During, and After, Tuberculosis: How can we make life better for TB survivors?

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Should we consider a 'fourth 90' for tuberculosis?

A. D. Harries,[1,2] R. A. Dlodlo,[1] G. Brigden,[1] K. Mortimer,[1,3] P. Jensen,[1] P. I. Fujiwara,[1] J. L. Castro,[1] J. M. Chakaya[1,4]

Table 90-(90)-90 Stop TB partnership global targets for TB (adapted from[4])

- Reach and treat at least 90% of all people with TB*
- As a part of this approach reach and treat at least (90%) of the key populations†
- Achieve at least 90% treatment success for all people diagnosed with TB‡

* Includes people with drug-susceptible and drug-resistant TB and people who require preventive therapy (for example, people living with HIV and those in contact with TB patients).
† Includes at-risk populations which can vary depending on country context.
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TB = tuberculosis.

Harries, IJTLD, 2019

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A Proposed 4th 90

'Ensuring that 90% of all people successfully completing treatment for TB can have a good health related quality of life'.

- Diabetes
- HIV
- Smoking
- Alcohol
- Mental Health
- Pulmonary rehabilitation

Harries, IJTLD, 2019

TABLE 2

Cumulative number of deaths averted by TB and TB/HIV interventions 2000–2020 (in millions), globally and by WHO region[a]

WHO REGION	HIV-NEGATIVE PEOPLE		HIV-POSITIVE PEOPLE		TOTAL	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
African Region	6.6	5.5–7.7	8.2	6.9–9.5	15	13–17
Region of the Americas	1.8	1.7–2.0	0.34	0.31–0.38	2.3	2.0–2.3
South-East Asia Region	23	19–28	2.8	1.9–3.8	26	22–31
European Region	2.1	1.8–2.3	0.30	0.26–0.34	2.4	2.1–2.6
Eastern Mediterranean Region	4.7	4.1–5.3	0.08	0.06–0.10	4.8	4.2–5.4
Western Pacific Region	15	14–16	0.48	0.40–0.57	16	14–17
Global	54	47–60	12	11–14	66	59–73

Due to improvements in TB detection and treatment, we have a growing population of TB survivors

WHO Global TB Report, 2021

Quantifying the global number of tuberculosis survivors: a modelling study

Dodd, Lancet ID, 2020

	African region	Region of the Americas	Eastern Mediterranean region	European region	South-East Asia region	Western Pacific region	Global
Total new tuberculosis cases, 1980–2019	72 400 000 (60 800 000–84 000 000)	11 500 000 (10 700 000–12 400 000)	25 600 000 (2 230 000–48 900 000)	14 300 000 (12 200 000–16 300 000)	161 000 000 (95 100 000–227 000 000)	77 800 000 (51 800 000–104 000 000)	363 000 000 (287 000 000–438 000 000)
New treated tuberculosis cases, 1980–2019	32 300 000 (31 900 000–	9 120 000 (9 000 000–	12 500 000 (12 400 000–	12 000 000 (11 800 000–	68 500 000 (66 500 000–	37 300 000 (36 400 000–	172 000 000 (169 000 000–
1980–2020	(378 000 000–620 000 000)	(143 000 000–151 000 000)	(199 000 000–374 000 000)	(175 000 000–188 000 000)	(1 230 000 000–1 960 000 000)	(588 000 000–955 000 000)	(3 040 000 000–3 920 000 000)
Post-tuberculosis life-years among treated individuals, 1980–2020	267 000 000 (164 000 000–370 000 000)	127 000 000 (123 000 000–130 000 000)	166 0 (160 00 171 000				000 000– 000)
Post-tuberculosis life-years among untreated individuals, 1980–2020	232 000 000 (168 000 000–295 000 000)	20 200 000 (18 000 000–22 400 000)	121 0 (33 400 208 000 000)	26 900 000)	1 170 000 000)	533 000 000)	000 1 970 000 000)
Total tuberculosis survivors alive in 2020	25 700 000 (18 600 000–32 800 000)	5 510 000 (5 320 000–5 700 000)	12 600 000 (9 430 000–15 800 000)	6 710 000 (6 460 000–6 960 000)	72 200 000 (58 700 000–85 700 000)	31 900 000 (26 600 000–37 200 000)	155 000 000 (138 000 000–171 000 000)
Treated tuberculosis survivors alive in 2020	15 200 000 (8 460 000–21 900 000)	4 780 000 (4 610 000–4 950 000)	7 750 000 (7 470 000–8 030 000)	6 020 000 (5 820 000–6 220 000)	41 700 000 (39 500 000–43 900 000)	21 000 000 (20 200 000–21 900 000)	96 400 000 (89 300 000–104 000 000)
Untreated tuberculosis survivors alive in 2020	10 500 000 (8 200 000–12 800 000)	734 000 (653 000–815 000)	4 870 000 (1 690 000–8 060 000)	693 000 (540 000–846 000)	30 500 000 (17 200 000–43 900 000)	10 800 000 (5 580 000–16 100 000)	58 200 000 (43 300 000–73 000 000)

Data are number of cases (95% UI) or life-years (95% UI). Rounding means that the sums of treated and untreated might not equal the totals exactly. UI=uncertainty interval.

Table 1: **Tuberculosis cases, life-years lived, and 2020 tuberculosis survivors globally and by WHO region**

Interpretation The number of tuberculosis survivors alive in 2020 is more than ten times the estimated annual tuberculosis incidence. Interventions to alleviate respiratory morbidity, screen for and prevent recurrent tuberculosis, and reduce stigma should be immediately prioritised for recently treated tuberculosis survivors.

155 *Million Survivors*

Long Term Mortality in People Treated for Tuberculosis

A systematic review and meta-analysis

Kamila Romanowski MSc, Brett Baumann MD, C Andrew Basham MSc, Faiz Ahmad Khan MD, Greg J Fox MD, James C Johnston MD

BC Centre for Disease Control
Provincial Health Services Authority

CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

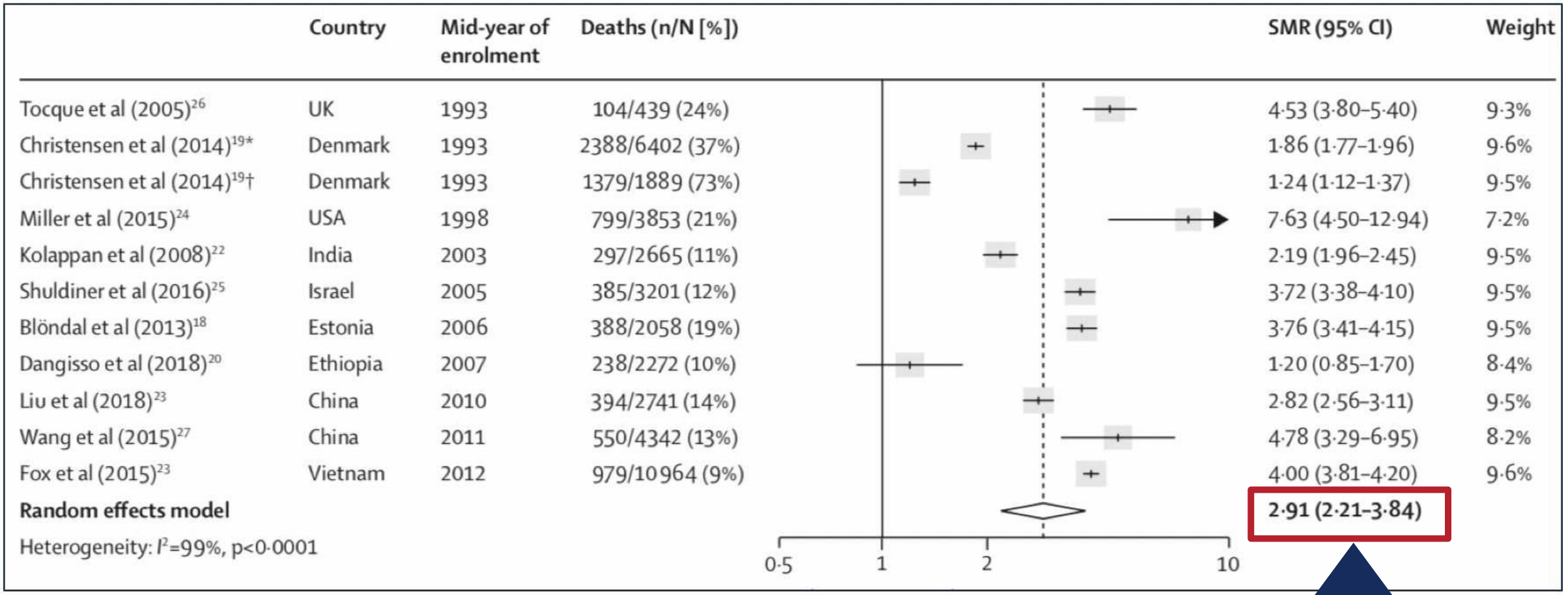
UBC

What do we know about the health of TB survivors?

- Often experience long-term disability after treatment completion
- Remain at-risk for recurrent TB disease
- Have high rates of socioeconomic marginalization and co-morbid disease

Lönnroth et al Soc Sci Med (2009)
Pasipanodya et at. BMC Public Health (2010)
Hargreaves et al Am J Public Health (2011)

Do people treated for active TB have high mortality post-treatment?

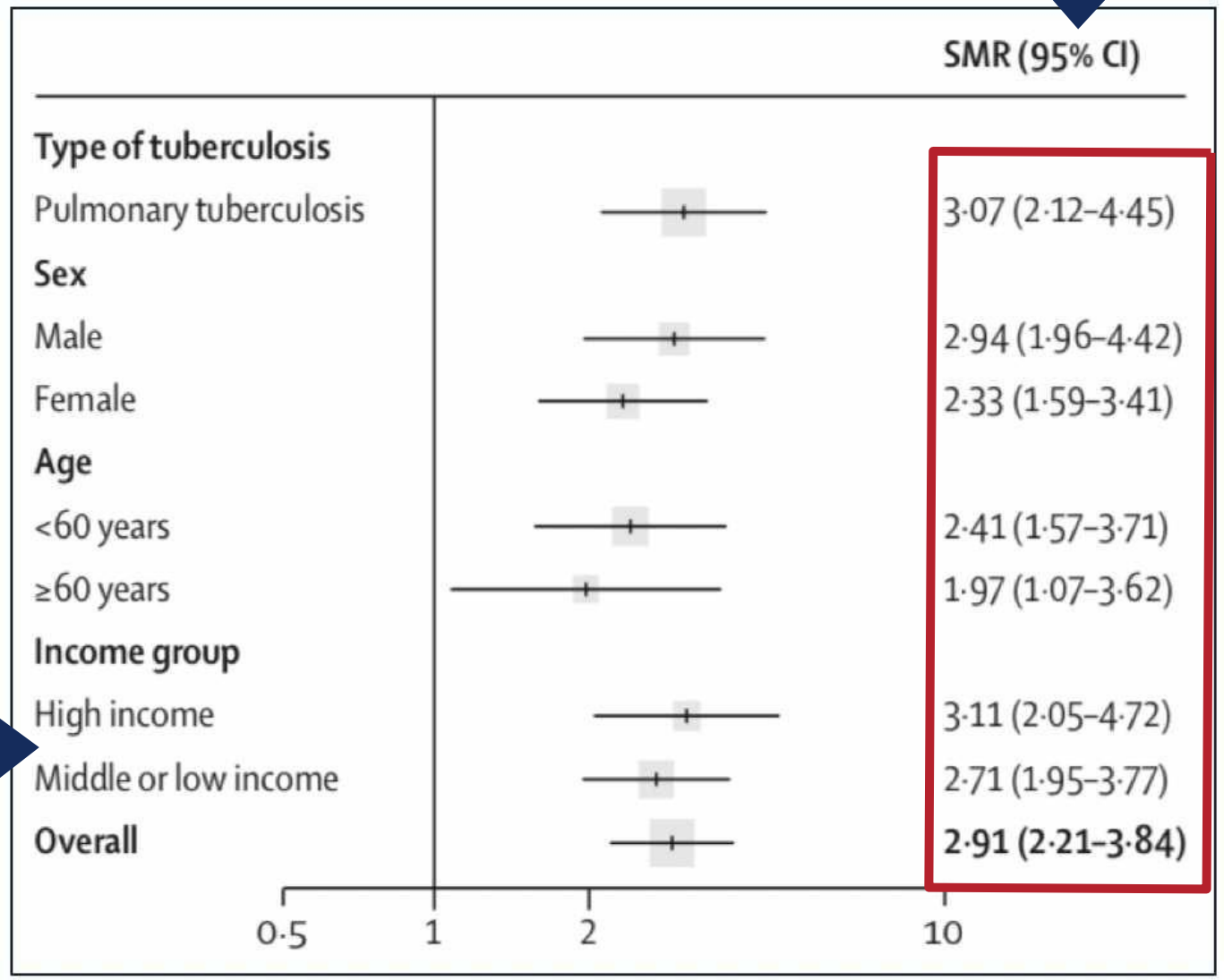


	Country	Mid-year of enrolment	Deaths (n/N [%])	SMR (95% CI)	Weight
Tocque et al (2005)[26]	UK	1993	104/439 (24%)	4·53 (3·80–5·40)	9·3%
Christensen et al (2014)[19]*	Denmark	1993	2388/6402 (37%)	1·86 (1·77–1·96)	9·6%
Christensen et al (2014)[19]†	Denmark	1993	1379/1889 (73%)	1·24 (1·12–1·37)	9·5%
Miller et al (2015)[24]	USA	1998	799/3853 (21%)	7·63 (4·50–12·94)	7·2%
Kolappan et al (2008)[22]	India	2003	297/2665 (11%)	2·19 (1·96–2·45)	9·5%
Shuldiner et al (2016)[25]	Israel	2005	385/3201 (12%)	3·72 (3·38–4·10)	9·5%
Blöndal et al (2013)[18]	Estonia	2006	388/2058 (19%)	3·76 (3·41–4·15)	9·5%
Dangisso et al (2018)[20]	Ethiopia	2007	238/2272 (10%)	1·20 (0·85–1·70)	8·4%
Liu et al (2018)[23]	China	2010	394/2741 (14%)	2·82 (2·56–3·11)	9·5%
Wang et al (2015)[27]	China	2011	550/4342 (13%)	4·78 (3·29–6·95)	8·2%
Fox et al (2015)[23]	Vietnam	2012	979/10964 (9%)	4·00 (3·81–4·20)	9·6%
Random effects model				**2·91 (2·21–3·84)**	
Heterogeneity: I^2=99%, p<0·0001					

The number of observed deaths for TB survivors was almost three times higher than the expected number of deaths

Romanowski et al. Lancet ID (2019)

Results remained consistent in sub-group analysis

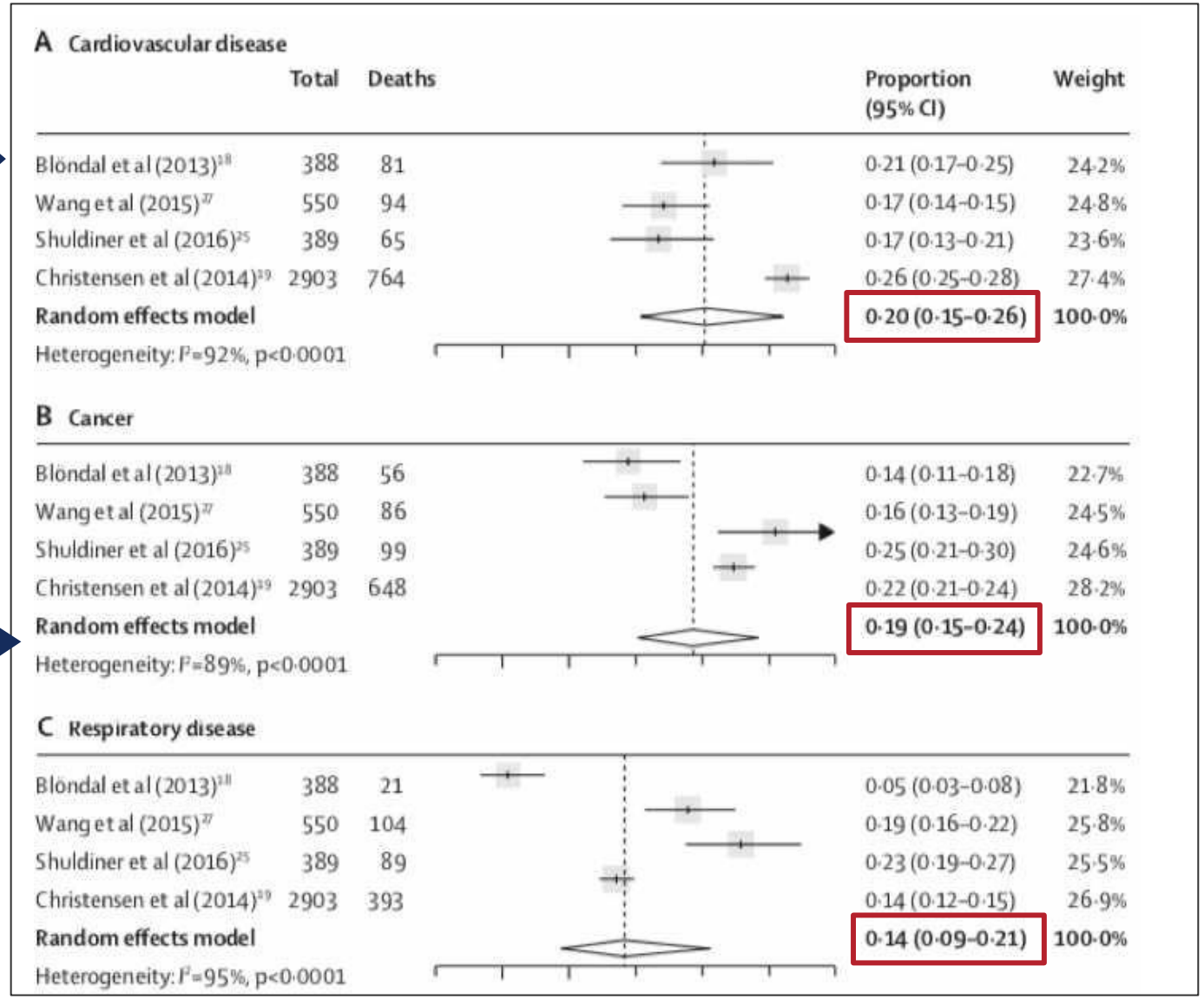


Similar findings for both high and low income countries

Romanowski et al. Lancet ID (2019)

Cardiovascular disease was the leading cause of post-treatment mortality

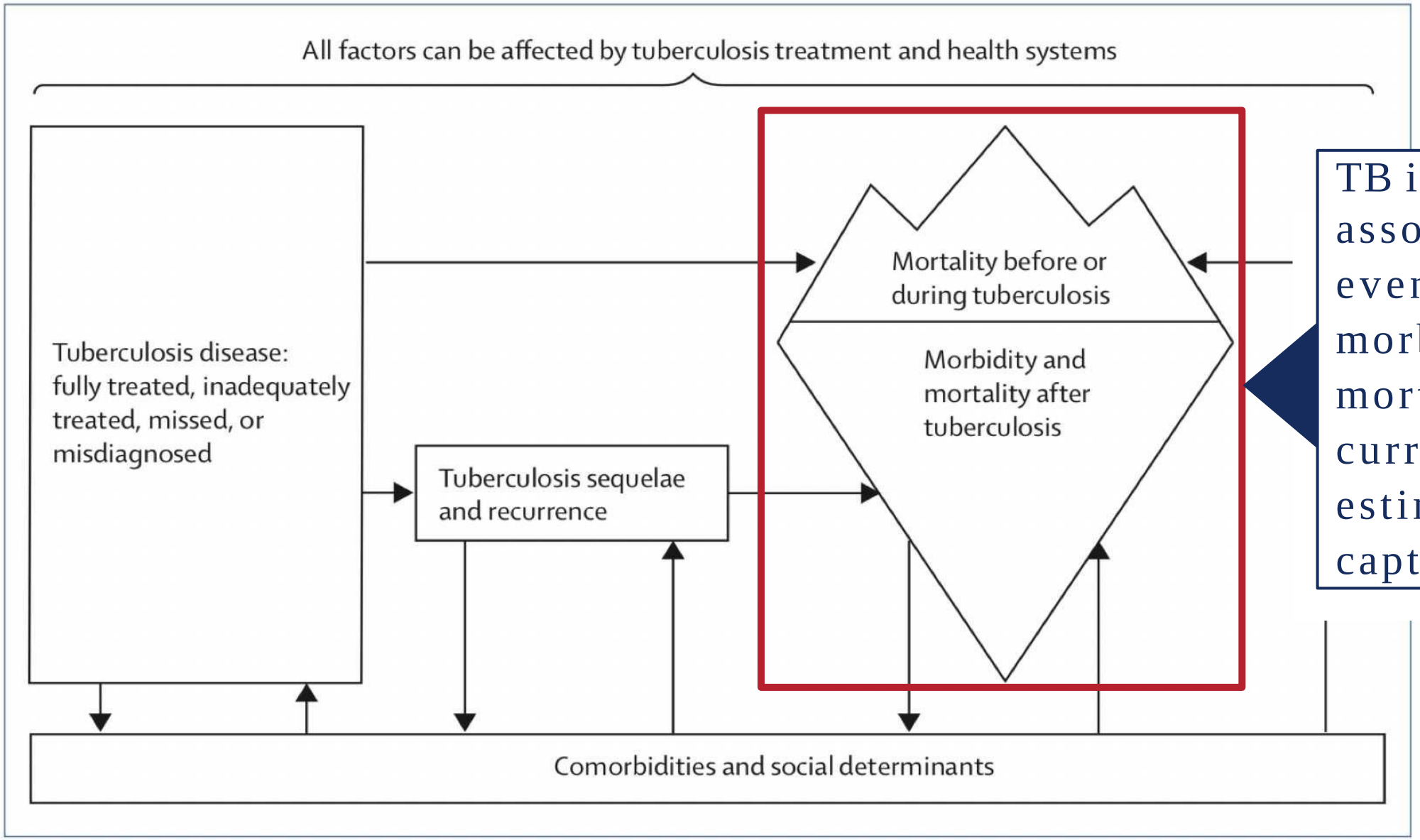
Followed by cancer and respiratory disease



Death due to TB or TB/HIV accounted for 9% of the causes of mortality

Romanowski et al. Lancet ID (2019)

The relationship between TB and mortality is complex



TB is likely associated with even greater morbidity and mortality than current estimates capture

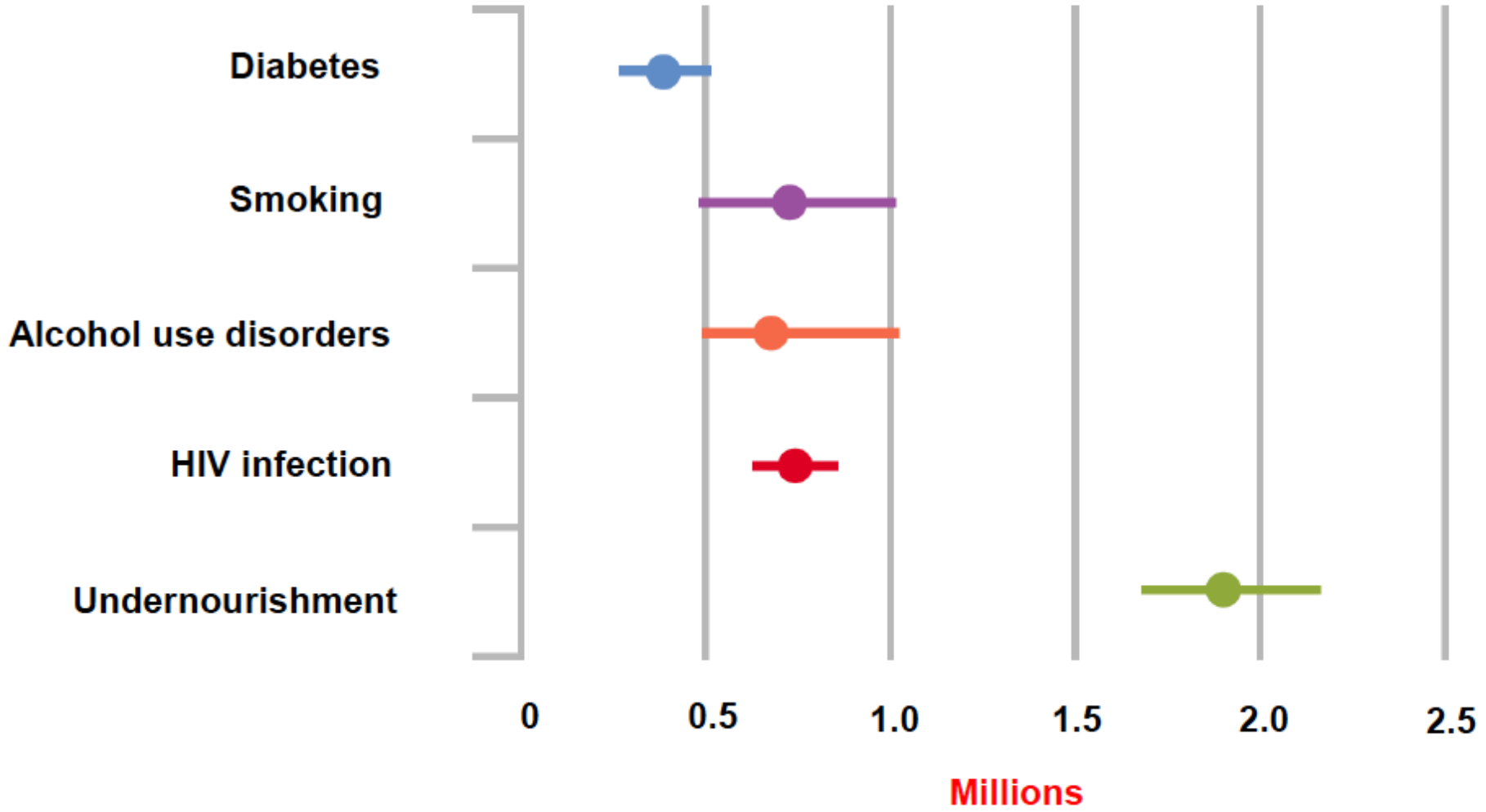
Datta et al. Lancet ID (2019).

TABLE 6.3.1 Global estimates of the number of TB cases attributable to selected risk factors, 2020

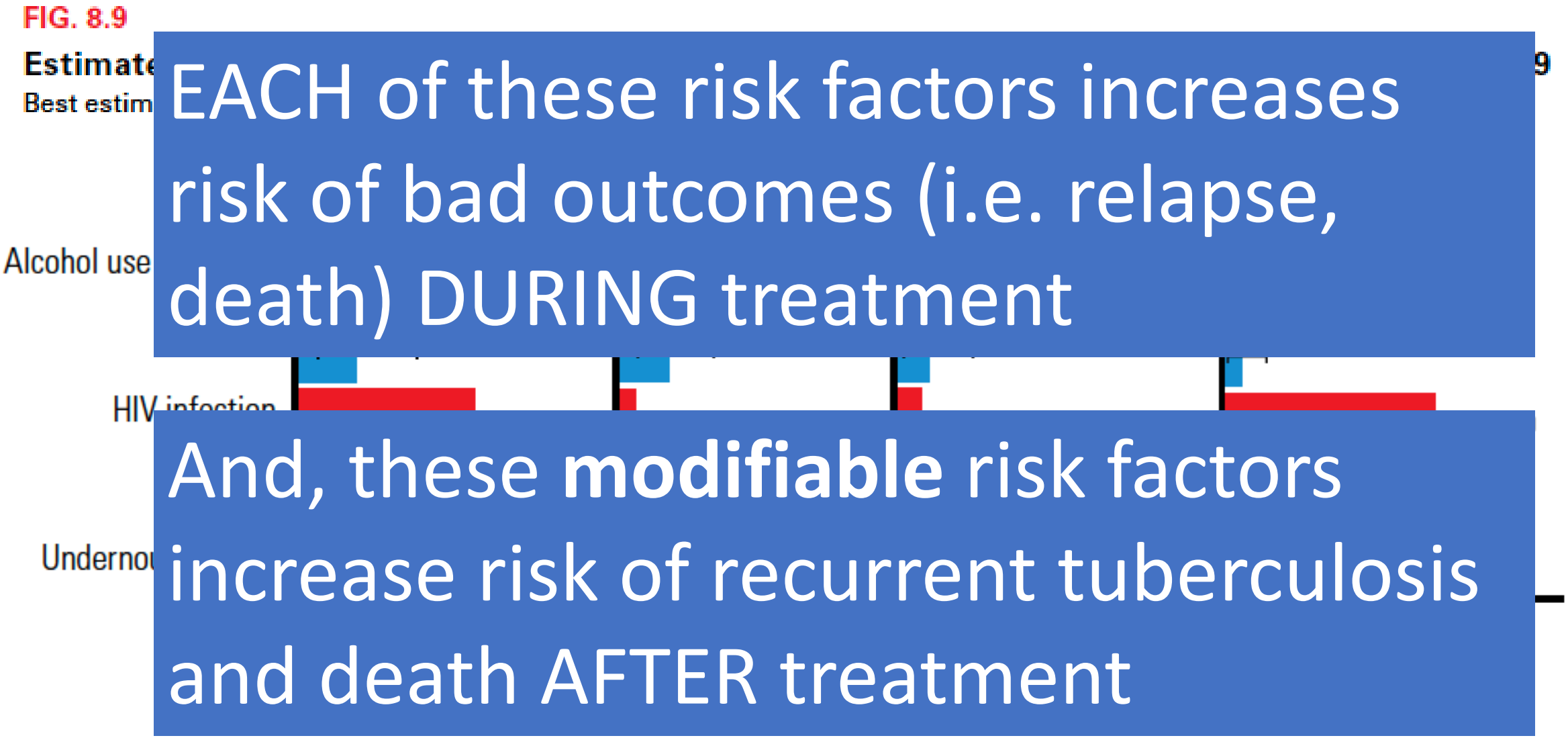
Risk Factor	Relative risk (uncertainty interval)	Exposed (millions)	Population attributable fraction (%)	Attributable TB cases (millions, uncertainty interval)
Alcohol use disorders	3.3 (2.1–5.2)	291 000	8.1	0.74 (0.31–1.3)
Diabetes	1.5 (1.3–1.8)	496 000	3.1	0.37 (0.15–0.68)
HIV infection	18 (15–21)	37 500	7.6	0.74 (0.65–0.83)
Smoking	1.6 (1.2–2.1)	1 050 000	7.1	0.73 (0.25–1.5)
Undernourishment	3.2 (3.1–3.3)	637 000	15	1.9 (1.3–2.6)

TB determinants

Estimates of TB cases attributable to 5 risk factors in 2020



World Health Organization



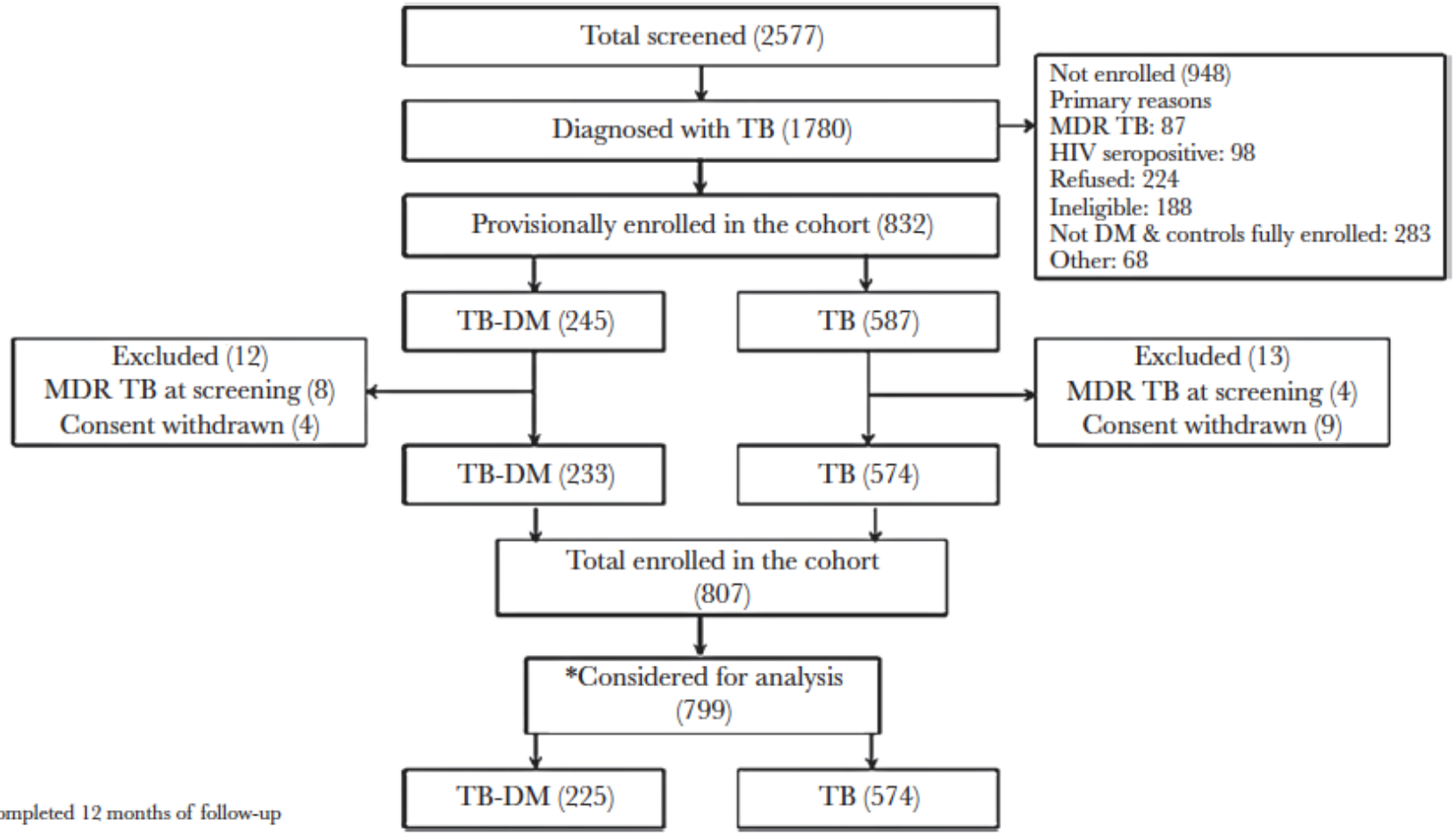
EACH of these risk factors increases risk of bad outcomes (i.e. relapse, death) DURING treatment

And, these **modifiable** risk factors increase risk of recurrent tuberculosis and death AFTER treatment

WHO Global Report 2021

Diabetes Mellitus and Tuberculosis Treatment Outcomes in Pune, India

Vidya Mave,[1,2] Sanjay Gaikwad,[1,3] Madhusudan Barthwal,[4] Ajay Chandanwale,[1,3] Rahul Lokhande,[1,3] Dileep Kadam,[1,3] Sujata Dharmshale,[1,3] Renu Bharadwaj,[1,3] Anju Kagal,[1,3] Neeta Pradhan,[1] Sona Deshmukh,[1] Sachin Atre,[4] Tushar Sahasrabudhe,[4] Shailesh Meshram,[4] Arjun Kakrani,[4] Vandana Kulkarni,[1] Swapnil Raskar,[1] Nishi Suryavanshi,[1] Hardy Kornfeld,[6] Kelly E. Dooley,[2] Sandy Chon,[2] Akshay Gupte,[5] Amita Gupta,[1,2,5] Nikhil Gupte,[1,2] and Jonathan E. Golub[2,5]



*Completed 12 months of follow-up

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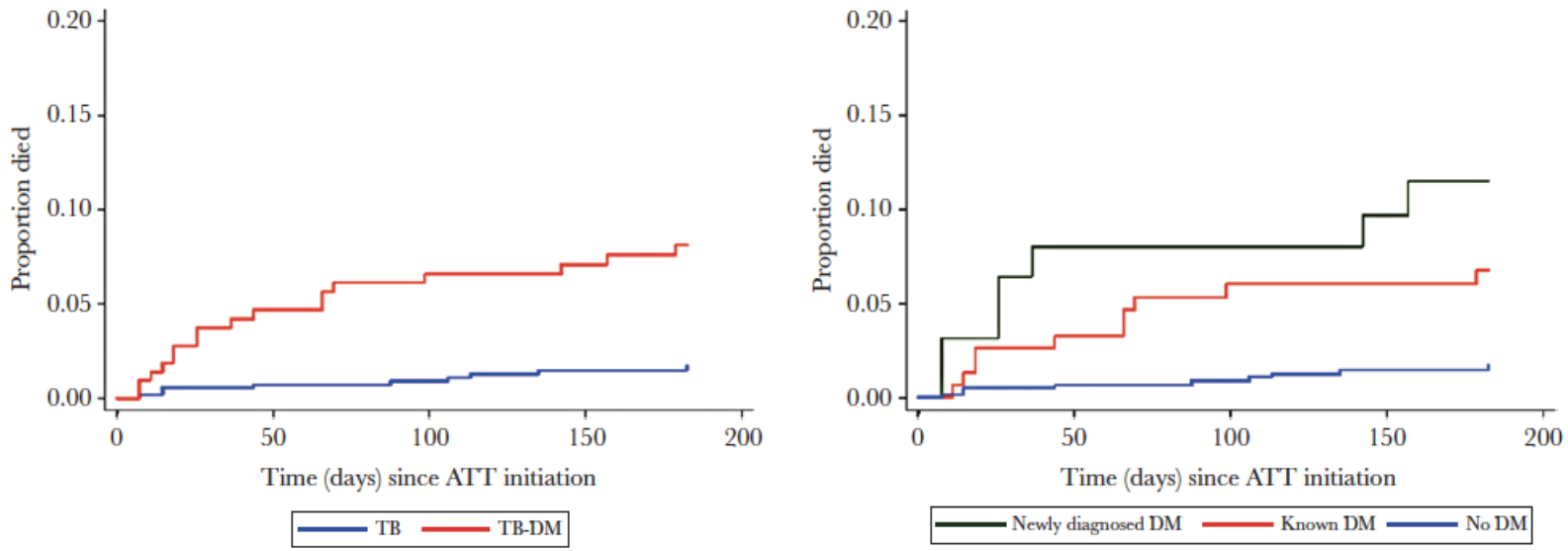


Figure 2. A, Kaplan-Meier curve showing time to early mortality (death during the period of tuberculosis treatment) among patients with tuberculosis (TB) by diabetes mellitus (DM) status. The red line represents patients with DM, and the blue line represents patients without DM. B, Kaplan-Meier curve showing time to early mortality by newly diagnosed diabetes mellitus (DM) and known DM among patients with tuberculosis (TB). The blue line represents patients with TB without DM, the green line represents newly diagnosed DM, and the red line represents known DM.

Diabetes is associated with early mortality

Outcomes	Yes	No	Unadjusted Risk Ratio (RR) (95% CI%)	#Adjusted RR (95% CI)
Unfavourable outcomes, n (%)				
No DM (n=574)	119 (21%)	455 (79%)	1	1
DM (n=225)	44 (20%)	181 (80%)	1.01 (0.71 – 1.42)	1.07 (0.66 – 1.72)
All-cause mortality (HR)				
No DM (n=574)	42 (7%)	532 (93%)	1	1
DM (n=225)	23 (10%)	202 (90%)	1.55 (0.93 – 2.59)	1.52 (0.75 – 3.08)
Early Mortality (HR)				
No DM (n = 574)	9 (2%)	565 (98%)	1	R1ef
DM (n = 225)	17 (8%)	208 (92%)	**5.06 (2.26 – 11.35)**	**4.77 (1.41 – 16.11)**

#adjusted for sex, age, household income, alcohol, body mass index, smear grade, cavitary disease and daily vs. intermittent regimen

Mave, OFID, 2021

Estimated risk of TB outcomes by DM status among a prospective TB cohort in Pune, India.

	Rate (95% CI)	Univariable Analysis		Multivariable Analysis[a]	
Outcome		Ratio[b] (95% CI)	p-value	Ratio[b] (95% CI)	p-value
Composite unfavorable outcome					
TB-only (n=574)	20.0 (16.6–24.0)	Ref		Ref	
TB-DM (n=225)	20.1 (14.6–27.0)	1.01 (0.71–1.42)	>0.95	1.13 (0.75–1.70)	0.56
HbA1c					
Treatment					
TB-only (					
TB-DM (n=225)	14.0 (7.4–23.8)	0.56 (0.30–1.06)	0.08	0.75 (0.36–1.58)	0.46
Recurrence					
TB-only (n=424)	12.2 (8.7–16.5)	Ref		Ref	
TB-DM (n=159)	7.5 (3.4–14.2)	0.62 (0.30–1.27)	0.19	0.73 (0.31–1.70)	0.46
Mortality					
TB-only (n=574)	6.5 (4.7–8.8)	Ref		Ref	
TB-DM (n=225)	9.9 (6.3–14.9)	1.55 (0.93–2.59)	0.09	1.54 (0.85–2.79)	0.16

TB with and without DM did NOT differ in composite outcome

BUT, mortality MAY be increased among people with DM

[a]adjusted for sex, age, household income, alcohol, BMI, smear grade and cavitary disease and daily vs. intermittent regimen

Estimated risk of EARLY mortality by DM subtype (new or known) among a prospective TB cohort in Pune, India

	Rate (95% CI)	Univariable Analysis		Multivariable Analysis[a]	
Outcome		HR (95% CI)	p-value	aHR (95% CI)	p-value
TB-only (n=574)	3.4 (1.6–6.5)	Ref		Ref	
TB-DM (n=225)	17.5 (10.2–28.0)	5.06 (2.26–11.35)	<0.001	4.36 (1.62–11.76)	0.004
New DM (n=70)	24.7 (10.0–51.0)	7.17 (2.67–19.27)	<0.001	6.56 (2.18–19.71)	0.001
Known DM (n=155)	14.5 (6.9–26.7)	4.20 (1.70–10.33)	0.002	3.14 (1.03–9.61)	0.045
DM on metformin (n=117)	11.4 (4.2–24.8)	3.30 (1.18–9.28)	0.02	2.32 (0.67–8.08)	0.20
DM no metformin (n=1	24.8 (13.4–44.4)	7.13 (2.96–17.21)	<0.001	6.17 (2.24–17.04)	<0.001

TB patients with DM at greater risk of death DURING TB treatment.
True for NEW DM and KNOWN DM.
DM on metformin had increased risk of early mortality.
DM NOT on metformin had a 6-fold increased risk of mortality!

[a]adjust

Estimated risk of POST-TREATMENT mortality by DM subtype (new or known) among a prospective TB cohort in Pune, India

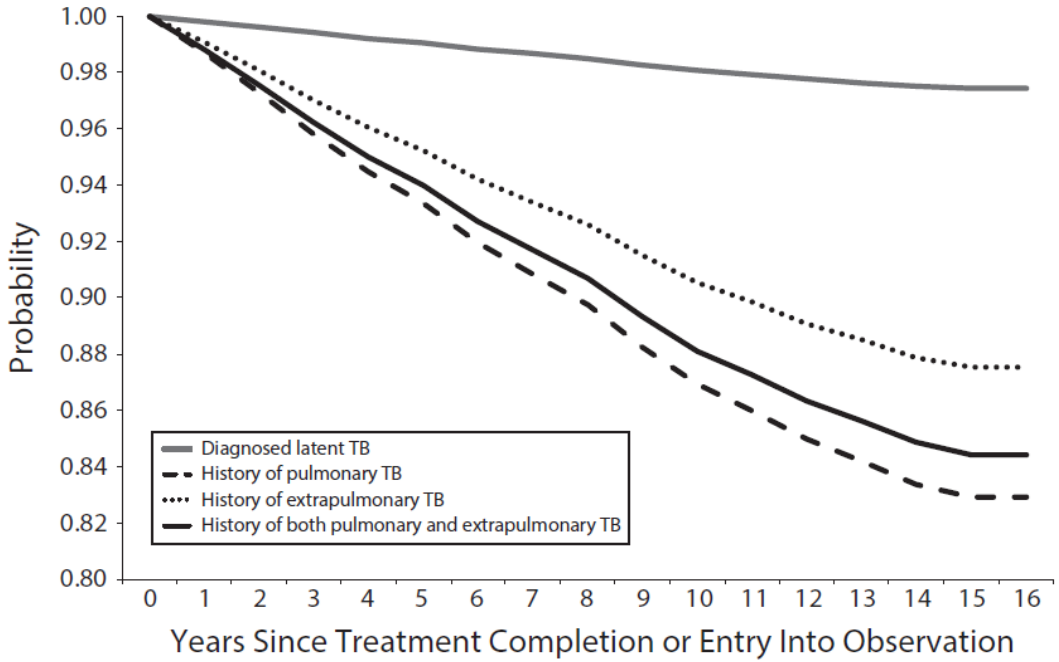
	Rate (95% CI)	Univariable Analysis		Multivariable Analysis[a]	
Outcome		HR (95% CI)	p-value	aHR (95% CI)	p-value
TB-only (n = 487)	8.6 (5.9 – 12.1)	Ref		Ref	
TB-DM (n = 176)	4.5 (1.6 – 9.7)	0.54 (0.22 – 1.28)	0.16	0.58 (0.22 – 1.51)	0.27
New DM (n = 49)	5.3 (0.6 – 19.1)	0.64 (0.15 – 2.69)	0.55	0.42 (0.10 – 1.6)	0.25
Known DM (n = 126)	4.2 (1.1 – 10.7)	0.50 (0.18 – 1.41)	0.19	0.72 (0.23 – 2.22)	0.57
DM on Metformin (n = 98)	2.6 (0.3 – 9.5)	0.31 (0.07 – 1.29)	0.11	0.47 (0.10 – 2.17)	0.33
DM no Metformin (n =	6.8 (1.9 – 17.5)	0.84 (0.30 – 2.39)	0.75	0.65 (0.22 – 1.96)	0.45

TB patients with DM are NOT at greater risk of death AFTER TB treatment.

[a]adjusted for sex, age, household income, alcohol, BMI, smear grade and cavitary disease and daily vs. intermittent regimen

Higher risk of death following TB treatment

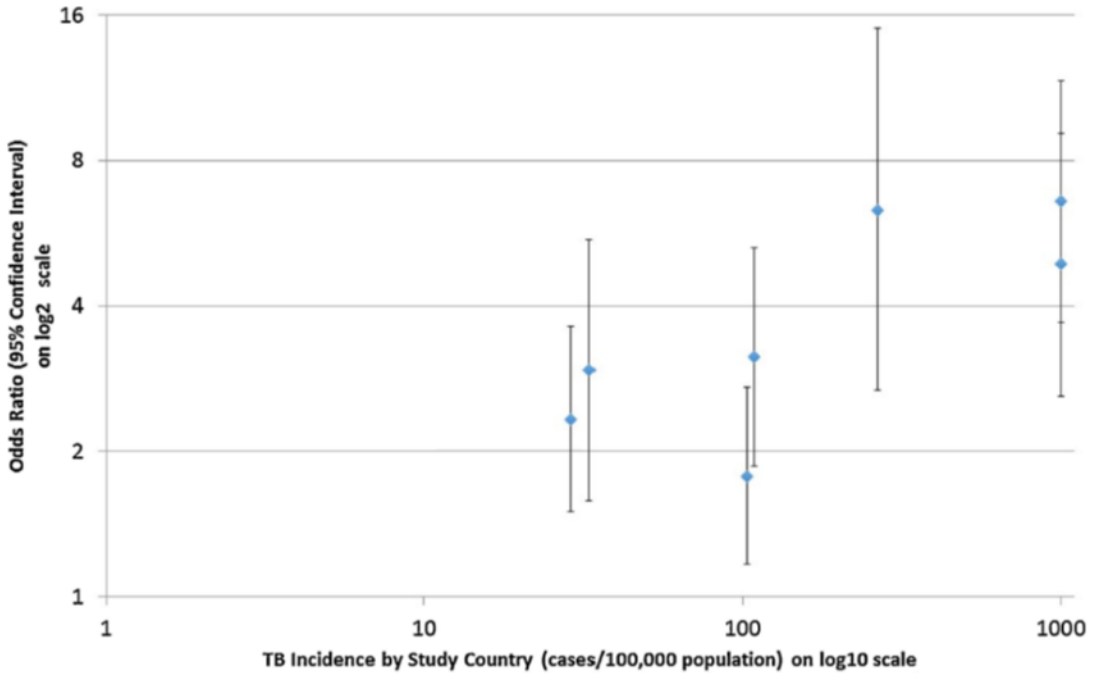
- Treated TB patients have higher risk of death
- SMR ~ 3 to 4
- Excess of 7.6 deaths /1000 p-yrs
- Multifactorial
- *Chronic lung diseases* thought to play an important role in excess mortality



Romanowski et al 2019, Shuldiner et al 2016

Higher prevalence of airflow obstruction in individuals with a history of TB

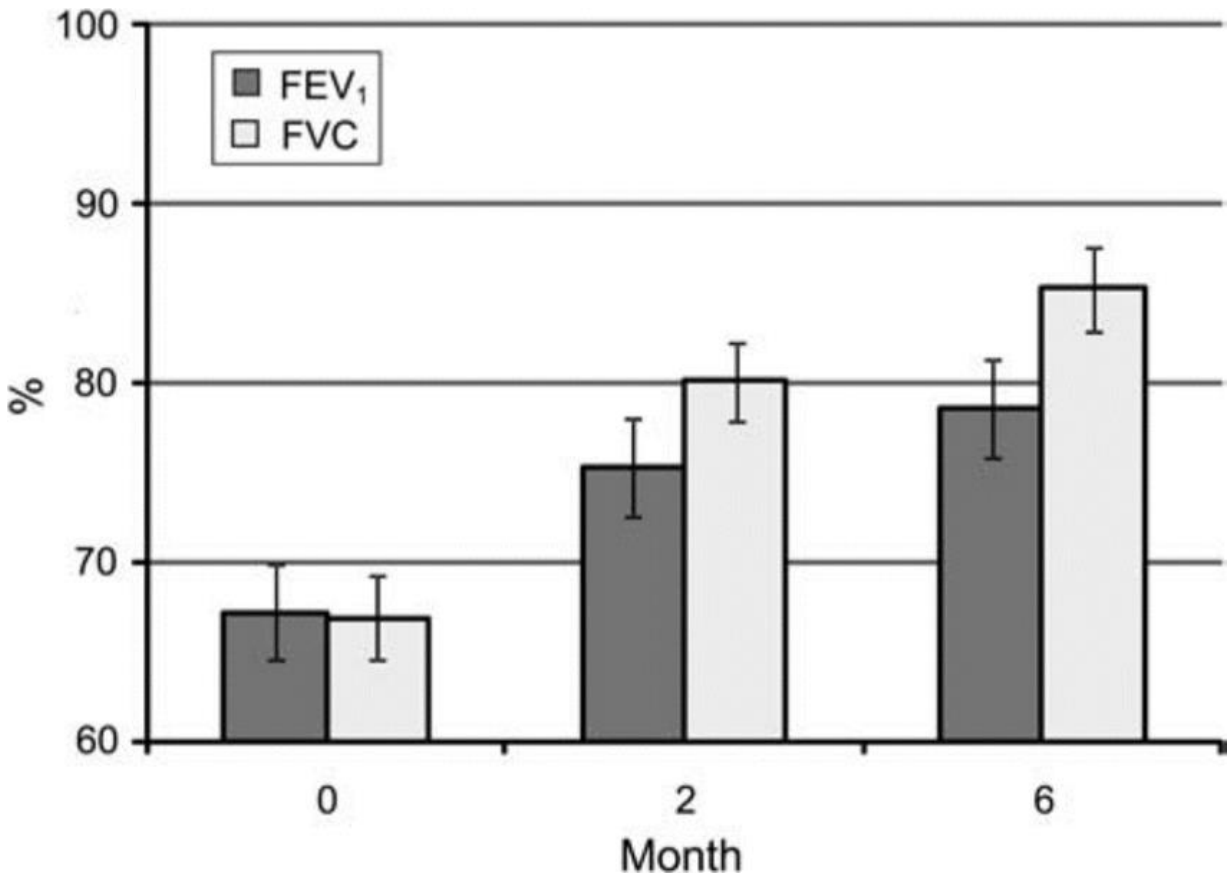
- Higher prevalence of chronic obstructive pulmonary disease (COPD) from global surveys
- Pooled OR = 3.05 (95%CI 2.42-3.82) adjusting for smoking and self-report bio-mass fuel use
- Association stronger in high-burden settings



Byrne et al 2015

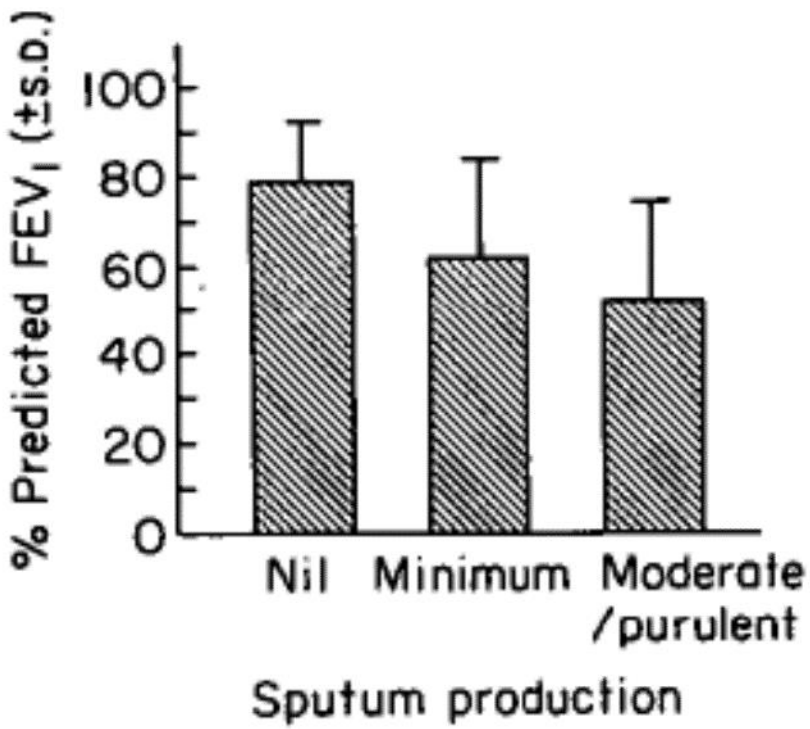
Lung function improves with treatment but may not normalize despite microbiologic cure

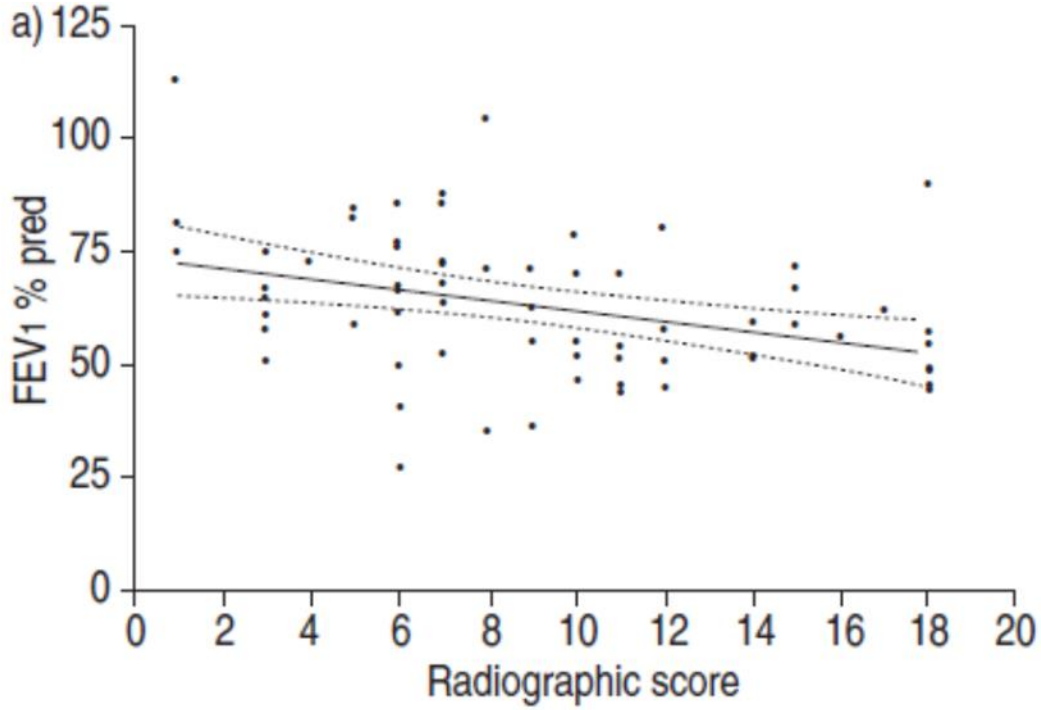
- 50% with lung function impairment at treatment initiation
- 25% with residual lung function impairment by treatment completion
- Greatest improvement in first 2 months



Maguire et al 2009

Respiratory impairment (RI) is common in treated PTB cases





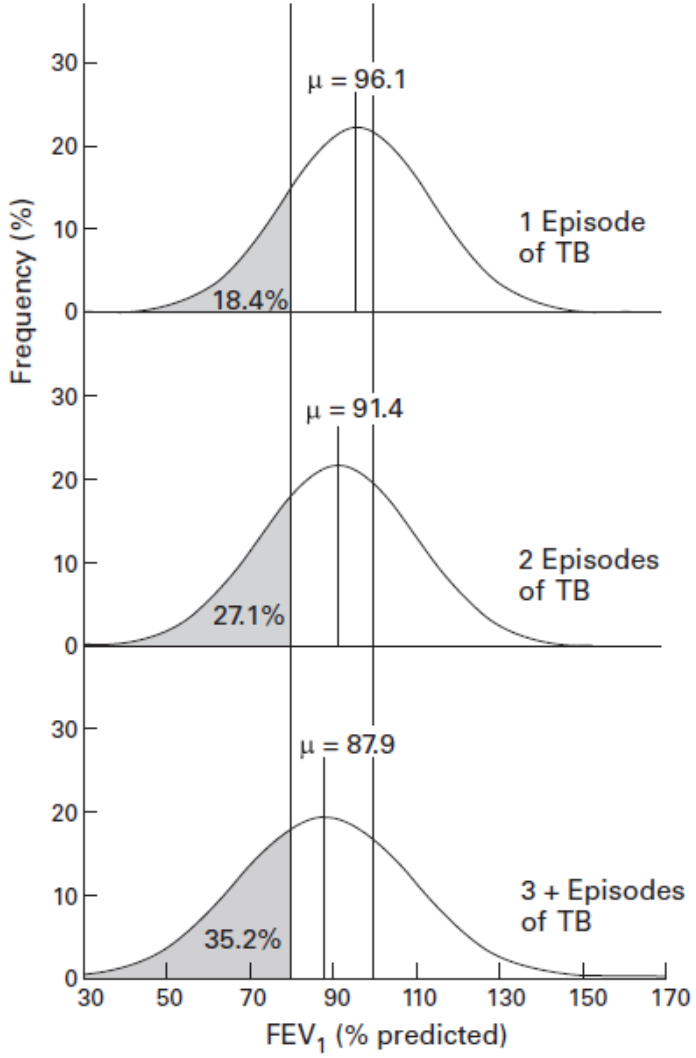
- 20-70% of treated PTB cases have lung function impairment
- Degree of impairment may correlate with extent of disease

Willcox et al 1989, Plit et al 1998

PTB-associated RI persists beyond treatment completion

- 65% of PTB patients had abnormal lung function 14-18 years after successful treatment

- Every episode of PTB was associated with approx. 200ml (5-10%) permanent and irreversible loss of lung function



Hnizdo et al 2006, Rekha et al 2009

Assessment of persistent depression among TB patients

Authors: Suryavanshi, N. [1]; Sane, M. [1]; Gaikwad, S. [2]; Paradkar, M. [1]; Mave, V. [3]; Chandrasekaran, P. [4]; Shivakumar, S. V. B. Y. [5]; Gupta, A. [6]; Gupte, N. [3]; Thomas, B. [4]; for CTRIUMPH RePORT India study

Source: The International Journal of Tuberculosis and Lung Disease, Volume 24, Number 11, 1 November 2020, pp. 1208-1211(4)

Publisher: International Union Against Tuberculosis and Lung Disease

DOI: https://doi.org/10.5588/ijtld.20.0231

Objective and study design

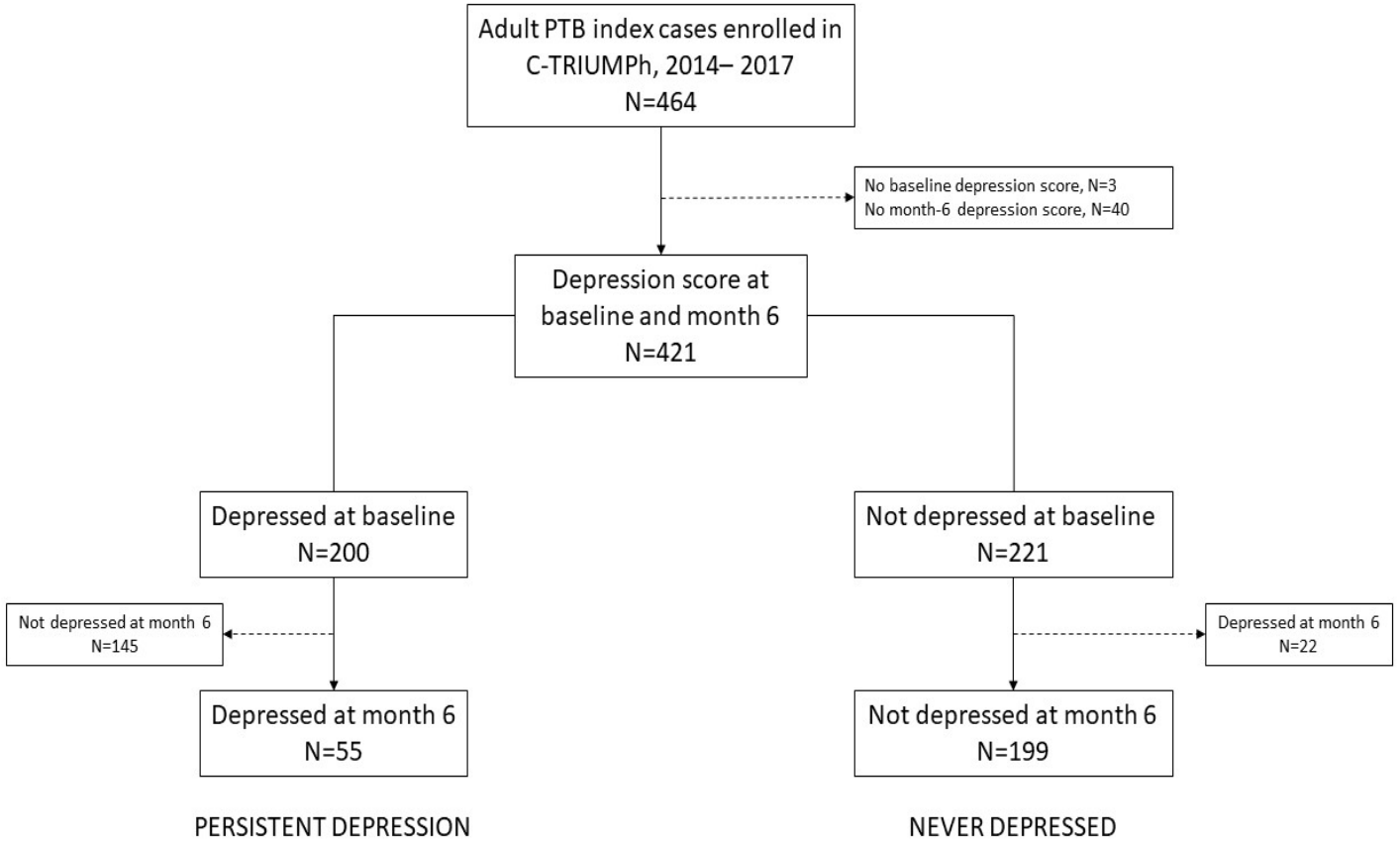
Prospective observational cohort study to assess the prevalence and risk factors of PDS among adult (>18 years) pulmonary TB patients enrolled in the Cohort for Tuberculosis Research by the Indo-US Medical Partnership (CTRIUMPh) study in India.

Depression was assessed using a validated Centre for Epidemiological Scale-Depression-10 scale (CESD-10) at ATT initiation and at the EOT.

Participants having cut off score of >9 were considered depressed.

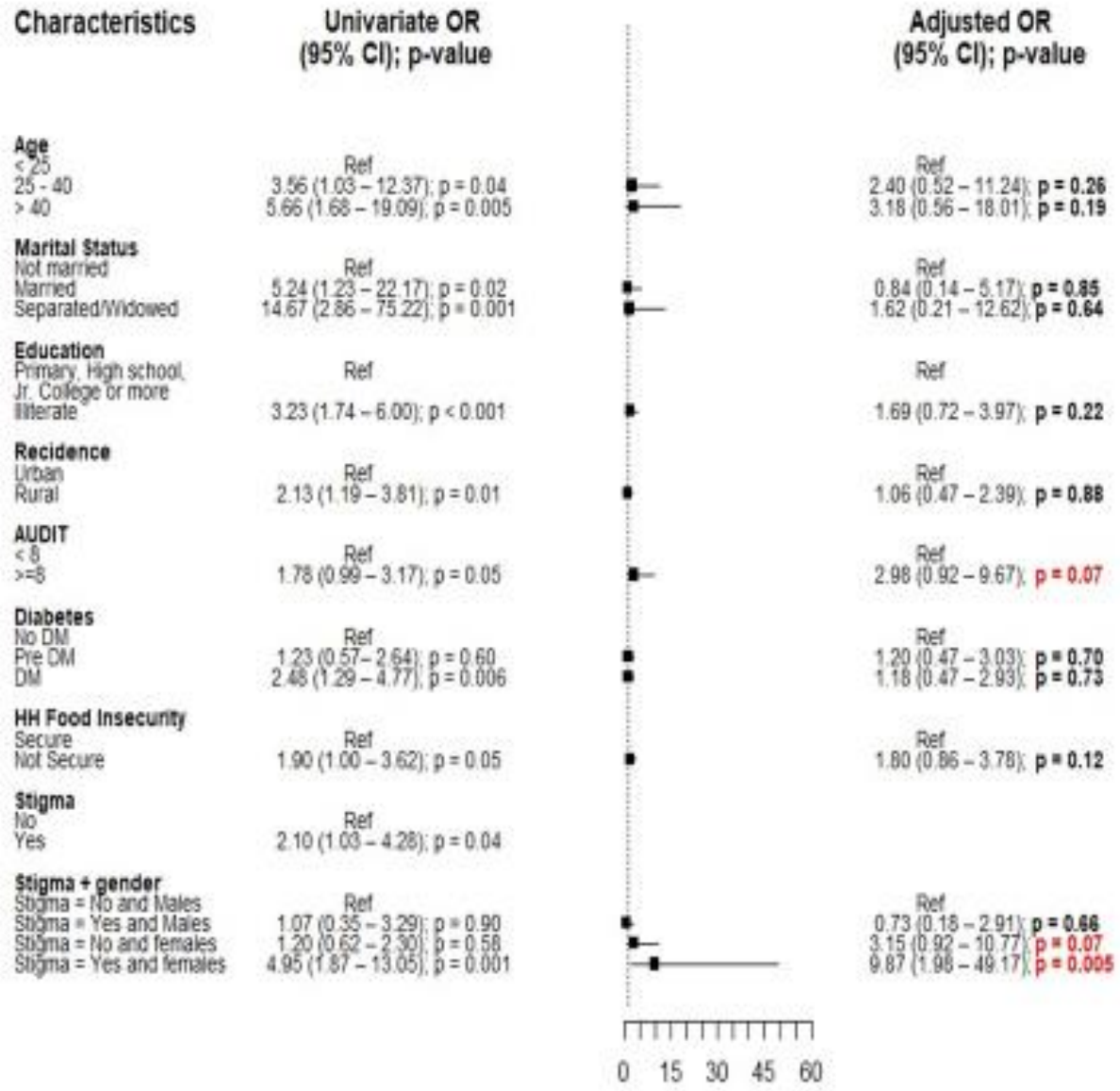
Results

- Of 464 adult TB patients enrolled, 40 were lost to follow-up, and 3 did not have baseline depression data.
- Among the remaining 421 participants, 200 (47.5%) had BDS but depression symptoms disappeared for 145 patients at the end of treatment.
- Of 254 participants included, 55 (22%) had PDS



Assessment of persistent depression symptoms among Tuberculosis patients in India

- Prevalence of baseline depression symptoms was 47. 5% (200/421)
- Prevalence of persistent depression symptoms (PDS: Depressed at ATT initiation and at EOT)) among those depressed at baseline was 27.5% (55/200).
- PD symptoms were correlated with more disadvantage and vulnerable group
  - Female tuberculosis (TB) patients with stigma are at increased risk PDS symptoms.
  - AUDIT ≥ 8 is risk factor for PDS
- Integrating screening for depression and TB stigma into routine TB care would facilitate early identification and timely intervention with the potential to enhance TB care.



Conclusions:

Our study identified a high prevalence of PDS among adult TB patients and particularly among women reporting TB stigma.

Recommendations

Integrating screening for depression and TB stigma into routine TB care along with counseling support would facilitate early identification and timely intervention.

This has the potential to enhance treatment adherence and overall TB care.

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Unhealthy alcohol use independently associated with unfavorable TB treatment outcomes among Indian men

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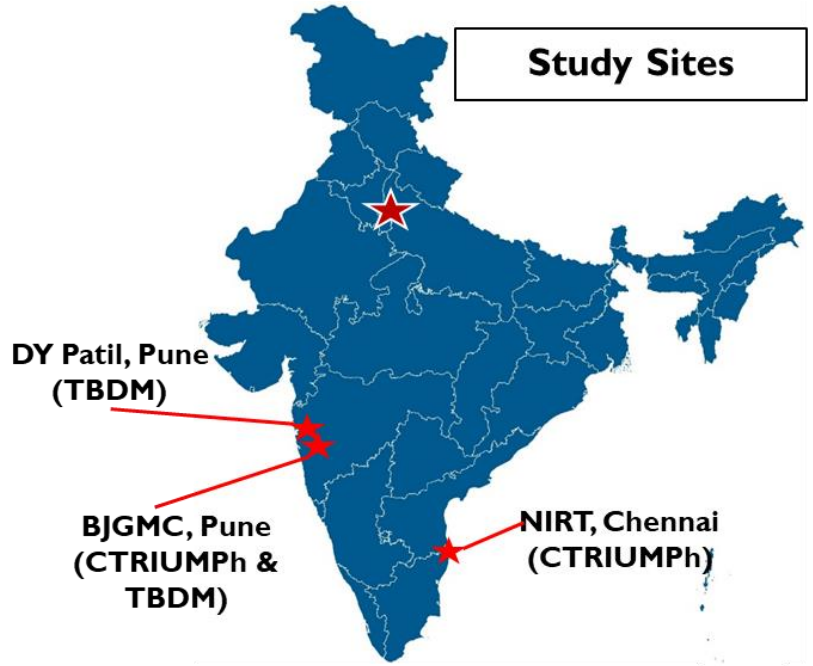
[1]Johns Hopkins University (JHU), School of Medicine, Baltimore, USA; [2]National Institute of Research in Tuberculosis (NIRT), Chennai, [3]Byramjee Jeejeebhoy Government Medical College (BJGMC) and Sassoon General Hospital, Pune, [4]BJGMC Clinical Research Site, Pune, [5]Dr DY Patil Medical College Hospital and Research Centre, Dr DY Patil Vidyapeeth, Pune, [6]Johns Hopkins India Private Limited, Pune, India

Study Overview

We used the validated Alcohol Use Disorders Identification Test-Concise (AUDIT-C) scale to determine whether unhealthy alcohol use was independently associated with unfavorable TB treatment outcomes among men with drug-susceptible pulmonary TB (PTB) in well-defined longitudinal cohorts in India.

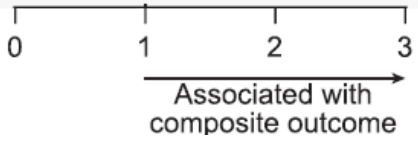
- Enrolled adults (≥18 yrs) with newly diagnosed pulmonary TB (PTB) (2013-2018).
- Restricted to men given very low prevalence of alcohol use among women (<1%).
- Unhealthy alcohol use = AUDIT-C ≥4 at entry.
- Why study alcohol & TB in India?
  - India has the world's largest burden of TB.
  - Alcohol use is on the rise in India.
  - Unhealthy alcohol use is a challenge for many TB patients (22-55% of TB patients in India).



Association of alcohol use with poor TB treatment outcomes

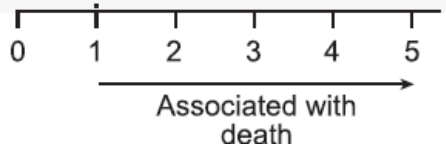
A

Parameter	Exposed			Unexposed			Model	IRR (95% CI)	*P* value
	Total	Event	py	Total	Event	py			
Ever had a drink containing alcohol	407	131	473	344	67	393	Unadjusted	1.87 (1.30–2.69)	<0.001
							Adjusted	1.62 (1.14–2.31)	0.01
Unhealthy alcohol use (AUDIT-C ≥ 4)	302	106	347	449	92	520	Unadjusted	1.99 (1.40–2.81)	<0.001
							Adjusted	1.47 (1.05–2.06)	0.03
AUDIT-C (continuous)	—	—	—	—	—	—	Unadjusted	1.10 (1.05–1.15)	<0.001
							Adjusted	1.06 (1.01–1.10)	0.01



D

Parameter	Exposed			Unexposed			Model	IRR (95% CI)	*P* value
	Total	Event	py	Total	Event	py			
Ever had a drink containing alcohol	407	59	520	344	17	410	Unadjusted	2.83 (1.55–5.15)	0.001
							Adjusted	2.37 (1.24–4.55)	0.01
Unhealthy alcohol use (AUDIT-C ≥ 4)	302	51	386	449	25	544	Unadjusted	2.88 (1.69–4.91)	<0.001
							Adjusted	1.90 (1.08–3.34)	0.03
AUDIT-C (continuous)	—	—	—	—	—	—	Unadjusted	1.14 (1.06–1.22)	<0.001
							Adjusted	1.07 (1.00–1.14)	0.05



Adjusted for location, age, BMI, education, smoking, smear grade. Tx=Treatment; IRR=incidence rate ratio; OR=Odds Ratio; BMI=body mass index.

Key findings

1. **Unhealthy alcohol use was common - identified in 40% of men with active TB in our study** (302 of 751 men).
2. **Unhealthy alcohol use is independently associated with higher risk of unfavorable TB treatment outcomes and specifically with death.**
   - **About 50% increased risk of unfavorable TB treatment outcomes.**
   - **Nearly two-fold increased risk of death within 2 years of TB diagnosis.**
3. **Majority of deaths occurred prior to TB treatment completion and among men with unhealthy alcohol use.**
4. **Malnutrition and unhealthy alcohol use had a combined adverse effect.**
   - **Checking AUDIT-C, height and weight may be a simple screening tool at TB treatment initiation to identify high-risk patients in need of additional services, such as alcohol reduction counseling.**

Thus, a TB diagnosis is an opportunity…

- To provide/improve health care linkage:
  - Diabetes treatment
  - Smoking cessation counseling/treatment
  - Alcohol reduction
  - Mental health
  - HIV treatment
  - Physical rehabilitation therapy for lung impairment
  - Financial improvement

Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, Annie Oravec, Madison Billingsley, Kate Shearer, Akshay Gupte, Moises A. Huaman, Greg J. Fox, Jonathan E. Golub, and James C. Johnston

BC Centre for Disease Control
Provincial Health Services Authority

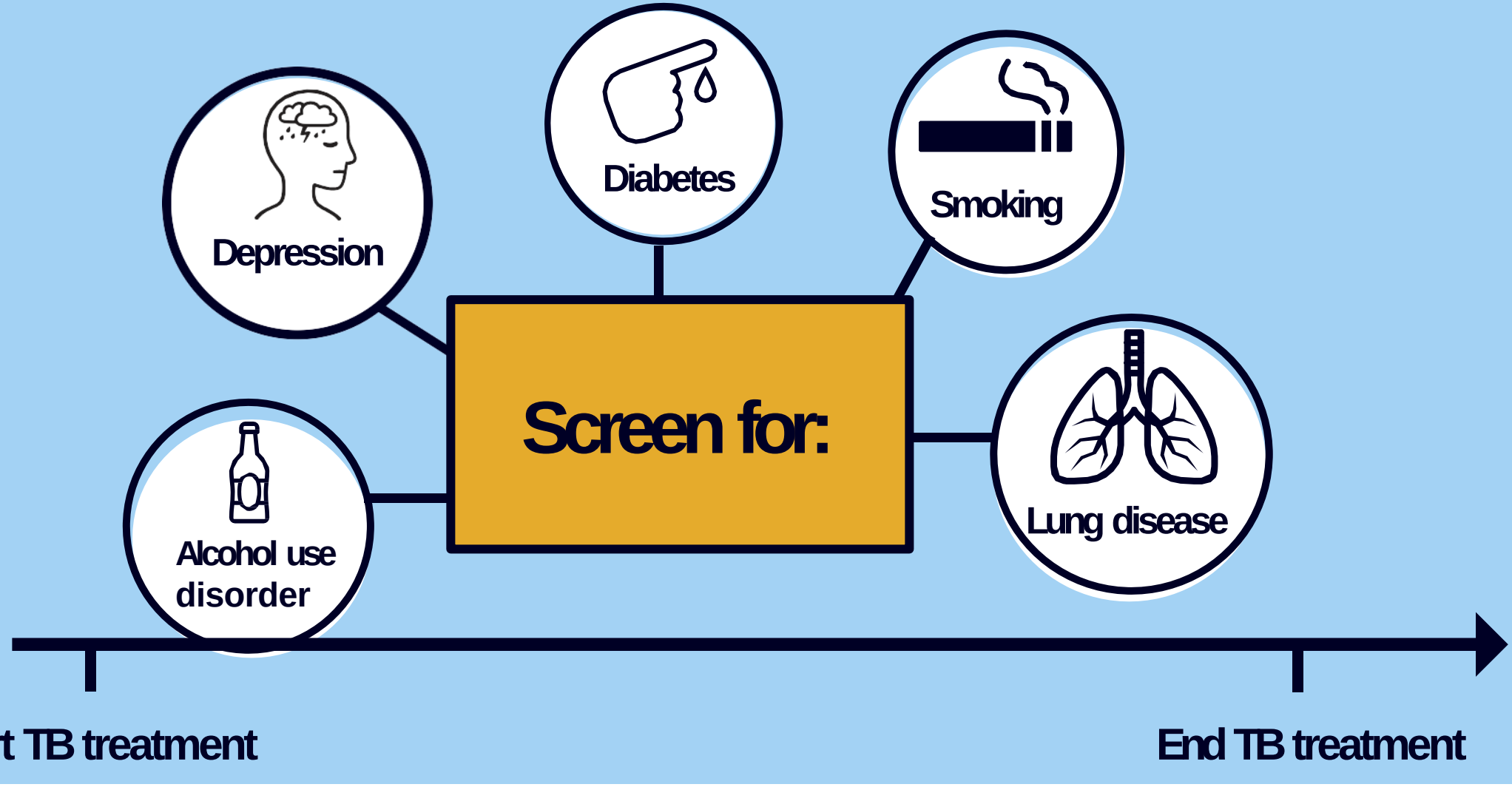
CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

UBC

Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

Category: Implementation
E-poster #: Oral Abstract



Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

Category: Implementation
E-poster #: Oral Abstract

What is the existing evidence on interventions that address common non-communicable diseases among people with TB?

Smoking cessation works in people with TB

REVIEW ARTICLE

A systematic review of the effectiveness of smoking cessation interventions among patients with tuberculosis

E. Whitehouse,[1] J. Lai,[2] J. E. Golub,[2,3] J. E. Farley[1,4]

Smoking is a significant risk factor for morbidity and mortality, particularly among patients with tuberculosis (TB). Although smoking cessation is recommended by the World Health Organization and the International Union Against Tuberculosis and Lung Disease, there has been no published evaluation of smoking cessation interventions among people with TB. The purpose of this review was to synthesize the evidence on interventions and suggest practice, research and policy implications. A systematic re- view of the literature identified 14 peer-reviewed studies describing 13 smoking cessation interventions between 2007 and 2017. There were five randomized controlled trials, three non-randomized interventions, and five pro- spective cohort studies. The primary types of interventions were brief advice (*n* = 9), behavioral counseling (*n* = 4), medication (*n* = 3), and community-based care (*n* = 3). A variety of health care workers (HCWs) implemented inter- ventions, from physicians, nurses, clinic staff, community health workers (CHWs), as did family members. There was significant heterogeneity of design, definition of smoking and smoking abstinence, and implementation, making comparison across studies difficult. Although **all smoking interventions increased smoking cessation between 15% and 82%**, many studies had a high risk for bias, including six without a control group.

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Inclusion:

- **Population:** people enrolled or completed treatment for active TB
- **Intervention:** structured program of care, implemented within a TB program to prevent or manage common NCDs
- **Common NCDs:** respiratory disease, cardiovascular disease, substance use disorder, and mental health disorders
- Assessed implementation and effectiveness outcomes

Exclusion:

- Screened but resulted in no further intervention.
- Only used TB treatment adherence or treatment completion as an outcome
- Evaluated interventions for infectious disease comorbidities, smoking cessation interventions, or surgical or pharmacological interventions

Interventions to Mitigate Common Non-Communicable Diseases in People Who Experience Tuberculosis: A Scoping Review of the Evidence

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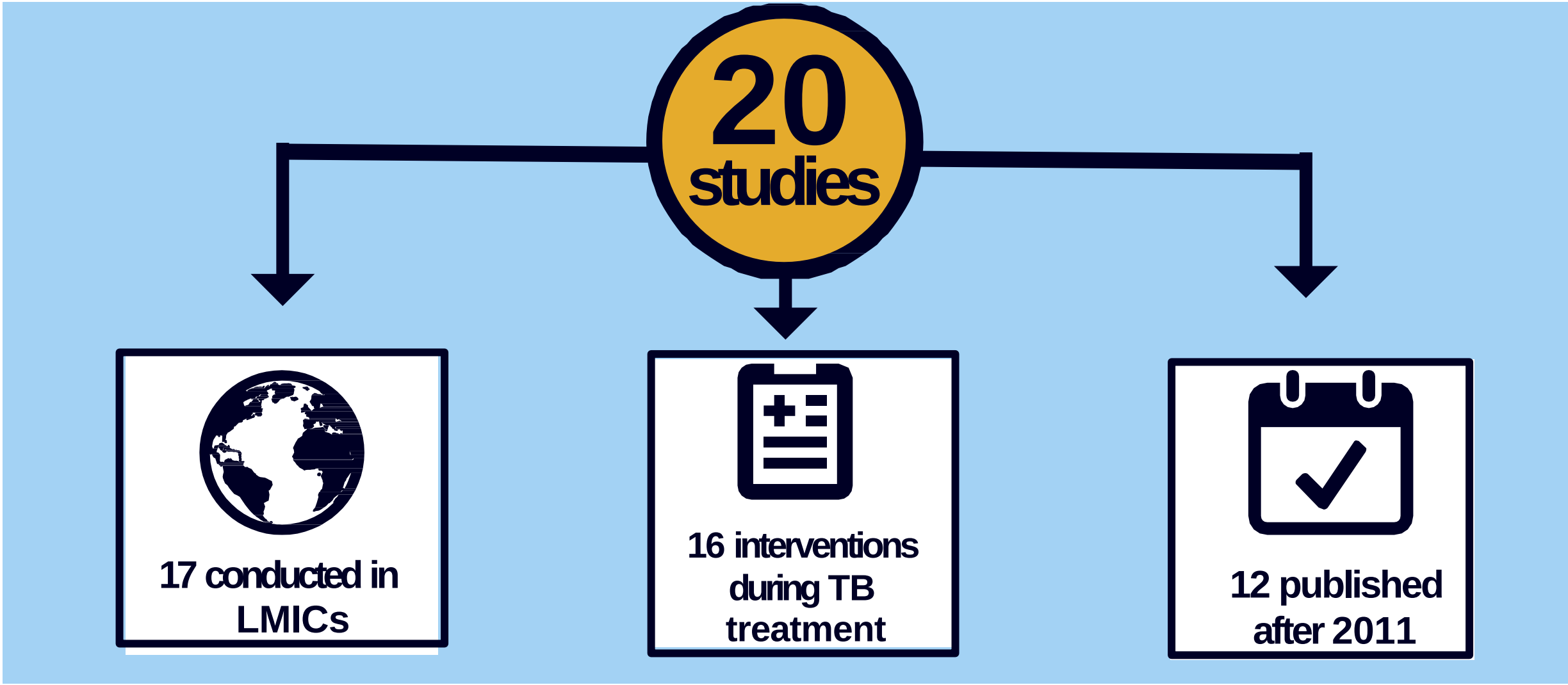

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Kamila Romanowski, UBC-BCCDC

Category: Implementation
E-poster #: Oral Abstract

Common NCDs among people who experience TB

Respiratory disease	Cardiovascular disease	Substance and alcohol use disorder	Mental health disorder
↓	↓	↓	↓
Pulmonary rehabilitation: 5 studies	Referral for diabetes and hypertension care: 6 studies	Care programs for alcohol use disorder: 4 studies	Individual counselling and psychosocial support: 5 studies

Interventions identified

Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

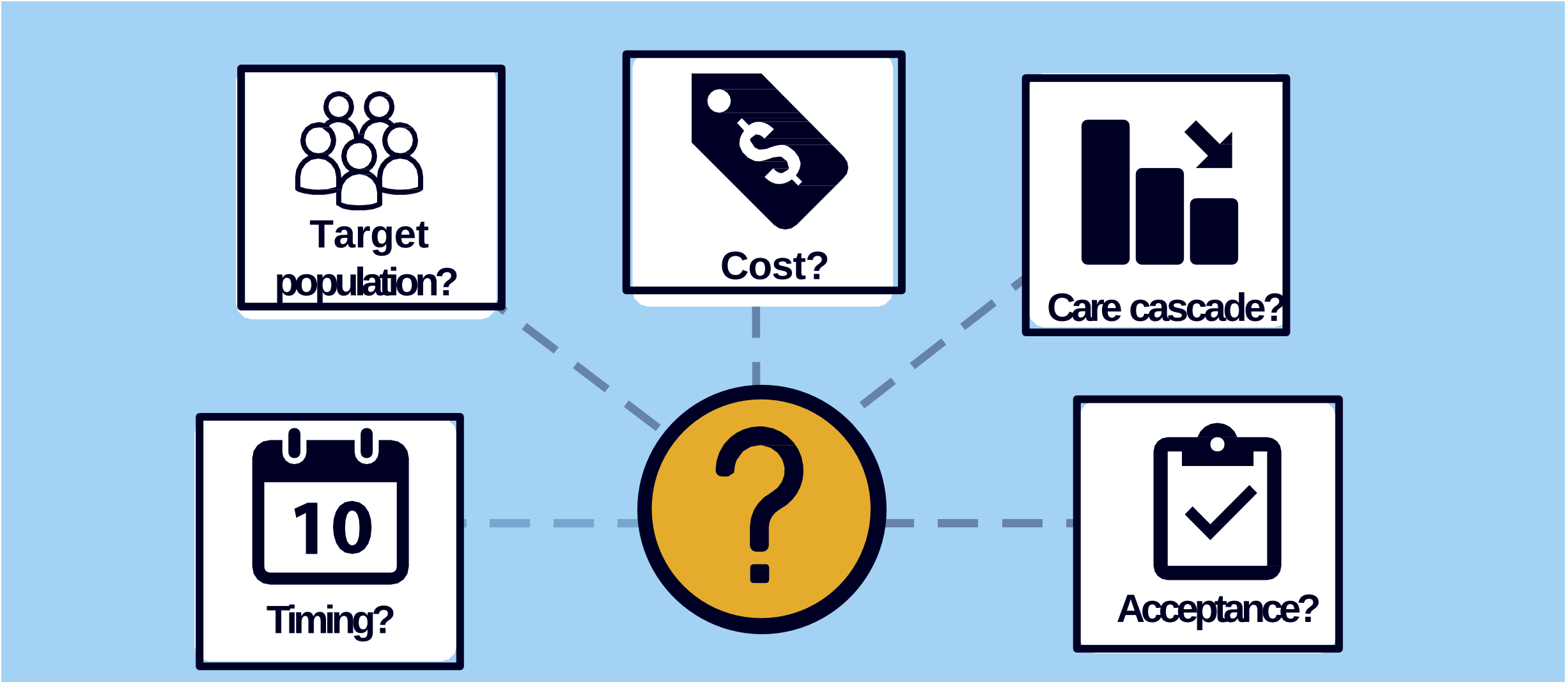
Category: Implementation
E-poster #: Oral Abstract

Is the decision to screen, a decision to treat?

Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

Category: Implementation
E-poster #: Oral Abstract



Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

Category: Implementation
E-poster #: Oral Abstract

Further evidence demonstrating the feasibility and effectiveness of interventions is needed before scale up to ensure resources are well invested, and the cascade of chronic disease care is addressed.

Tropical Medicine and Infectious Disease

MDPI

Article

Is It Feasible to Conduct Post-Tuberculosis Assessments at the End of Tuberculosis Treatment under Routine Programmatic Conditions in China?

Yan Lin [1,2,†], Yuqin Liu [3,†], Guanghui Zhang [4], Qinghe Cai [5], Weihua Hu [3], Lixin Xiao [6], Pruthu Thekkur [1,7], Jonathan E. Golub [8] and Anthony D. Harries [1,9,*]

This study, carried out under routine program conditions in patients completing standard anti-TB treatment in five clinics in China between April and June 2021, showed that post-TB assessments were feasible to conduct, they could be conducted in an average time of about 20 min and the health care workers involved found them useful. About half of the patients who were fully assessed had on-going symptoms, the most common being cough, shortness of breath and fatigue. Over 90% had some chest radiographic abnormality at the end of treatment and one fifth had a 6MWT below 400 m. There is significant morbidity amongst TB patients completing anti-TB treatment and this needs to be addressed if we are to honor the Lancet Commission pledge of providing good quality patient-centered care.

NEW study: <u>Assess</u> TB patients with drug-sensitive TB at three time points:

a) as they start anti-TB treatment;
b) as they complete anti-TB treatment; and
c) one month after completion of anti-TB treatment.

Assessment will comprise smoking, alcohol use, malnutrition and exposure to silica through mining work, diabetes mellitus, hypertension, COVID-19 and measuring disability using the 6MWT.

Table 4. Results of post-TB assessment in patients completing anti-TB Treatment.

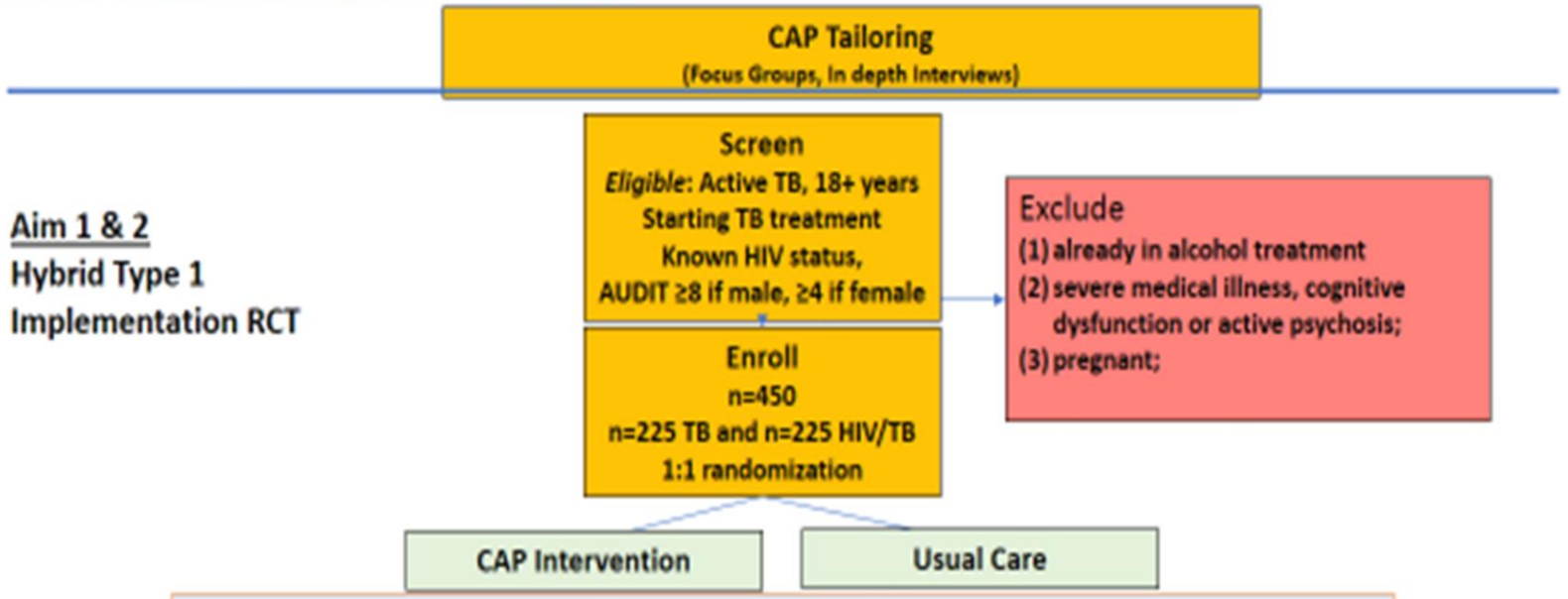
Variables	Number	(%) [a]
Total patients evaluated	115	
Male	70	(61)
Rural	65	(57)
Pulmonary TB	106	(92)
Extrapulmonary TB	9	(8)
Previously treated TB	12	(10)
Multidrug-resistant TB	6	(5)
Did not feel healthy and had continuous symptoms	54	(47)
Cough	21	(19)
Shortness of breath	13	(11)
Tiredness and fatigue	20	(17)
Chest pain	9	(8)
Other	8	(7)
Known diabetes mellitus diagnosed elsewhere	19	(17)
Newly diagnosed diabetes mellitus during this TB visit	3	(3)
Current smoker	12	(10)
Currently drinking alcohol	1	(1)
Currently injecting drugs	0	(0)
Systolic blood pressure ≥ 140 mmHg	2	(2)
Diastolic blood pressure ≥ 90 mmHg	8	(7)
Fasting blood glucose ≥ 7.0 mmol/L [b]	15	(13)
Any chest radiographic abnormality	106	(92)
Unilateral chest radiographic abnormality	39	(34)
Bilateral chest radiographic abnormality	36	(31)
Chest radiographic shadowing	17	(15)
Chest radiographic cavitation	11	(10)
Chest radiographic scarring	11	(10)
Chest radiographic pulmonary shrinkage	1	(1)
Other chest radiographic abnormality	18	(16)
Number of meters walked within 6 min:		
30–299	8	(7)
300–399	16	(14)
400–499	49	(43)
500–599	27	(23)
600–750	15	(13)

[a] denominator for all percentages is the total number of patients assessed (n = 115) [b] this includes 12 patients with known diabetes and 3 newly diagnosed with diabetes.

Overview of HATHI study

- Aim 1. To examine the effectiveness of CAP (Counseling for alcohol problem) alcohol reduction intervention, integrated into TB and HIV/TB care compared to usual care on alcohol reduction.
  - CAP has 4-session combined Cognitive Behavioral Therapy (CBT) + 3 booster Motivational Enhancement Therapy (MET).
  - Aim 1 will occur in two phases, the intervention tailoring phase and the RCT phase.
- Aim 2. To examine the effectiveness of CAP (CBT/MET) integrated into TB and HIV/TB care compared to usual care on TB and HIV treatment outcomes.
- Aim 3: To understand multi-level factors that influence alcohol reduction intervention integration into these clinical settings.
  - 3a) evaluate patient, provider and organizational barriers and facilitators to integrated alcohol treatment in TB and HIV/TB settings, and
  - 3b) measure incremental costs from health system and societal perspectives, and to estimate their incremental cost-effectiveness, compared to treatment as usual.

Figure 1: Overview of HATHI Aims and Trial Schema



Study Sites

BJGMC and Sassoon General Hospital, Pune, India

Dr. D.Y. Medical College, Pune, India

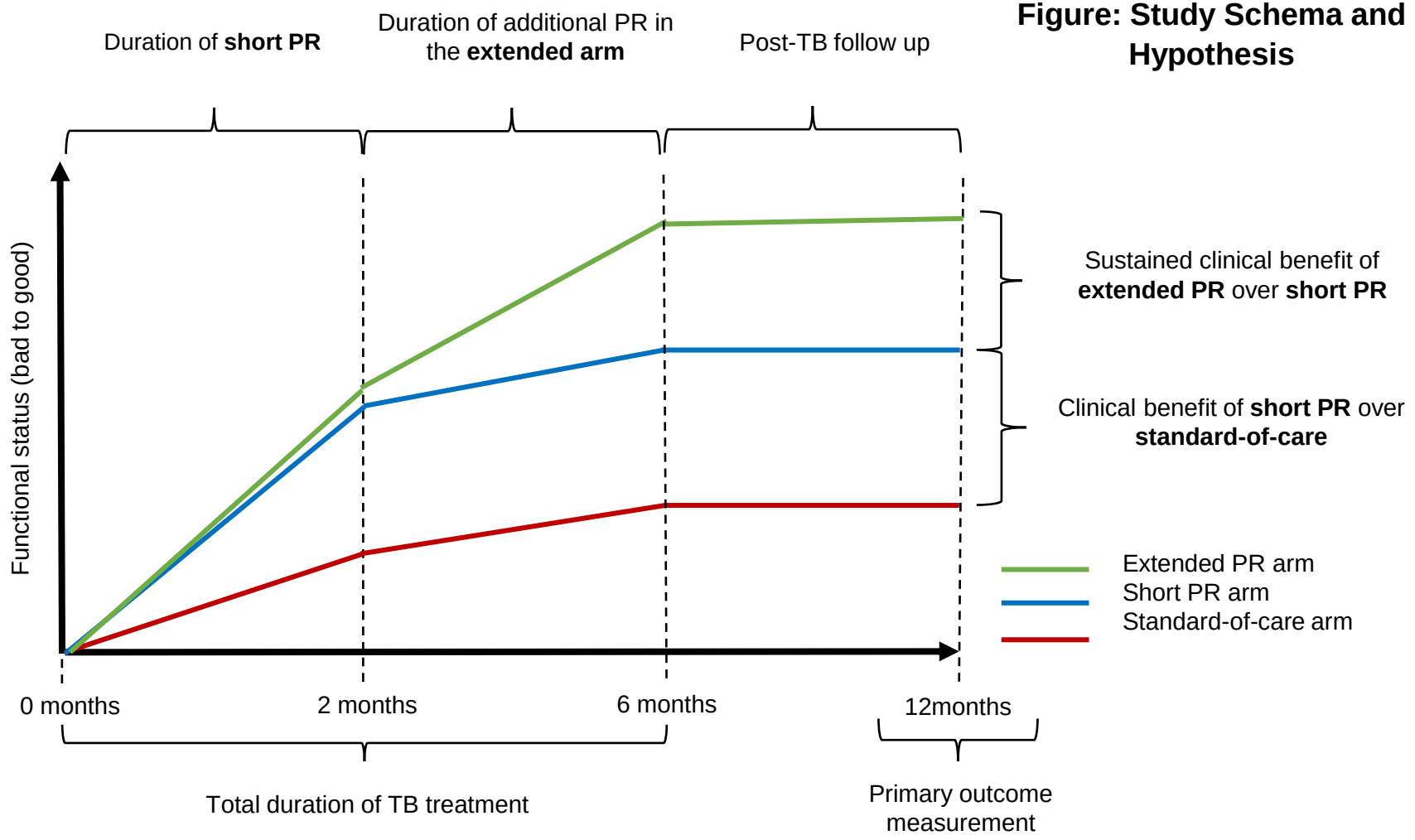
Policy and program level stakeholders (n=10-15). Ministry of health officials, key informants in the HIV/TB health system and community advisors to the India ART and TB program will be interviewed using in-depth interviews.

TB PuRe: Pulmonary Rehabilitation to Reduce Post-Tuberculosis Morbidity (NIH; NIAID; Golub, Gupte, Mave)

<u>Overall objective:</u>

To measure the effectiveness, feasibility and cost-effectiveness of a pulmonary rehabilitation (PR) program to prevent post-tuberculosis (TB) respiratory morbidity in India

Figure: Study Schema and Hypothesis



Sites: a) Bharati Vidhyapeeth Medical College and Hospital (BVMC), Pune; b) Kashibai Navle Medical College and General Hospital (KNMC), Pune; c) Yenepoya Medical College (YMC), Mangalore

Published in final edited form as:
Lancet Glob Health. 2018 April ; 6(4): e426–e435. doi:10.1016/S2214-109X(18)30022-6.

Tuberculosis control interventions targeted to previously treated people in a high-incidence setting: a modelling study

Florian M Marx[*], **Reza Yaesoubi**[*], **Nicolas A Menzies**, **Joshua A Salomon**, **Alyssa Bilinski**, **Nulda Beyers**, and **Ted Cohen**

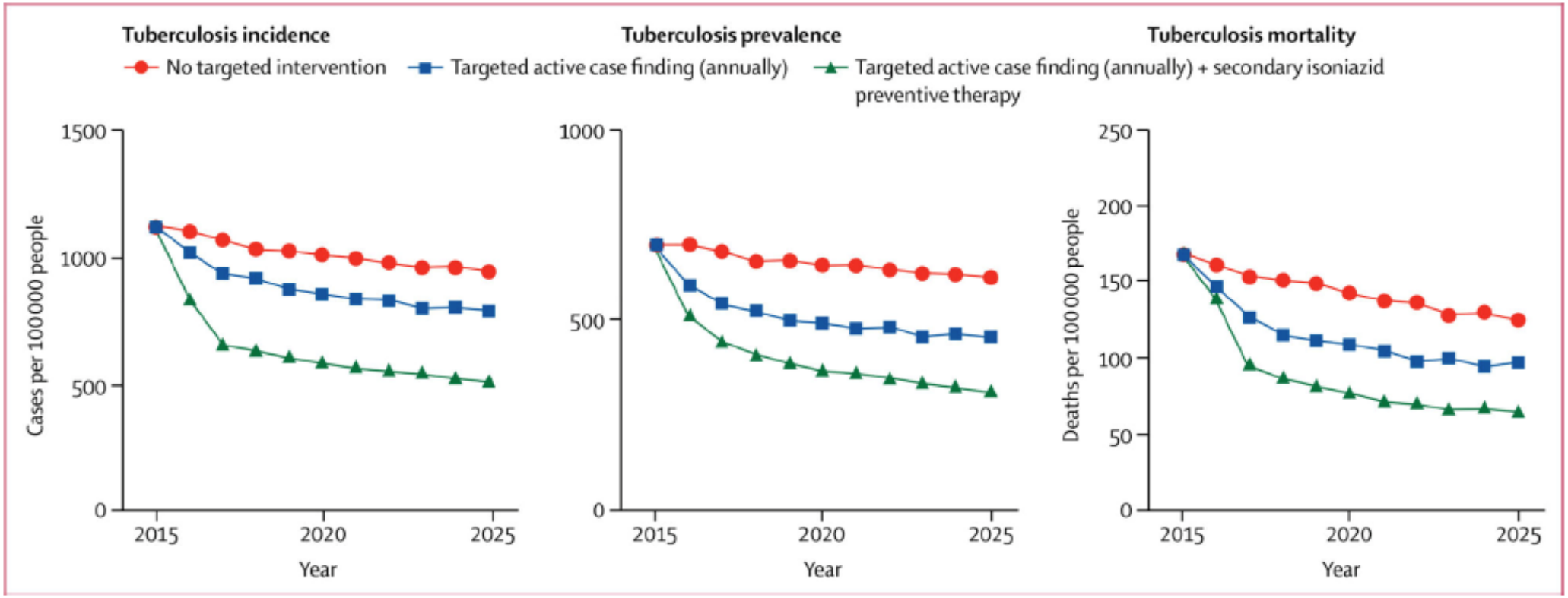
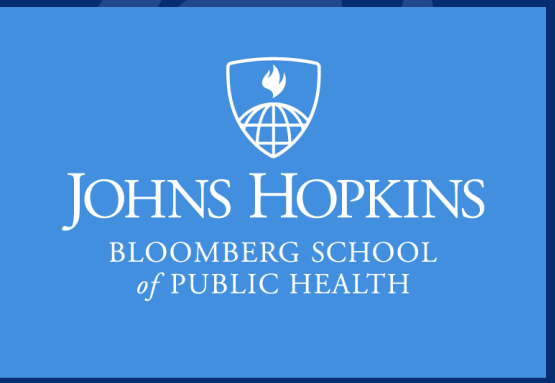


Figure 4. Projected epidemiological effect of interventions targeted to individuals with a history of previous complete tuberculosis treatment in a high-incidence setting in suburban Cape Town, 2016–2025



TB Aftermath

A hybrid type I effectiveness-implementation non-inferiority randomized trial in India comparing two active case finding (ACF) strategies among individuals treated for TB and their household contacts

Principal Investigators:
Vidya Mave, MD, TM, MPH
Madhusudan Barthwal, MBBS, MD, DM
Jonathan E. Golub, PhD, MPH

Background & Evidence Gap

- **Optimized active case finding (ACF) strategies targeting high-risk population are needed.**

- **Individuals recently treated for TB are a high-risk group**
  - 7% of reported TB cases worldwide are recurrent
  - 10-13% of treatment-completed individuals develop TB again

Image credit: pih.org

- **Standard of Care** per India's National TB Elimination Program (NTEP):
  - Follow-up of index patients at 6, 12, 18, and 24 months after TB treatment completion.
  - No defined approach for detecting TB among treated patients and their household contacts.

- **Evidence gap**:
  - No published ACF trials targeting treated TB patients
  - Only conditional recommendation by WHO

Global TB Report, WHO 2020; *Vega, Thorax 2021; WHO, Global TB Report 2020; Azhar, Lung India 2012; Velayutham PLOS ONE 2018; WHO, Consolidated guidelines on TB, 2021*

Aims

1. To conduct a non-inferiority randomized trial to measure the comparative effectiveness of two potentially implementable ACF strategies within the NTEP, conducted by existing NTEP healthcare workers (HCWs): (i) Home-based ACF (HACF) and (ii) Telephonic ACF (TACF).

2. To characterize implementation processes of the ACF strategies using the RE-AIM framework to inform their future scale-up and sustainability

3. To model the impact and cost-effectiveness of the ACF strategies evaluated in the trial, and of potential alternative strategies for the targeting and timing of those strategies.

4. To measure the association of the severity, chronicity, and progression of post-TB lung impairment with recurrent TB disease.

Design & Setting

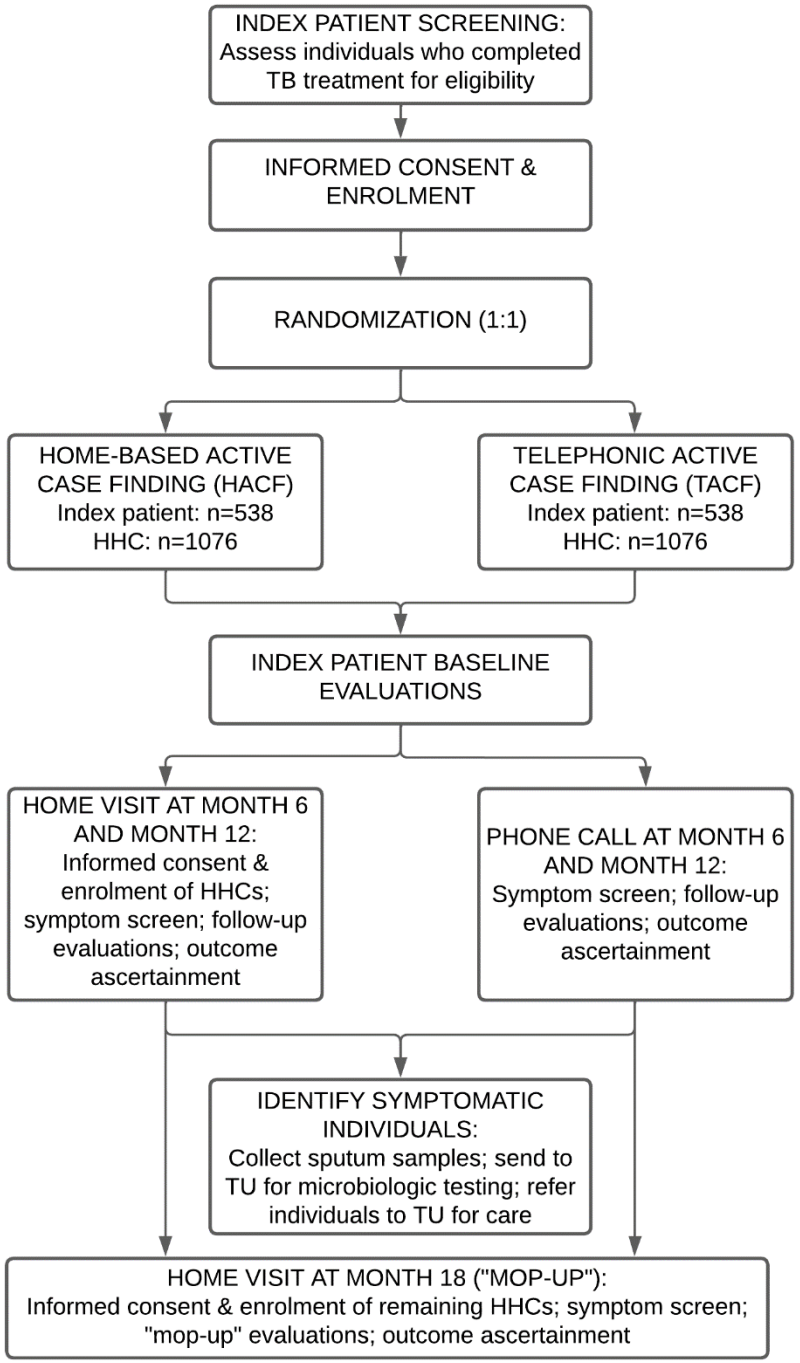
- **Hybrid Type I effectiveness-implementation non-inferiority trial with individual randomization**
- **Setting:** Six public TB units in Pune district, India
- **Index Case Eligibility Criteria**
  - Adults (≥18 years)
  - Completed TB treatment within 60 days of enrolment
  - Informed consent
- **All household contacts (HHC) eligible**

1 TU covers 0.3-0.5 million population

Urban TUs
Sahakarnagar
YCM
Jijamata

Rural TUs
Khed
Paud
Maval

TB Aftermath Study Schema



Acknowledgements

- TB Aftermath study team and PIs
- TB Aftermath participants and their families
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