TB Update

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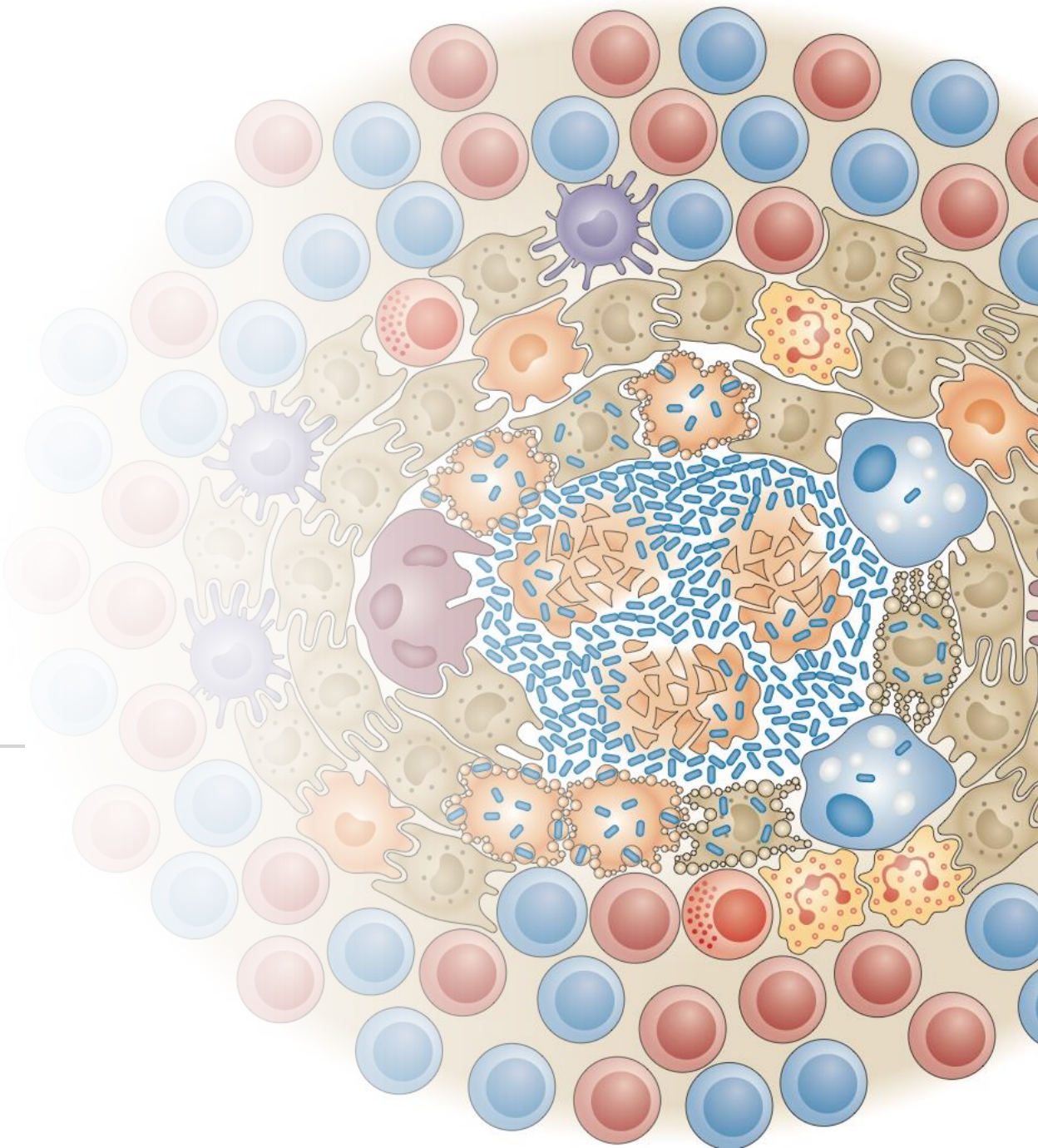
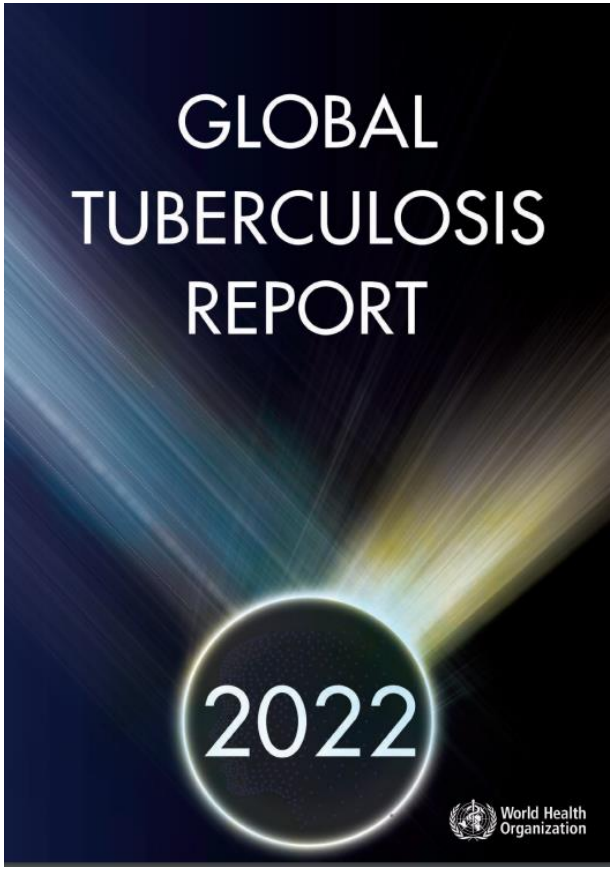


TB Vignette

- Sept: ~50 M PLWH from TB endemic setting 20 years ago reports to urgent care for productive cough >2 months, F, >25# WL and fatigue
- Diagnosed with atypical pneumonia and treated with Z-pack
- Think TB?

2021 Global TB Epidemiology



- Estimated 10.6M people developed TB
  - 4.5% increase from 2020
- 1.6M died from TB
  - Estimated deaths are increasing since 2020

TB: Major Cause of Suffering and Death

First cases Heidelberg (4000 BC), Egypt (3700 BC), Peru (700 AD)

White Plague, scrofula, King's Evil, phthisis, consumption

England 1815: 1 in 4 deaths

France 1918: 1 in 6 deaths

During 20th C: ~100 million deaths

King Louis XIII of France

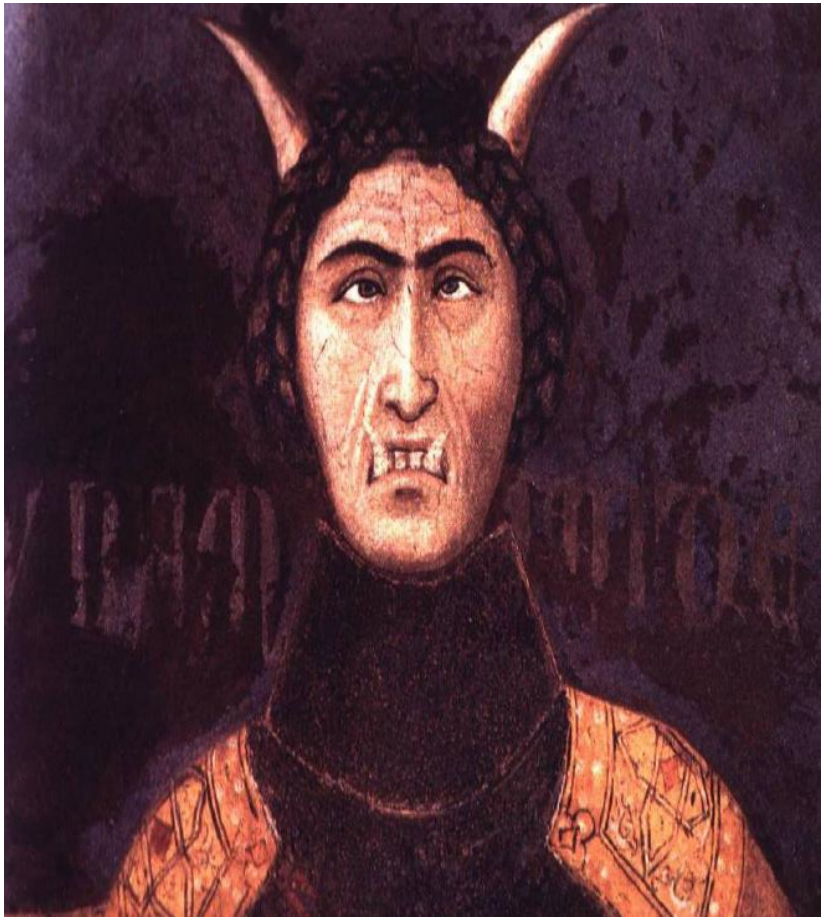
1601-1643

TB Changed Course of Human History

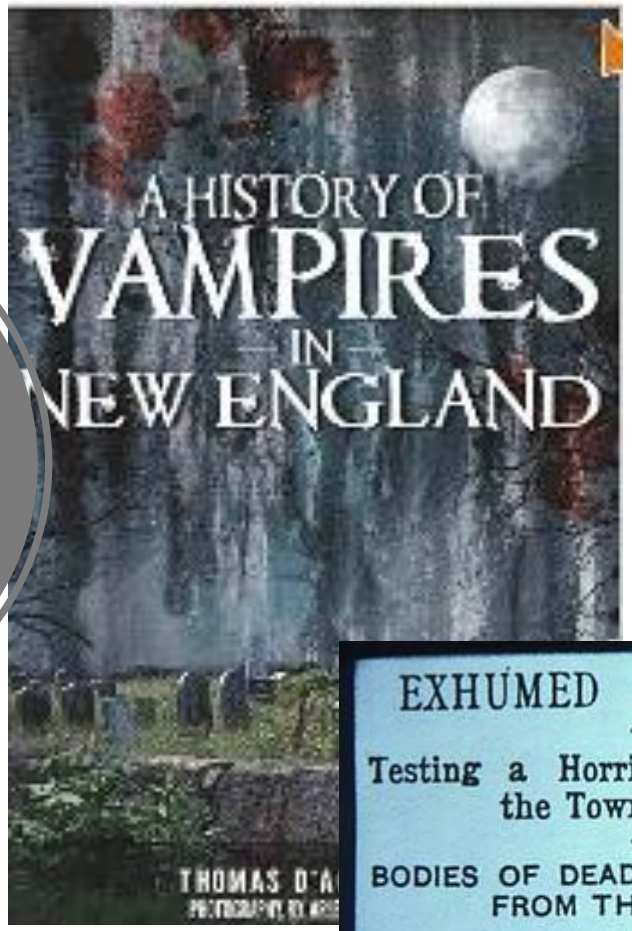
- Bronte Family
- Cardinal Richelieu
- Katherine Mansfield
- Luigi Boccherini
- Amedeo Modigliani
- Sir Walter Scott
- Franz Kafka
- Fyodor Dostoyevsky
- Eleanor Roosevelt
- Jimmie Rogers
- Robert Louis Stevenson
- Anton Chekov
- Doc Holiday
- Igor Stravinsky
- D H Lawrence
- Eugene O'Neill
- Johann von Goethe
- Freidrich Schiller
- Frédéric Chopin
- George Orwell
- Christy Mathewson
- Gavrilov Princip

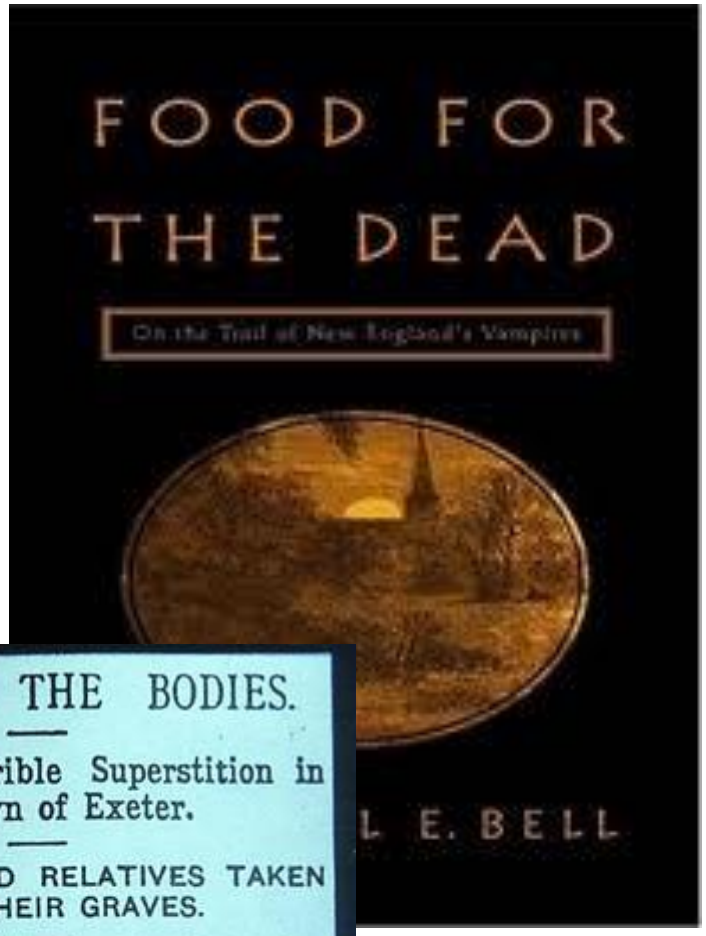
Historic Theories About What Caused TB

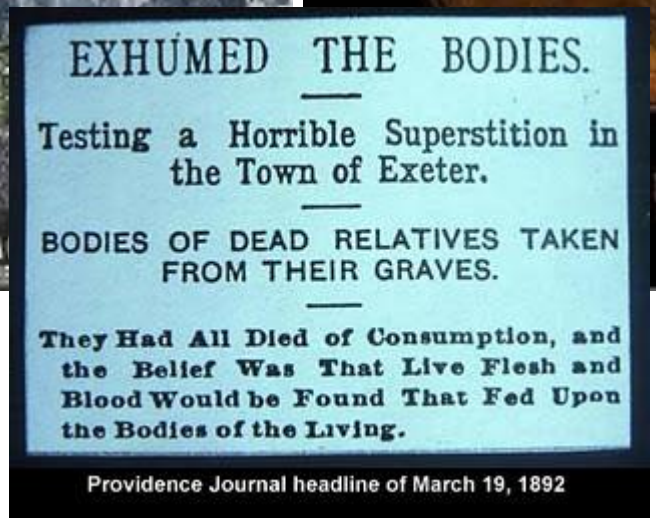
- Sadness, fasting, pregnancy, fatigue
- Hippocrates (400 BC)
  - Hereditary
- Galen (200 AD)
  - Person to person
- Ibn Sina (1020)
  - Dirt and water
- Vampirism
  - Pale skin
  - Coughing blood
  - Effect on family



New England Vampire Epidemic






EXHUMED THE BODIES.

Testing a Horrible Superstition in the Town of Exeter.

BODIES OF DEAD RELATIVES TAKEN FROM THEIR GRAVES.

They Had All Died of Consumption, and the Belief Was That Live Flesh and Blood Would be Found That Fed Upon the Bodies of the Living.

Providence Journal headline of March 19, 1892

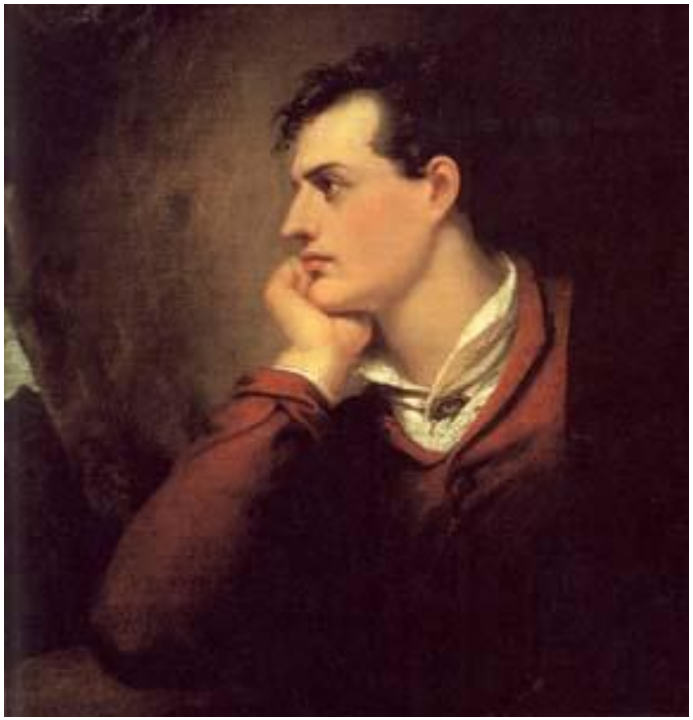
TB: A Romantic Affliction

- Violetta: La Traviata
- Mimi: La Boheme
- Leonora: La Favorata
- Fantine: Les Miserables
- Smike: Nicholas Nickleby
- Tiny Tim: Christmas Carol
- Little Blossom: David Copperfield
- Marguerite Gautier La Dame au Camelias

Society Linked Artistic Ability and TB

- The price that artists paid for their talent
- Elizabeth Barrett Browning: “Is it possible that genius is only scrofula?”
- “In the consumptive patient, mind and body were imagined as existing at odds with one another: even as the body becomes ‘consumed’ and ‘wasted’ by disease, the mind continues to expand and create.”

Tuberculosis: Illustrated History of a Disease



“I look pale . . . I should like to die of consumption – because the ladies would say ‘Look at poor Byron, how interesting he looks in dying’.”

- Lord Byron (1788-1824)

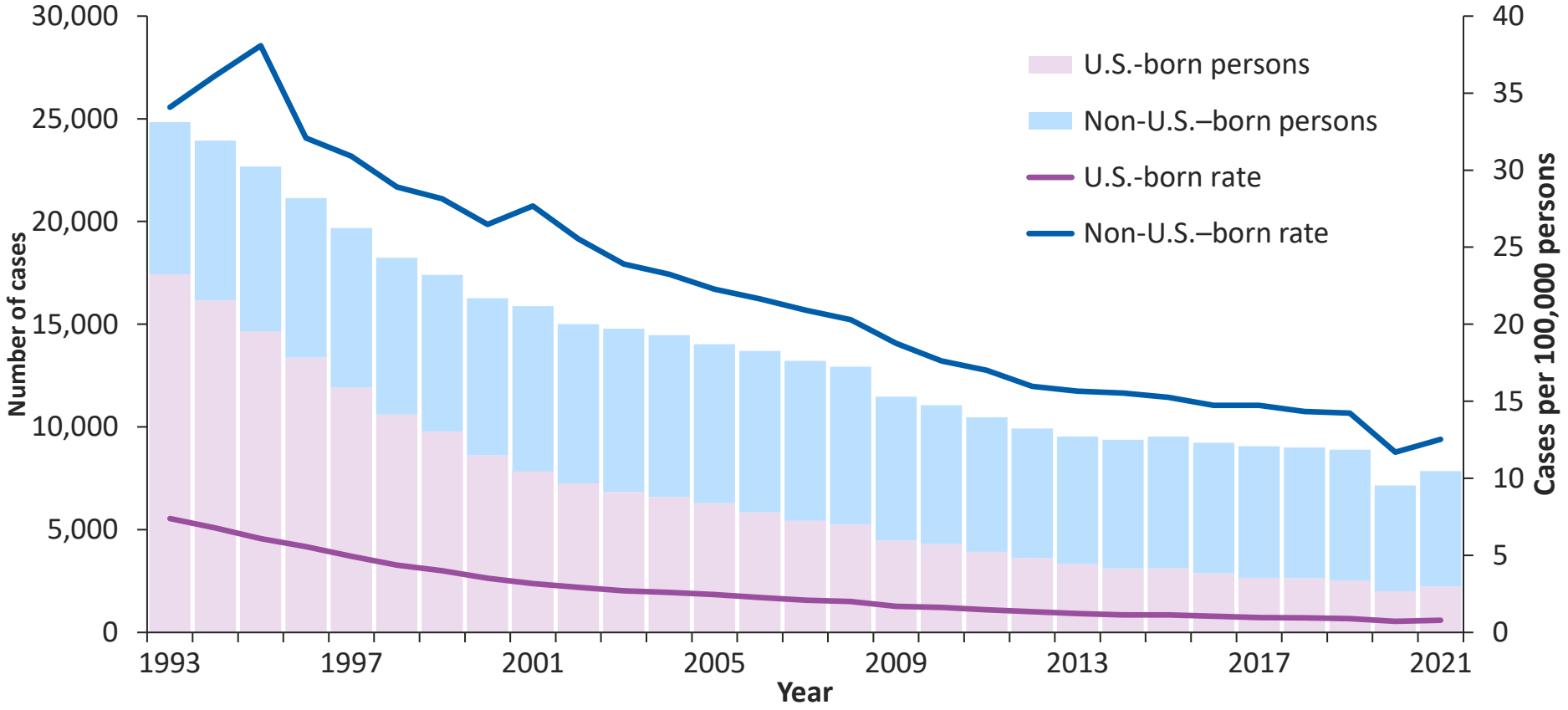
Century of the Sanatorium

- Galen 200AD: fresh air, rest, nutrition
- 1838 Croghan brought TB patients into Mammoth Cave
  - All died
- Revised recipe: *mountain* air, rest, and nutrition

Anecdotal Origin

- Hermann Brehmer
  - TB cured in Himalayas
  - 1859: 1st TB sanatorium in Germany
- Edward Livingston Trudeau
  - TB cured in Saranac Lake in NY's Adirondacks
  - 1884: Established first TB sanatorium in US
- NH's Glencliff Sanatorium in 1901
  - TB most common cause of death in ages 20-40
  - >4000 TB patients over 50 years

US TB Cases and Incidence Rates by Origin of Birth,* 1993–2021



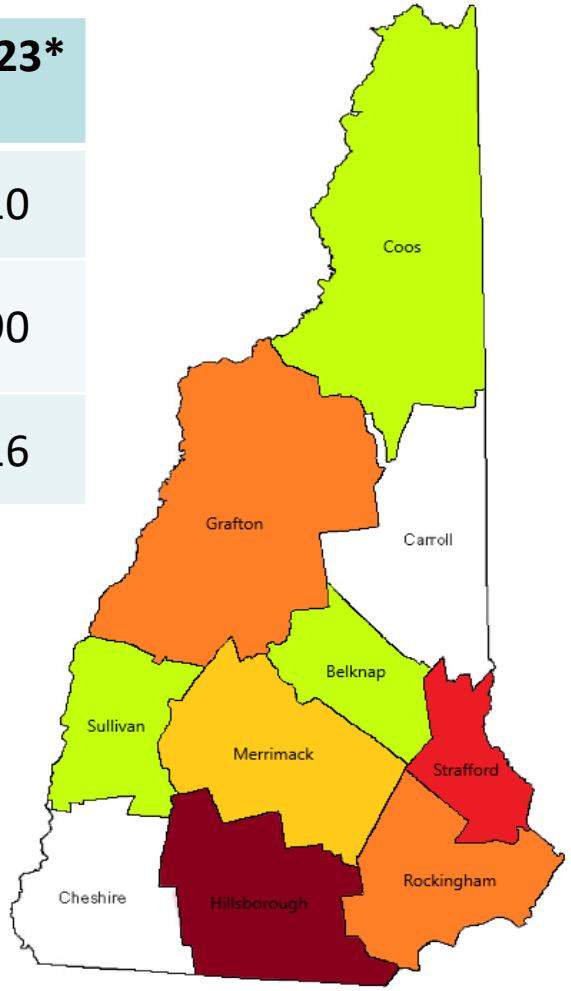
*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

CDC Slide Set

TB in New Hampshire

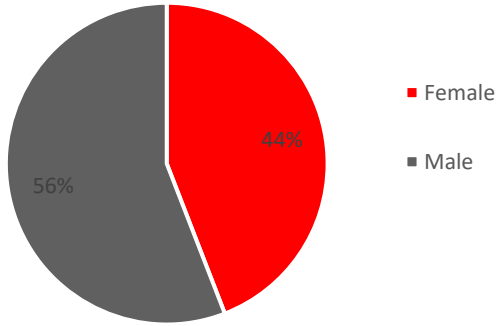
	2018	2019	2020	2021	2022	2023*
Active TB	12	6	12	12	11	10
Proportion FB (%)	83	100	92	75	91	90
Contacts	66	14	56	167	97	16

*Includes Q1&Q2 of 2023

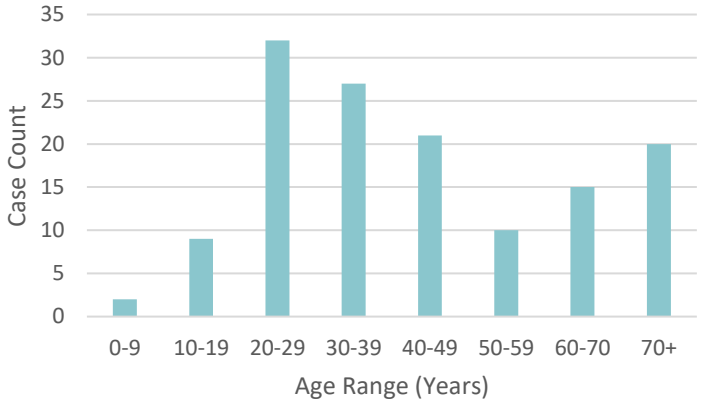


NH Demographic Breakdown

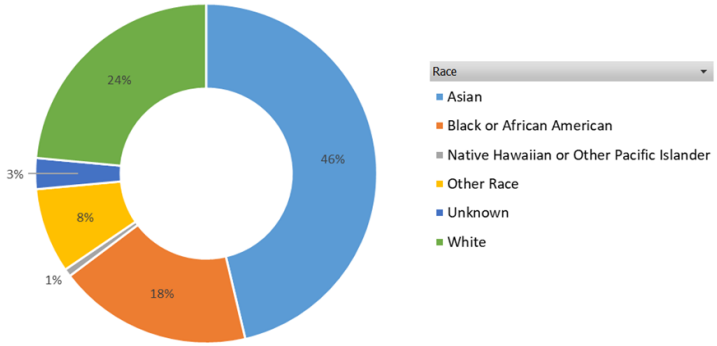
TB Cases by Gender (2013-2023)

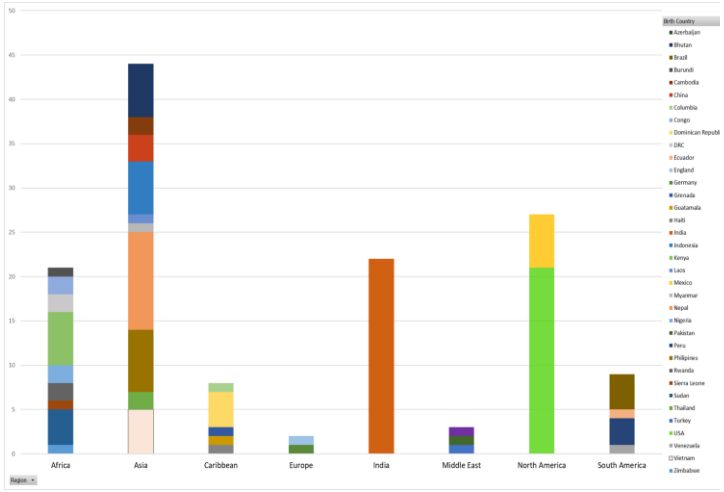


TB Cases by Age Range (2013-2023)

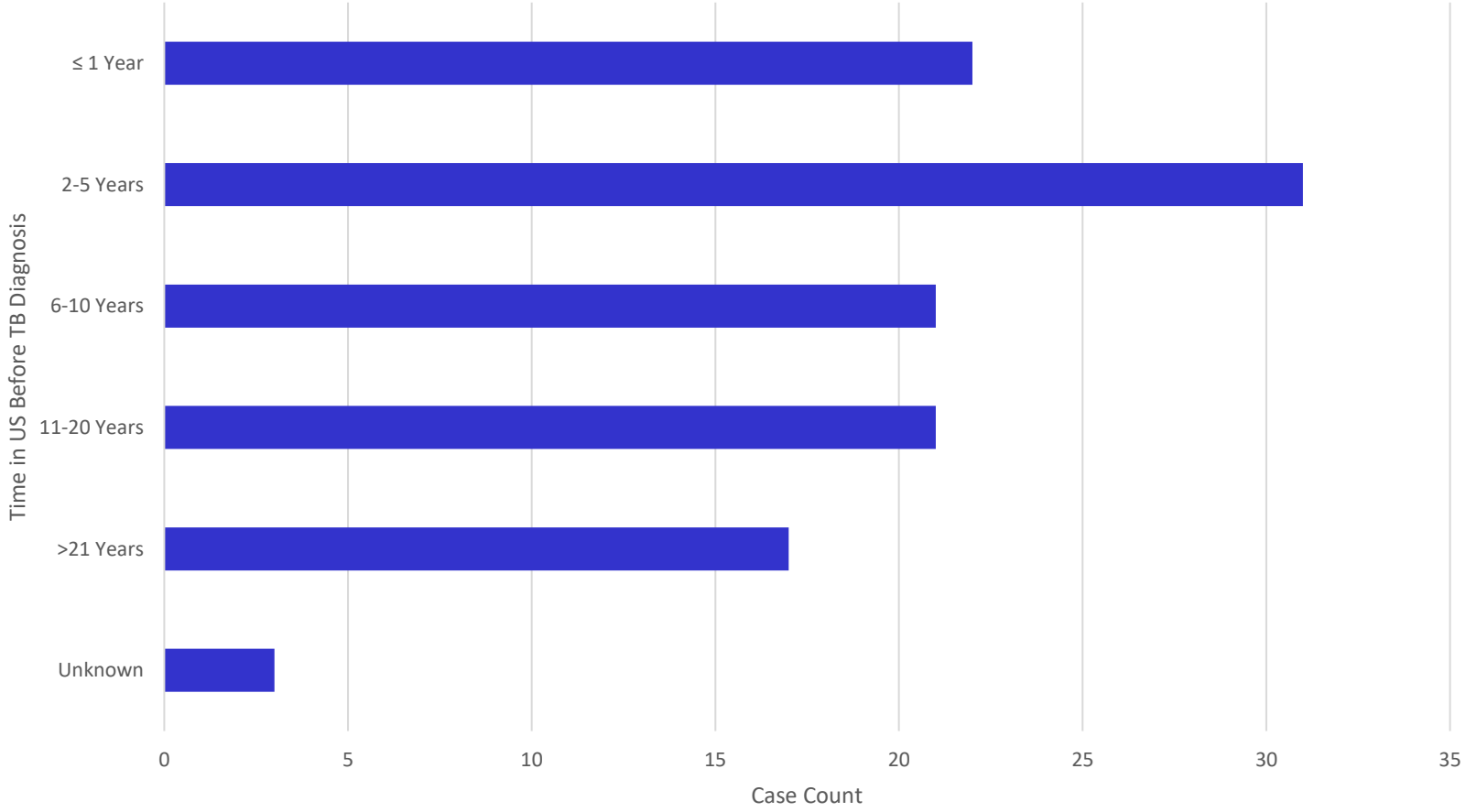


TB Cases by Race (2013-2023)



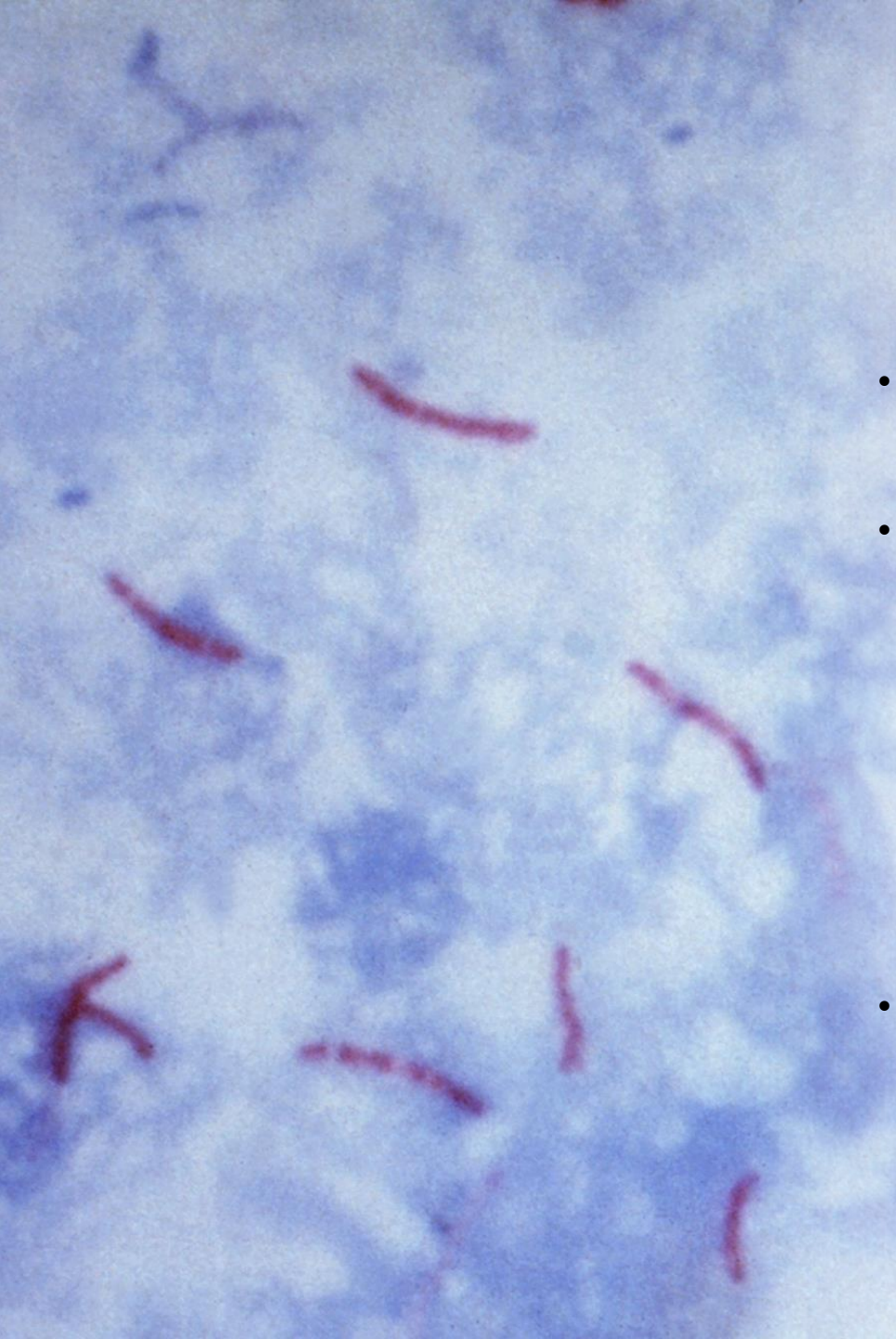


How Long are NH TB Patients in the US Before Diagnosis (2013-2023)?



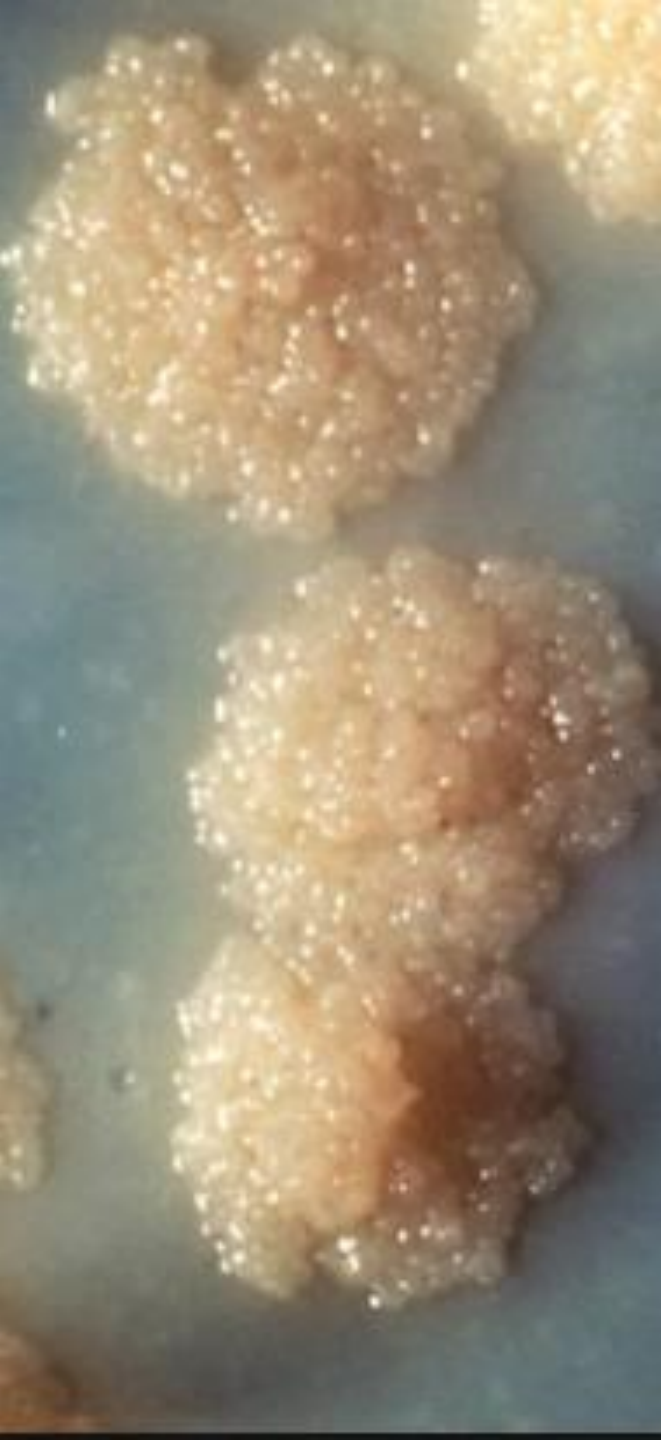
TB Vignette (2)

- Mid-Oct: reports to PCP with worsening symptoms
  - CXR extensive, bilateral, confluent nodular infiltrates with upper lobe predominance
  - IGRA ordered
- Late-Oct: returns to PCP; admitted to hospital
  - IGRA noted to be positive
  - Chest CT: multilobar bronchopneumonia most extensive in upper lobes with areas of cavitation, axillary and mediastinal LAD
  - 3 AFB collected: 2-3+ smear, culture pending



NH TB Program

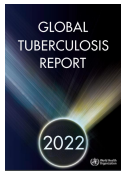
- TB/LTBI-related support and guidance for clinicians including navigating medication shortages, screening, diagnosis and treatment
- For those with suspected or confirmed active TB and high risk LTBI
  - Expert consultation
  - Case management services: ongoing education and support, assisting with adherence through directly observed therapy (DOT, vDOT), and navigating assistance programs
    - TB Financial Assistance Program (TBFA) for eligible patients supports testing, TB meds and monitoring
  - Specimen collection and testing
    - Best, fastest approaches to resistance testing
- For those exposed to TB
  - Community contact investigations and supports screening, testing and treatment
  - If there is exposure in a facility (e.g., medical facility, congregate setting), collaborative

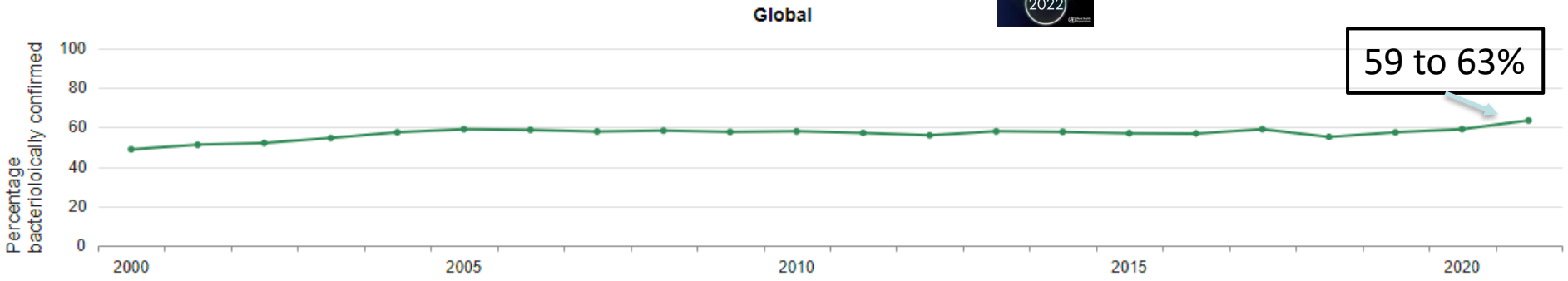


TB Diagnosis

Breakthroughs at last

Lack of Diagnostics Threatens Global TB Control

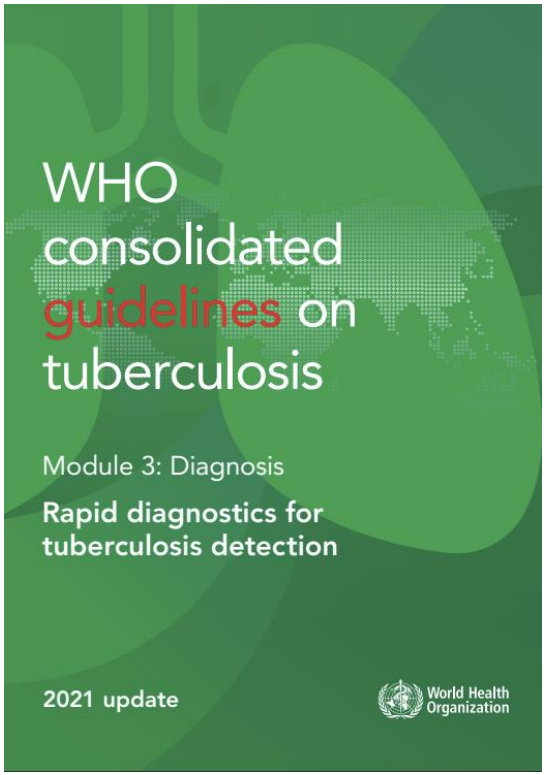




People diagnosed with TB using culture, rapid molecular tests recommended by WHO, lateral flow urine LAM or sputum smear microscopy

Of 10.6M estimated global TB cases in 2021, only 6.4M were reported so 4.1M are 'missing': combo of not diagnosed and not reported. Of those reported:

- 1 in 3 are bacteriologically-confirmed
- 1 in 5 diagnosed with recommended PCR (also known as NAAT or molecular) diagnostic test
- 1 in 3 with DR-TB are tested and appropriately treated



What is in our tool box – in NH, US and global?

DIAGNOSTIC TOOLS CURRENTLY AVAILABLE

Currently Recommended Diagnostic Tests For Pulmonary TB

ATS/CDC/IDSA 2017

Sputum smear microscopy	Strong recommendation
Liquid AND solid culture	Strong recommendation
Molecular test	Conditional recommendation
Molecular test for RIF +/- INH resistance	Strong recommendation

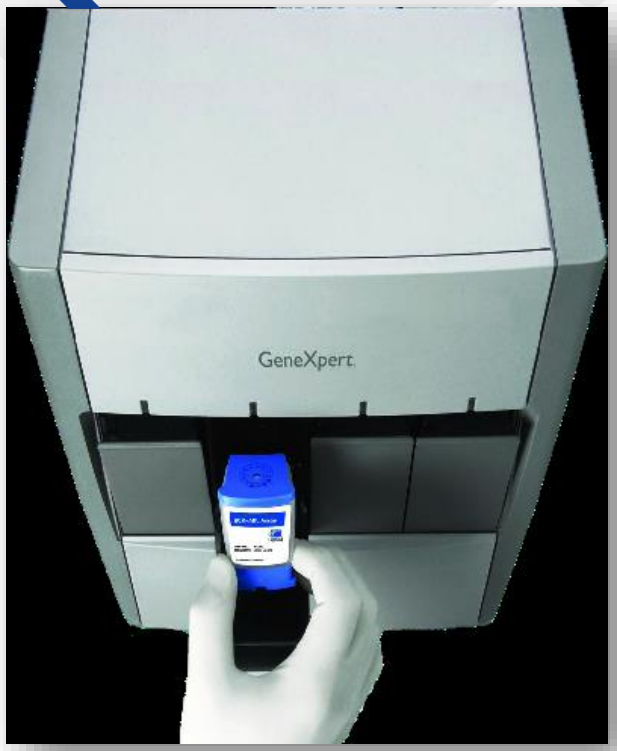
LTBI Tests for Presumptive TB??

 **Person with Latent TB Infection**	 **Person with TB Disease**
Few TB bacteria that are alive but inactive	Have more TB bacteria that are alive and active
Cannot spread TB bacteria to others	May spread TB to others
Does not feel sick in any way referable to infection	May feel sick and may have symptoms such as a cough, fever, and/or weight loss
Usually has a positive TB skin test (TST) or TB blood test (IGRA)	Usually has a positive TST or IGRA indicating TB infection predated disease
Should consider TB preventive treatment (TPT)	Needs treatment for TB disease
AFB smear - / culture - / NAAT -	AFB smear +/-, culture probably positive, NAAT positive

Xpert MTB/RIF (Cepheid)

here

- Automated, real-time PCR
  - 100 minutes to TB and rifampin resistance
    - Sensitivity for TB diagnosis higher than culture
    - 98% sensitivity for rifampin resistance
- Simple, modular system
  - Cartridges for other diseases



http://www.cdc.gov/mmwr/pdf/wk/mm6241.pdf

WHO/HTM/TB/2013.14

Currently Available Diagnostic Tests For Pulmonary TB

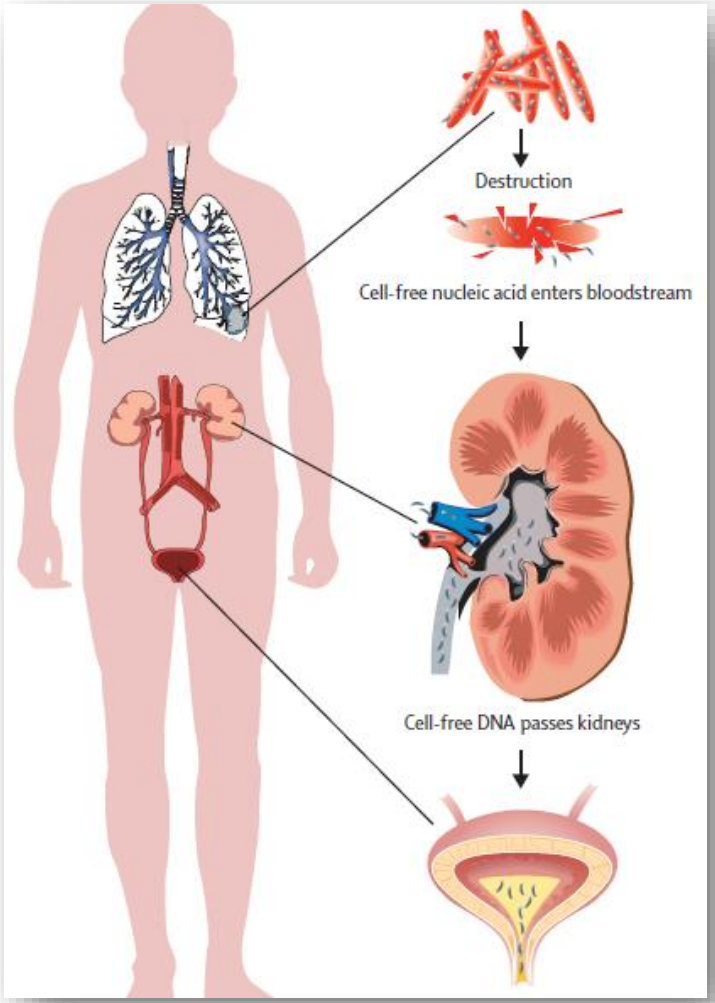
ATS/CDC/IDSA 2017

Sputum smear microscopy	Strong recommendation
Liquid AND solid culture	Strong recommendation
Molecular test	Conditional recommendation
Molecular test for RIF +/- INH resistance	Strong recommendation

WHO 2021

Rapid molecular test as first line	Strong recommendation
Universal testing for RIF +/- INH resistance	Strong recommendation
Urine LAM for HIV+ inpatients	Strong recommendation
Urine LAM for HIV outpatients	Strong recommendation

TB Diagnosis: Urine Lateral Flow Lipoarabinomannan (LF-LAM)



- Point of care, non-sputum sample
- Simple, 30m to results
- Alere Determine™ TB LAM Ag, USA is only commercially available urinary LAM test
  - Only recommended for PLWH under certain circumstances

Pipeline Report » 2022

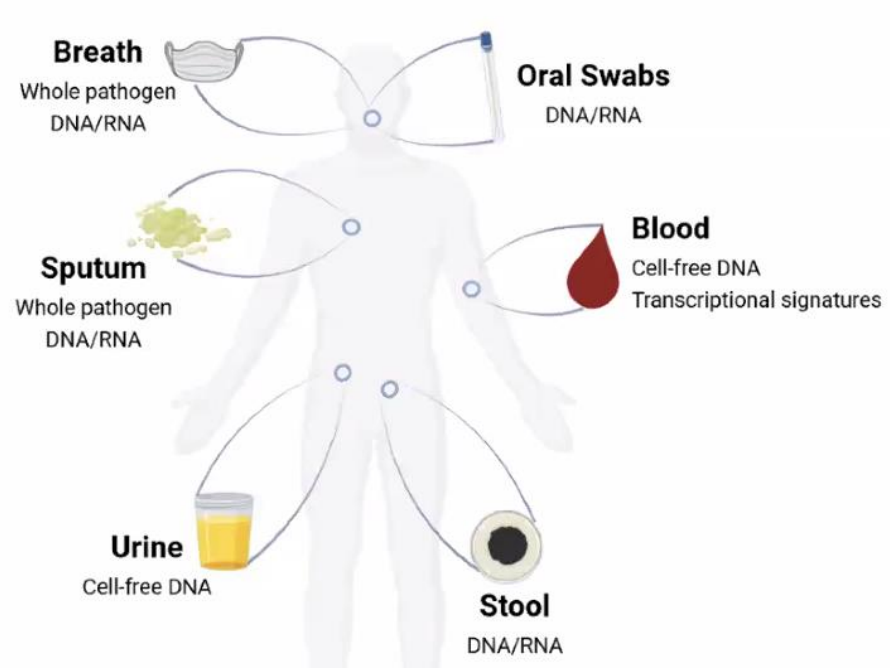
Tuberculosis Diagnostics

Test/Tool (Instrument)	Manufacturer (Country)	Type: Use case	Specimen type: Performance*	Intended level of use	Time to results	Price**	Stage of development
SILVAMP TB LAM	**Fujifilm** (Japan)	**Lateral flow:** Diagnosis for PLHIV (Evaluation among HIV-negative people and children ongoing for expanded indication)	**Urine:** PLHIV SE: 70.7% SP: 90.9%[88] HIV-negative SE: 53.2% SP: 98.9%[89] Children (irrespective of HIV status) SE: 60.0% SP: 95.0%[90]	**Community/ Primary care setting**	1 hour	Estimated price per test: $6[91]	Late-stage development (Optimization of production for quality stabilization is ongoing) **Projected ERPD review:** late 2023/early 2024 **Projected WHO review:** late 2024/early
Flow-TB	**Salus Discovery** (USA)	**Lateral flow, urine concentration:** Diagnosis for all people being evaluated for TB	**Urine:** Target sensitivity (irrespective of HIV status): 90.0–95.0%[93]	**Community/ Primary care setting**	1.5 hours[94] (including urin… con…	Not yet…	…ge …ent
High-sensitivity TB LAM	**Abbott** (USA)	**Lateral flow:** Diagnosis for all people being evaluated for TB	**Urine:** Not yet availabl…	**C…**		Not yet available	Early-stage development **Projected ERPD and WHO review:** 2025[95]
Third-generation LAM	**Bodi…**	…ll people …g evaluated for TB	**Urine:** Not yet available	**Community/ Primary care setting**	Not yet available	Not yet available	Early-stage develop-ment[96]
Third-g… LAM	…mic (Sweden)	**Lateral flow:** Diagnosis for all people being evaluated for TB	**Urine:** Not yet available	**Community/ Primary care setting**	Not yet available	Not yet available	Early-stage develop-ment[97]

"Potential Game Changers" for POC TB Diagnosis?

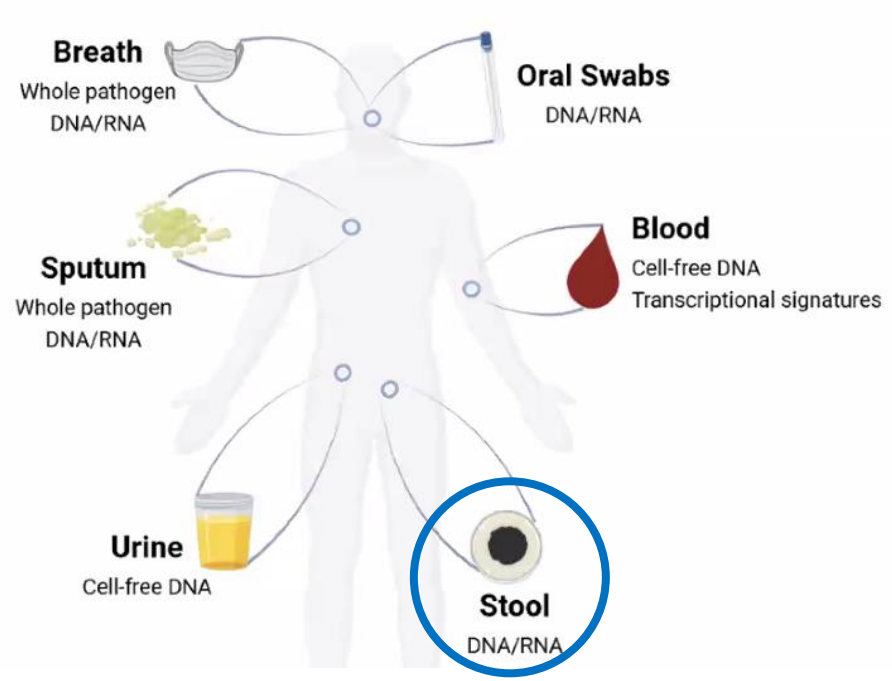
[WHO Operational Handbook on TB: Screening]

[TAG Pipeline Report]



For persons with presumptive TB who cannot produce sputum

NONSPUTUM SAMPLES FOR MOLECULAR DETECTION



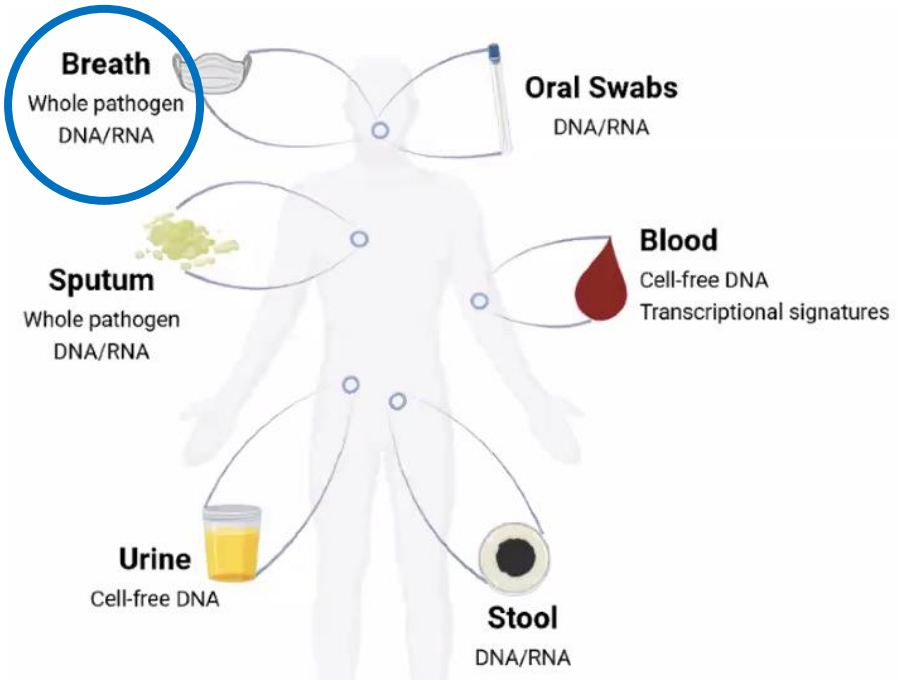
For persons with presumptive TB who cannot produce sputum

NONSPUTUM SAMPLES FOR MOLECULAR DETECTION

Stool Sample Processed for Xpert

- MTB DNA can be detected in stool specimens because sputum is coughed up and swallowed
- Systematic review and meta-analysis of Xpert Ultra data found heterogeneity by processing:
  - Sensitivity 53% (95% CI: 35–70)
  - Specificity of 98% (95% CI: 93–99)
- 2021: WHO recommended stool for Xpert MTB/RIF and Ultra as initial diagnostic test TB and detection of rif resistance in children <10y with signs/symptoms of pTB
- Practical manual for processing stool
  - Optimized Sucrose Flotation
  - Simple One Step method

Kay AW, et al. Diagnostic accuracy of Xpert MTB/RIF Ultra using different sample types in children: a systematic review and meta-analysis. 2021. Available at STOPTB



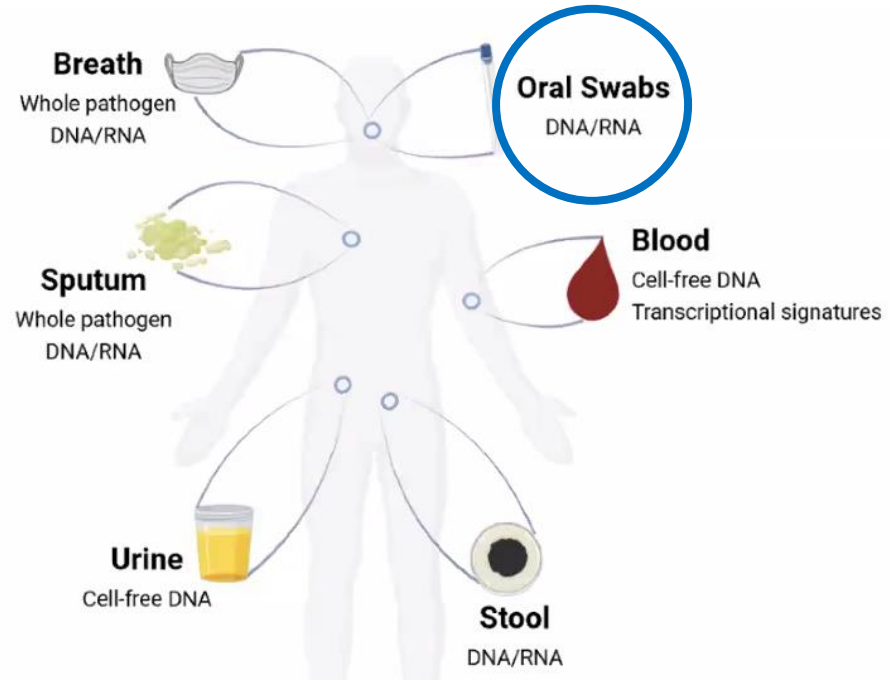
For persons with presumptive TB who cannot produce sputum

NONSPUTUM SAMPLES FOR MOLECULAR DETECTION

Advances in Sampling Methods:
Face Mask Sampling

- Presumptive TB patient wears mask for 30-60 min to capture breath aerosols containing DNA or pathogens, dissolve embedded strip, and test using Xpert
- "Exhaled *M tuberculosis* output showed no diurnal pattern and did not associate with cough frequency, sputum bacillary content, or chest radiographic disease severity"
- Early performance results promising: sensitivity<culture but perfect specificity

Williams C, Lancet ID 2020



For persons with presumptive TB who cannot produce sputum

NONSPUTUM SAMPLES FOR MOLECULAR DETECTION

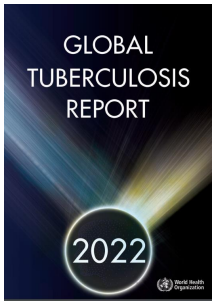
Advances in Sampling Methods: Tongue Swabs (Oral Swab Analysis)

Andama et al J Clin Microbiol 2022
Steadman et al, medRxiv 2023

- Optimized processing for Xpert Ultra
  - Self-swabs tongue dorsum for 10 seconds using Copan FLOQSwabs
  - 1 or 2 swabs with usual sample reagent per cartridge
  - 1 swab boiled, incubated, mixed without Cepheid sample reagent
- Early promising results approaching sensitivity of sputum Xpert and perfect specificity among 183 adults with cough >2w in 2 clinics in Kampala

TB Vignette (3)

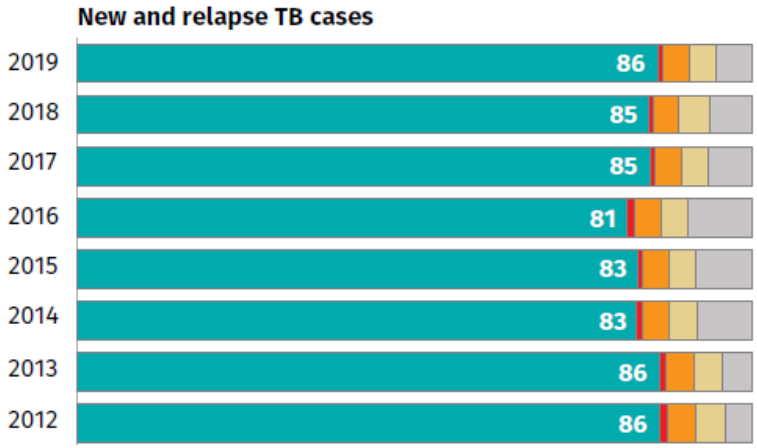
- Report to NH DHHS
  - 603-271-4496
- Facilitates sputum for Xpert which is positive for TB, with no mutations for rifampin resistance detected



Global TB Treatment Outcomes 2012-2019

Stagnation of drug susceptible TB treatment success at ~85%

- 77% among PLWHIV



WHO Global TB Report 2022

TB Treatment

Breakthroughs at last

Traditional TB Treatment

Drug	Properties	Usual Dose	Common Side Effects
Isoniazid (INH or I)	Cidal	300mg/d	Hepatitis, neuropathy
Rifampin (RMP or R)	Cidal	600mg/d	Hepatitis, flu reaction, drug interactions
Pyrazinamide (PZA or P)	Cidal for intracellular organisms	15-30mg/kg/d	Hepatitis, GI, rash, myalgias
Ethambutol (EMB or E)	Static, used to prevent resistance	15mg/kg/d	Ocular toxicity

- RIPE 2m (intensive phase)
- INH+RMP 4m (continuation phase)
- Administer by directly observed therapy (DOT)

2023 Global New TB Drug Pipeline[1] Updated 7/14/2023

Discovery | Preclinical Development | Clinical Development

Lead Optimization | Early Stage Development | GMP / GLP Tox. | Phase 1 | Phase 2 | Phase 3 | Regulatory Market Approvals

Lead Optimization

- Indazole sulfonamides
- Diarylthiazoles
- DprE1 Inhibitors
- Direct InhA Inhibitors
- Mtb energy metabolism
- Gyrase Inhibitors
- Arylsulfonamides
- Inhibitors of MmpL3, Translocase-1, ClpC1, ClpP1P2, PKS13, F-ATP synthase, RNAP
- Oxazolidinones
- DnaE1 / Nargenicin analogs

Early Stage Development

- TBD10 (MK-3854)
- CLB-073*
- SPR720*
- MPL-447*
- JSF-3285*
- CPZEN-45*
- NTB-3119*
- MBX-4888A (1810)*
- FNDR-10045*, FNDR-20364*

GMP / GLP Tox.

- GSK-839*
- OTB-658

Phase 1

- TBD09 (MK-7762)
- GSK-286*
- TBAJ-876
- TBAJ-587
- TBI-223
- Macozinone* (PBTZ-169)

Phase 2

- Telacebec* (Q203)
- Alpibectir* (BVL-GSK098)
- Sanfetrinem
- Delpazolid
- Sutezolid
- Sudapyridine (WX-081)
- BTZ-043*
- TBA-7371*
- Quabodepistat (OPC-167832*)
- Ganfeborole (GSK-656*/070)
- Pyrifazimine (TBI-166)
- SQ-109*

Phase 3

- Bedaquiline*
- Delamanid*
- Pretomanid*

Underline = updates since November 2022

*New chemical class. Known chemical classes for any indication are color coded: rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone, imidazopyridine amide, beta-lactam.

[1] New Molecular Entities not yet approved, being developed for TB or only conditionally approved for TB. Showing most advanced stage reported for each. Details for projects listed can be found at http://www.newtbdrugs.org/pipeline/clinical

Ongoing projects without a lead compound identified: http://www.newtbdrugs.org/pipeline/discovery

WORKING GROUP ON NEW TB DRUGS

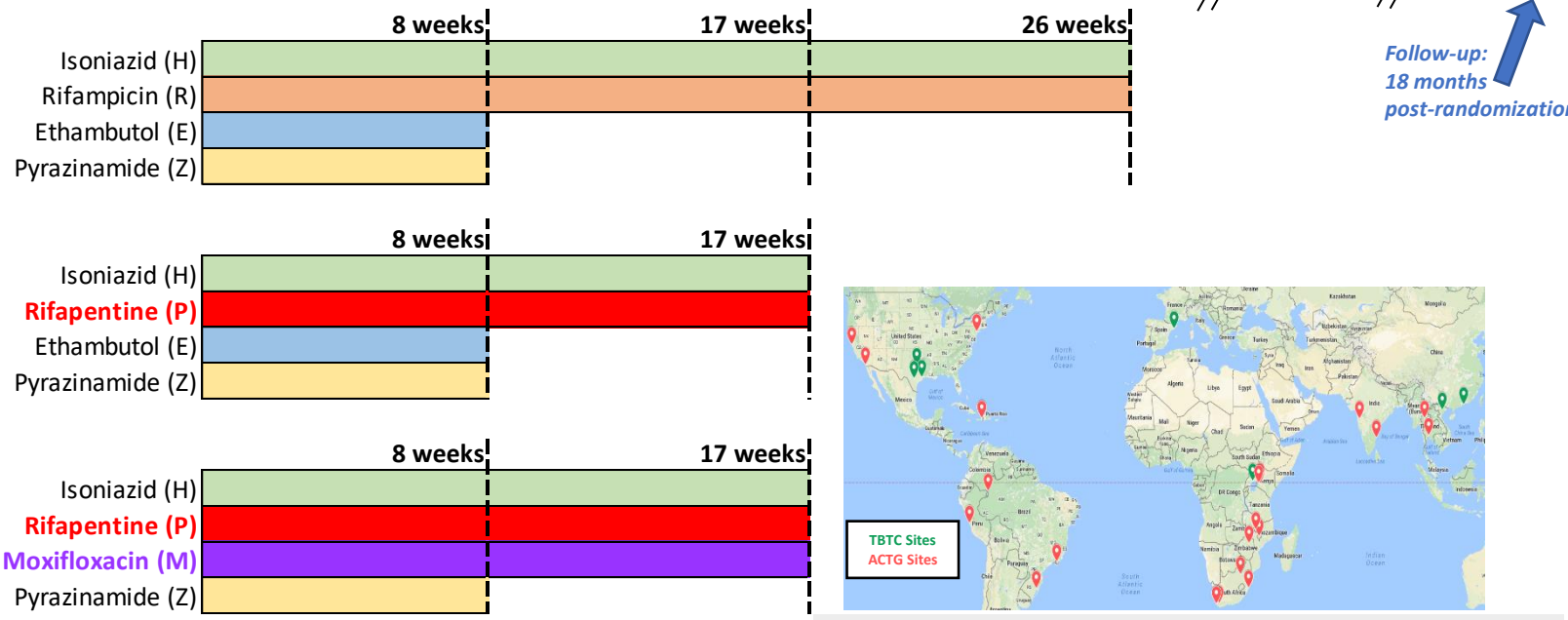
www.newtbdrugs.org

Updated: July 2023

Study 31/ACTG5349
Phase 3 Non-Inferiority Trial

Primary efficacy endpoint: outcome at 12-months post-randomization

3 arms randomization 1:1:1



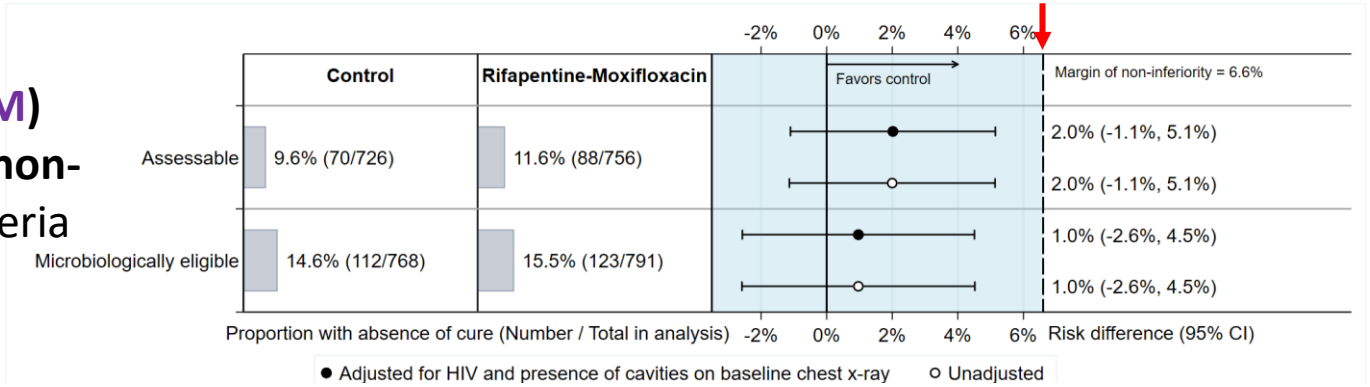
- 2516 adolescents (≥12 y.o.) and adults enrolled
- HIV-infected (CD4≥100) and HIV-uninfected
- All treatment: daily 7/7, **DOT 5/7**
- Flat RPT dose of 1200 mg; MOX dose of 400 mg
- Open label: food with RPT, no food with RIF

Sputum, safety labs & AE checks: Weeks 2, 4, 8, 12, 17, 22, 26
Post-tx completion f/u visits Months 9, 12, 15, 18

Courtesy of Payam Nahid, UCSF, TBTC/ACTG

Study 31/A5349: Primary Efficacy Results

RPT-MOX (2HPZM/2HPM) regimen met non-inferiority criteria for efficacy in <u>both</u> analyses



Courtesy of Payam Nahid, UCSF, TBTC/ACTG

N Engl J Med. 2021 May 6;384(18):1705-1718

here

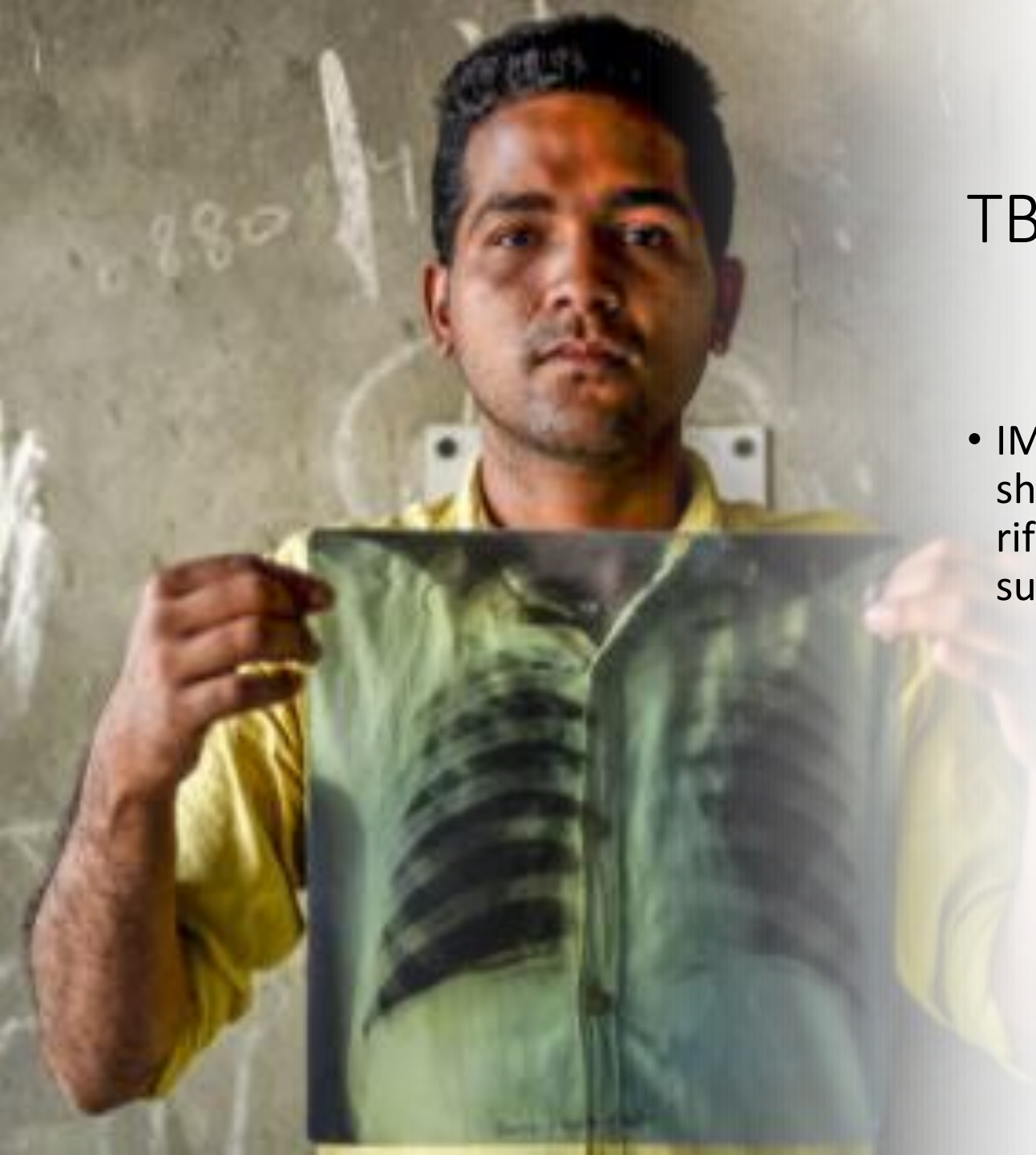
Morbidity and Mortality Weekly Report (*MMWR*)

Interim Guidance: 4-Month Rifapentine-Moxifloxacin Regimen for the Treatment of Drug-Susceptible Pulmonary Tuberculosis — United States, 2022

Weekly / February 25, 2022 / 71(8);285–289

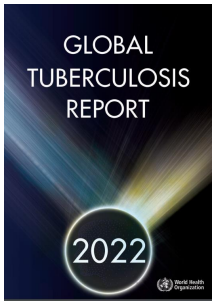
Wendy Carr, PhD[1]; Ekaterina Kurbatova, MD[1]; Angela Starks, PhD[1]; Neela Goswami, MD[1]; Leeanna Allen, MPH[1]; Carla Winston, PhD[1] (VIEW AUTHOR AFFILIATIONS)

"CDC recommends the 4-month regimen as a treatment option for U.S. patients aged ≥12 years with drug-susceptible pulmonary TB and provides implementation considerations for this treatment regimen."



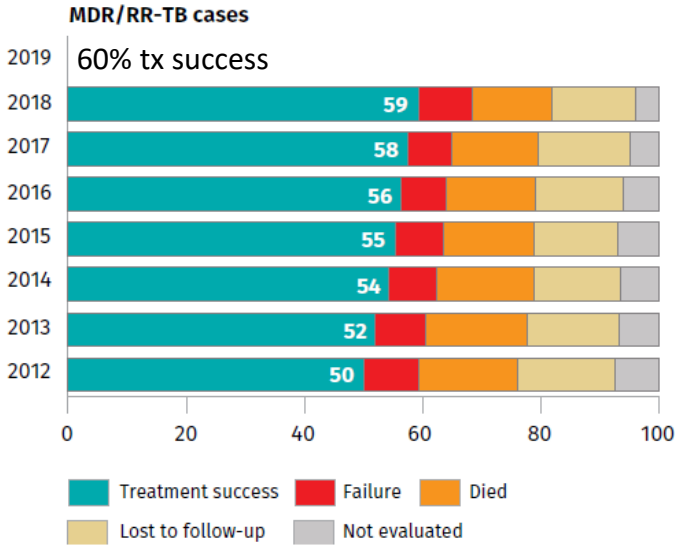
TB Vignette (alt3)

- IMAGINE that the Xpert showed there were rifampin mutations that suggested MDR-TB



Global TB Treatment Outcomes 2012-2019

- 15–21m of treatment after culture conversion with 4–7 drugs that are less effective, more toxic, and more costly than those for drug-susceptible TB
- Recent steady improvement in treatment outcomes with improved drugs and regimens
  - 124 countries using bedaquiline
  - 109 using all-oral longer regimens
  - 92 using shorter regimens



WHO Global TB Report 2022

here

Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease

Print

Updated May 4, 2023

CDC endorsed pretomanid 200mg in combination with bedaquiline and linezolid (BPaL) in adults with pulmonary extensively drug resistant (XDR), treatment-intolerant, or nonresponsive MDR TB

2 Feb. 2022

4 May 2023

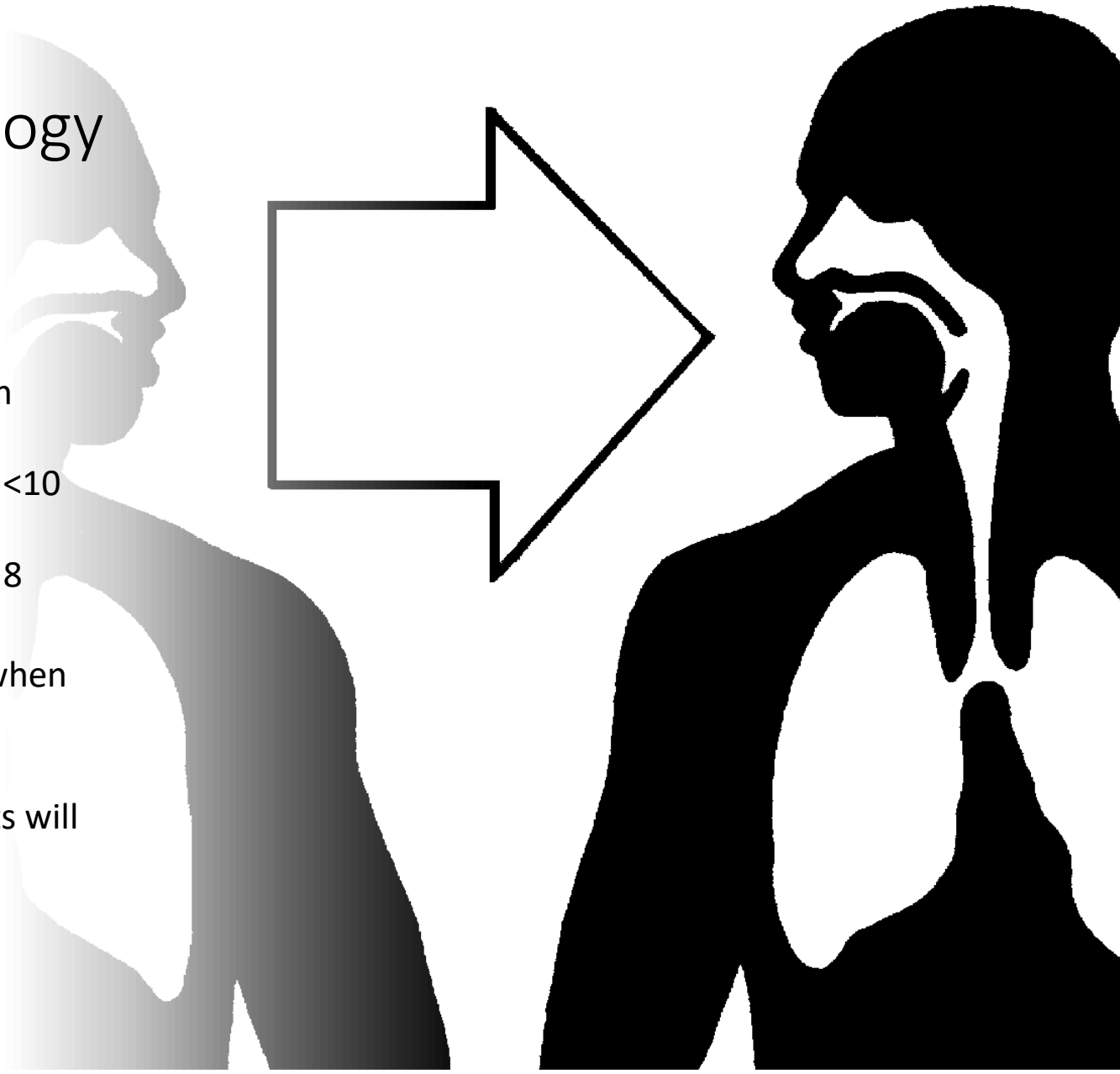
Linezolid dose within BPaL regimen changed from 1200 mg to 600 mg

TB Vignette (4)

- Collaboration with NH DHHS toward contact investigation reveals patient has multiple household, occupational and nosocomial contacts during his infectious period

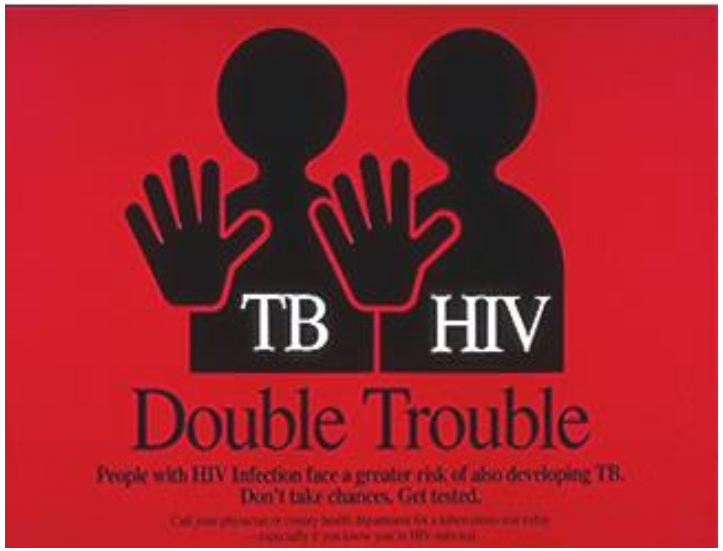
Pathophysiology of TB

- Bacteria aerosolized in "droplet nuclei"
  - Each may contain <10 bacilli
  - Linger in air up to 8 hours
- Transmission occurs when share airspace with infectious TB patient
- ~30% of close contacts will be infected



Progression From LTBI to TB

Risk of progressing is highest first 2 years after infection and for those with immunocompromise, but progression possible over lifespan of someone with LTBI



10% lifetime if HIV-

10% annual if HIV+

Increased Risk for Progressing to TB

It's all about host factors that allow progression

- People infected with *M. tuberculosis* within past 2 years
- People living with HIV
- People with medical conditions known to increase the risk for TB
- Infants and children <4 years old
- People who inject drugs

Two Types of Tests for LTBI

- Tuberculin skin test (TST)
- Interferon gamma release assays (IGRA)
  - T-SPOT.*TB* test (Quest Diagnostics)
  - QuantiFERON-TB Gold Plus (Qiagen)

IGRAs Compared to TST

Advantages

Single patient visit

No booster phenomenon

Less likely to have incorrect reading

Not affected by prior BCG vaccination and most nontuberculous mycobacteria (NTMs)

Disadvantages

More expensive up front (1.5x at DHMC)

Time constraints to process blood samples

Limited data on children < age 2

TST and IGRA Similarities

Both cost money: cost effectiveness analyses show equivalence

Both have compromised sensitivity in immunocompromised

Specificity issues

- TST: NTM or BCG history
- IGRA: especially in low LTBI incidence populations

Quantitative results important for both

Neither differentiates between LTBI and active TB

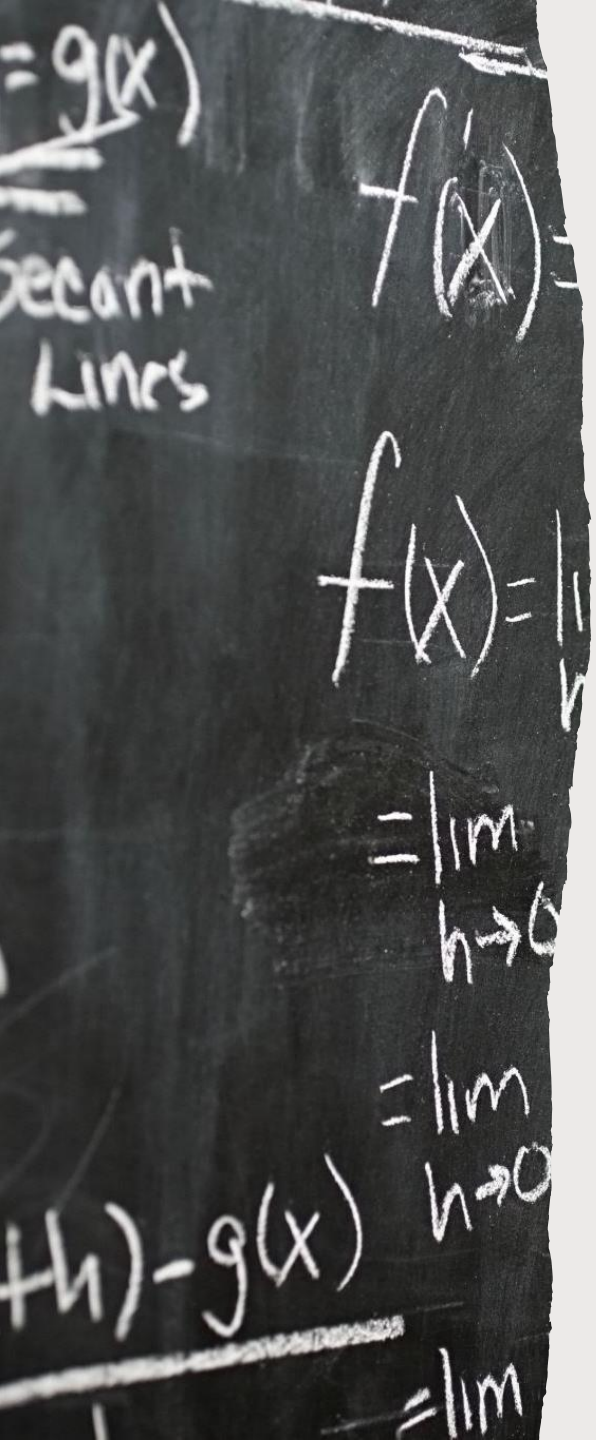
Neither predicts risk for progression to active TB

Altet et al. Ann Am Thor Soc 2015; 12(5):680; Andrews J et al. Serial QFT . . . Lancet 2017.

Case: Positive IGRA in Low LTBI Risk

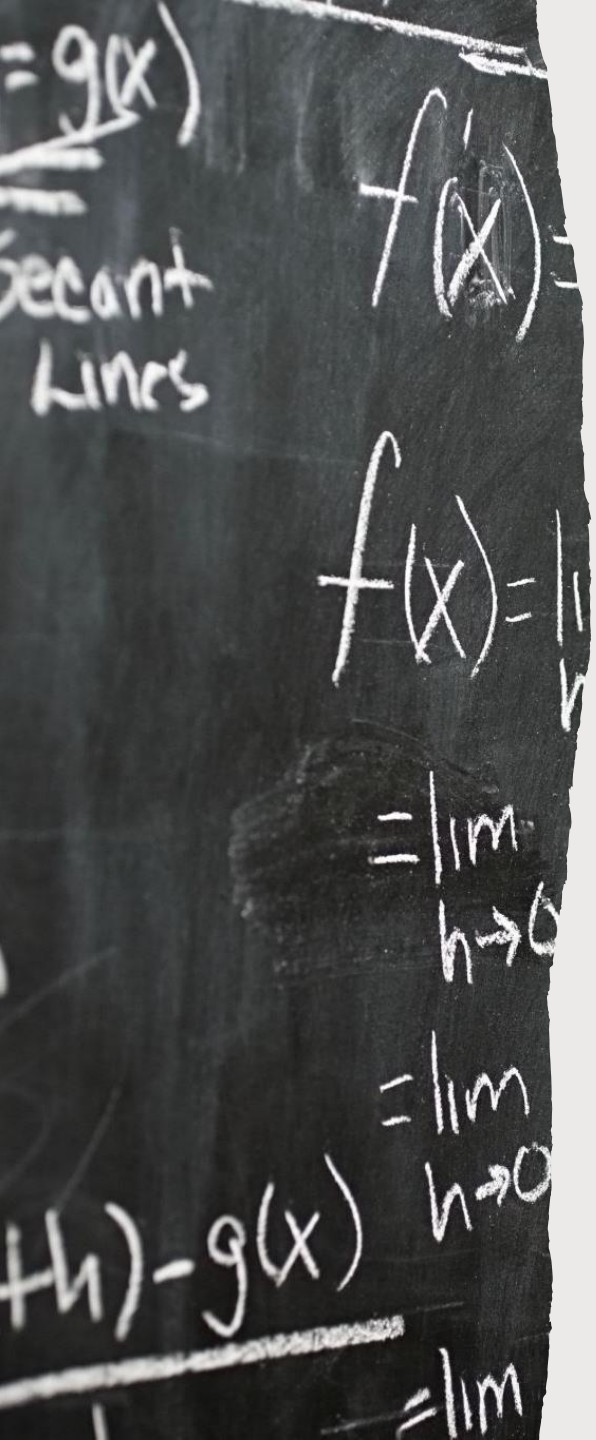
- Farmer from northern NH who never left his farm needs an IGRA because he will start TNF-alpha inhibitor for steroid-resistant RA
- QuantiFERON Plus comes back as positive:
  - TB1-nil=0
  - TB2-nil=0.36

Q. What do you do about an unexpected positive IGRA?



Next Step?

1. Nothing – probably false positive because low positive, no LTBI risk (but high risk of progression if infected)
2. Repeat same IGRA
3. Do the other IGRA
4. Place TST
5. Go right to a CXR, rule out active TB, consider TPT



Next Step?

1. **Nothing – probably false positive because low positive, no LTBI risk (but high risk of progression if infected)**
2. **Repeat same IGRA**
3. **Do the other IGRA**
4. **Place TST**
5. Go right to a CXR, rule out active TB, consider TPT

New LTBI Tests Coming

- TB Ag-based skin tests (TBST) accurate (76%se/98%sp), acceptable, feasible and cost-effective
  - Alternative to TST and IGRAs
- Globally available products:
  - C-Tb (Serum Institute of India, India)
  - C-TST (Anhui Zhifei Longcom, China)
  - Diaskintest (Generium, Russian Federation)

C-TB Recent Reference
WHO Recommendation

Latent Tuberculosis Infection Treatment Regimens

Treatment regimens for latent TB infection (LTBI) use isoniazid (INH), rifapentine (RPT), or rifampin (RIF). **CDC and the National Tuberculosis Controllers Association preferentially recommend short-course, rifamycin-based, 3- or 4-month latent TB infection treatment regimens over 6- or 9-month isoniazid monotherapy.**

Clinicians should choose the appropriate treatment regimen based on drug susceptibility results of the presumed source case (if known), coexisting medical conditions (e.g., HIV*), and potential for drug–drug interactions.

https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm?s_cid=rr6901a1_w

	DRUG	DURATION	FREQUENCY	TOTAL DOSES	DOSE AND AGE GROUP
Preferred	**ISONIAZID† AND RIFAPENTINE†† (3HP)**	3 months	Once weekly	12	**Adults and children aged ≥12 yrs** INH: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT: 10–14.0 kg; 300 mg 14.1–25.0 kg; 450 mg 25.1–32.0 kg; 600 mg 32.1–49.9 kg; 750 mg ≥50.0 kg; 900 mg maximum
					Children aged 2–11 yrs INH†: 25 mg/kg; 900 mg maximum RPT††: See above
	RIFAMPIN§ (4R)	4 months	Daily	120	**Adults:** 10 mg/kg; 600 mg maximum
					Children: 15–20 mg/kg‖; 600 mg maximum
	ISONIAZID† AND RIFAMPIN§ (3HR)	3 months	Daily	90	**Adults** INH†: 5 mg/kg; 300 mg maximum RIF§: 10 mg/kg; 600 mg maximum
					Children INH†: 10-20 mg/kg#; 300 mg maximum RIF§: 15-20 mg/kg; 600 mg maximum
Alternative	**ISONIAZID† (6H/9H)**	6 months	Daily	180	**Adults** Daily: 5 mg/kg; 300 mg maximum Twice weekly: 15 mg/kg; 900 mg maximum
			Twice weekly¶	52	
		9 months	Daily	270	**Children** Daily: 10–20 mg/kg#; 300 mg maximum Twice weekly: 20–40 mg/kg#; 900 mg maximum
			Twice weekly¶	76	

*For persons with HIV/AIDS, see Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/367/overview.
†Isoniazid is formulated as 100-mg and 300-mg tablets.
††Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.
¶Intermittent regimens must be provided via directly observed therapy (i.e., a health care worker observes the ingestion of medication).
§Rifampin (rifampicin) is formulated as 150-mg and 300-mg capsules.
‖The American Academy of Pediatrics acknowledges that some experts use rifampin at 20–30 mg/kg for the daily regimen when prescribing for infants and toddlers (**Source**: American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:829–53).
#The American Academy of Pediatrics recommends an INH dosage of 10–15 mg/kg for the daily regimen and 20–30 mg/kg for the twice weekly regimen.

CDC

CDC and the National TB Controllers Association
LTBI Treatment Guidelines

Morbidity and Mortality Weekly Report (*MMWR*)

Tuberculosis Testing and Latent Tuberculosis Infection Treatment Practices Among Health Care Providers — United States, 2020–2022

Weekly / November 3, 2023 / 72(44);1183–1189

- CDC recommends testing persons at increased risk for LTBI routinely, using IGRAs, and, if a diagnosis of LTBI is made, prescribe short-course regimen
- Among 3,647 primary health care providers
  - 53% reported routinely testing non–USB patients
    - 35.7% used IGRAs, 44.2% used TSTs and 20.2% used both
  - >Half (59%) reported prescribing any LTBI treatment
    - 33% reported prescribing short-course regimens
  - 41% referred patients to a health department

Summary

- TB causes massive global morbidity and mortality
- Think TB and partner with NH DHHS
- Imperfect diagnostic tests
  - Xpert a major breakthrough for active TB
  - IGRAs becoming mainstay for LTBI
- Treatments are also improving
  - DS TB treatment is 2m of RIPE, 4m of RI
    - New 4 month regimen
  - MDR TB treatment all oral, short course via BPaL
  - LTBI favored regimen is rif-based 3 or 4m