Diabetes and tuberculosis: double trouble?

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Objectives

- Epidemiology of diabetes and tuberculosis
- Evidence for an association
- The situation in South Africa
- Testing for diabetes in TB patients

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Diabetes

- Chronic disease
- Due to either lack of insulin (Type I) of resistance to insulin (Type II)
- One of four priority non- communicable diseases (NCDs) targeted for action by world leaders

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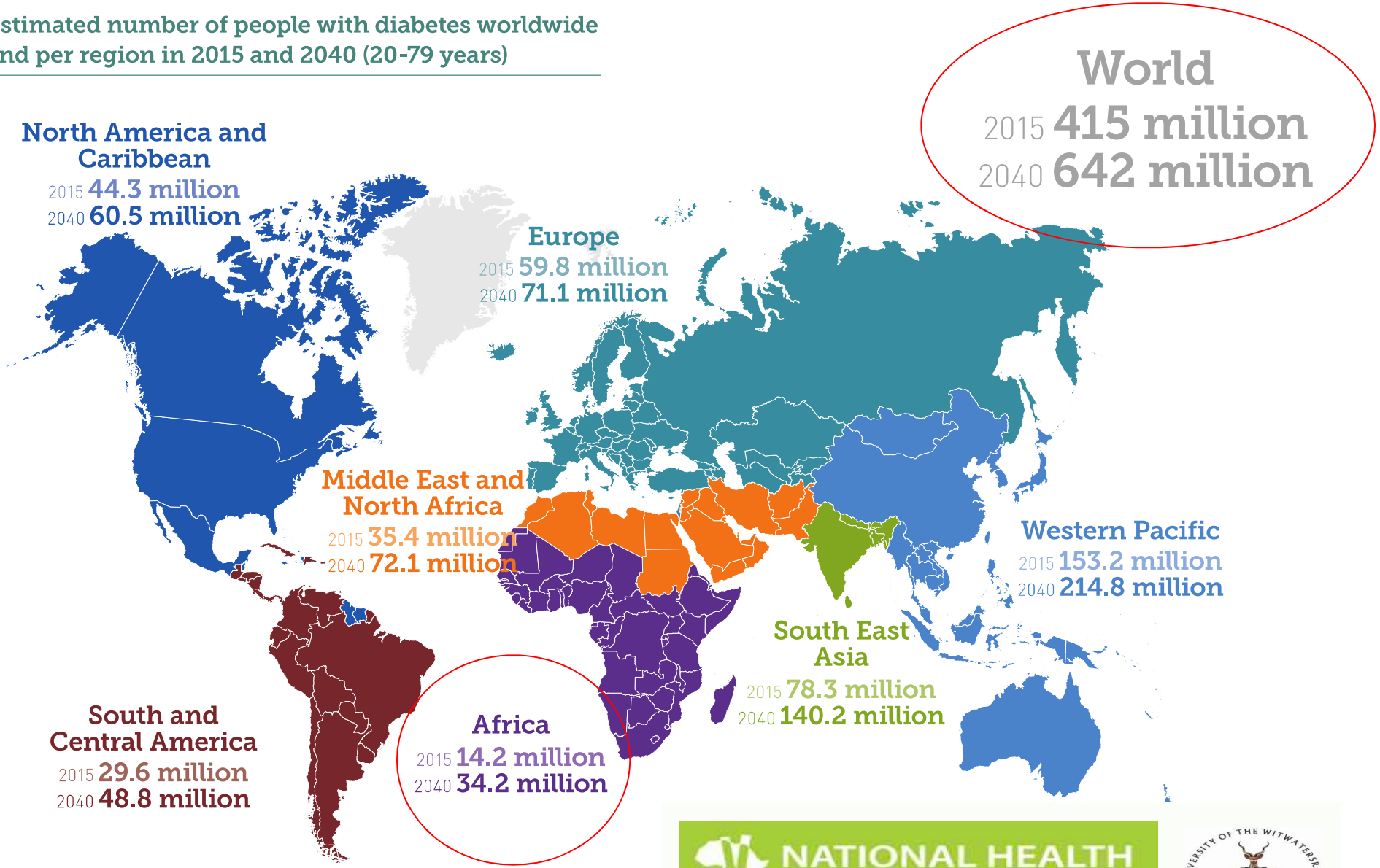
Diabetes: A global emergency

International Diabetes Federation

Estimated number of people with diabetes worldwide and per region in 2015 and 2040 (20-79 years)



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Diabetes mellitus: the epidemic of the century

	Fasting blood glucose (mmol/L)	2 hour post prandial (mmol/L)	HbA1c %
Diagnostic cut points			
Impaired fasting glucose	5.6-6.9	5.6-6.9	
Impaired glucose tolerance		7.8-11	
Diabetes	≥ 7.0	> 11	≥ 6.5%

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Prevalence of diabetes and IGF among Black African Women in Soweto

Disorder	Prevalence (%)
Diabetes (fasting glucose ≥7mmol/L)	8.86
Impaired fasting glucose (≥5.6mmol/L)	7.62
Metabolic syndrome	49.6

Jaffe et al 2015

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Prevalence of metabolic abnormalities in African and Indian adults

	Africans n=371 (%)	Indian n=350 (%)
IFG/DM	18	32
↑ BP	62	52
↑ Waist circumference	59	79
Low HDL	34	35
High Trigs	14	30

George et al 2013

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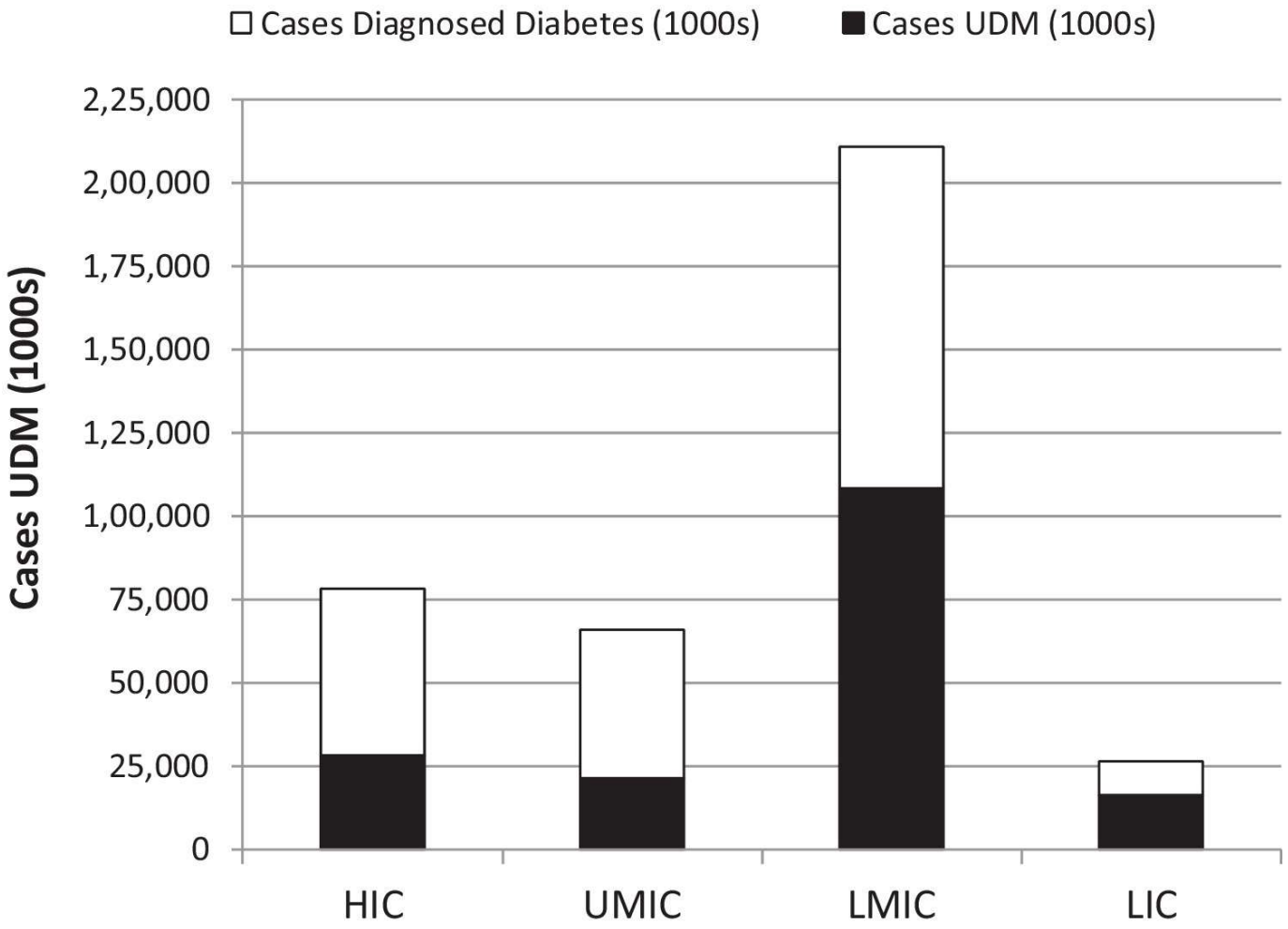
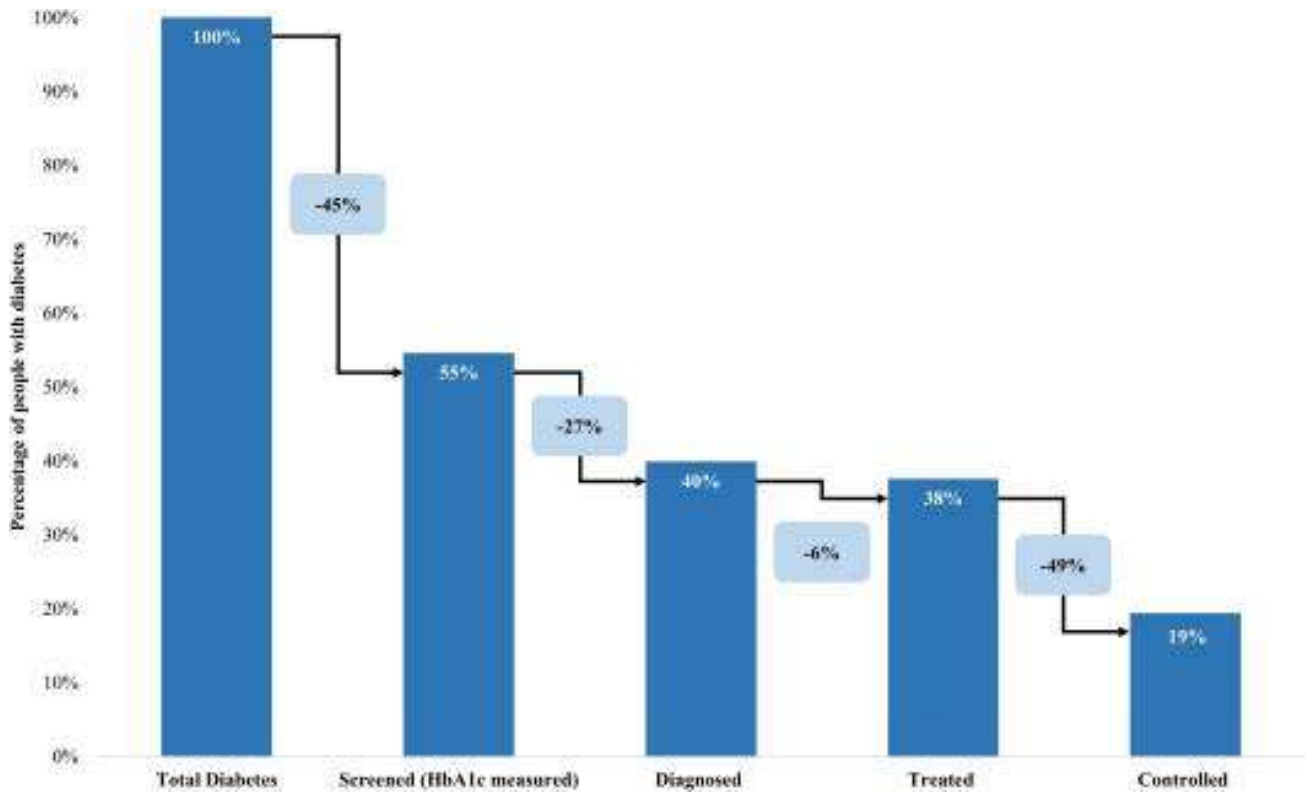
Undiagnosed diabetes



Diabetes Research and Clinical Practice
Volume 103(2): p 150-160

The diabetes care cascade, South Africa 2011–2012.



PLoS One. 2017; 12(10): e0184264.

Mortality

Adults who died from diabetes, HIV/AIDS, tuberculosis, and malaria

5.0 million
from diabetes
2015
IDF

1.5 million
from HIV/AIDS
2013
WHO Global Health Observatory Data Repository 2013

1.5 million
from tuberculosis
2013
WHO Global Health Observatory Data Repository 2013

0.6 million
from malaria
2013
WHO Global Health Observatory Data Repository 2013

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Tuberculosis
“the captain of all these men of death”

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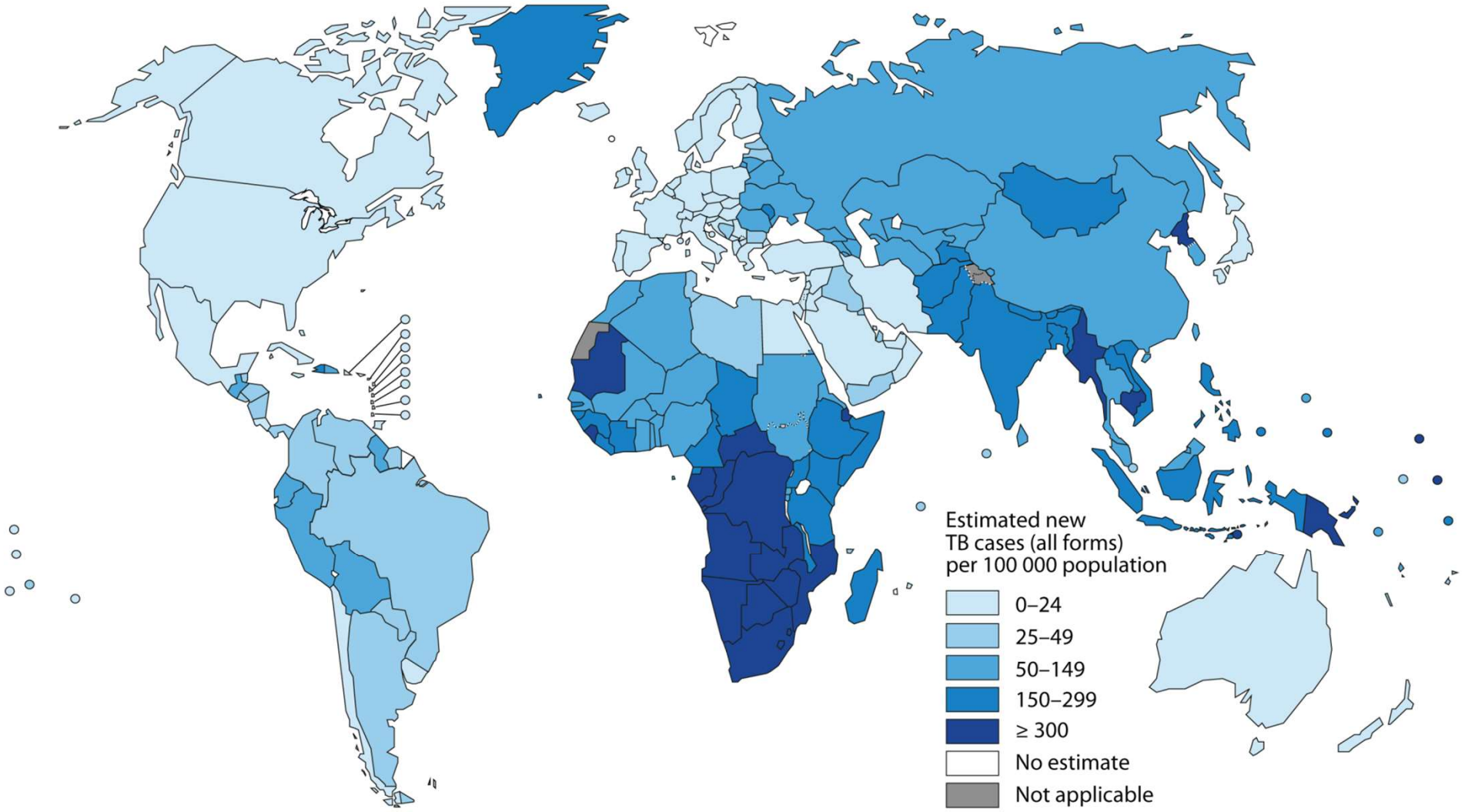
2011 Global TB Incidence Rates:



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WHO Global Tuberculous Control , 2012

Risk factors for the development of TB

- HIV/AIDS
- Other causes of immune suppression (e.g., treatment with corticosteroids)
- Silicosis
- Malnutrition
- Indoor air pollution
- Cigarette smoking
- Harmful alcohol use and other drug abuse
- Diabetes mellitus

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Global Distribution of DM and TB

Diabetes Mellitus: 2011
[IDF Atlas 5th Edition 2011]

- South East Asia 19.5%
- Western Pacific 36%
- Africa 5%
- 79% in LIC and MIC

Tuberculosis: 2011
[WHO- Global TB Control 2012]

- South East Asia 41.6%
- Western Pacific 20.8%
- Africa 20.8%
- 95% in LIC and MIC

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Objectives

- Epidemiology of diabetes and tuberculosis
- Tuberculosis in diabetics
- Diabetes in patients with tuberculosis
- Newer/alternate screening methods for diabetes

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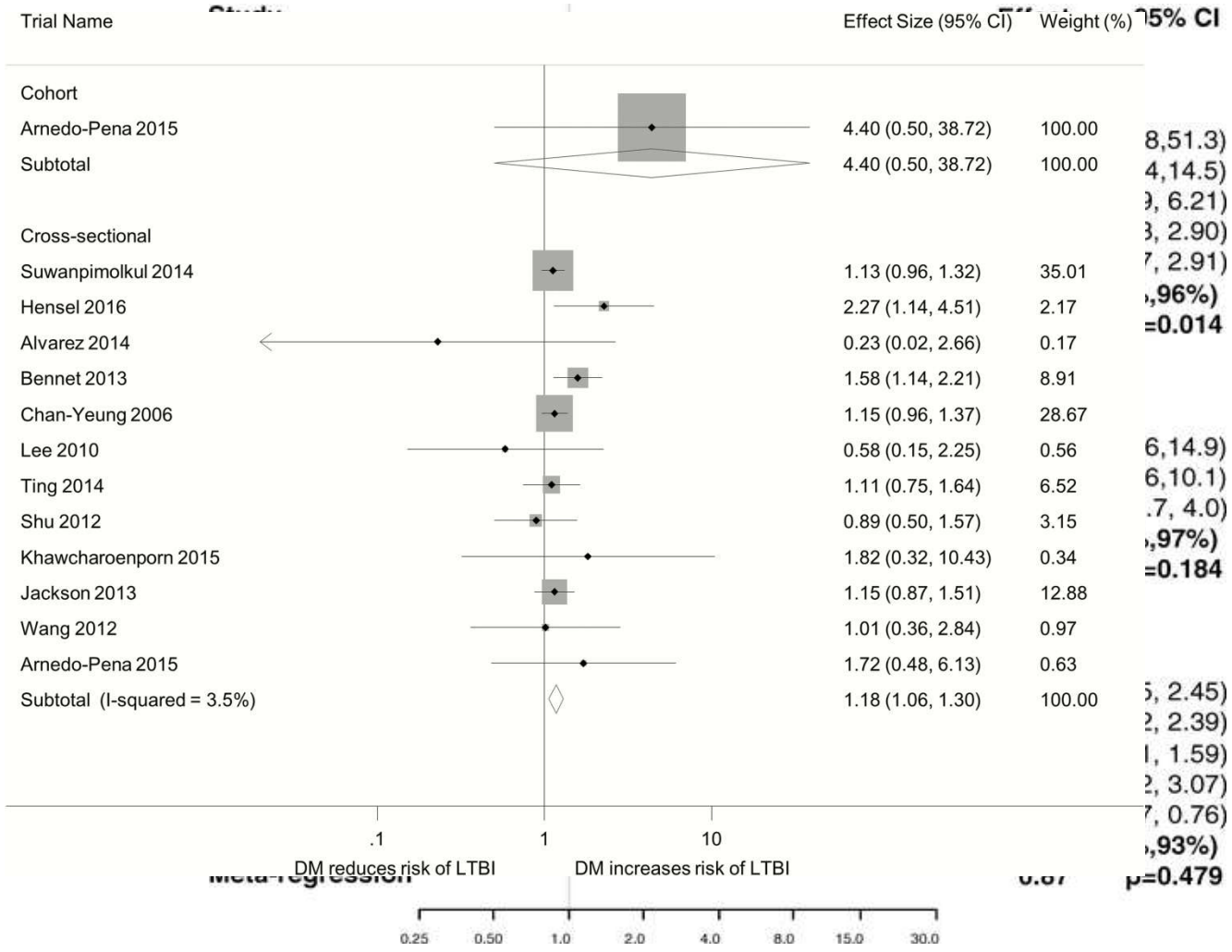
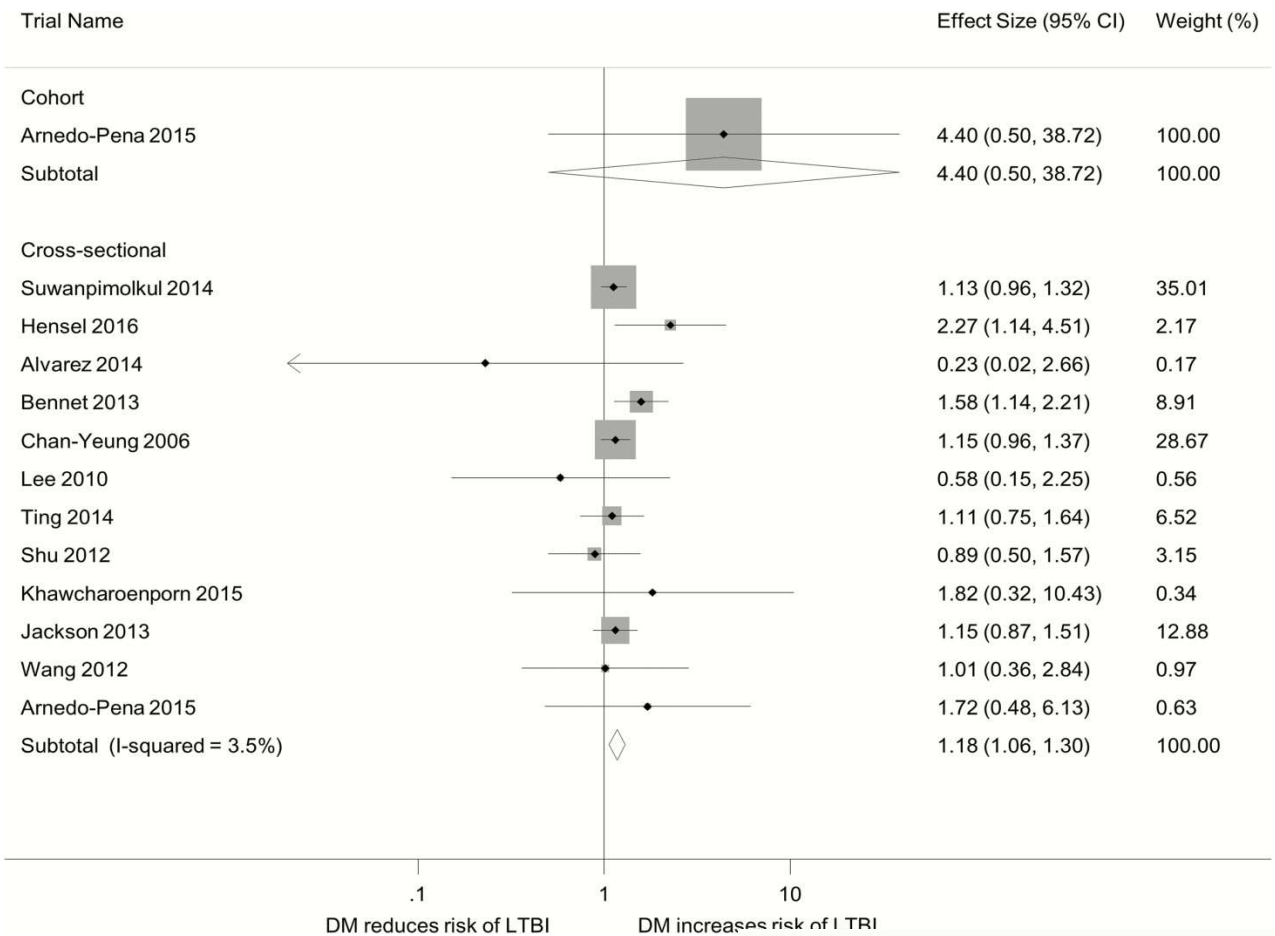
Diabetes and active tuberculosis



Jeon CY, Murray MB (2008) Diabetes Mellitus Increases the Risk of Active Tuberculosis: A Systematic Review of 13 Observational Studies. PLO 0050152
http omed.0050152

Diabetes Mellitus and Latent Tuberculosis Infection



Clinical Infectious Diseases, Volume 64, Issue 6, 15 March 2017, Pages 719–727, https://doi.org/1(

The Effect of DM on TB treatment outcomes

Longer time to sputum conversion

Treatment failure or death ((OR 2.06, (95% CI: 1.68–2.53))

Recurrence ((1.57, 1.38–1.79))

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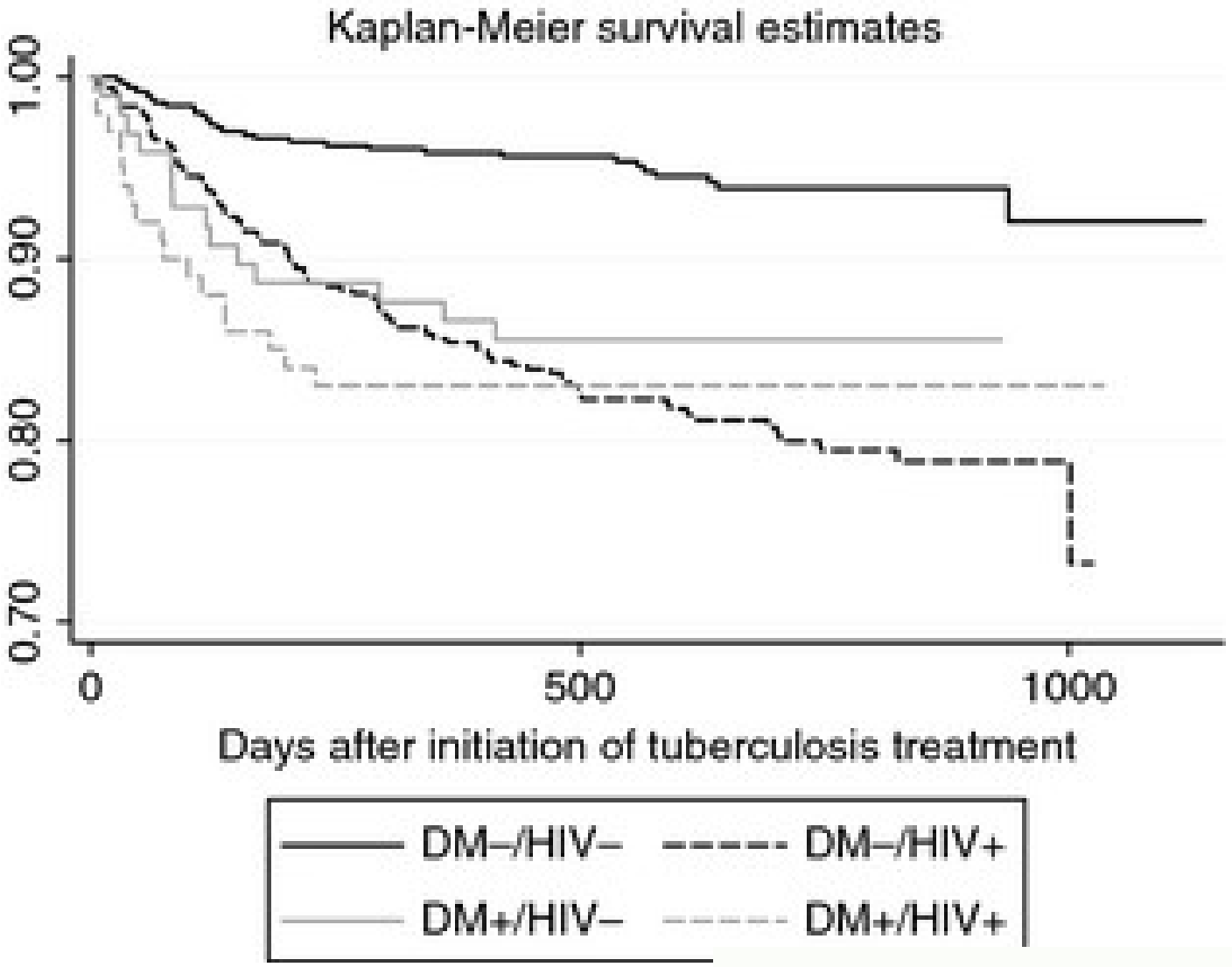
Diabetes is a strong predictor of mortality during tuberculosis treatment: a prospective cohort study among tuberculosis patients from Mwanza, Tanzania



Tropical Medicine & International Health
Volume 18, Issue 7, pages 822-829, 6 MAY 2013 DOI: 10.1111/tmi.12120
http://onlinelibrary.wiley.com/doi/10.1111/tmi.12120/full#tmi12120-fig-0001

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Diabetes in active tuberculosis

- Global 15·3% (95% CI 14.1-16.6;)
- Africa 8.0%(5.9-10.4)
- Range
- 1.9% (Benin)-34.4% (Ethiopia)
- Higher in high income, low TB burden countries

Lancet Glob Health. 2019 Apr;7(4):e448-e460.

Global prevalence of diabetes in active tuberculosis

Region	Prevalence
North America	19.7%
S E Asia	19.0%
Western Pacific	19.4%
North Africa/Middle East	17.5%
Africa	8.0%
South and Central America	7.7%
Europe	7.5%
Global	15.3%

Recommendations for screening

- People with diabetes should be screened for chronic cough at the time of their diagnosis and if possible, during regular check-ups.
- Patients with TB should be screened for diabetes at the start of their
- treatment, where resources for diagnosis are available.
- The type of screening and diagnostic tests should be adapted to the context of local health systems and the availability of resources

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Tuberculosis program requirements for DM screening

DM assay that requires

- no patient preparation,
- is acceptably accurate, sensitive and specific,
- is low cost,
- requires minimal infrastructure and is easy to use

- Preferably POC

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Local data
N= 83

	OGTT	HbA1c
IFG %)	3.61	75.9
IGT (%)	18.1	
DM (%)	2.41	14.1**

INT J TUBERC LUNG DIS 21(2):208–213

Multivariate linear regression models for HbA1c levels

Independent variables	Laboratory HbA1c	POC HbA1c
Age (years)	0.31 (0.009)	0.17 (0.002)
Weight (kg)	0.31 (0.009)	0.12 (0.03)
Duration of TB treatment (weeks; log)	-0.17 (0.004)	-0.15 (0.01)

INT J TUBERC LUNG DIS 21(2):208–213

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Associations with duration of TB treatment

Variables	Quartiles of duration of TB treatment			
	1 (n=80)	2 (n=79)	3 (n=79)	4 (n=79)
POC HbA1c (%)	5.73±0.41	5.54±0.45*	5.55±0.45*	5.67±0.43*
Lab HbA1c (%)	5.91± 0.61	5.58±0.53**	5.69±0.49*	5.77±0.48
Fasting glucose (mmol/l)	4.96 ± 0.66	4.87 ± 0.70	4.68 ± 1.05	4.75 ± 0.61
Two hour glucose (mmol/l)	6.65 ± 1.39	6.37 ± 1.44	6.24 ± 2.23	6.14 ± 1.50

INT J TUBERC LUNG DIS 21(2):208–213

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Prevalence of diabetes and impaired glucose regulation (IGR), including previously diagnosed diabetes, by diagnostic test

Diabetes	Overall	Non-TB	TB
FPG	4.1 (3.0–5.7)	3.9 (2.4–6.2)	4.4 (2.8–6.9)
OGTT	3.3 (2.3–4.8)	3.5 (2.1–5.8)	3.1 (1.7–5.3)
HbA1c	8.2 (6.5–10.2)	6.2 (4.3–8.9)	10.2 (7.7–13.6)
IGR			
Any test	57.3 (53.7–60.8)	50.0 (45.1–54.9)	65.2 (60.0–70.0)
FPG	10.6 (8.6–13.1)	12.5 (9.5–16.1)	8.6 (6.1–12.2)
OGTT	10.6 (8.6–13.0)	4.9 (3.1–7.5)	16.9 (13.3–21.2)
HbA1c	39.5 (36.1–43.0)	34.1 (29.6–38.9)	45.4 (40.3–50.6)

Eur Respir J

2017 Jul; 50(1): 1700004.

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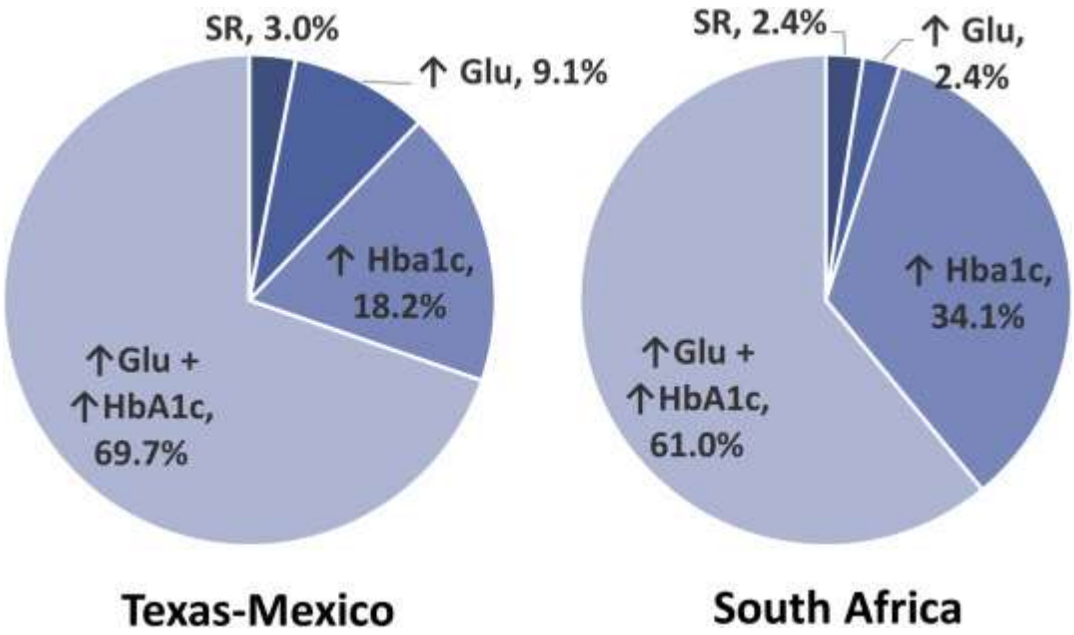
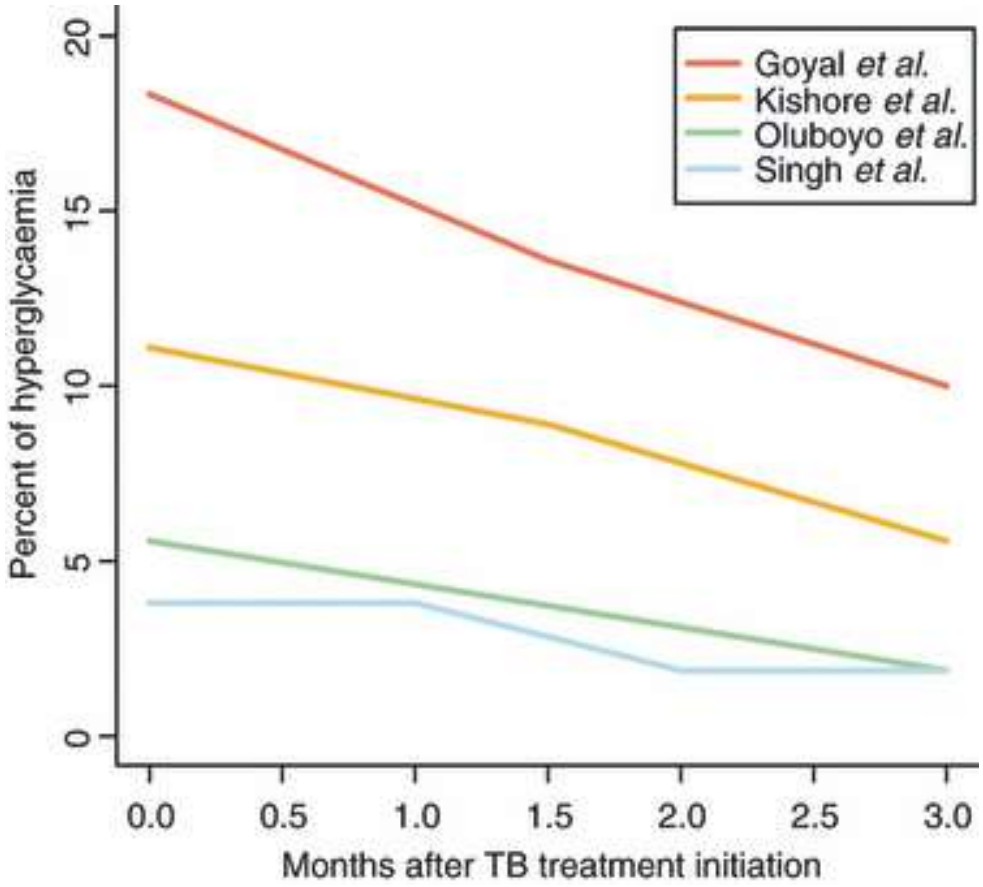
Diabetes screening in Cape Town

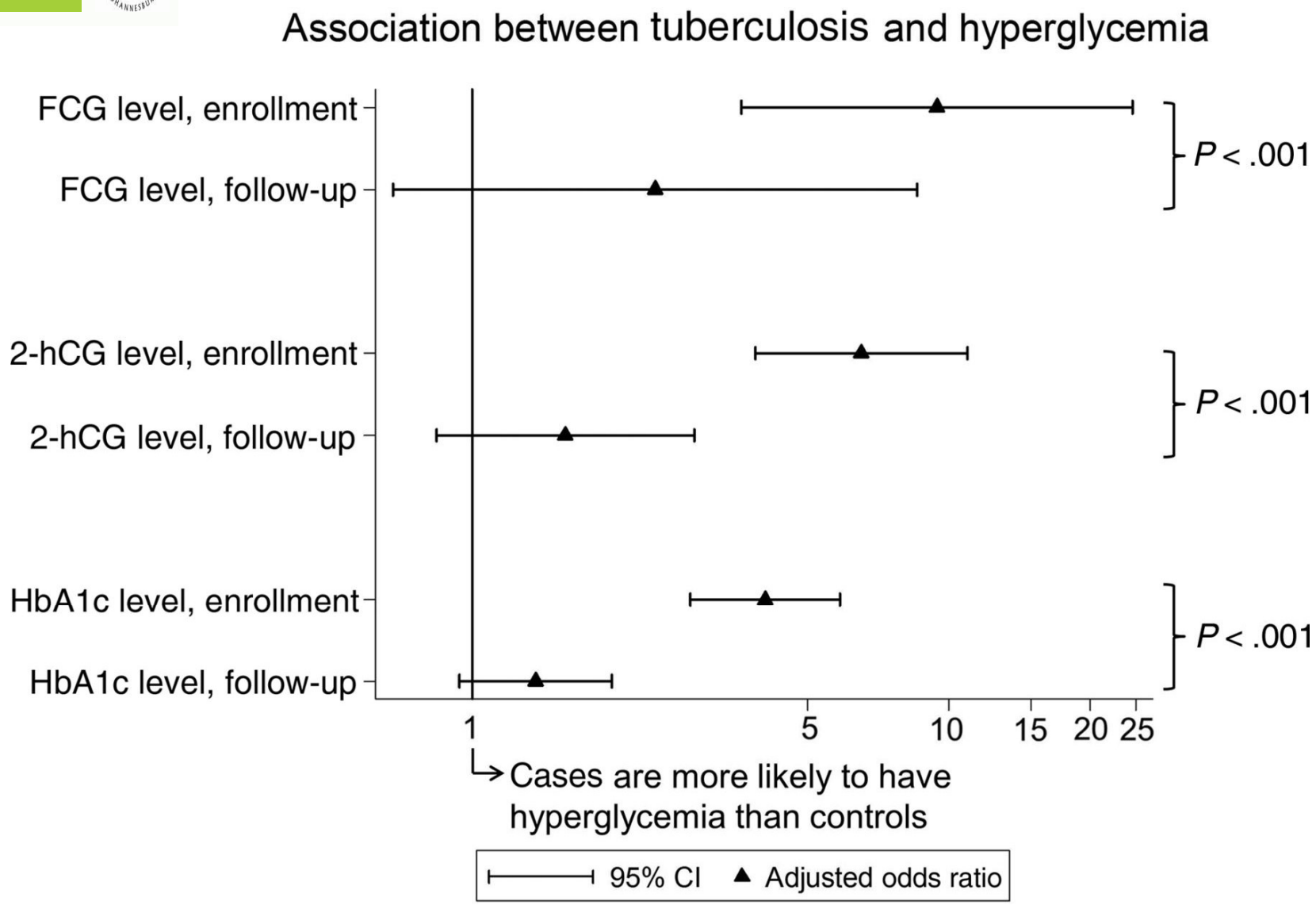


Tuberculosis
Volume 113, December 2018, Pages 10-18



Tropical Medicine & International Health, Volume: 15, Issue: 11, Pages: 1300-1314, First published: 24 September 2010, DOI: (10.1111/j.1365-3156.2010.02632.x)

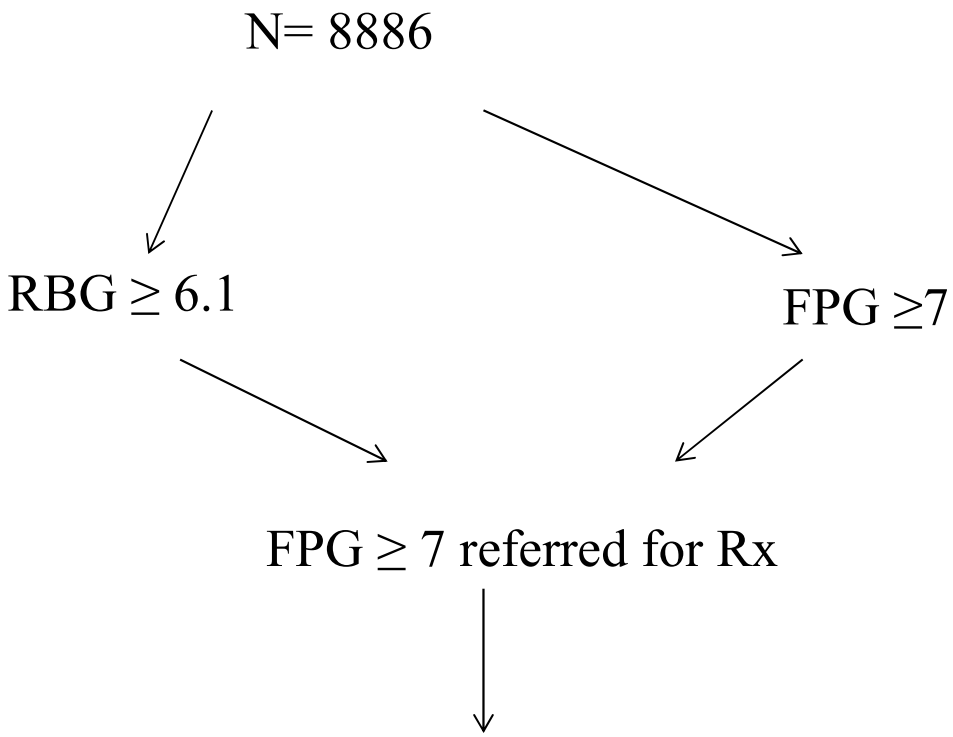
All tests show evidence of declining glycaemia



Noémie Boillat-Blanco et al. J Infect Dis. 2016;213:1163-1172

The Journal of Infectious Diseases

Yes : the China example

- China
- 

Conclusions

- There is strong evidence for the association between TB and DM
- This association results in poor outcomes.
- Linked to hyperglycaemia and its consequences
- The association of DM with TB has to be evaluated further
- With regard to DM in TB :
- Questions remain as to who should be screened, when they should be screened and what test should be used.
- Evidence from SA suggests that HbA1c is not suitable for screening

Future work

- How best to test for these in our populations?
- When to test?
- Can changes in blood glucose indicate response to TB treatment?

- How does our disease burden affect HbA1c?