


**Tuberculosis and Diabetes**

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27 September 2018

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## Disclosures

- I have no actual or potential conflict of interest in relation to this presentation.

## Learning Objectives

1. To review the epidemiology of TB-DM co-infection
2. To review the impact of DM on TB disease
3. To review management issues of TB-DM

## Diagnosis of Diabetes

Fasting plasma glucose (FPG)  
≥126 mg/dL (7.0 mmol/L)

*OR*

2-h plasma glucose ≥200 mg/dL  
(11.1 mmol/L) during an OGTT

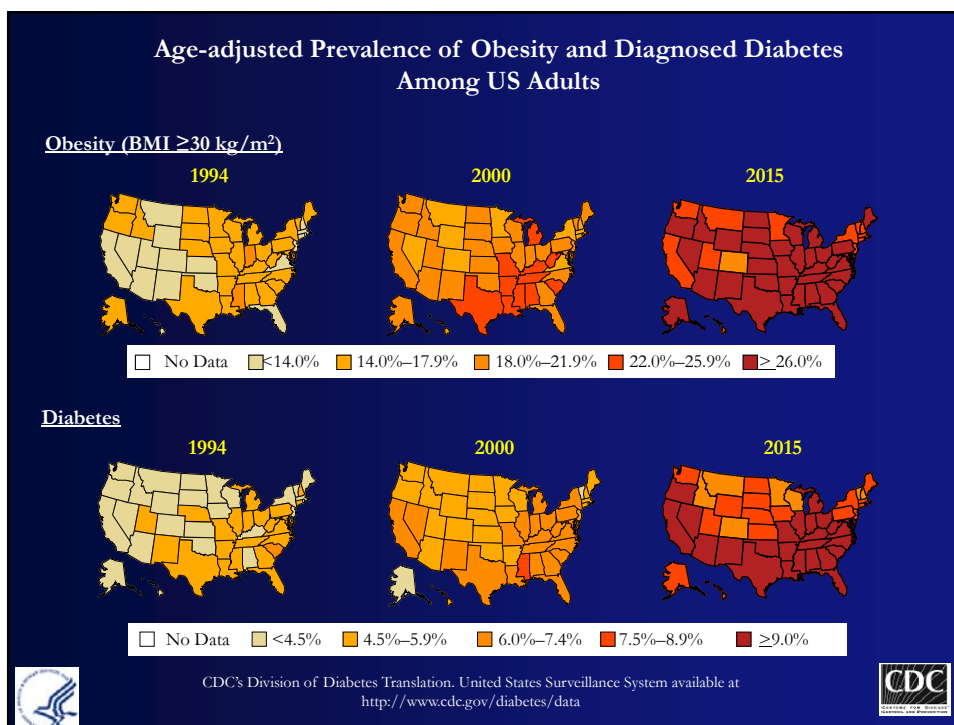
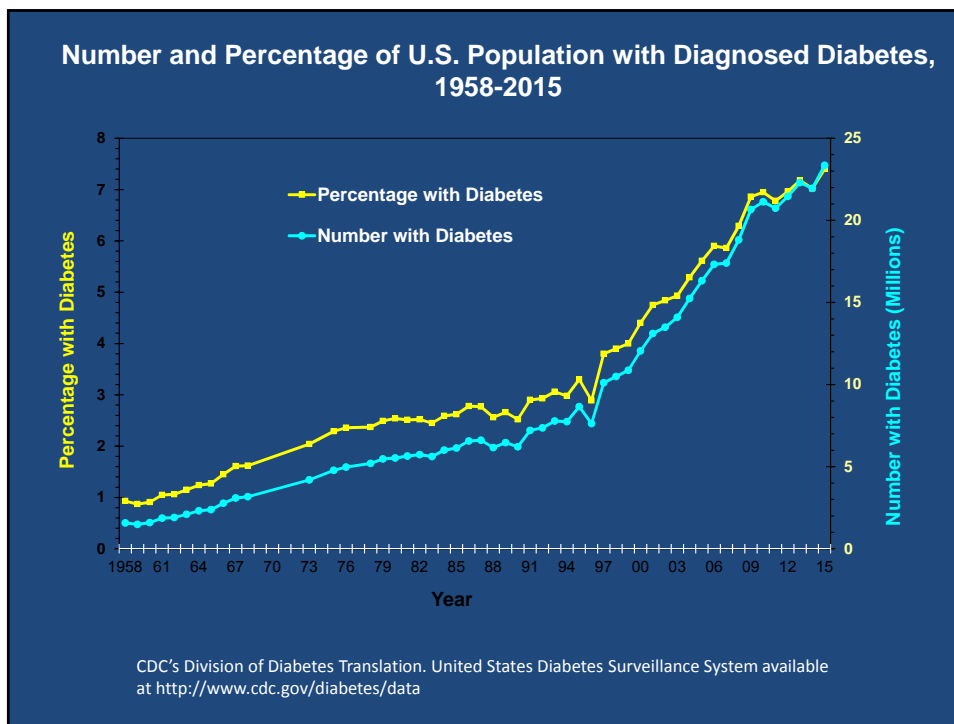
*OR*

A1C ≥6.5%

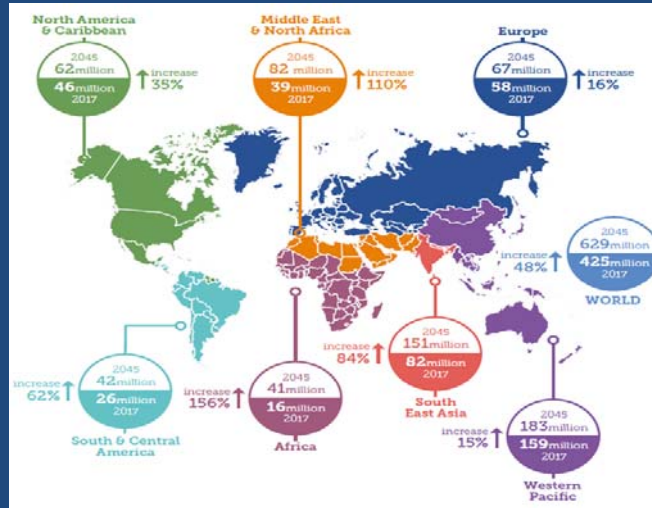
*OR*

Classic diabetes symptoms + random plasma glucose  
≥200 mg/dL (11.1 mmol/L)

American Diabetes Association Standards of Medical Care in Diabetes.  
Classification and diagnosis of diabetes. Diabetes Care 2017; 40 (Suppl. 1): S11-S24

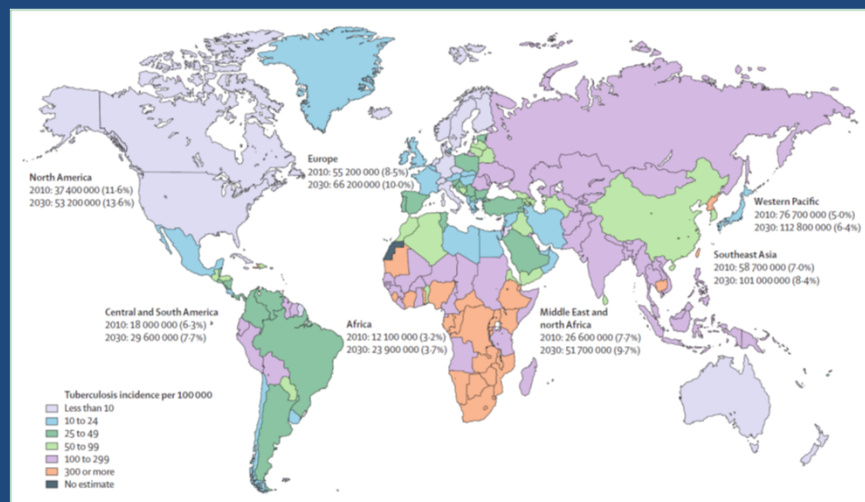


## Diabetes Projected Increase 2045



IDF: Diabetes Atlas, 8<sup>th</sup> ed, 2017

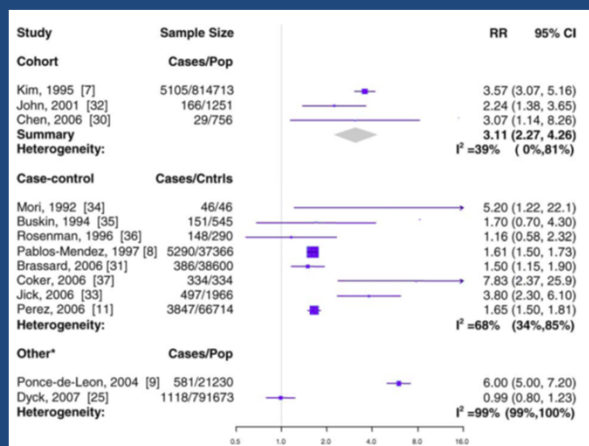
## DM and TB 2030



Dooley K; Lancet Infect Dis 2009; 9: 737-46

# Convergence of Two Epidemics

## DM and Risk for Active TB



Jeon CY, Murray MB; PLoS Med 2008;5:e152.

## Attributable Risk

TABLE 1: Relative risk, prevalence and population attributable risk of selected risk factors for TB.

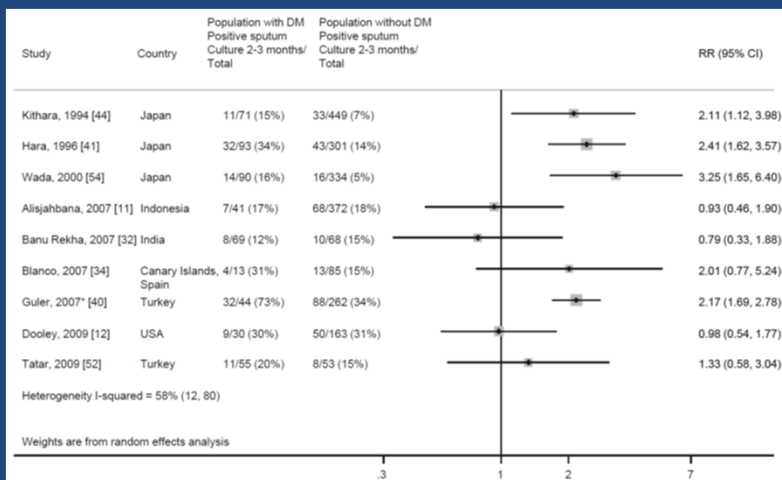
Risk factor (reference)	Relative risk for active TB disease (range) <sup>a</sup>	Weighted prevalence, total population, 22 TB high burden countries <sup>b</sup>	Population attributable fraction (range) <sup>c</sup>
HIV infection	8.3 (6.1–10.8)	1.1%	7.3% (5.2–6.9)
Malnutrition	4.0 (2.0–6.0)	17.2%	34.1% (14.7–46.3)
Diabetes	3.0 (1.5–7.8)	3.4%	6.3% (1.6–18.6)
Alcohol use > 40 g/day	2.9 (1.9–4.6)	7.9%	13.1% (6.7–22.2)
Active smoking	2.6 (1.6–4.3)	18.2%	22.7% (9.9–37.4)
Indoor pollution	1.5 (1.2–3.2)	71.1%	26.2% (12.4–61.0)

Narasimhan et al. Pulm Med;2013:828939

## DM and TB Outcomes

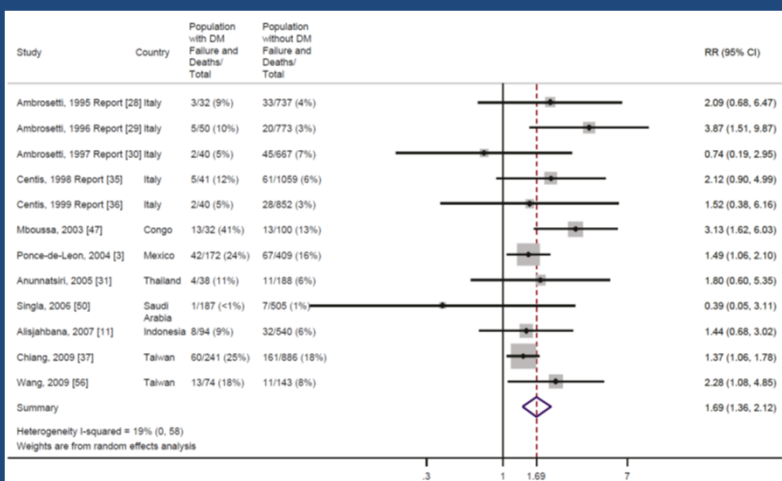
- WORSE!

## DM and TB: Culture Conversion (by 2 months)



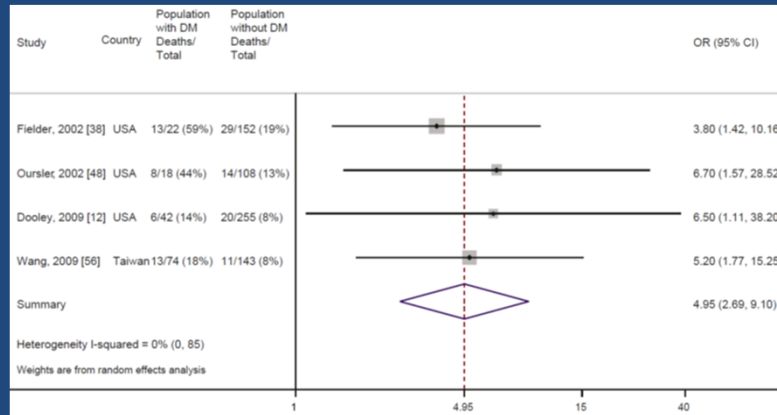
Baker et al. BMC Medicine 2011, 9:81

## DM and TB: Failure and Death



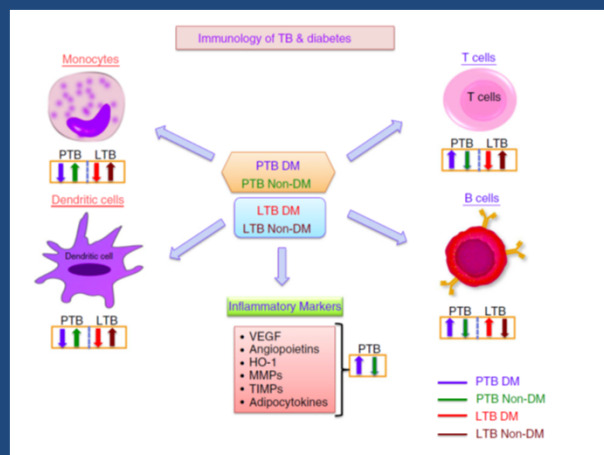
Baker et al. BMC Medicine 2011, 9:81

## DM and TB: Death, Adjusted OR



Baker et al. *BMC Medicine* 2011, 9:81

## DM Alters TB Immunity



Nathella. *Immunology*. 2017;152:13-24.



## Active TB in Diabetic Patients

- Often more advanced disease
- More cavitory disease
- ? Lower lobe disease

Dooley K; Lancet Infect Dis 2009; 9: 737–46

## Active TB in Diabetic Patients

### People with DM and TB have...

- 2x risk of remaining culture positive
- 3x risk of progression to TB disease
- 4x risk of relapse after standard tx
- 5x risk of death during TB treatment



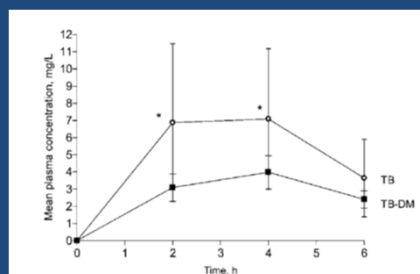
## Managing DM-TB Patient

- 2016 ATS/CDC Guidelines:
- Always give pyridoxine
- Consider prolonging treatment and drug level monitoring

Activity	Baseline	Month of Treatment Completed								End of Treatment Visit
<b>MICROBIOLOGY</b>										
Sputum smears and culture <sup>1</sup>	□	□	□	□	□	□	□	□	□	□
Drug susceptibility testing <sup>2</sup>	□	□	□	□	□	□	□	□	□	□
<b>IMAGING</b>										
Chest radiograph or other imaging <sup>3</sup>	□	□	□	□	□	□	□	□	□	□
<b>CLINICAL ASSESSMENT</b>										
Weight <sup>4</sup>	□	□	□	□	□	□	□	□	□	□
Symptom and adherence review <sup>5</sup>	□	□	□	□	□	□	□	□	□	□
Vision assessment <sup>6</sup>	□	□	□	□	□	□	□	□	□	□
<b>LABORATORY TESTING</b>										
AST, ALT, bilirubin, alkaline phosphate <sup>7</sup>	□	□	□	□	□	□	□	□	□	□
Platelet count <sup>8</sup>	□	□	□	□	□	□	□	□	□	□
Creatinine <sup>9</sup>	□	□	□	□	□	□	□	□	□	□
HIV <sup>10</sup>	□	□	□	□	□	□	□	□	□	□
Hepatitis B and C screen <sup>11</sup>	□	□	□	□	□	□	□	□	□	□
Diabetes Screen <sup>12</sup>	□	□	□	□	□	□	□	□	□	□

## TB-DM: Rifampin levels

- Rifampin levels can be 50% lower in diabetics
- Obesity dosing is not “established”
- Consider checking levels



**Figure 1.** Mean plasma concentration (mg/L) over time (h) of rifampin in 17 patients with tuberculosis (TB; *open circles*) and 17 patients with TB and with type 2 diabetes (DM; *closed squares*), with standard deviations. *P* value of comparison between groups <.05.

Rifampicin in Patients with TB and Type 2 Diabetes • CID 2006;43

## TB-DM: Drug Interactions

- Rifampin affects hepatic metabolism
- Sulfonylureas: glyburide, glipizide –DECREASES levels
- Thiazolidinediones -decreased
- Insulin is not metabolized, so not affected
- Metformin?
- Take Away: Need to manage diabetes and TB, DM may worsen initially

## Metformin Interaction

- Rifampin enhances glucose lowering effect of metformin
- Complex mechanism: rifampin increases organic cation transporters (OCT1), increases drug absorption of metformin

## TB-DM Drug Issues

- Increase glucose monitoring
- Monitor renal and hepatic function more closely due to drug interactions and propensity for renal disease
- Establish endocrine support, since infectious patients will not be able to attend regular clinics

## Latent TB Infection

- Diabetes is a risk factor for active TB, therefore suggest prioritizing treatment for diabetics with LTBI
- Screening for DM in LTBI, usually not feasible, but consider for high risk diabetic populations

# BCG Vaccination and DM

npj Vaccines

www.nature.com/npjvaccines

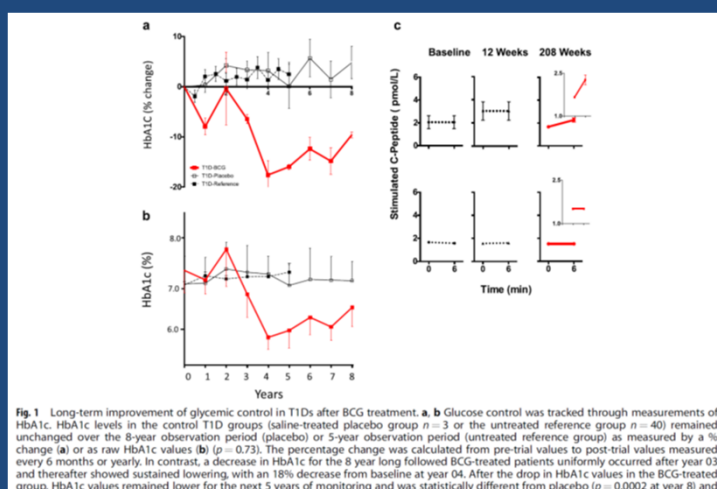
ARTICLE OPEN

## Long-term reduction in hyperglycemia in advanced type 1 diabetes: the value of induced aerobic glycolysis with BCG vaccinations

Willem M. Kühtreiber<sup>1</sup>, Lisa Tran<sup>1</sup>, Taesoo Kim<sup>1</sup>, Michael Dybala<sup>1</sup>, Brian Nguyen<sup>1</sup>, Sara Plager<sup>1</sup>, Daniel Huang<sup>1</sup>, Sophie Janes<sup>1</sup>, Audrey Defusco<sup>1</sup>, Danielle Baum<sup>1</sup>, Hui Zheng<sup>2</sup> and Denise L. Faustman<sup>1</sup>

- Type 1 diabetics given BCG x2, followed for 8 years, and compared to control (placebo) subjects

# BCG Vaccination and T1D



npj Vaccines volume 3, Article number: 23 (2018)

## Conclusions

- Watch for poor outcomes in diabetic patients
- Prioritize diabetic patients for LTBI treatment
- Watch for drug interactions
  
- If possible, Try to treat the TB and the diabetes together

Questions?

Thank you