Tuberculosis and Diabetes Connections

Michigan World TB Day Conference

April 8, 2016

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CDR USPHS

TB-DM Connections

1) TB-DM Epidemiology
2) Screening for DM in TB Cases
3) Screening for TB in DM Cases
4) Enhanced TB case management
5) Michigan approach?
6) Big Finish!

Global Burden of DM and TB

Diabetes Mellitus: 2013

- **383 million people living with DM**
- **10 million new cases per annum**
- **~5 million people died of DM during the year**

[IDF Diabetes Atlas 2013]

Tuberculosis: 2013

- **11.0 million people living with TB**
- **9.0 million new cases in the year**
- **1.5 million people died of TB during the year**

[WHO- Global TB Control 2014]

From: Prof Tony Harries

Global Distribution of DM and TB

Diabetes Mellitus: 2013

- South East Asia 19%
- Western Pacific 36%
- Africa 4%

80% in LIC and MIC

[IDF Diabetes Atlas 2013]

Tuberculosis: 2013

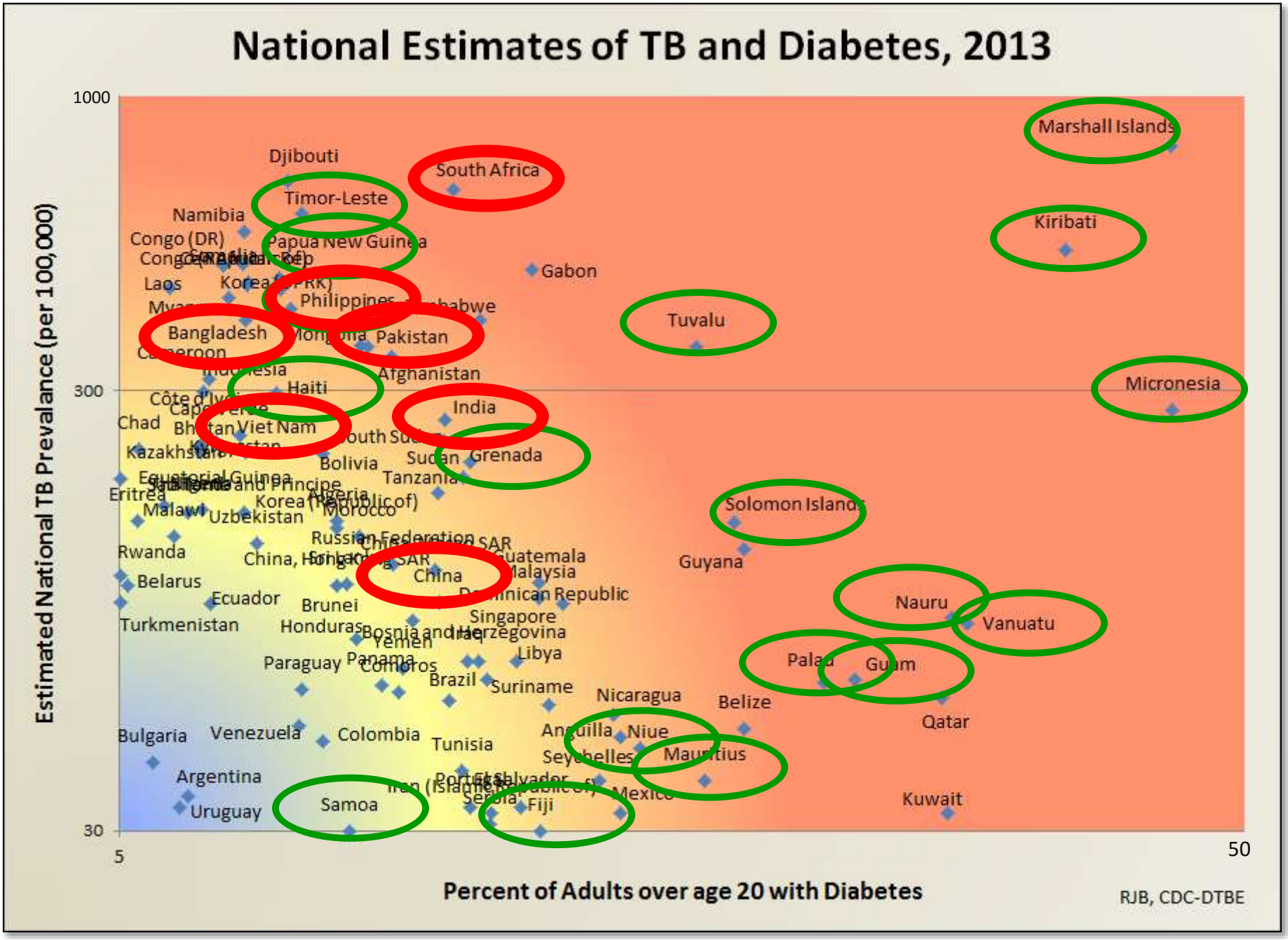
- South East Asia 38%
- Western Pacific 18%
- Africa 29%

95% in LIC and MIC

[WHO- Global TB Control 2014]

From: Prof Tony Harries

National Estimates of TB and Diabetes, 2013



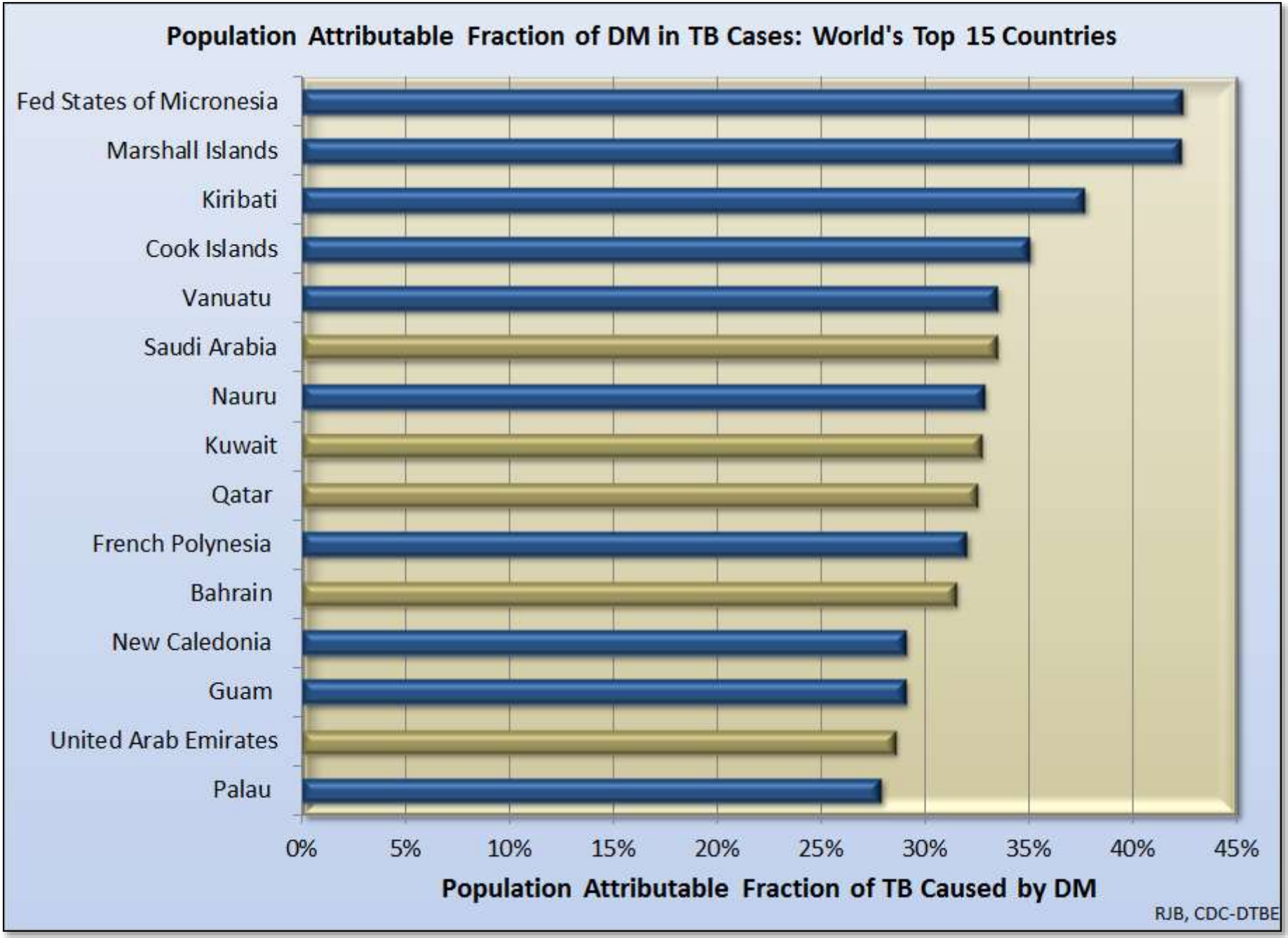

Population Attributable Fraction of DM in TB Cases: World's Top 15 Countries
Fed States of Micronesia
Marshall Islands
Kiribati
Cook Islands
Vanuatu
Saudi Arabia
Nauru
Kuwait
Qatar
French Polynesia
Bahrain
New Caledonia
Guam
United Arab Emirates
Palau
0%
5%
10%
15%
20%
25%
30%
35%
40%
45%
Population Attributable Fraction of TB Caused by DM
RJB, CDC-DTBE

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	
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	

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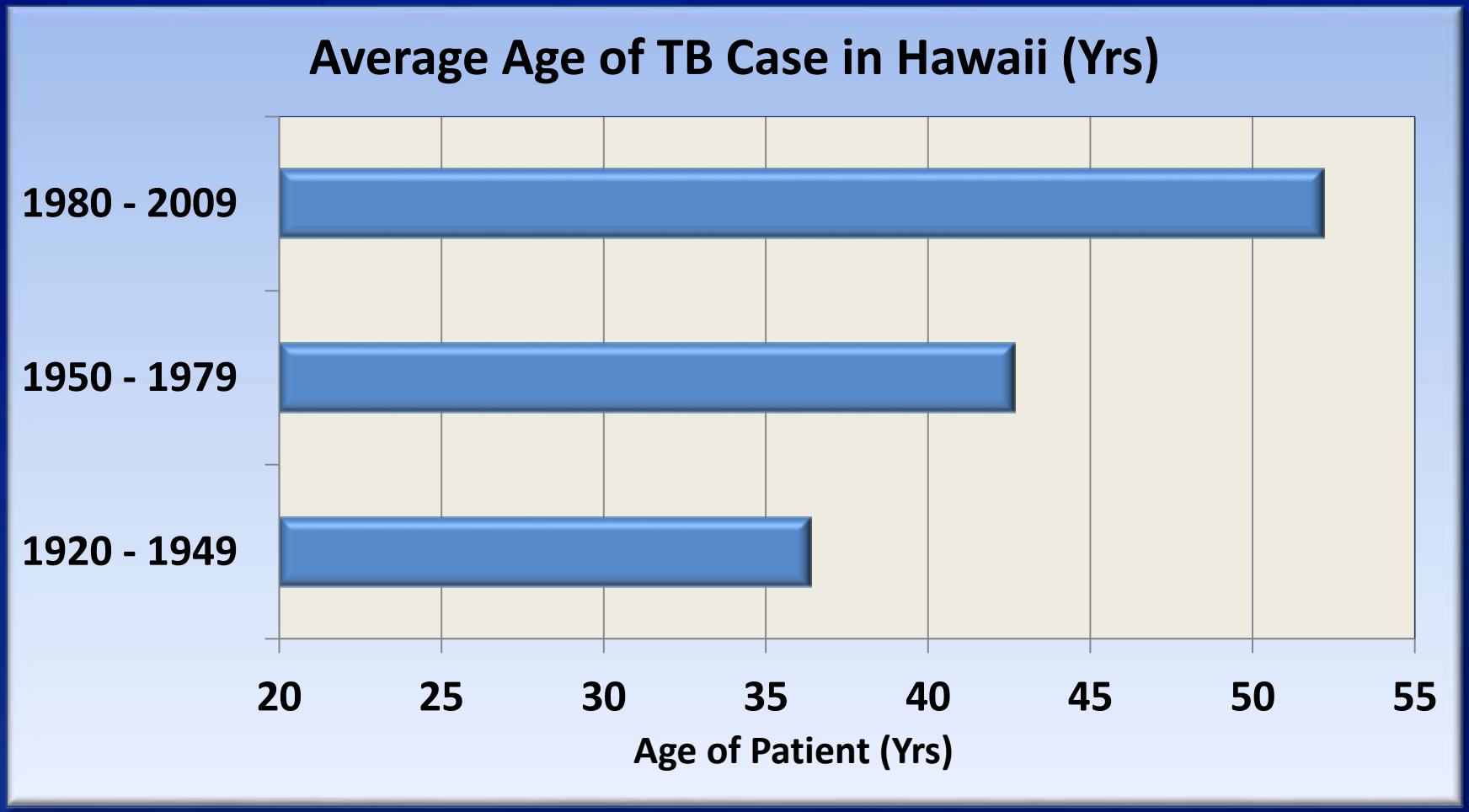
Oh, the good old days……



*Hawaii Case Reports for 1920 – 2014 N=211

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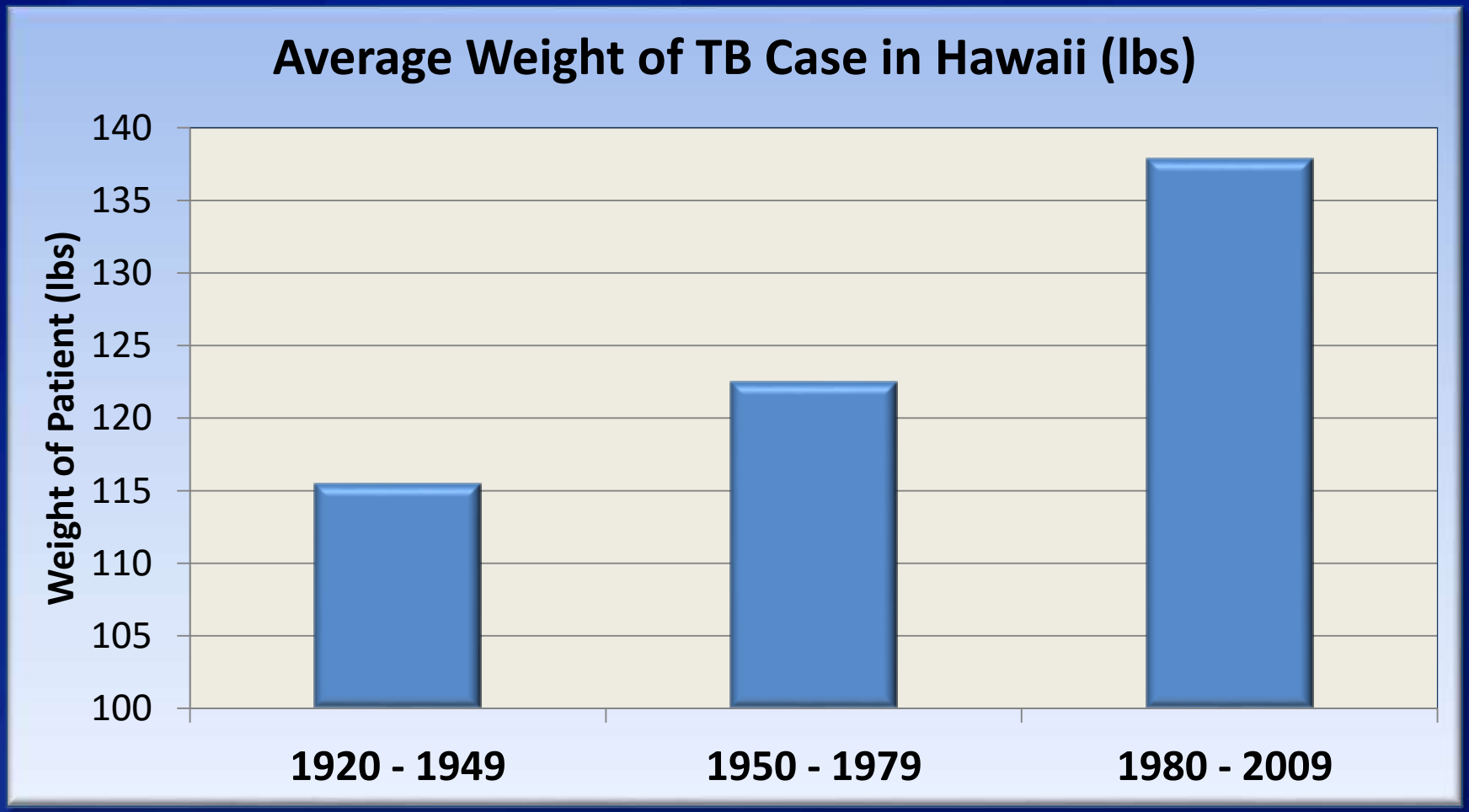

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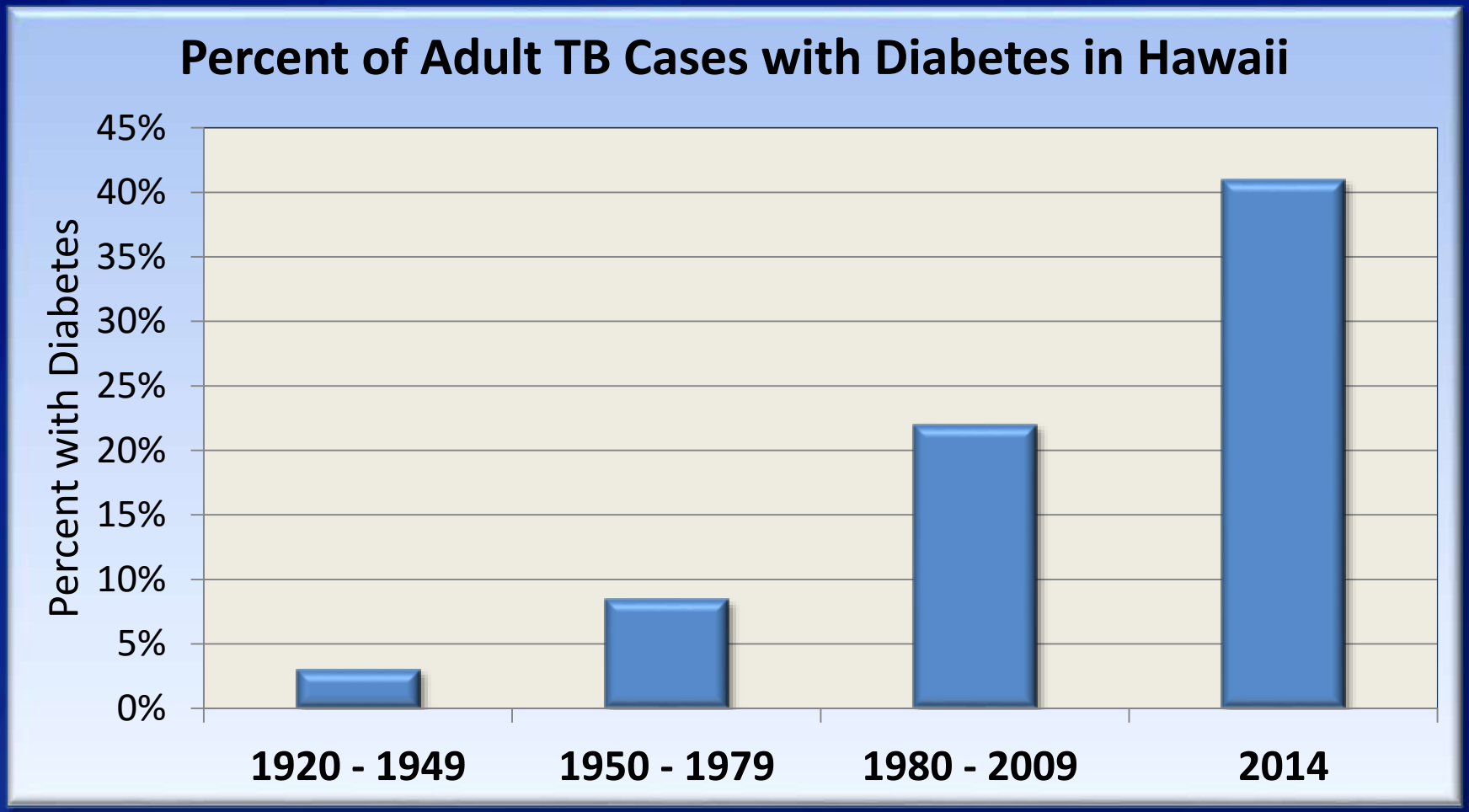


*Hawaii Case Reports for 1920 – 2014 N=211

EpiAnywhere Data Entry Page

DM: Prior History of Diabetes Before TB Diagnosis?

DM Testing at TB Diagnosis?

Test Date: _/_/__

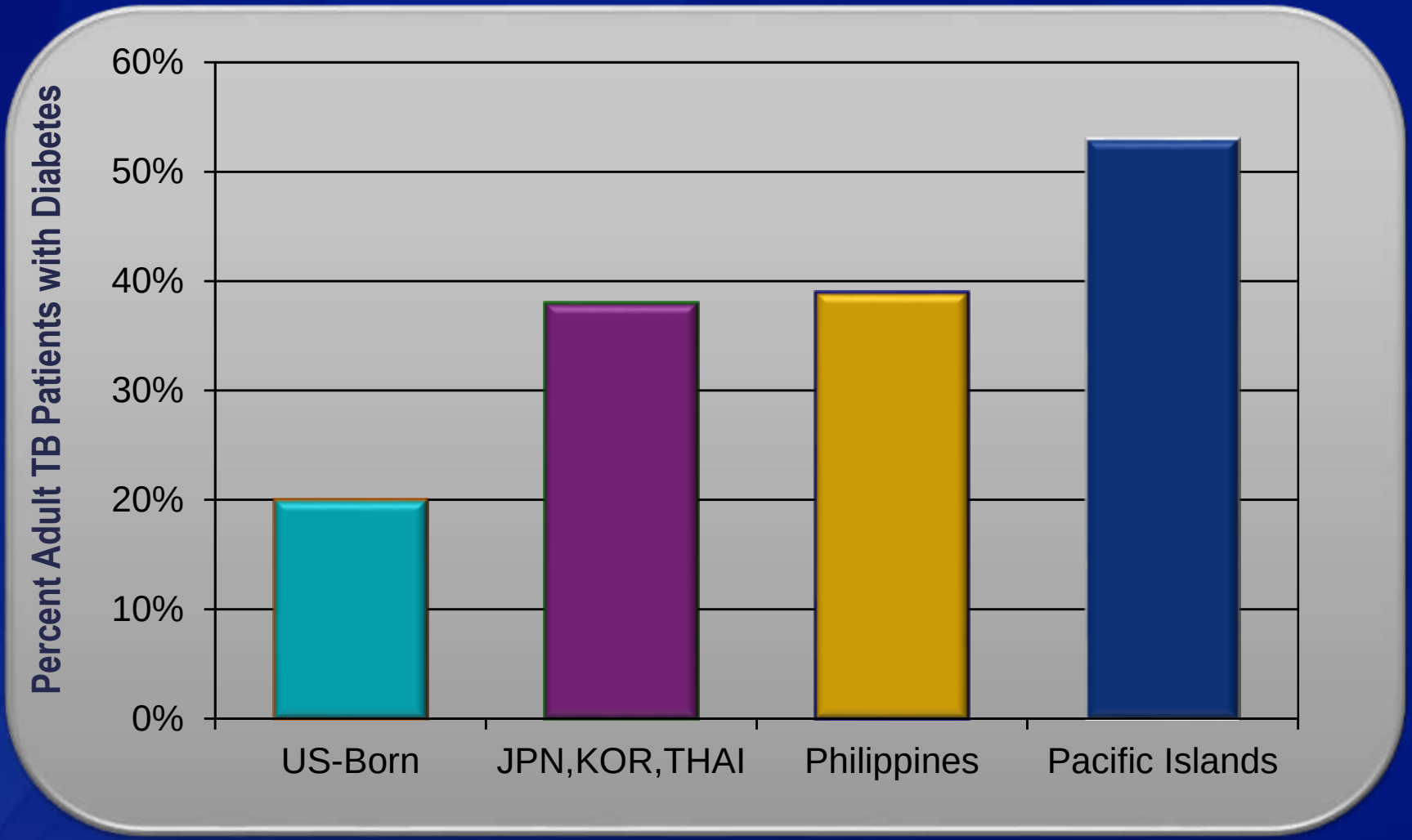
DM Test Type:

DM Test Result: ___.__

Hawaii Adult TB cases with Diabetes

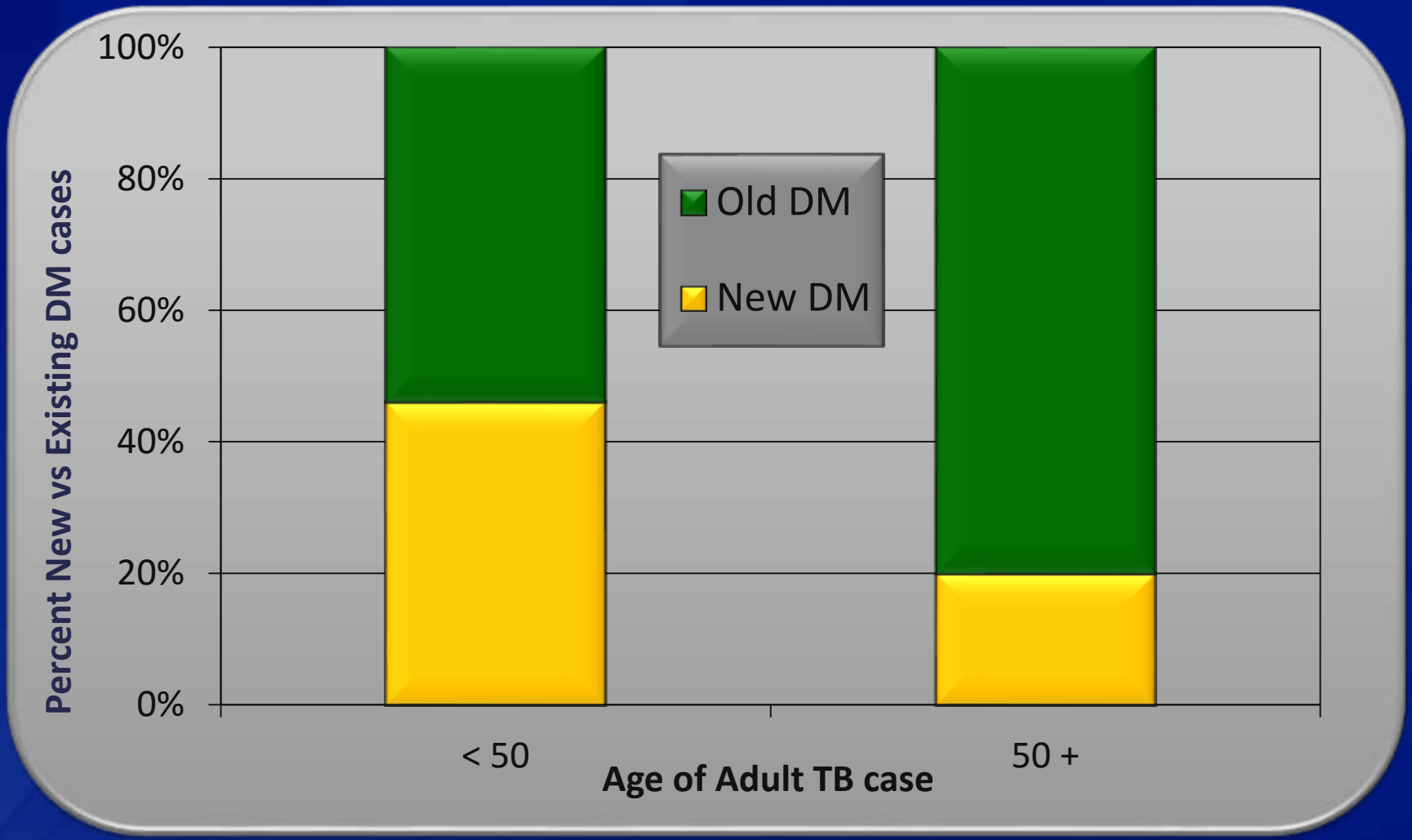
Brostrom, R and Young, B Hawaii TB Control Program 2015

Adult TB cases with DM in Hawaii: 2014



*Hawaii Case Reports for 2014

TB as the “Diabetes Defining Illness”



*Hawaii Case Reports for 2014

DM Screening Methods for TB Programs

Method	Advantages	Disadvantages	Cost*
Glucose ≥ 200 (random)	Inexpensive. Easily available. Point of care possible. No phleb. required	Many false (-) Some false (+) Poorly reproducible	$750
A1c ≥ 6.5	Most accurate. Point of care possible. Few false (-),(+)	More expensive. Not always avail in rural setting. May require phleb.	$8,000
Random glucose ≥ 140 followed by A1c ≥ 6.5 to confirm	Less expensive than universal A1c. Few false (+)	Some false (-). Requires follow-up.	$3,150

* Cost per 1000 TB cases screened for DM ($8 for A1c, $0.75 for Glucose)

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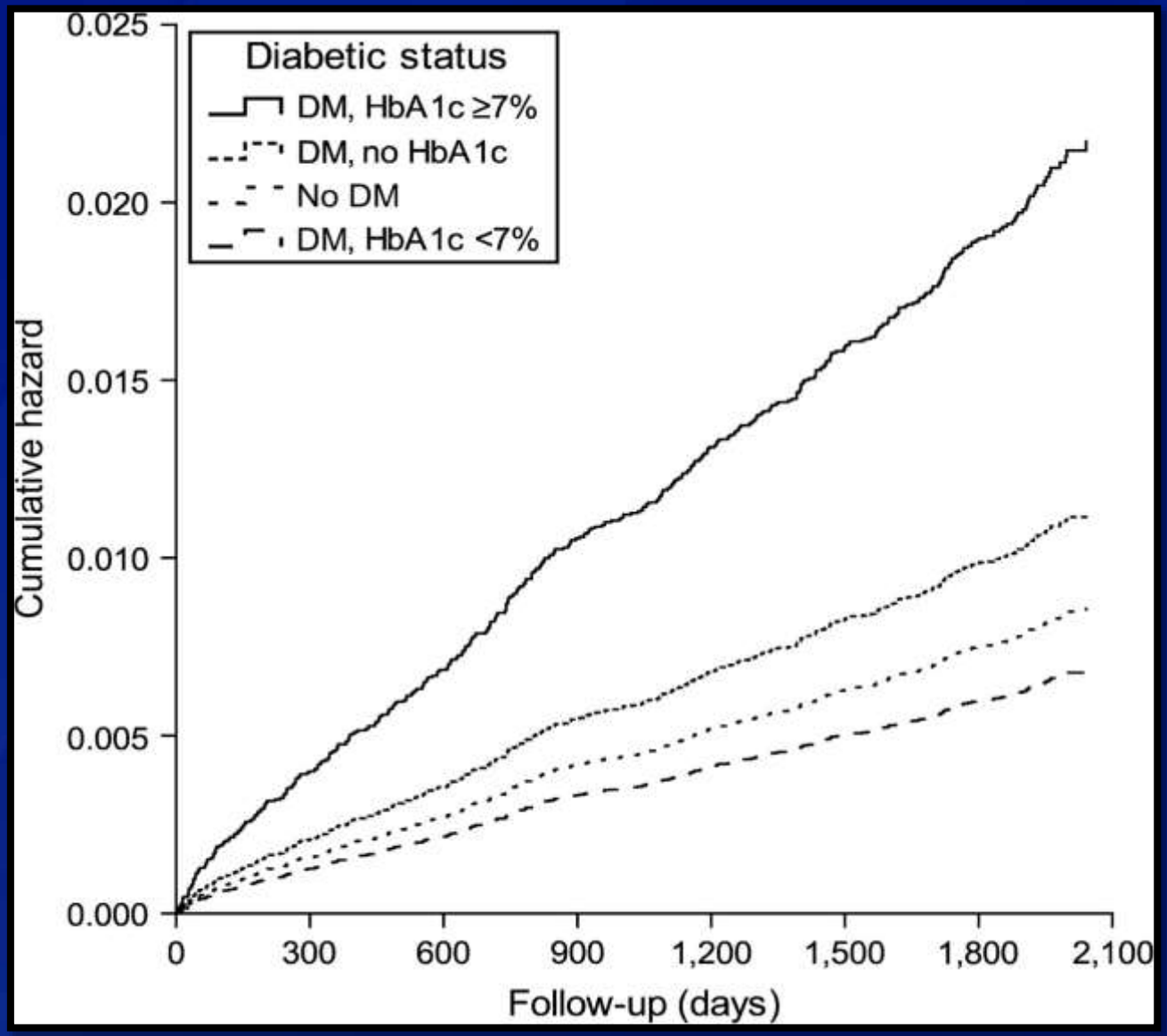
Diabetic status
DM, HbA1c ≥7%
DM, no HbA1c
No DM
DM, HbA1c <7%
Cumulative hazard
0.025
0.020
0.015
0.010
0.005
0.000
0
300
600
900
1,200
1,500
1,800
2,100
Follow-up (days)

TB-DM: Younger DM Cases at Risk

Table 2—*Incidence rates (per 100,000 person-years) among diabetic and nondiabetic populations (clustering within 1 year of diagnosis)*

Age-group (years)	TB patients with diabetes (*n*)	Incidence rate of TB among diabetic population	TB patients without diabetes (*n*)	Incidence rate of TB among nondiabetic population	Ratio of rates (95% CI)	*P*	Population attributable risk (%)
Clustered cases							
20–44	18	127.3	62	6.9	18.6 (10.3–31.8)	<0.0001	21
45–64	15	39.3	25	8.0	4.9 (2.4–9.6)	<0.0001	29
65–89	9	30.2	12	10.1	3.0 (1.1–7.8)	0.01	28
Total	42	51.2	99	7.4	6.9 (4.7–9.9)	<0.0001	25
Reactivated cases							
20–44	25	176.8	192	21.2	8.3 (5.3–12.7)	<0.0001	10
45–64	78	204.1	75	24.1	8.5 (6.0–11.8)	<0.0001	44
65–89	27	90.7	43	36.1	2.5 (1.5- 4.2)	0.0004	23
Total	130	158.3	310	23.2	6.8 (5.5–8.4)	<0.0001	25

Ponce De-Leon, A. Tuberculosis and Diabetes in Southern Mexico, Diabetes Care 27:1584–1590, 2004

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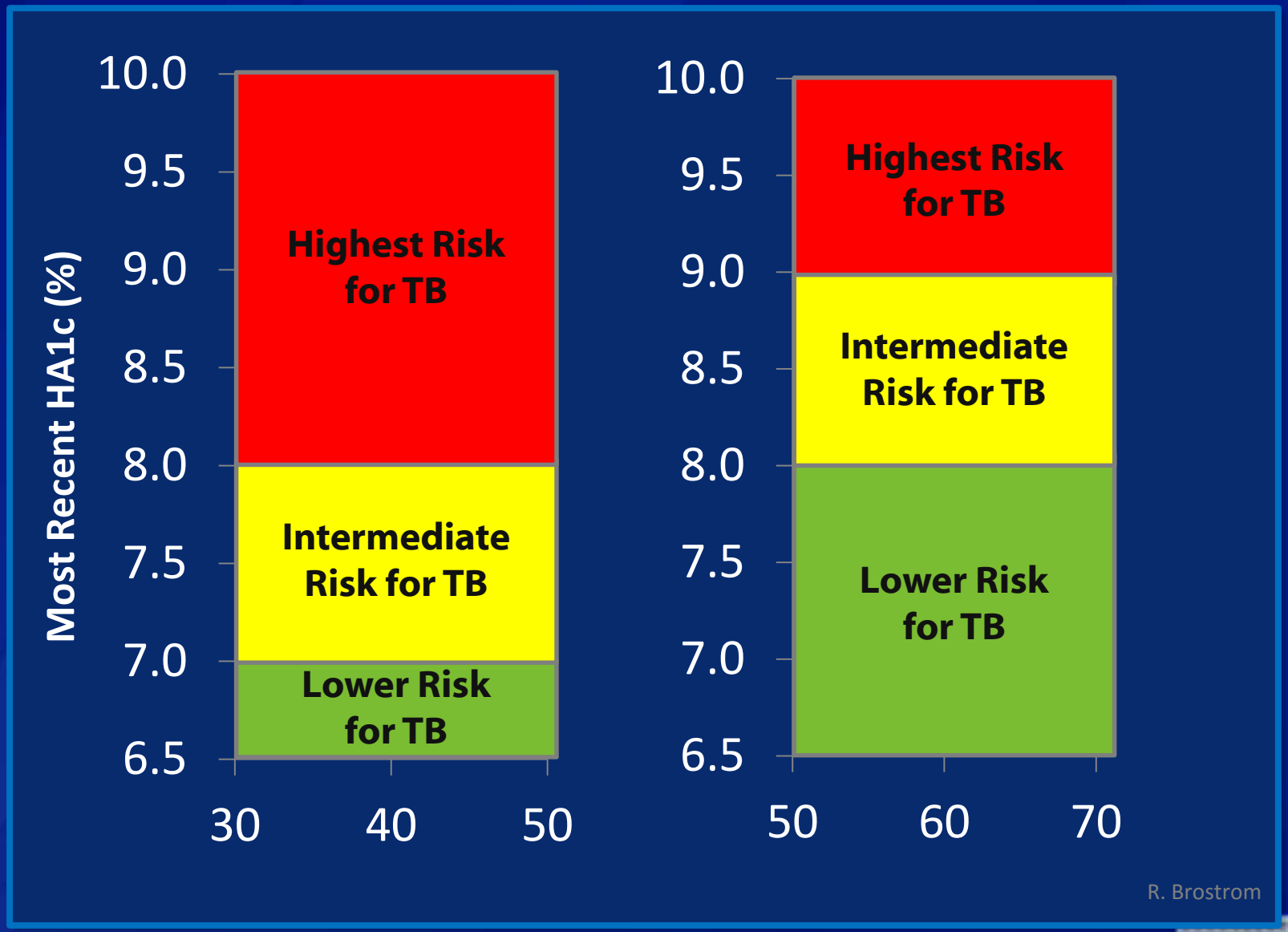
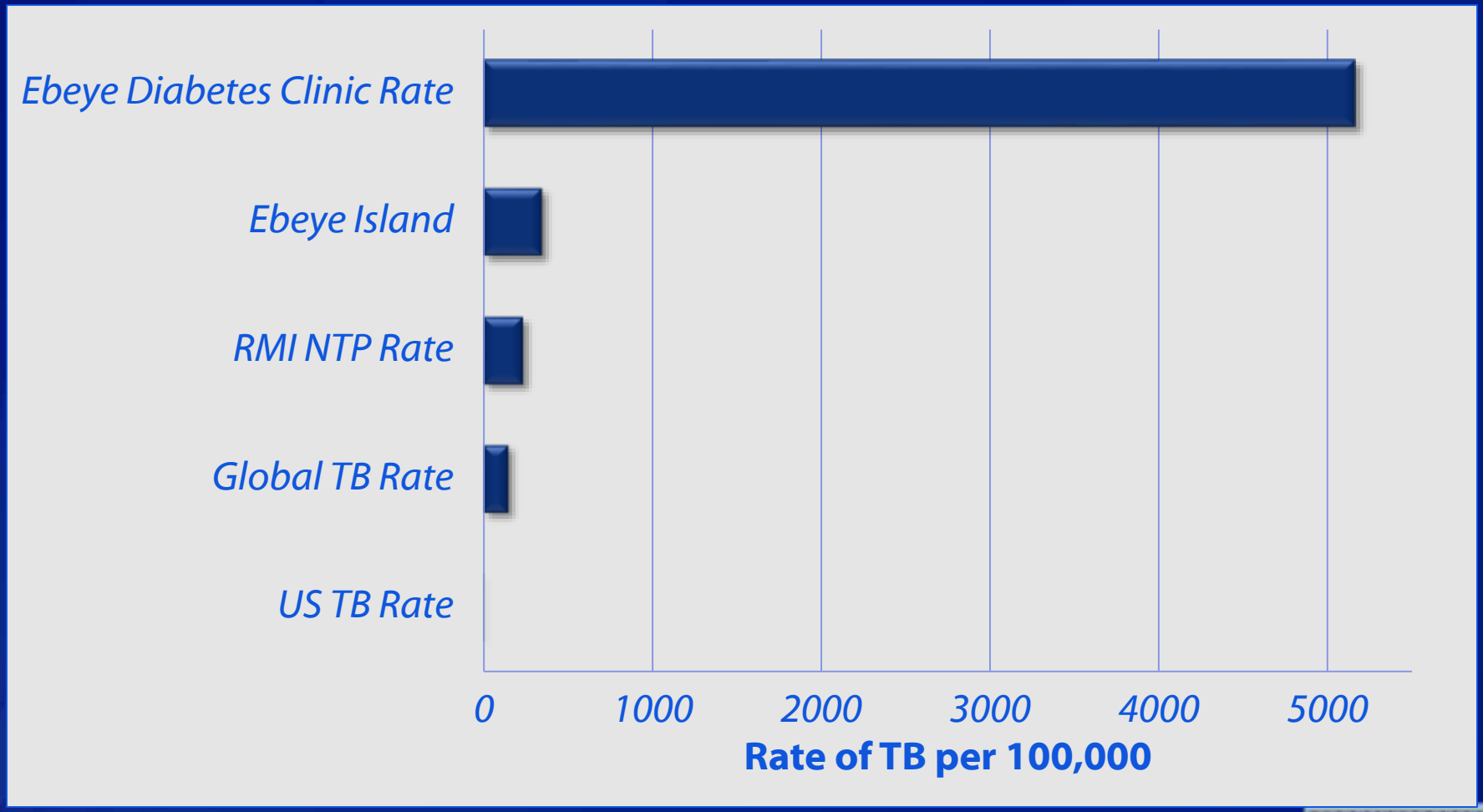
Testing and Treating TB infection for DM Cases

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

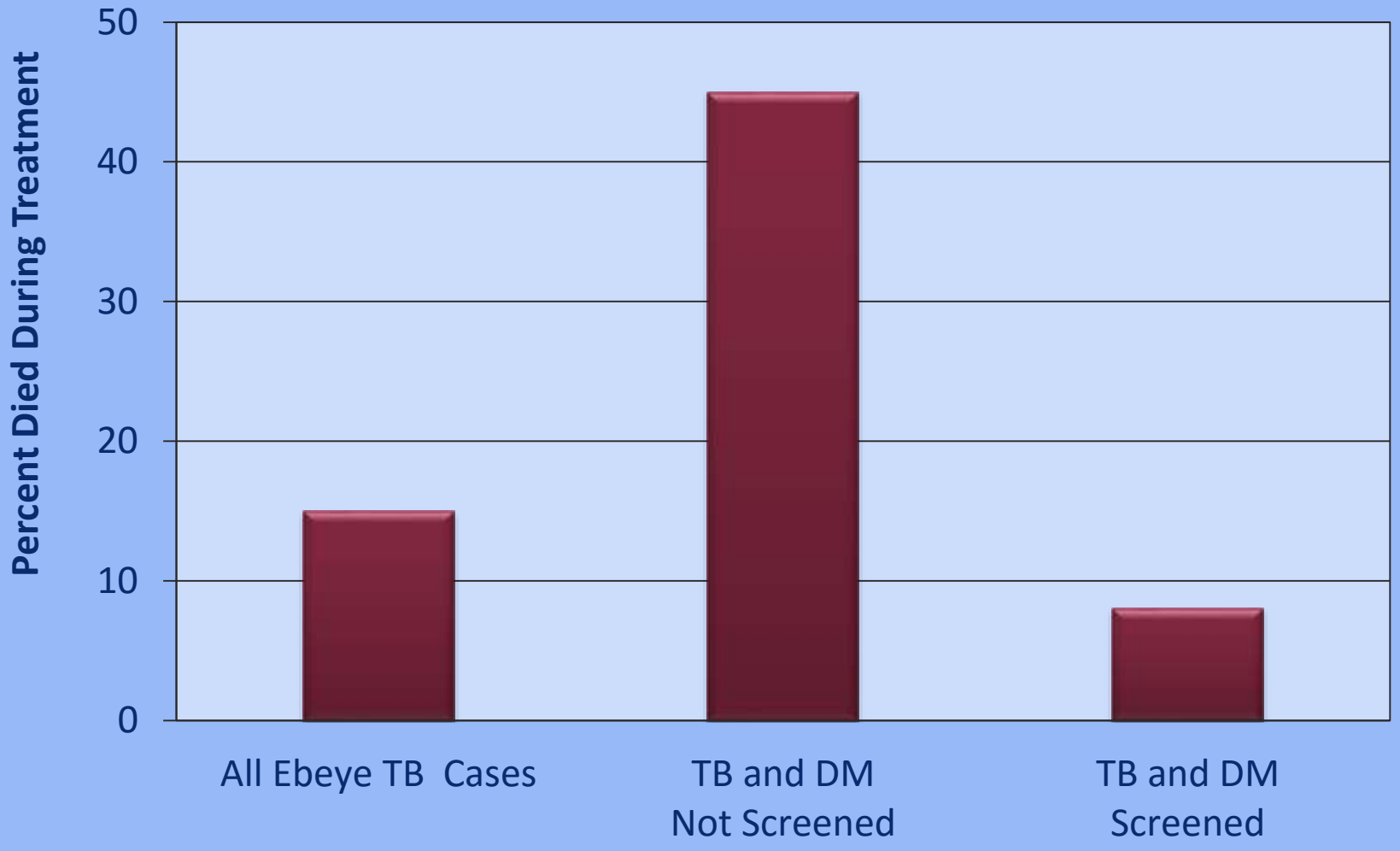
Possible Risk Profile for TB Prevention in Persons with DM



TB Screening in Diabetes Clinic: Finding TB



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



Screening for TB Disease in DM Clinic

Method	Advantages	Disadvantages	Cost*
Symptom Screen every 6 months to 1 year	No cost. Should minimize exposure in DM Clinic. Raises awareness in DM Clinic.	False (-), (+) Will miss early TB.	$ 0
Chest x-ray every 1 to 5 years	Most accurate, especially when baseline CXR known. Sensitive for TB.	Most expensive. Not always avail in rural setting.	$10,000

* Cost per 1000 DM cases screened for TB ($50 for CXR divided by 5years)

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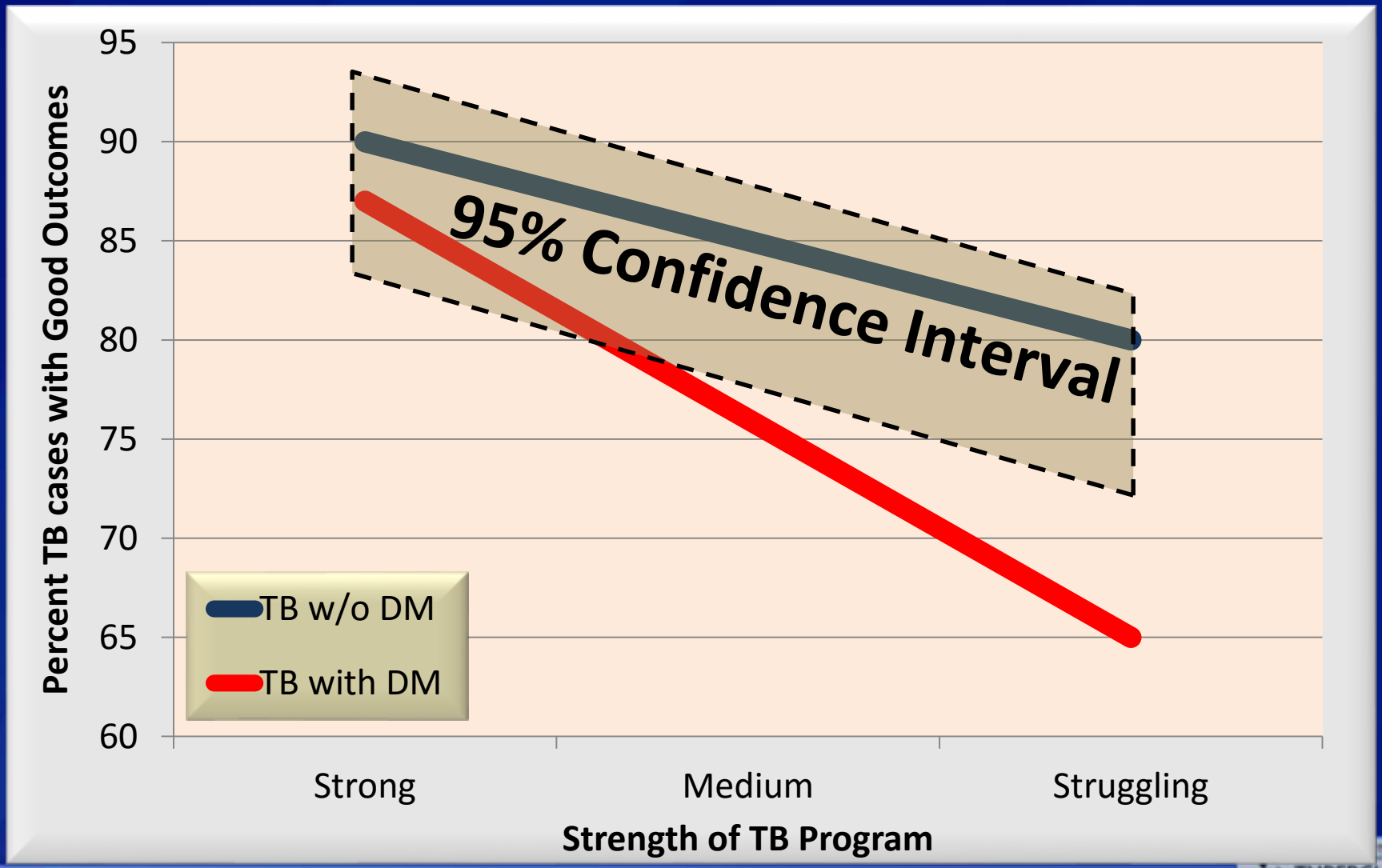
TB-DM: Strength of Association

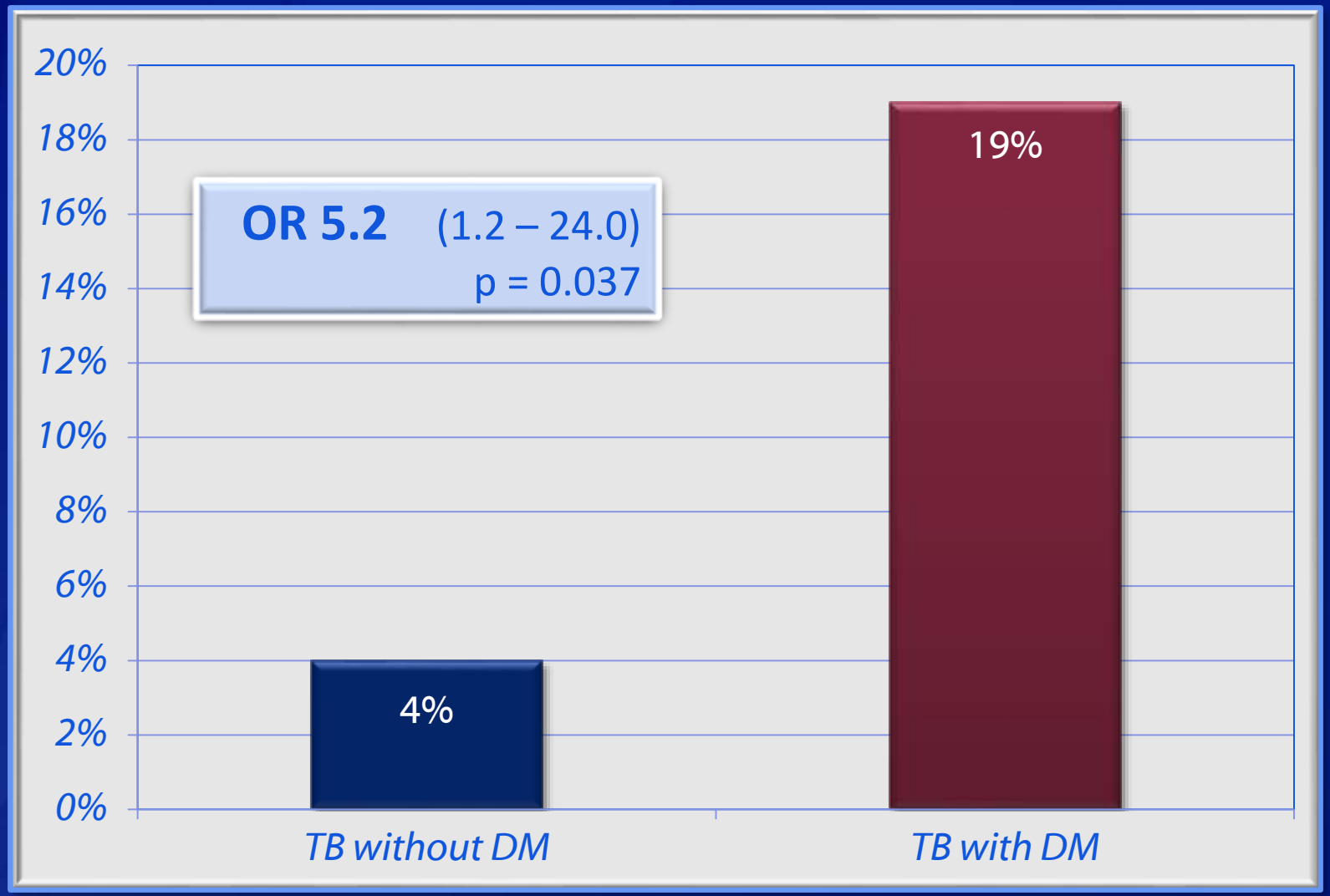


TB and Diabetes Summary: 2-3-4-5

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

All-Cause Mortality During TB Treatment*



* Pacific Islands TB Cases, 40 – 60 years old, 2010–2012, n=129
Data excludes "lost", "discontinued", "moved", "unknown"

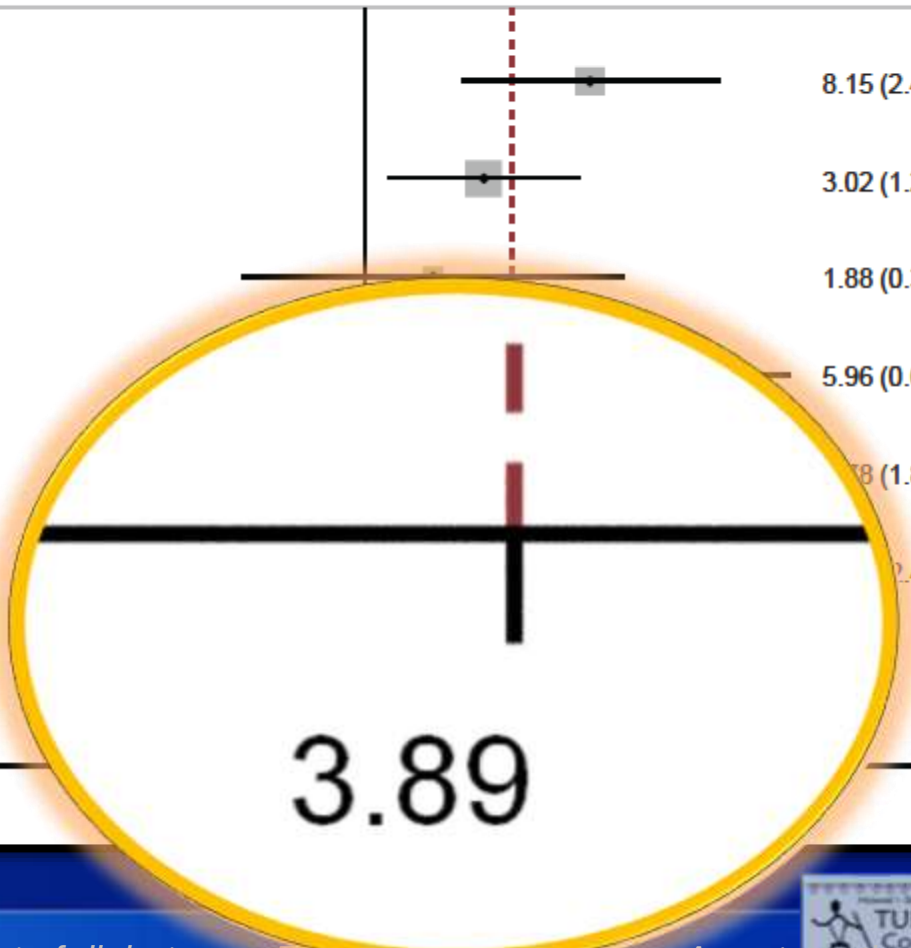
R.Brostrom

TB-DM Outcomes: Relapse

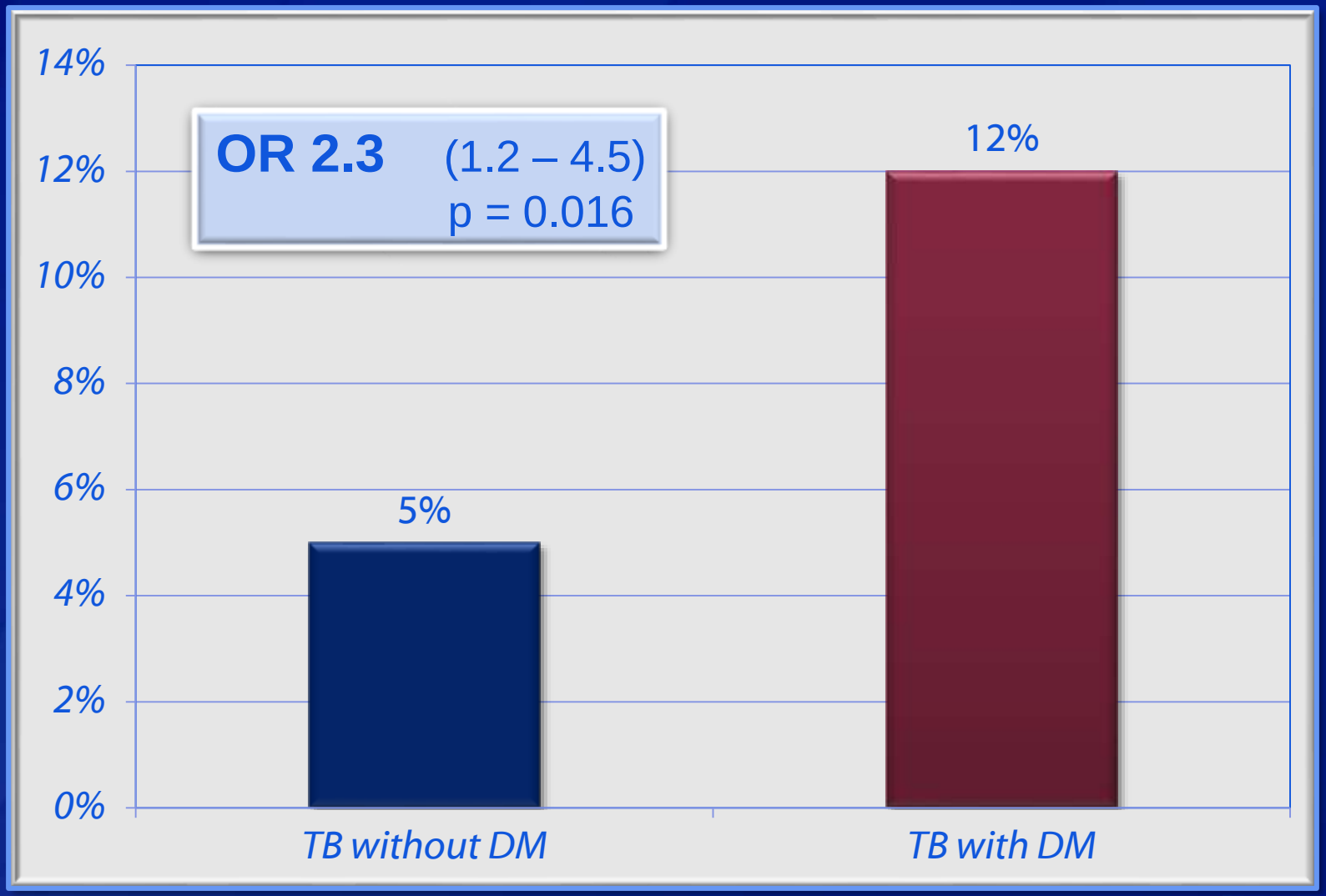
Study	Country	Population with DM Relapse/ Total	Population without DM Relapse/ Total	RR (95% CI)
Wada, 2000 [54]	Japan	7/61 (11%)	4/284 (1%)	8.15 (2.46, 26.97)
Mboussa, 2003 [47]	Congo	6/17 (35%)	9/77 (12%)	3.02 (1.24, 7.35)
Singla, 2006 [50]	Saudi Arabia	2/130 (2%)	3/367 (1%)	1.88 (0.32, 11.14)
Maalej, 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%)	3.78 (1.87, 7.65)
Summary				3.89 (2.43, 6.23)

Heterogeneity I-squared = 0% (0, 79)

Weights are from random effects analysis



History of Prior TB*

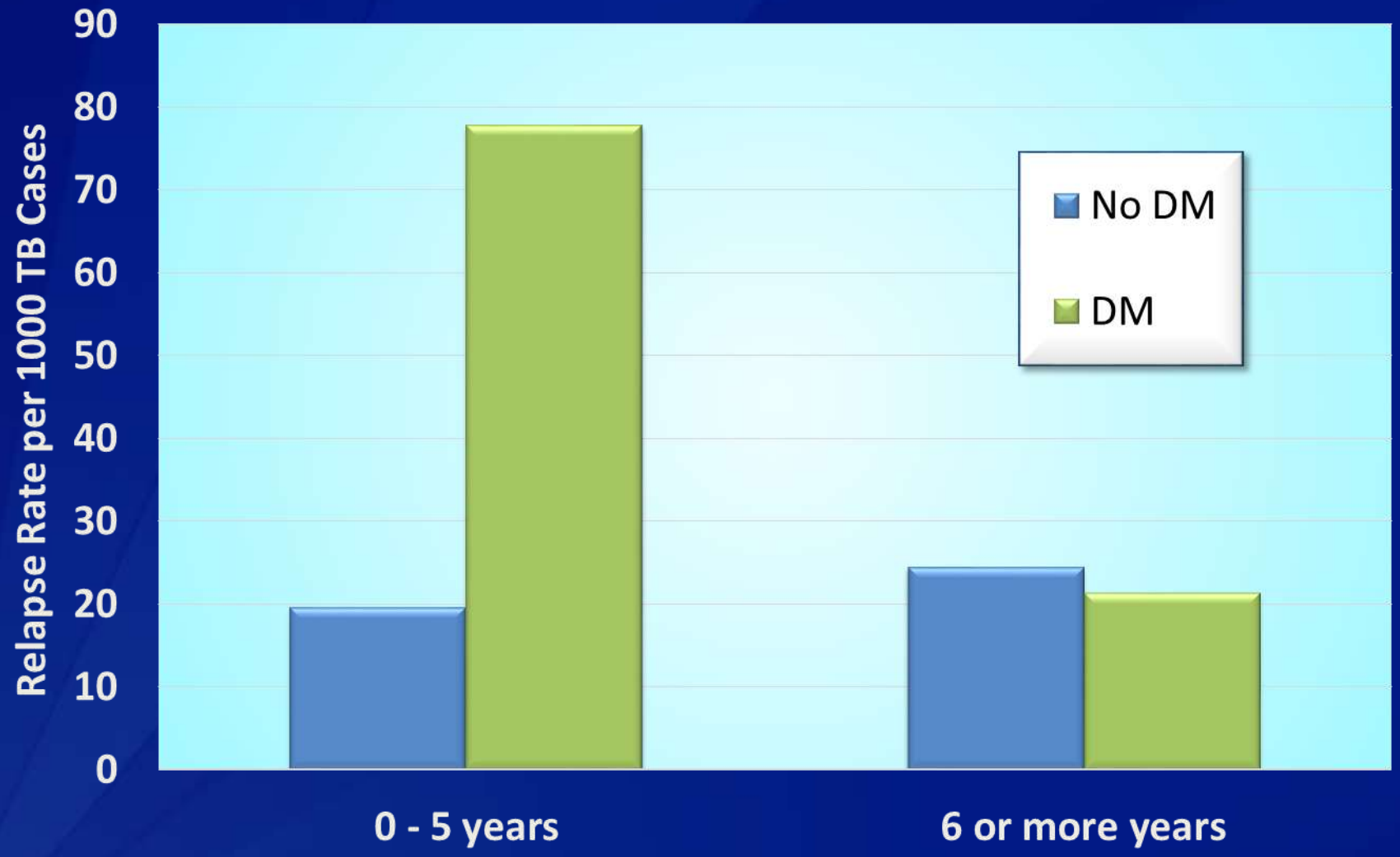


* Adult Pacific Islands TB Cases, 2010 – 2012, n = 511

R.Brostrom

History of Prior TB Treatment

Pacific Island Adults > 30, 2010 - 2014, n=657



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Diabetes complicates TB Care:

- Greatly increases num
- Harder to
-
- of TB recurrance
- Increased risk of death during treatment

Diabetes is the HIV of the Pacific!

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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)

1.1 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 person with DM should be screened for TB disease and TB infection

2.1 Persons with TB symptoms or TB disease should be referred to the local TB Program for TB management.

2.2 A test for TB infection should be done at the time of DM diagnosis.

2.3 Screening should be repeated as often as the local TB epidemiology may warrant.

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.

6.2 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/

PITCA

Pacific Chronic Disease Coalition

Basic DM Management for TB Clinic

Treating TB in persons with DM

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Enhanced DM Management for TB Clinic

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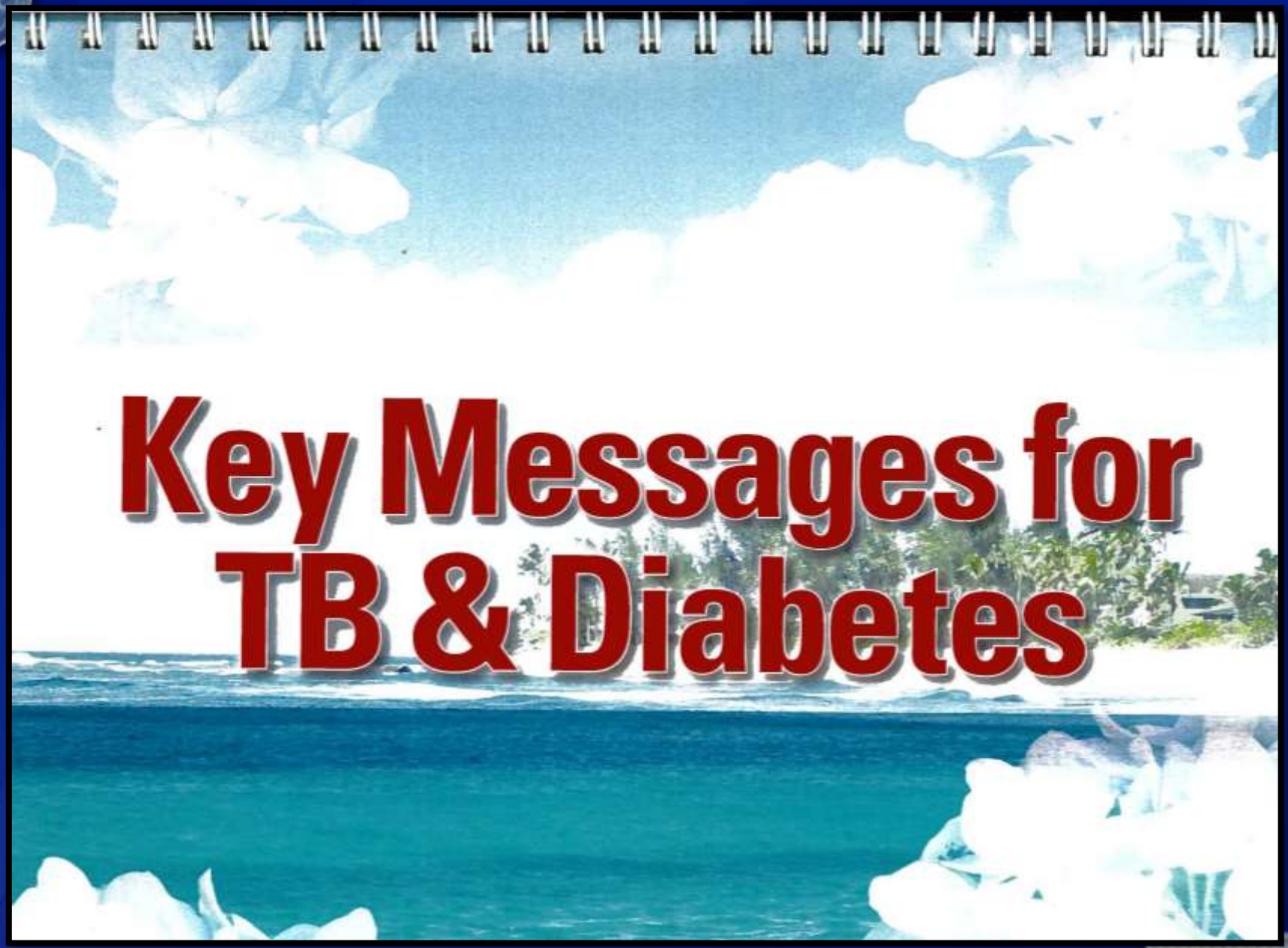
Battle Creek Sanitarium: Exercises, 1911


Key Messages for
TB & Diabetes

Hawaii TB Nurses Documentation

Hawaii TB-Diabetes Patient Care Worksheet

Patient Name: _____ **CC#:** _____

Date and Initials	/ /	/ /	/ /	/ /	/ /
DM education	☐ None ☐ <5 min ☐ 5-10 min ☐ 10-30 min	☐ None ☐ <5 min ☐ 5-10 min ☐ 10-30 min	☐ None ☐ <5 min ☐ 5-10 min ☐ 10-30 min	☐ None ☐ <5 min ☐ 5-10 min ☐ 10-30 min	☐ None ☐ <5 min ☐ 5-10 min ☐ 10-30 min
DM test results	Gluc: ____mg/dL A1c: _____%	Gluc: ____mg/dL A1c: _____%	Gluc: ____mg/dL A1c: _____%	Gluc: ____mg/dL A1c: _____%	Gluc: ____mg/dL A1c: _____%
Seeing DM provider?	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Taking DM medications?	☐ Yes ☐ No ☐ None needed	☐ Yes ☐ No ☐ None needed	☐ Yes ☐ No ☐ None needed	☐ Yes ☐ No ☐ None needed	☐ Yes ☐ No ☐ None needed
Comments:					

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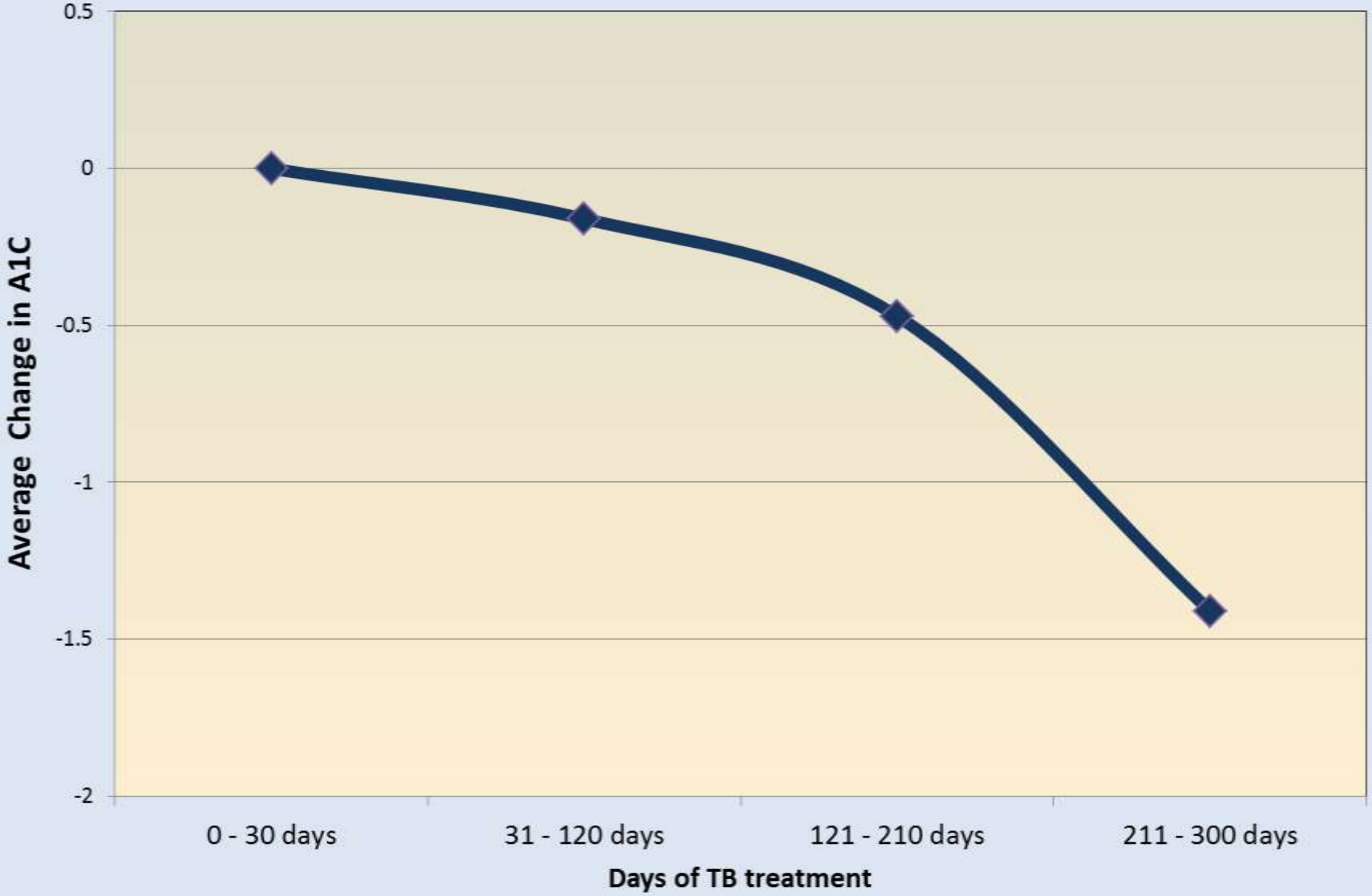
Can the TB clinic help with glucose control?

- A1c data collection (586 tests)
- Initial (intake package)
- 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)



Can the TB Program take credit for this?

What is the natural change in A1c during TB treatment?	
A1c should drop during treatment	***A1c should rise during treatment***
Infections usually elevate blood glucose. Glucose is an "acute phase reactant".	Rifampin (and INH) will elevate blood glucose throughout treatment and can interfere with some DM medications.
Patients may use this as an opportunity to address multiple health problems.	Almost all patients gain weight during TB treatment

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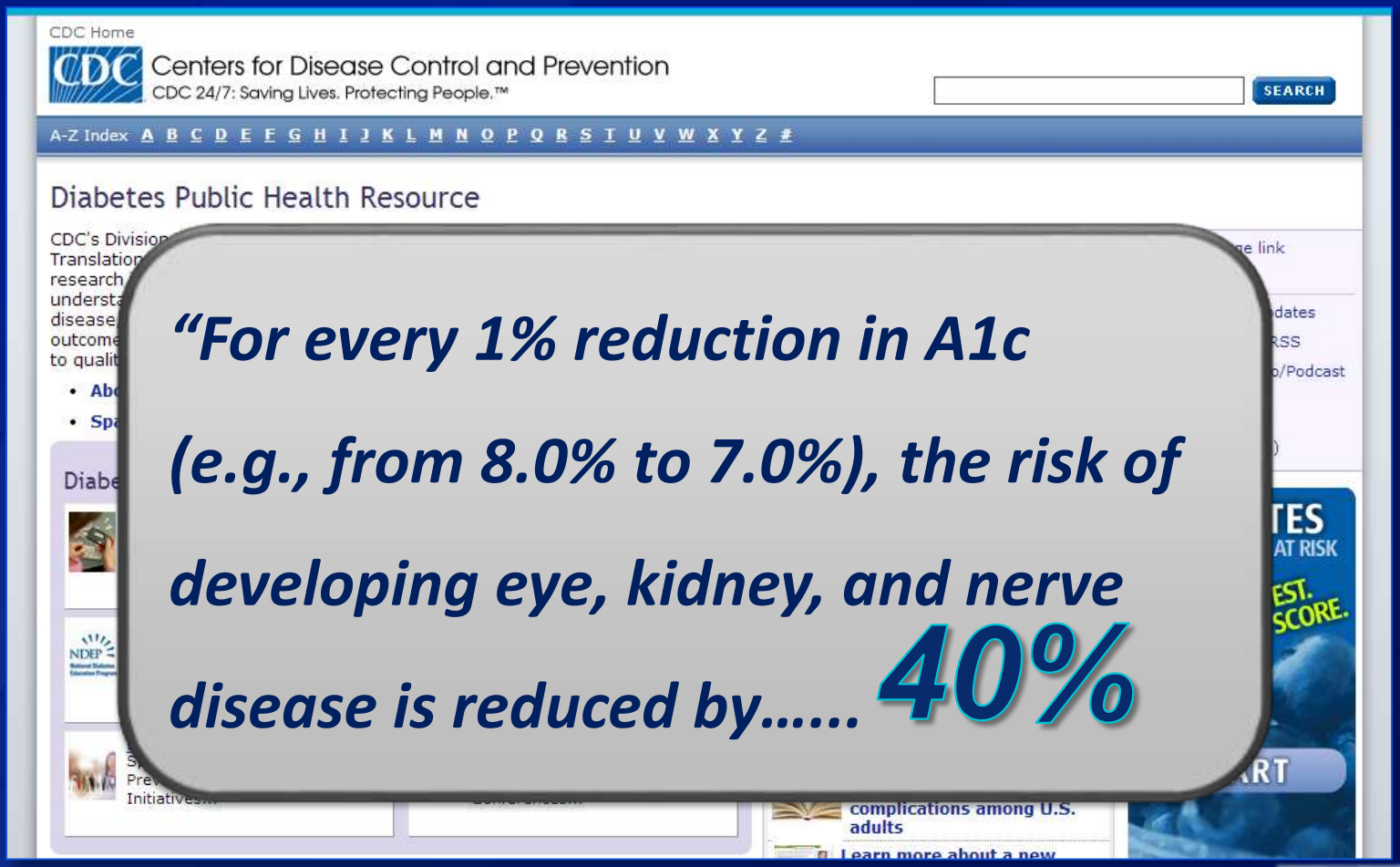
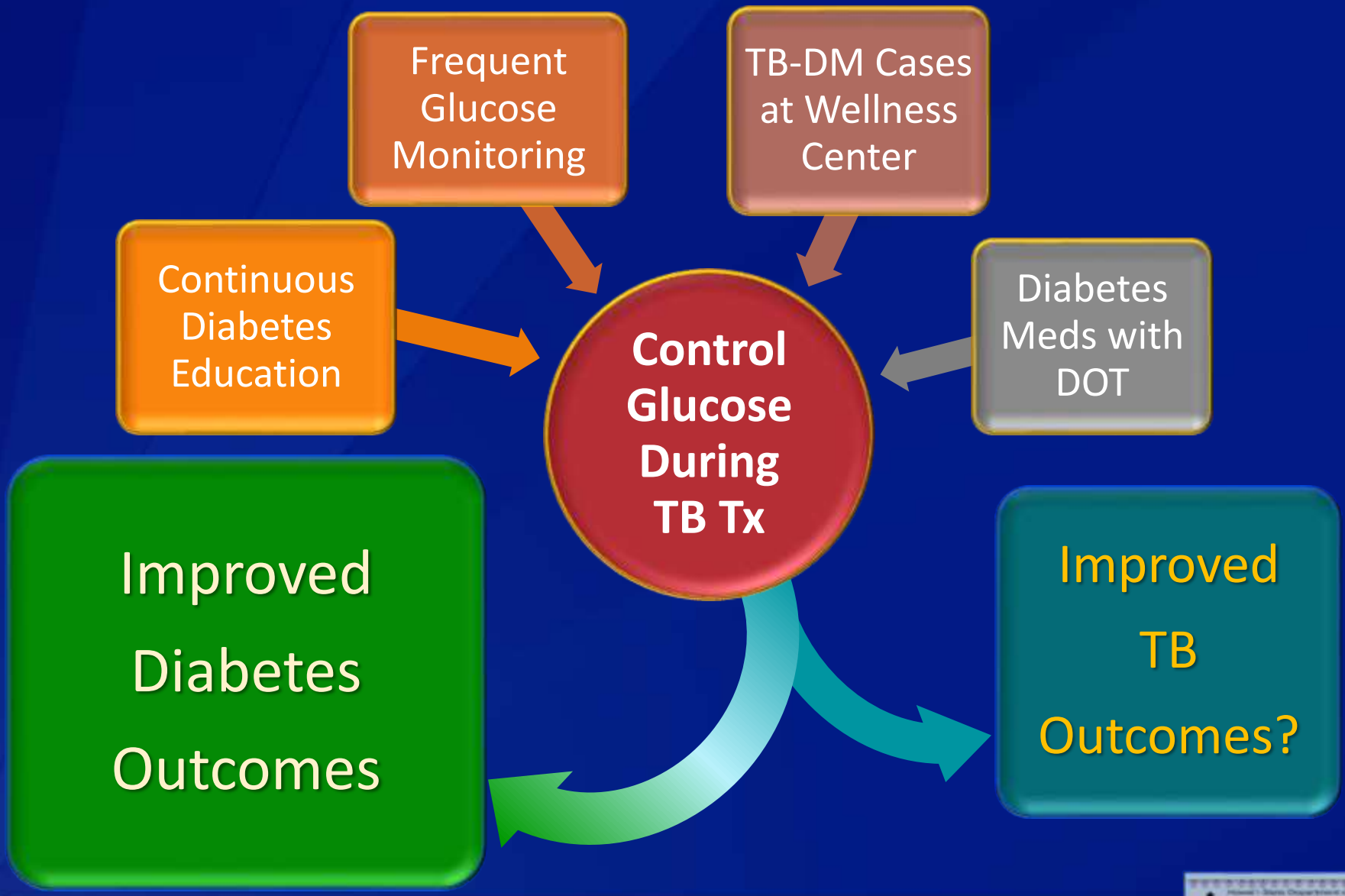
The 1% Solution……



TB-DM Program Integration Efforts



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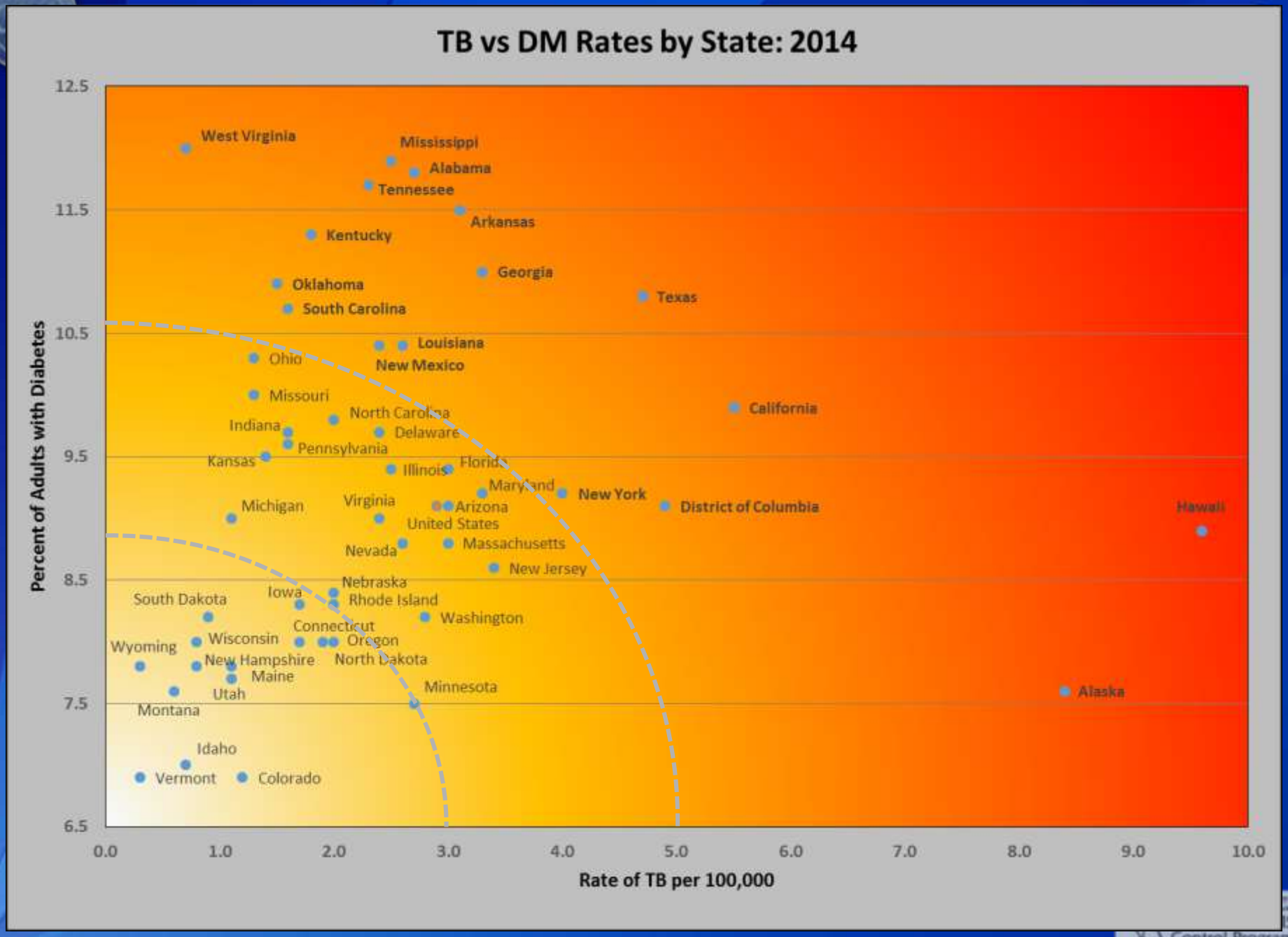
TB vs DM Rates by State: 2014



Screening for DM in TB cases in Michigan

Who? Every adult TB case, regardless of age or country of birth

When? At time of diagnosis for TB

How? A1c as a routine panel test, or RBG > 140 with A1c (reflex pos)

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Screening for TB in DM cases in Michigan

Who? All DM who are FB
All DM with poor glucose control under age 50

When? At time of diagnosis for DM, repeat eval every 5 years

How? TST ok, unless poorly controlled

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TB-DM Enhanced Case Management in Michigan

- Limit interventions to just those with poorly controlled DM (A1c > 8.5)
- Refer all DM for DM management
- Provide DM education in clinic
- Consider A1c or glucose in clinic

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Other advanced possibilities for TB-DM in Michigan

- Routine RIF/INH levels for TB cases with DM?
- Provide DM meds with DOT?
- Joint TB-DM Meeting

Enhanced TB-DM Program Collaboration

- Seek out and meet with your DM 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?

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It's not my Job!

1) A three year-old for immuni
   Drinking Kool-aid
2) Prenatal ca OB smoking
3) A with laceration: Drinking
   Grandpa in clinic with poor
   appetite: Daughter obese

EVERY HEALTHCARE VISIT IS AN NCD VISIT

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Resources

Collaborative framework for care and control of tuberculosis and diabetes:

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

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/TBandDiabetes.aspx