 (7200-26 300)	4·3 (2·1-7·7)	6·8%
Philippines	6600 (5700-7500)	3·7 (3·2-4·2)	3·0%
Russia	1200 (500-2400)	0·9 (0·4-1·8)	0·5%
South Africa	8400 (4400-14 300)	10·3 (5·4-17·6)	3·9%
Tanzania	3100 (1700-5200)	2·2 (1·2-3·7)	1·4%
Thailand	500 (200-900)	0·9 (0·4-1·6)	0·2%
Uganda	2600 (1400-4400)	2·3 (1·2-3·8)	1·2%
Vietnam	900 (700-1100)	0·8 (0·7-1·0)	0·4%
Zimbabwe	2400 (1400-4100)	7·9 (4·6-13·4)	1·1%
Total	166 200 (143 000-195 500)	2·5 (2·1-2·9)	77·0%

*Total percentage does not sum to 100% because list only shows % of global burden in pregnant women for each of the WHO 22 high tuberculosis burden countries.

Table 3: Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden amongst pregnant women for the 22 high tuberculosis burden countries as classified by the WHO

110

Improvements → TB Elimination

- Redirect resources towards TB prevention & treatment
- Enhanced TB screening at household level
  - Especially among children < 5 years
  - Enhance contact tracing
- Continue BCG vaccination of infants

111

Improvements → TB Elimination

- Increase treatment of those with TB infection –
  - ***discussed in a future webinar***
- Increased access to shorter (1–3 months) regimens (TB infection)
  - ***discussed in a future webinar***

112

https://www.tballiance.org/news/one-million-child-friendly-tuberculosis-medicines

113

114

10 MIN

115

Clinical Case Discussion

116

Clinical Case – Family Cohort (7+)

- Refugees from Afghanistan
  - Urgently evacuated
- Arrived to US in early 2022
  - Father
  - Mother (pregnant at time of arrival)
  - 5 children (2 yo, 3yo, 5 yo, 8 yo, 9yo)

- Overseas pre-immigration screening not available
- Family tested for TB upon arrival to the U.S.

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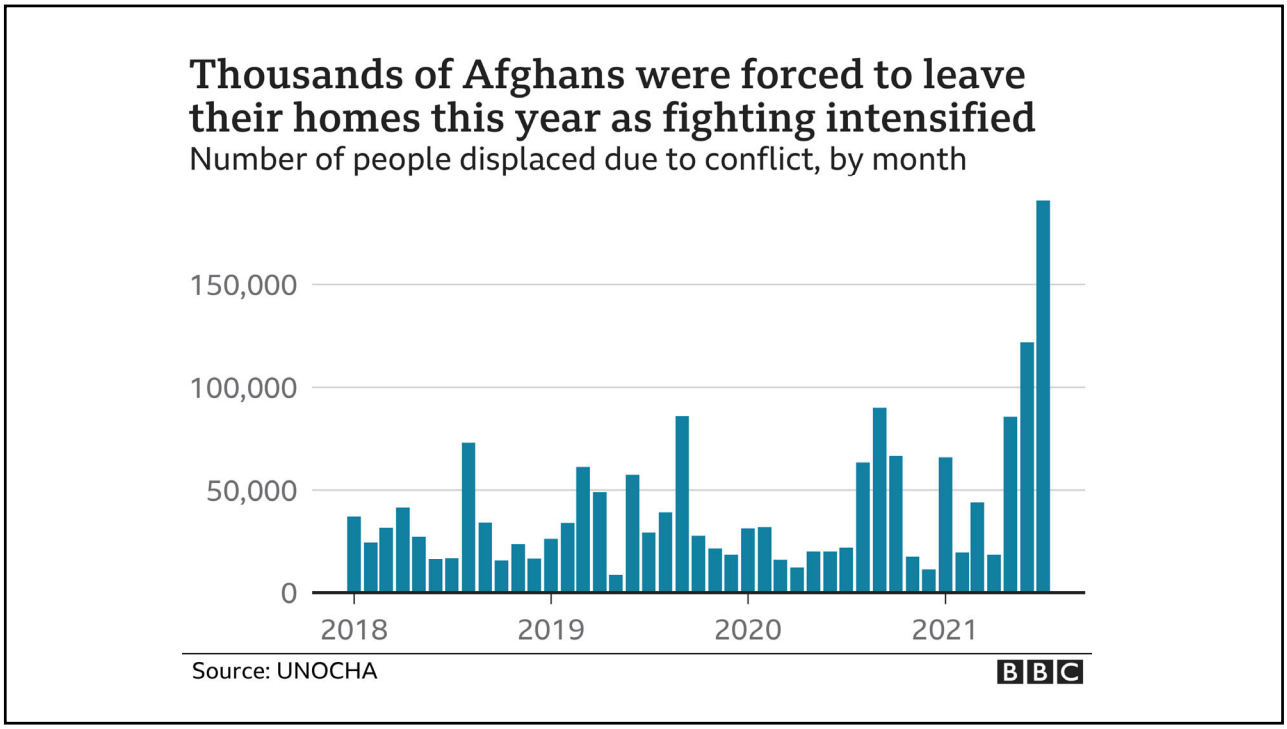
TB in Afghanistan?

118


Thousands of Afghans were forced to leave their homes this year as fighting intensified
Number of people displaced due to conflict, by month
150,000
100,000
50,000
0
2018
2019
2020
2021
Source: UNOCHA
BBC

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BBC

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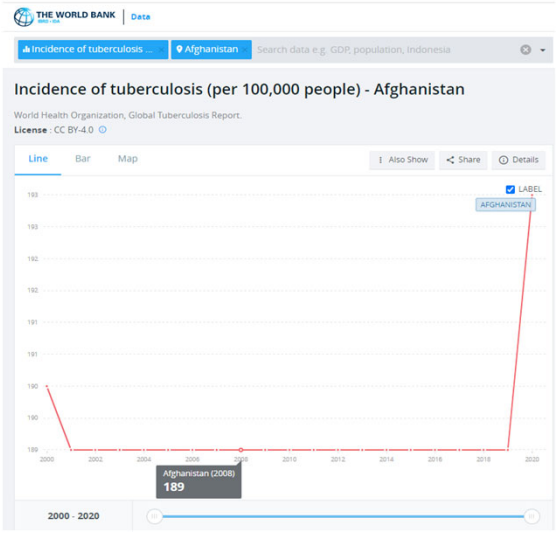
TB in Afghanistan

- A major health problem
- Lack of recent statistics
  - 2016: 65K cases, 11K deaths
  - 2020: 73K cases
    - 15,000 children
    - 11,000 TB related deaths
- 2021 – estimated ***600K cases!***



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journal homepage: www.elsevier.com/locate/amsu

Correspondence

Highlighting the forgotten: Tuberculosis amidst the humanitarian crisis and COVID-19 in Afghanistan

TB CASES
(including DR)

124

? Parents

- Dad – (asymptomatic)
  - Normal CXR, +IGRA, receiving 3HP
- Mom – (asymptomatic)
  - +IGRA ***(at end of pregnancy)***
  - CXR with RUL calcification, otherwise normal

125

Case Discussion

- ***Management of the mother (during pregnancy)?***
- ***Following delivery (now breastfeeding)?***

126

- Mom – (asymptomatic)
  - +IGRA ***(at end of pregnancy)***
  - CXR with RUL calcification, otherwise normal
  - Sputa collected: smear negative, NAAT negative, cultures negative to date (4 weeks)

127

Mother

- ***Treat or not treat? For infection or disease?***

128

Children

- 2mo, 2 yo, 3yo, 5 yo, 8 yo, 9yo

- ***Should they all be tested for TB infection? If so, how?***

129

Children – upon arrival to U.S.

- 2mo, 2 yo, 3yo, 5 yo, 8 yo, 9yo

- 2mo
  - asymptomatic, no test of infection to date

- 2yo, 3yo, 5 yo, 8 yo, 9yo
  - all asymptomatic, +IGRAs

130

- ***All referred to the TCH TB Clinic***

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Children

- 2mo
  - asymptomatic, no test of infection, normal exam & CXR
  - ***Recommended timing of a test of infection?***
  - ***Recommended treatment?***
- 2yo
  - asymptomatic, +IGRA, normal exam & CXR
  - ***Recommended treatment for infection?***
- 3yo, 5 yo, 8 yo
  - all asymptomatic, +IGRAs, normal exams & CXRs
  - ***Recommended treatment for infection?***

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Children

- 2mo
  - asymptomatic, no test of infection, normal exam & CXR
  - PPD to be placed @ 3 mo of age
  - receiving INH biweekly
- 2yo
  - asymptomatic, +IGRA, normal exam & CXR
  - Receiving daily RIF
- 3yo, 5 yo, 8 yo
  - all asymptomatic, +IGRAs, normal exams & CXRs
  - Receiving 3HP

133

TB Clinic Evaluation

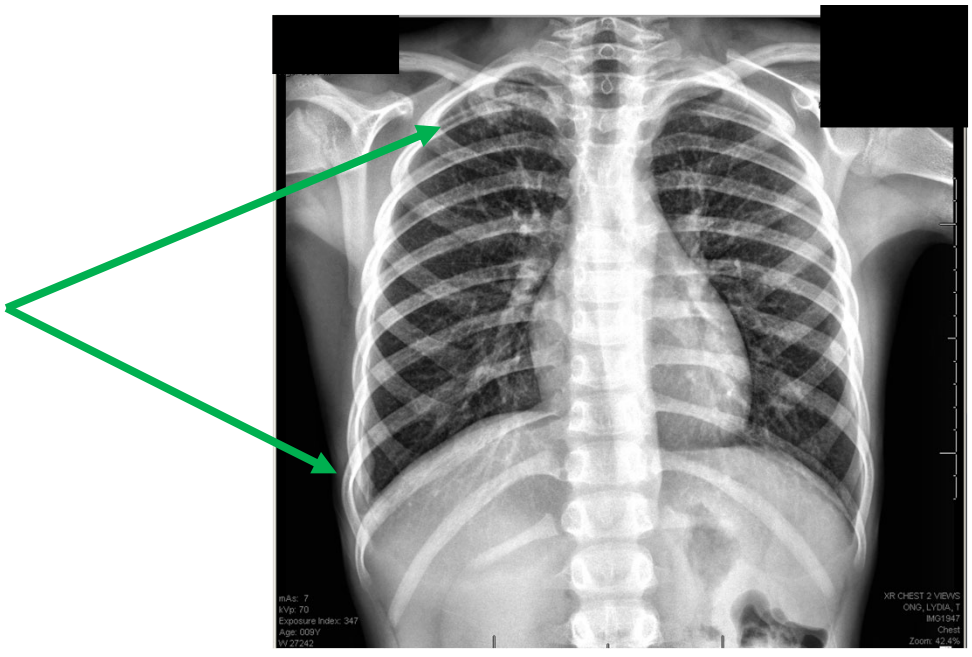
- Interviewed with a Pashto interpreter
- No known contacts with TB
- “has felt warm at night, + night sweats”
- “no cough, no change in activity”

134

Physical Exam

- Afebrile, Weight 25kg (7%) ↓ 1 kg
- Small for age, thin
- No BCG scar
- Normal pulmonary exam

135



136

- ***How should he be managed?***

137

Management

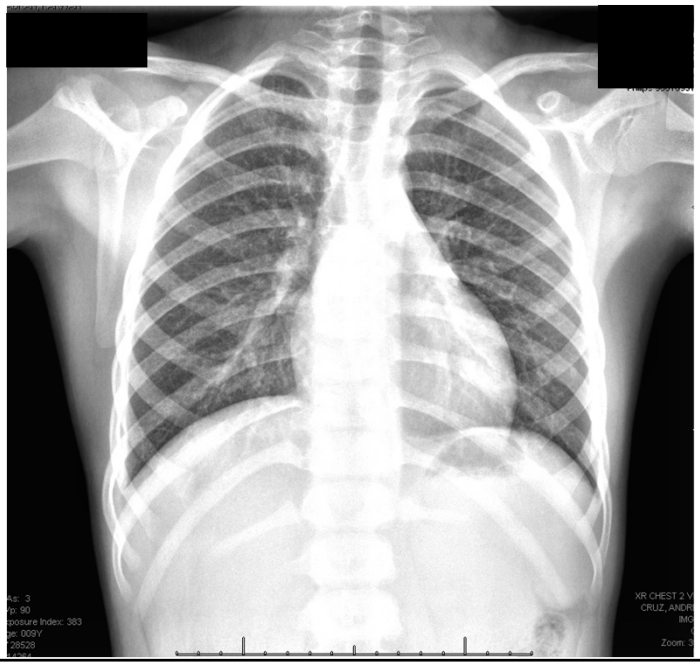
- HIV negative
- Cultures & NAAT obtained in field
  - Negative smear, +NAAT
- Started on RIPE therapy

138

F/U 2 months

- Resolved fever/night sweats
- Weight +2 kg

- Pansusceptible isolate
  - PZA & EMB discontinued



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- ***Final thoughts/discussion from panelists.***

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Clinical Case

- 6yo M, Guatemalan immigrant, BCG immunized
  - Arrived to Houston in July, TX 2021
  - Father came to work for a construction company
    - (3 year term)
  - Mother and 2 siblings remain in rural Guatemala
  - Father speaks Kiche' (some Spanish)
  - Child only speaks Kiche'

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- Developed a soft tissue swelling in R paraspinal region (December 2021)
  - No fevers/systemic symptoms
- Seen by PCP
  - Positive quantiferon (0.87, 0.75)

142

- ***Referred to Dermatology & TB Clinic***

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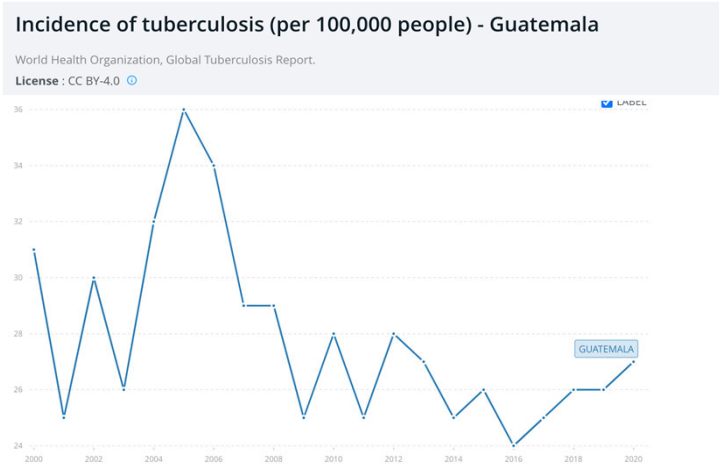
TB in Guatemala?

- Incidence/prevalence in:
  - rural vs. urban areas?

144

- 25 cases/100,000 (WHO)
- 4,900 cases in 2020
  - 530 children
  - 410 TB associated deaths
- Likely underestimated
  - Rural>>>urban areas



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Global health

CASE REPORT

Delays in diagnosis and treatment of extrapulmonary tuberculosis in Guatemala

Pooja Ajay Shah,[1] Merida Coj,[2] Peter Rohloff[3,5]

Patient's perspective

This all started when I was working as a storekeeper. I began to feel some strange symptoms, like the fever and the growths that appeared around my neck. I was worried, but I didn't know what to do. I didn't have a solution. I went to many doctors, and they asked for tests but I could not afford them. I am so thankful that when I came to this clinic, you fought for me. The doctors and the *compañera* [patient care navigator] did a great favor for me by getting me to the hospital in the capital. Then, in the hospital they did all the tests I needed and finally figured out what was happening. They told me I had tuberculosis. The truth is, when I went to the hospital, I was hopeless. But I thank God that it worked out. Now I am very satisfied with the treatment I received.

Shah PA, *et al. BMJ Case Rep* 2017. doi:10.1136/bcr-2017-220777

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Learning points

- In a country with a medium incidence of tuberculosis (TB; 25 cases per 100 000 people), health system segmentation can lead to significant delays in diagnosis and treatment of a classic clinical presentation of extrapulmonary TB.
- Vertical healthcare programmes, in contrast to integrated care, can be highly inefficient, due to provision of redundant testing and incomplete preventative care.
- Public–private partnerships can be employed to overcome some of the inefficiencies in a highly segmented health system, including shortcomings in the laboratory referral network.
- Indigenous people in Guatemala experience poor healthcare access and health outcomes due to barriers of poverty, language and rural residence.
- Patient accompaniment provides a potential solution to the barriers of health system segmentation faced by marginalised populations.

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Clinical case Cont.

- Afebrile, normal RR
- <<3% weight & height
- Poor dentition
- + murmur
- Decreased BS on R
- No HSM
- Non tender back swelling

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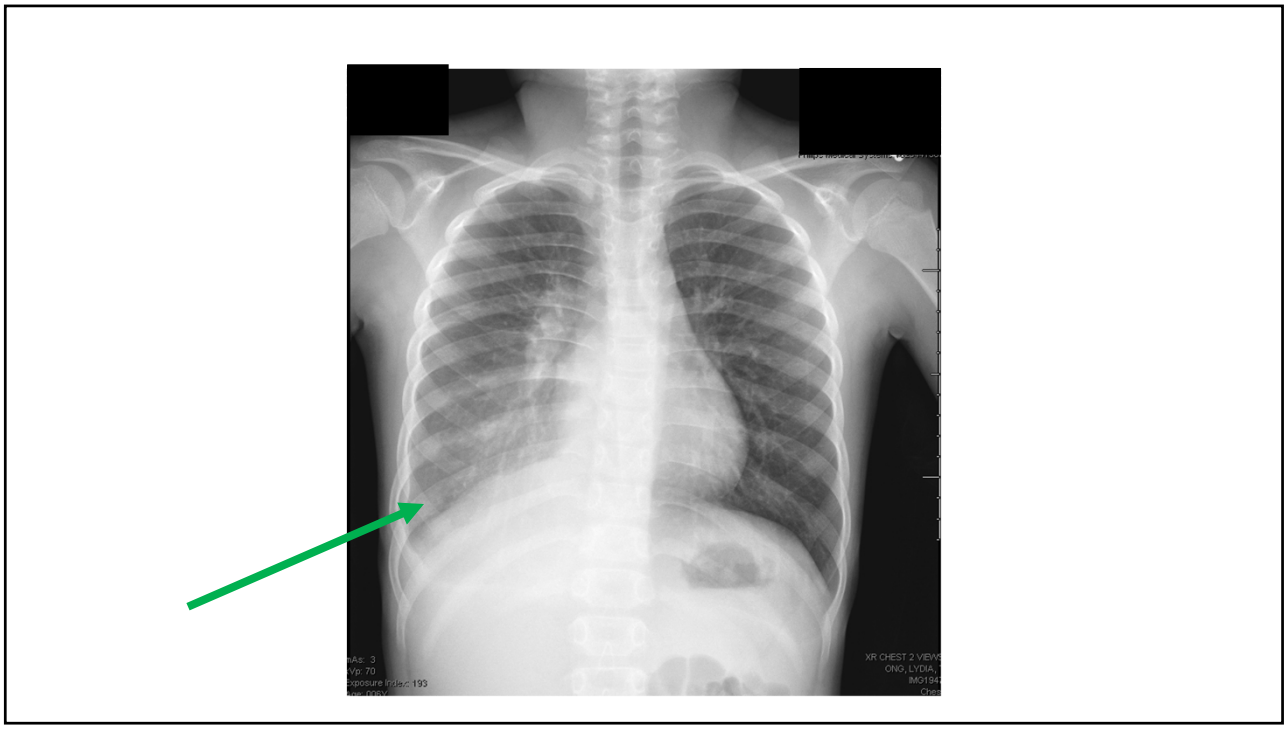

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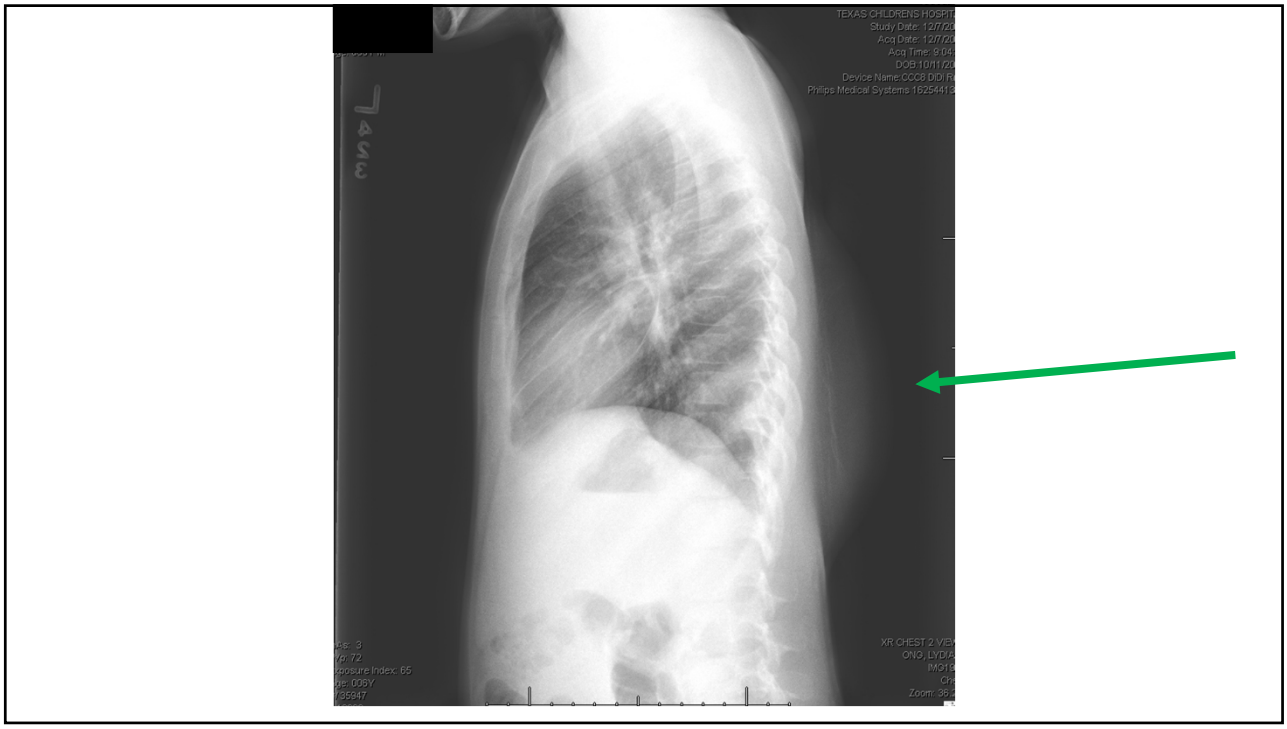
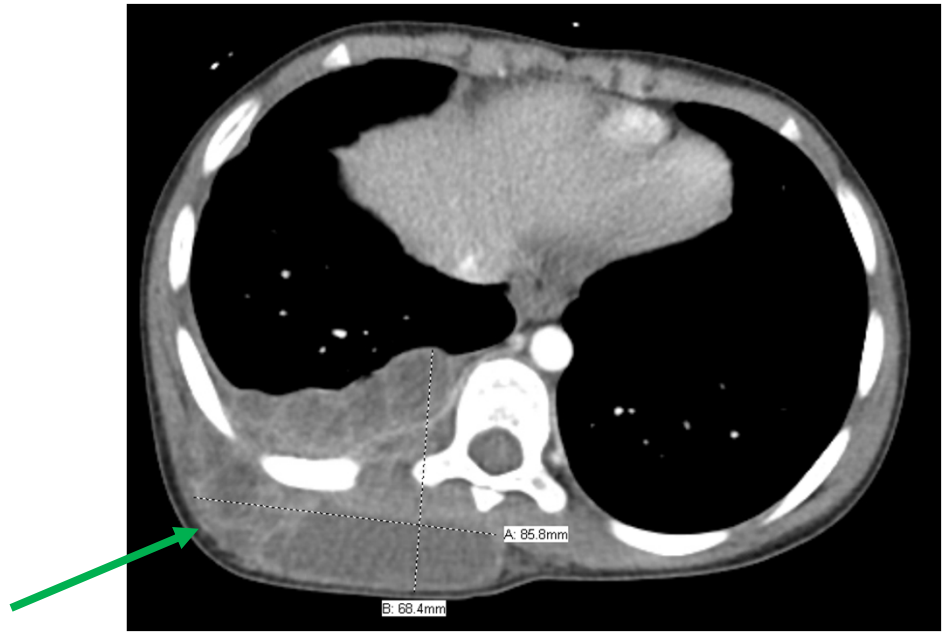


150

- ***How should he be managed?***

151



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Radiologic Diagnosis: Empyema necessitans

- +/- contiguous osteomyelitis of the R 10th rib
- L axillary adenopathy
- R hilar and mediastinal adenopathy
- Multifocal tree-in-bud opacities and nodules
  - Throughout R lung

153

- ***Next steps in management?***

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IR Drainage

- 80mL, pink tinged purulent fluid drained
- 4 pleural biopsies obtained

155

Diagnostics

- HIV negative
- Repeat QFT: 1.9, 1.76
- Pleural fluid
  - Smear negative (degenerated/necrotic debris on pathology)
  - **MTB PCR positive**
  - **Cultures pending**
- **Father's chest radiograph (TCH) → NORMAL**

156

- ***How should the patient be managed?***

157

Management

- Started on RIPE therapy
- + prednisone x4 weeks → taper

158

Mycobacterial Culture Results

- ***Mycobacterium tuberculosis* isolated on culture (19 days)**

Isoniazid 0.1 ug/mL	Suscept
Rifampin 1.0 ug/mL	Suscept
Ethambutol 5.0 ug/mL	Suscept
Pyrazinamide 100 ug/mL	Suscept

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Follow-up – 1 month

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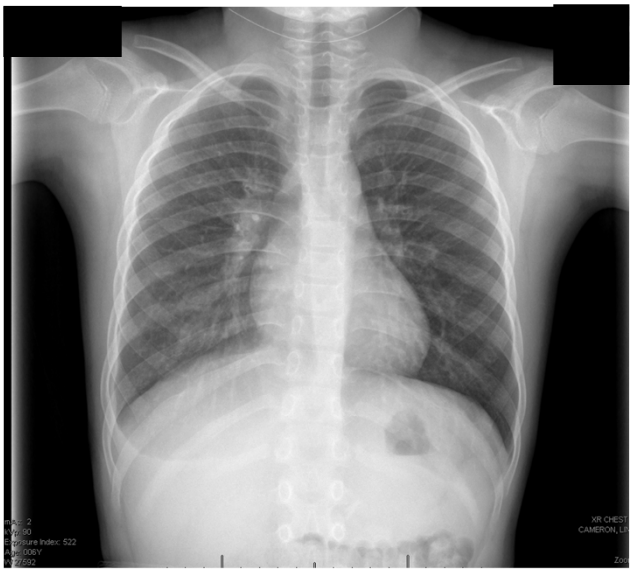
Follow-up – 2 months



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- ***Final thoughts/discussion from panelists.***

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Clinical Case

- 2 mo, U.S. born, ex-full term M
- Asymptomatic

- Exposed to father
  - Household contact
  - Symptomatic x2 months
  - **Smear positive**
  - **Xpert MTB PCR positive**
- Moved to the U.S. from Cameroon in early 2021

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- ***Eek! Based on this what is the infant's risk?***

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Evaluation

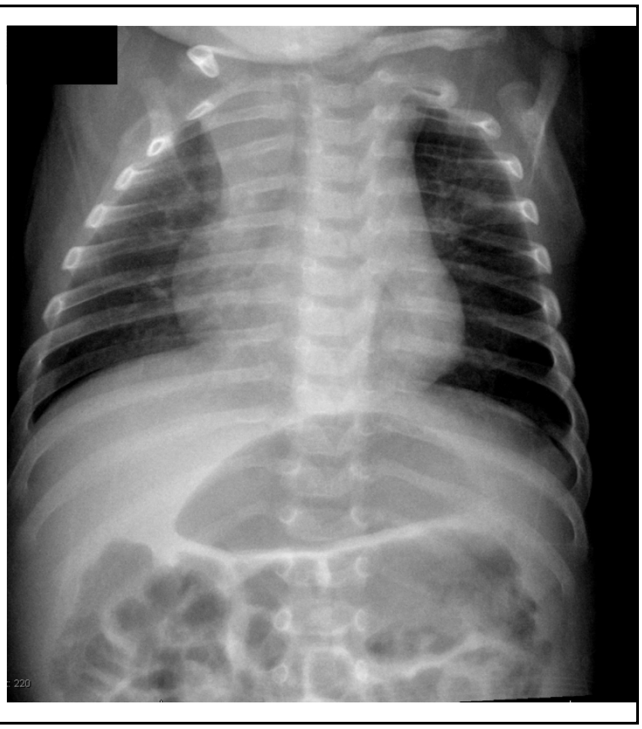
- Well appearing
- Normal exam
- **Quantiferon >10, >10**

- ***Does a "wicked positive" QFT suggest disease over infection?***

166

- Hyper-aerated lungs are clear.
- No lymphadenopathy identified.

Is the lung hyper-aeration concerning?



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Admitted to TCH

- First morning gastric aspirates x3 collected
  - Smear negative
  - MTB PCR negative
  - Cultures pending

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9 mm solid pulmonary nodule in LUL.

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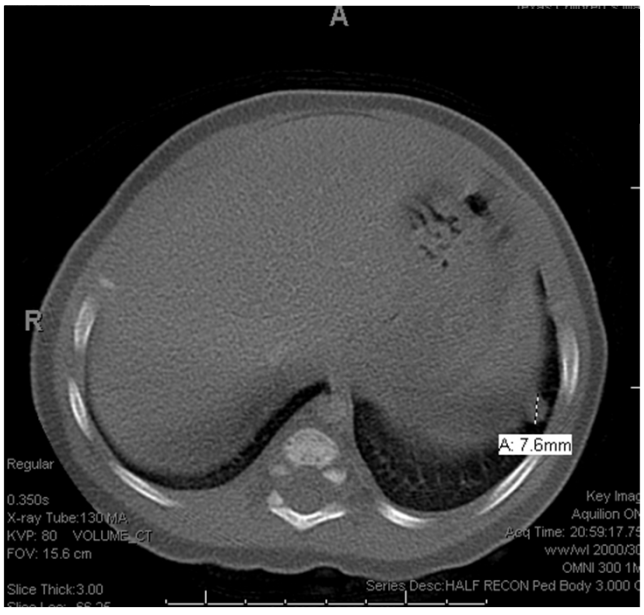

6 mm solid pulmonary nodule in LLL.

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CNS Evaluation

- LP/CSF evaluation
  - WBC 16 (slightly elevated, L 72%)
  - RBC 2,000
  - Protein 99 (slightly elevated)
  - Glucose normal
- MRI brain w/o contrast
  - No evidence of TB meningitis

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- ***Why is his treatment complicated?***

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Management

- PO Levofloxacin, 10 mg/kg, BID (4/27/22 - present)
- PO Isoniazid 150mg once daily (4/29/22 - present)
- PO Linezolid 90 mg daily (4/29/22 - present)
- IV Imipenem 100 mg q12 (4/29/22 - present)
- Augmentin (amoxicillin-clavulanate ES 40mg/kg dose) (4/29/22 - present)

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Update: Source Case – Susceptibility

- Silent RIF mutation (molecular)
- DST – pan-susceptible
- Receiving RIPE therapy (Galveston Co HD)

174

Definitive Management

- RIPE therapy
- High dose RIF

175

- ***Final thoughts/discussion from panelists.***

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Question & Answer

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