Linking TB Biomarkers to Clinically Relevant Outcomes

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April 1, 2024

New Directions in TB
April 1 – 2, 2024
Houston, Texas

Anna Mandalakas, MD, PhD has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

GLOBAL TB PROGRAM
TEXAS CHILDREN'S HOSPITAL
BAYLOR COLLEGE OF MEDICINE

Linking TB Biomarkers to Clinically Relevant Outcomes

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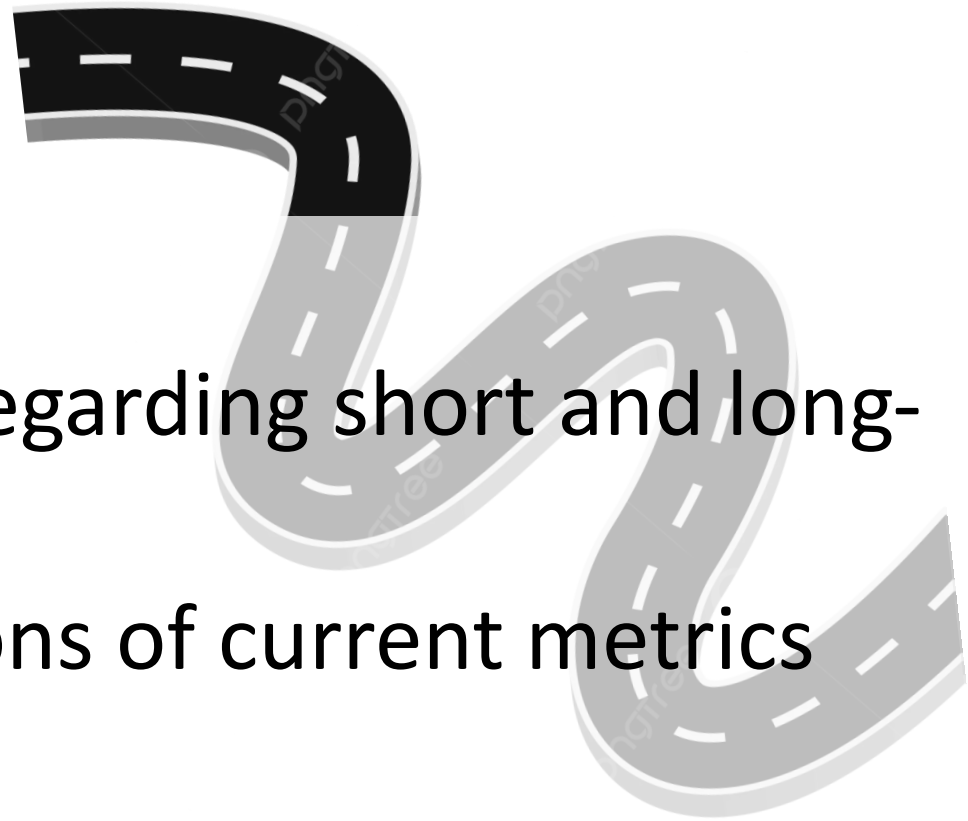
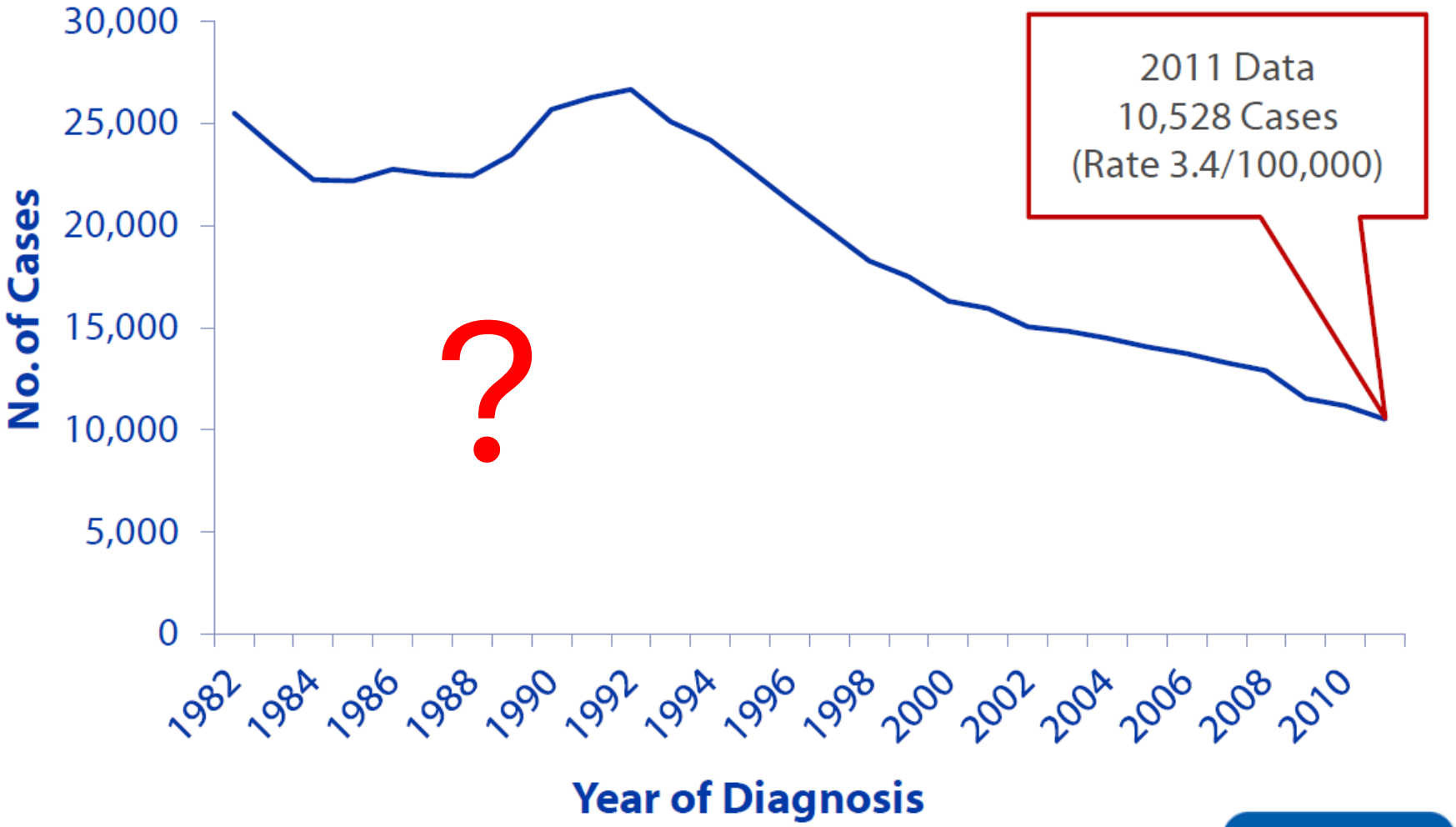
30-minute roadmap

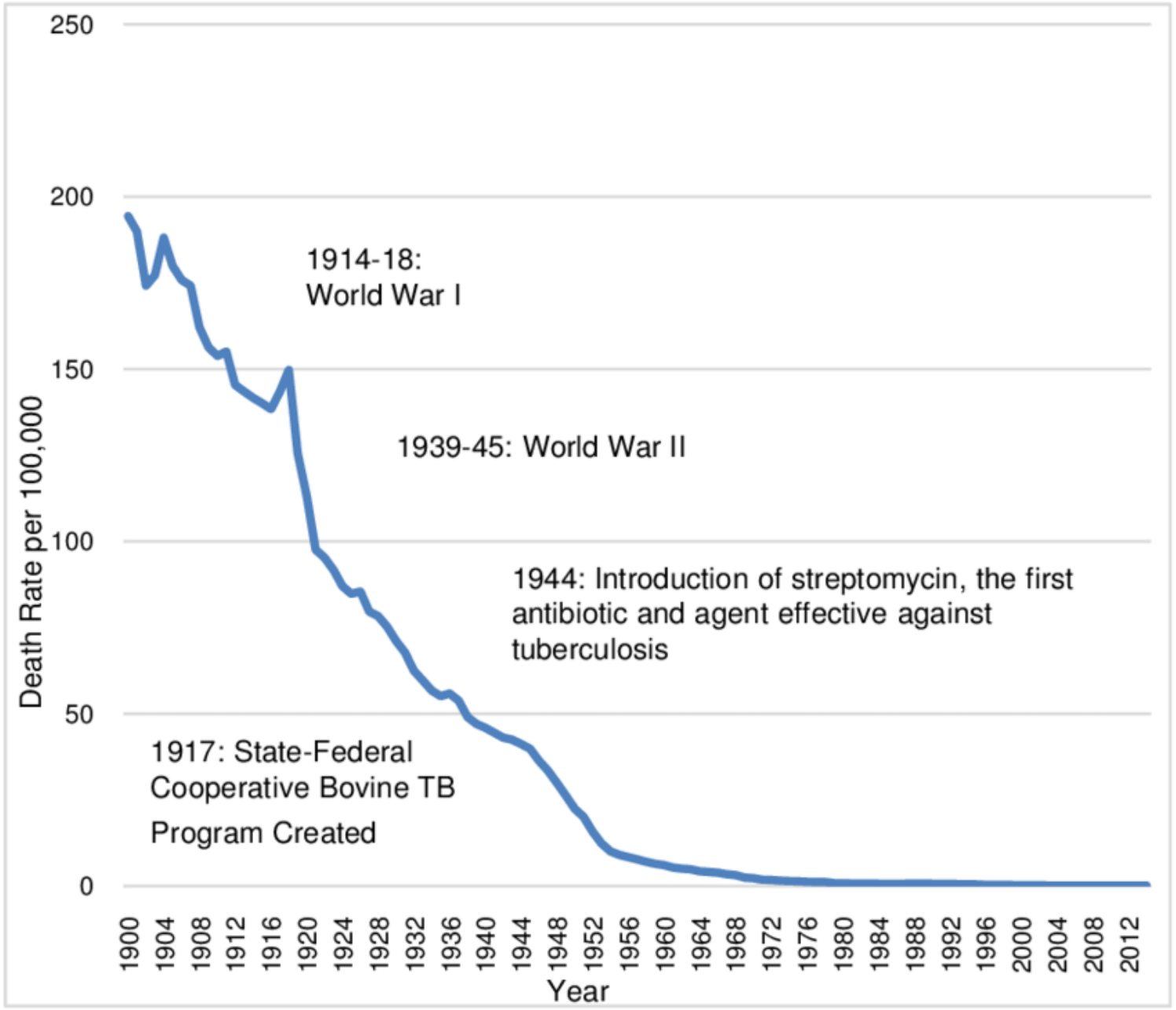


- Examine emerging evidence regarding short and long-term outcomes of TB
- Review strengths and limitations of current metrics describing TB outcomes
- Explore opportunities to inform TB care and optimize outcomes for patients combatting TB

Reported TB Cases
United States, by Year, 1982–2011*

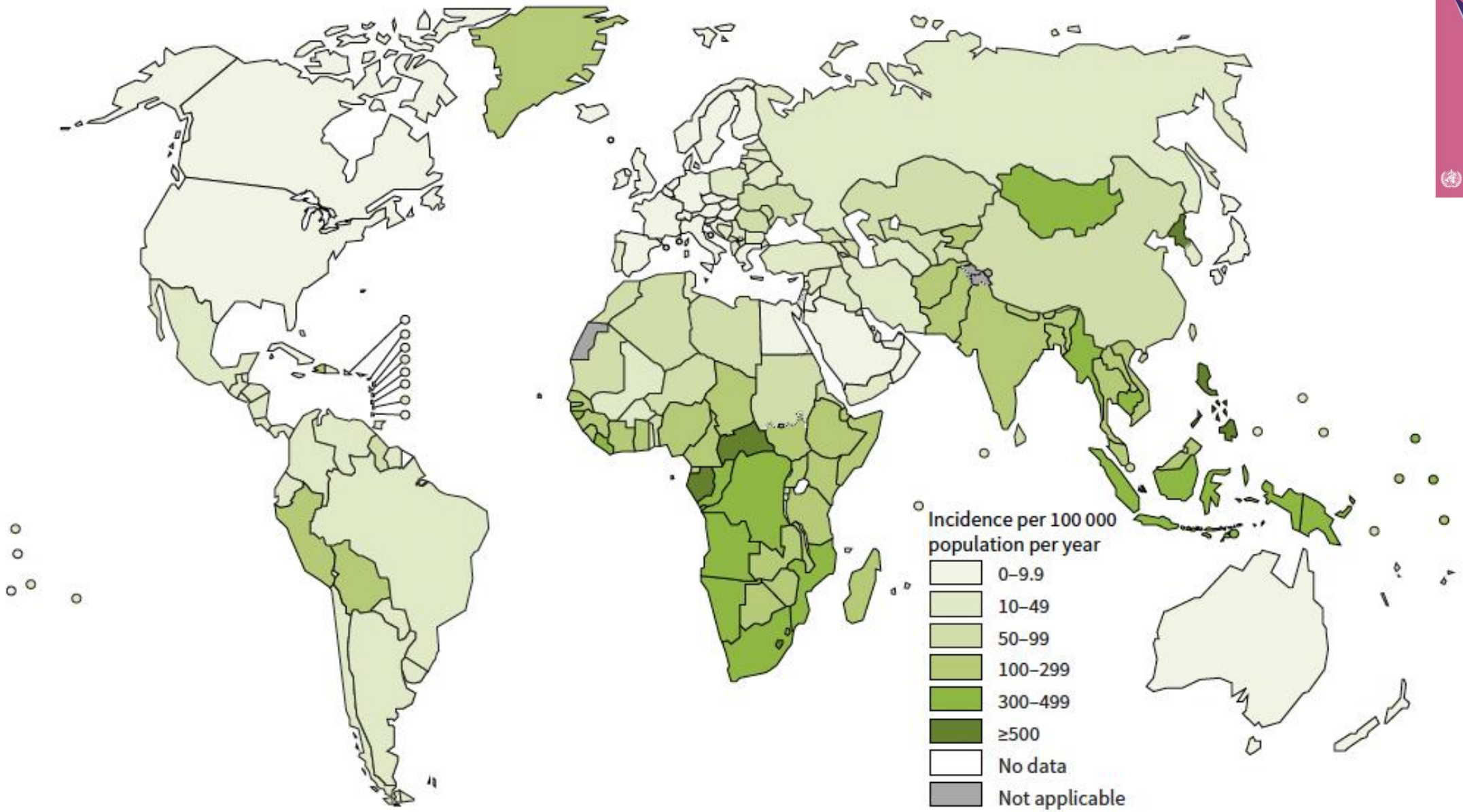


*Updated July 2012

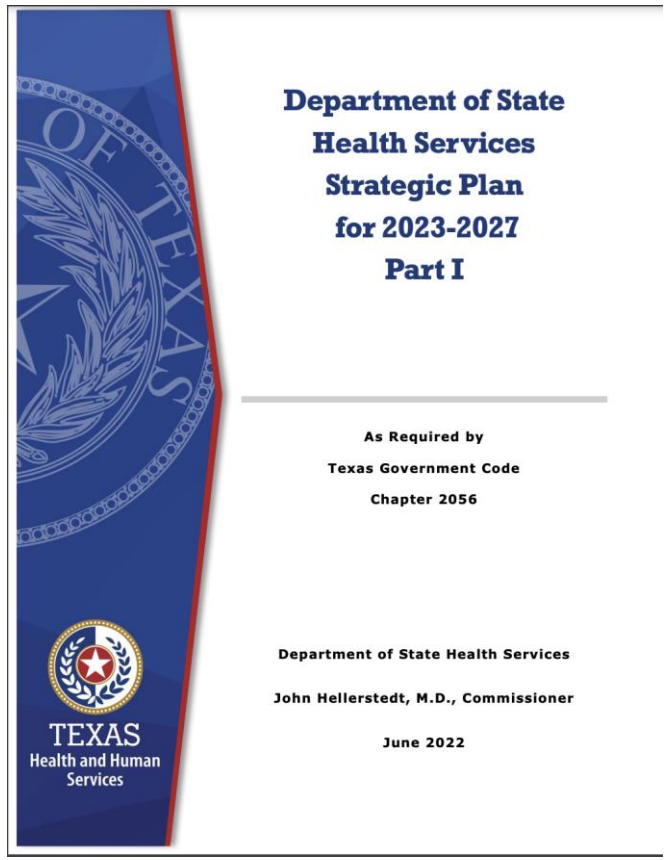


Merrill et al. Journal of Tuberculosis Research > Vol.4 No.3, September 2016

Estimated TB incidence rates, 2022



GLOBAL TUBERCULOSIS REPORT 2023



Our Vision

A Healthy Texas

Our Mission

To improve the health, safety, and well-being of Texans through good stewardship of public resources, and a focus on core public health functions.

Our Values

- Lead with a vision.
- Driven by science and data.
- Partner with a purpose.
- Engage and connect as a team.

Our Goals

- Improve and support health outcomes and well-being for individuals and families
- Ensure efficient access to appropriate services
- Protect the health and safety of vulnerable Texans
- Continuously enhance efficiency and accountability

In 2020...

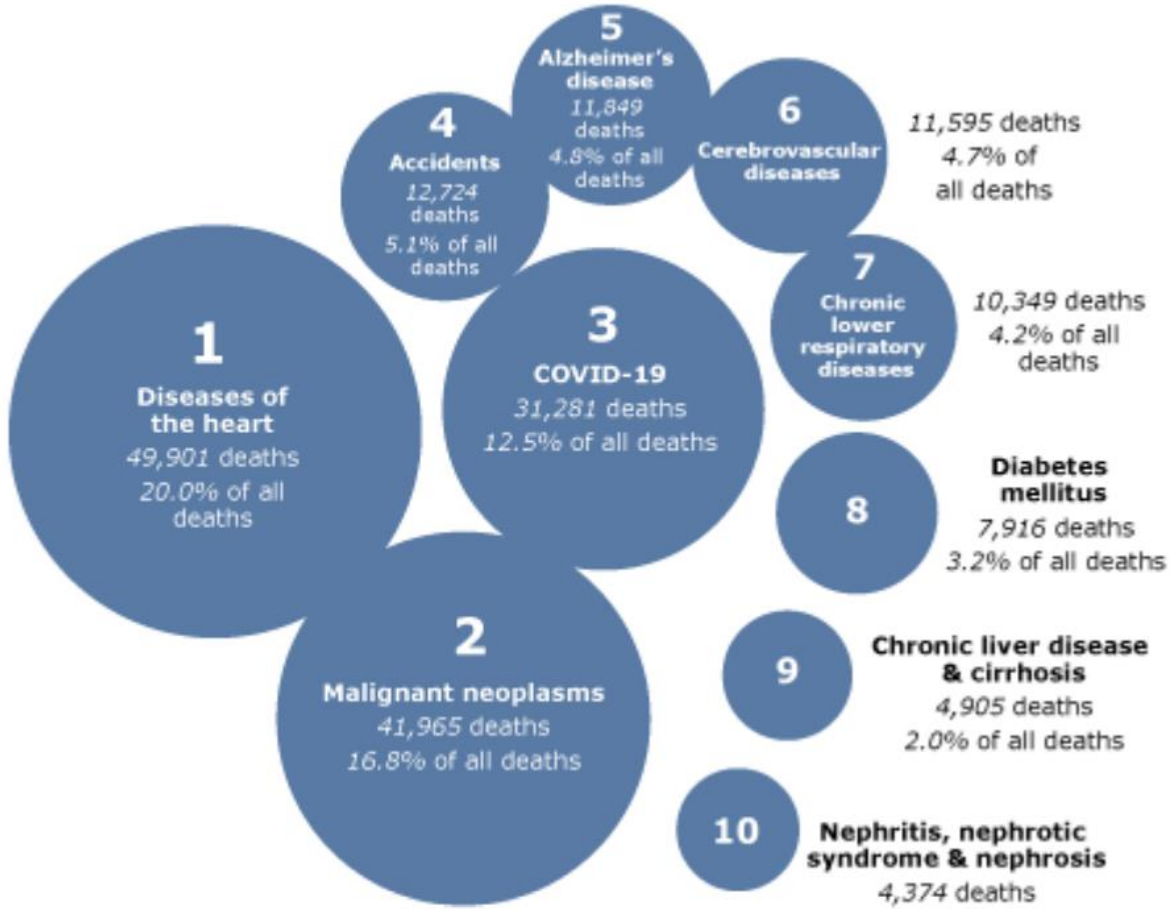
...there were:

249,267
total deaths

...there were:

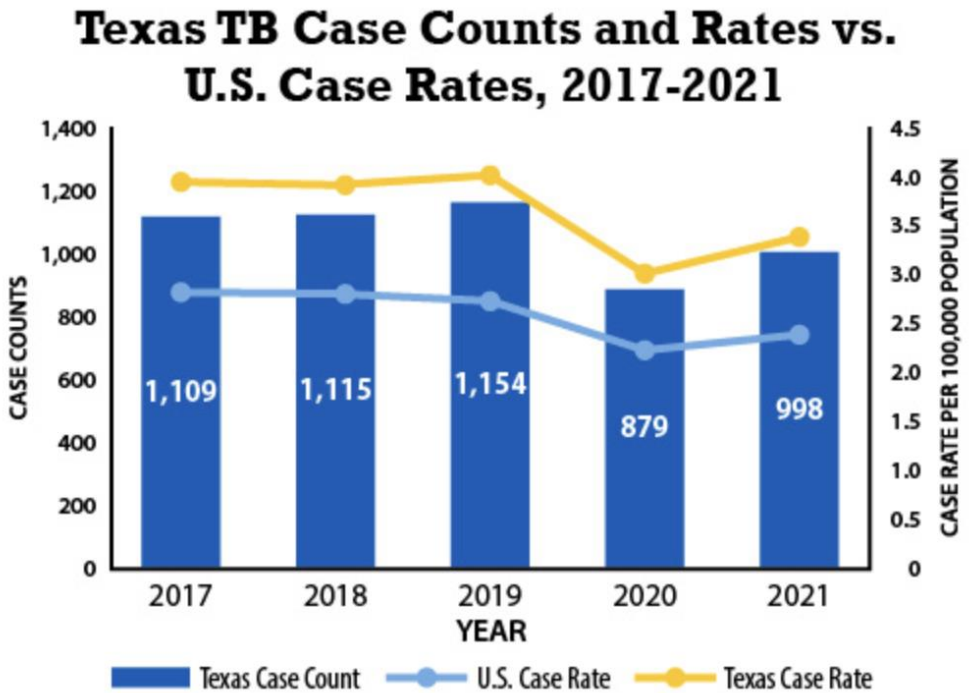
839.9
deaths per
100,000 population

...the top 10 causes of death among Texas residents were:

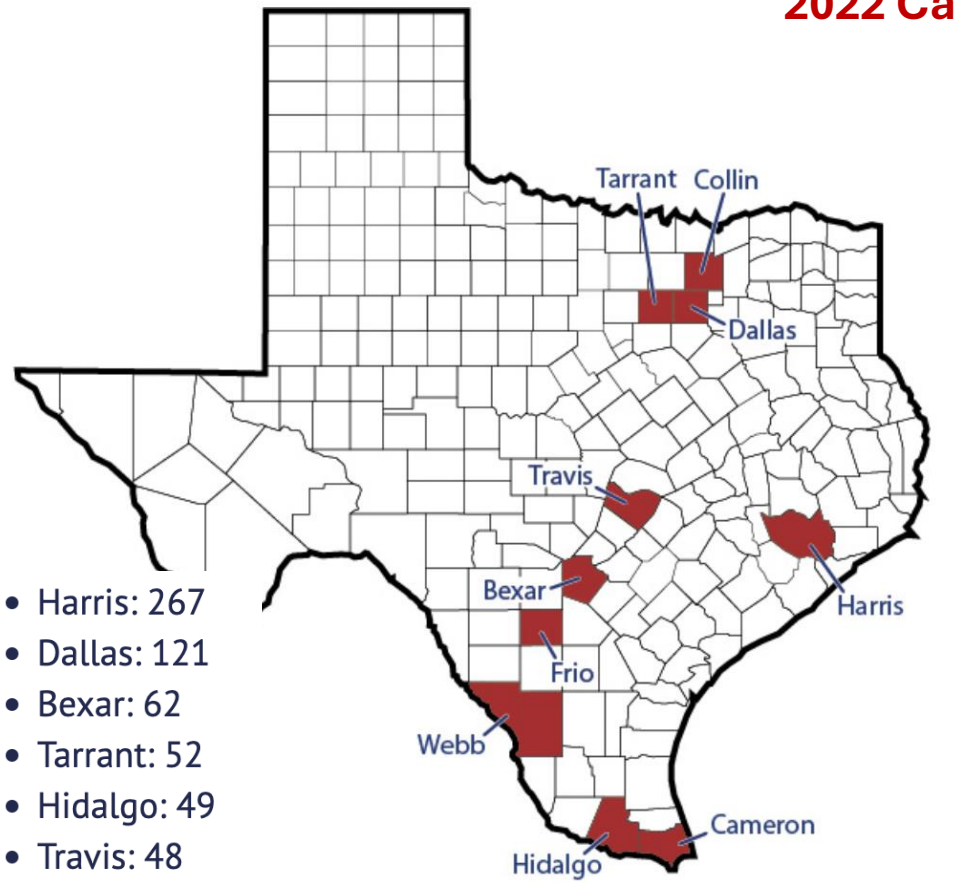


Please note that all data for 2020 are provisional. See data notes for further detail

Is TB thwarting our efforts to achieve our shared vision of a HEALTHY TEXAS?



2022 Cases



- Harris: 267
- Dallas: 121
- Bexar: 62
- Tarrant: 52
- Hidalgo: 49
- Travis: 48
- Cameron: 46
- Frio: 46
- Collin: 35
- Webb: 32

https://www.dshs.texas.gov/tuberculosis-tb/tb-data-statistics#

7,415

Number of people exposed to TB in 2022

>2,900

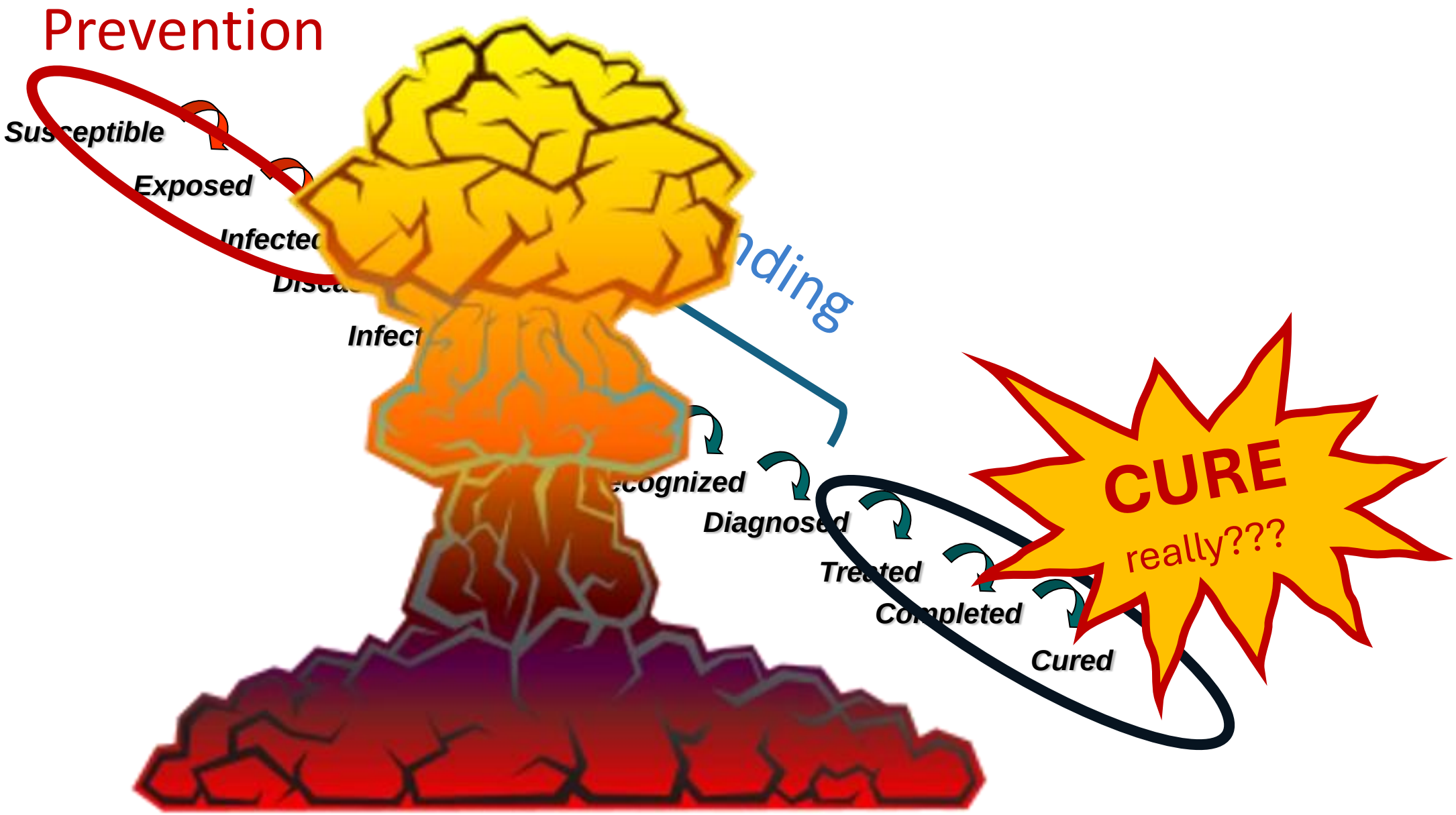
Number of people treated to prevent TB disease in 2022

1,097

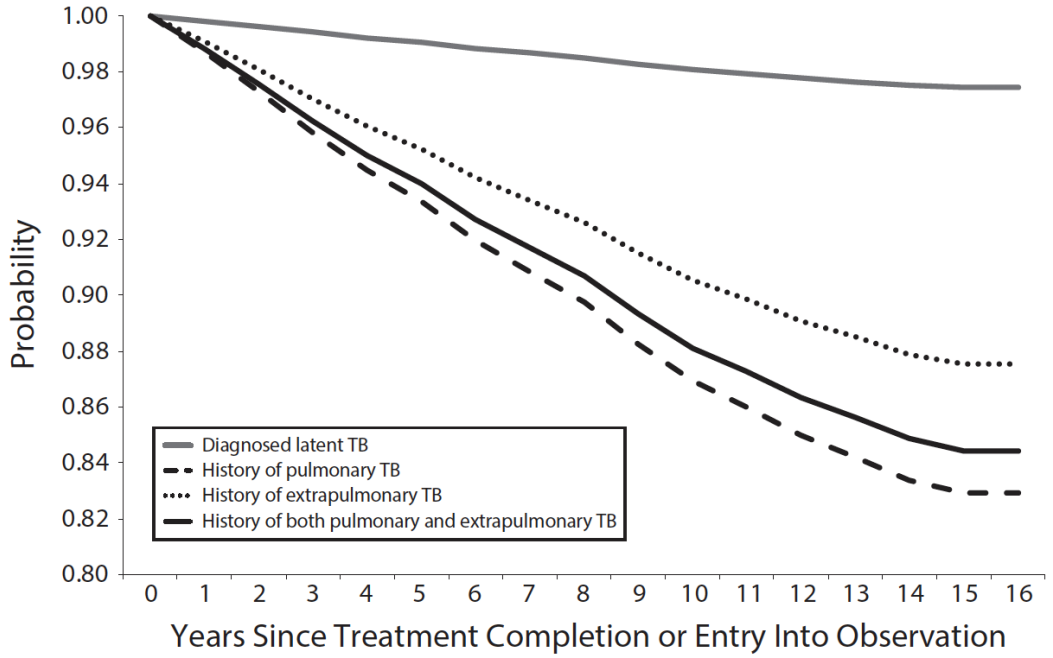
Number of Texas TB cases in 2022

https://www.dshs.texas.gov/tuberculosis-tb/tb-data-statistics#

Traditional Tuberculosis Cascade Of Care

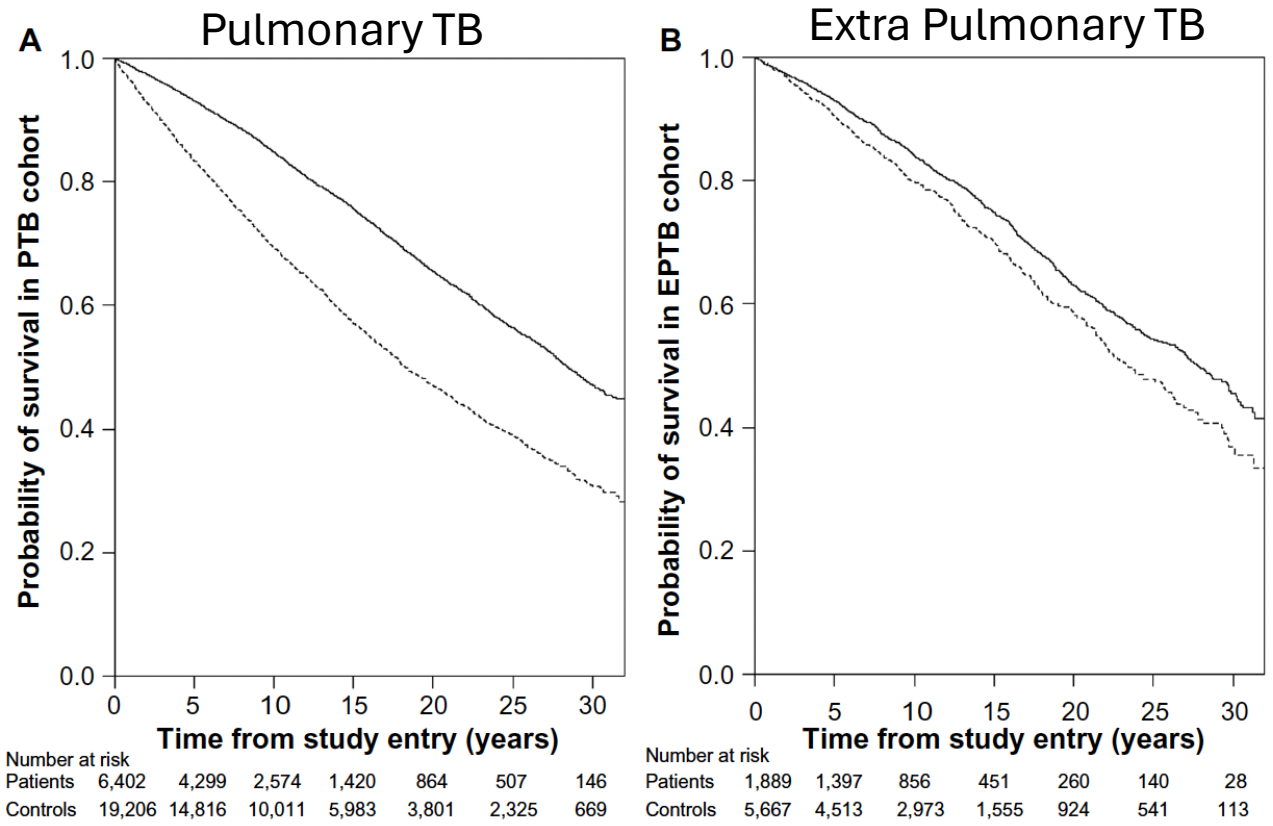


Mortality post “successful TB treatment”



Note. TB = tuberculosis. Treatment completion indicates a history of active TB; entry into observation indicates no history of active TB.

FIGURE 1—Age, gender, race/ethnicity, HIV status, and nativity-adjusted Cox regression survival probability by tuberculosis history: Centers for Disease Control and Prevention's National Death Index; Texas, Massachusetts, and Seattle and King County, WA; 2008.

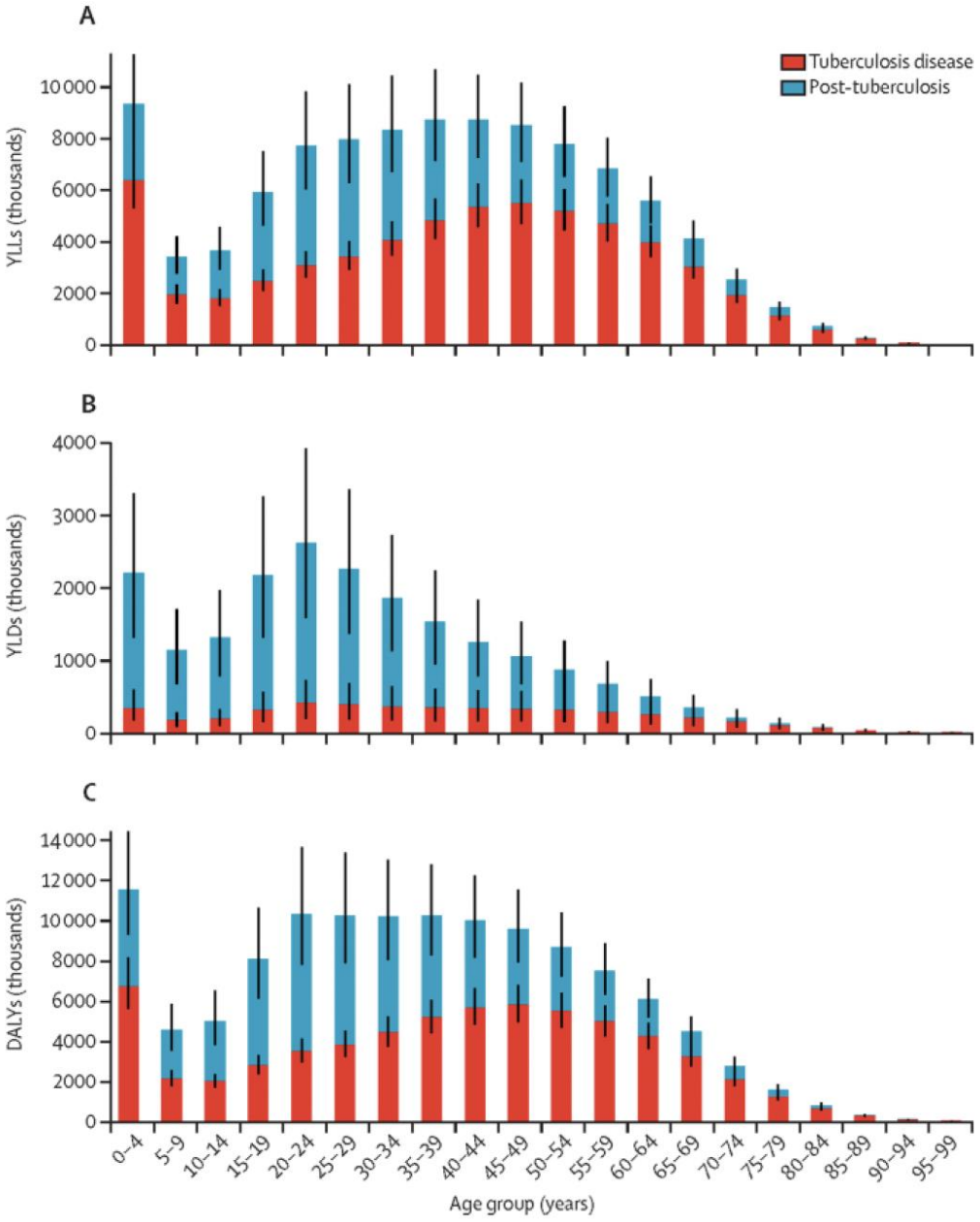


Increased long-term mortality in PTB stems from alcohol, tobacco, and drug abuse as well as immune suppression, and family-related factors.

Miller et al. AJPH. 2014

Christensen et al. Clin Epi 2014

Lifetime burden of disease due to incident tuberculosis



YLL = years of life lost.

YLD = years lived with disability.

DALYs = disability-adjusted life-years.

One DALY represents the loss of the equivalent of one year of full health. DALYs are the sum of the years of life lost to due to premature mortality (YLLs) and the years lived with a disability (YLDs)

Menzies et al. Lancet Global Health. 2021

Estimated long-term outcomes for 10^7 TB patients

~10,000,000
TB Cases a year

5-year Post-TB Outcomes

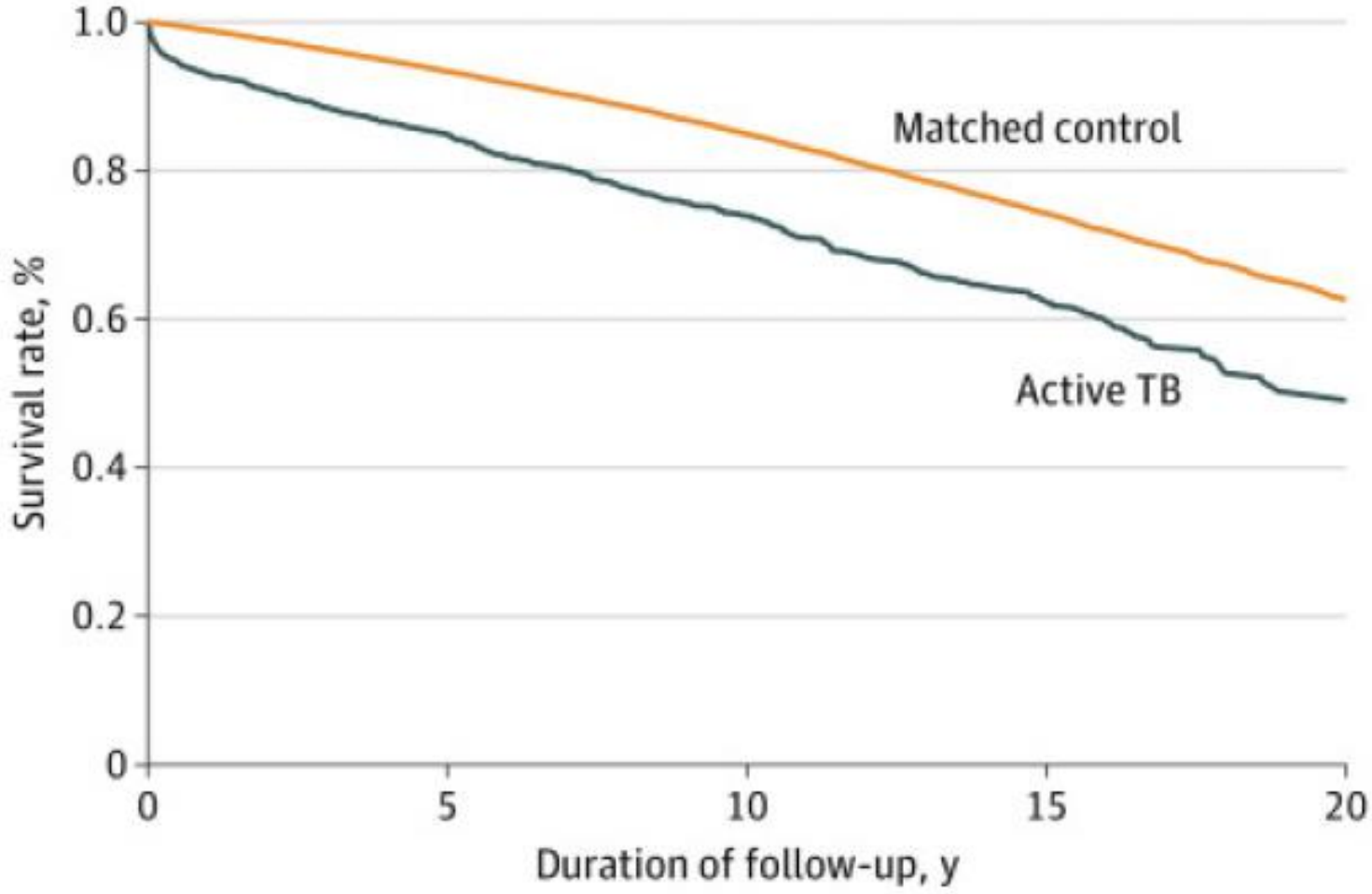
Pre/ In-Rx Death	10-15% *	1.5 million deaths/ yr.
Relapse	~2%	200,000 relapses/ yr.
Post-Rx death	2-6 deaths/ 100 PYs	105-300,000 deaths
Post-Rx CVD	1.7 CVD deaths/ 100 PYs	88,000 CVD deaths
Post-Rx cancer (Ca)	1.2 Ca deaths/ 100 PYs	60,000 Ca deaths
Lung Dysfunction	15% w severe disease	1.5 million w severe PTLD

References & Notes
1: 2021 WHO Report; * TB mortality dramatically reduces once antimicrobial therapy is started.
2: Vega et al 2021, BMJ Thorax, PMID: 33547088; alternative reference PMID: 20074418
3: Romanowski & Lee-Rodriguez;
4: Blondal: 81 post-TB Cardiovascular (CVD) deaths; * only represents deaths, not all CVD morbidity.
5: Christensen; 22% Post-TB mortality due to Cancer; only represents Cancer deaths, not all cancer morbidity
6: Ravimohan 2018; 2020; Pasipanodya 2007

SLIDE CREDIT: Andrew DiNardo

Survival Probability Among Patients With Active TB

Kaiser Permanente Northern California, 1997-2017



YEARS of POTENTIAL LIFE LOST
7.0 (95% CI 8.4 to 5.5)

2,522 TB patients → 17K p-y follow-up
COMPARED TO
101K Age-, Sex-, and Date of Diagnosis–Matched Cohort of Patients Without TB → 736K p-y follow-up

Lee-Rodrigues et al. JAMA. 2020

Estimated long-term outcomes for 10^3 TB patients

~1,100

TB Cases a year

5-year Post-TB Outcomes

Pre/ In-Rx Death	10-15% *	110- 165	deaths/ yr.
Relapse	~2%	22	relapses/ yr.
Post-Rx death	2-6 deaths/ 100 PYs	115 - 330	deaths
Post-Rx CVD	1.7 CVD deaths/ 100 PYs	97	CVD deaths
Post-Rx cancer (Ca)	1.2 Ca deaths/ 100 PYs	66	Ca deaths
Lung Dysfunction	15% w severe disease	165	w severe PTLD

References & Notes

1: 2021 WHO Report; * TB mortality dramatically reduces once antimicrobial therapy is started.

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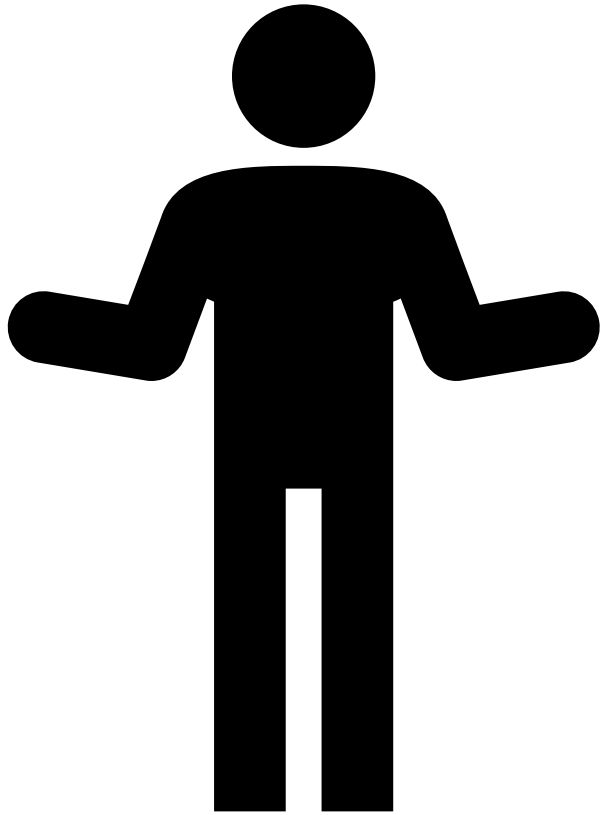

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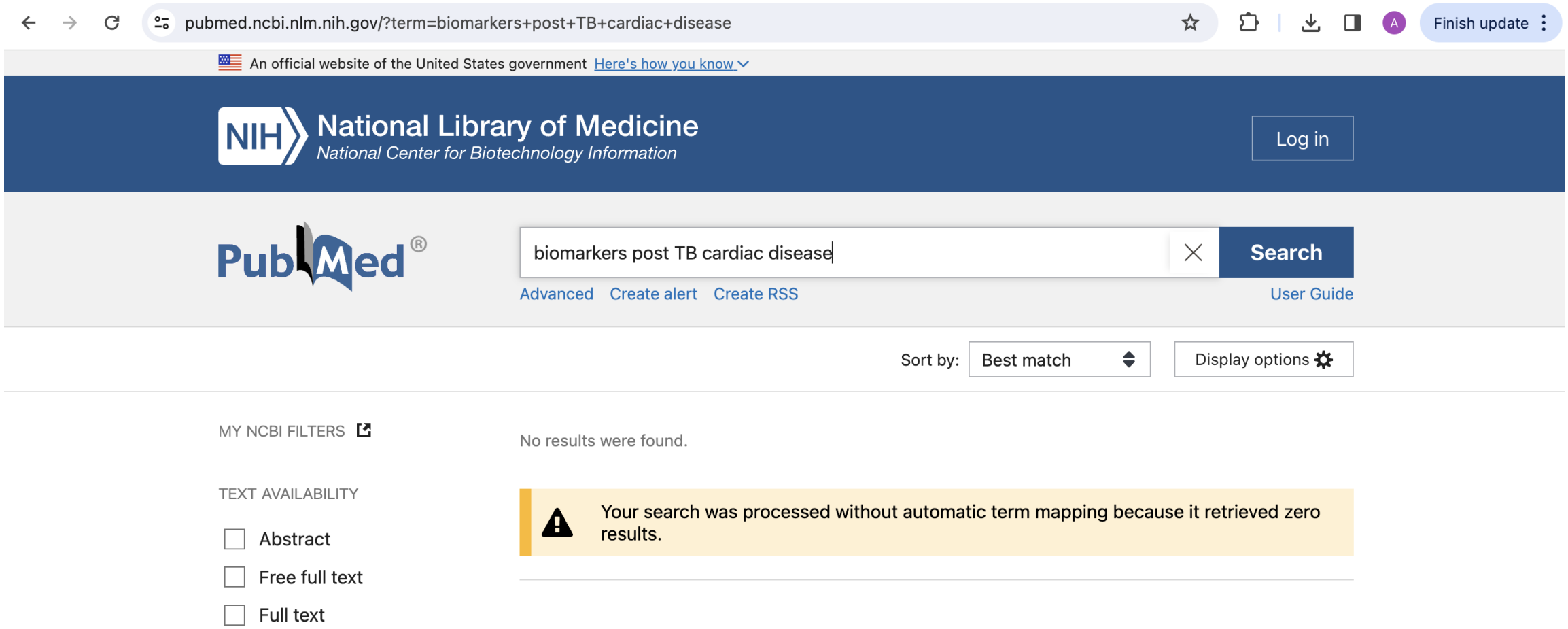
pubmed.ncbi.nlm.nih.gov/?term=biomarkers+post+TB+cardiac+disease
Finish update
An official website of the United States government Here's how you know
NIH National Library of Medicine
National Center for Biotechnology Information
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biomarkers post TB cardiac disease
Search
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Display options
MY NCBI FILTERS
No results were found.
TEXT AVAILABILITY
Abstract
Free full text
Full text
Your search was processed without automatic term mapping because it retrieved zero results.

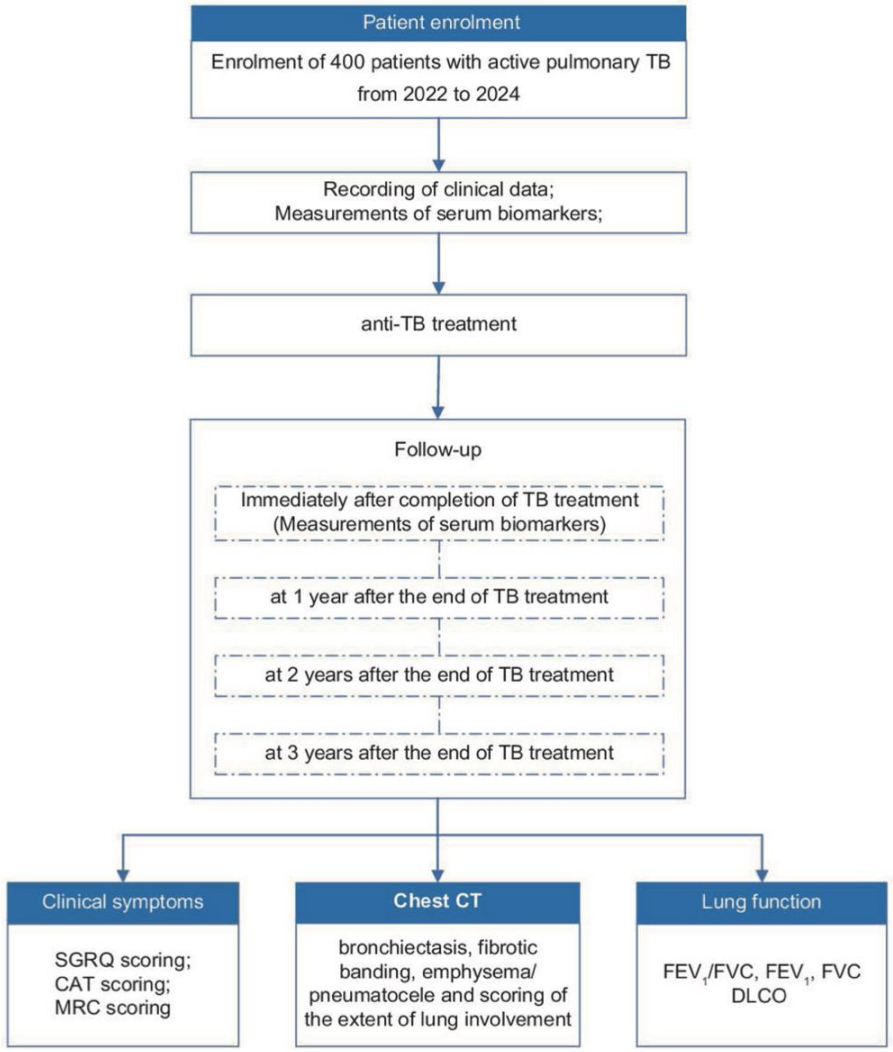
PTLD: Limited but Emerging Evidence

- PTLD has a very wide disease spectrum
  - a single immunologic or radiographic marker will likely not be sufficient
  - No definitive immunologic markers have been identified
  - Positron emission tomography (PET) with 18FDG in combination with CT
  - *Singh et all. Tuberculosis. 2022 September*
- Elevated IL-6 and slow-to-resolve TGF-β
  - Adults in Chennai (30 confirmed PTB evaluated at baseline, 2 mos, EOT)
  - *Gupte et al. ERJ Open Res 2021*
- Elevated matrix metalloproteinase (MMP)-1 (~~TGF-β & IFN-ɣ~~)
  - Adults in Delhi (10 PTBSx, 10 PTBnoSx, 10 Control)
  - *Shunmugasundaram et al. Tuberc Respi Dis 2022 April*

Open access Protocol

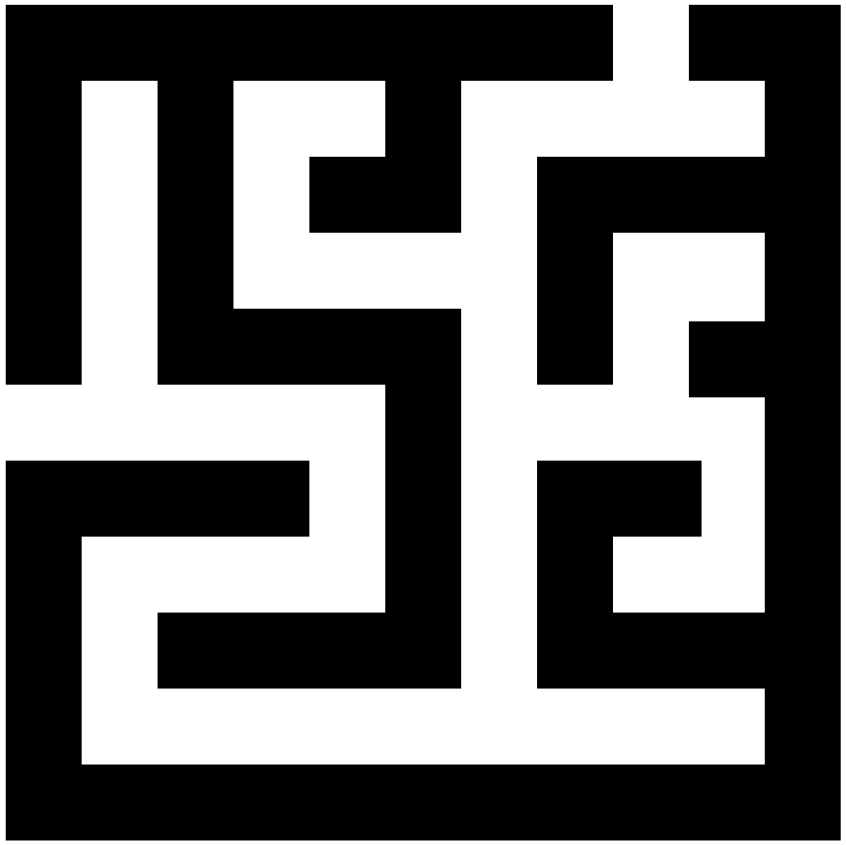
BMJ Open

Risk factors and biomarkers for post-tuberculosis lung damage in a Chinese cohort of male smokers and non-smokers: protocol for a prospective observational study



Texas – sized Questions

- Is TB thwarting our efforts to achieve a **Healthy Texas**?
- How many Texans are suffering from post-TB lung disease?
- How many Texans are dying early due to post-TB mortality?
- Can we predict who is at greatest risk?
- Can we develop targeted interventions to mitigate poor outcomes?
- Can we join forces to answer these questions in the communities that we serve and leave no one behind?



Lot's of estimates &
a good bit of uncertainty

Where do we begin?

INT J TUBERC LUNG DIS 25(10):797–813

http://dx.doi.org/10.5588/ijtld.21.0425

CLINICAL STANDARDS FOR LUNG HEALTH

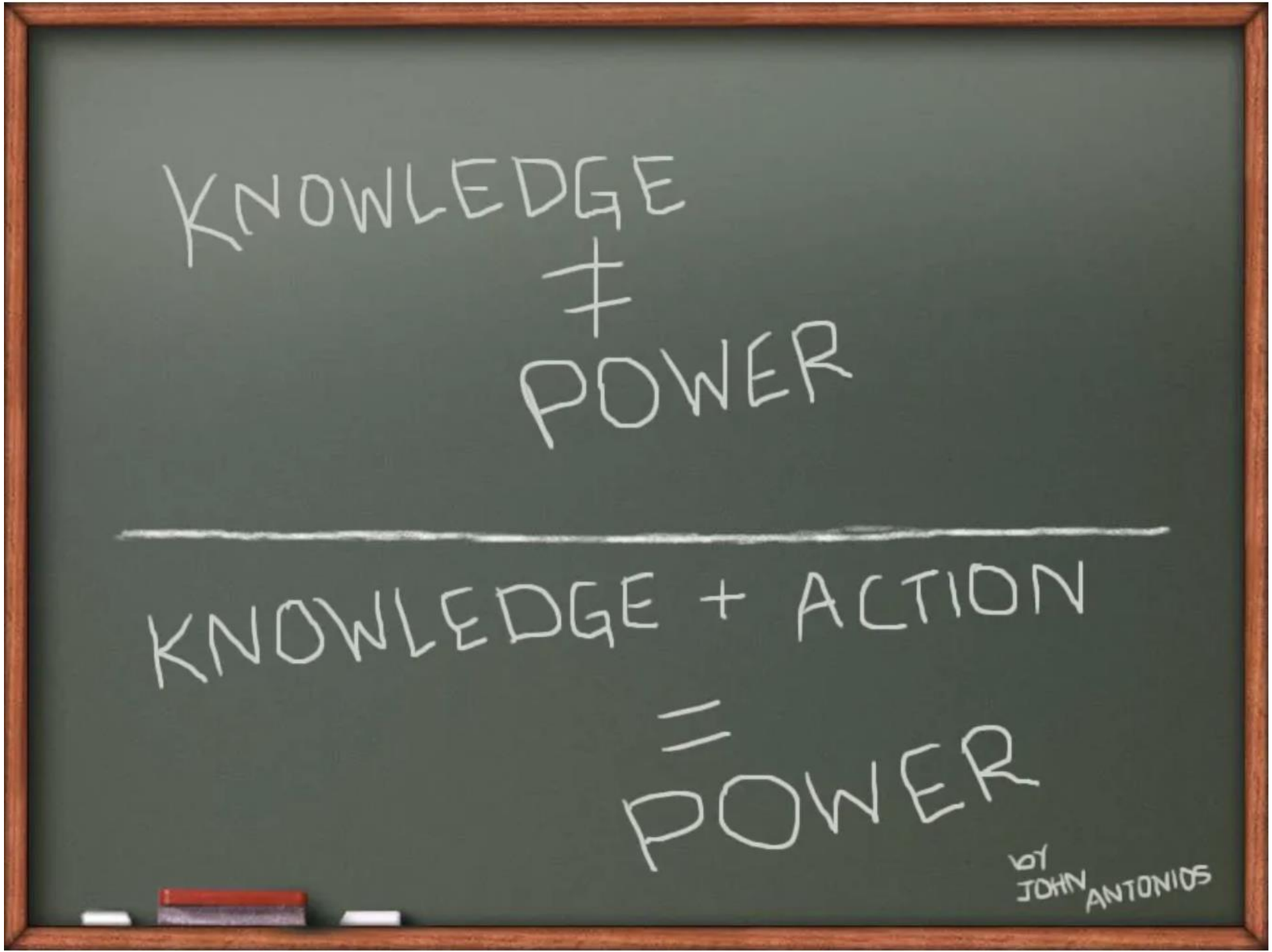
Clinical standards for the assessment, management and rehabilitation of post-TB lung disease

- Standard 1: all TB patients should be assessed for PTLD


mrcscore
trolox
sgrqscore
alcohol
ethnicity
familial
mri
race
chestct
il6
fev1
18fdg
petct
ifny
pft
hiv
dlco
gender
easyone
mmp
age
tgfß
fvc
crp
petscan
cxr
fev1fvc
nativity
tobacco
catscore
bronchiectasis

Implementing screening spirometry is feasible (<15 minutes) and possible in out-patient settings

EasyOne Spirometer


KNOWLEDGE
≠
POWER
KNOWLEDGE + ACTION
=
POWER
by JOHN ANTONIOS

THANK YOU for LISTENING

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