

Double Trouble: The Surprising Connection Between Diabetes and Tuberculosis and Opportunities for Meaningful Collaboration



October 27, 2015

The findings and conclusions in this webinar are those of the presenters and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



National Diabetes Education Program

A program of the National Institutes of Health and the Centers for Disease Control and Prevention



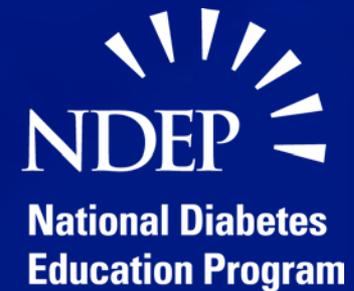
Double Trouble:

The Surprising Connection Between Diabetes and Tuberculosis and Opportunities for Meaningful Collaboration

Sundari Mase, MD-MPH

Richard Brostrom, MD-MSPH

NDEP Webinar Series



Learning Objectives:

- Identify effective communication or education strategies that can be used in diabetes prevention or self-management programs.
- Identify evidence-based approaches to diabetes prevention or self-management that can be used in community or clinical settings.
- Describe strategies for reducing diabetes related health disparities.
- Describe tools and resources to support the implementation of best practices in improving diabetes education and communication and/or reducing diabetes related health disparities.

Objectives for Today

By the end of today's webinar, you will be able to:

- Describe the interaction between TB and Diabetes.
- Identify at least 2 ways diabetes and TB impact outcomes for both conditions.
- Identify individuals with diabetes who may be at high-risk from TB, and the procedures to refer for TB testing.
- Identify at least 2 opportunities for program collaboration between TB and diabetes programs.

Today's Presenters



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CDC Tuberculosis Medical Officer
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Branch Chief, Hawaii State
Tuberculosis Program

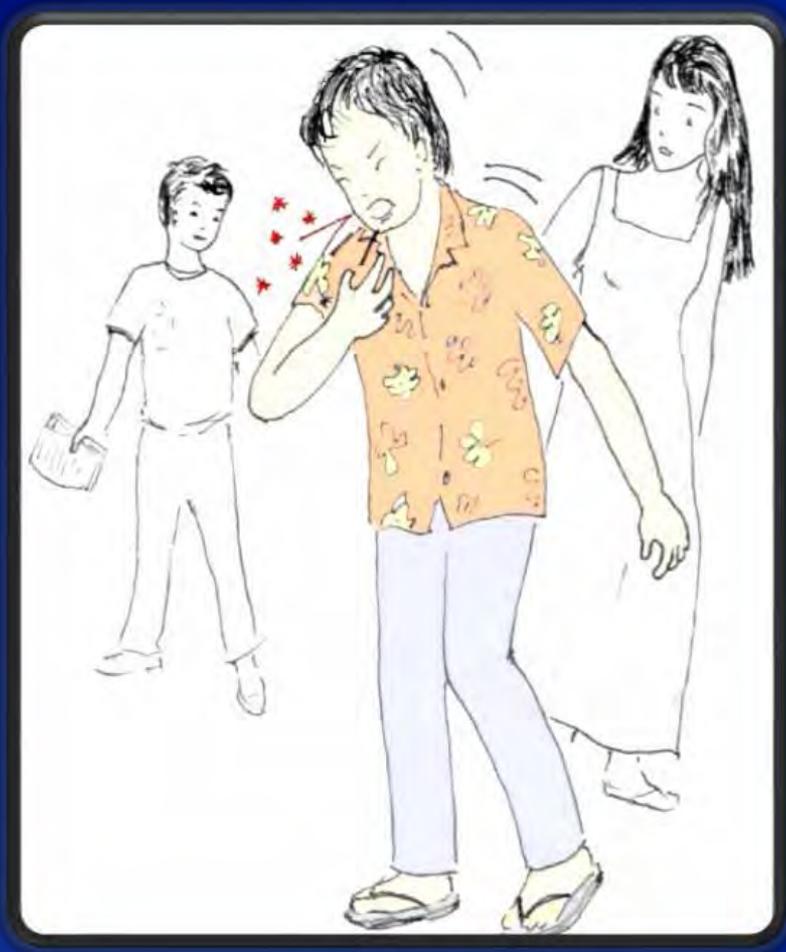
TB-DM: Opportunities for Collaboration

- **TB 101: A few of the basics**
- TB-DM Current Epidemiology
- TB-DM Literature Update
- TB-DM Current Collaborations
- TB-DM Opportunities for Partnership

What is Tuberculosis(TB)?

1. Tuberculosis (TB) is a disease caused by bacteria
2. TB usually affects the lungs (85%), but it can also affect other parts of the body such as the brain, bones, kidneys, or the spine
3. TB disease is curable, but it can be fatal if not treated properly

There are Two Forms of TB



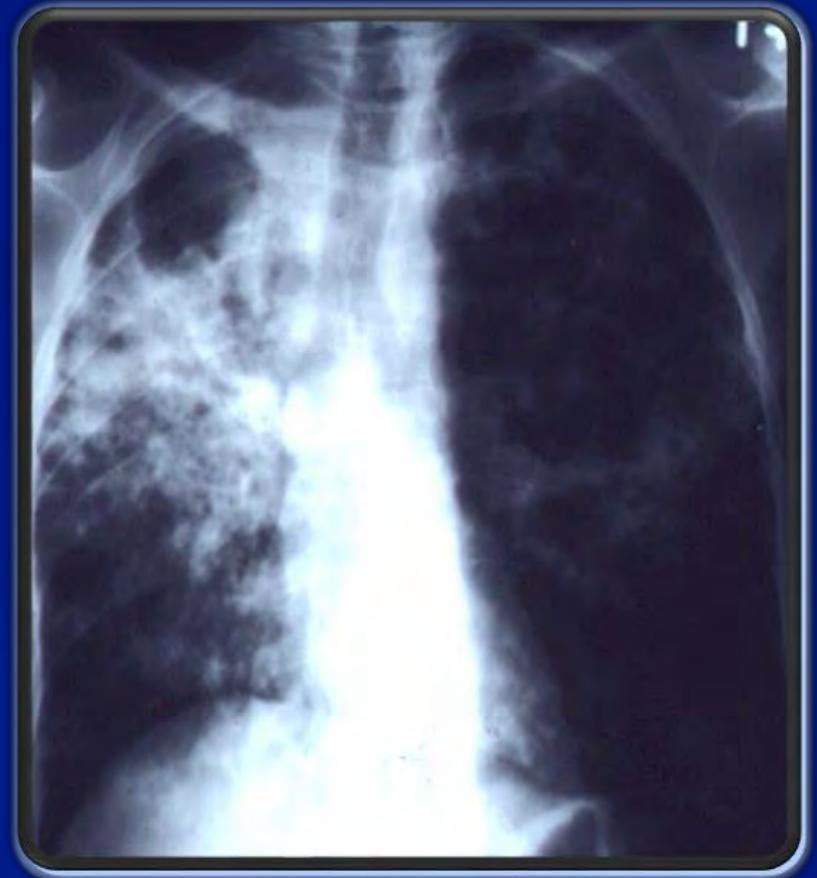
TB Disease



TB Infection

TB Disease

- Person has breathed in TB bacteria
- Immune system does not contain the TB bacteria
- TB is awake and multiplying
- Person sometimes feels sick
- Chest X-ray is abnormal
- **If the TB is in the lungs, the person may be contagious**

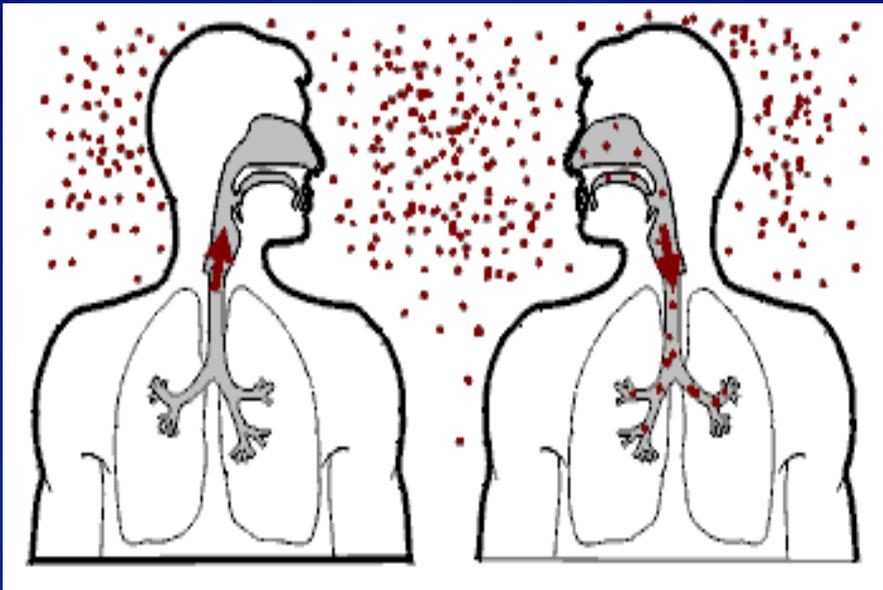


Symptoms of TB Disease

- Prolonged Cough (>2-3 weeks duration)
- Productive or Dry Cough
- Coughing Up Blood
- Feeling Weak or Constantly Tired
- Fever
- Night Sweats
- Loss of Appetite
- Weight Loss
- Chest Pain

How is TB Spread?

TB bacteria can be spread when a person with TB disease:



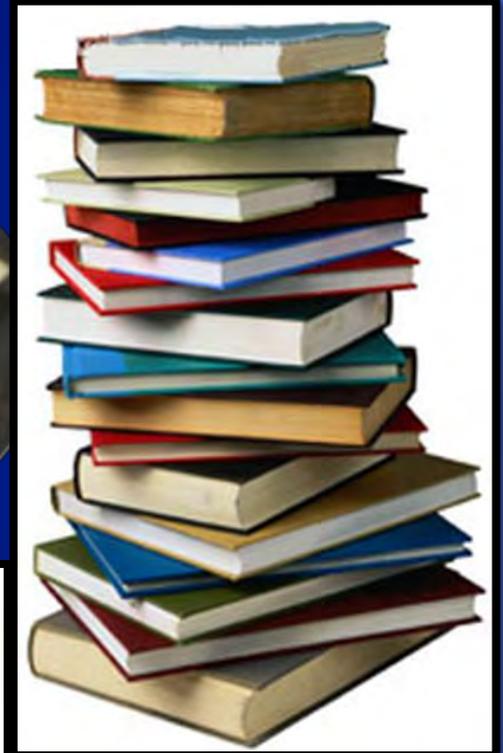
- Coughs
- Sneezes
- Speaks
- Sings
- Shouts
- Laughs

These actions send TB germs into the air



TB is NOT Spread by Sharing

- Paper or pencils
- Books
- Desks
- Toilets
- Food
- Eating utensils
- Bedding



TB Infection

- Person has breathed in TB bacteria
- TB skin test is positive



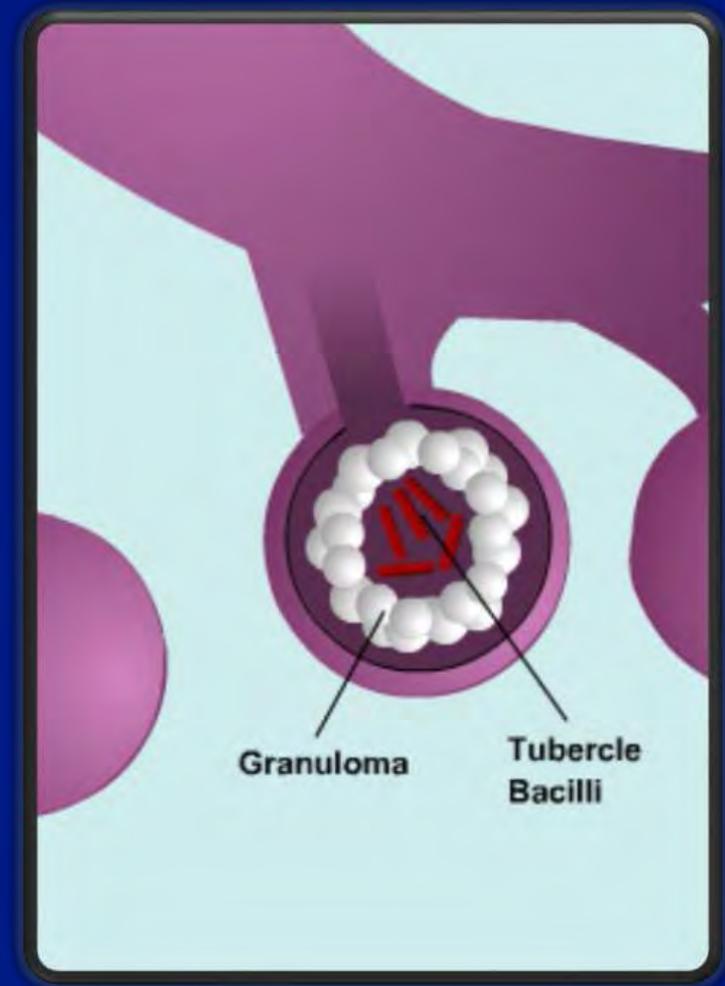
TB Infection

- Person has breathed in TB bacteria
- TB skin test is positive
- Chest X-ray is normal



TB Infection

- Person has breathed in TB bacteria
- TB skin test is positive
- Chest X-ray is normal
- Immune system has contained the TB bacteria
- Bacteria becomes dormant (sleeping)
- Person is not sick
- **Person is NOT contagious**
- **Medicine is available to treat the infection and prevent TB disease in the future**



TB Infection vs. TB Disease

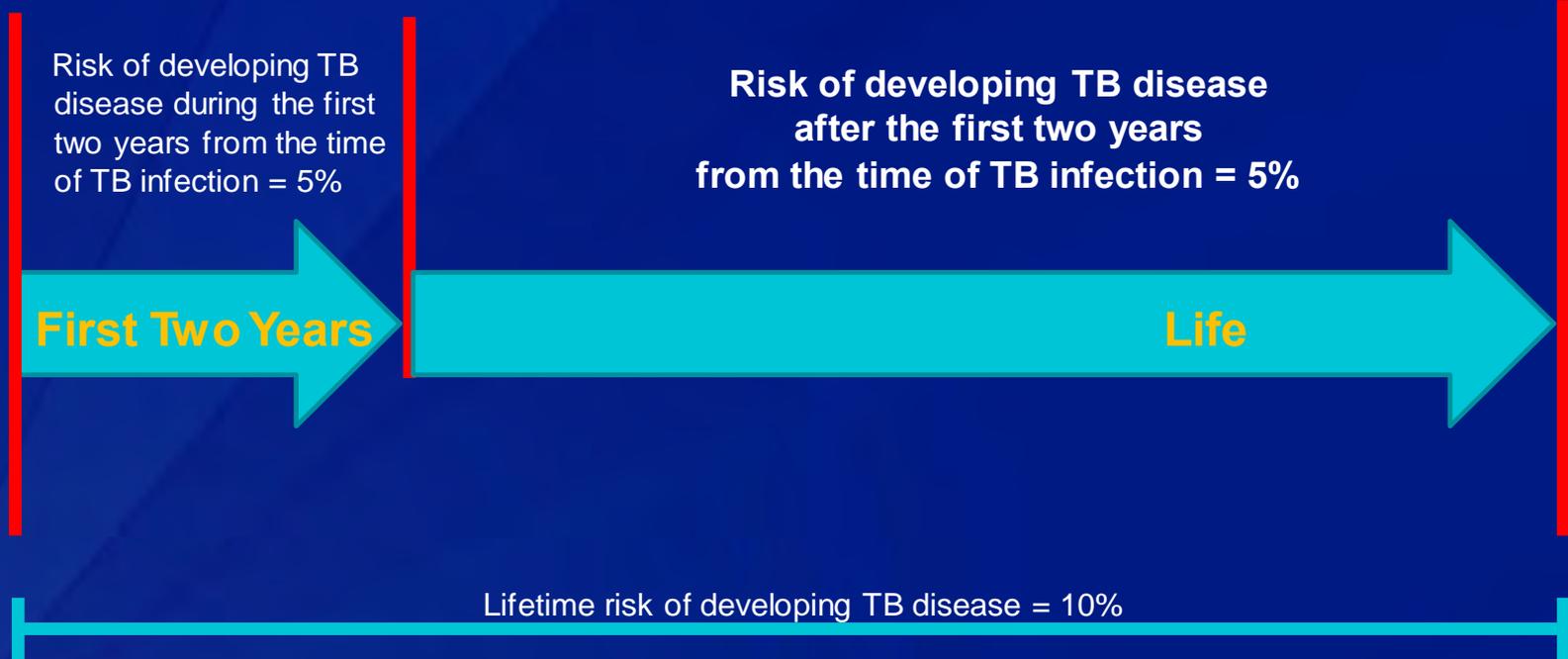
TB Infection	TB Disease (in the lungs)
Tubercle bacilli in the body	
Tuberculin skin test reaction usually positive	
Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and/or cultures positive
No symptoms	Cough, fever, weight loss, night sweats, loss of appetite
Not infectious	Often infectious before treatment
Not a "case" of TB	A case of TB

TB Infection to TB Disease

- For healthy adults, if you have TB infection (positive TB skin test and normal chest X-ray), your highest risk (5%) of going from TB infection to TB disease is in the first two years after you have been infected
- After the first two years, for the rest of your life there is a 5% risk of going from TB infection to TB disease
- 10% total lifetime risk of developing TB disease
- The risk of developing TB disease is higher for people with weak immune systems (e.g., children <5 years old and people with diabetes, cancer, HIV, or kidney disease)

TB Infection to TB Disease

Time of TB
infection



TB Pathogenesis

Progression to TB disease

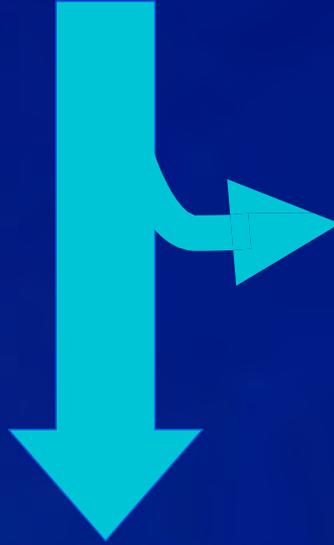
TB infection
No risk factors



TB infection
(no TB disease)

TB
Disease
(10% over
a lifetime)

TB infection
and diabetes



TB infection
(no TB disease)

TB
Disease
(30% over
a lifetime)

TB infection
and HIV



TB infection
(no TB disease)

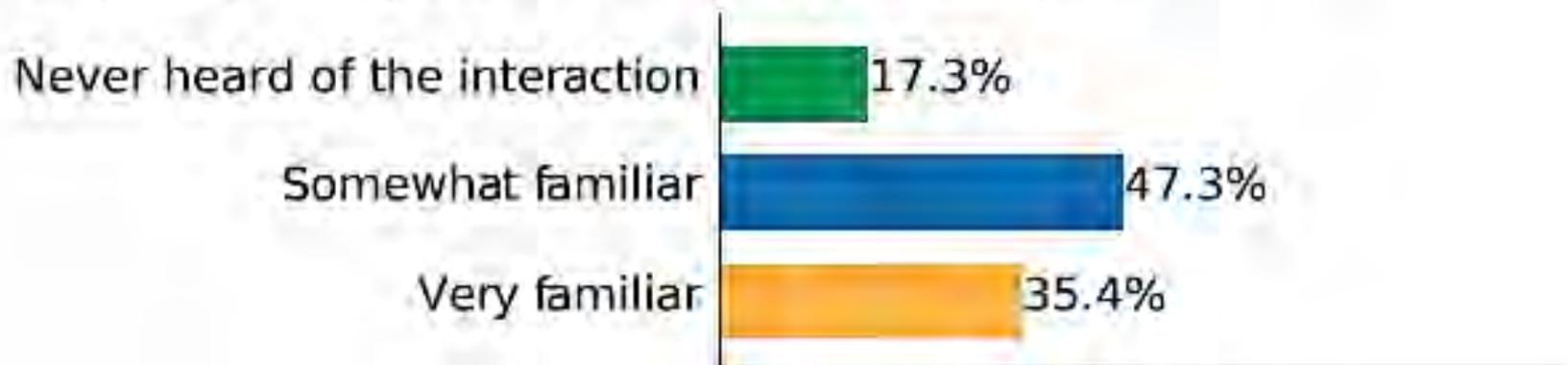
TB
Disease
(7-10% per
year.)

Poll 1:

How familiar are you with the risk of TB disease in your diabetes population?

- Never heard of the interaction
- Somewhat familiar
- Very familiar

How familiar are you with the risk of TB disease in your DM population?



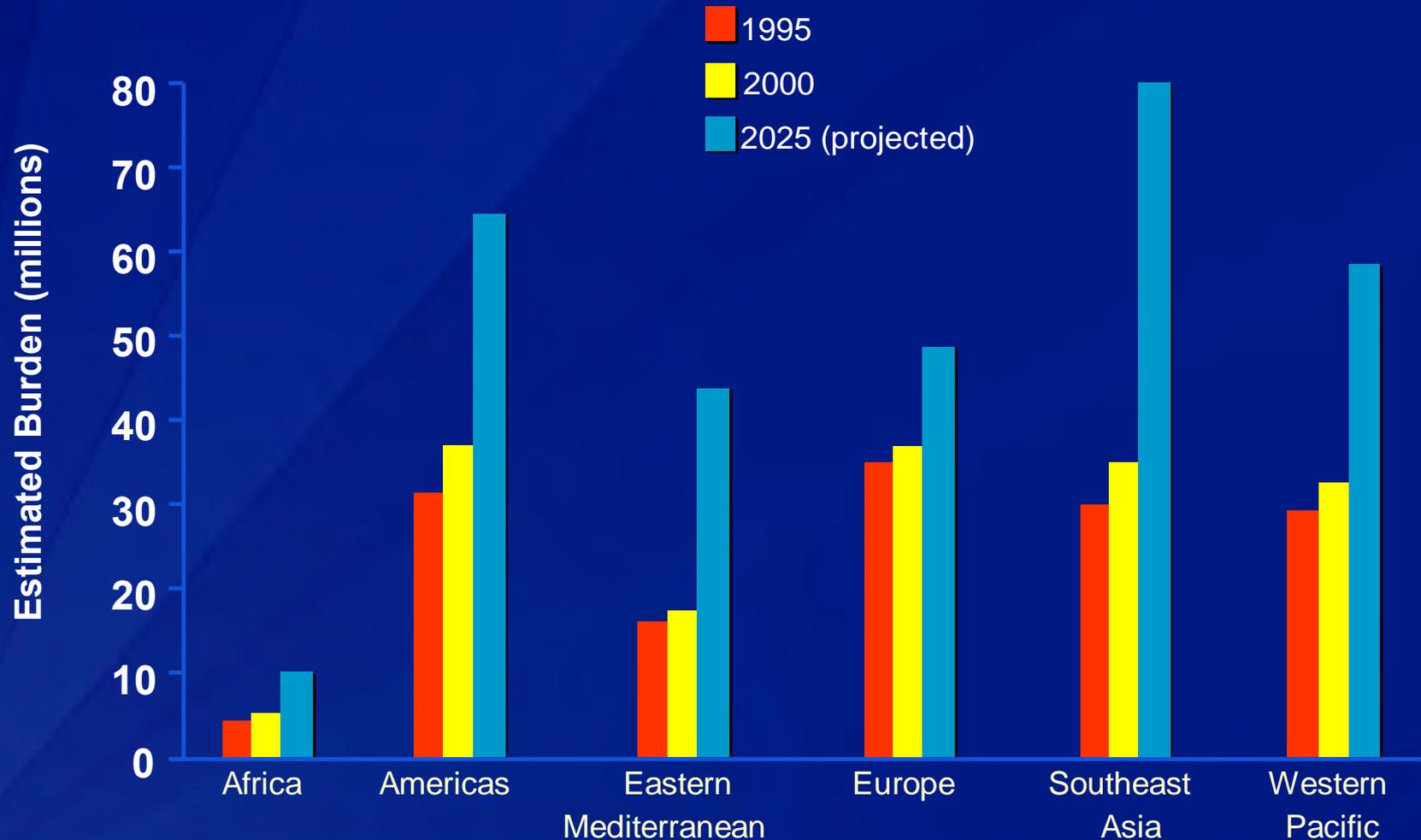
TB-DM: Opportunities for Collaboration

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Epidemiology



Worldwide Diabetes Burden



The Global Burden of TB - 2012



All forms of TB

8.6 (8.3-9.0) million

- 0.5 m in children
- 2.9 m in women

Estimated number of deaths

1.3 (1.0-1.6) million*

- 74,000 in children
- 410,000 in women

HIV-associated TB

1.1 (1.0-1.2) million
(13%)

320 000 (300k-340k)

Multidrug-resistant TB

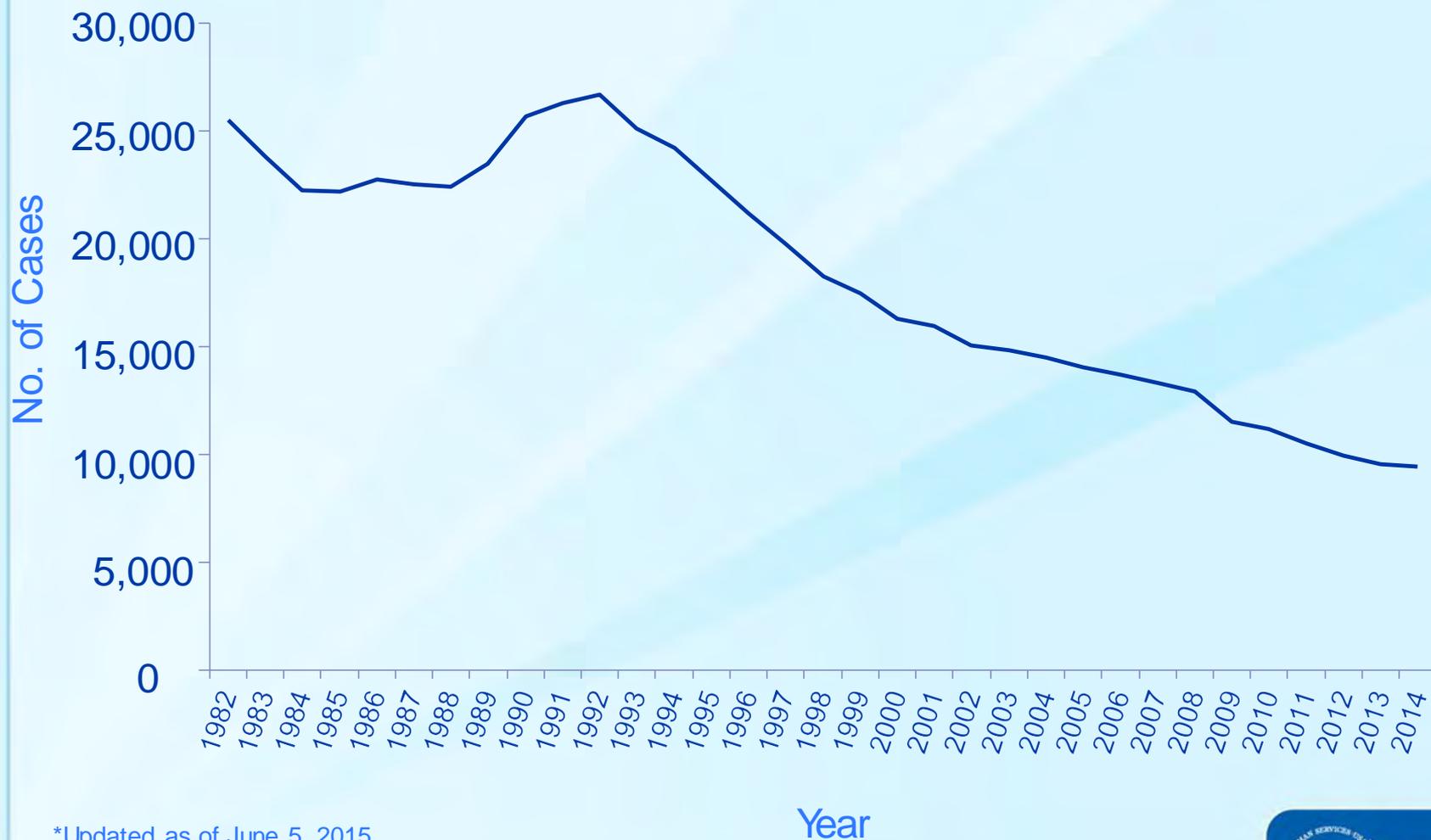
450 000 (300k-600k)

170 000 (102k-242k)

Source: WHO Global Tuberculosis Report 2013

* Including deaths attributed to HIV/TB

Reported TB Cases United States, 1982–2014*



*Updated as of June 5, 2015.



TB Morbidity

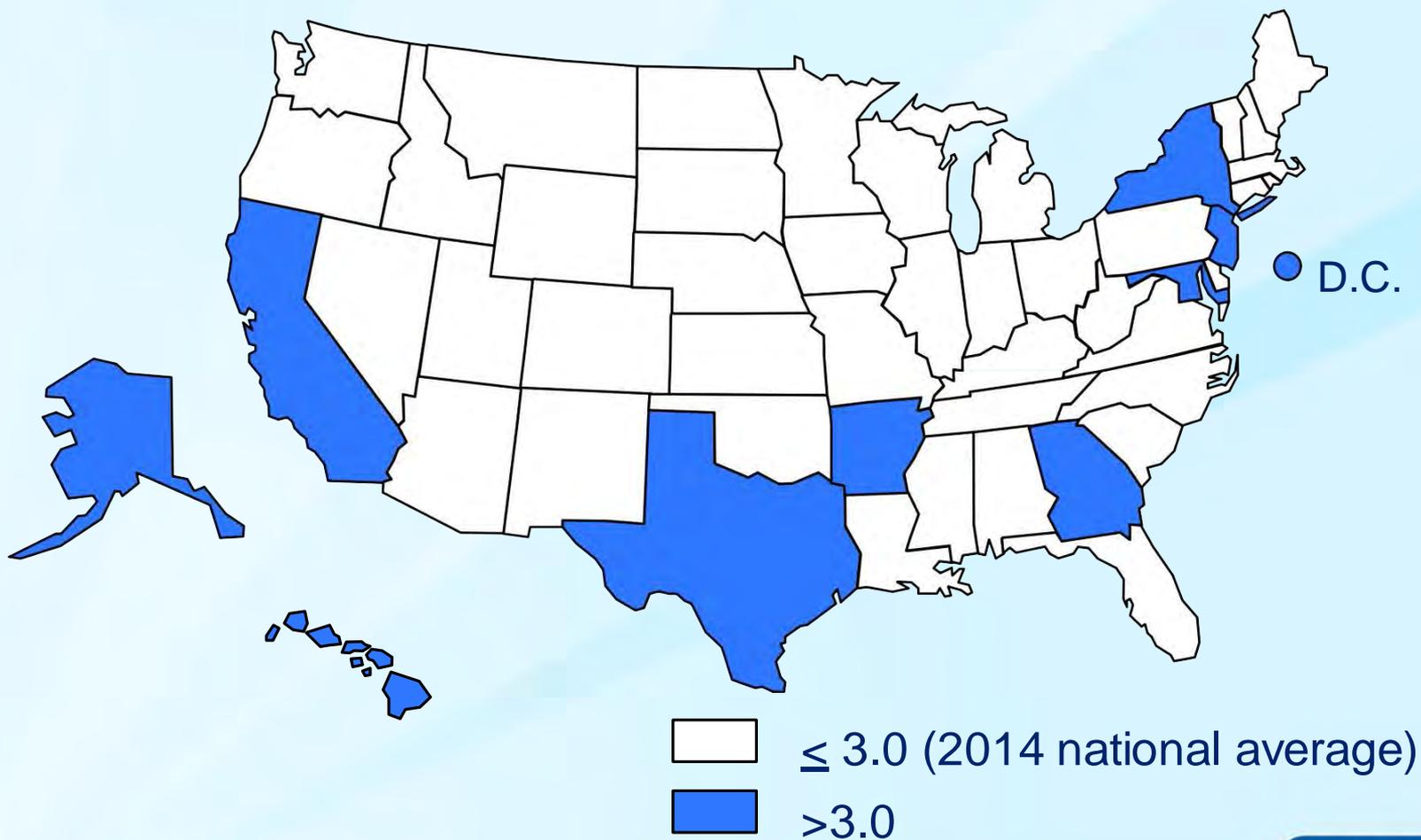
United States, 2009–2014

Year	No.	Rate*
2009	11,523	3.8
2010	11,161	3.6
2011	10,510	3.4
2012	9,941	3.2
2013	9,565	3.0
2014	9,421	3.0

*Cases per 100,000. Updated as of June 5, 2015.



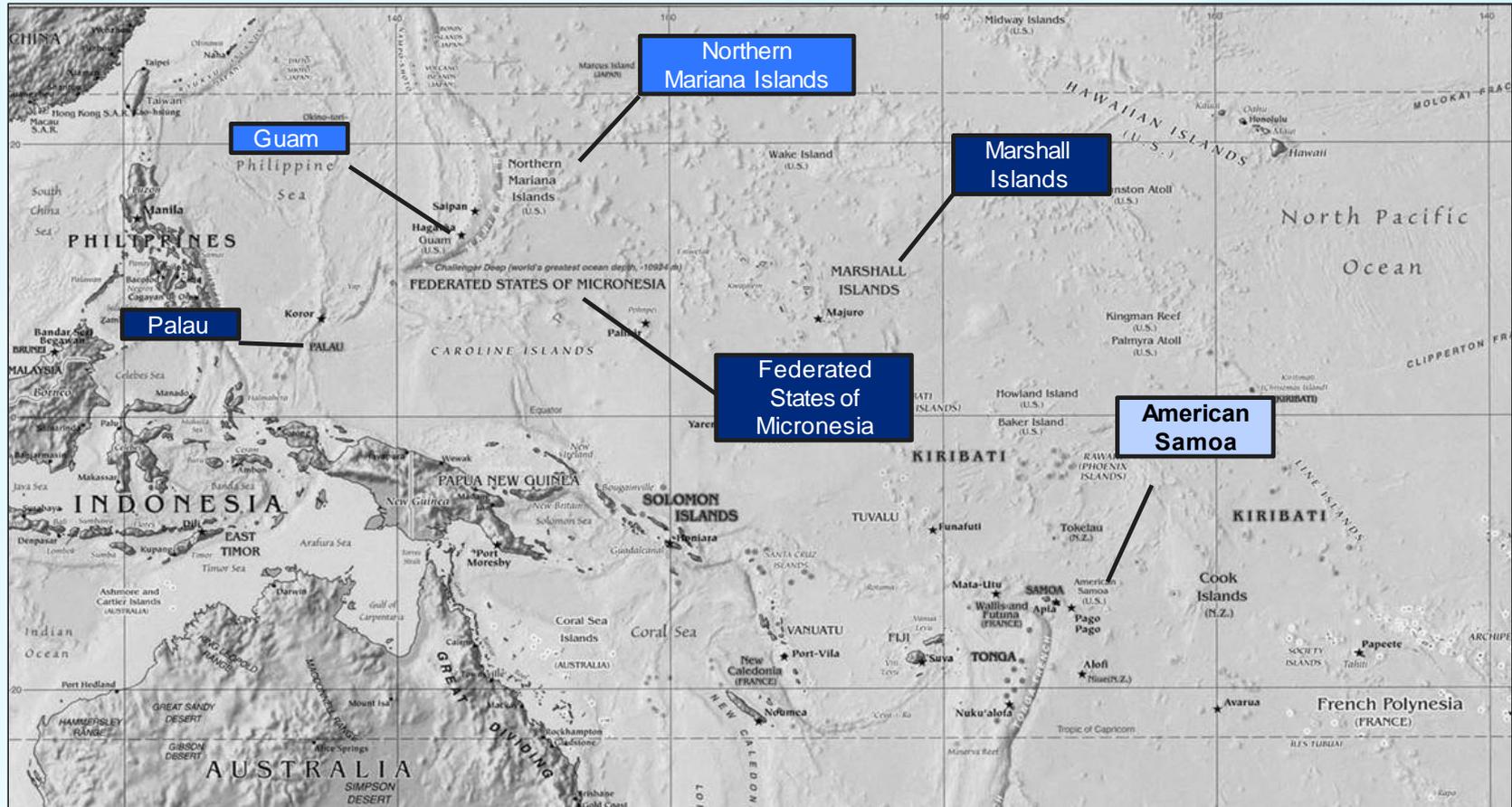
TB Case Rates,* United States, 2014



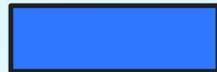
*Cases per 100,000.



Map of U.S.-Affiliated Pacific Islands by TB Case Rates,* 2014



≤ 9.9



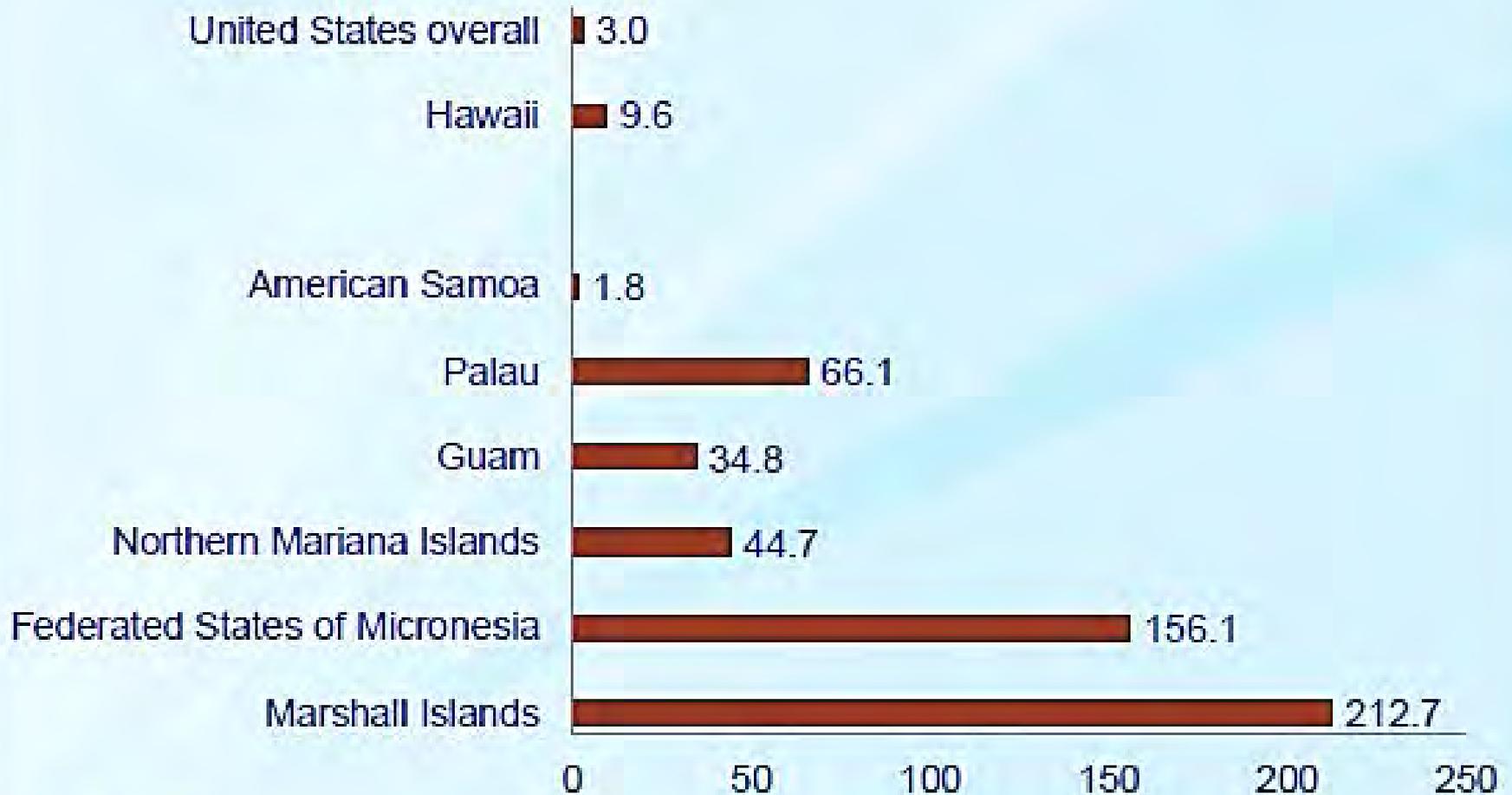
10–49.9



≥ 50

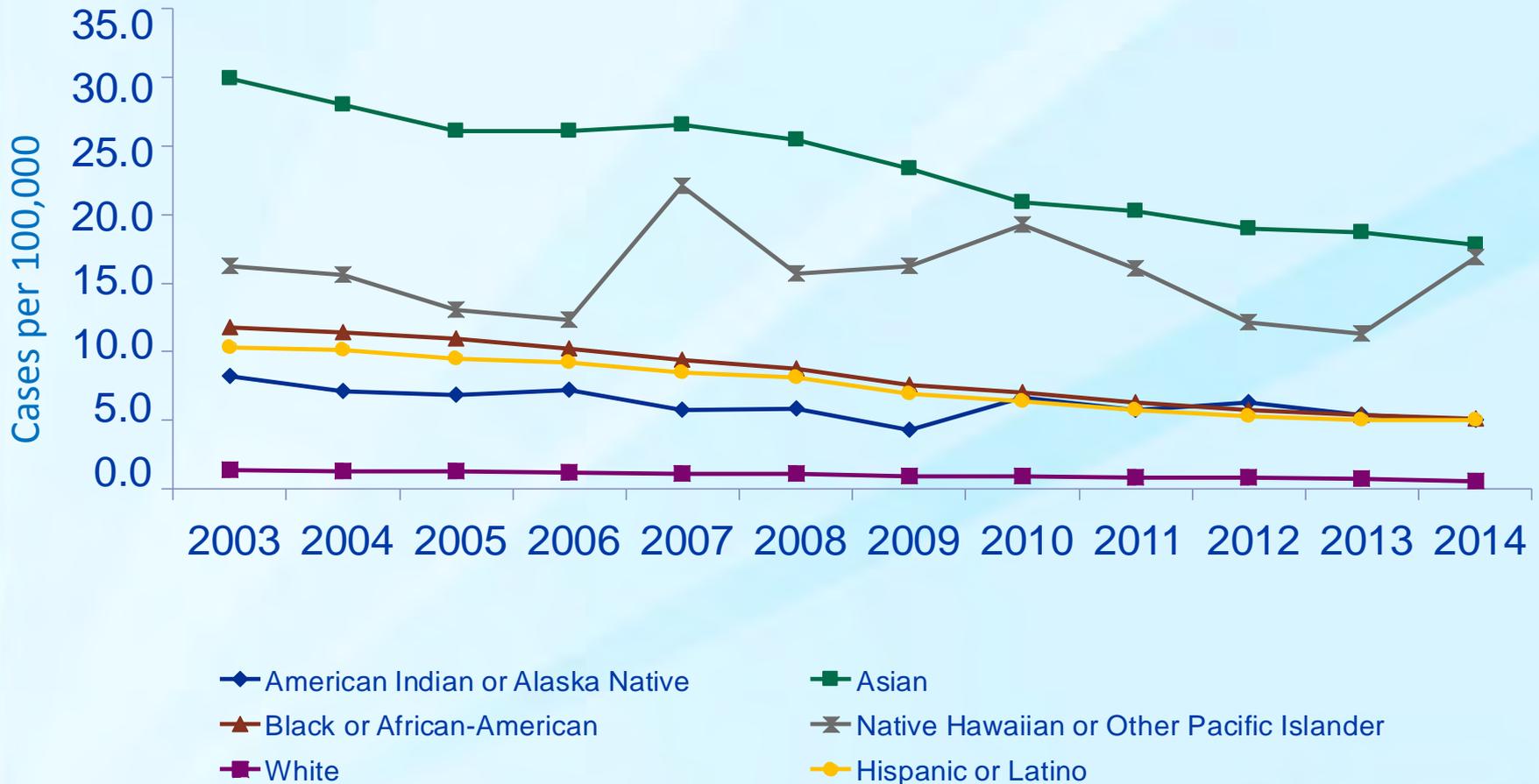
*Cases per 100,000

TB Case Rates,* U.S.-Affiliated Pacific Islands, 2014



*Cases per 100,000

TB Case Rates by Race/Ethnicity,* United States, 2003–2014**

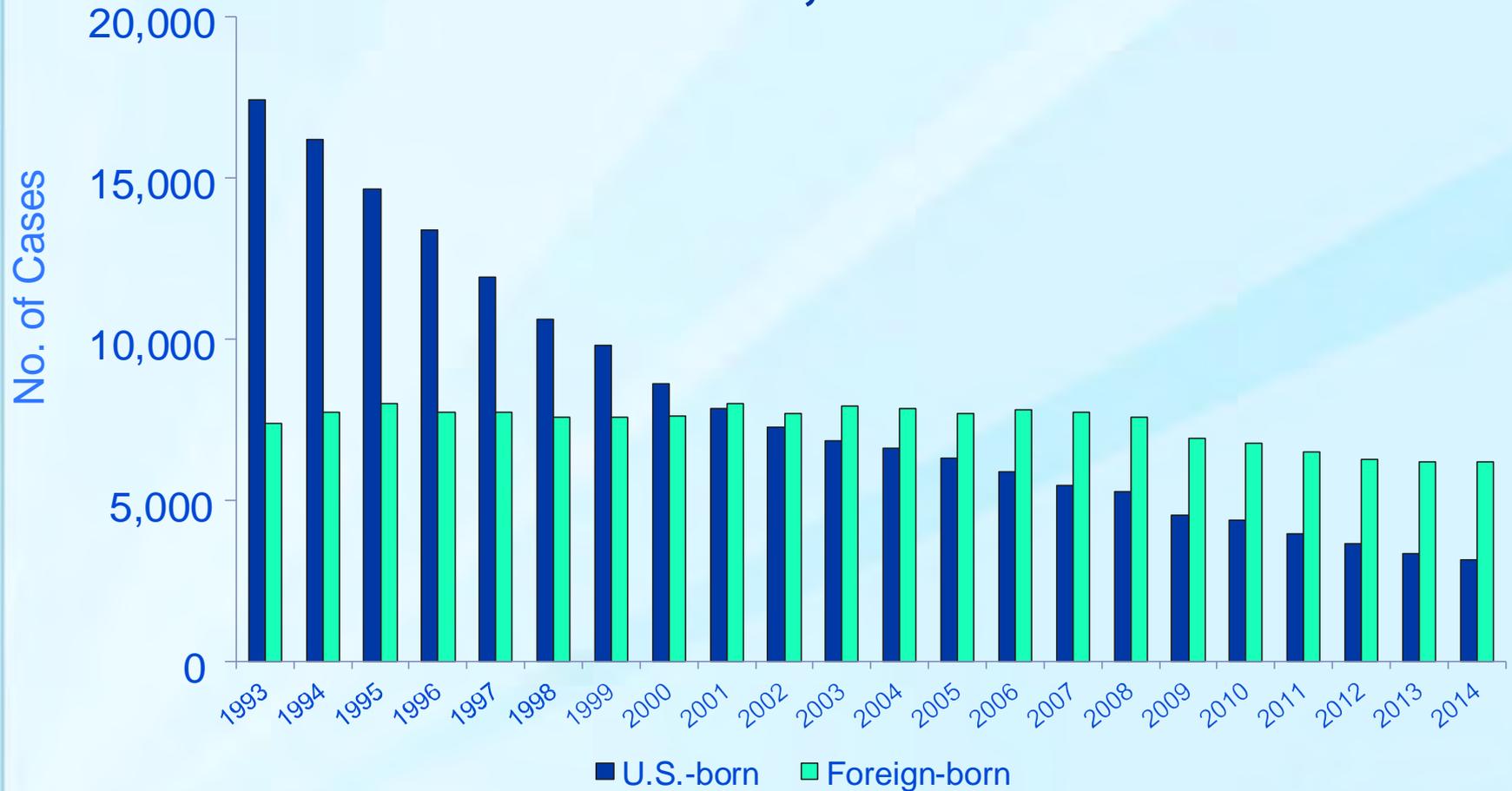


*All races are non-Hispanic.

**Updated as of June 5, 2015.



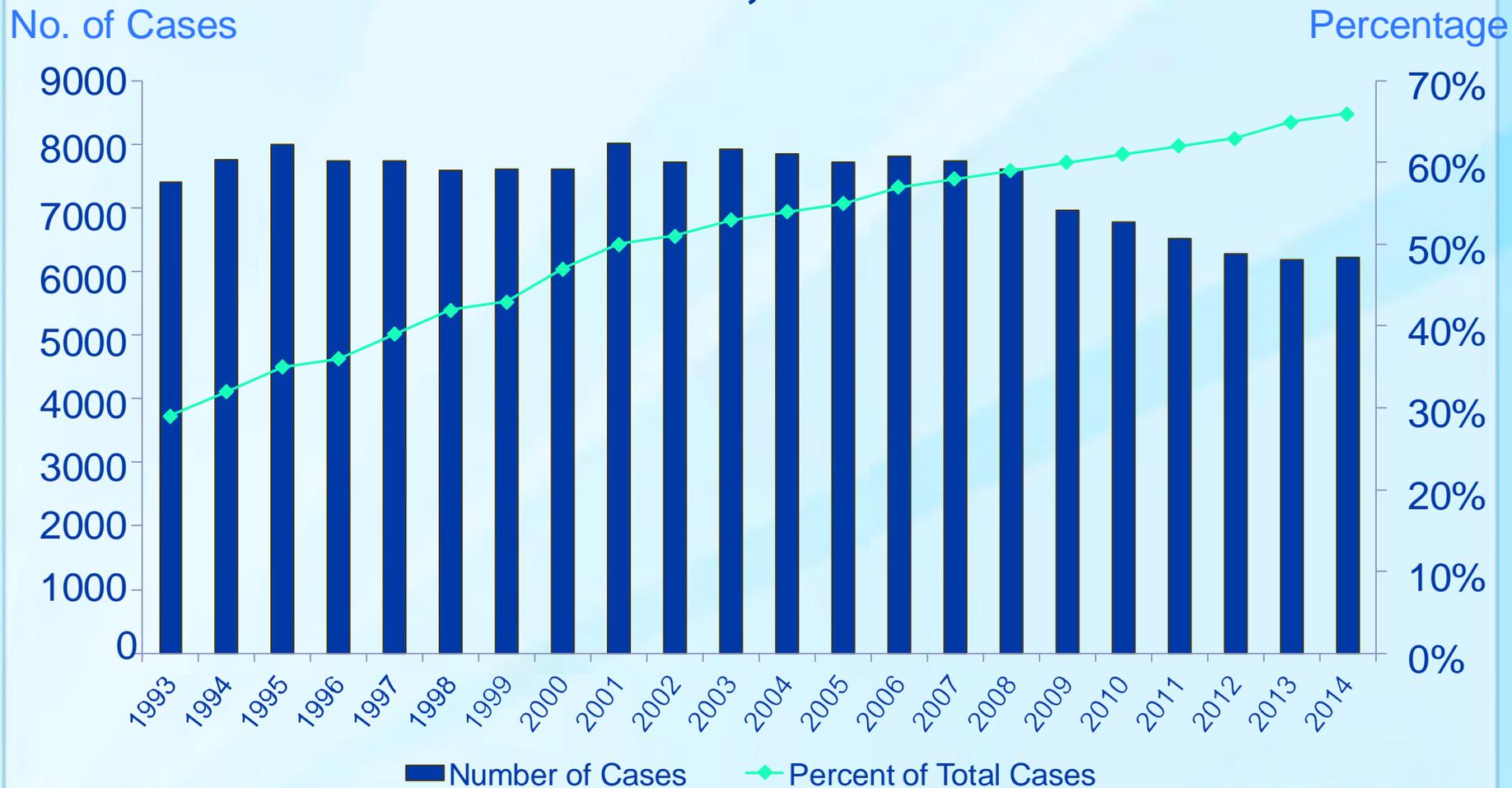
Number of TB Cases in U.S.-born vs. Foreign-born Persons, United States, 1993–2014*



*Updated as of June 5, 2015.



Trends in TB Cases in Foreign-born Persons, United States, 1993 – 2014*

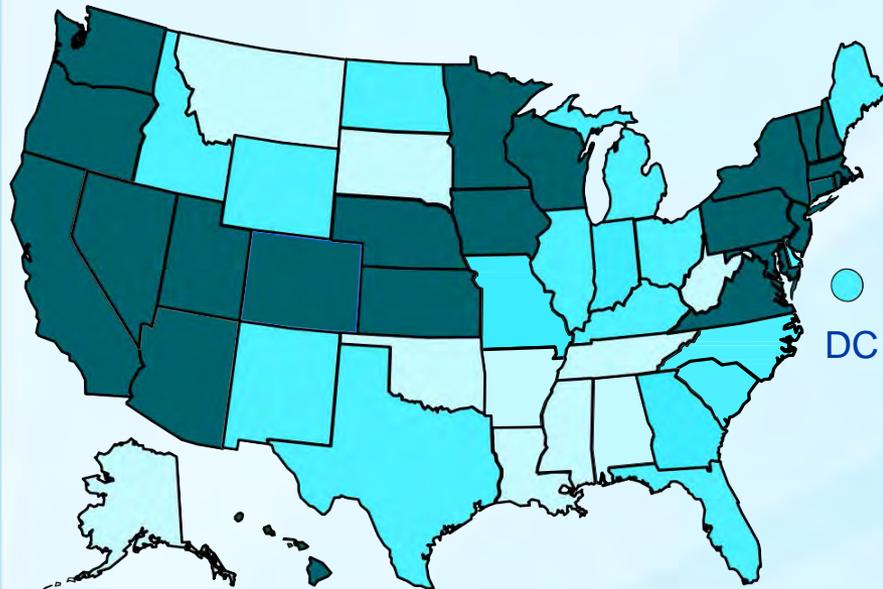


*Updated as of June 5, 2015.

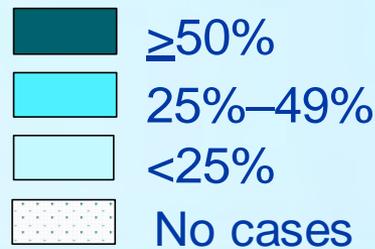
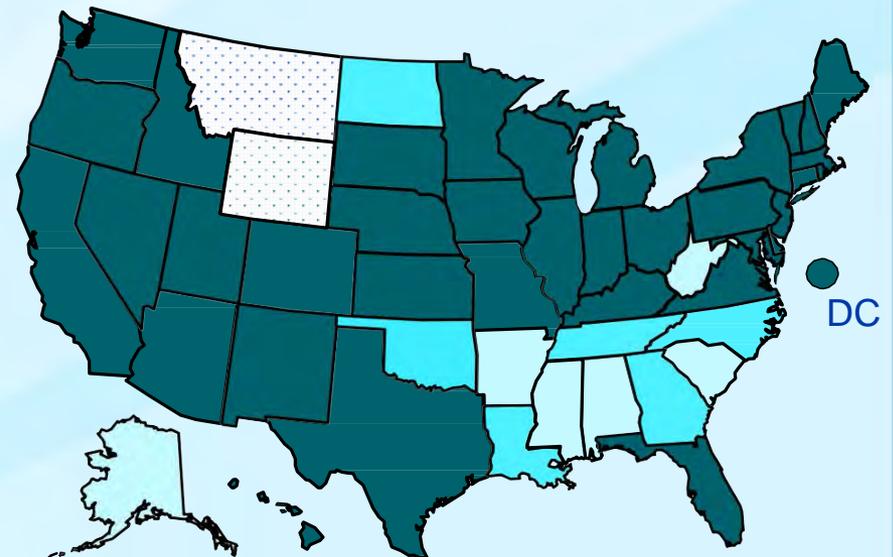


Percentage of TB Cases Among Foreign-born Persons, United States*

2004



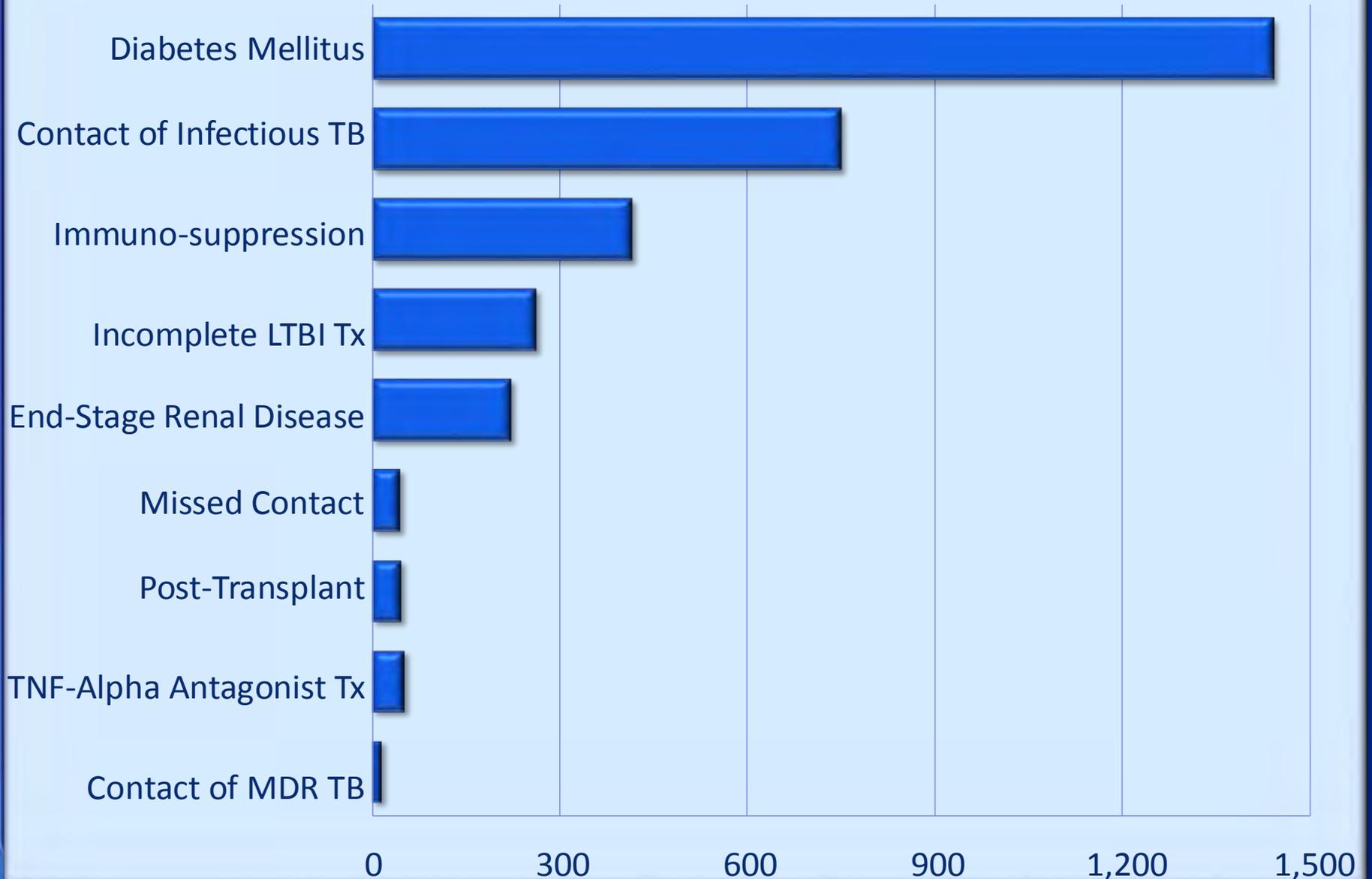
2014



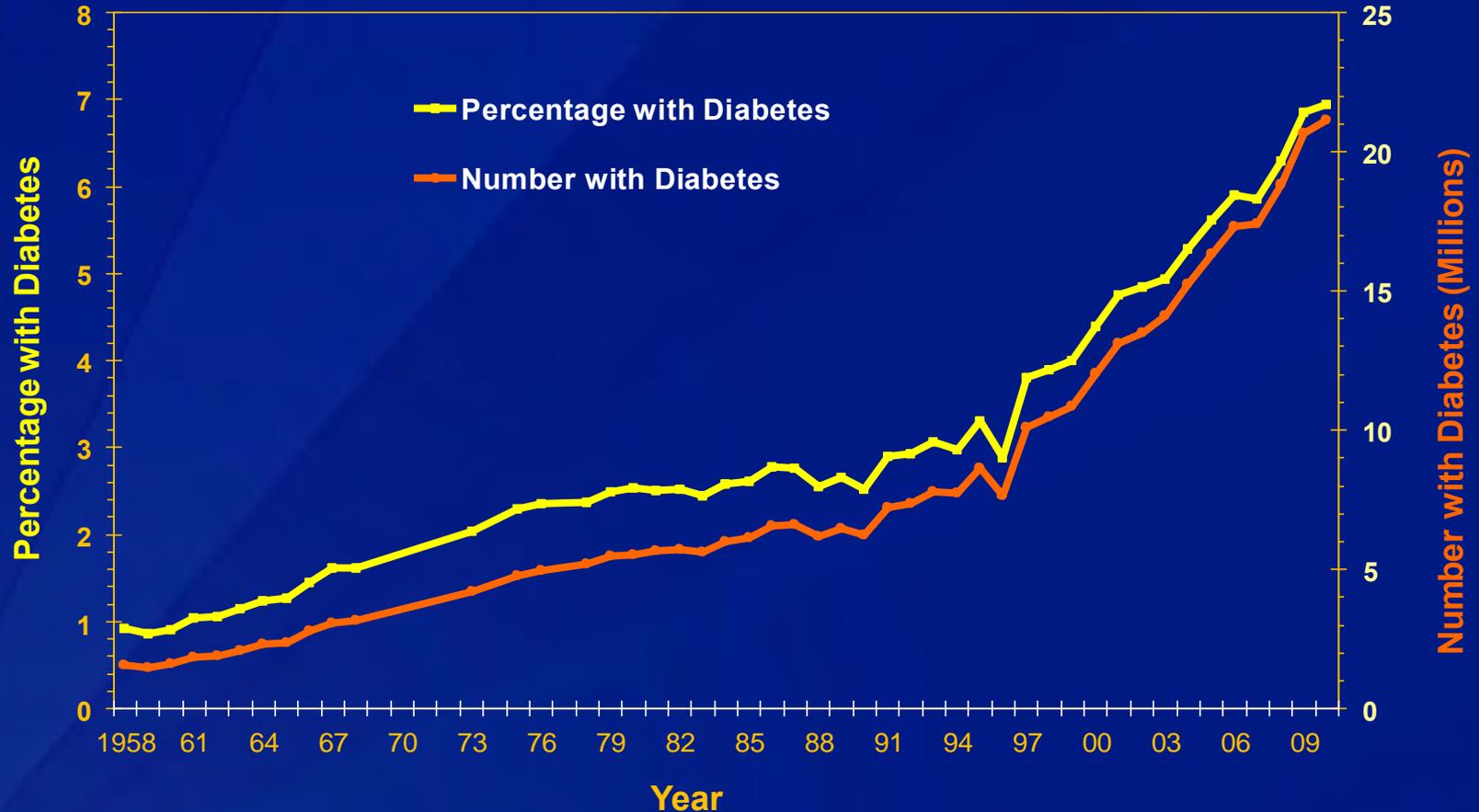
*Updated as of June 5, 2015.



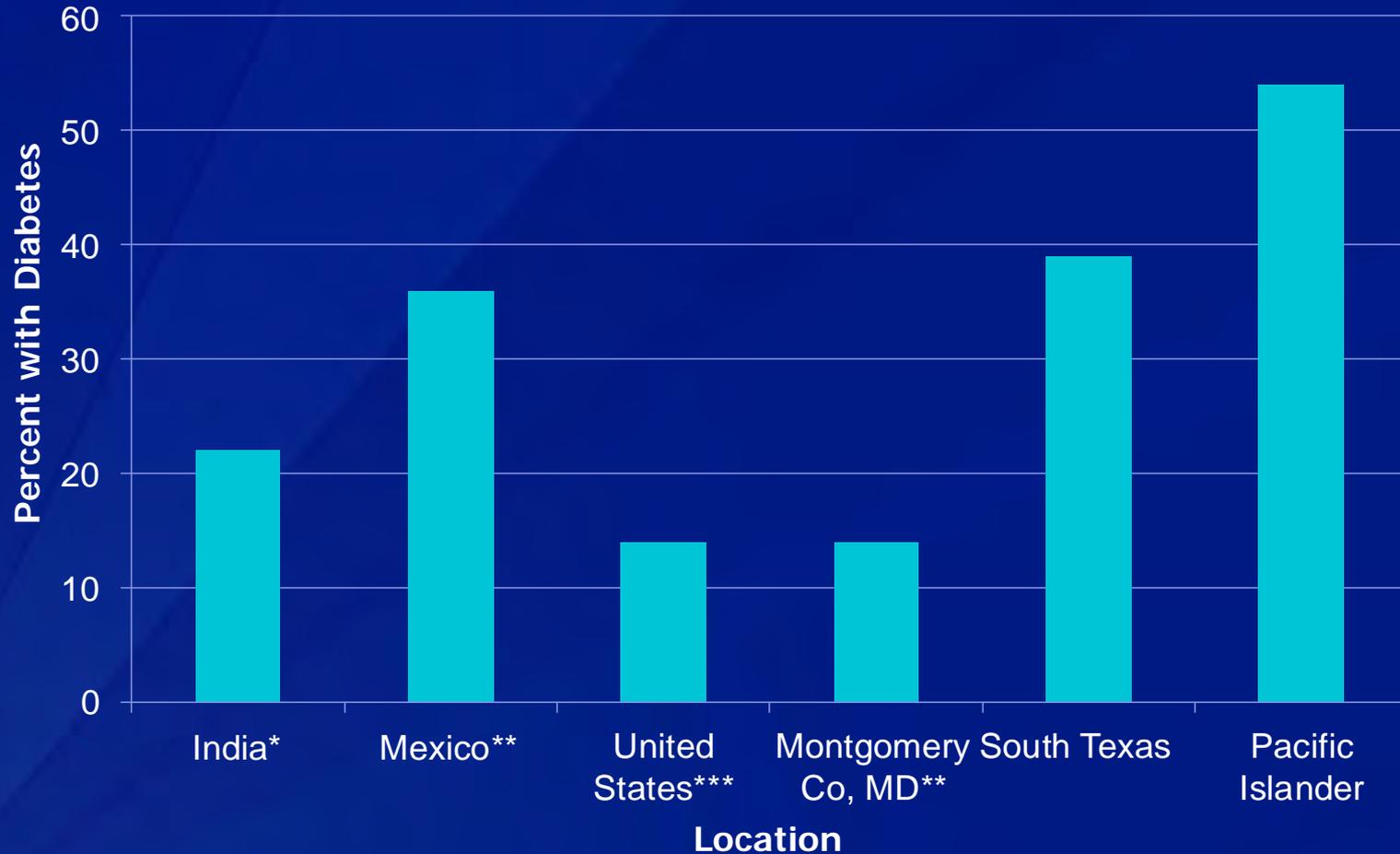
TB Risk Factors in the US - 2012



Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958–2010



Adult TB Cases with DM





TB and Diabetes in Kiribati

- Setting: South Tarawa (capital of Kiribati)
- Participants: TB patients and community members without signs and symptoms of active TB
- Case control study: 275 TB patients and 499 controls from the community

TB Rate: 378/100,000

(Source: WHO, 2013)

DM Rate: 29%

(Source: IDF Diabetes Atlas, 6th edition, 2013. In people aged 20-79 years)





Impact of Diabetes on TB in Kiribati:

Summary

- Additional burden of TB, attributable to diabetes was 25%.
- Additional burden of smear positive TB among people with diabetes was significant – impacting TB transmission in the community
- Treatment outcomes were not statistically significant – but very small sample.
- Undiagnosed diabetes (~50%)



TB and Diabetes in Kiribati

- 275 cases and 499 controls enrolled (774 in total)
- 195 (25%) people had diabetes (94 controls, 101 TB pts)
- Number of TB pts with diabetes: 101 (37%)
- Number of TB pts with known diabetes: 54 (53%)
- Number of TB pts newly diagnosed with diabetes: 47 (47%)
- Number of controls newly diagnosed with diabetes: 61 (64.8%)

Balakrishnan et al. PLoS One (2012). 552 TB patients screened; 243 (44%) had diabetes. Of these, 128 (53%) known diabetes, 115 (47%) newly diagnosed.



TB Treatment Outcomes

	Successful outcome N (%)	Poor outcome N (%)	Relative Risk (95% Confidence Interval)
Patients with diabetes	93 (92)	8 (8)	0.99 (0.92 – 1.06)
Patients without diabetes	162 (93)	12 (7)	Referent



No differences in chest x-ray changes or sputum conversion at two months, however sample size was small

Pacific Bi-Directional Screening for TB and DM

Country	Proportion of TB patients with DM	Diabetes status
Kiribati	37%	Known and newly diagnosed DM
Fiji	13%	Known DM only. A further 21% had elevated random glucose, referred for fasting glucose
Marshall Islands	45%	Known and newly diagnosed DM
Federated States of Micronesia	24%	Known and newly diagnosed DM
Country	Proportion of DM patients with TB	TB status
Marshall Islands (Ebeye)	5%	Newly diagnosed only
Federated States of Micronesia	3%	Known and newly diagnosed A further 25% had evidence of latent TB

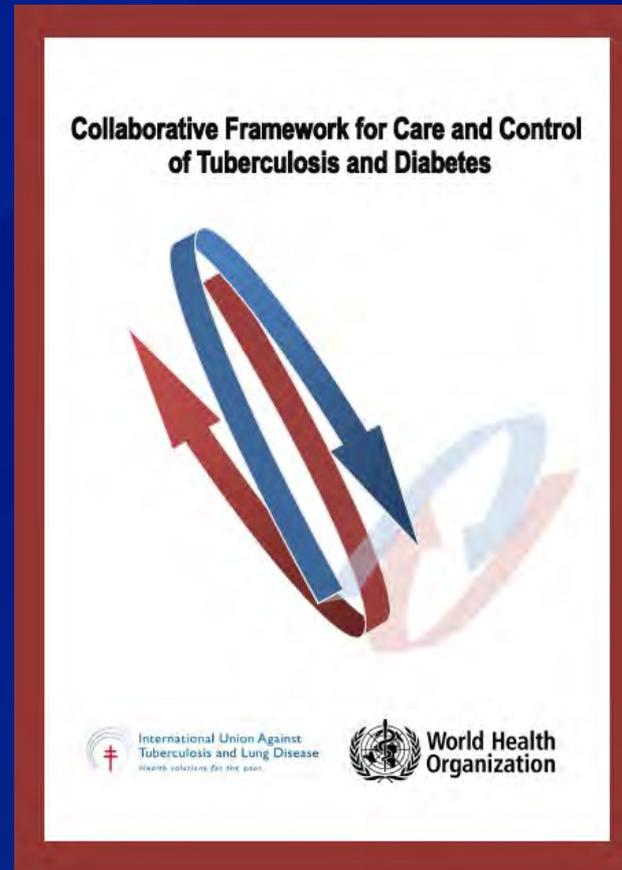
Impacts of DM on TB Control

“Increases in diabetes prevalence in populations with high ongoing tuberculosis transmission rates.... counteract the positive effects of TB control efforts.

In 2013, an estimated 15% (*nearly 1 out of every 6 cases*) of TB in adults worldwide were attributed to diabetes, which corresponds to over 1 million cases of diabetes-associated TB per year.”

Lonroth , et al. *Lancet Diabetes Endocrinol.* 2014 Dec;2(12):932.

2010: WHO Collaborative Framework for Care and Control of TB and Diabetes

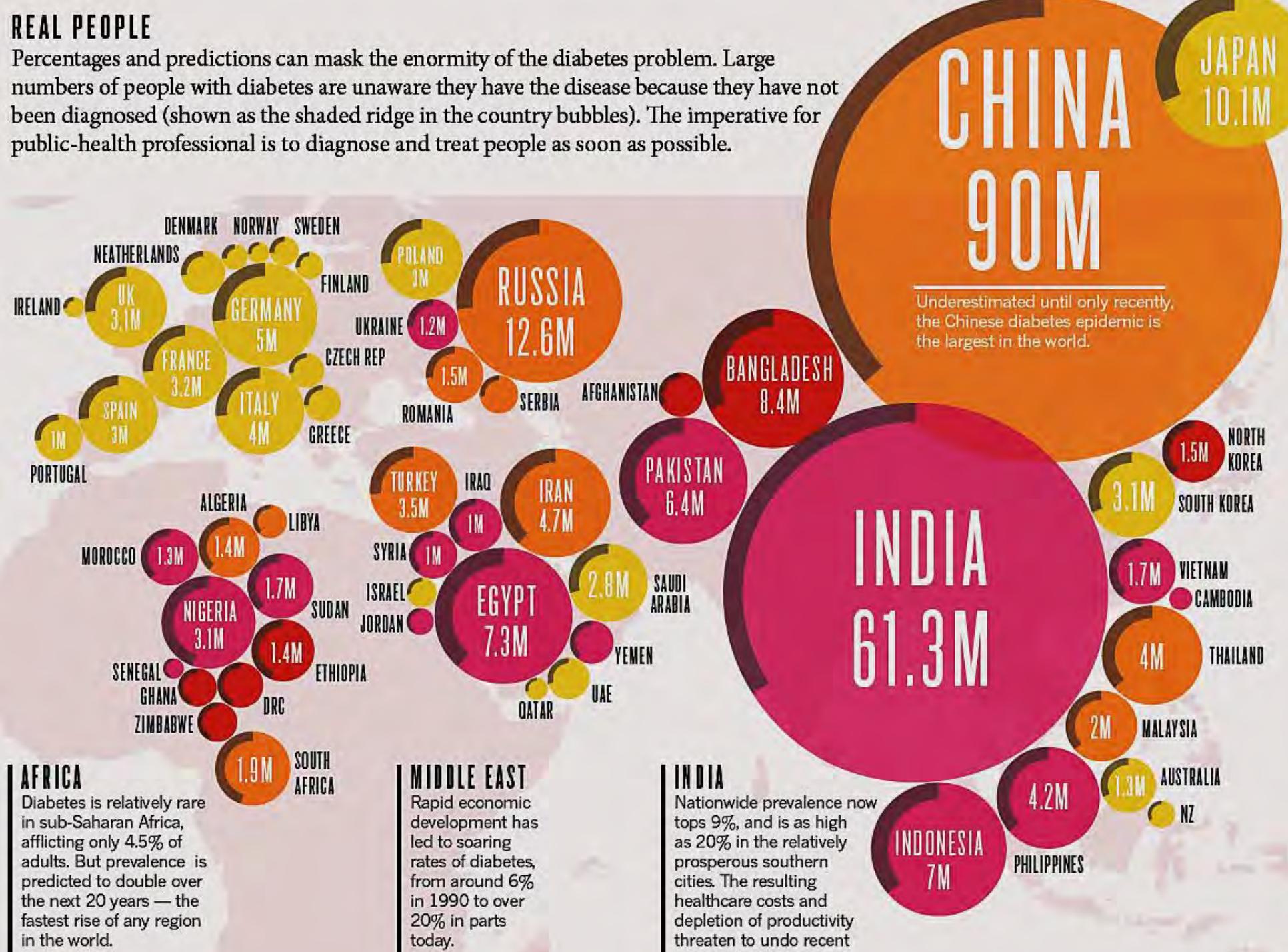


TB-DM: Opportunities for Collaboration

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REAL PEOPLE

Percentages and predictions can mask the enormity of the diabetes problem. Large numbers of people with diabetes are unaware they have the disease because they have not been diagnosed (shown as the shaded ridge in the country bubbles). The imperative for public-health professional is to diagnose and treat people as soon as possible.



Underestimated until only recently, the Chinese diabetes epidemic is the largest in the world.

AFRICA

Diabetes is relatively rare in sub-Saharan Africa, afflicting only 4.5% of adults. But prevalence is predicted to double over the next 20 years — the fastest rise of any region in the world.

MIDDLE EAST

Rapid economic development has led to soaring rates of diabetes, from around 6% in 1990 to over 20% in parts today.

INDIA

Nationwide prevalence now tops 9%, and is as high as 20% in the relatively prosperous southern cities. The resulting healthcare costs and depletion of productivity threaten to undo recent

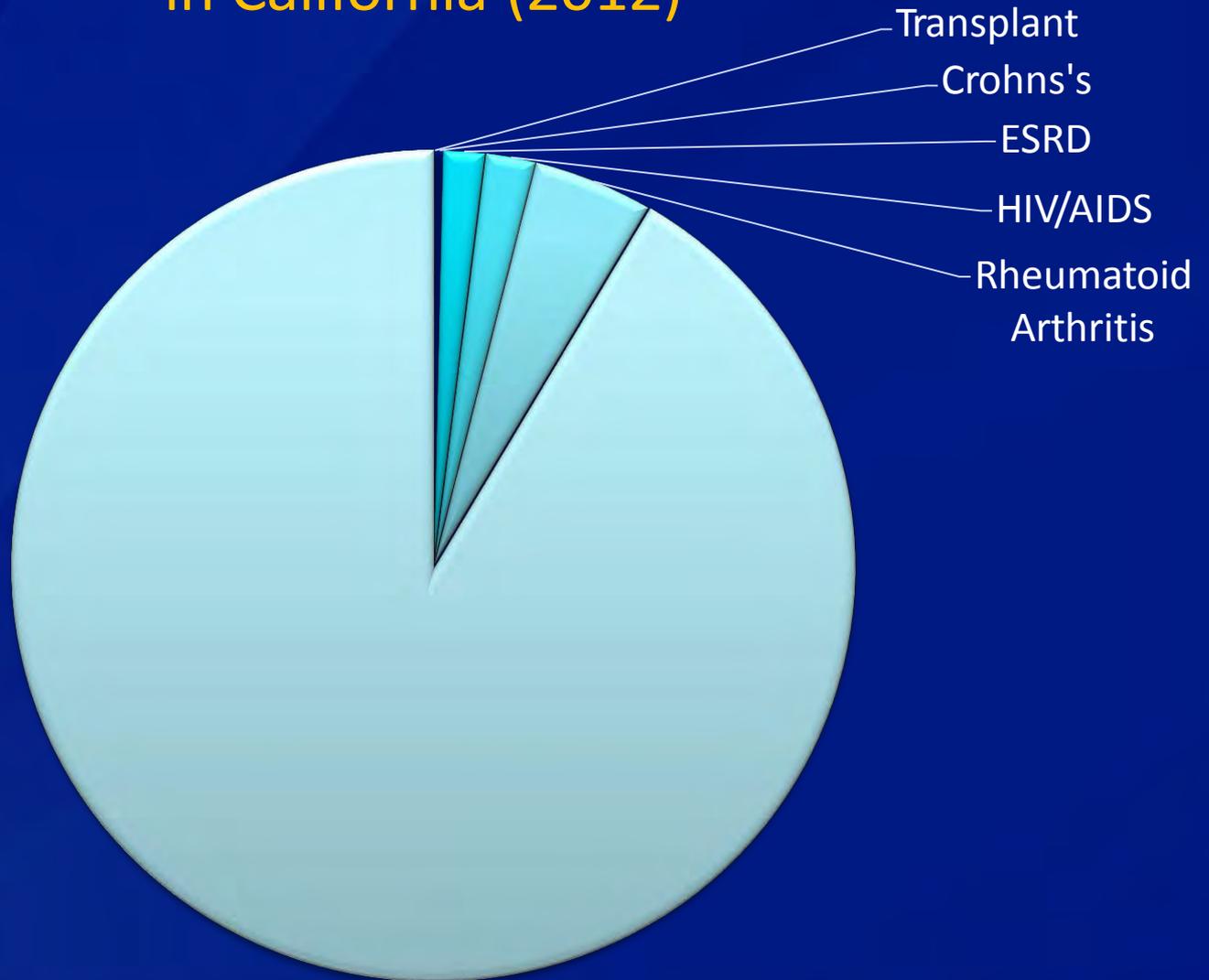
Table 2.3 Undiagnosed diabetes (20-79 years) by IDF Region and income group, 2013

IDF REGION	PROPORTION UNDIAGNOSED %	CASES MILLIONS
Africa		12.4
Low-income countries	75.1	
Middle-income countries	46.0	
Europe		20.1
Low-income countries	29.3	
Middle-income countries	35.1	
High-income countries	36.6	
North America and Caribbean		
Low-income countries		29.4
Middle-income countries		25.0
High-income countries		27.7
Middle-income countries	25.0	
High-income countries	27.7	
South and Central America		5.8
Middle-income countries	24.1	
South-East Asia		35.1
Low-income countries	43.6	
Middle-income countries	49.1	
Western Pacific		74.7
Low-income countries	63.0	
Middle-income countries	54.1	
High-income countries	49.4	

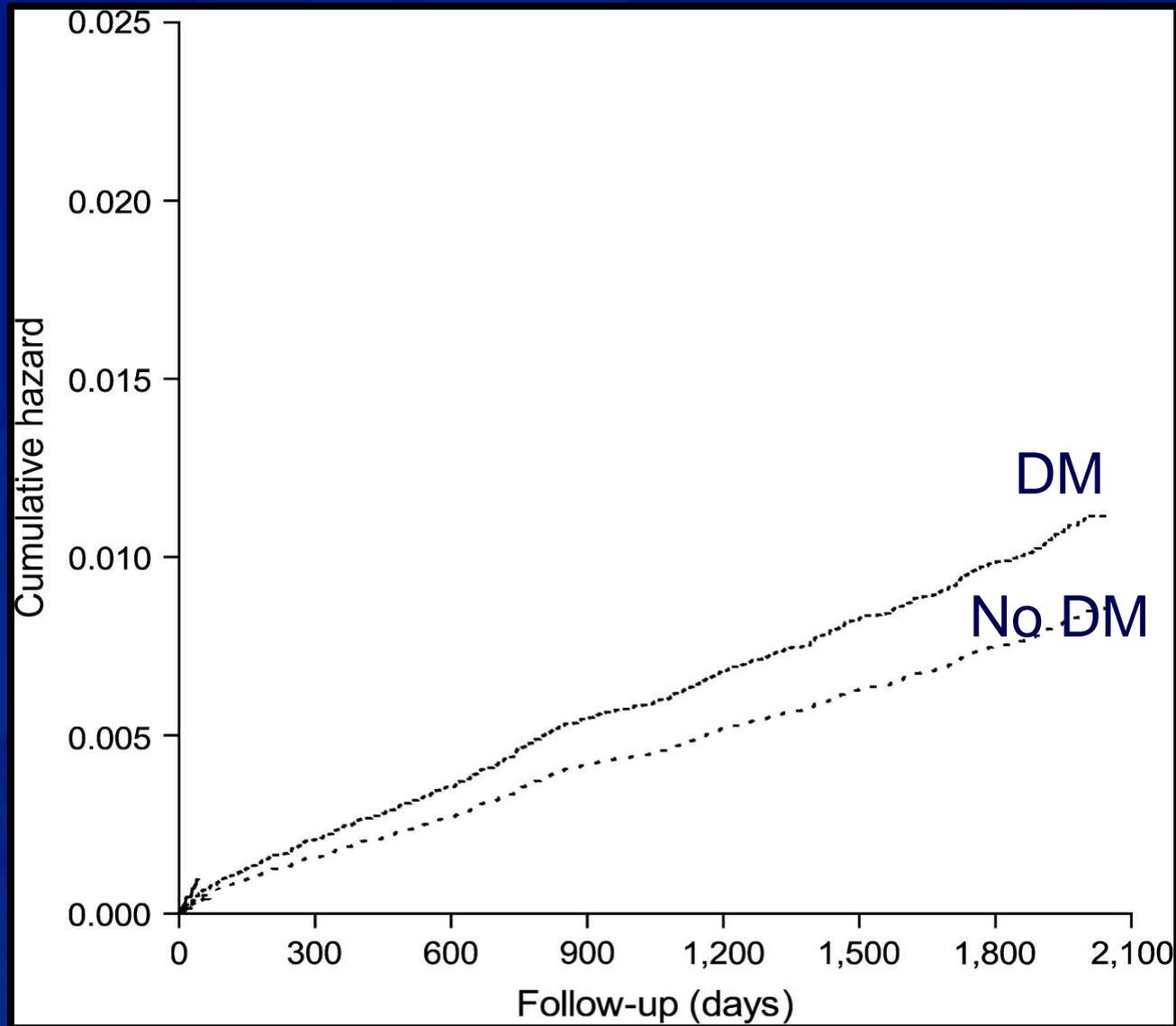
Double Trouble: TB-DM Lit Review

1. Does DM cause TB?
2. Does Diabetes affect TB treatment?
3. Can we make a difference?

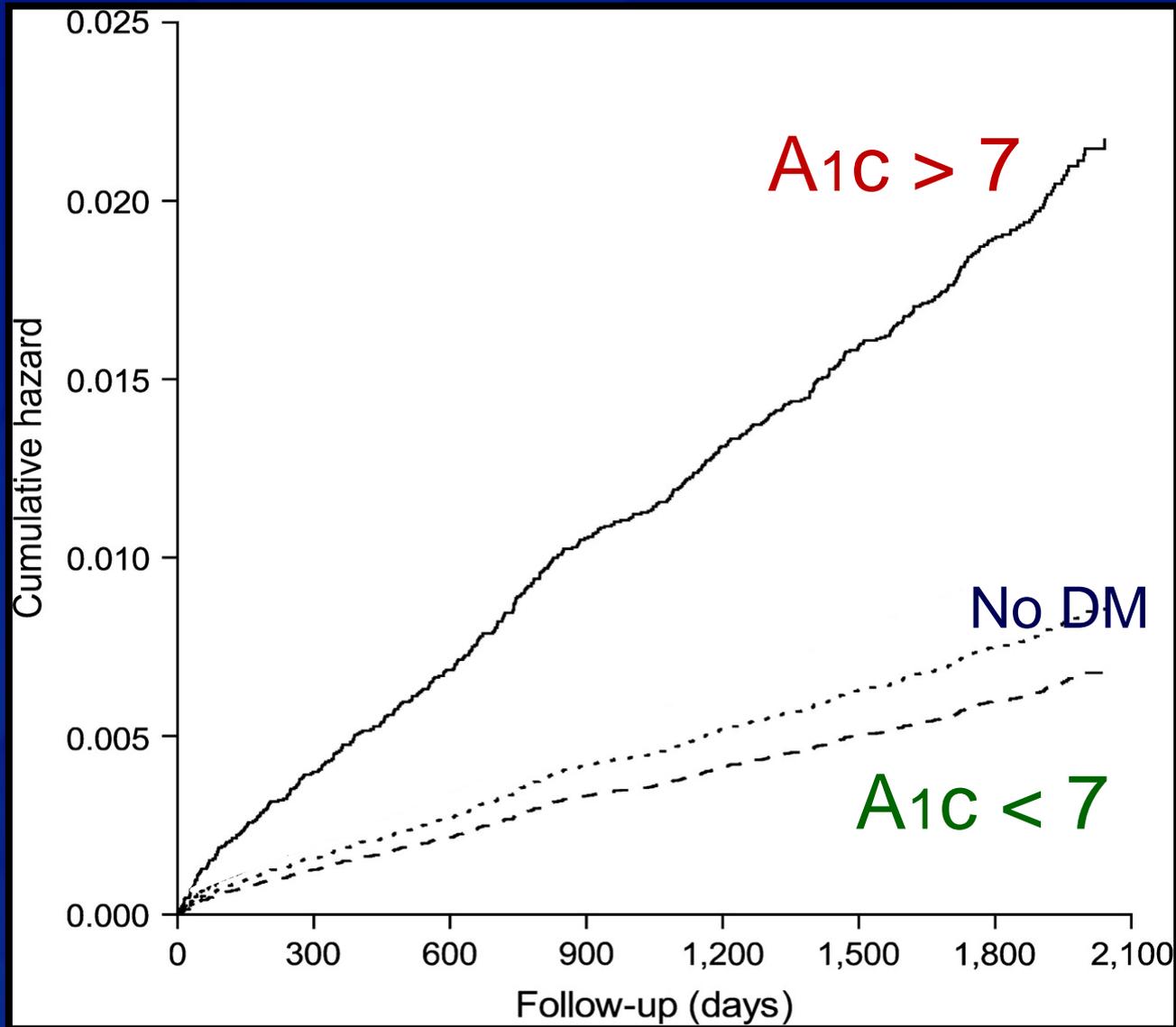
Risk Factors among Foreign-born with TB Infection in California (2012)



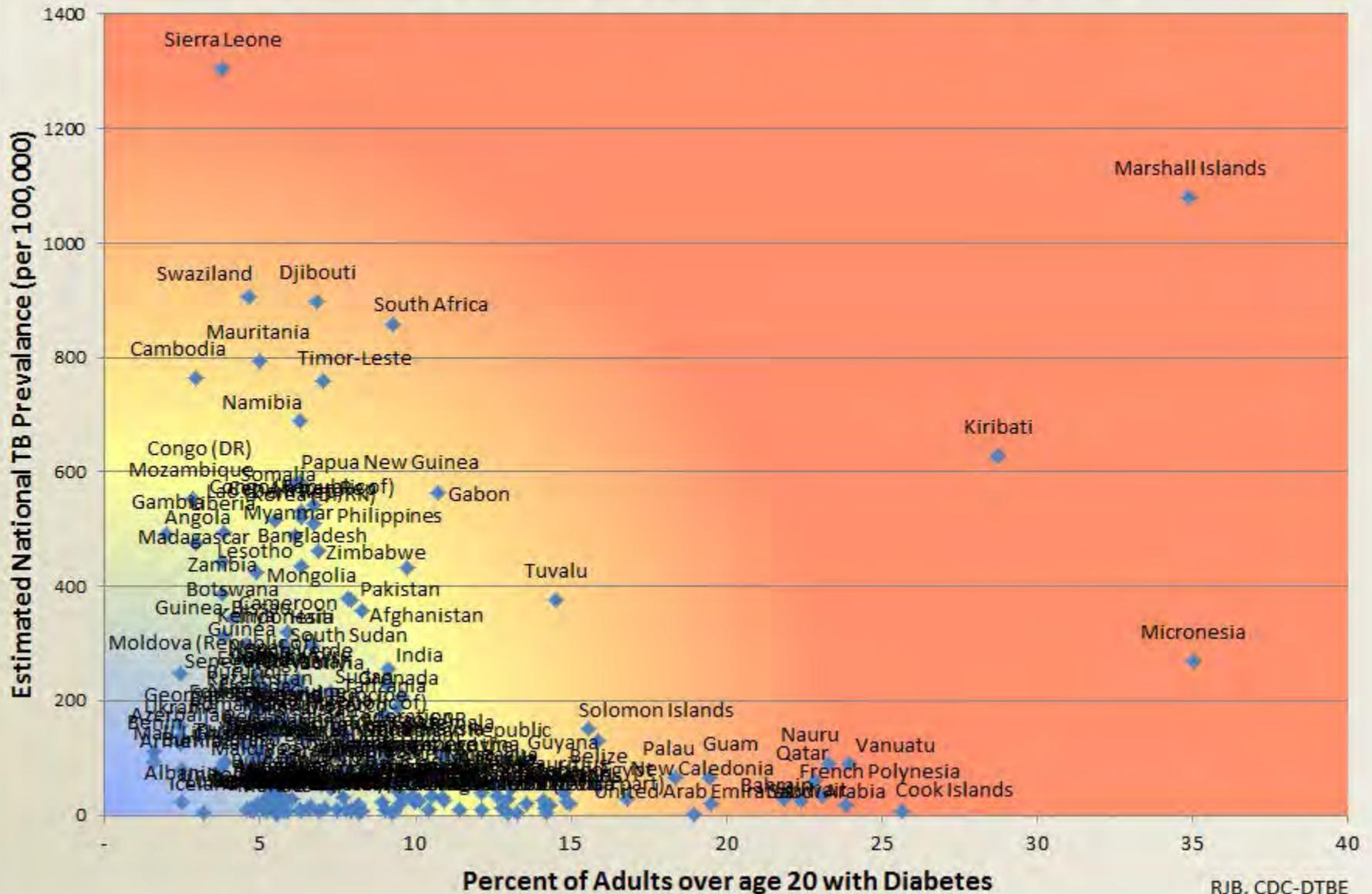
TB-DM: Diabetes Control



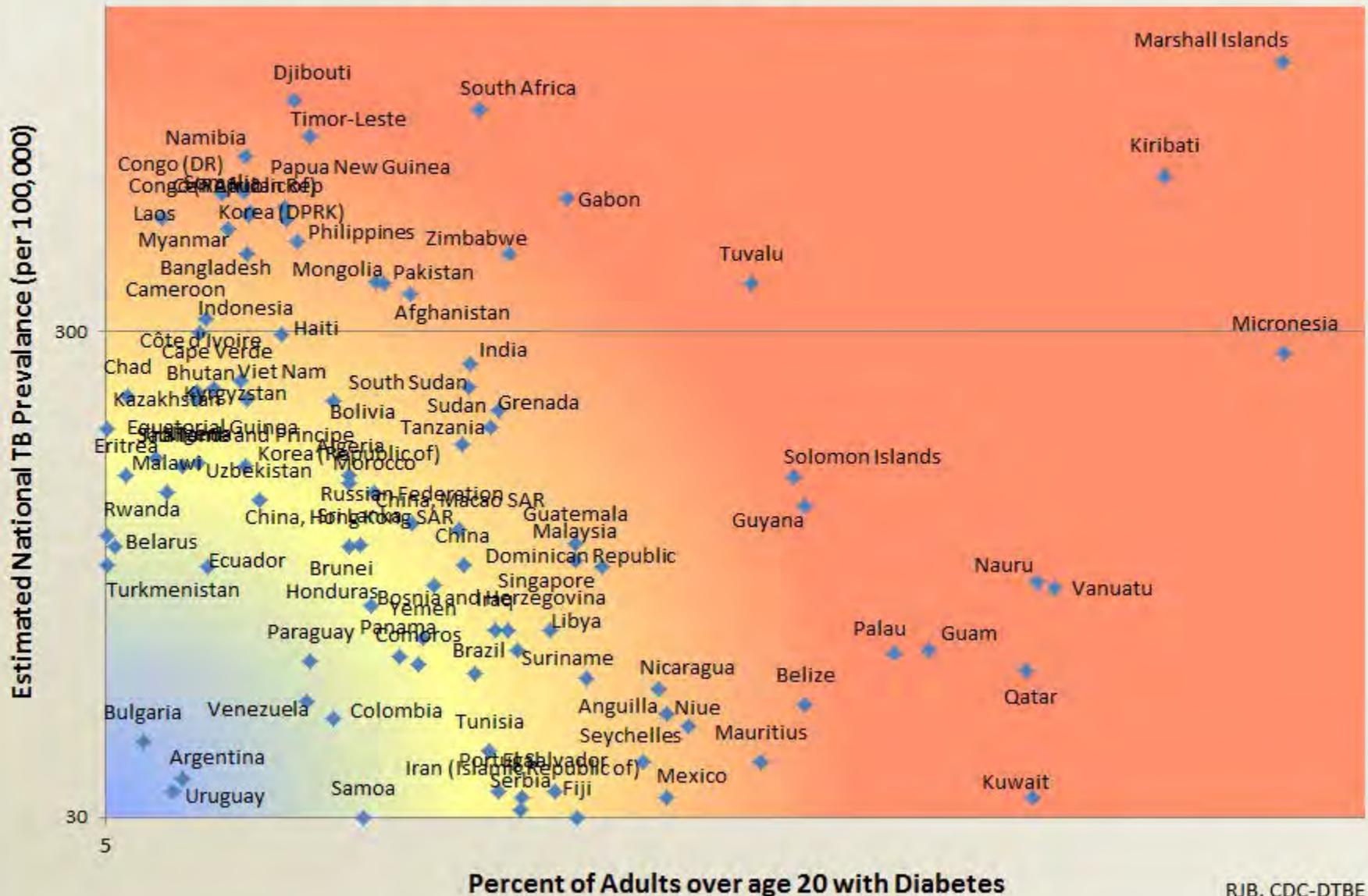
TB-DM: Diabetes Control



National Estimates of TB and Diabetes, 2013



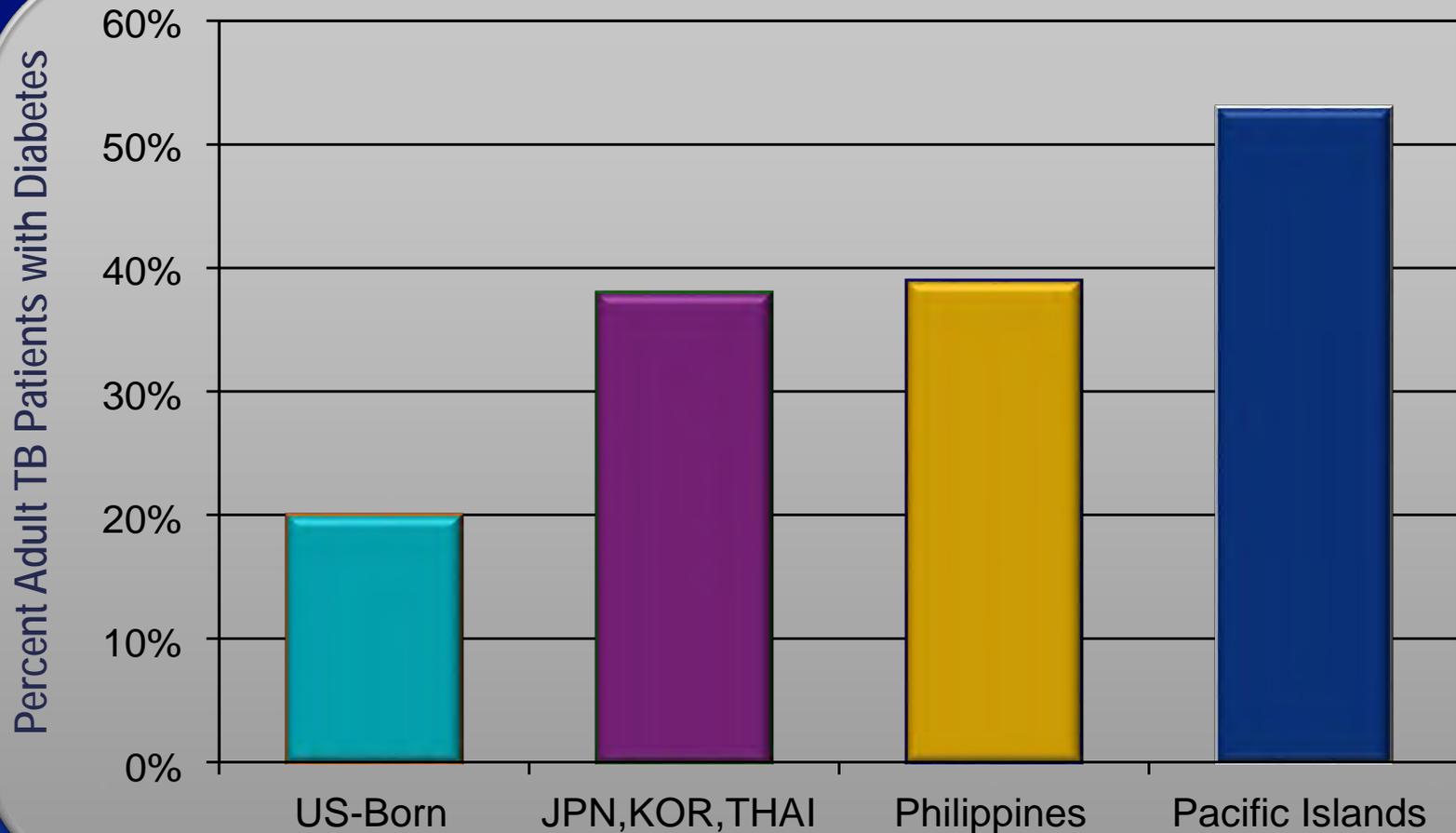
National Estimates of TB and Diabetes, 2013



Hawaii Adult TB Cases with Diabetes

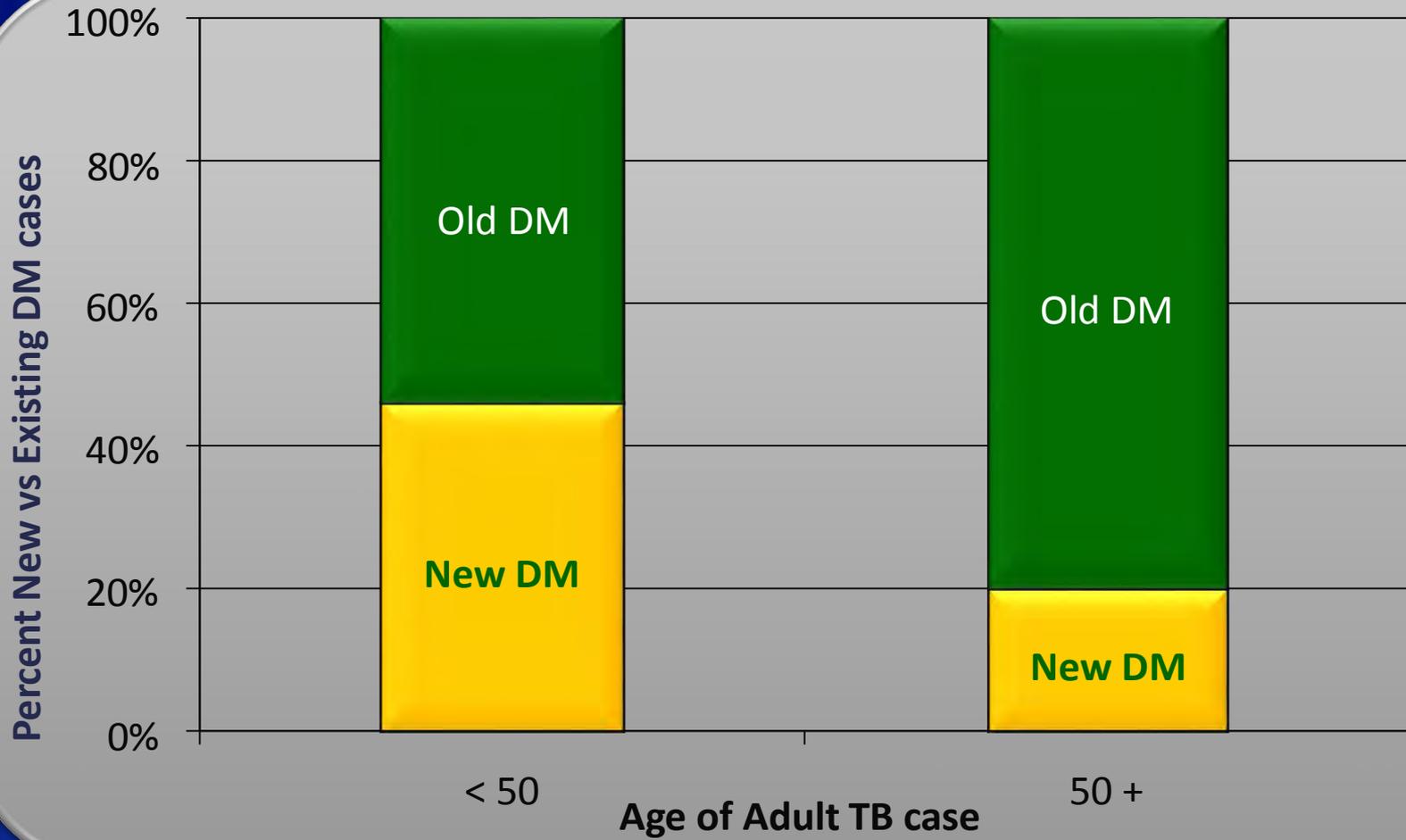


Adult TB Cases with DM in Hawaii: 2014



*Hawaii Case Reports for 2014

TB as the “Diabetes Defining Illness”



*Hawaii Case Reports for 2014

Double Trouble: TB-DM Lit Review

1. Does DM lead to TB? **Yes!**
2. Does diabetes affect TB treatment?
3. Can we make a difference?

TB and Diabetes: Case Management

People with DM and TB have....

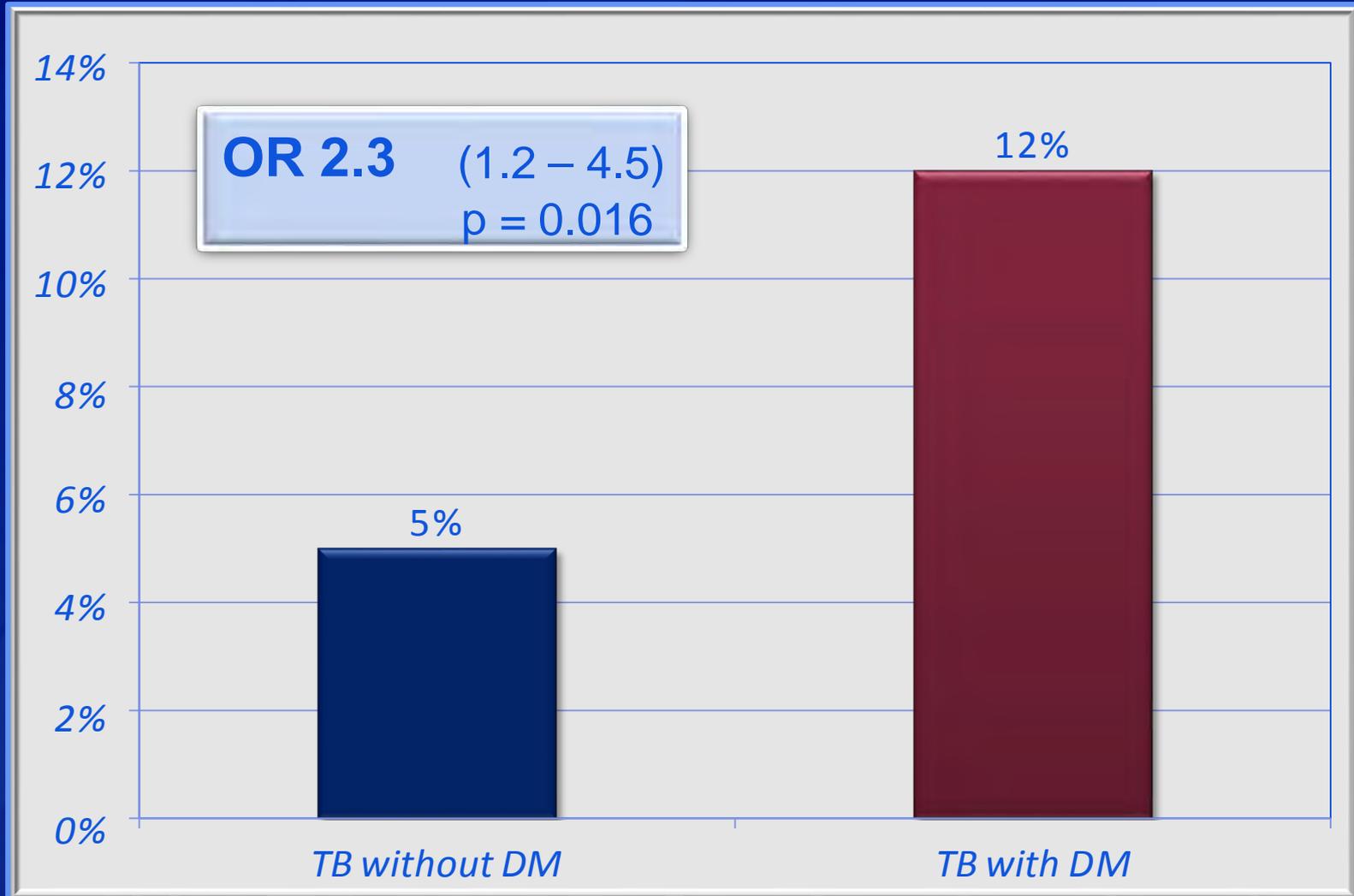
- More atypical TB presentations
- A multitude of med interactions
- Longer periods of infectiousness
- Higher risk of hepatitis from TB meds

TB-DM Outcomes: Relapse

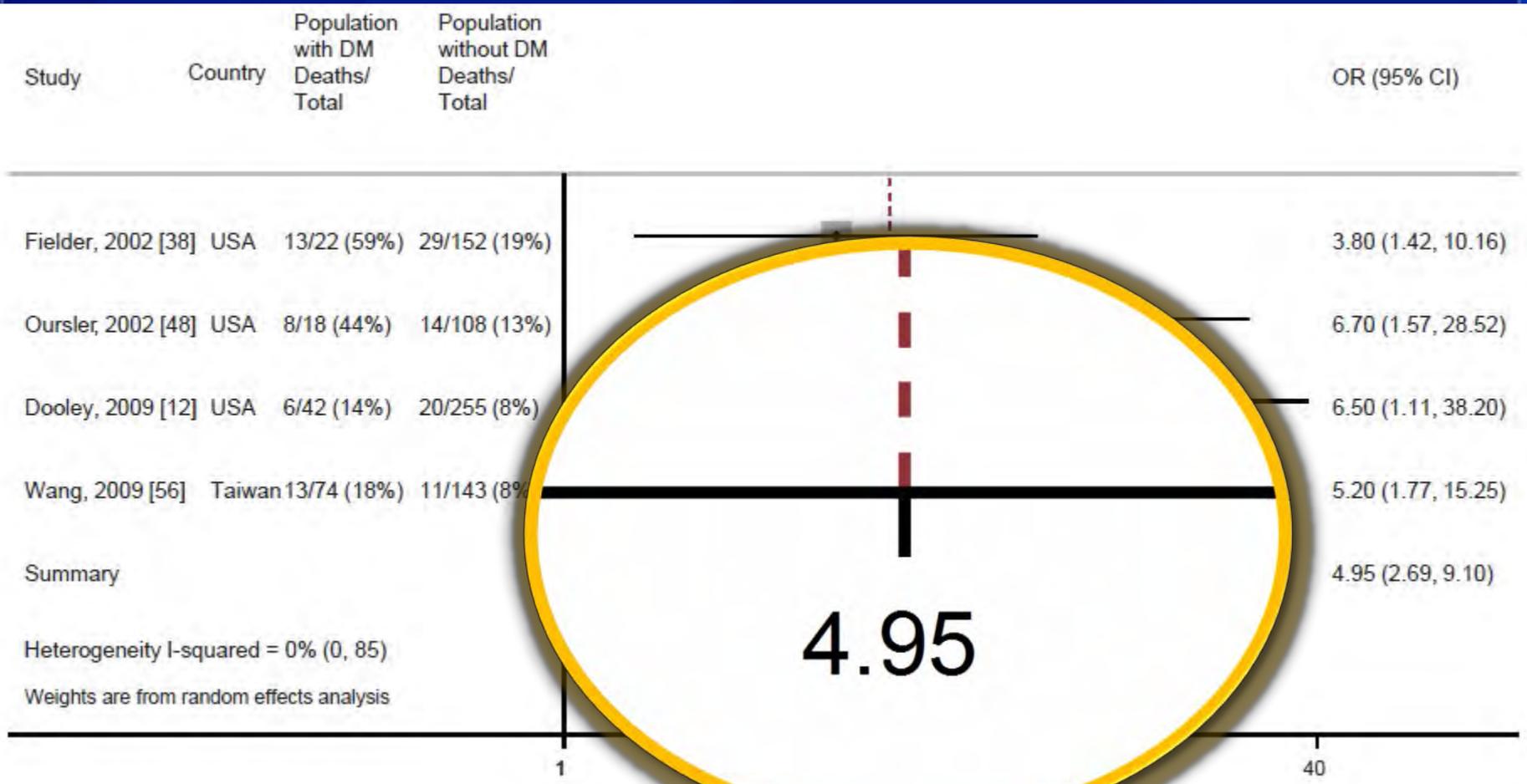
Study	Country	Population with DM Relapse/ Total	Population without DM Relapse/ Total	RR (95% CI)
Wada, 2000 [54]	Japan	7/61 (11%)	4/284 (1%)	8.15 (2.46, 26.97)
Mboussa, 2003 [47]	Congo	6/17 (35%)	9/77 (12%)	3.02 (1.24, 7.35)
Singla, 2006 [50]	Saudi Arabia	2/130 (2%)	3/367 (1%)	1.88 (0.32, 11.14)
Maalej, 2009 [46]	Tunisia	4/55 (7%)	1/82 (1%)	5.96 (0.68, 51.95)
Zhang, 2009 [57]	China	33/165 (20%)	9/170 (5%)	(1.87, 7.65)
Summary				2.43, 6.23)

Heterogeneity I-squared = 0% (0, 79)	<p style="font-size: 2em; font-weight: bold;">3.89</p>
Weights are from random effects analysis	

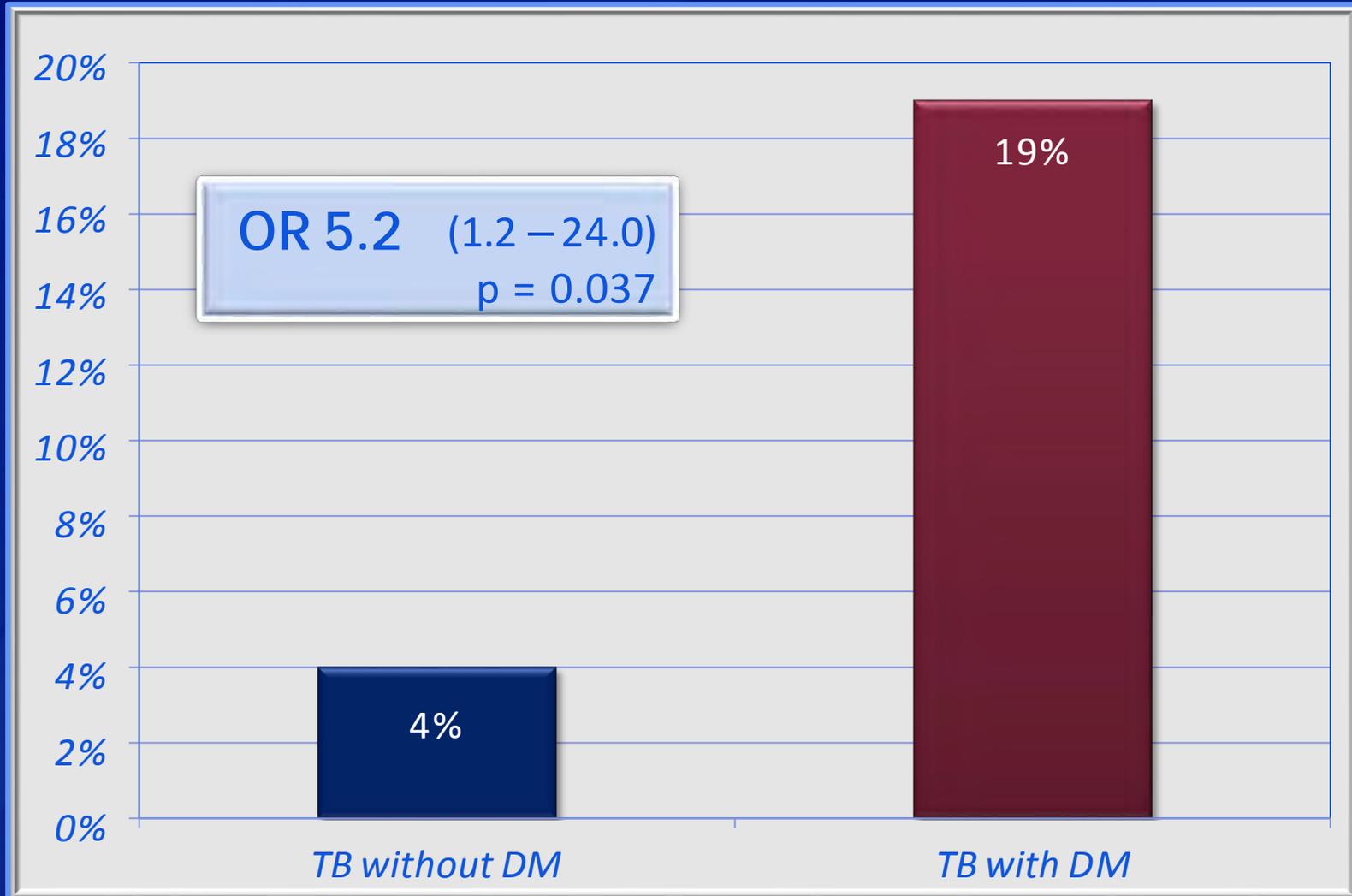
History of Prior TB*



TB-DM Outcomes: Death during TB Tx



All-Cause Mortality During TB Treatment*



More DM Complications: More TB Risk

Table 4. Multivariate Associations for Tuberculosis Disease, by Complications of Diabetes Mellitus

Variable	Tuberculosis Cases	Total Population	Adjusted Hazard Ratio (95% CI)	<i>P</i>
Complications of DM				.0016
No DM	44	16 557	1.00	
Treated DM and ≤1 complication	4	609	1.73 (.61–4.89)	
Treated DM and ≥2 complications	9	549	3.45 (1.59–7.50)	
Diabetes Complications Severity Index				
No DM	44	16 557	1.00	.0002
Treated DM and severity score ≤3	6	881	1.72 (.72–4.13)	
Treated DM and severity score ≥4	7	277	5.05 (2.11–12.04)	

Abbreviations: CI, confidence interval; DM, diabetes mellitus.

Meghan A Baker, Hsien-Ho Lin, Hsing-Yi Chang, and Megan B Murray. The Risk of Tuberculosis Disease Among Persons With Diabetes Mellitus: A Prospective Cohort Study, *Clin Infect Dis*. 2012 doi:10.1093

Higher A1C: Worsening TB Presentation

	A1C<7%		A1C 7%–9%		A1C>9%	
	AdjRRR	(95% CI)	AdjRRR	(95% CI)	AdjRRR	(95% CI)
Any Cavity	0.79	(0.42–1.49)	2.00	(1.30–3.09)	3.59	(2.53–5.11)
Location (field)						
Upper	0.89	(0.46–1.62)	1.86	(1.20–2.88)	2.71	(1.92–3.83)
Lower	1.02	0.30–3.51)	2.28	(1.10–4.71)	4.47	(2.62–7.62)
Number of cavities						
Single	0.97	(0.41–2.29)	2.46	(1.40–4.32)	3.97	(2.53–6.25)
Multiple	0.68	0.30–1.53)	1.71	(1.02–2.88)	3.37	(2.26–5.03)
Size of cavity						
Small	0.80	(0.36–1.77)	2.20	(1.32–3.67)	3.34	(2.19–5.08)
Large	0.79	(0.34–1.88)	1.77	(1.01–3.12)	3.87	(2.54–5.90)

Chiang CY, Lee JJ, Chien ST, Enarson DA, Chang YC, et al. (2014) Glycemic Control and Radiographic Manifestations of Tuberculosis in Diabetic Patients. PLoS ONE 9(4): e93397. doi:10.1371/journal.pone.0093397

TB and Diabetes Summary: 2-3-4-5

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

Double Trouble: TB-DM Lit Review

1. Does DM cause TB? **Yes!**
2. Does diabetes affect TB treatment? **Yes!**
3. Can we make a difference?

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Pacific Standards for Management of Tuberculosis and Diabetes

Screening for DM in persons with TB

Standard 1 Every person with tuberculosis (TB) over the age of 18 should be screened for diabetes mellitus (DM)

1. The diagnosis of DM may be made using one of the following criteria:
 - Fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l)
 - Random plasma glucose ≥ 200 mg/dl (11.1 mmol/l)
 - Hemoglobin A1c ≥ 6.5 % (48 mmol/mol)
- 1.2 Abnormal glucose values should be verified in patients who have no symptoms of DM.
- 1.3 Rifampin can elevate blood glucose in TB patients. Glucose testing may be repeated after 2-4 weeks of TB treatment, or if symptoms of hyperglycemia develop during TB treatment.

Screening for TB in persons with DM

Standard 2 Every high-risk person with DM should be periodically screened for TB disease and TB infection

1. Program may choose to screen all patients with DM for TB, or may choose to screen highest risk patients only:
 - People with DM under age 50.
 - People with poorly controlled DM (A1C $\geq 8.0\%$)
- 2.2 Persons with TB symptoms or TB disease should be referred to the local TB Program for TB management.
- 2.3 A test for TB infection should be done at the time of DM diagnosis.
- 2.4 Screening should be repeated as often as the local TB epidemiology may warrant. Annual symptom screening for TB disease is reasonable. Screening for TB infection every 2 - 5 years is reasonable.

Standard 3 Persons with DM and TB infection should be encouraged to take preventive therapy

- 3.1 Persons with DM are at increased risk of peripheral neuropathy. If INH is used for prevention, give B6 to prevent neuropathy (10 – 25 mg/day).
- 3.2 Monitor for adherence and side effects of preventive treatment.

Treating TB in persons with DM

Standard 4 Clinicians may need to adjust TB treatment in persons with DM

- 4.1 Make sure that TB medications are properly dosed. Check creatinine for diabetic nephropathy, and if present, adjust the frequency of PZA and EMB according to ATS-CDC guidelines.* Administer B6 to prevent INH-induced neuropathy (10 – 25 mg/day).
- 4.2 Observe closely for TB treatment failure in persons with DM. Be aware of poor absorption of some TB meds in DM. Manage the many interactions between TB and DM meds. Some programs follow INH or RIF levels in persons with DM.
- 4.3 “Assure the Cure” Consider extending treatment to 9 months for persons with DM, especially persons with cavitary disease or delayed sputum clearance.* Upon completion of therapy, obtain sputum for AFB smear and culture. Evaluate at one year after treatment for evidence of relapse.

*Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society, MMWR 2003;52

Managing DM in persons with TB

Standard 5 Use TB clinic visits to help persons manage their DM

- 5.1 There should be a glucometer in every TB clinic for monitoring glucose.
- 5.2 TB patients with DM should have their glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if diabetes is controlled. Monthly glucose testing during treatment is recommended.
- 5.3 All clinic staff should reinforce lifestyle changes at TB clinic visits.
- 5.4 If available, refer persons with DM to the Diabetes Clinic for diabetes care. Ensure DM clinician is aware of TB diagnosis and TB medications.

Standard 6 Use DOT visits to help persons manage their DM

- 6.1 DOT workers should encourage lifestyle changes at every encounter. DOT workers should use structured and culturally-appropriate diabetes educational materials.* Dietary changes and physical activity are the most important in this effort.
2. Consider delivering DM meds with TB meds via DOT for persons with poorly-controlled DM who have non-adherence to diabetic medications.

* ARC TB and DM Flipchart: <http://www.thearc.org.au/TBAndDiabetes.aspx>

* NDEP, US Dept of Health and Human Services: <http://www.yourdiabetesinfo.org/>



Best Practices: RMI Diabetes Clinic

Program Collaboration

In 2010, the KAHCB adopted and started implementing the *USAPI Standards for the Management of Tuberculosis and Diabetes*. In this guideline – standards were set for DM screening in persons with active TB; screening for TB in persons with DM; treating TB in persons with DM; and managing DM in persons with active TB.

To improve implementation of the USAPI clinical guidelines – KAHCB have set the following measures to accomplish the collaborative initiatives:



DM Screening and Glucose Monitoring for TB Cases

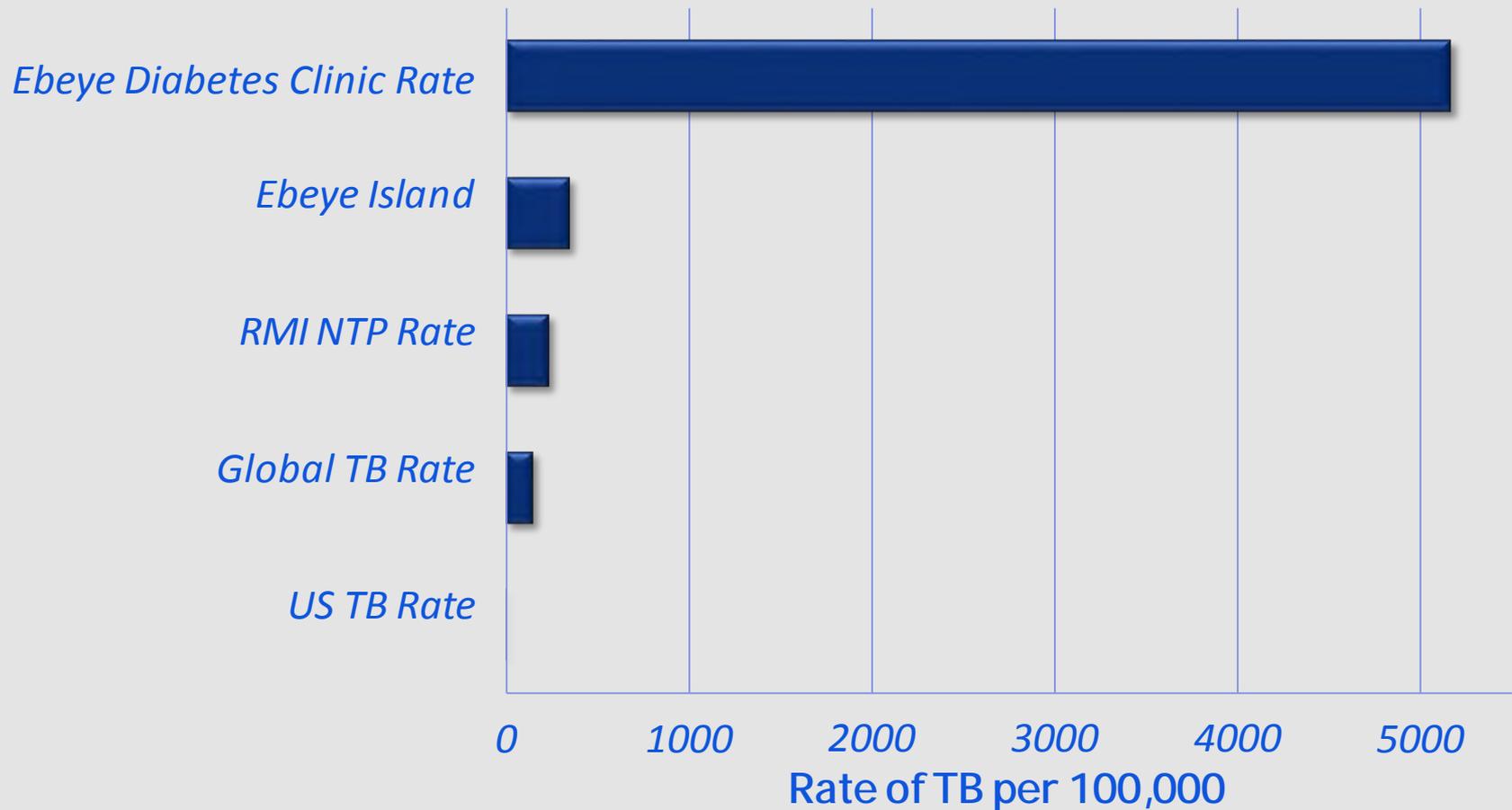


Tuberculosis screening in the DM Clinic

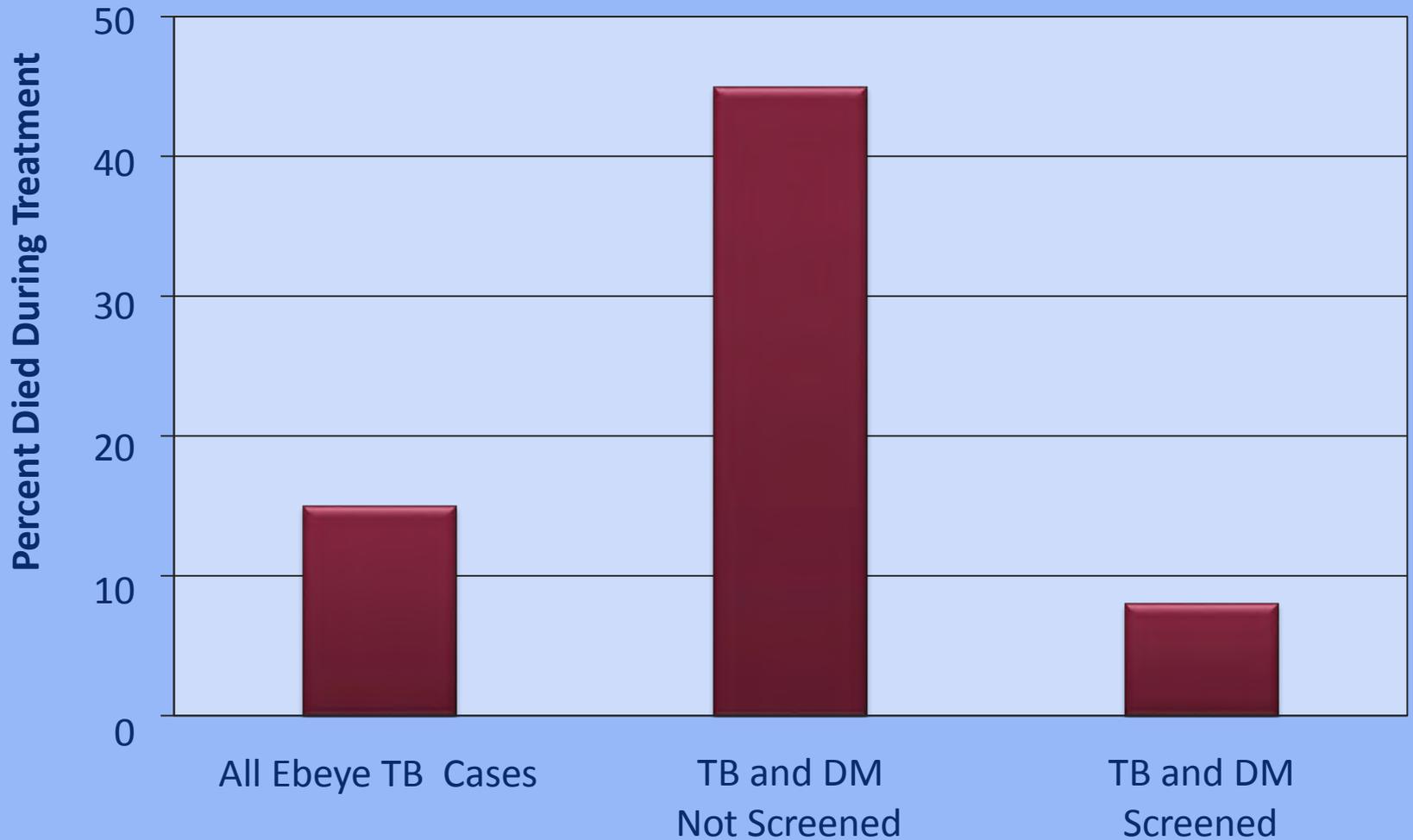


Strengthening DM-TB co-morbid clinical management

TB Screening in Diabetes Clinic: Finding TB



Death During TB Treatment in Ebeye (2010 – 2012, n=23)



What Happens After Bidirectional Screening?



**"Geez, I had no idea there was a Nobel Prize
for accounting."**



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now revised and updated

Diabetes

FOR DUMMIES®

2nd Edition

Dr Alan L. Rubin

Diabetes specialist

Dr Sarah Jarvis, GP

*Fellow of the Royal College of
General Practitioners*



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Battle Creek Sanitarium: Exercises, 1911



Basic DM Management for TB Clinic

Treating TB in persons with DM

Standard 4 Clinicians may need to adjust TB treatment in persons with DM

4.1 Make sure that TB medications are properly dosed.

Check creatinine for diabetic nephropathy, and if present, adjust the frequency of PZA and EMB according to ATS-CDC guidelines.*

Administer B6 to prevent INH-induced neuropathy (10 – 25 mg/day).

4.2 Observe closely for TB treatment failure in persons with DM.

Be aware of poor absorption of some TB meds in DM.

Manage the many interactions between TB and DM meds.

Some programs follow INH or RIF levels in persons with DM.

4.3 “Assure the Cure”

Consider extending treatment to 9 months for persons with DM, especially persons with cavitary disease or delayed sputum clearance.*

Upon completion of therapy, obtain sputum for AFB smear and culture.

Evaluate at one year after treatment for evidence of relapse.

*Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society, MMWR 2003;52

Enhanced DM Management for TB Clinic

Managing DM in persons with TB

Standard 5 Use TB clinic visits to help persons manage their DM

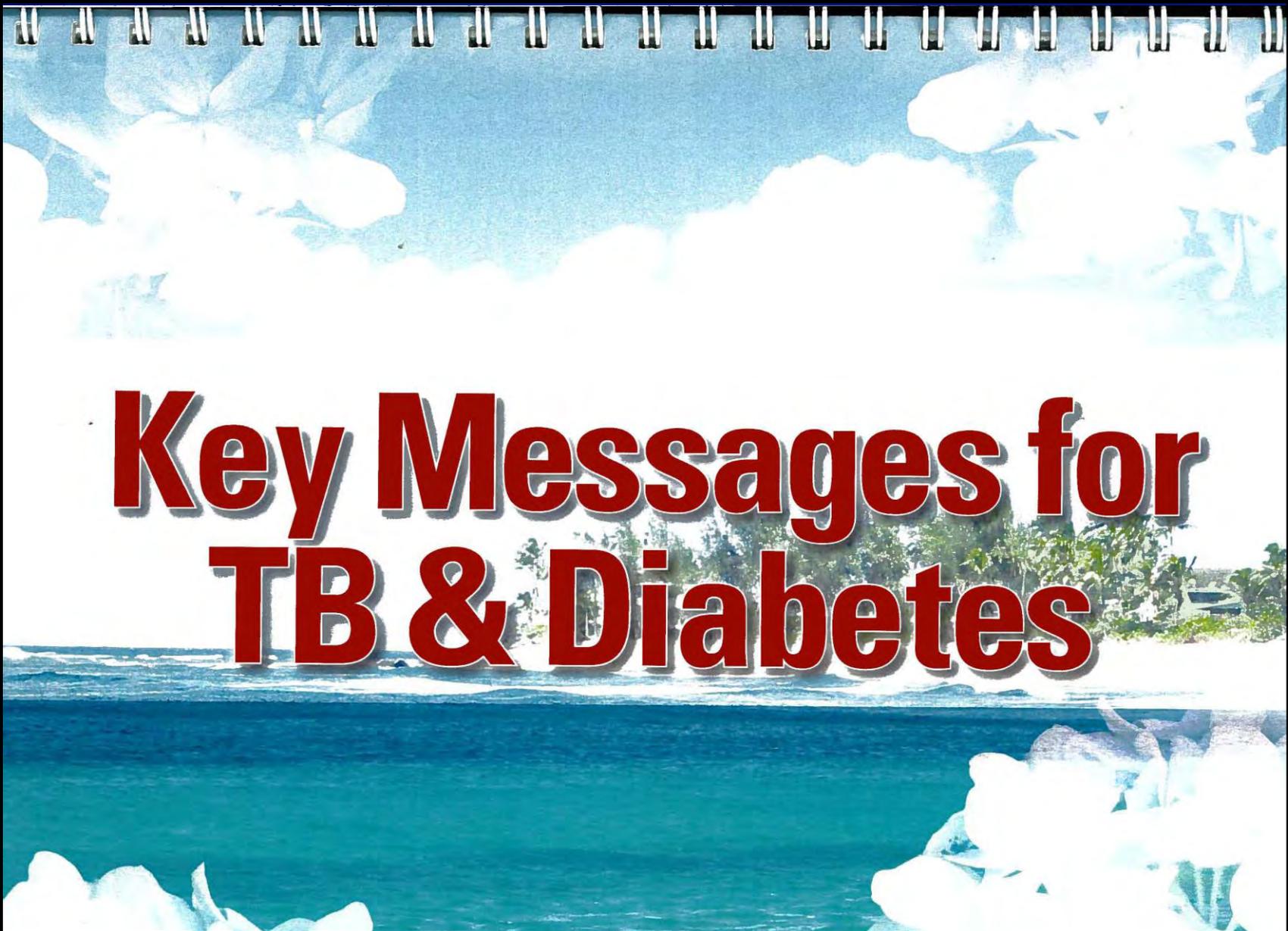
- 5.1 There should be a glucometer in every TB clinic for monitoring glucose.
- 5.2 TB patients with DM should have their glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if diabetes is controlled. Monthly glucose testing during treatment is recommended.
- 5.3 All clinic staff should reinforce lifestyle changes at TB clinic visits.
- 5.4 If available, refer persons with DM to the Diabetes Clinic for diabetes care. Ensure DM clinician is aware of TB diagnosis and TB medications.

Standard 6 Use DOT visits to help persons manage their DM

- 6.1 DOT workers should encourage lifestyle changes at every encounter. DOT workers should use structured and culturally-appropriate diabetes educational materials.*
Dietary changes and physical activity are the most important in this effort.
- 6.2 Consider delivering DM meds with TB meds via DOT for persons with poorly-controlled DM who have non-adherence to diabetic medications.

* ARCTB and DM Flipchart: <http://www.thearc.org.au/TBAndDiabetes.aspx>

* NDEP, US Dept of Health and Human Services: <http://www.yourdiabetesinfo.org/>



Key Messages for TB & Diabetes

Week 2 (Day 1)

DOT helps cure TB!

Why does a health worker need to see you every day for TB medication?



Week 2 (Day 1)

DOT helps cure TB!

Why does a health worker need to see you every day for TB medication?

- "DOT" means Directly Observed Therapy. DOT makes it easy to take your pills. DOT is when a nurse or health care worker sees you every day to give you TB medicine. A health worker can meet with you every day or a few times a week to watch you take your TB pills. He or she will bring you your pills at the place and time that is most easy for you. This is the best way to make sure you get all the medicine you need and your treatment is working. If there is a problem with your medication it can be fixed right away
- Our goal is to ensure that everyone completes their treatment and is cured
- **Note for the healthworker:** if your local policy requires, you may need to obtain agreement from the patient to complete DOT and / or to record their signature on each day they take their medication

Week 2 (Day 1)

DOT helps cure TB!

Why does a health worker need to see you every day for TB medication?



Week 5 (Day 1)

You have also been diagnosed with diabetes

What do you know about diabetes?



Hawaii TB Nurses Training



Hawaii TB Nurses Documentation

Hawaii TB-Diabetes Patient Care Worksheet

Patient Name: _____ CC#: _____

Date and Initials	/ /	/ /	/ /	/ /	/ /
DM education	<input type="checkbox"/> None <input type="checkbox"/> <5 min <input type="checkbox"/> 5-10 min <input type="checkbox"/> 10-30 min	<input type="checkbox"/> None <input type="checkbox"/> <5 min <input type="checkbox"/> 5-10 min <input type="checkbox"/> 10-30 min	<input type="checkbox"/> None <input type="checkbox"/> <5 min <input type="checkbox"/> 5-10 min <input type="checkbox"/> 10-30 min	<input type="checkbox"/> None <input type="checkbox"/> <5 min <input type="checkbox"/> 5-10 min <input type="checkbox"/> 10-30 min	<input type="checkbox"/> None <input type="checkbox"/> <5 min <input type="checkbox"/> 5-10 min <input type="checkbox"/> 10-30 min
DM test results	Gluc: ___ mg/dL A1c: ___ %				
Seeing DM provider?	<input type="checkbox"/> Yes <input type="checkbox"/> No				
Taking DM medications?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> None needed	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> None needed	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> None needed	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> None needed	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> None needed
Comments:					

Can the TB Clinic Help with Glucose Control?

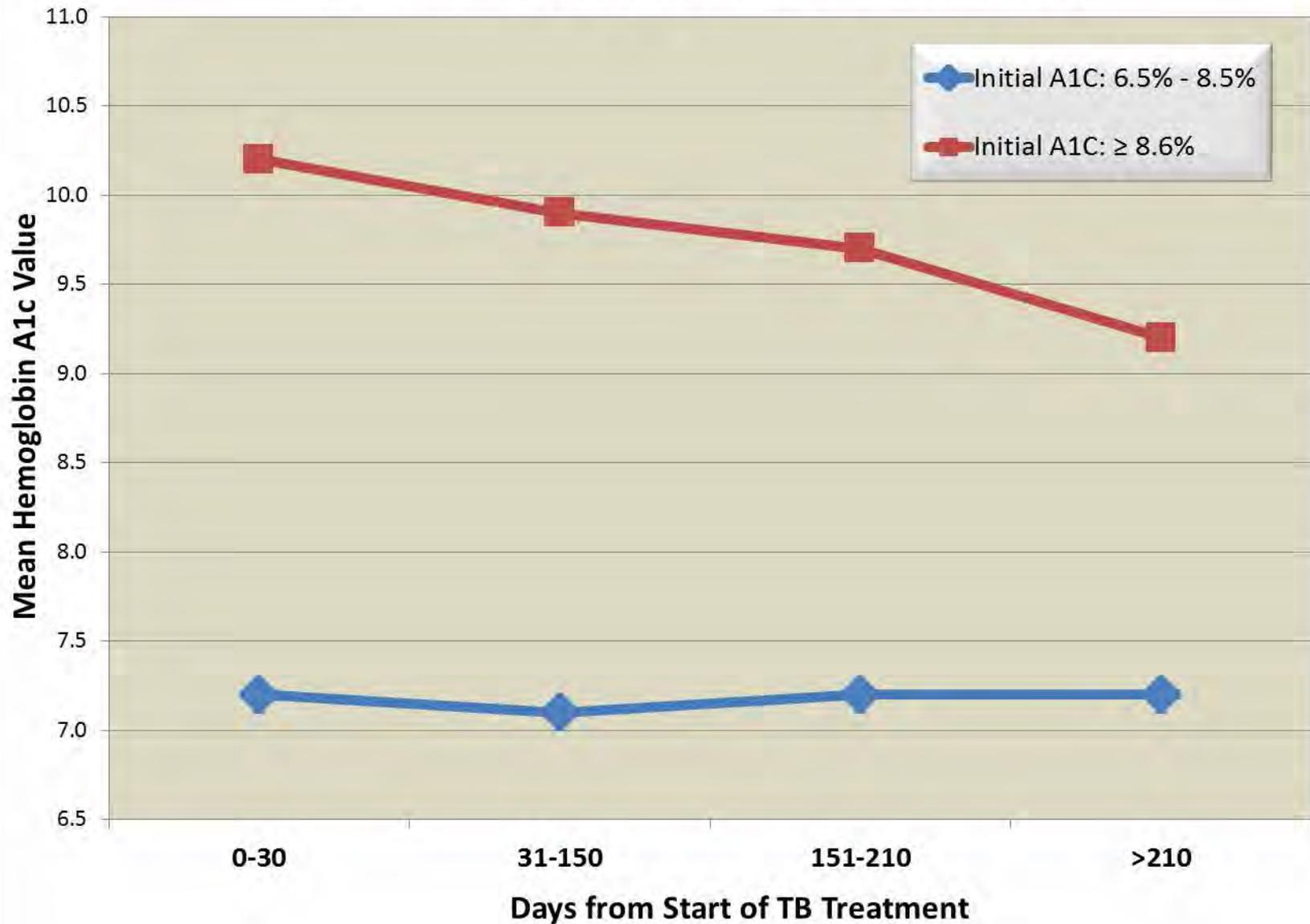
- A1c data collection (586 tests)
- Initial A1C on intake
- For follow-up, standing order for every 3 months (ADA standard)
- 55 patients with 2 or more results
 - 154 A1c tests in this cohort

Average A1C during TB treatment in Hawaii

(at least 2 measurements, 2011 - 2013, Cases=55, A1C's=154)



**Mean hemoglobin A1c during TB treatment: 2013 - 2014
(by initial HbA1c category, Hawaii TB-DM cases, n=50)**



Can Our TB Program Take Credit for This?

What is the natural change in A1c during TB treatment?

A1c should drop during treatment

Infections usually elevate blood glucose. Glucose is an “acute phase reactant”.

Patients may use this as an opportunity to address multiple health problems.

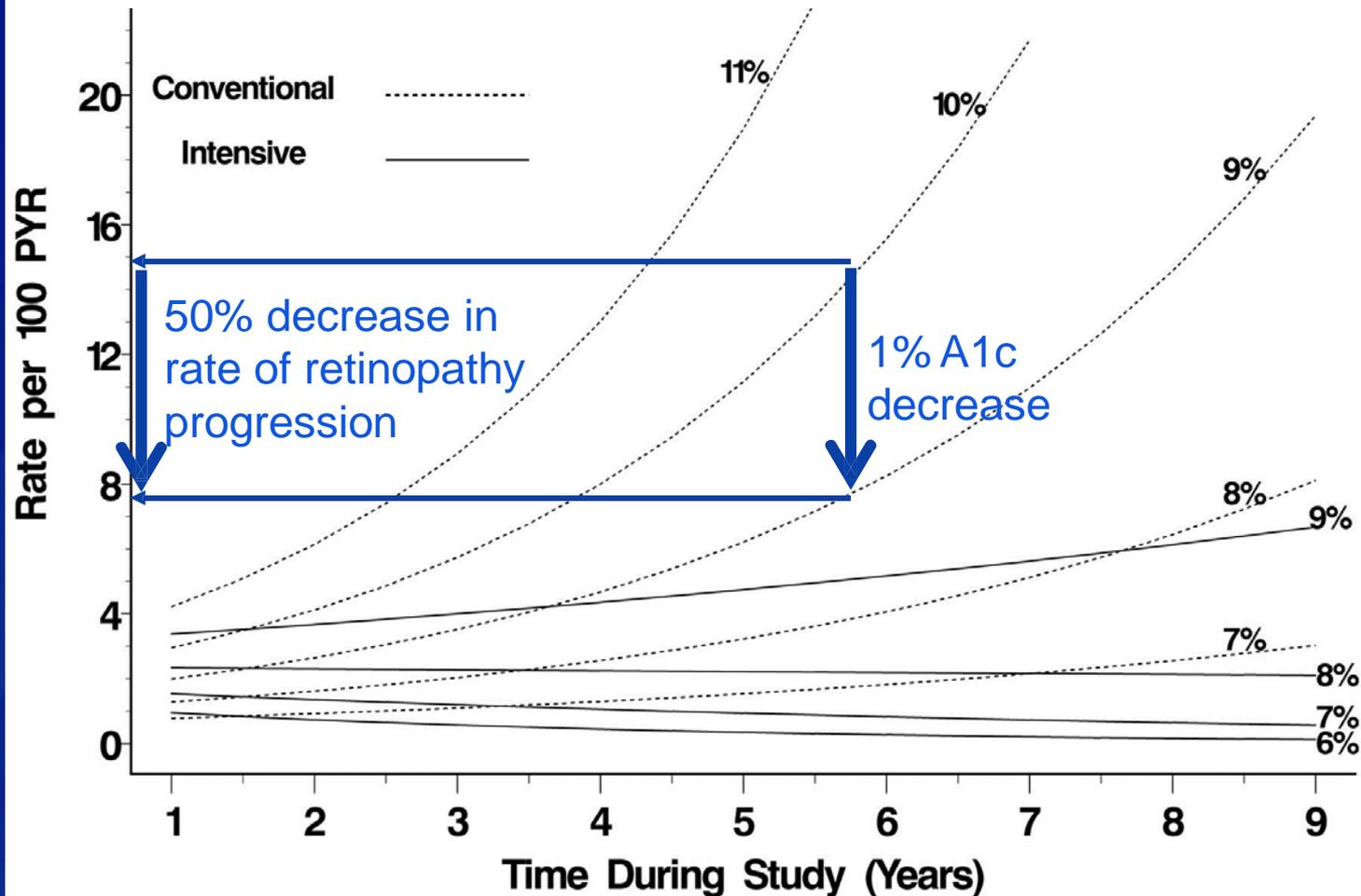
A1c should rise during treatment

Rifampin (and INH) will elevate blood glucose throughout treatment and can interfere with some DM medications.

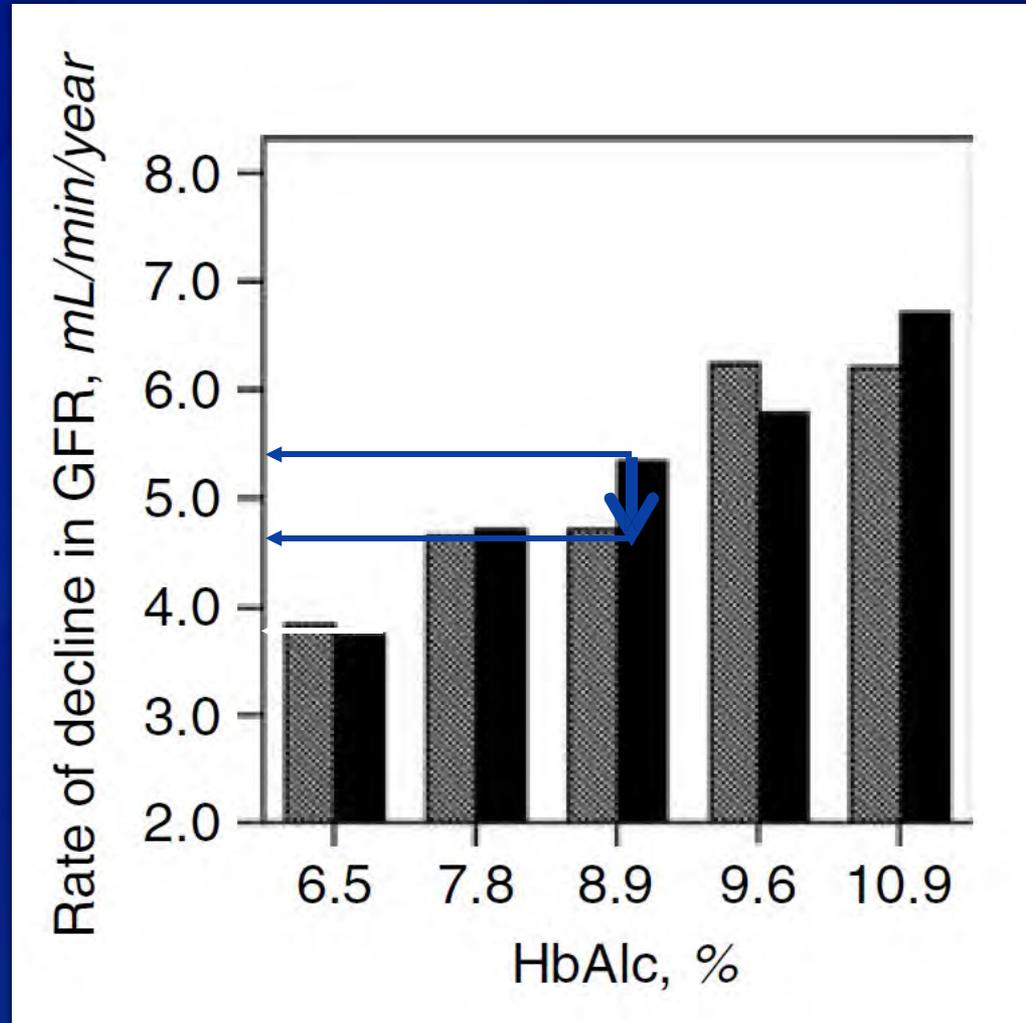
Almost all patients gain weight during TB treatment

1% A1c Change and Retinopathy

Risk of sustained retinopathy progression at assumed fixed levels of A1c over time within the intensive and conventional treatment groups.



1% A1c Change and Nephropathy



1% A1c Change and All-Cause Mortality

Table 4. Baseline predictors of time to death (all-cause mortality) in 227 type 2 diabetic patients with nephropathy followed for 6.5 years (Cox proportional hazard model)

Baseline	Hazard ratio (95% CI)	<i>P</i> value
Age per 10 years	1.82 (1.32 to 2.63)	<0.001
Albuminuria log ₁₀	2.56 (1.34 to 4.88)	<0.01
Systolic blood pressure per 10 mm Hg	1.14 (1.00 to 1.29)	0.049
HbA1c per 1%	1.24 (1.05 to 1.47)	<0.01

The 1% Solution...

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 Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

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Diabetes Public Health Resource

CDC's Division of Diabetes Translation translates diabetes research into daily practice to understand the impact of the disease, influence health outcomes, and improve access to quality health care.

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Type 2 Diabetes: Resolve to Prevent or Delay

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Diabetes Topics



Diabetes & Me

Basic Information, Frequently Asked Questions, Prevent Diabetes...



Data & Trends

Statistics, Surveillance Data, National Diabetes Fact Sheet, Maps...



Education Resources

Partner Information, Community Intervention Tools, Education...



Publications

Fact Sheets, Reports, Prevention & Control Materials Brochures...



Projects & Programs

Special Projects, State Diabetes Prevention Control Programs, Initiatives...



News & Resources

News, Press Releases, Diabetes Issues, For the Media, Conferences...

National Diabetes Prevention Program

Learn about this CDC-led program for preventing type 2 diabetes.

Find local programs in CDC's national registry.

Apply for program recognition by CDC .

Diabetes Spotlight

 CDC data show declines in 5 major diabetes-related complications among U.S. adults

[Learn more about a new](#)

DIABETES

YOU COULD BE AT RISK

TAKE THE TEST. KNOW YOUR SCORE.

[START](#)

The 1% Solution...

The image is a screenshot of the CDC website's "Diabetes Public Health Resource" page. At the top, the CDC logo and name are visible, along with the tagline "CDC 24/7: Saving Lives. Protecting People.™". A search bar is located on the right. Below the navigation menu, the page title "Diabetes Public Health Resource" is displayed. The main content area features a section for "Type 2 Diabetes:" with a background image of a person. A large, rounded rectangular callout box is overlaid on the page, containing the text: "For every 1% reduction in A1c (e.g., from 8.0% to 7.0%), the risk of developing eye, kidney, and nerve disease is reduced by.....". To the right of the callout box, there are links for "Email page link" and "Print page".

CDC Home
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CDC 24/7: Saving Lives. Protecting People.™

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Diabetes Public Health Resource

CDC's Division of Diabetes Translation translates diabetes research into daily practice to understand the disease, influence outcomes, and improve quality of life.

Type 2 Diabetes:

“For every 1% reduction in A1c (e.g., from 8.0% to 7.0%), the risk of developing eye, kidney, and nerve disease is reduced by.....”

- About
- Spanish

Diabetes

Diabetes Risk

ES RISK

T. MORE.

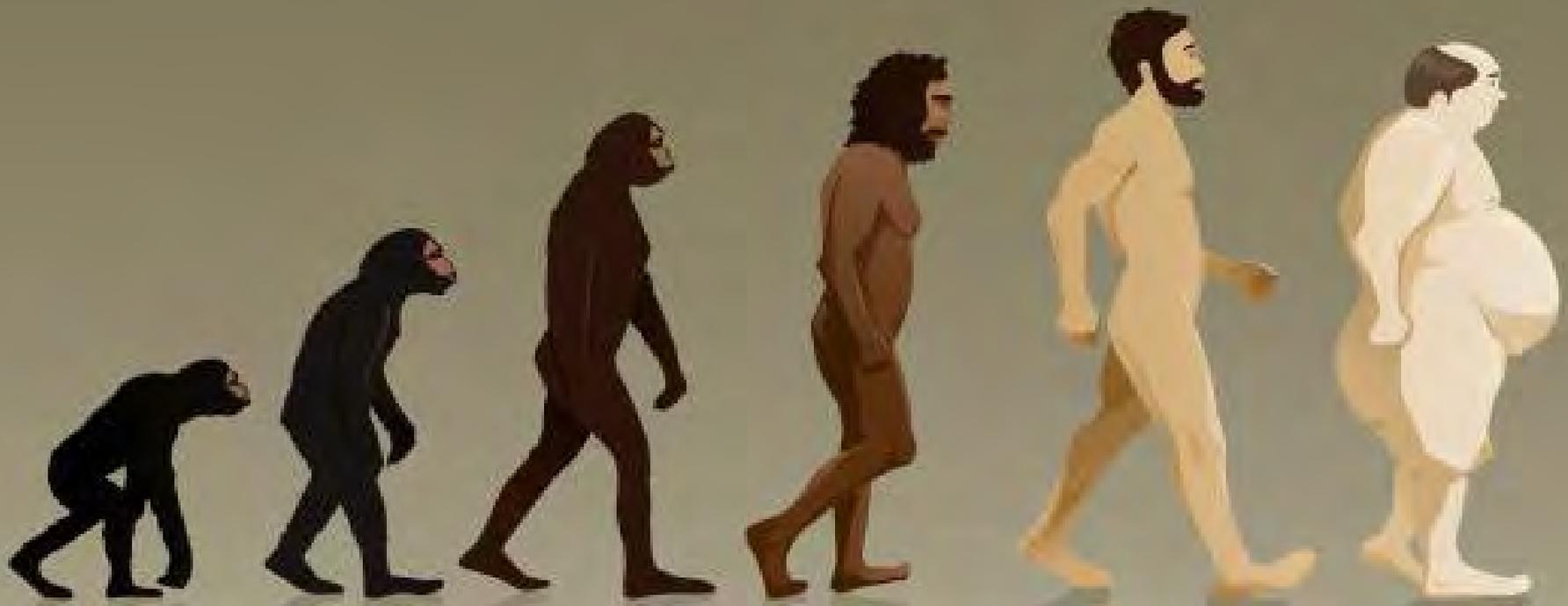
Double Trouble: TB-DM Lit Review

1. Does DM cause TB? **Yes!**
2. Does diabetes affect TB treatment? **Yes!**
3. Can we make a difference?
 - We can diagnose TB with active case-finding for early diagnosis to improve outcomes
 - We can identify high-risk individuals in DM clinics for TB prevention

TB-DM: Opportunities for Collaboration

- TB 101: A few of the basics
- TB-DM Current Epidemiology
- TB-DM Brief Research Update
- TB-DM Current Collaborations
- **TB-DM Opportunities for Partnership**

TB-DM: Evolution of Man



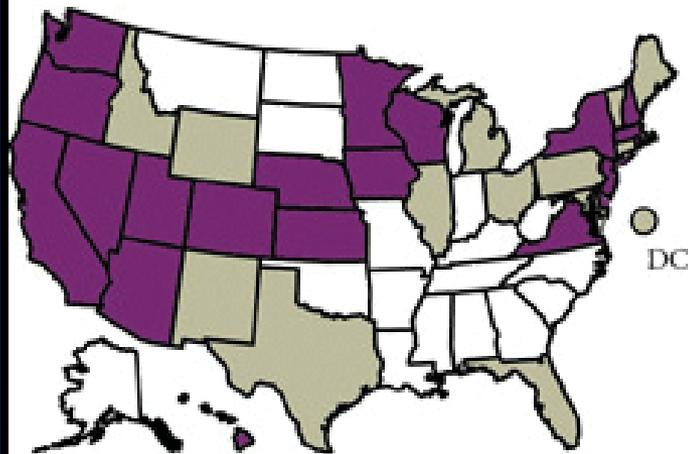
TB Screening in DM Clinic

- 1. Where was my patient born?**
2. What is the current level of glucose control?
3. What is the age of my patient?
4. What test should I use?

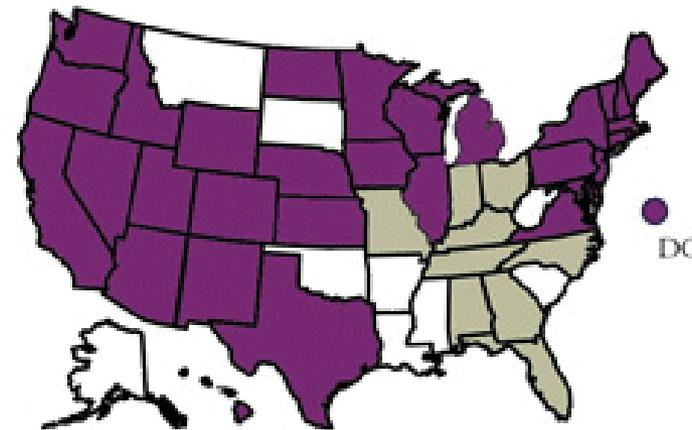
TB Screening in DM Clinic

Percentage of TB Cases Among Foreign-born Persons, United States*

2000



2010



$\geq 50\%$ 25%–49% $<25\%$

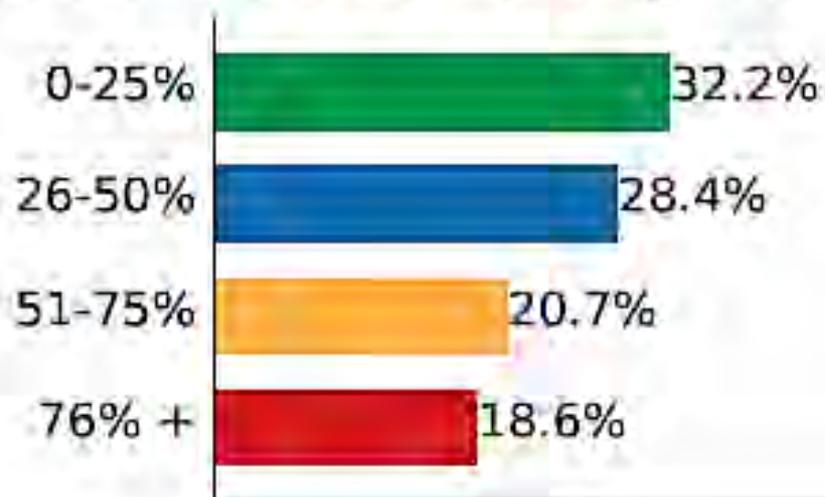
*Updated as of July 21, 2011.

Poll 2:

Approximately what percent of your DM patients are foreign born?

- 0-25%
- 26-50%
- 51-75%
- 76%+

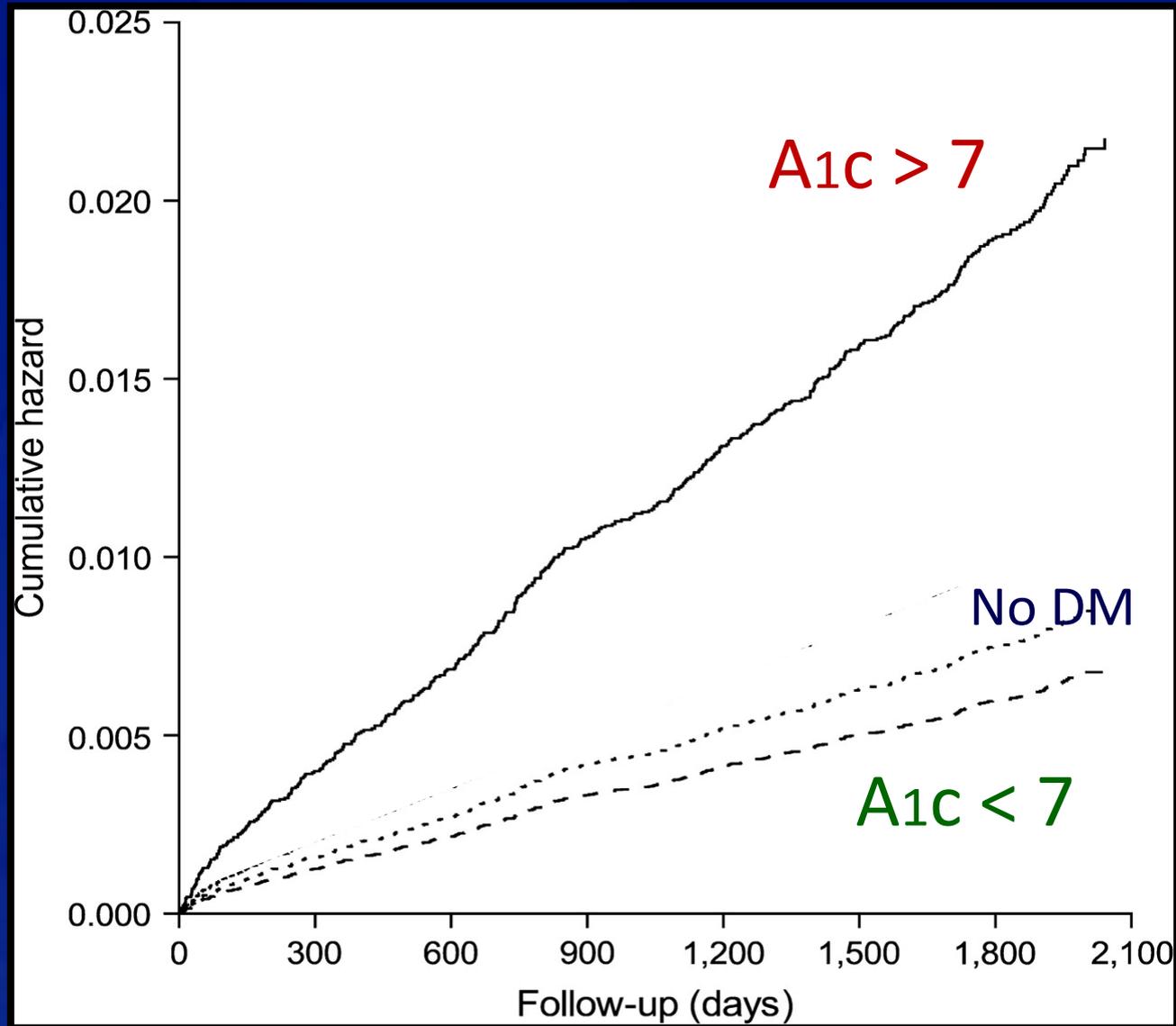
Approximately what percent of your DM patients are foreign born?



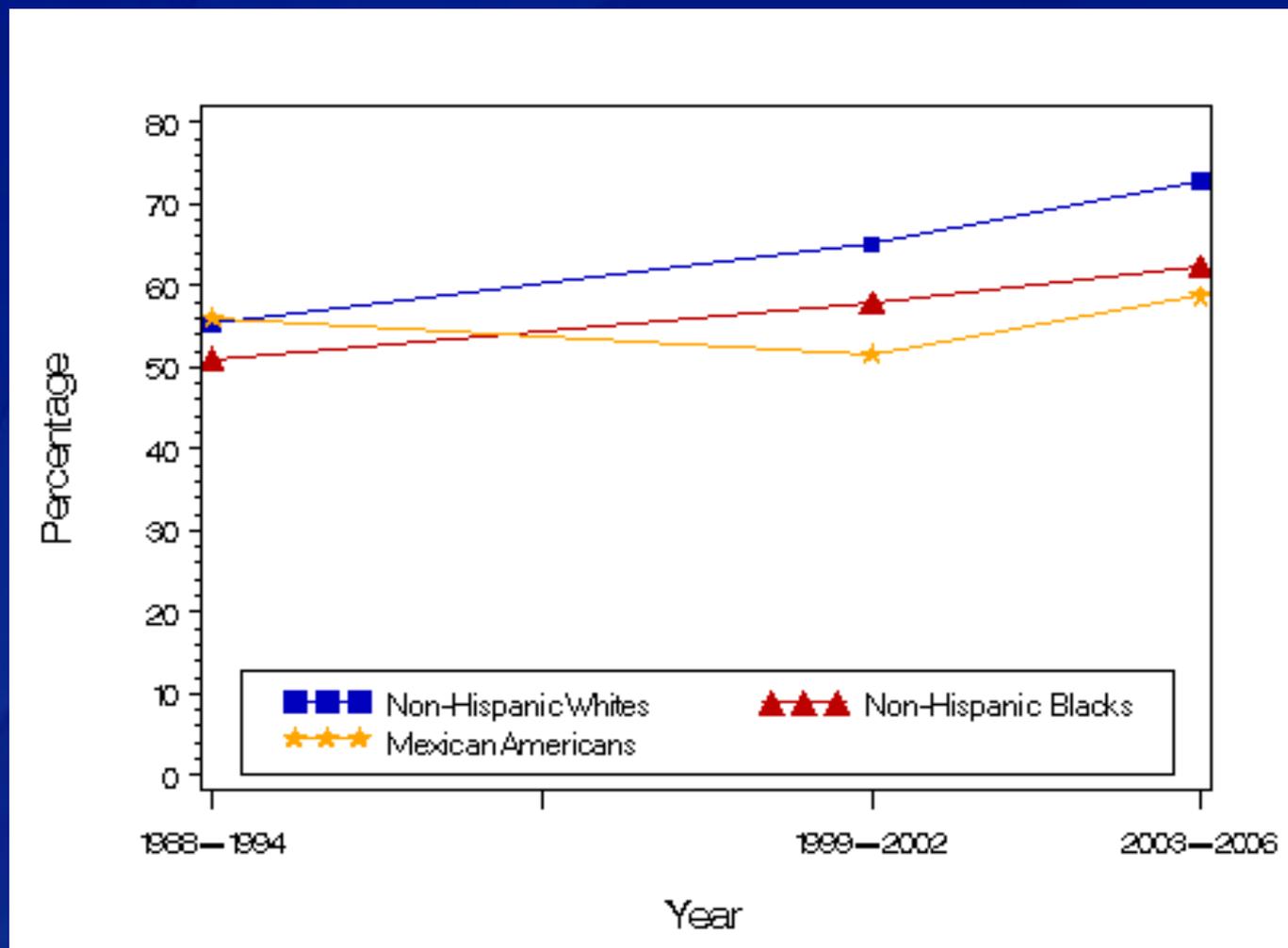
TB Screening in DM Clinic

1. Where was my patient born?
- 2. What is the current level of glucose control?**
3. What is the age of my patient?
4. What test should I use?

TB-DM: Diabetes Control



Percentage of DM with A1c < 8% by Race/Ethnicity, United States, 1988 - 2006

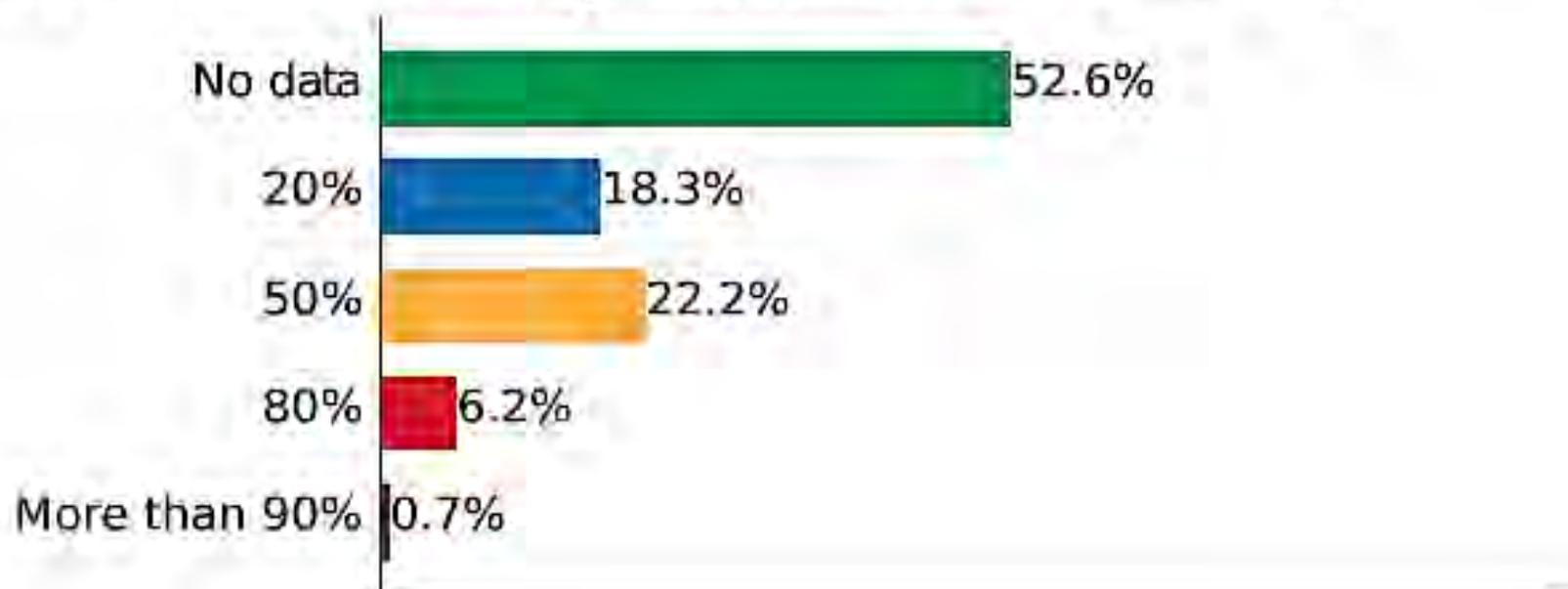


Poll 3:

Approximately what percent of your DM patients currently have an A1C < 8.5?

- No data
- 20%
- 50%
- 80%
- More than 90%

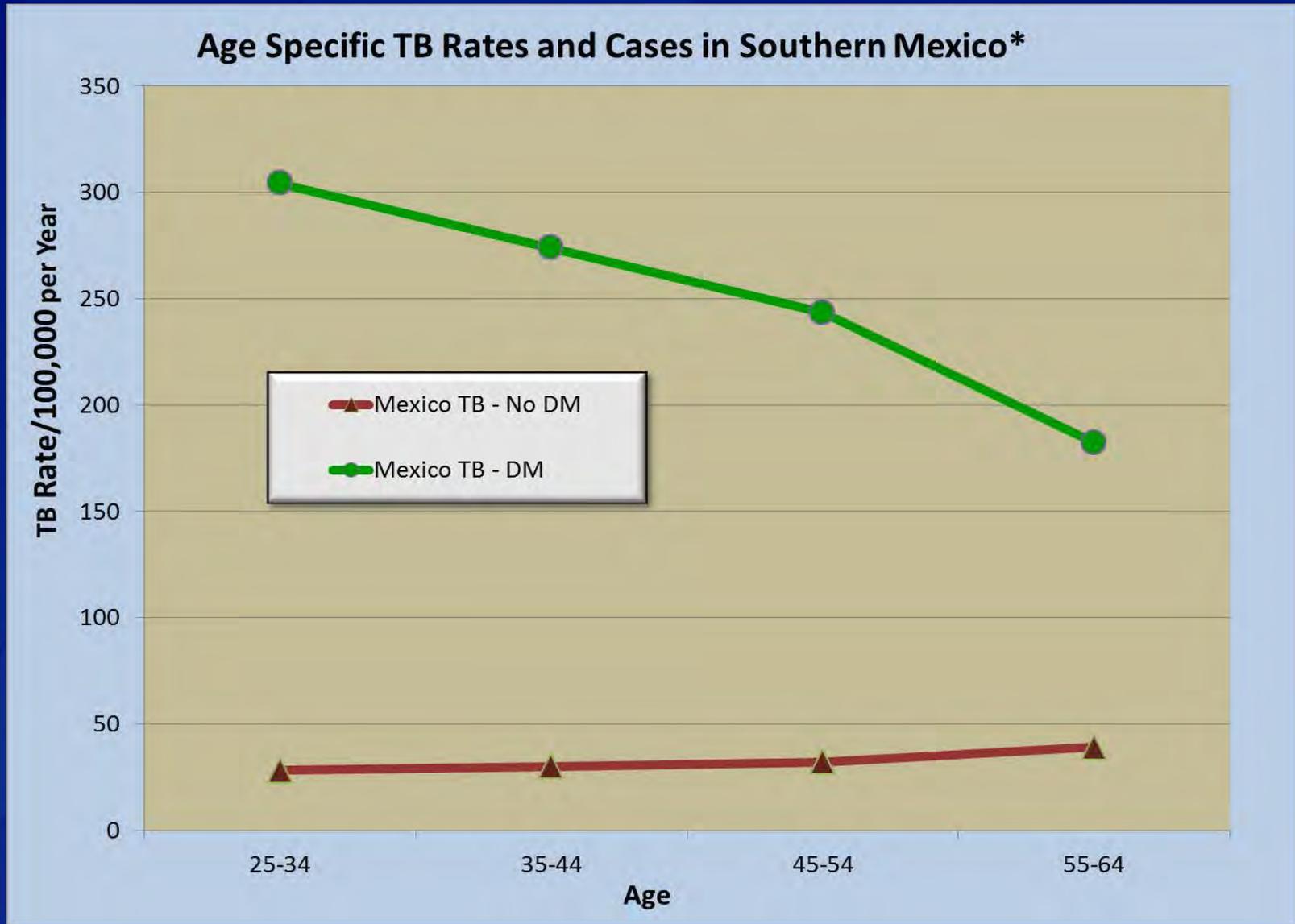
Approximately what percent of your DM patients currently have an A1C < 8.5?



TB Screening in DM Clinic

1. Where was my patient born?
2. What is the current level of glucose control?
- 3. What is the age of my patient?**
4. What test should I use?

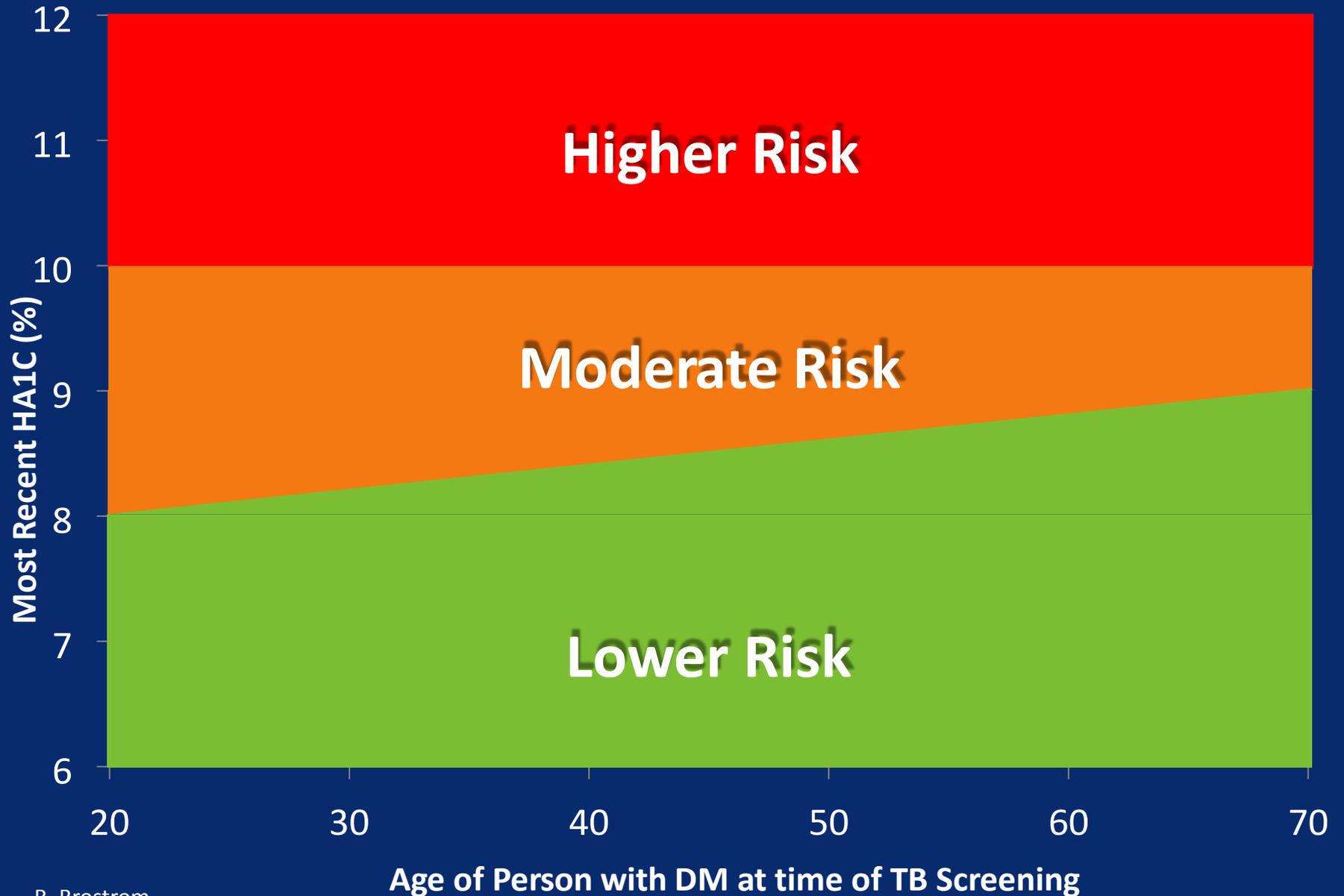
TB-DM: Younger DM Cases at Highest Risk



Summary: TB Infection for DM Cases

- 1) Younger DM cases seem to be at a higher relative risk of TB.
 - ? Younger DM cases may be closer to their initial TB exposure
- 2) Younger DM cases tolerate preventive treatment better
- 3) Younger DM cases will realize more long-term benefit from preventive treatment

Possible Risk Profile for TB Screening in Persons with DM



TB Screening in DM Clinic

1. Where was my patient born?
2. What is the current level of glucose control?
3. What is the age of my patient?
4. **What TB screening test should I use?**

TB Screening Cornucopia



- TB skin test: TST
- TB blood test: IGRA
- TB Symptom Screen
- Chest X-ray (CXR)
- Sputum AFB Smear
- GeneXpert MTB-Rif

TST and IGRA

TST

- Skin test
- 2 patient visits
- **BCG falsely positive**
- Less expensive
- Reader variability
- Results in 2 to 3 days

IGRA

- Blood test
- 1 patient visit
- Specific antigens
- More expensive
- Lab variability
- Results in 1 or 2 days

IGRA or TST? Diabetes

- For DM cases with good control
 - TST seems to work fairly well
 - Test placement and reading requires
- For younger individuals with DM
 - TST has more false positives (ex. BCG vaccination) and IGRA should reduce the number of TB-infections you will need to treat.
- For older individuals with DM (ex. ESRD)
 - TST has many false negatives and can miss 30% to 50% of TB-infected individuals. IGRA seems to perform better in this population.

TB-DM for DM Clinics: Where to Start?

Screening in DM Clinic for TB Disease

- WHO?** All persons with diabetes, especially foreign born individuals from high-risk countries
- HOW?** Use a routine periodic **TB-symptom screen** to find TB cases
- WHEN?** Annual symptom screening
- THEN?** Refer all positives to TB Clinic for chest x-ray and further workup

TB-DM for DM Clinics: Where to Start?

Screening in DM Clinic for TB Infection

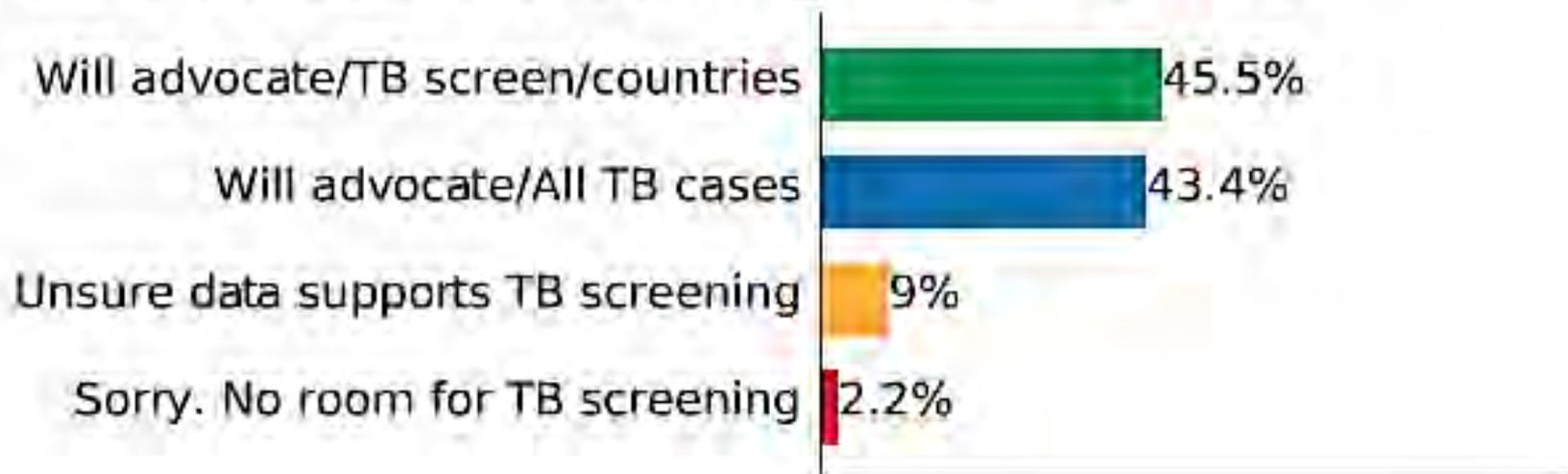
- WHO?** Focus on those with **A1C > 8%**
Focus on those under **age 50 y.o.**
- HOW?** Use **TST or IGRA** to dx TB infection
- WHEN?** Test for TB infection **every 2 to 5 years**
- THEN?** Refer all positives to TB Clinic for treatment. 3HP ideal for short course treatment

Poll 4:

Tuberculosis screening in your DM clinic—

- I will advocate for TB screening for DM cases from countries with high TB rates.
- I will advocate for TB screening for all DM cases.
- I need to think about this. I am still not sure the data supports routine TB screening.
- Sorry Dr B, but we have enough problems with DM control. Right now, there's no room for TB screening in my DM program.

Tuberculosis screening in DM clinic:



Enhanced TB-DM Program Collaboration



Enhanced TB-DM Program Collaboration

- Seek out and meet with your TB program
 - Choose a pilot DM clinic serving high-risk cases.
 - Decide together which DM cases need to be screened for TB?
 - Who is going to perform the TB screening?
 - Who is going to pay for the TB screening?
 - How are the screening results going to be recorded and communicated?

How Else Can DM Programs Help?

- Provide culturally appropriate patient education materials to TB clinic
- Provide feedback on TB materials
- Offer to teach basic DM principles to TB nurses and DOT workers
 - Teach RBG, A1C, DM education
- Consider TB-only DM classes



Metformin could be used to treat tuberculosis

Discussion in 'Diabetes News' started by DCUK NewsBot, Nov 20, 2014.

Sci Transl Med 19 November 2014:

Vol. 6, Issue 263, p. 263ra159

Sci. Transl. Med. DOI: 10.1126/scitranslmed.3009885

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RESEARCH ARTICLE

TUBERCULOSIS

Metformin as adjunct antituberculosis therapy

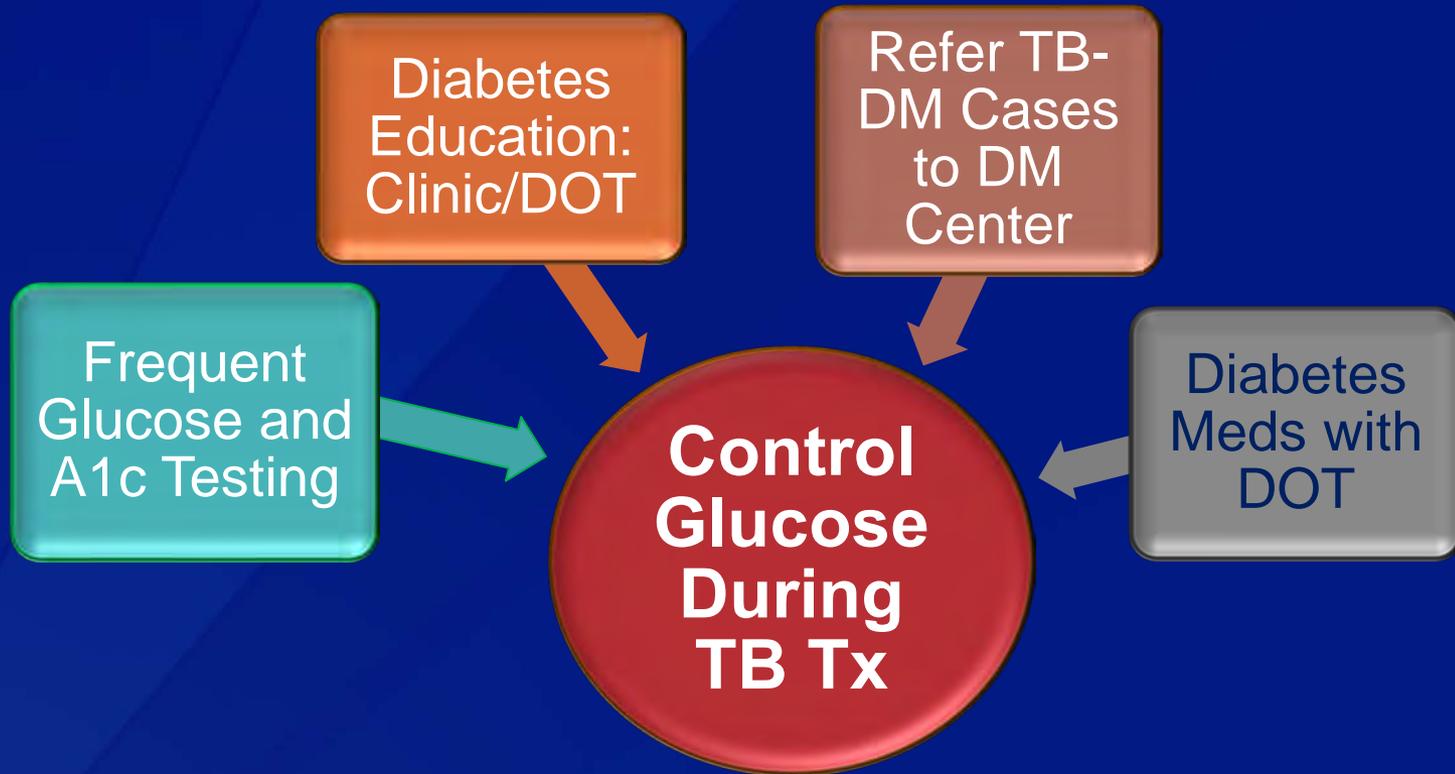
Amit Singhal^{1,*}, Liu Jie^{1,†}, Pavanish Kumar^{1,†}, Gan Suay Hong², Melvin Khee-Shing Leow^{3,4},

Bhairav Paleja¹, Liana Tsenova^{5,6}, Natalia Kurepina⁵, Jinmiao Chen¹, Francesca Zolezzi¹,

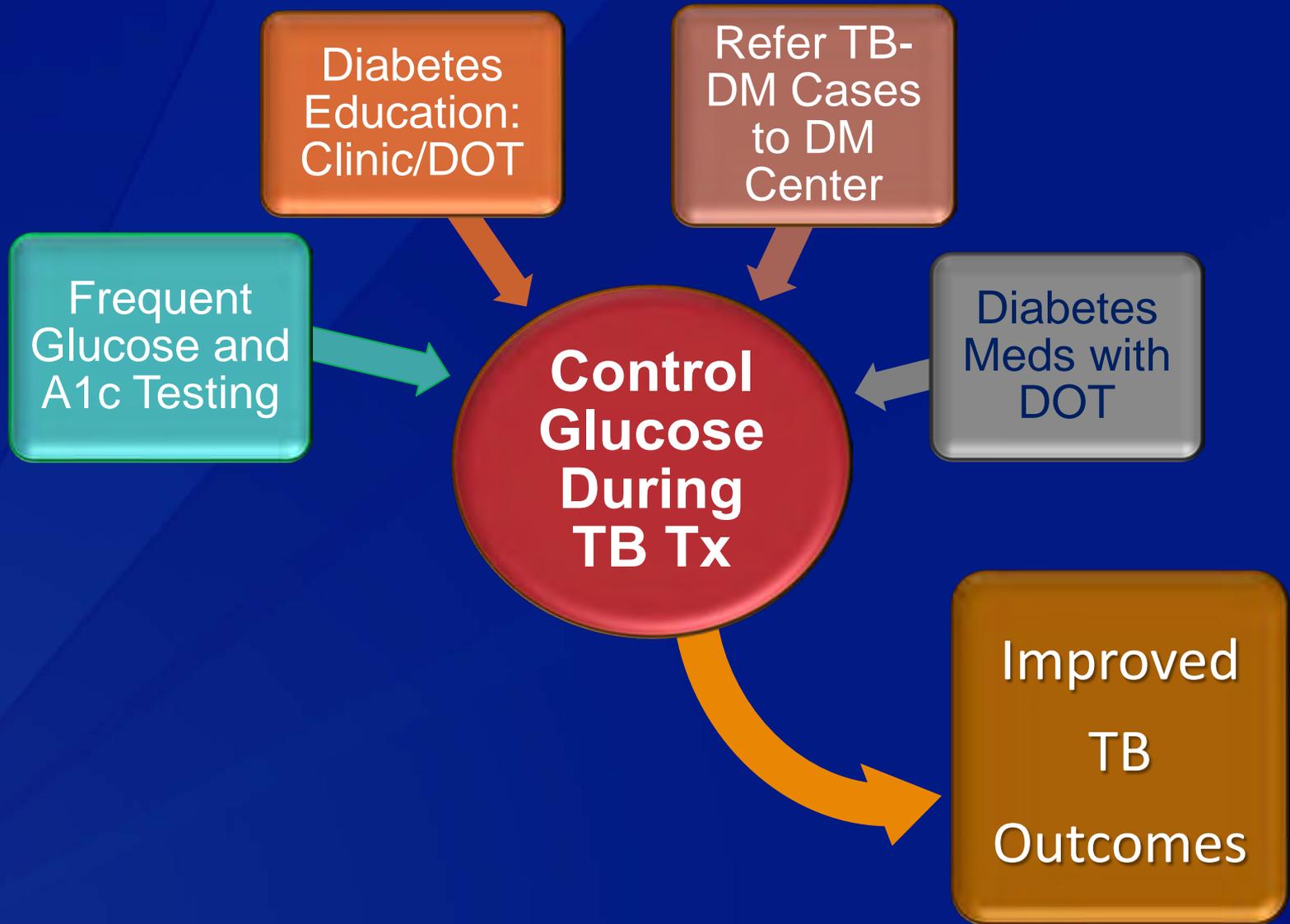
Barry Kreiswirth⁵, Michael Poidinger^{1,7}, Cynthia Chee², Gilla Kaplan^{5,8}, Yee Tang Wang² and

Gennaro De Libero^{1,9,*}

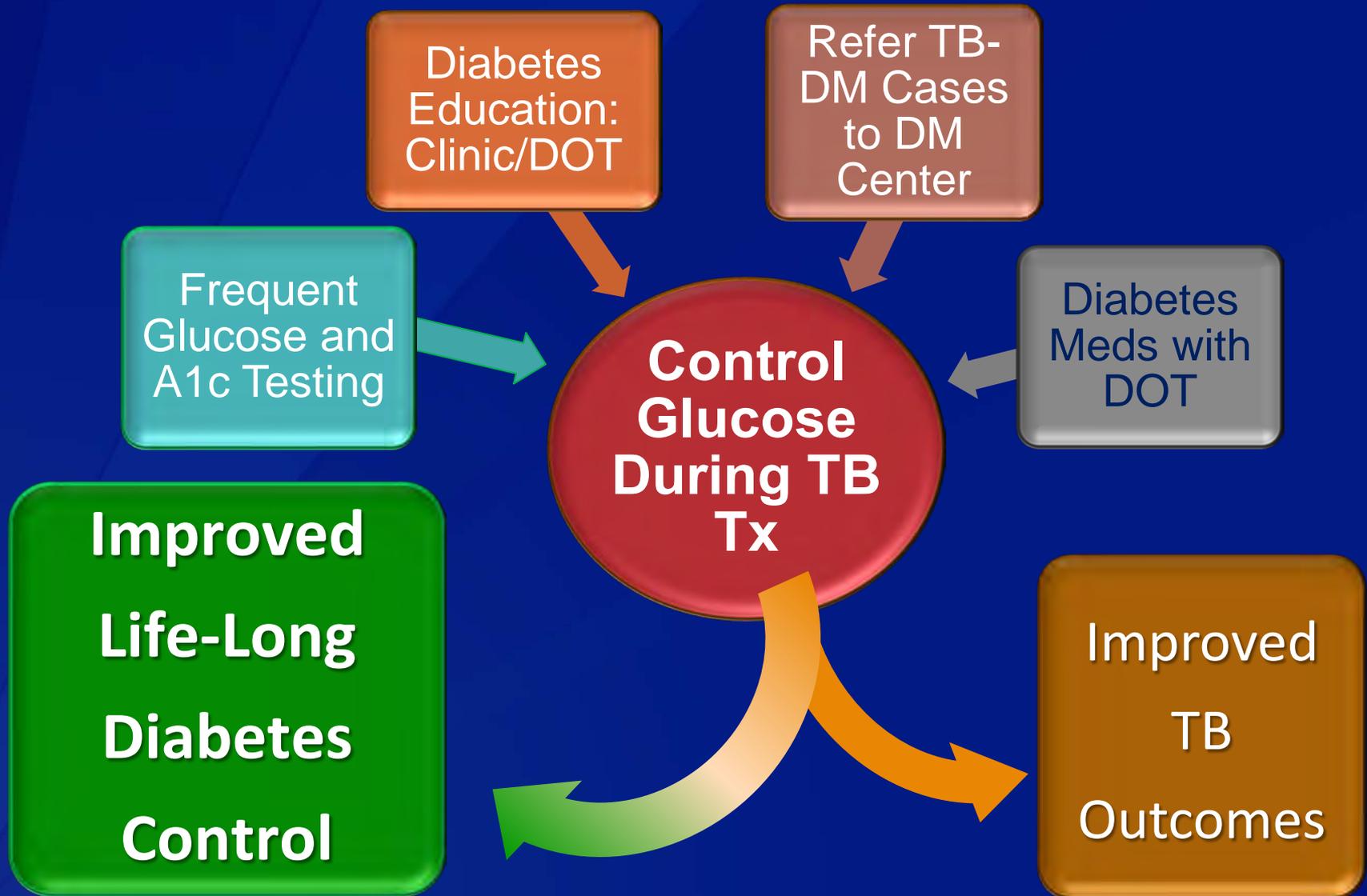
TB-DM – Framework Summary



TB-DM – Framework Summary



TB-DM – Framework Summary



Resources

Collaborative framework for care and control of tuberculosis and diabetes:

http://www.who.int/diabetes/publications/tb_diabetes2011/en/

Pacific Standards for Management of TB and DM:

<http://www.spc.int/tb/component/content/article/75-pacific-standards-for-management-of-tb-and-diabetes>

Key Messages for TB and DM:

<http://www.thearc.org.au/resources/flipchart>



TB-DM: Opportunities for Collaboration

TB DM Cases

- Screening for TB Disease (Active TB)
- Screening for TB Infection (Latent TB)

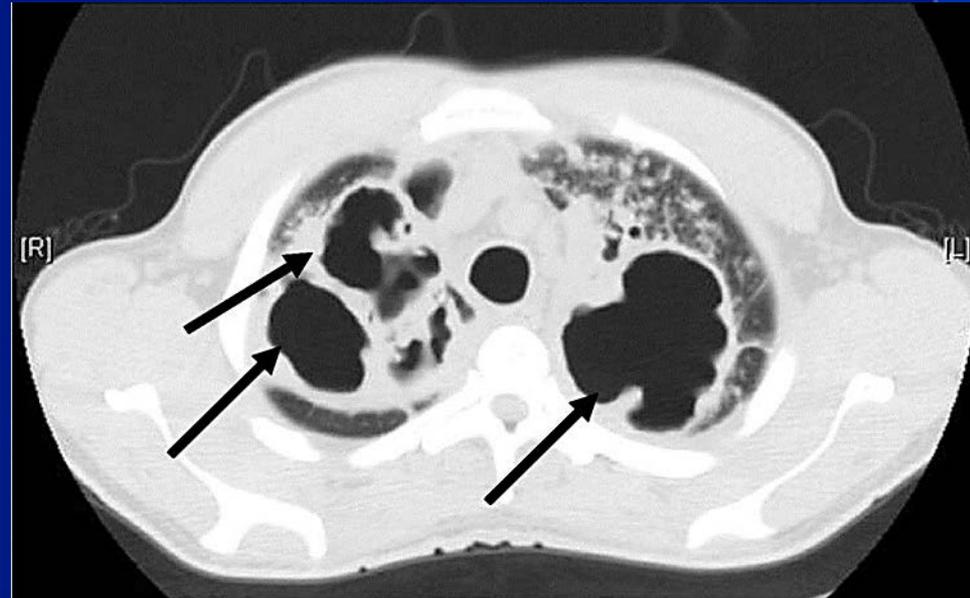
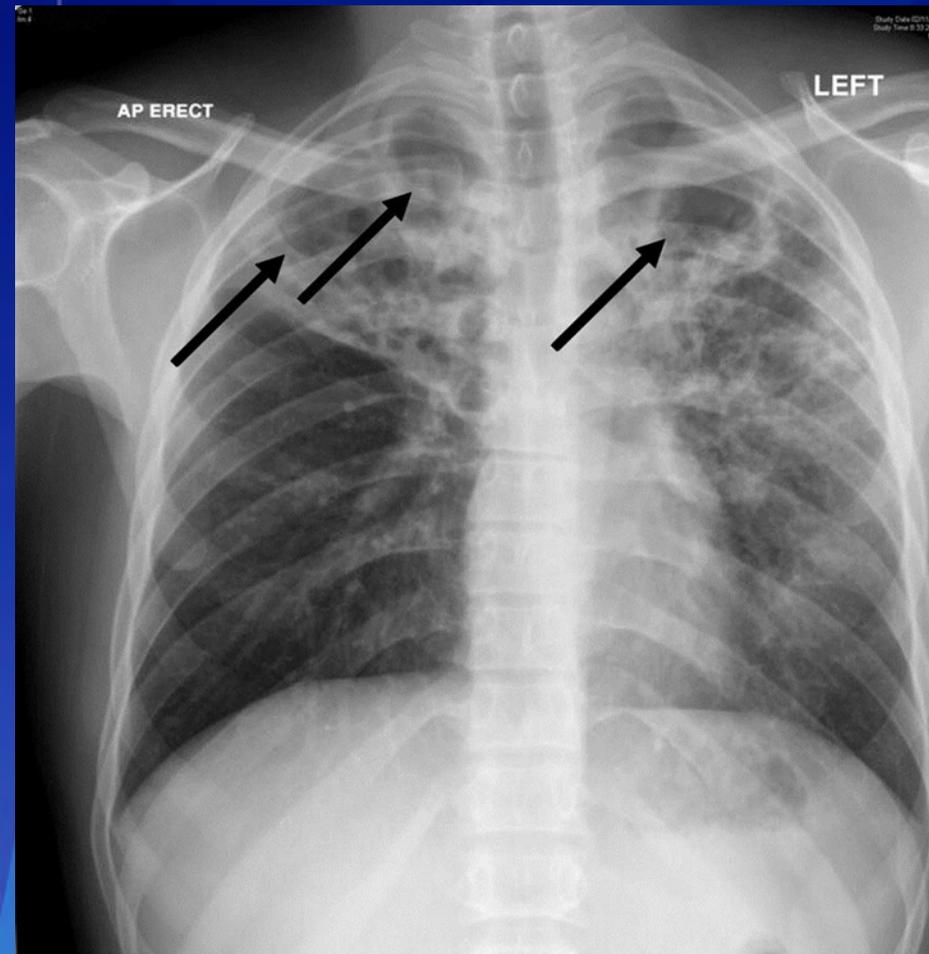
TB-DM for DM Clinics: Case

- Mr. Hernandez is a 43 year old male from Mexico, living and working in Houston TX
- Complains of blurry vision and nocturia
- Primary care clinician ordered a RBG (276 mg/dl)
- Referral made to DM clinic for care
- He is admitted to DM clinic, initial A1C is 9.2%
- He is very compliant and attends a total of 6 weekly group sessions (2 hours each) for DM education
- After 3 months, his A1C is down to 8.7%

TB-DM for DM Clinics: Case

- After 4 months, another patient noted that Mr. Hernandez had been coughing in the waiting area over the past three weeks
- DM clinic told him to see his primary care doc to manage his “cold”
- 4 weeks later, he sees his primary care clinician who tries to manage him with some outpatient antibiotics (levofloxacin 500mg x 1 week). It helped some, but the cough persisted
- CXR was ordered:

TB-DM for DM Clinics: Case



TB-DM for DM Clinics: Case

- Sputum was ordered for AFB and was 4+
- Referral made to public health for TB treatment
- Started on 4 medications (R-I-P-E)
- Initial RBG after treatment initiated was 340 mg/dl
- After 2 weeks, public health inquired about other patients seen at DM clinic
- Contact investigation was initiated for 23 other people with DM who had significant contact to this case
 - 16 other patients, 7 DM clinic staff

TB-DM for DM Clinics: Case

- After 6 weeks, TB culture was confirmed and was sensitive to all 4 TB medications
- From the workplace contact investigation, a total of 8 contacts (7 patients, 1 staff) were found to have a positive IGRA test
 - 5 of these had no prior TB test
 - 3 had positive TSTs in the past
 - All 8 individuals are placed on preventive treatment with 3HP

TB-DM for DM Clinics: Case

- After 2 months, he continued to have positive AFB. In response, TB treatment was extended to 9 months
- TB and DM clinic met to optimize his treatment. Sulfonylureas were discontinued and metformin was increased. Patient returned to DM clinic after he was deemed non-infectious by the TB program
- DM lifestyle changes were reinforced by both programs, and patient received DM education and monitoring as part of his DOT for TB
- After 9 months, patient completed treatment

TB-DM for DM Clinics: Where to Start?

Screening in DM Clinic for TB Disease

- WHO?** All persons with diabetes, especially foreign born individuals from high-risk countries
- HOW?** Use a routine periodic **TB-symptom screen** to find TB cases
- WHEN?** Annual symptom screening
- THEN?** Refer all positives to TB Clinic for chest x-ray and further workup

Symptoms of TB Disease

- Prolonged Cough (>2-3 weeks duration)
- Productive or Dry Cough
- Coughing Up Blood
- Feeling Weak or Constantly Tired
- Fever
- Night Sweats
- Loss of Appetite
- Weight Loss
- Chest Pain

Who is at Highest Risk of TB?

A. 32 y.o. born in the Cambodia

A1c = 7.5 Loss of appetite

B. 57 y.o. Caucasian from New York

A1c = 8.7 Homeless Cough 2 weeks

TB-DM for DM Clinics: Where to Start?

Screening in DM Clinic for TB Infection

- WHO?** Focus on those with **A1C > 8%**
Focus on those under **age 50 y.o.**
- HOW?** Use **TST or IGRA** to dx TB infection
- WHEN?** Test for TB infection **every 2 to 5 years**
- THEN?** Refer all positives to TB Clinic for treatment. 3HP ideal for short course treatment

Who Needs Latent TB Screening?

A. 32 y.o. born in the Philippines

A1c = 9.3

B. 67 y.o. Caucasian from Iowa

A1c = 7.3

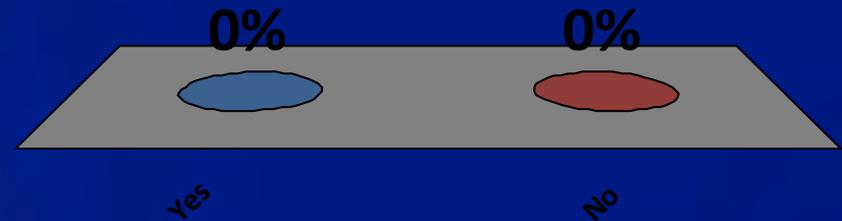
Case Study

- 36 yr old Latino woman with close exposure to an infectious individual with drug susceptible pulmonary TB
- She has a long history of poorly controlled diabetes

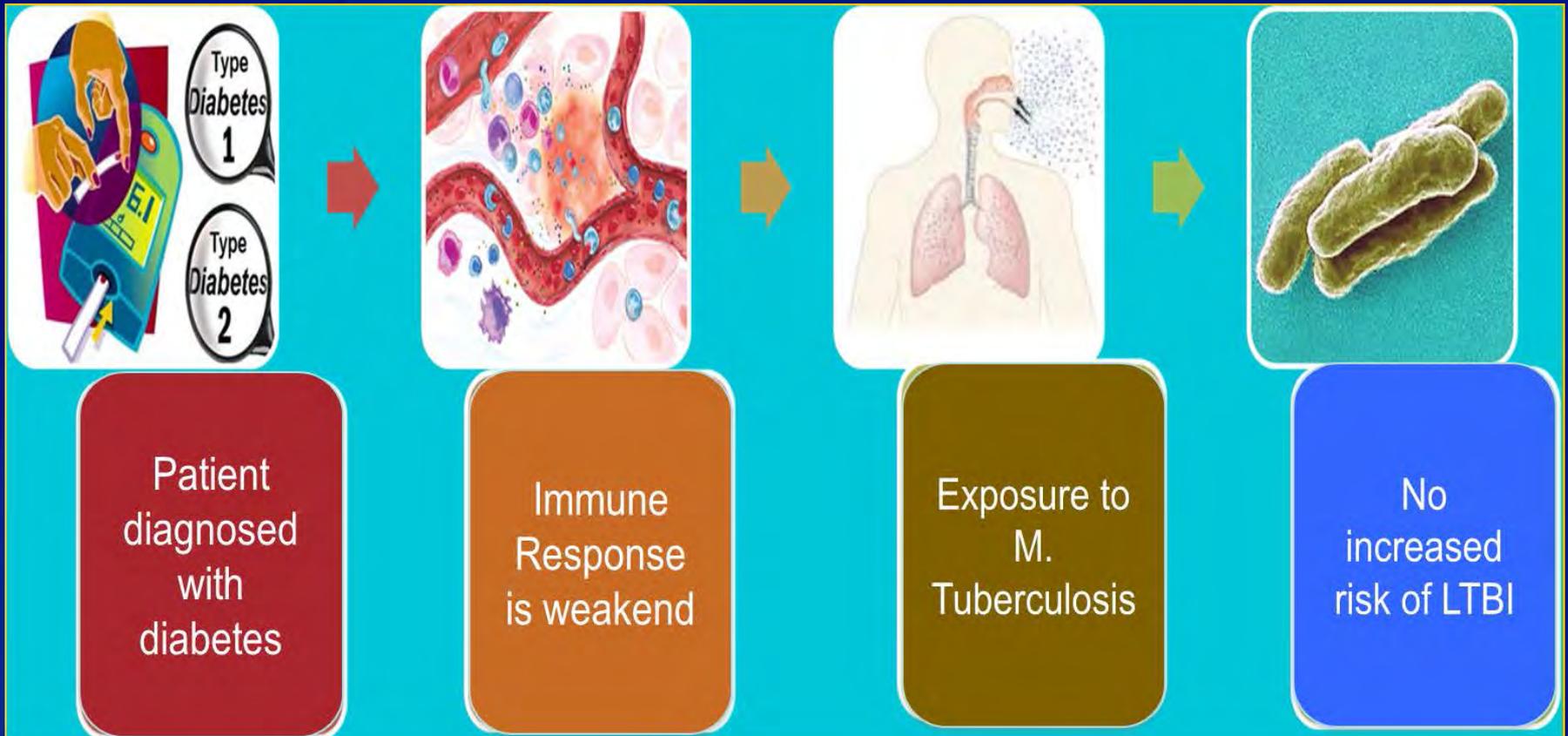
Compared to other contacts to the source case is she more at risk of developing LTBI?

A. Yes

B. * No



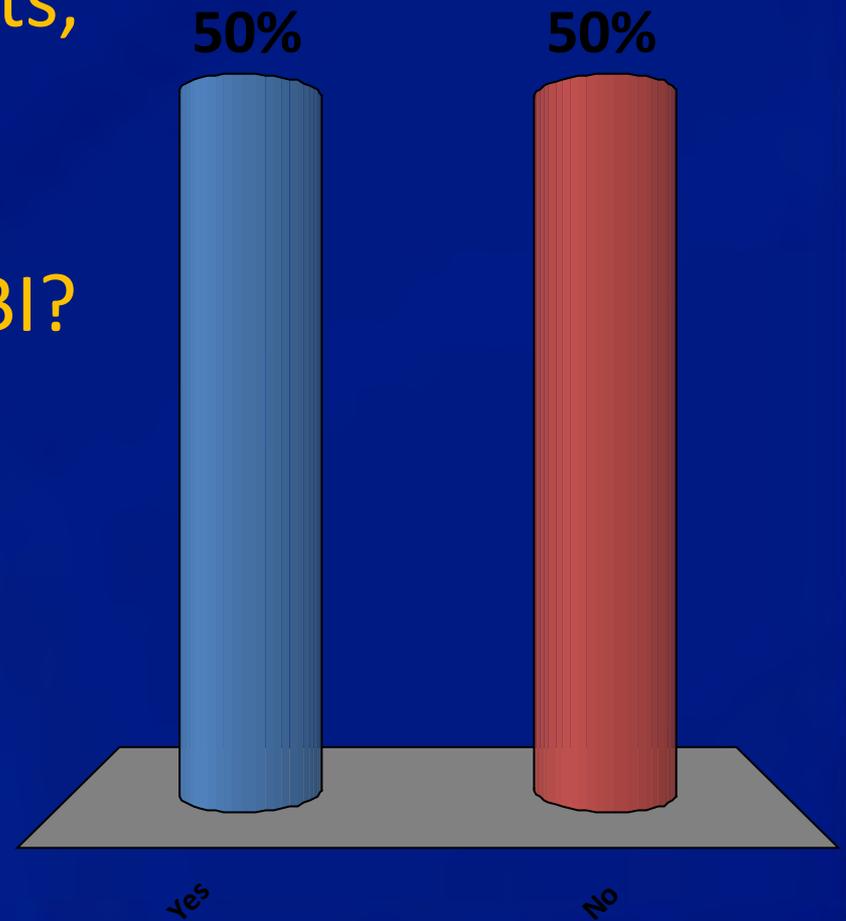
Linkage Between Tuberculosis and Diabetes



Compared to other contacts,
is she more at risk of
progressing to active TB
disease if she develops LTBI?

A. *Yes

B. No



WHO 2009

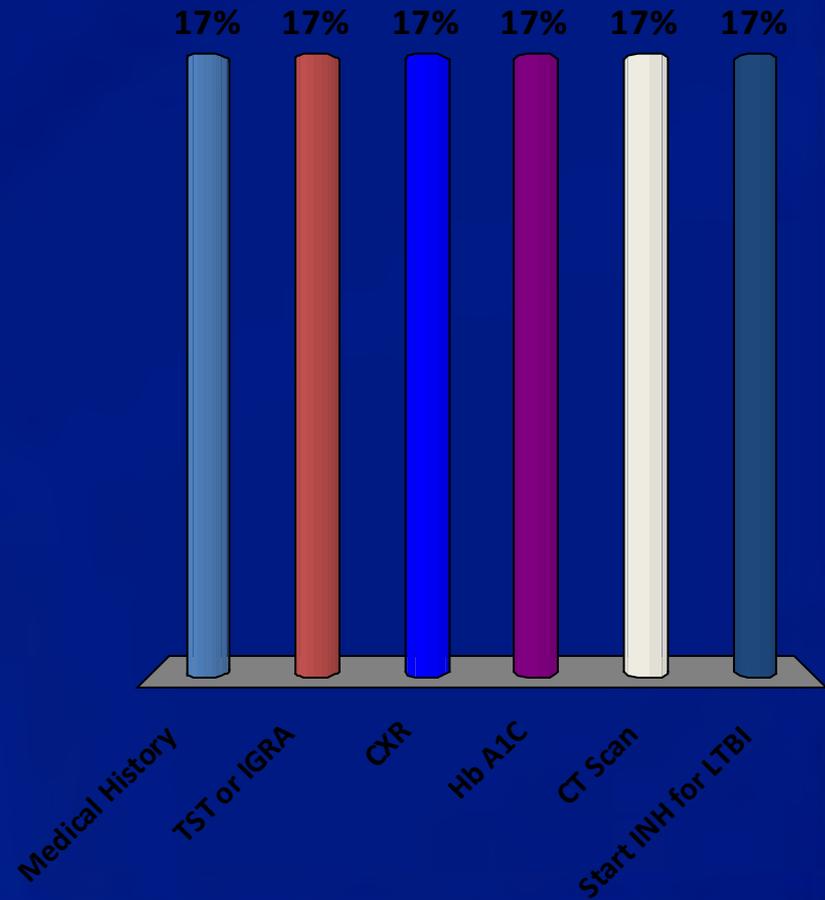
People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB

People with diabetes have a 2-3 times higher risk of TB compared to people without diabetes

About 10% of TB cases globally are linked to diabetes

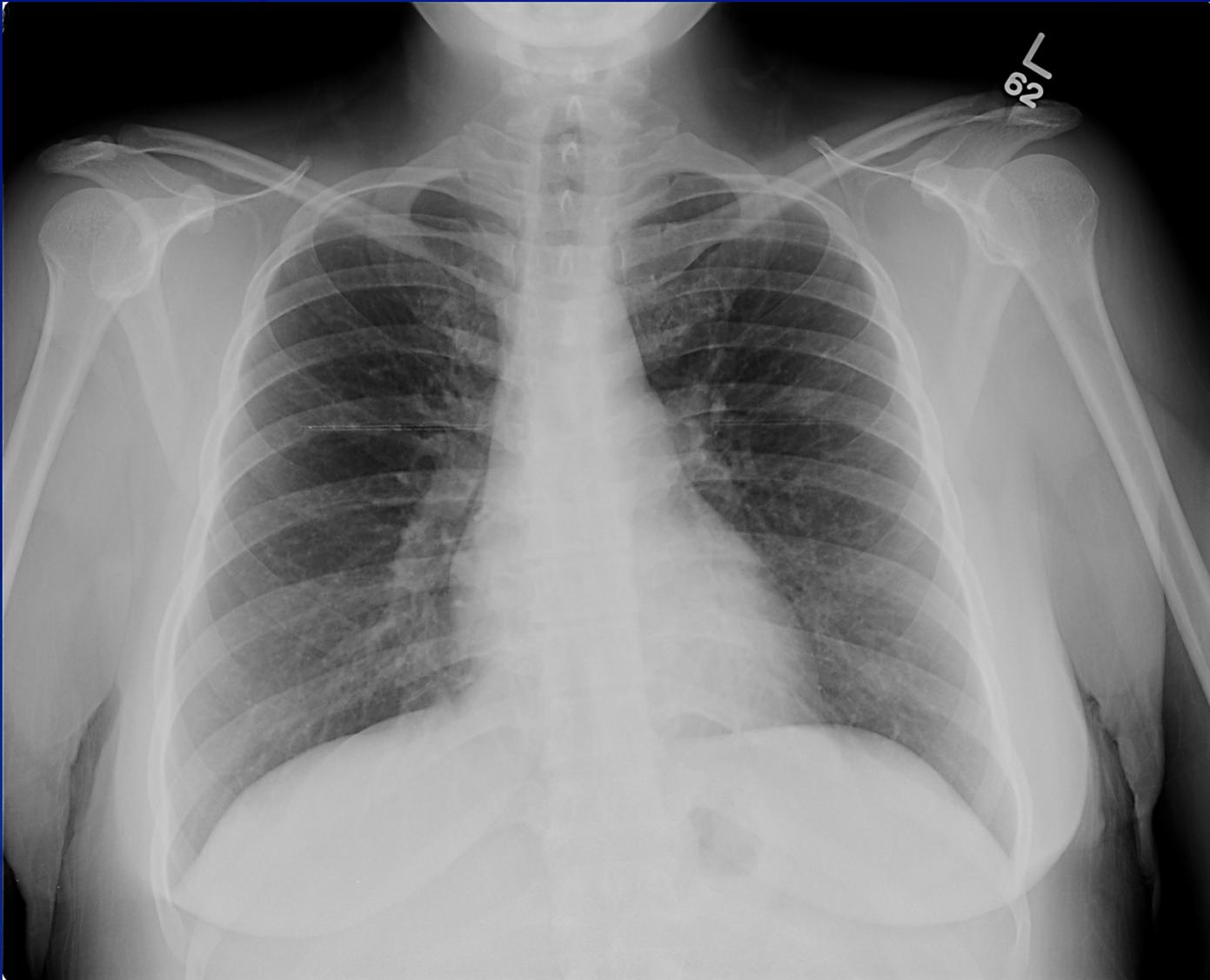
What Additional Evaluation or Treatment Should This Patient Have?

- A. Medical History
- B. TST or IGRA
- C. CXR
- D. Hb A1C
- E. Start INH for LTBI
- F. A and B



Case Study

- TST 20 mm
- Patient notes several weeks of dry cough but is otherwise well
 - Incidentally her HB A1C is $> 8.9\%$
- Now what?



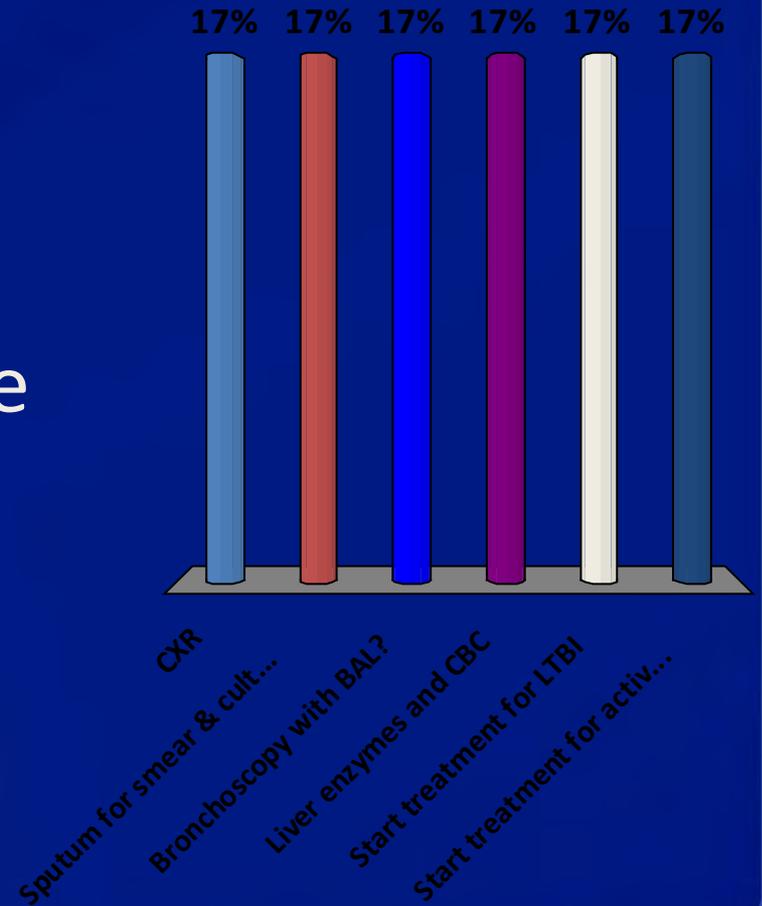
April 27, 2011

Case Study

- CXR was read as normal by radiologist
- Exam was normal
- Patient reported frequent allergies
- One sputum specimen was submitted
 - Smear negative for AFB

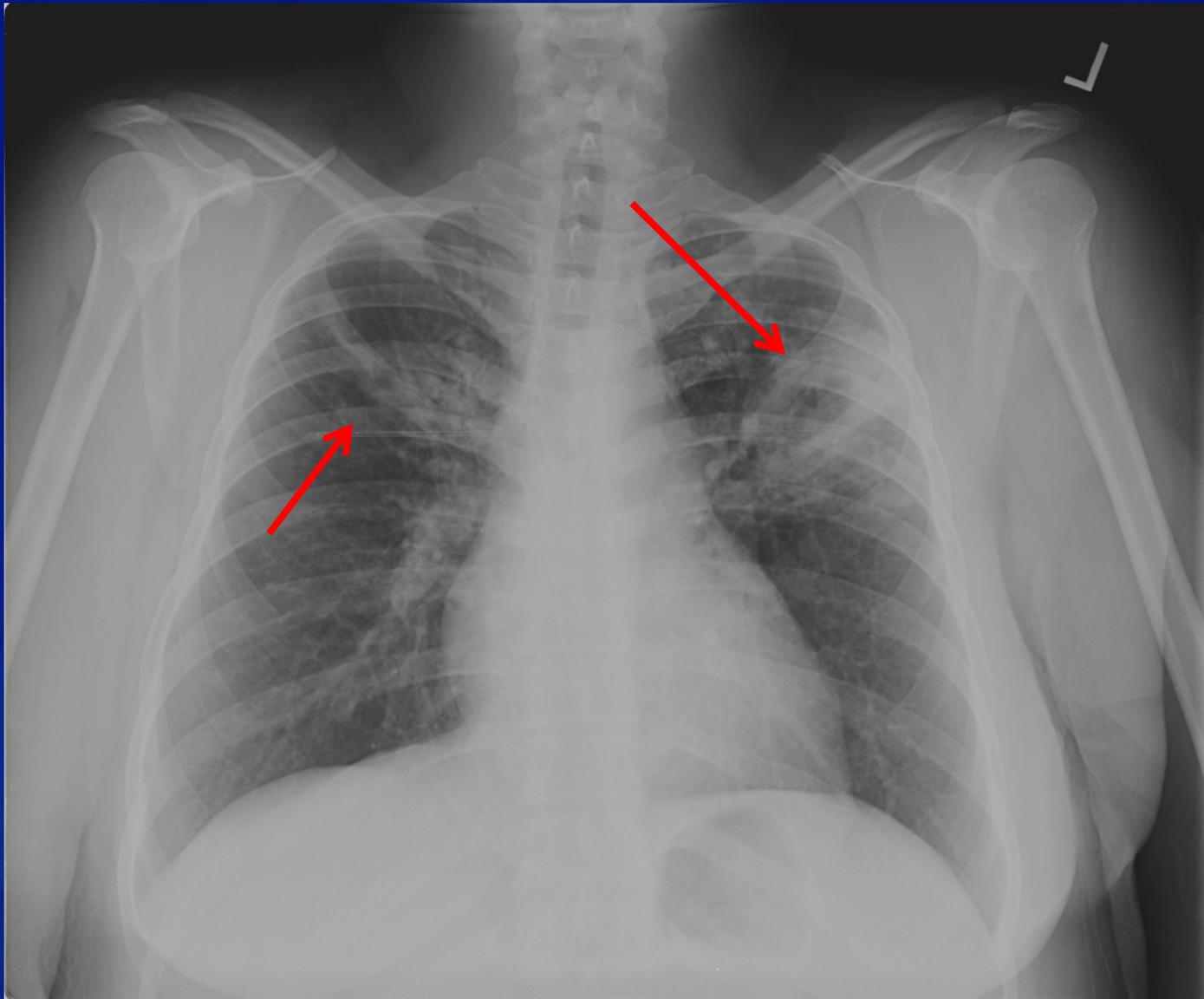
What Else Should Be Done?

- A. Sputum for smear & culture x 3
- B. Bronchoscopy with BAL?
- C. Start treatment for LTBI
- D. Start treatment for active TB disease (RIPE)
- E. A and C
- F. *A and D



Case Study

- 3 months later:
 - Fever
 - Productive cough
 - Hemoptysis



August 26, 2011

Case Study

Smear + for AFB

CXR notes bilateral upper lobe
opacifications and cavitation

What Now?

A. *Start RIPE

B. Stop INH continue RPE

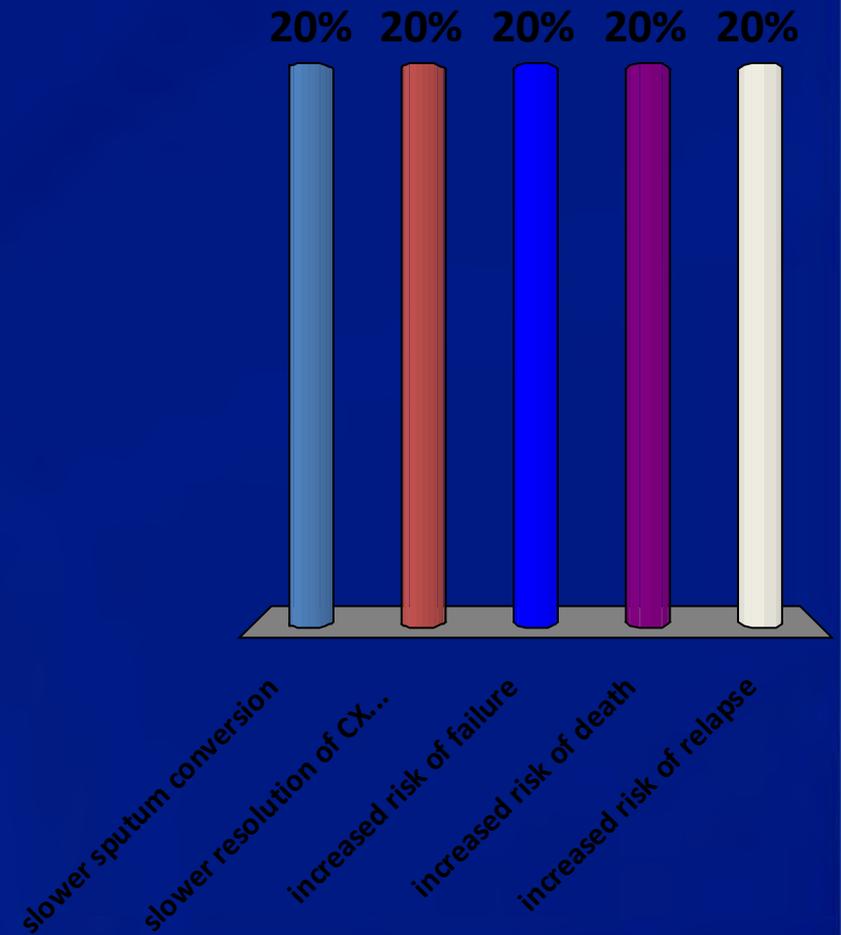
C. Stop INH, start RPE and add a
fluoroquinolone

Case Study

- Culture grows M TB
Later found resistant to INH

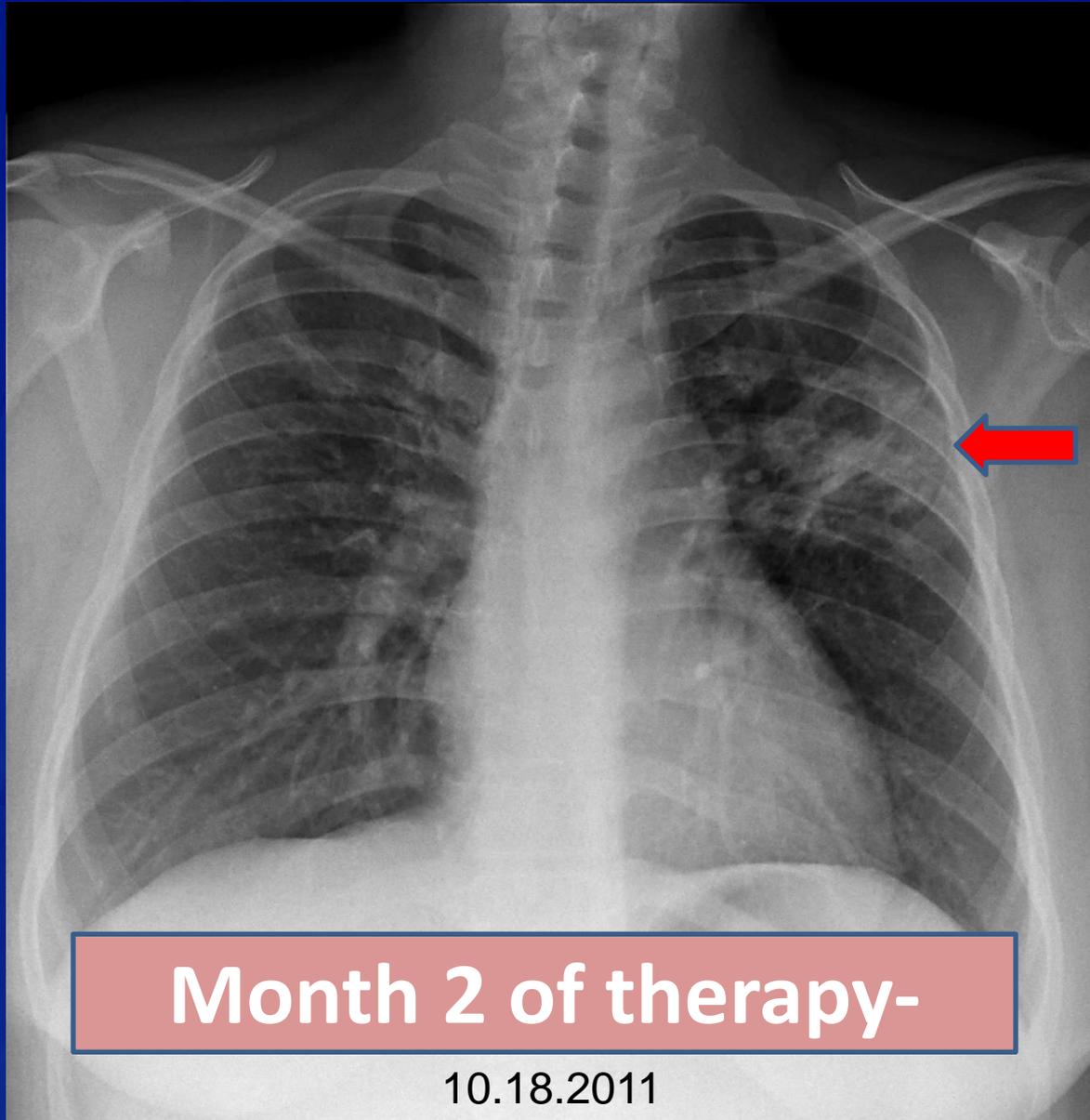
Are Outcomes Different Than For Other TB Patients?

- A. Slower sputum conversion
- B. Increased risk of failure
- C. Increased risk of death
- D. Increased risk of relapse
- E. * All of above



Case Study

- Slow conversion of cultures and smears after $> 2 \frac{1}{2}$ months of therapy
- Slow radiographic improvement
- HB A1C remains $> 9\%$
- Nausea and some vomiting after TB meds
- Rifampin level (900 mg qd) - trace - (nl 8 – 24)

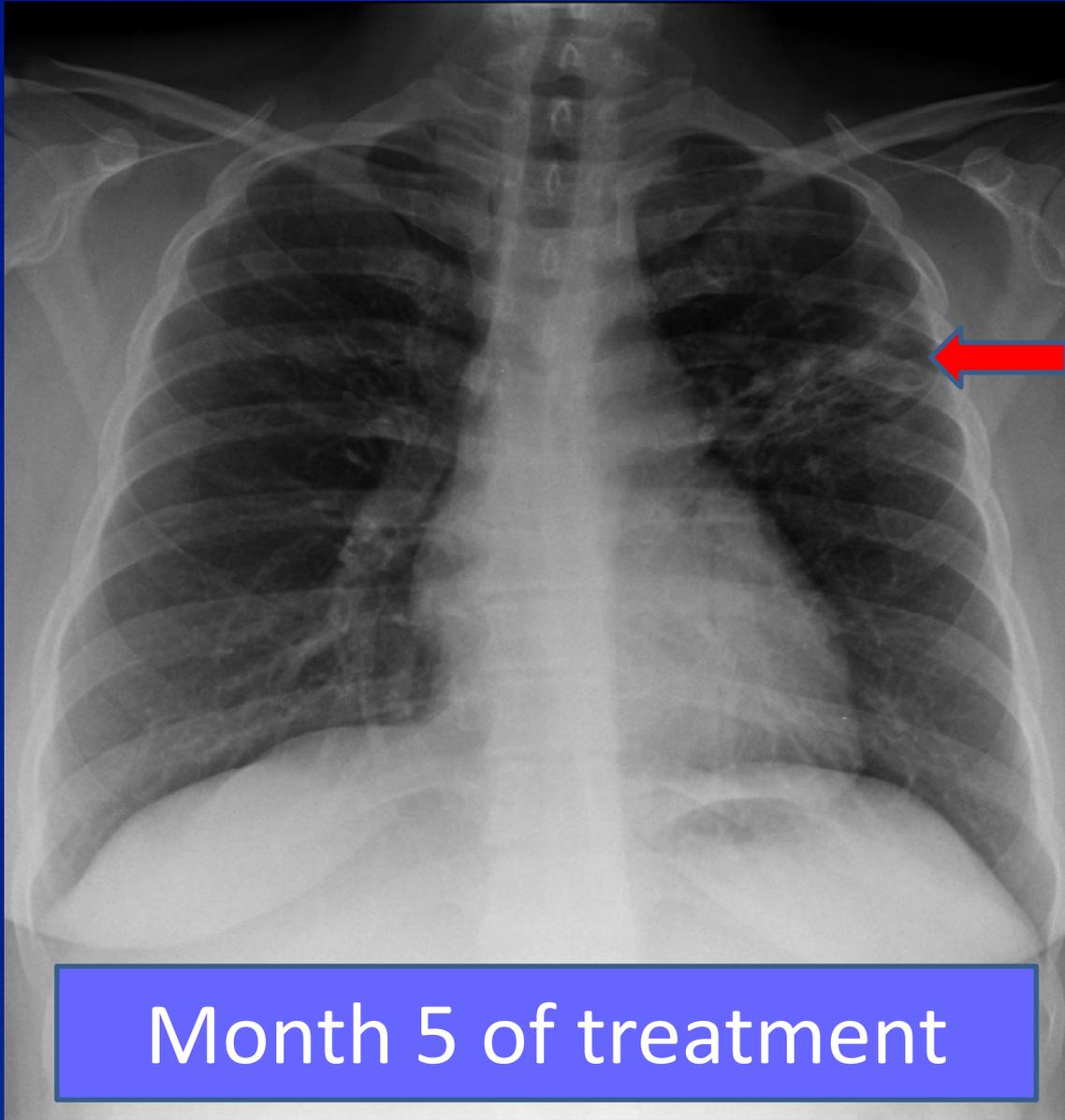


Month 2 of therapy-

10.18.2011

Case Study

- Improved diabetic control with diet modification, exercise and medication
- Increase in rifampin dosage due to low serum level
- Clinically improved
- Radiographically improved



Month 5 of treatment



XDR-TB



National Diabetes Education Program

A program of the National Institutes of Health and the Centers for Disease Control and Prevention

Q&A



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