

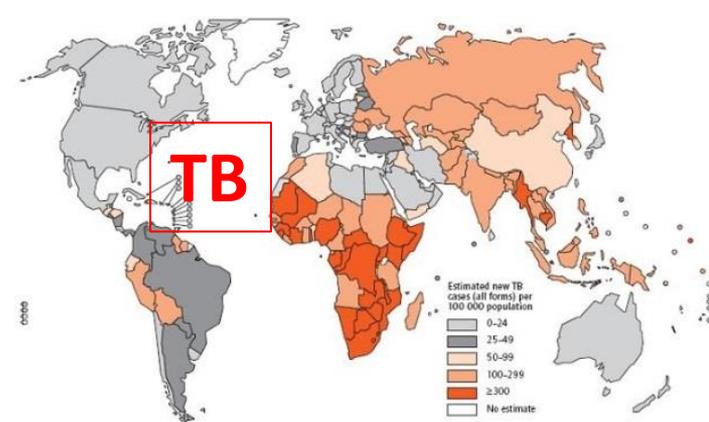
Improving TB outcomes for diabetics

Scott Heysell MD, MPH



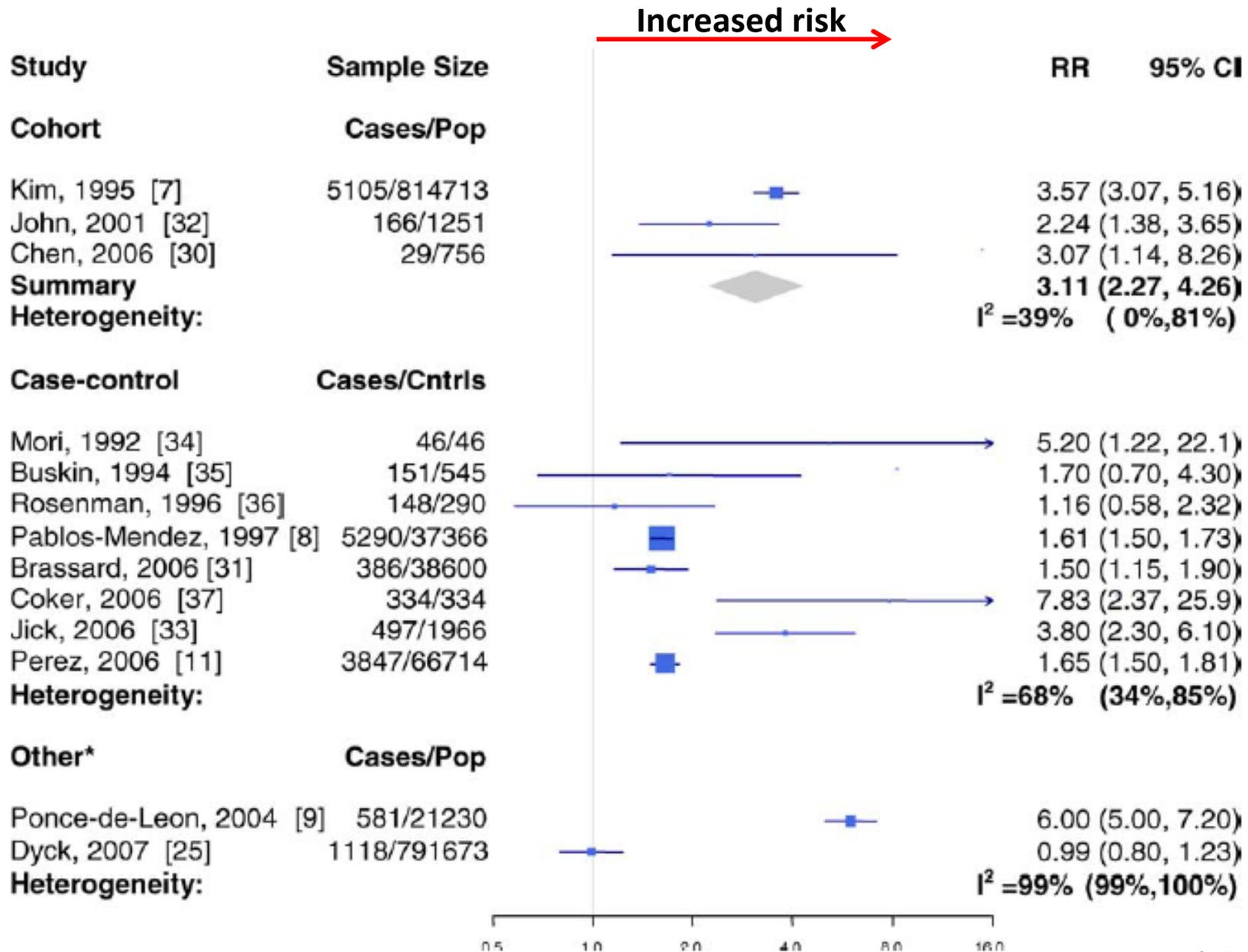


Outline

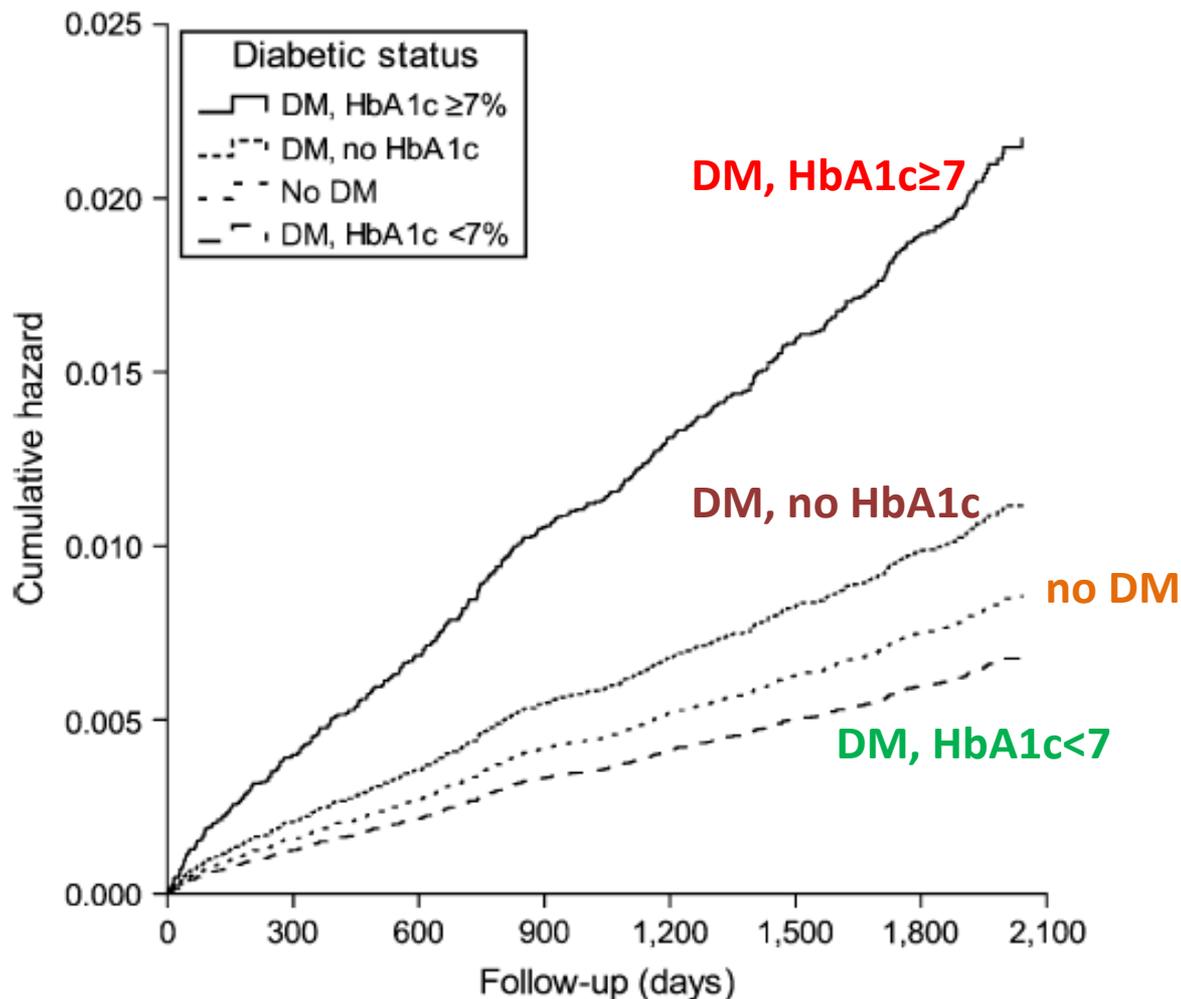


- **Overview** of diabetes (DM) and tuberculosis (TB) interaction
- **Global case study:** Dhaka, Bangladesh
- What we are doing in **Virginia** →
 - early therapeutic drug monitoring
 - patient/provider education (DM-TB flipchart)
- What can we do in **2016 and beyond** →
 - screening for DM in TB patients (hemoglobin A1c)
 - linkage to DM care

Diabetes is consistently a risk factor for developing active TB



Severity of diabetes increases the risk for TB



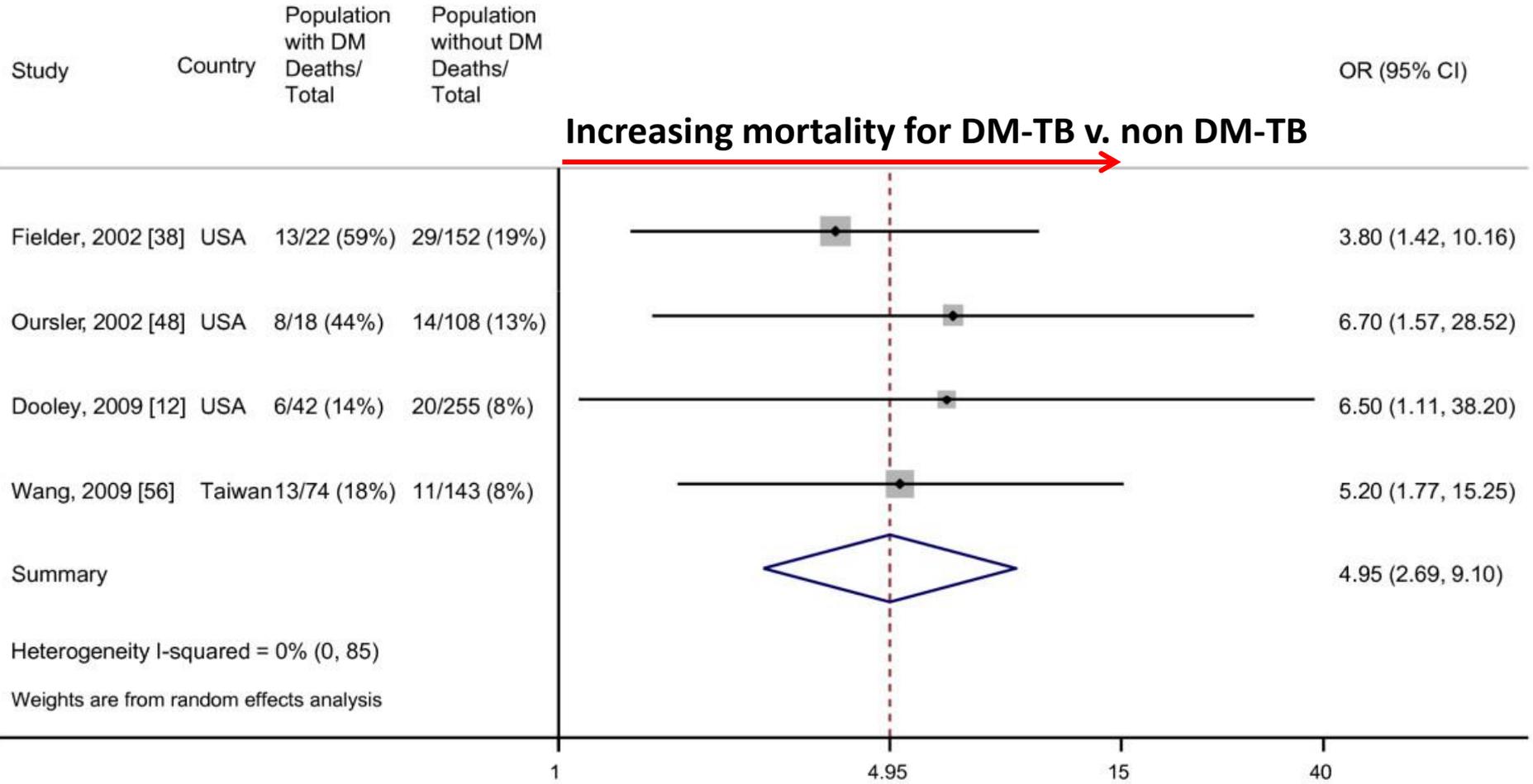
42,000 adults >65 years old from Hong Kong*

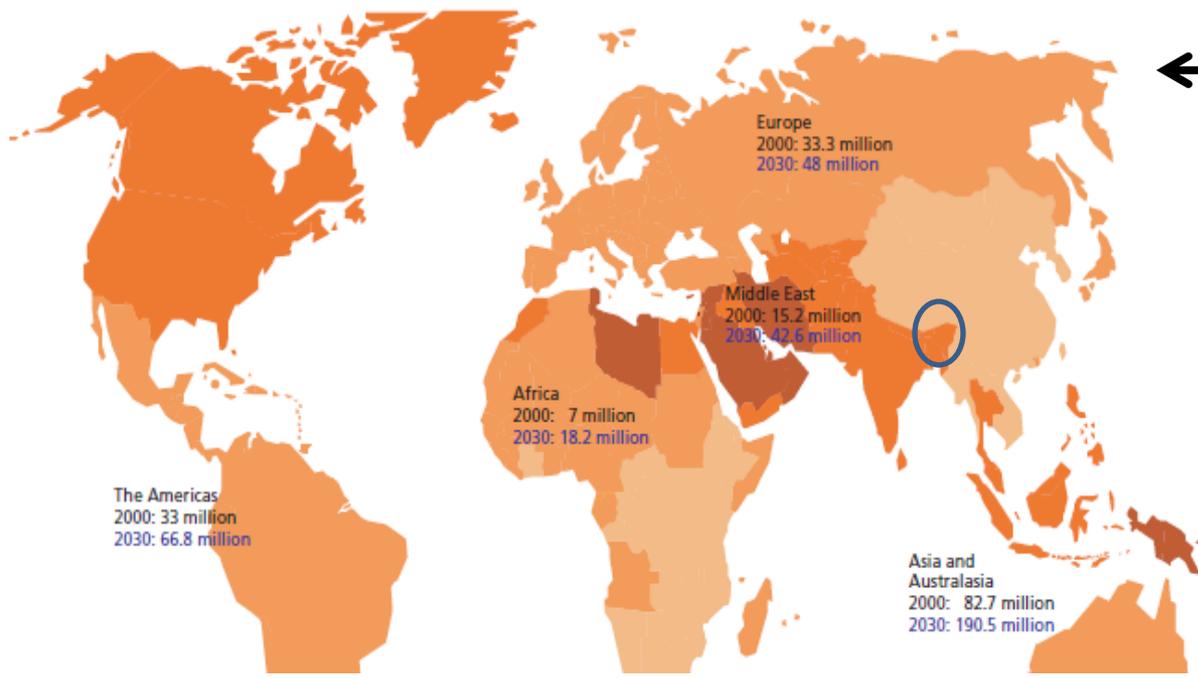
Diabetes with HbA1C ≥7 compared to <7; odds for developing active PTB were **3.63 (1.79-7.33)***

1. Pablos-Mendez et al. *Am J Pub Health* 1997

*2. Leung et al. *Am J Epi* 2008

All cause mortality increased in diabetics during TB treatment (compared to non-diabetics)





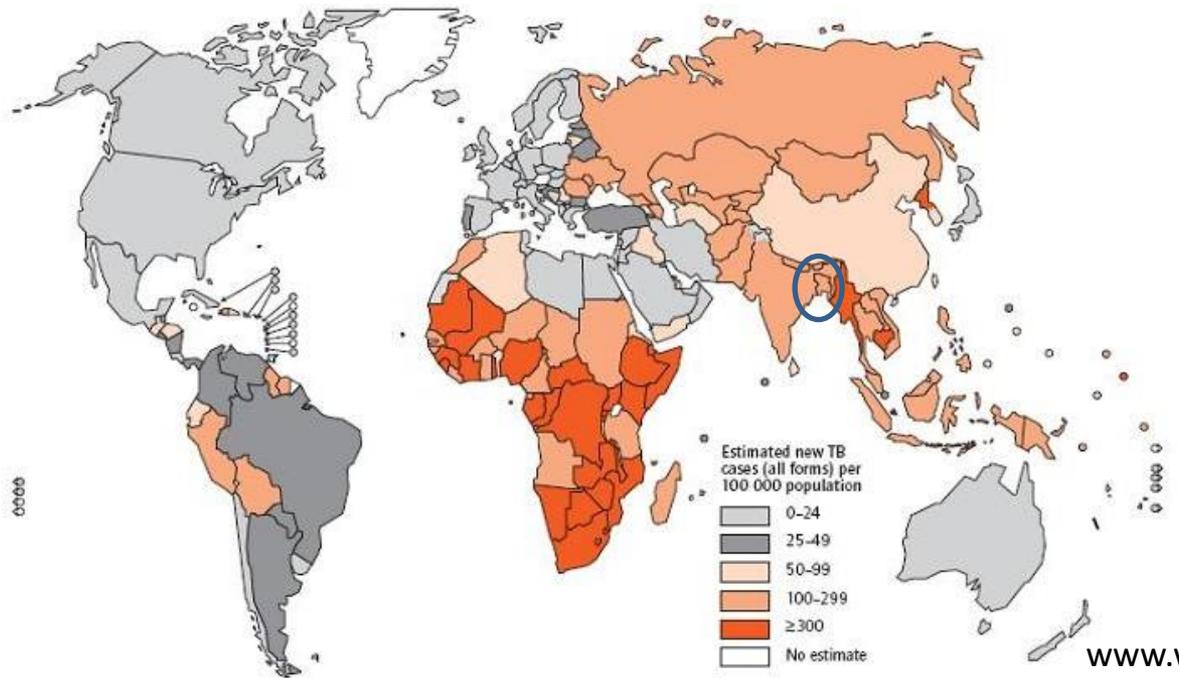
← Global diabetes burden

2010: 285 million
2030: 439 million
(75% in developing countries)

1/3 of diabetics in 48 least developed countries live in Bangladesh

Global TB burden

| ranking | country |
|---------|-------------------|
| 1 | India |
| 2 | China |
| 3 | Indonesia |
| 4 | Nigeria |
| 5 | South Africa |
| 6 | Bangladesh |



The city of Dhaka, Bangladesh

2030

OUR GOAL IS TO END THE GLOBAL TB EPIDEMIC
WITHIN 1 GENERATION

UNITE TO → **END
TB**

WORLD TB DAY 24 MARCH 2016

ঐক্যবদ্ধ হলে সবে
যক্ষ্মামুক্ত দেশ হবে



THE CHEST & HEART ASSOCIATION OF BANGLADESH
E-mail : chab@dhaka.net
Website : www.chestheart.org

Courtesy: **BEXIMCO PHARMA** here's to life

of only \$3,100 USD

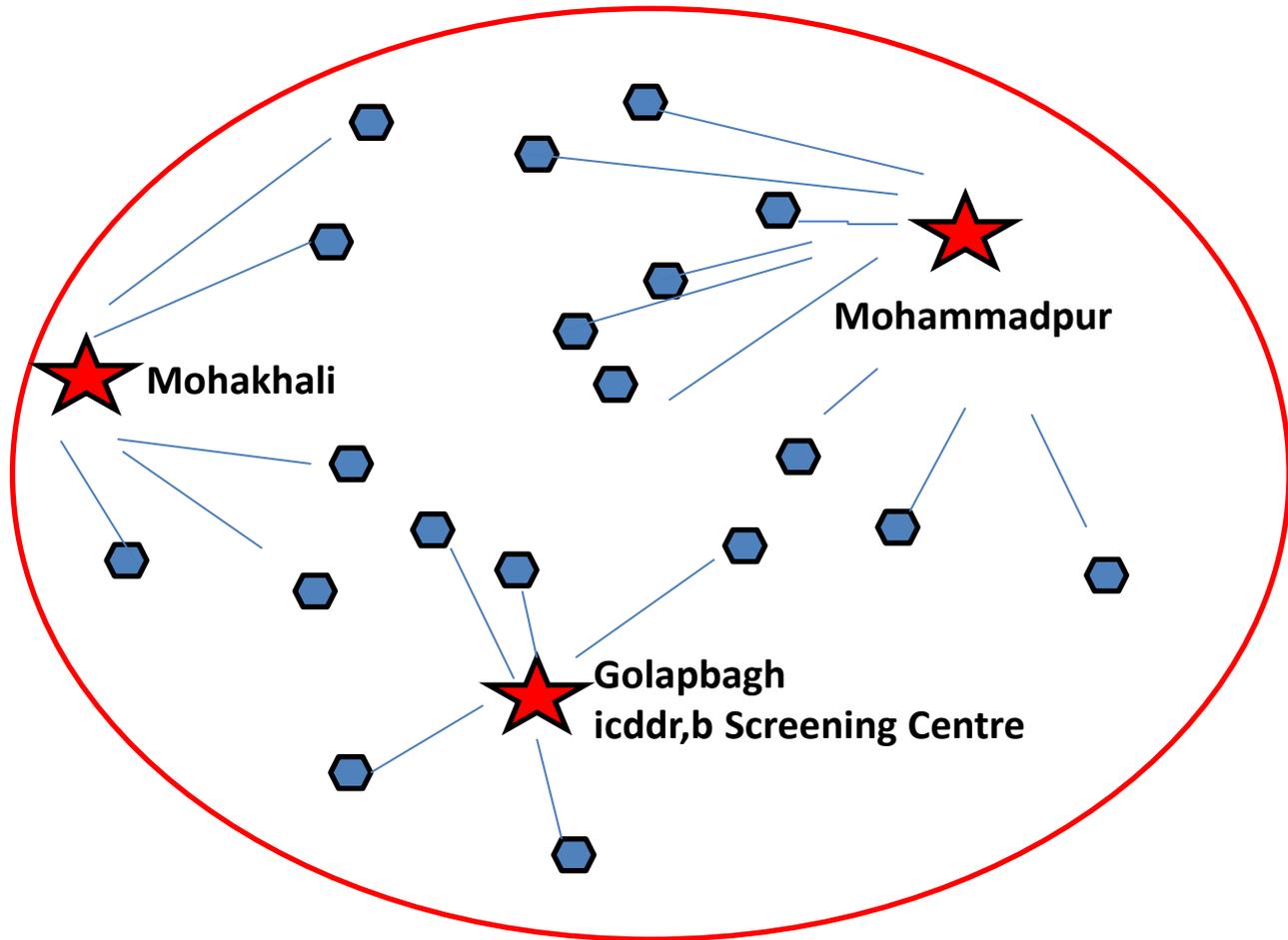
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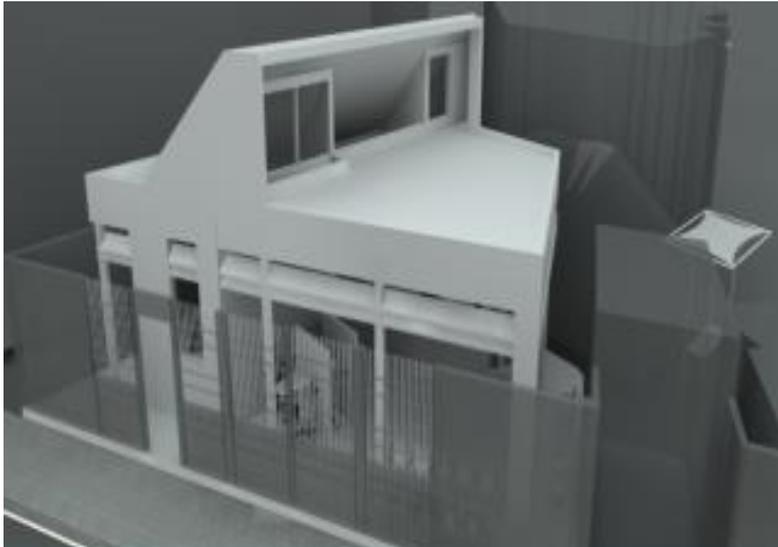
Screening Centre network of private clinics/ providers in Dhaka

● Private clinic in icddr,b network
N= 1,300 physicians or clinics!
• 1 Community Screener at clinic

★ icddr,b Screening Centre
N= 3
• ~24,000 CAD4 x-rays annually
• ~2,200 new TB patients identified annually



Target population:
~8 million working poor accessing low-cost private clinics



Purposeful architecture of Screening Centre

Waiting area with high air exchange



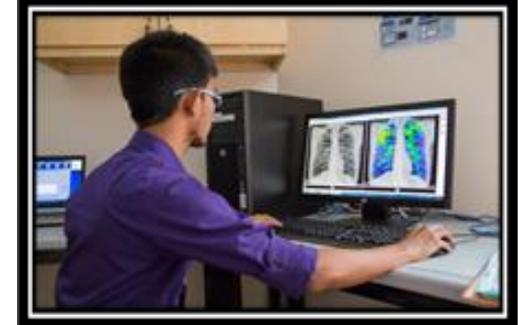
In 12 months, glucometry in 3,348 patients:

19% with diabetes among those with positive Xpert MTB/RIF



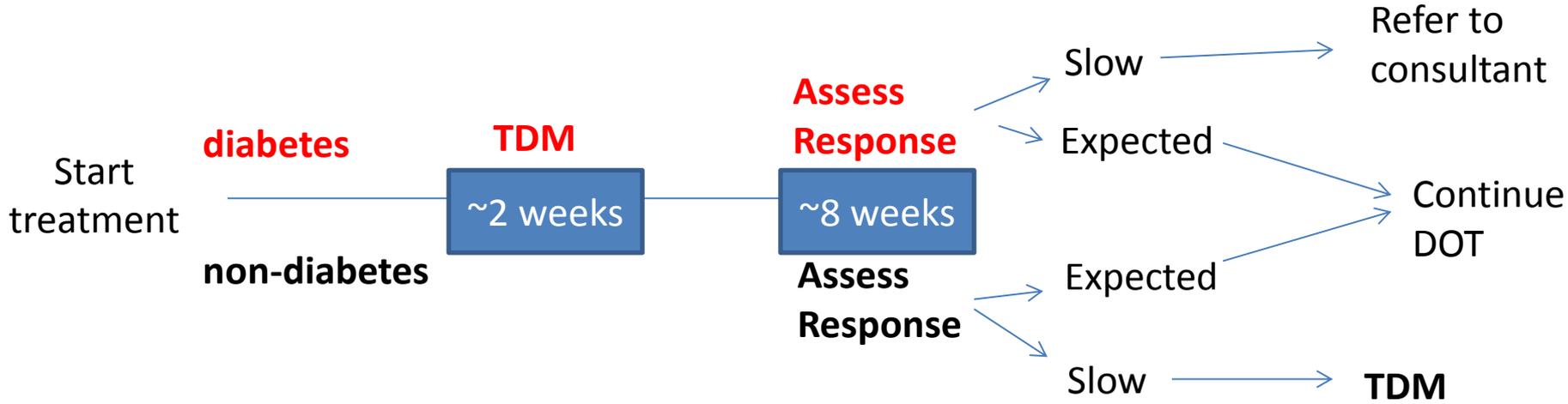
Xpert MTB/RIF

CAD4 chest x-ray: automatic TB score



Back to Virginia: rationale for therapeutic drug monitoring (TDM)

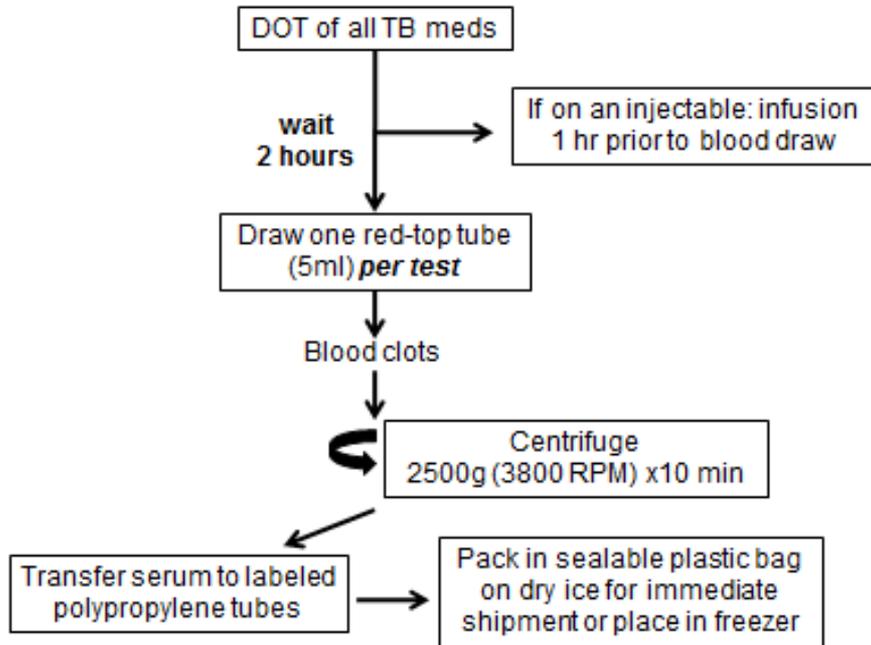
- Previously, in Virginia, DM made up ~15% of all TB patients, but **DM-TB accounted for 40% of those with slow treatment response**, and were **more likely to have low serum rifampin** levels compared to non-diabetes TB.¹
- 2013 → state recommendations for **early TDM** and dose correction for **isoniazid** and **rifampin** for **all diabetes/TB patients**²



1. Heysell et al, *Emerg Infect Dis* 2010

2. Heysell et al, *Tuberc Res Treat* 2013

TDM resources are available



Resources for Diabetes/TB and therapeutic drug monitoring (TDM):
(Virginia Dept. Health)

<http://www.vdh.virginia.gov/TB>

Table 2. Dose adjustment for d

| | Normal drug level | Sub-target INH and Sub-target RIF |
|----------------------|--|---|
| Initiation regimen* | Continue INH 300 mg M-F; RIF 600 mg M-F | Finish initiation with INH 450 mg M-F; RIF 900 mg M-F |
| Continuation regimen | Continue INH and RIF (biweekly acceptable) | INH 900 mg and RIF 900 mg, thrice weekly |

Recommended dose adjustment for sub-target INH and RIF:
Initiation M-F →
 INH 300 mg increase to 450 mg
 RIF 600 mg increase to 900 mg

Continuation (M/W/F) →
 INH 900 mg
 RIF 900 mg

*All initiation phase regimens assume a normal drug level. Sub-target doses of isoniazid (INH) of 5 mg/kg and rifampin (RIF) of 10 mg/kg. M-F= Monday through Friday, 5 x weekly schedule. Sub-target concentrations are any below the expected C_{2hr} range.

Does early TDM make a difference? Recent preliminary results:

diabetes/TB patients were older than non-diabetes/TB

New pulmonary drug-susceptible TB patients from Jan 2013- Dec 2014 (N=112)

| Characteristic | Diabetes (N=22) | Non-diabetes (N=90) | p-value |
|----------------------------|-----------------|---------------------|-------------------|
| Male gender, % N | 13 (59%) | 51 (57%) | p=0.84 |
| Age, mean years± SD | 60 ±11 | 42 ±18 | p<0.001 |
| Smear positive, % N | 19 (86%) | 75 (83%) | p=0.73 |
| Cavitary chest x-ray, % N* | 12 (57%) | 42 (48%) | p=0.47 |

*missing report in 1 diabetes and 3 non-diabetes

Results of early therapeutic drug monitoring (TDM):

majority with a drug concentrations **below** expected range

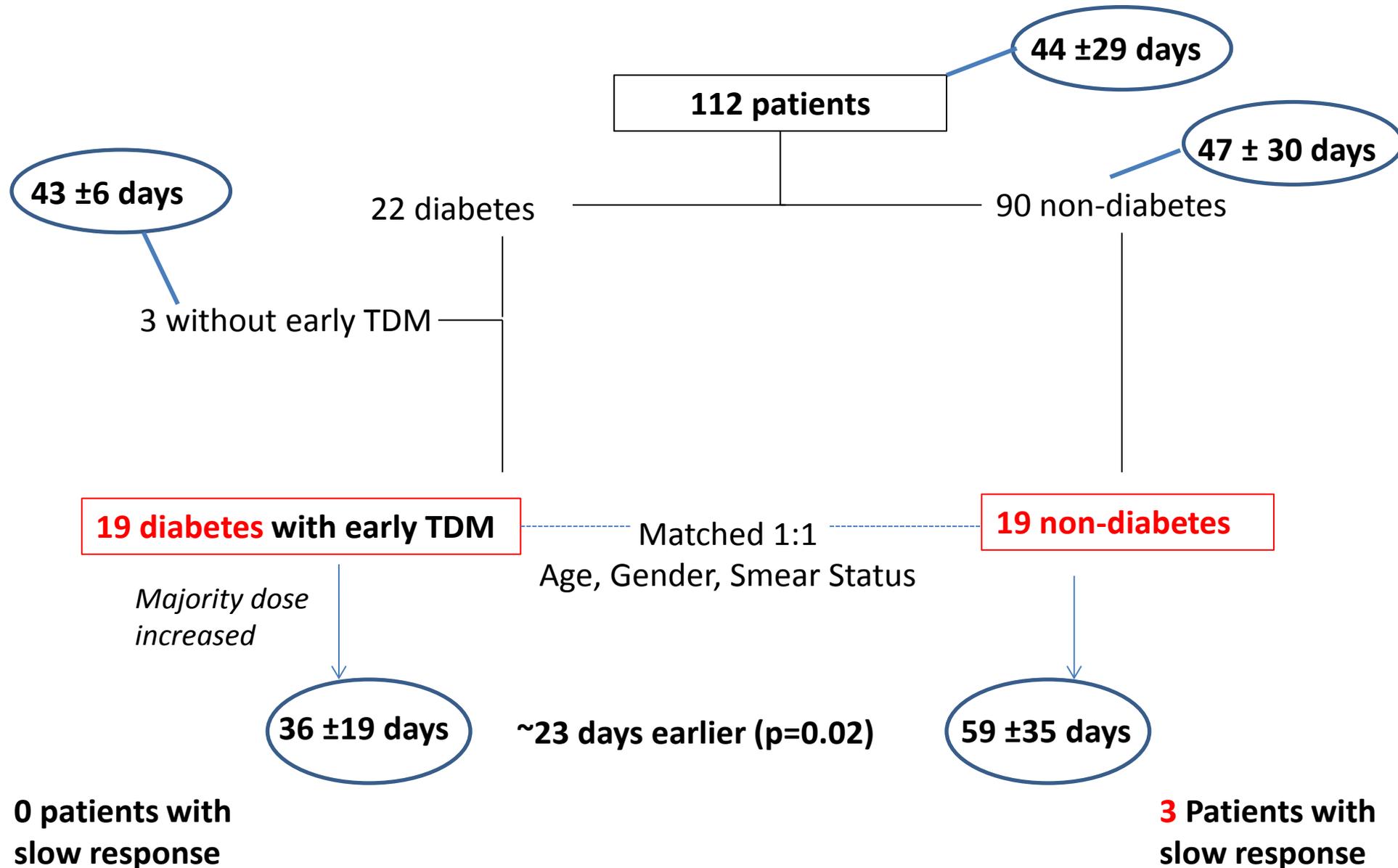
diabetes/TB patients with early TDM

| Medication* (daily or 5 x/ week) | C2hr expected range | Mean C2hr | below expected range |
|---|---------------------|----------------|----------------------|
| Isoniazid (n=18) | 3-5 µg/mL | 2.5 ±1.8 µg/mL | 11 (61%) |
| Rifampin (n=17) | 8-24 µg/mL | 7.7 ±6.5 µg/mL | 8 (47%) |
| Rifabutin (n=1) | 0.3-0.9 µg/mL | 0.57 µg/mL | 0 |
| Total with at least one medication checked (n=19) | | | 12 (63%) |

*one patient each with only isoniazid or rifampin reported; one patient with rifabutin instead of rifampin

No reported adverse events with dose increase

Results cont'd: **diabetes**/TB with early TDM had a **faster** time to sputum **culture conversion** than matched non-diabetes/TB

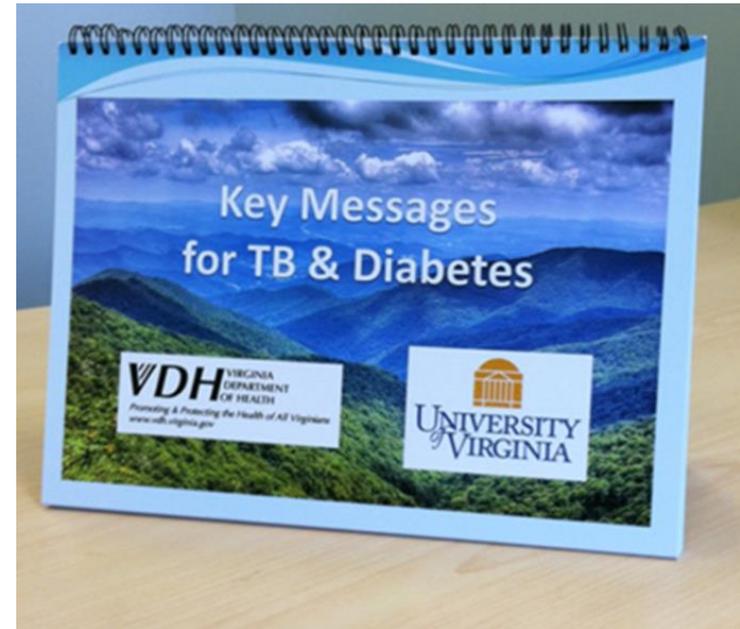


Other explanations and interventions:

- Were other interventions responsible for diabetes patients improved culture conversion?
patient-provider
educational flipchart

← **Metformin may have independent anti-TB effect**

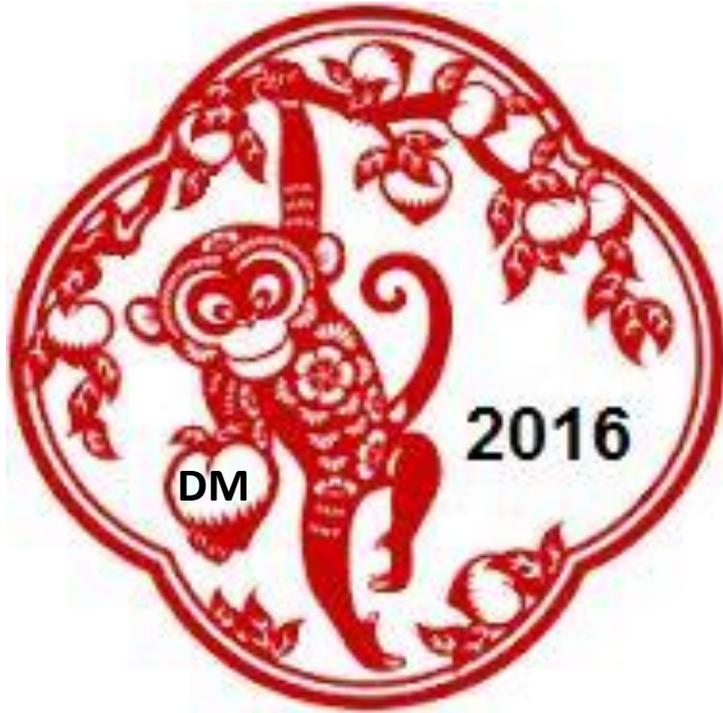
Singhal et al, *Science Trans Med* 2014



Adapted from ARC and
Hawaii DOH

2016: I would recommended studying ***how best to use the flipchart***

2016 and beyond: we can't treat what we don't diagnose



Diabetes diagnosis is the
proverbial low-hanging fruit

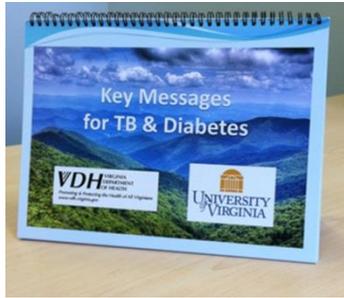
This is the year of the
Red Fire Monkey
(Chinese Astrology)
and the year of:

HbA1c testing!

TB diagnosis:
DDP-tb intake

HbA1C checked
on all clients

HbA1C \geq 6.5



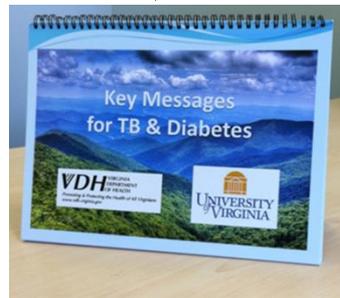
Early TDM (at 2 weeks)

and



Linkage to DM care

HbA1C <6.5, on
diabetes treatment



Early TDM (at 2 weeks)

Continue current
diabetes regimen



HbA1C <6.5, no
prior diabetes

No intervention
(~80% clients)

Bali Declaration: November, 2015

“That tuberculosis and diabetes represent two of the greatest global health challenges of our time, and their convergence globally represents a looming co-epidemic,

That this looming co-epidemic threatens progress against TB,

That, based on what we have learned from past co-epidemics, particularly TB-HIV, we must act early and decisively to avoid large numbers of avoidable deaths”



International Union Against
Tuberculosis and Lung Disease
Health solutions for the poor



WORLD **DIABETES** FOUNDATION

Recommended reading → WHO: Collaborative framework for care and control of tuberculosis and diabetes. WHO/HTM/TB/2011.15