Tuberculosis & Co-Morbidities

Megan Devine, MD

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Has the following disclosures to make:

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

Tuberculosis and Co-Morbidities

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Pulmonary Medicine

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University of Texas at Tyler

Global Impact of Co-Morbid Conditions on TB cases

TABLE 7.2

TB cases attributable to selected risk factors

RISK FACTOR	RELATIVE RISK[a]	EXPOSED (MILLIONS IN 2015)	GLOBAL POPULATION ATTRIBUTABLE FRACTION (%)	ATTRIBUTABLE TB CASES (MILLIONS IN 2015)
Undernourishment	3.1 – 3.3	734	18	1.9
HIV infection	22	36	9.4	1.0
Smoking	1.6 – 2.5	1047	7.9	0.83
Diabetes	2.3 – 4.3	460	7.5	0.79
Harmful use of alcohol	1.9 – 4.6	407	4.7	0.49

[a] Source: Lönnroth K, Castro KG, Chakaya JM et al. Tuberculosis control and elimination 2010–50: cure, care, and social development. Lancet. 2010 May 22;375(9728):1814–29. The relative risk for HIV infection is based on data from UNAIDS and estimates from this Global TB report.

WHO Global Tuberculosis Report 2017

TB and Co-Morbidities 2016
Closer to Home

	Diabetes	HIV	IVDU	Non-injecting drug use	Excessive Alcohol
US	16.5%	5.6%	1.3%	6.8%	10%
Texas	19%	6%	2%	9%	15%
Region 4/5N	14.8%	3.7%	0	7.4%	18.5%

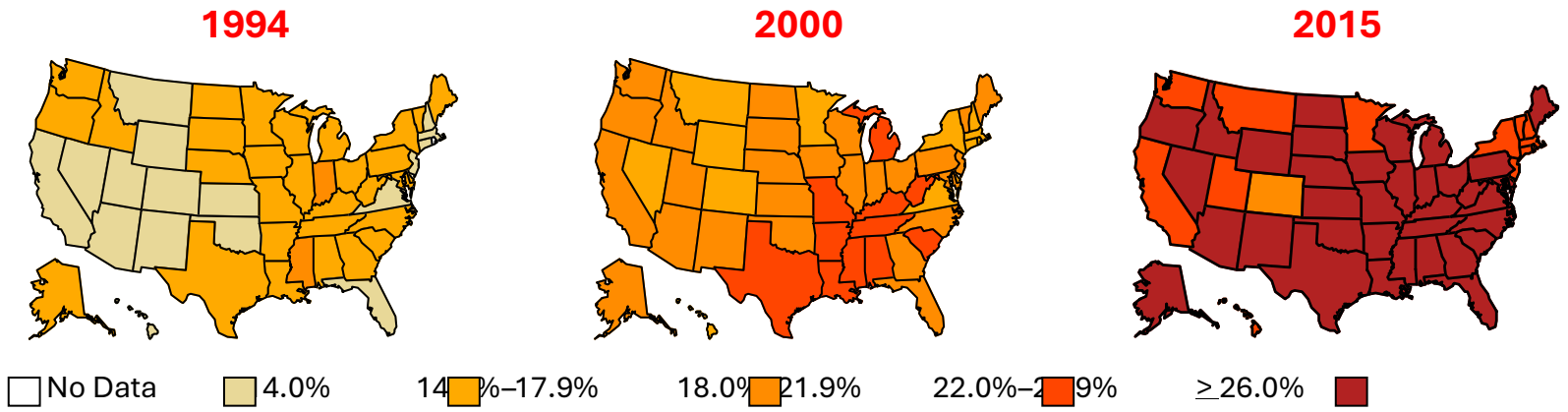
2016 REPORTED TUBERCULOSIS IN THE UNITED STATES
Texas TB Surveillance Report 2016
Region 4/5 data provided by:
Daniele Fedonni and Jie Deng
DSHS TBHIVSTDdata

TB and Diabetes

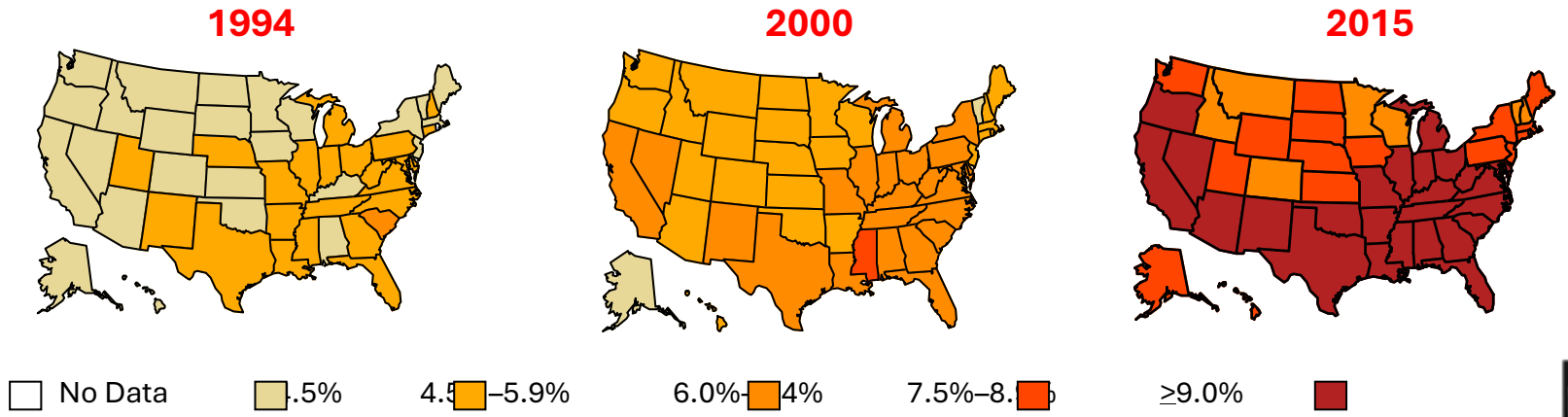
The Fattening and Sweetening of the US

Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI ≥30 kg/m²)



Diabetes



CDC's Division of Diabetes Translation. United States Surveillance System available at http://www.cdc.gov/diabetes/data

Type 2 Diabetes in the US

Prevalence: In 2015, 30.3 million Americans (9.4% of the population) had diabetes.

- Of those, approximately 1.25 million American children and adults had type 1 diabetes.

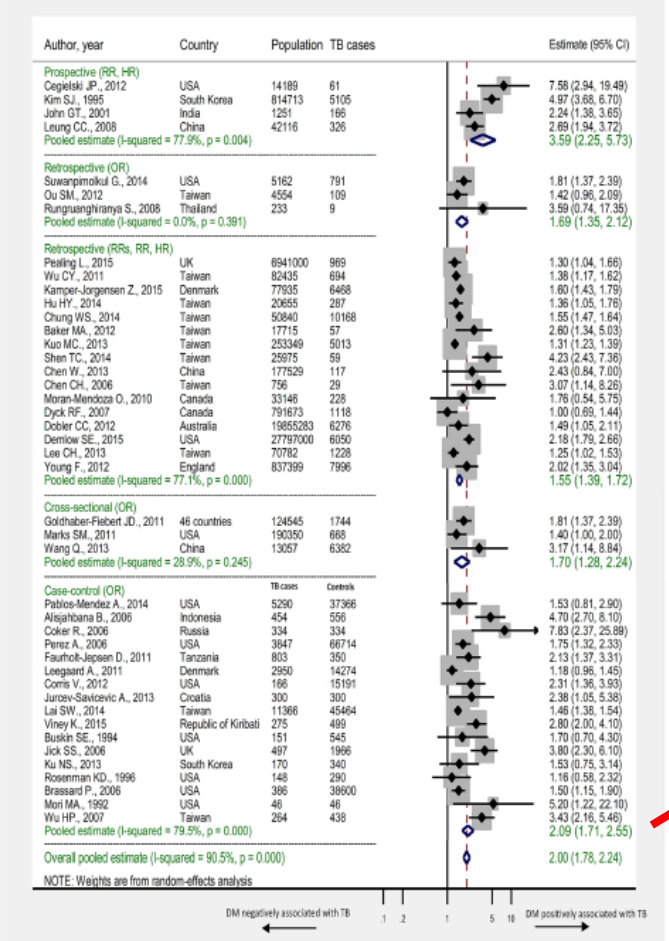
For 2018

JAMA

> "The estimated unadjusted prevalence was 11.2% for diagnosed diabetes (95% CI, 9.8%-12.5%), 3.4% for undiagnosed diabetes (95% CI, 2.5%-4.3%), and 14.6% for diabetes (95% CI, 12.8%-16.3%) (Table 1)."
>
> — **Li Wang, PhD1**, *et al.*, School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai, China and other institutions
>
> Trends in Prevalence of Diabetes and Control of Risk Factors in Diabetes Among US Adults, 1999-2018. JAMA. June 24, 2021.

Association between diabetes mellitus and active tuberculosis:

A systematic review and meta-analysis



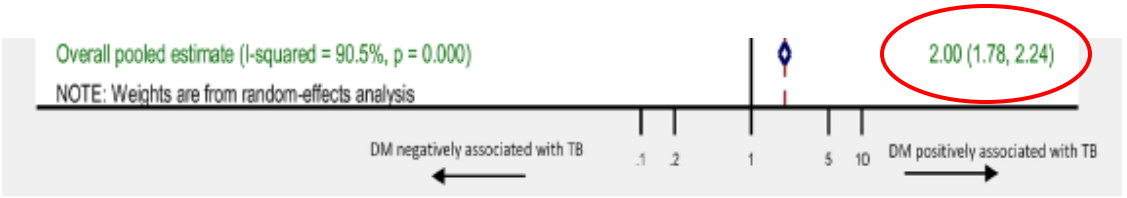
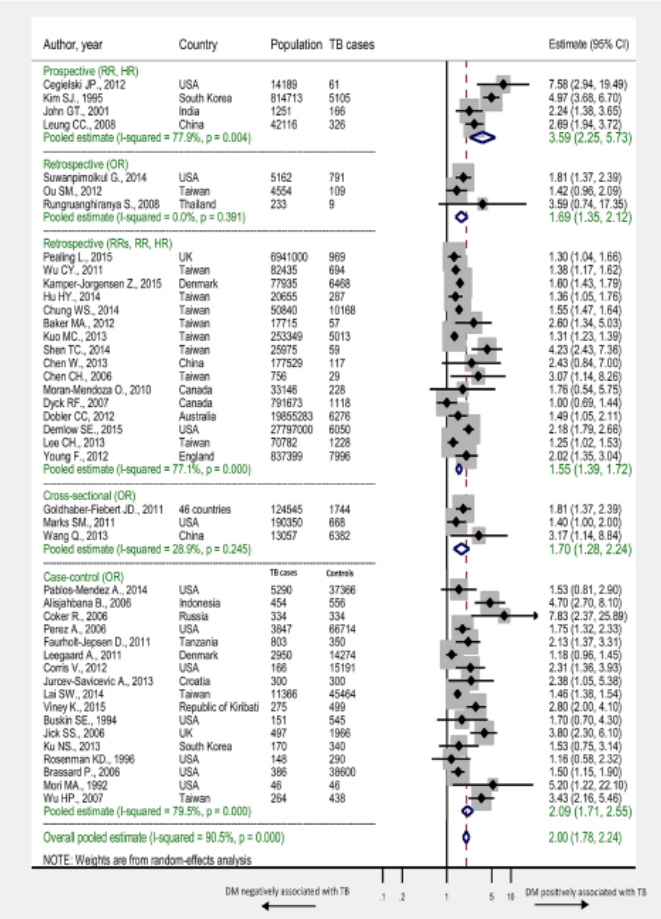


Fig 2. Forest plot of the meta-analyses. Pooled findings of 44 studies reporting adjusted estimates of the association between TB and DM, stratified according to study design. Size of the square is proportional to the precision (weight) of the study-specific effect estimates. Circle is the study–specific effect point estimate. Arrows indicate that the bars are truncated to fit the plot. The diamond is centered on the summary effect estimate, and the width indicates the corresponding 95% CI. RRs: relative risk; RR: rate ratio; OR: odds ratio; HR: hazard ratio.

Al-Rifai et al. PLoS ONE 2017 12(11): e0187967

Association between diabetes mellitus and active tuberculosis:

A systematic review and meta-analysis



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Increase in risk

- By study type
  - 3.59-fold (prospective)
  - 1.55-fold (retrospective)
  - 2.09-fold (case-control)
- By country income level
  - 3.16 fold low/middle income vs. 1.73-fold in high income
- By geographical region
  - 2.44-fold in Asia
  - 1.71-fold in Europe
  - 1.73-fold in USA/Canada

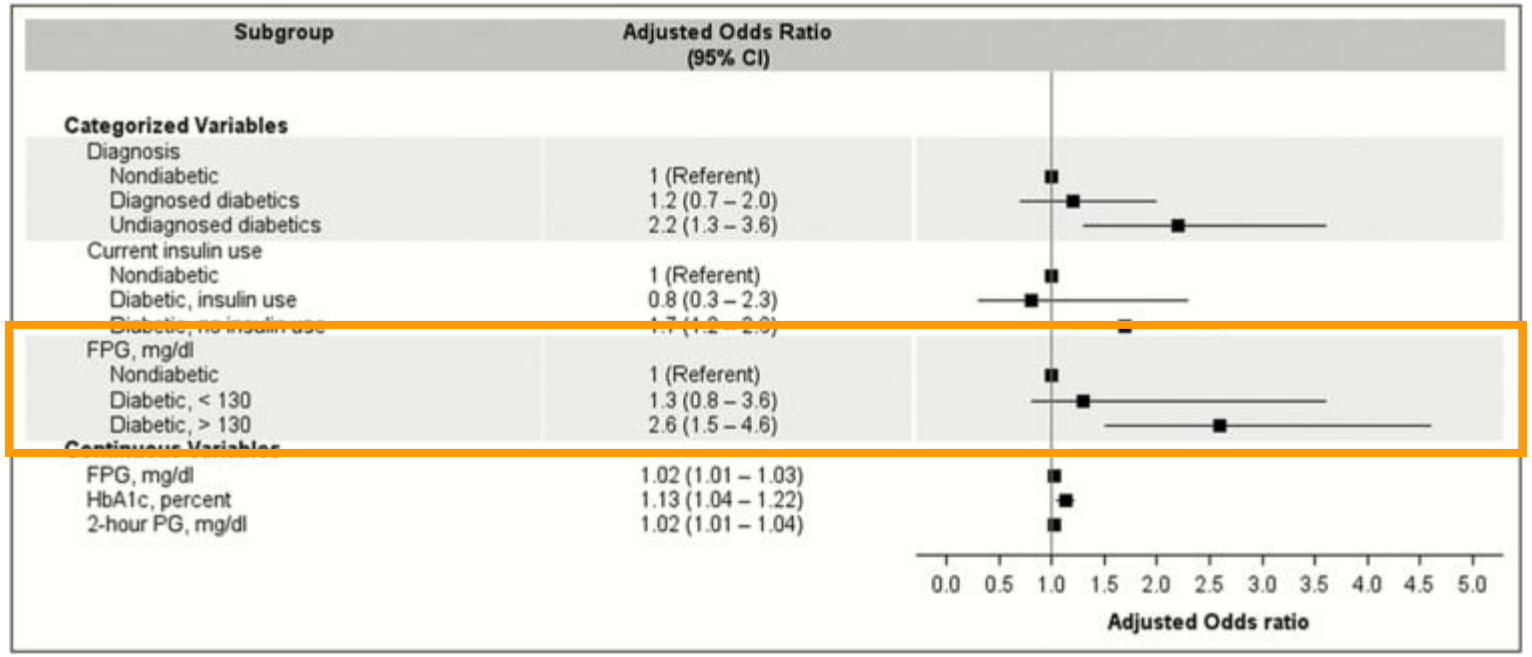
Conclusion:

DM is associated with a 1.5-fold- to 4-fold increased risk of active TB

Al-Rifai et al. PLoS ONE 12(11): e0187967

Association between diabetes mellitus and active tuberculosis:

A Population-based Observational Study



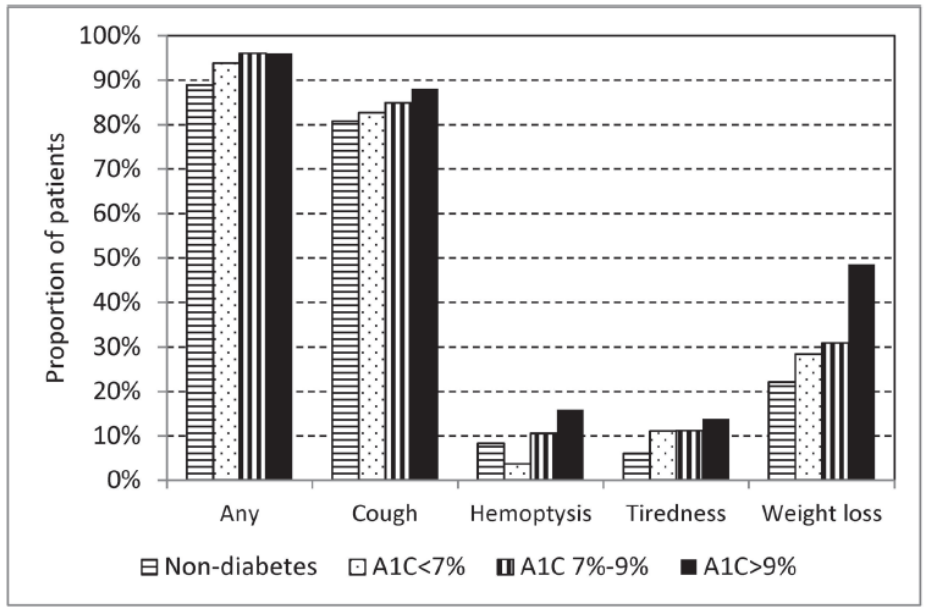
Leonardo Martinez et al. Clin Infect Dis. 2017. Nov 29. PMID: 29059298

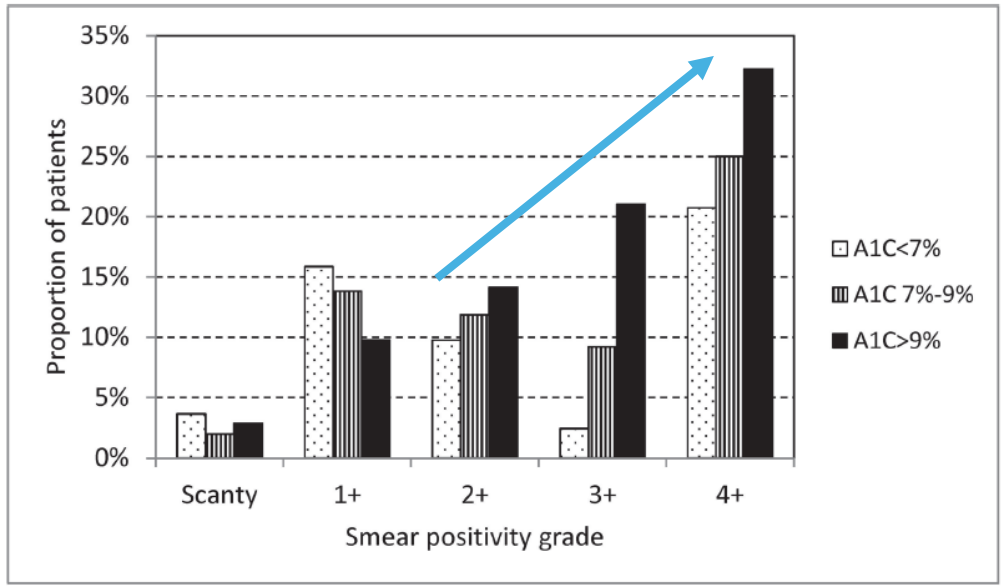
PLOS ONE

RESEARCH ARTICLE

The Influence of Diabetes, Glycemic Control, and Diabetes-Related Comorbidities on Pulmonary Tuberculosis

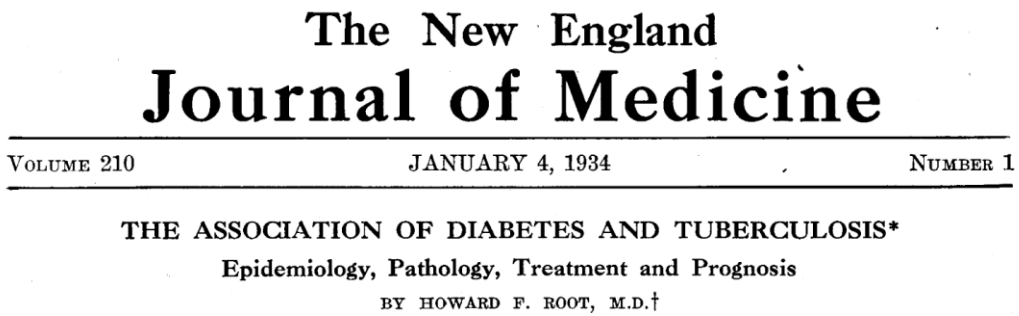
Chen Yuan Chiang[1,2,3], Kuan Jen Bai[2,4], Hsien Ho Lin[5], Shun Tien Chien[6], Jen Jyh Lee[7], Donald A. Enarson[1], Ting-I Lee[8,9], Ming-Chih Yu[2,4]*





Chiang et al. PLoS ONE 2015 10(3): e0121698

Diabetes and Clinical Presentation of TB



The New England
Journal of Medicine

VOLUME 210 JANUARY 4, 1934 NUMBER 1

THE ASSOCIATION OF DIABETES AND TUBERCULOSIS*

Epidemiology, Pathology, Treatment and Prognosis

BY HOWARD F. ROOT, M.D.†

- Autopsy series of 126 patients:
  - No pathological findings unique to “the tubercular diabetic”
- 245 TB cases in diabetic patients
  - “no special insidiousness” of signs or symptoms and similar CXR findings to non-diabetics
  - Noted that TB developed most frequently in patients with poor diabetic control

Dooley, & Chaisson, Lancet ID, Dec 2009

Does Diabetes Impact TB Treatment and Cure?

INT J TUBERC LUNG DIS 23(7):783–796

http://dx.doi.org/10.5588/ijtld.18.0433

STATE OF THE ART

STATE OF THE ART SERIES
TB and diabetes
Series editors: Matthew Magee, Hsien-Ho Lin
NUMBER 8 IN THE SERIES

The effects of diabetes on tuberculosis treatment outcomes: an updated systematic review and meta-analysis

P. Huangfu,* C. Ugarte-Gil,†,‡ J. Golub,§ F. Pearson,* J. Critchley*

There is an association between diabetes and

- Delayed culture conversion
- MDR-TB
- Treatment failure
- Relapse and recurrence
- Mortality

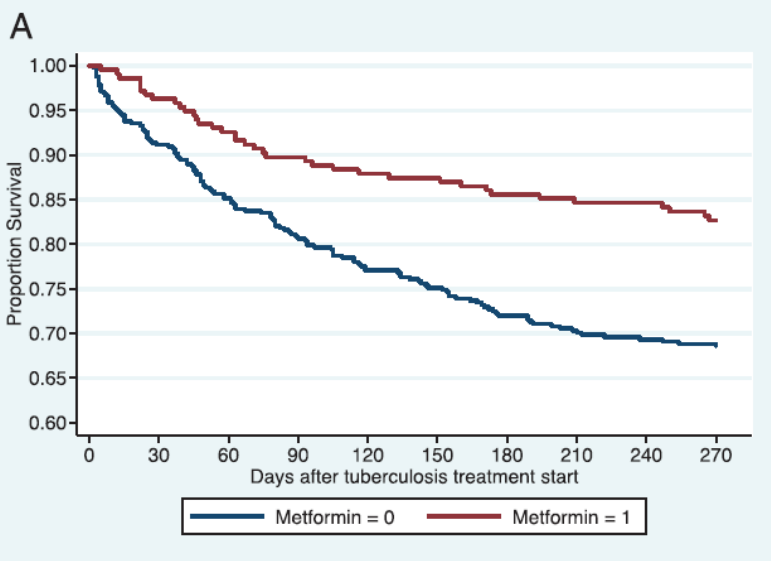
Dooly, 2009; Restrepo 2008; Wang 2008; Alisahlanda,2007

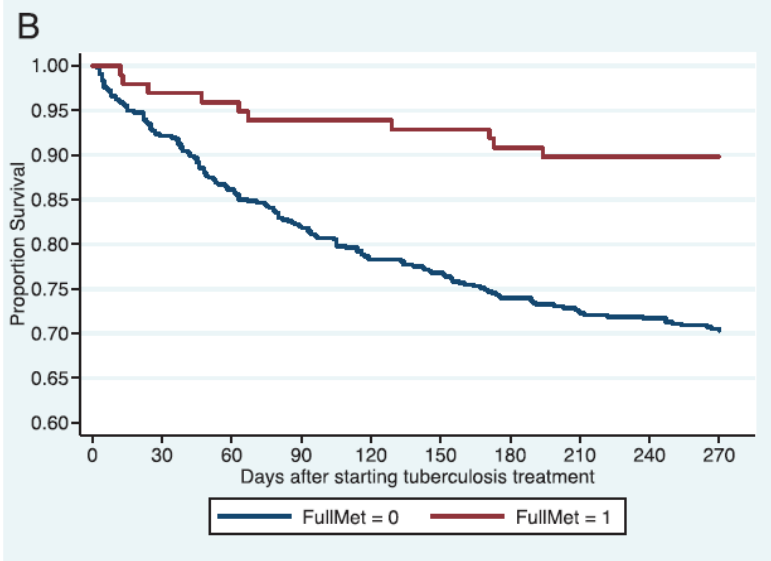
TB and Diabetes -Treatment Considerations

- **Rifampin interacts with** many of the older (affordable) hypoglycemic medications
  - Glipizide, glyburide, glimepiride, sitagliptin, pioglitazone (reduced efficacy)
- **Diabetic neuropathy** at baseline complicates therapy due to INH-related neuropathy
  - Baseline assessment of neuropathy
  - Vitamin B 6 (pyridoxine) to all diabetics on INH or ethionamide
- **Renal insufficiency** is associated with diabetes, especially long standing or poorly controlled diabetes
  - Adjust dose and dosing interval of EMB & PZA in those with Creatinine Cl < 30

Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America. 2016;63(7):853-67. doi:10.1093/cid/ciw566

Metformin Use Reverses the Increased Mortality Associated With Diabetes Mellitus During Tuberculosis Treatment





	Metformin (n=216)	Non-Metformin (n=418)	Total (n=634)	Log-Rank χ2
Death during tuberculosis treatment -%	17.6	31.3	26.7	<0.001

	Metformin (n=219)	Non-Metformin (n=358)	Total (n=577)	Log-Rank χ2
Death during tuberculosis treatment -%	10.2	29.7	26.7	<0.001

Degner et al. CID 2018; 66(2):198–205

Randomized Controlled Trial > Clin Infect Dis. 2022 Aug 31;75(3):425-434.
doi: 10.1093/cid/ciab964.

Randomized Trial of Metformin With Anti-Tuberculosis Drugs for Early Sputum Conversion in Adults With Pulmonary Tuberculosis

Chandrasekaran Padmapriydarsini [1], Megha Mamulwar [2], Anant Mohan [3], Prema Shanmugam [1], N S Gomathy [1], Aarti Mane [2], Urvashi B Singh [3], Nathella Pavankumar [1], Abhijeet Kadam [2], Hemanth Kumar [1], Chandra Suresh [1], Devaraju Reddy [1], Poornaganga Devi [1], P M Ramesh [4], Lakshmanan Sekar [1], Shaheed Jawahar [5], R K Shandil [5], Manjula Singh [6], Jaykumar Menon [5], Randeep Guleria [3]

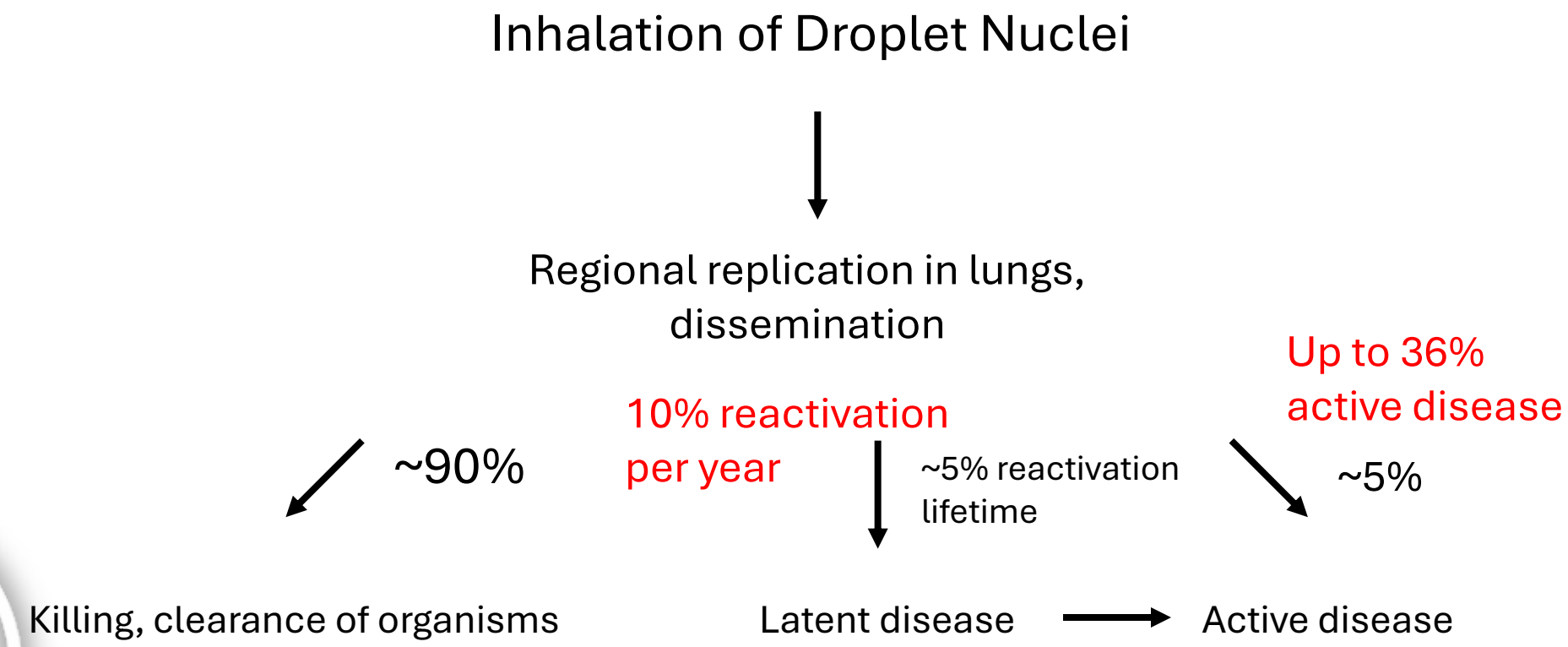
Affiliations + expand

PMID: 34849651 PMCID: PMC9427151 DOI: 10.1093/cid/ciab964

Control arm = RIPE
Study arm = RIPE + Metformin 1000mg daily
Study duration = 8 weeks
Primary endpoint = time to sputum culture conversion
Plasma inflammatory markers and time to CXR clearance also measured

TB and HIV

Outcomes of Exposure to *M. tuberculosis* in HIV-negative and HIV-positive patients



Clinical Presentation
HIV-positive vs. HIV-negative patients

- Driven mostly by degree of immunity
- HIV-positive patients are more likely to have:
  - Isolated extrapulmonary localization (53-63% in some studies)
  - Primary infection
  - Pulmonary basilar involvement
  - Tuberculous pneumonia
  - Hilar or mediastinal lymphadenopathies
  - Miliary or disseminated TB
  - Normal CXR (8-20% in some studies)

Clinical Microbiology and Infection, Volume 10 Number 5, May 2004

Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

HIV-infected persons, regardless of age, should be treated for LTBI *if they have no evidence of active TB* and exhibit the following characteristics:

- 1) a positive diagnostic test for LTBI and no prior history of treatment for active or latent TB (AI);
- 2) a negative diagnostic test for LTBI but are close contacts of persons with infectious pulmonary TB (AII); and
- 3) a history of untreated or inadequately treated healed TB (i.e., old fibrotic lesions on chest radiography) regardless of diagnostic tests for LTBI (AII)

TB and Smoking

Systematic Reviews and Meta-analyses evaluating tuberculosis and cigarette smoking

- Slama et al, Int J Tuberc Lung Dis 2007, 11; 1049
  - “Tobacco and tuberculosis: a qualitative systematic review and meta-analysis”
- Lin et al, PLoS Med 2007, 4; e20
  - “Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis”
- Bates et al Arch Intern Med 2007
  - “Risk of tuberculosis from exposure to tobacco smoke: a systematic review and meta-analysis”
- Conclusions:
  - Smokers almost twice as likely to be infected with TB and to progress to active disease
  - 2 of 3 studies suggest smokers almost twice as likely to die from TB

Tobacco and TB

OPEN ACCESS Freely available online PLOS MEDICINE

Tobacco Smoke, Indoor Air Pollution and Tuberculosis: A Systematic Review and Meta-Analysis

Hsien-Ho Lin[1], Majid Ezzati[2], Megan Murray[1,3,4*]

1 Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America, **2** Department of Population and International Health and Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, United States of America, **3** Division of Social Medicine and Health Inequalities, Brigham and Women's Hospital, Boston, Massachusetts, United States of America, **4** Infectious Disease Unit, Massachusetts General Hospital, Boston, Massachusetts, United States of America

January 2007 | Volume 4 | Issue 1 | e20

- Review of 33 papers on smoking and TB
- Compared with people who do not smoke, smokers have an increased risk of:
  - having a positive tuberculin skin test,
  - of having active TB,
  - and of dying from TB.

Conclusion: TB control programs might benefit from a focus on interventions aimed at reducing tobacco and indoor air pollution exposures, especially among those at high risk for exposure to TB.

Tobacco and Treatment Delay

INT J TUBERC LUNG DIS 16(6):822–827

http://dx.doi.org/10.5588/ijtld.11.0678
E-published ahead of print 9 April 2012

Longer delay in accessing treatment among current smokers with new sputum smear-positive tuberculosis in Nepal

T. S. Bam,* D. A. Enarson,† S. G. Hinderaker,‡ D. S. Bam§

*International Union Against Tuberculosis and Lung Disease (The Union), Jakarta, Indonesia; †The Union, Paris, France; ‡Centre for International Health, University of Bergen, Bergen, Norway; §Kathmandu Medical College, Kathmandu University, Kathmandu, Nepal

- 605 TB patients
  - 50.2% current smokers or ex-smokers,
  - 49.8% never smokers
- Median total delay in seeking treatment
  - current smokers **133 days**
  - ex-smoker **103 days**
  - never smokers 80 days.
- Longer delay was more common among current smokers (aOR 2.03, 95%CI 1.24–3.31).

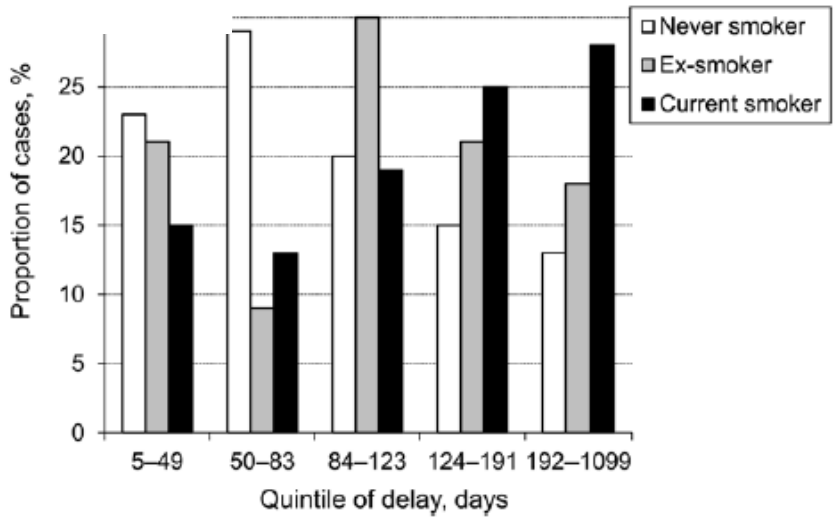


Figure 2 Association of total delay with smoking habit among new smear-positive pulmonary tuberculosis patients, Kathmandu 2006.

Tobacco and Culture Conversion

INT J TUBERC LUNG DIS 17(2):225–228

http://dx.doi.org/10.5588/ijtld.12.0426

Smoking and 2-month culture conversion during anti-tuberculosis treatment

E. L. Maciel,*† A. P. Brioschi,*† R. L. Peres,* L. M. Guidoni,*† F. K. Ribeiro,* D. J. Hadad,* S. A. Vinhas,* E. Zandonade,† M. Palaci,* R. Dietze,* J. L. Johnson‡

*Núcleo de Doenças Infecciosas, Centro de Ciências da Saúde, Universidade Federal do Espírito Santo, Vitória, Espírito Santo, †Programa de Pós-graduação em Saúde Coletiva, Centro de Ciências da Saúde, Universidade Federal do Espírito Santo, Vitória, Espírito Santo, Brazil; ‡Tuberculosis Research Unit, Department of Medicine, Division of Infectious Diseases, Case Western Reserve University, Cleveland, Ohio, USA

- 714 patients in Brazil, screened for Phase 2 trial, Dec 2002 – August 2006
- 2 months daily HRZE then 2 or 4 months daily HR, all evaluated after 2 months. Excluded if co-morbid conditions: DM, asthma, rheum dz, HIV

Patients who smoked had three-fold greater odds of remaining sputum culture-positive after 2 months of treatment than non-smokers

*Alcohol consumption did not affect culture conversion

Tobacco and Diabetes

OPEN ACCESS Freely available online

PLOS | ONE

Impact of Diabetes and Smoking on Mortality in Tuberculosis

George W. Reed[1], Hongjo Choi[2], So Young Lee[2], Myungsun Lee[2], Youngran Kim[2], Hyemi Park[2], Jongseok Lee[2], Xin Zhan[4], Hyeungseok Kang[5], SooHee Hwang[5], Matthew Carroll[6], Ying Cai[6], Sang-Nae Cho[2,3], Clifton E. Barry III[6], Laura E. Via[6], Hardy Kornfeld[7]*

February 2013 | Volume 8 | Issue 2 | e58044

- 657 subjects presenting at TB hospital, 25% with DM
- DM associated with greater radiographic severity and with recurrent or relapsed TB.
- Diabetes and cigarette smoking independently increased the risk of death in the first 12 months after enrollment.
- Estimating the combined impact of diabetes and smoking yielded a hazard ratio of 5.78.

Alcohol Misuse, Substance Abuse and TB

Review > BMC Public Health. 2009 Dec 5:9:450. doi: 10.1186/1471-2458-9-450.

The association between alcohol use, alcohol use disorders and tuberculosis (TB). A systematic review

> Addiction. 2017 Dec;112(12):2124-2131. doi: 10.1111/add.13926. Epub 2017 Aug 22.

Heavy alcohol consumption increases the risk of active tuberculosis in Taiwanese adults: a nation-wide population-based cohort study

Meta-Analysis > Int J Tuberc Lung Dis. 2018 Nov 1;22(11):1277-1285. doi: 10.5588/ijtld.18.0092.

Alcohol consumption and risk of tuberculosis: a systematic review and meta-analysis

Observational Study > PLoS One. 2020 Dec 17;15(12):e0240595.
doi: 10.1371/journal.pone.0240595. eCollection 2020.

Alcohol use and tuberculosis clinical presentation at the time of diagnosis in Puducherry and Tamil Nadu, India

Individuals with heavy alcohol consumption or alcohol use disorder (AUD) have a two- to five-fold increased risk of developing active TB compared to those who do not drink alcohol.

Alcohol Misuse and TB

Differences in disease characteristics between North Carolina tuberculosis cases reported 1994–2006 with and without excess alcohol use

Characteristic	Excess alcohol use		Prevalence ratio (95% confidence interval)
	Yes	No/unknown	
Site of disease			
Pulmonary (±extrapulmonary)	1227 (92.5%)	3266 (77.2%)	1.20 (1.17–1.23)
Extrapulmonary only	99 (7.5%)	964 (22.8%)	
Chest radiographic findings			
Cavitary	452 (36.8%)	920 (28.2%)	1.31 (1.19–1.43)
Non-cavitary	775 (63.2%)	2346 (71.8%)	
Sputum smear			
Positive	809 (65.9%)	1495 (45.8%)	1.44 (1.36–1.52)
Negative	418 (34.1%)	1771 (54.2%)	
Sputum culture			
Positive	1038 (84.6%)	2270 (69.5%)	1.22 (1.18–1.26)
Negative	189 (15.4%)	996 (30.5%)	

Chest radiographic, sputum smear, and sputum culture data are for cases with pulmonary involvement only.

› Int J Tuberc Lung Dis. 2012 Jul;16(7):886-90. doi: 10.5588/ijtld.11.0624. Epub 2012 May 8.

Tuberculosis and alcohol misuse in Scotland: a population-based study using enhanced surveillance data

B de la Haye [1], S H Wild, J Stevenson, F Johnston, O Blatchford, I F Laurenson

Pulmonary Disease: 92.3% vs 61.1%

Fiske et al Journal of Infection (2009) 58, 395-401

Alcohol Misuse and TB

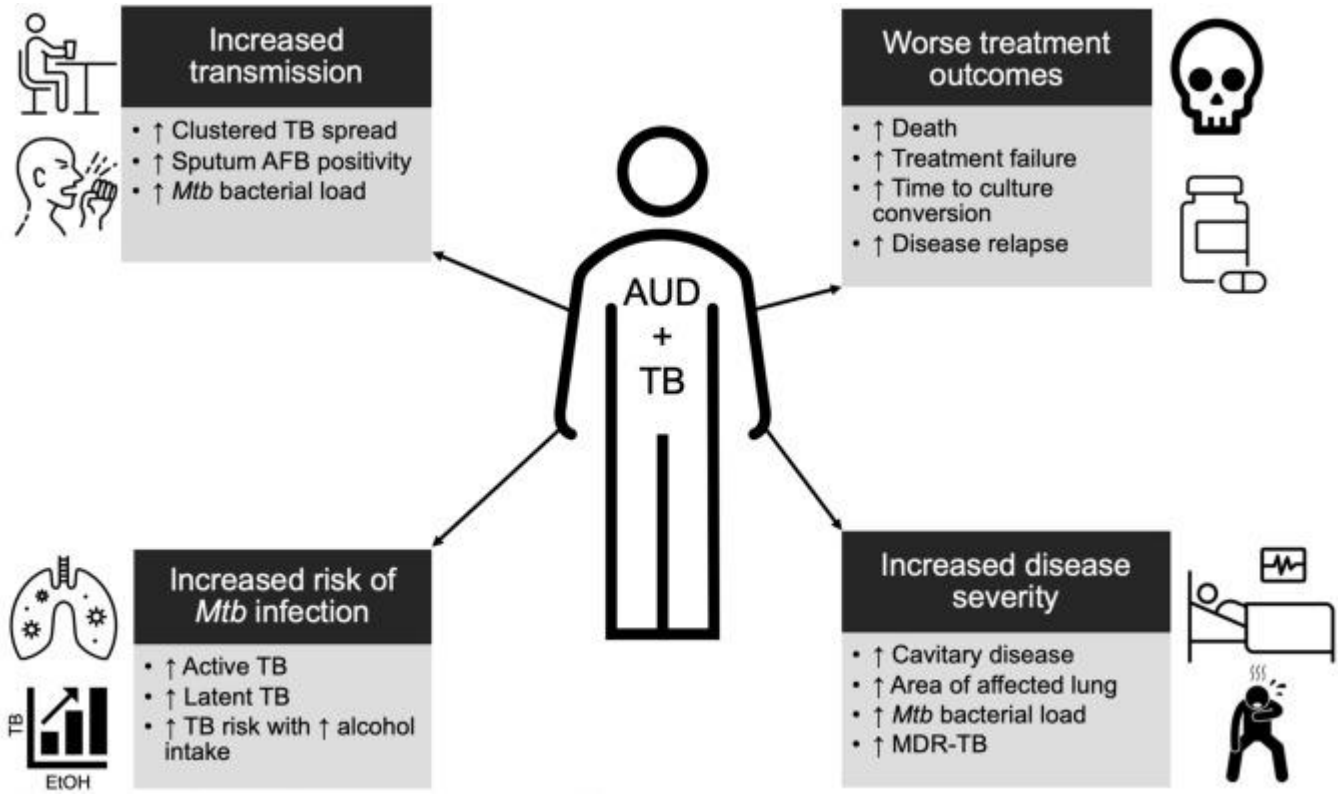


Figure 1

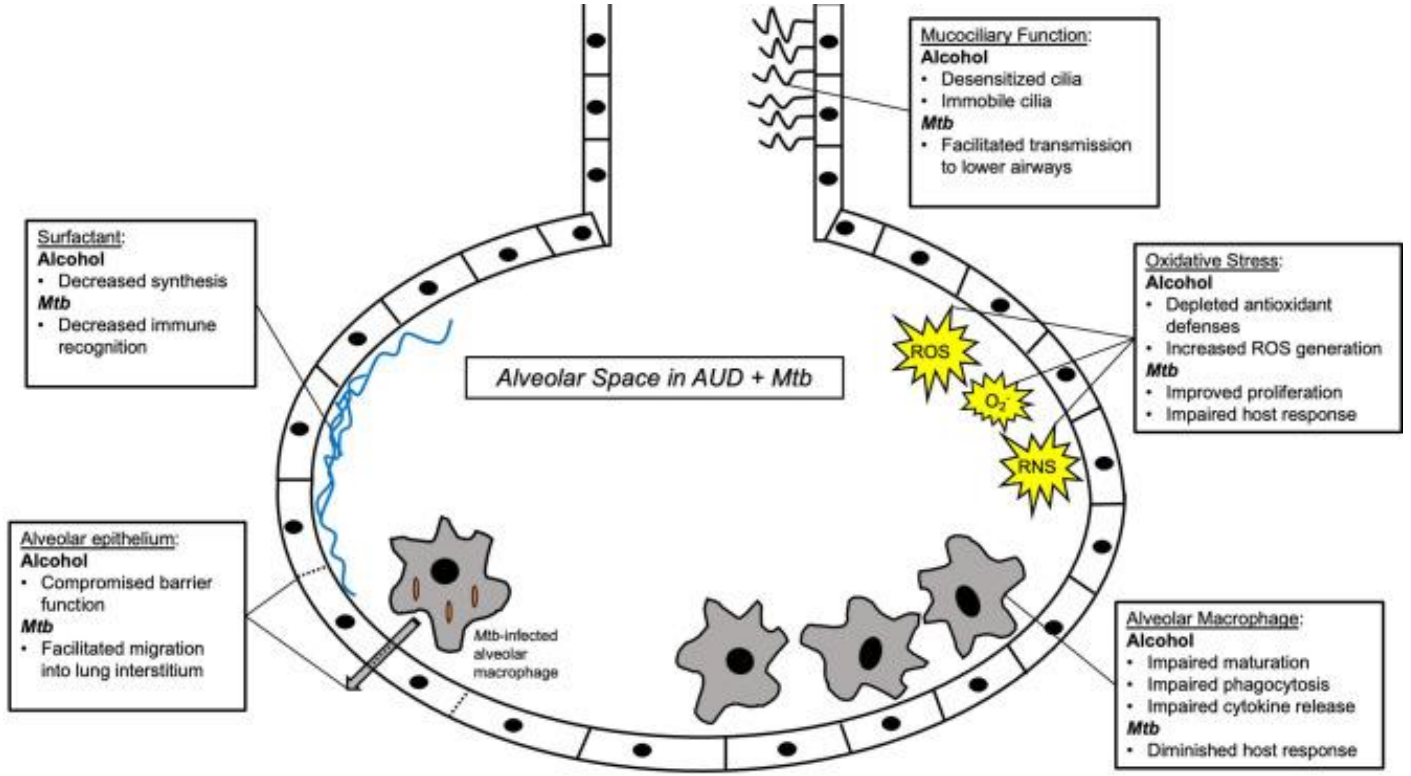
Summary schema of the epidemiologic data of alcohol use disorder (AUD) and tuberculosis (TB). Individuals with AUD are at a higher risk for TB, more infectious, have more severe disease, and are more likely to experience poor outcomes.

Gregory Wigger et al. Front Immunol. 2022 Mar 31:13:864817

Review > Front Immunol. 2022 Mar 31:13:864817. doi: 10.3389/fimmu.2022.864817.
eCollection 2022.

The Impact of Alcohol Use Disorder on Tuberculosis: A Review of the Epidemiology and Potential Immunologic Mechanisms

Gregory W Wigger [1], Tara C Bouton [2], Karen R Jacobson [2], Sara C Auld [1 3], Samantha M Yeligar [1 4], Bashar S Staitieh [1]



Alcohol and Hepatotoxicity in the Treatment of TB Disease

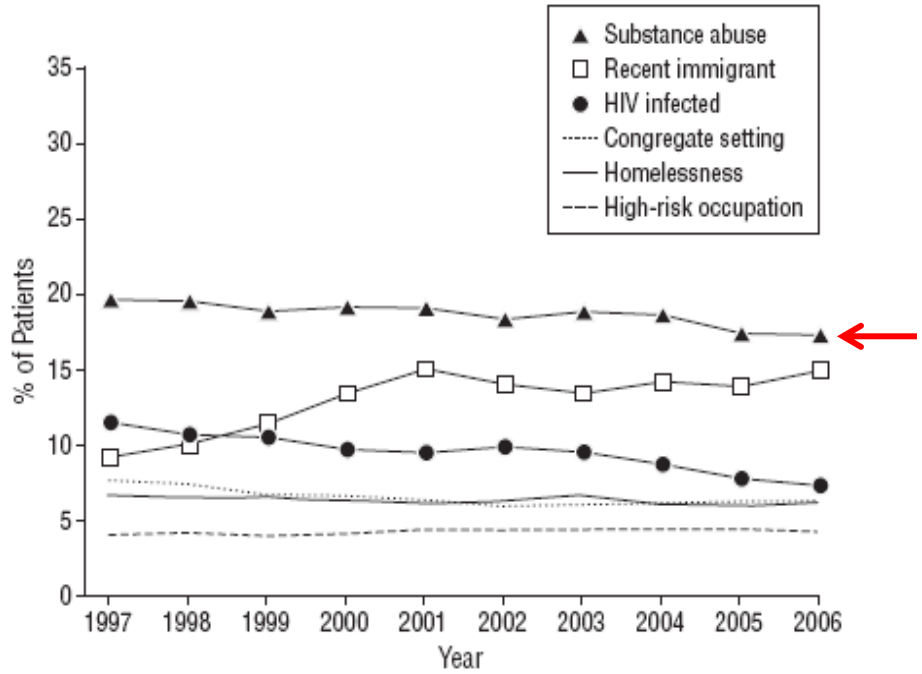
Table 5 Dichotomous variables in cases and controls

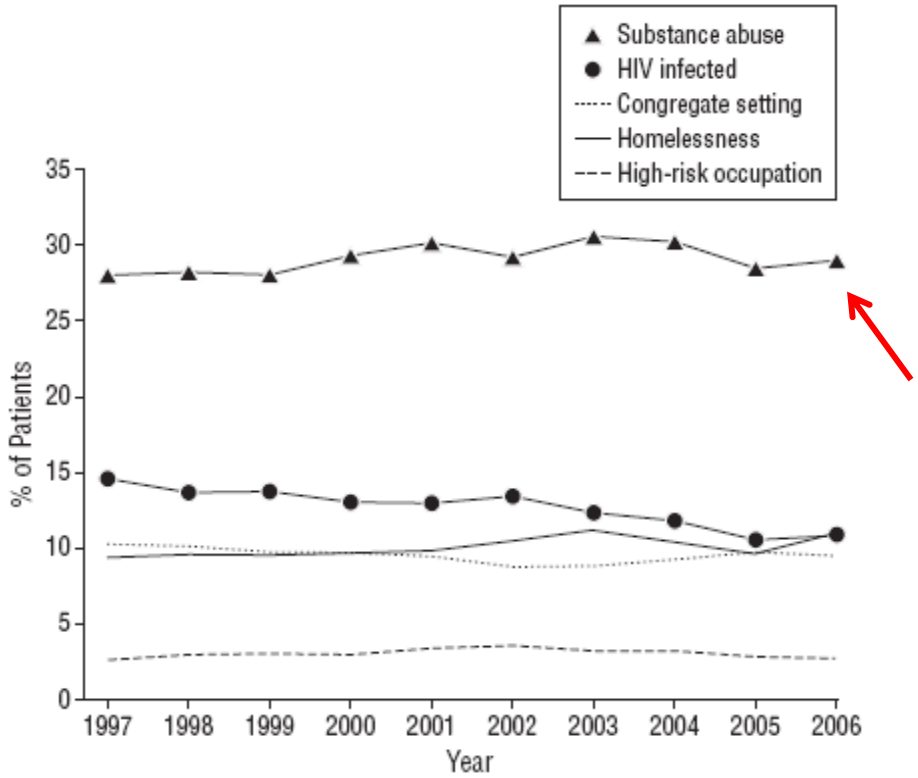
	Cases (n = 86)	*Controls (n = 406)*	*χ^2†*	*Odds ratio (95% CI)*
High alcohol intake	19·8%	4·9%	20·4	4·76 (2·25 to 10·05)*
Extensive disease	14·0%	3·5%	13·6	4·5 (1·88 to 10·93)*
Slow acetylator	82·9%	64·2%	5·60	2·72 (1·16 to 6·57)**
Jaundice in past	11·6%	10·8%	0·001	1·08 (0·49 to 2·35)
Pyrazinamide in regimen	62·8%	25·1%	44·78	5·03 (2·99 to 8·47)***

* $p<0·001$; ** $p<0·01$; *** $p<0·1 \times 10^{-7}$.
† Yates' corrected χ^2.

Pande Thorax 1996;51:132-136

Tuberculosis and Substance Abuse in the United States, 1997-2006





Oeltmann et al. Arch Intern Med. 2009;169(2):189-197

Tuberculosis Outbreak Investigations in the United States, 2002–2008

Kiren Mitruka, John E. Oeltmann, Kashef Ijaz, and Maryam B. Haddad

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 3, March 2011

Table 2. Tuberculosis risk factors for patients in CDC–investigated TB outbreaks, United States, 2002–2008*

Risk factor†	No. (%) patients
Total	398 (100)
Medical	
HIV co-infection	46 (12)‡
Diabetes	23 (6)
Immunosuppression (not HIV associated)	14 (4)
History of TB	16 (4)
Incomplete treatment	7 (44)
Social	
Any substance abuse	233 (58)
Alcohol abuse	204 (51)
Nonintravenous drug use	117 (29)
Intravenous drug use	19 (5)
Incarceration history§	126 (32)
Homelessness	78 (20)

Table 3. Predominant characteristics of CDC–investigated TB outbreaks, United States, 2002–2008*

Characteristic	No. (%) outbreaks†
Total	27 (100)
US born	24 (89)
Male sex	22 (81)
Substance abuse (alcohol/drugs)	18 (67)
Acid-fast bacilli smear positive	17 (63)
Non-Hispanic black	16 (59)
Incarceration history	8 (30)
Cavitary disease on chest radiograph	7 (26)
Non-Hispanic white	4 (15)
Homelessness	4 (15)
Hispanic	3 (11)
HIV co-infection	1 (4)

*TB, tuberculosis; CDC, Centers for Disease Control and Prevention.
†Outbreak had ≥50% of patients with the select characteristic.

Substance abuse in TB patients

- Tuberculosis Outbreak in Southern Mississippi, 2005-2007
  - Bloss et al. 2011. Southern Medical Journal 104 (11):731
  - All US-born, all HIV negative, 92% black, 82% substance abuse, 100% pulmonary disease, 170 contacts (45% TST+)

- Crack Cocaine and Infectious Tuberculosis
  - Story et al. 2008. EID 14 (9):1466
  - 64% UK-born, 64 % white or black Caribbean, crack use associated with 2.4X higher rate of smear positivity

- Tuberculosis and Drug Users in Iran
  - Shamaei et al. IJ STD & AIDS. 2009. 20:320
  - 91% Iranian, 98% men, heroin/opium, 89% sputum smear positive

- Tuberculosis Outbreak in Nevada and Arizona
  - Mitruka et al. Public Health Reports 129: 78
  - 100% Hispanic (born in Mexico), index case deported by ICE (returned), 130 contacts (54.6% TST positive), methamphetamines

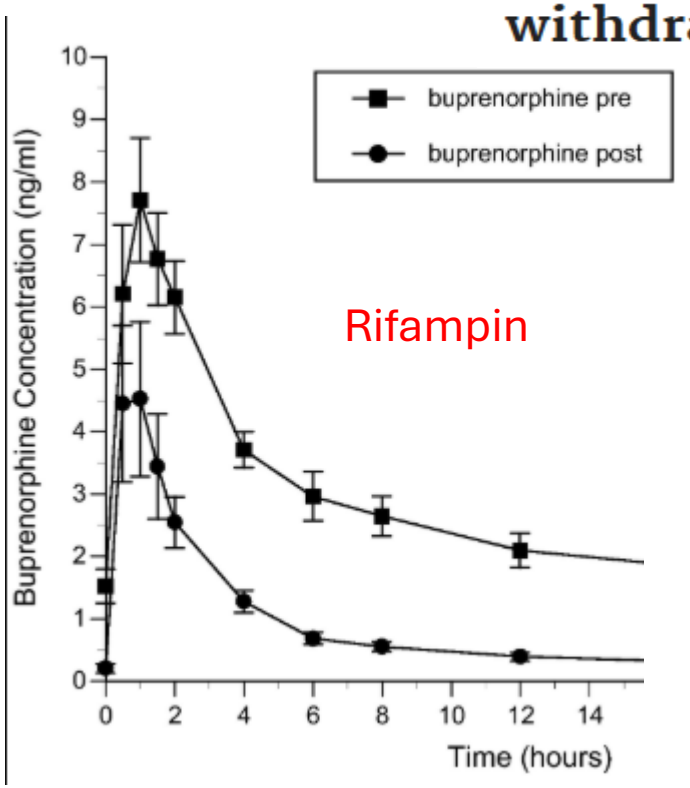
Rifampin and Opioids

- Methadone
  - Rifampin lowers the serum concentration of methadone by 33-66%
  - Administration of rifampin to patients on methadone has led to opioid withdrawal in patients on methadone replacement therapy
  - Need to increase methadone dose and monitor carefully to prevent withdrawal with co-administration of rifampin and methadone
- Suboxone (buprenorphine and naloxone)
  - Rifampin lowers the serum concentration of buprenorphine leading to reduced efficacy and risk of withdrawal
- Codeine
  - Administration with rifampin leads to decreased biotransformation to morphine (which is responsible for most of the analgesic effects)
  - Decreased serum concentration with rifampin
- Morphine
  - 28 % decrease in serum levels when given with rifampin
  - Loss of analgesic effect

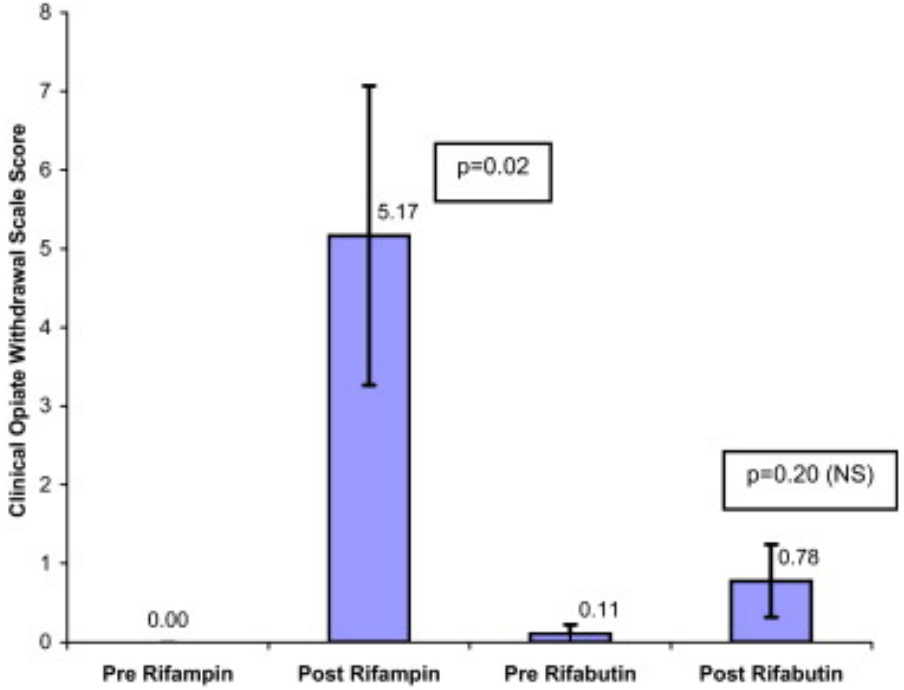
Niemi et al. Clin Pharmacokinet 2003 42 (9): 819-50
McCance-Katz et al. Drug and Alcohol Dependence. 2011; 118(2-3)326-34.

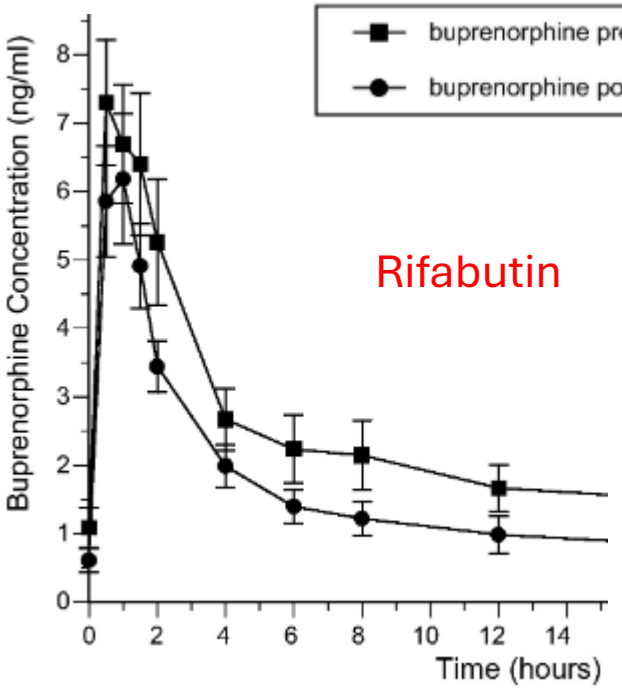
Drug Alcohol Depend. 2011 Nov 1;118(2-3):326-34. doi: 10.1016/j.drugalcdep.2011.04.013. Epub 2011 May 19.

Rifampin, but not rifabutin, may produce opiate withdrawal in buprenorphine-maintained patients



Rifampin





Rifabutin

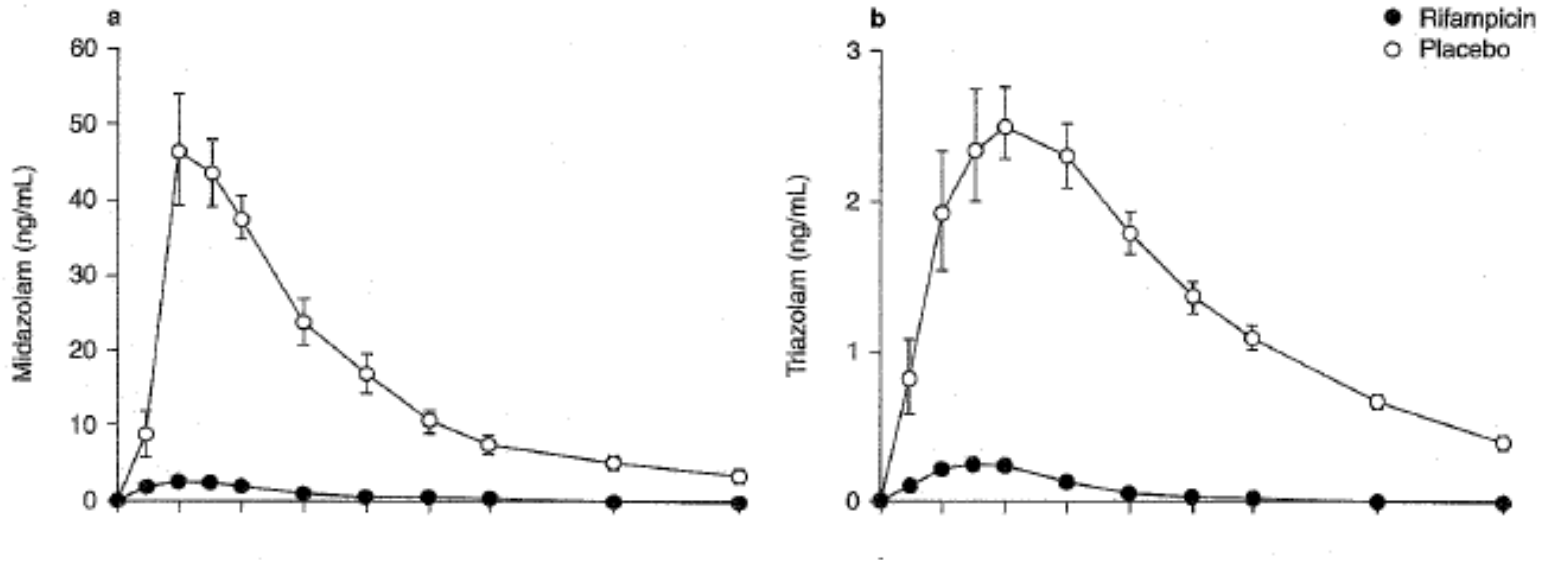
Rifampin and Benzodiazepines

- Diazepam
  - Reduction of half-life by 76%
  - Enhanced total body clearance by 300%
  - May require a 2-3 fold increase in dose for effect

- Midazolam and Triazolam
  - Decreased serum concentration to 2-4% of controls
  - Ineffective during co-administration with rifampin

Niemi et al. Clin Pharmacokinet 2003 42 (9): 819-50

Rifampin and Benzodiazepines



Niemi et al. Clin Pharmacokinet 2003 42 (9): 819-50

Rifabutin

- A substitute for rifampin for patients who are receiving drugs, especially antiretroviral drugs, that have unacceptable interactions with rifampin.

- Less severe induction of hepatic microsomal enzymes, therefore, less effect on the metabolism of other drugs

Biggest Barrier to care:
What is important to you? Your patient?

- Difference in focus between care providers and substance abuser
  - Providers are focused on
    - Compliance
    - Co-morbid conditions
    - Pill counts
  - Patient is frequently focused on
    - Available foods, foods I like
    - Avoiding withdrawal
    - Avoiding drugs that make me feel bad or ‘kill my buzz’
    - Next ‘fix’, next meal, a place to sleep
    - Avoiding incarceration

How do we help the patient?

- Let go of stigma and focus on walking with the patient to care
- See addiction as another co-morbidity to be addressed
- Answer the question: “What’s in it for me?”
  - A meal?
  - A bed?
- Explore available programs to help the patient effect a change

Anticoagulation, Anti-Platelet Agents and TB

Deep vein thrombosis, pulmonary embolism, atrial-fibrillation, cerebrovascular disease, coronary artery disease, and peripheral vascular disease.

Antiplatelet Agents

Clopidogrel (Plavix):

Rifampin markedly increases the formation of clopidogrel's active metabolite, leading to enhanced P2Y12 inhibition and a higher risk of bleeding.

Ticagrelor (Brilinta):

Rifampin induces CYP3A4, which substantially decreases ticagrelor exposure and efficacy. Rifampin may render ticagrelor ineffective

Prasugrel (Effient):

Unlike clopidogrel and ticagrelor, prasugrel's pharmacokinetics are largely unaffected by rifampin, making it a potential alternative if antiplatelet therapy is required in a patient receiving rifampin

MacDougall C et al. Pharmacotherapy. 2022; 42(4):343-361.

Anticoagulants

Warfarin

Rifampin decreases the efficacy of warfarin.

Warfarin dose often requires increase, sometimes 2 - to 5 - fold while using rifampin

When rifampin is stopped, warfarin doses often require decreases

Direct Oral Anticoagulants

Rifampin significantly reduces drug exposure (AUC reductions 20-67%)

Potentially leads to therapeutic failure

MacDougall C et al. Pharmacotherapy. 2022; 42(4):343-361.

› Antimicrob Agents Chemother. 2021 Aug 17;65(9):e0104321. doi: 10.1128/AAC.01043-21. Epub 2021 Aug 17.

Model-Based Comparative Analysis of Rifampicin and Rifabutin Drug-Drug Interaction Profile

Vianney Tuloup [1 2], Mathilde France [1], Romain Garreau [1 2], Nathalie Bleyzac [1], Laurent Bourguignon [1 2 3], Michel Tod [1 2 3], Sylvain Goutelle [1 2 3]

“On average, DDI caused by low-dose RIF were twice as potent as those caused by RBT. Contrary to RIF, RBT appears unlikely to cause severe DDI, even with sensitive CYP substrates.”

DDI: drug-drug interactions
RIF: rifampin 600mg
RBT: rifabutin 300mg

THEY ALWAYS COME BACK

Do It Right The First Time!

Barbara Seaworth, MD