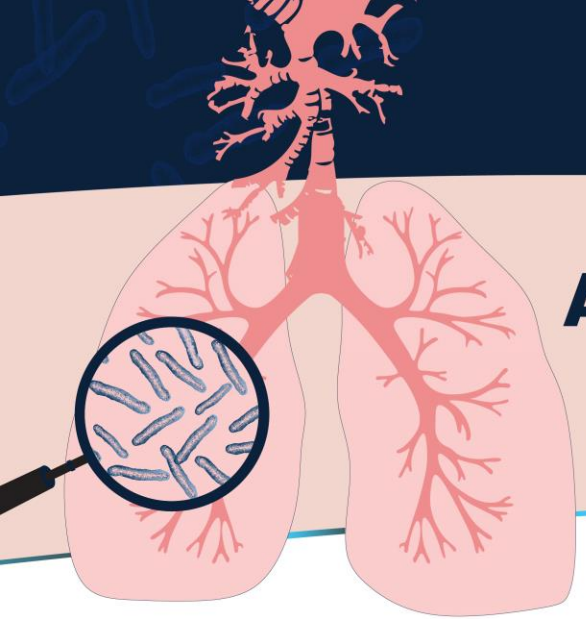

Accelerating progress to end TB

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Prior tuberculosis, radiographic lung abnormalities and prevalent diabetes in rural South Africa

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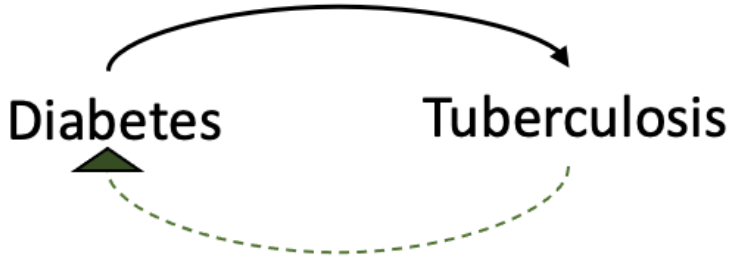
Background



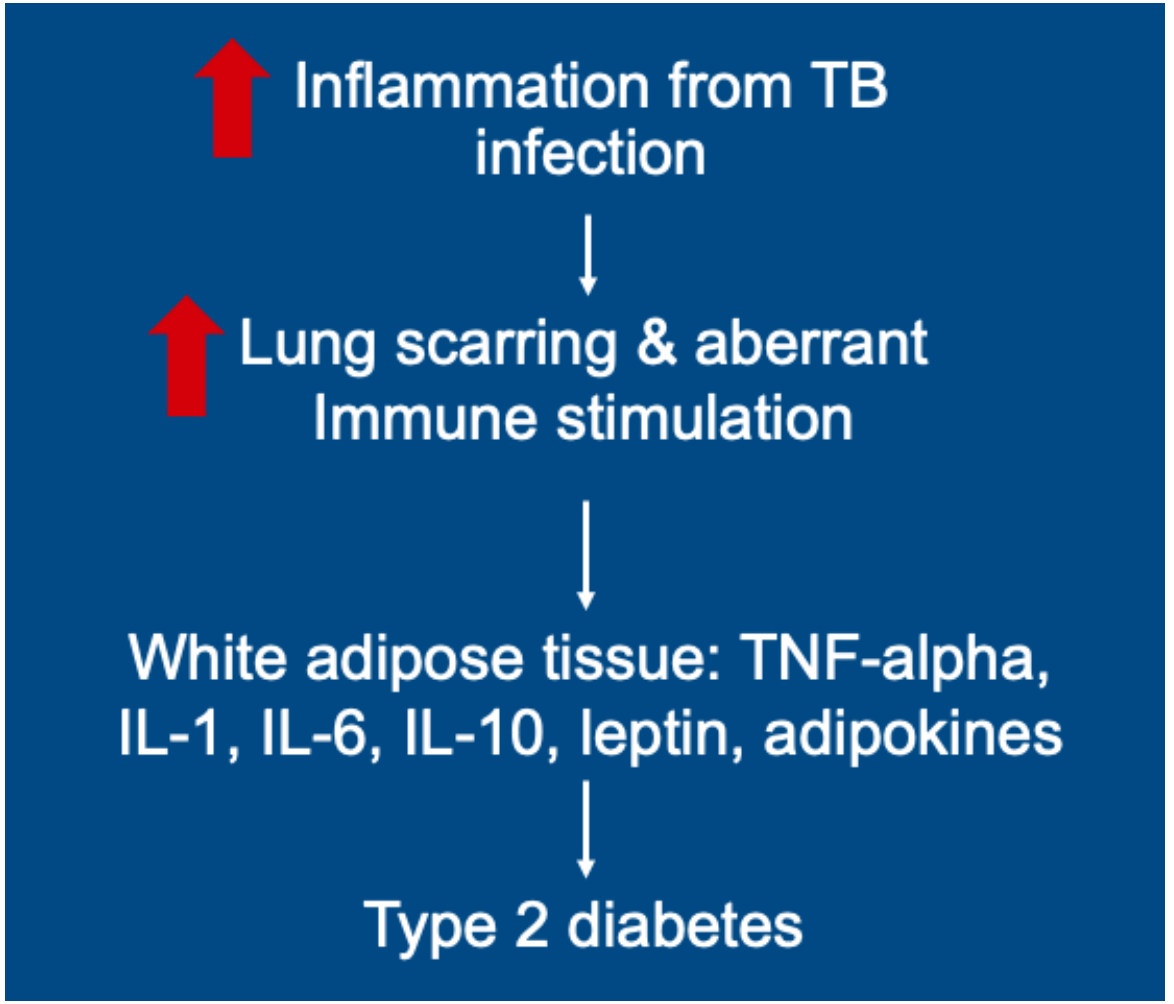
- Prior TB disease may increase diabetes risk.[1]
- The immune response to TB induces lung damage and has been associated with insulin resistance.[2,3]
- Chest X-ray lung abnormalities are a surrogate measurement of both the severity of TB disease and the host immune response.[4]
- We hypothesize that lung abnormalities on chest radiography in people with prior TB may be associated with prevalent diabetes.

(1) Pearson F, et al. J Epidemiol Community Health, 2019. (2) Brown TT, et al. Diabetes Care, 2010. (3) Martinez N, et al. Ebio Medicine, 2019. (4) Stek C, et al. Front Microbiol, 2018.

Objective

To explore the association between chest X-ray (CXR) abnormalities and prevalent diabetes among individuals with a history of TB.

Conceptual Framework



Tsalamandris et al. Eur Cardiol. 2019

Methods

Secondary data analysis from a cross-sectional, community-based study that enrolled >18,000 adults in KwaZulu-Natal, South Africa

Analytic sample: persons with prior TB defined as

1) self-report of prior TB treatment **or**
2) radiologist-diagnosed prior TB on CXR **and**
3) negative sputum culture/GeneXpert (i.e., absence of active TB)

Methods

- **Primary outcome** prevalent diabetes (HbA1c ≥ 6.5%)

- **Primary exposure** computer-aided detection CAD4TB scores of CXR, ranging from 10-100

Example CAD4TB CXR from participant: score 97

Statistical approach

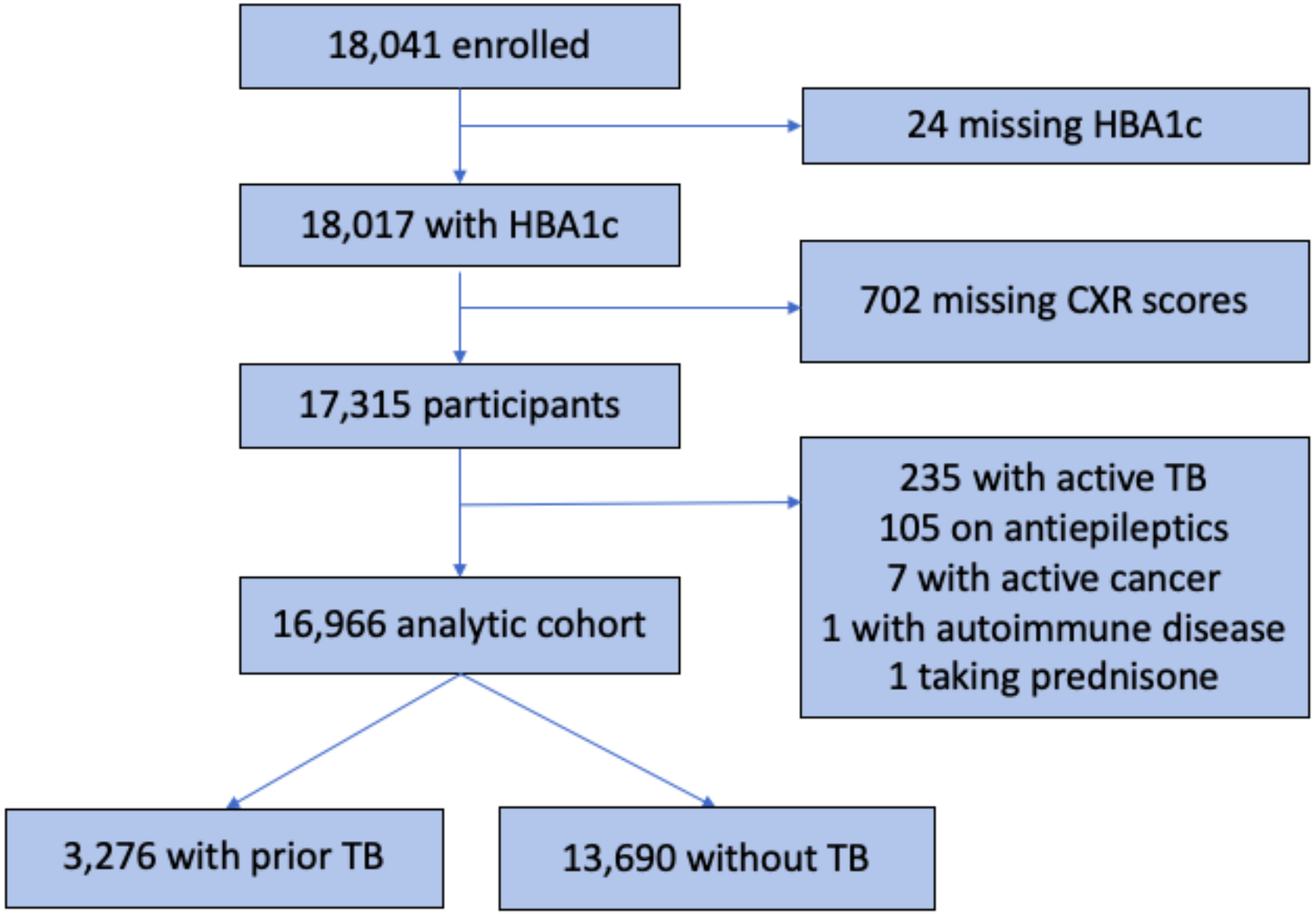
- Fitted logistic regression models to estimate the relationship between CAD4TB CXR scores and diabetes
- **Models were adjusted for** age, sex, smoking status, alcohol use, waist circumference, HIV serostatus, and socioeconomic status

Sensitivity Analyses

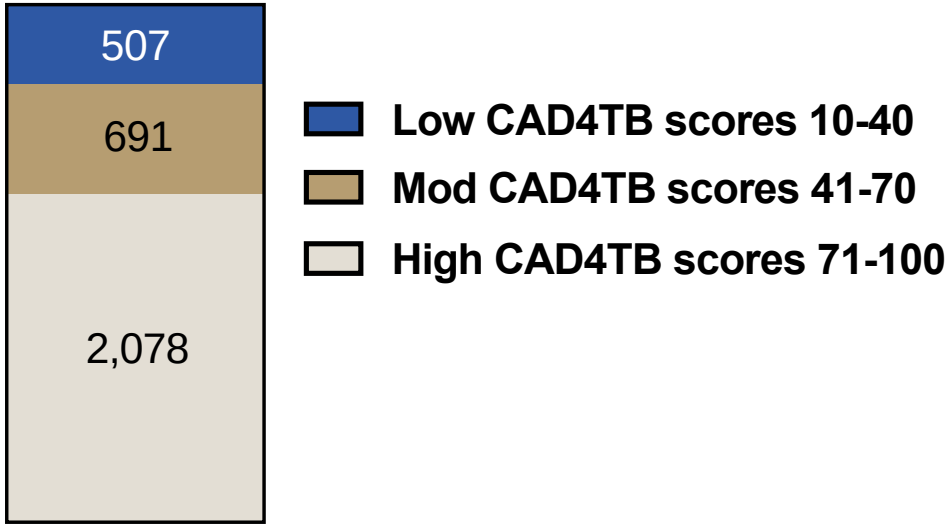
1) Modified exposure to be the presence of lung abnormalities characterized by study radiologist

2) Repeated the primary analysis with a comparator group with no history of TB

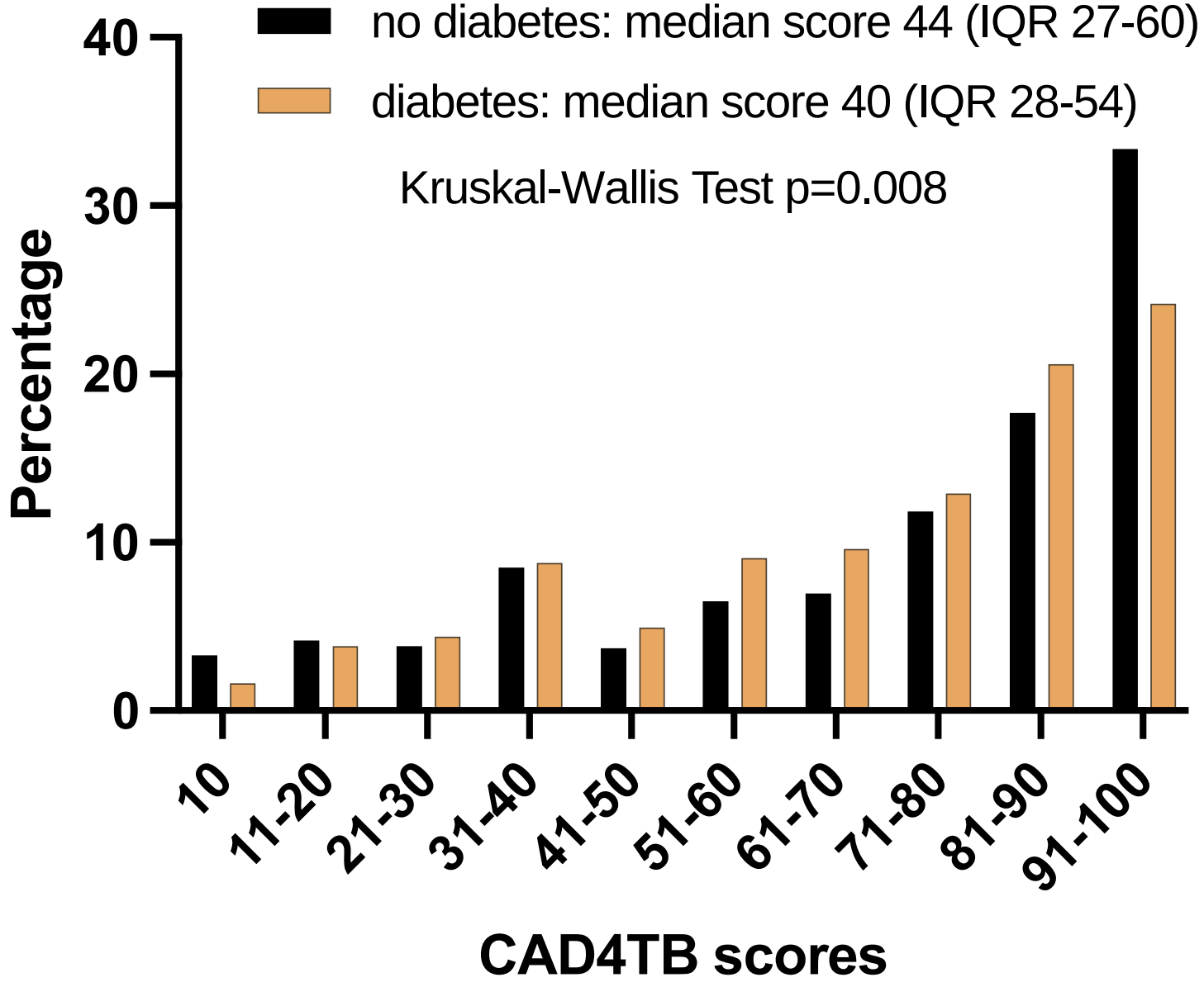
Results


18,041 enrolled
24 missing HBA1c
18,017 with HBA1c
702 missing CXR scores
17,315 participants
235 with active TB
105 on antiepileptics
7 with active cancer
1 with autoimmune disease
1 taking prednisone
16,966 analytic cohort
3,276 with prior TB
13,690 without TB

Sample characteristics



Unadjusted CAD4TB scores by diabetes status



For every 10-unit increase in CXR score, the odds of having prevalent diabetes decrease by 8%

Characteristic	Unadjusted Odds Ratio (95%CI)	p value	Adjusted Odds Ratio (95% CI)	p value
Model: Prior TB cohort with CAD4TB scores (n=3,276)				
CAD4TB scores	**0.97 (0.94-1.01)**	**0.210**	**0.92 (0.87-0.97)**	**0.002**
Female sex	2.50 (1.90-3.29)	<0.001	1.19 (0.87-1.64)	0.283
Age (years)	1.04 (1.03-1.05)	<0.001	1.03 (1.03-1.04)	**<0.001**
Waist Circumference (cm)	1.93 (1.74-2.13)	<0.001	1.57 (1.41-1.76)	**<0.001**
Living with HIV	0.37 (0.29-0.47)	<0.001	0.58 (0.44-0.77)	**<0.001**
Ever smoker	0.16 (0.08-0.32)	<0.001	0.51 (0.24-1.06)	0.071
Consumes alcohol	0.23 (0.14-0.38)	<0.001	0.50 (0.29-0.89)	**0.018**
Socioeconomic status	1.10 (1.03-1.16)	0.001	1.06 (1.00-1.13)	0.047

The presence of radiologist-detected abnormalities was associated with a 29% lower odds of having diabetes

Characteristic	Unadjusted Odds Ratio (95%CI)	p value	Adjusted Odds Ratio (95% CI)	p value
Model: Prior TB cohort with radiologist interpretation (n=3,276)				
Radiologist abnormalities	**1.23 (0.95-1.58)**	**0.114**	**0.71 (0.53-0.97)**	**0.030**
Female sex	2.50 (1.90-3.29)	<0.001	1.27 (0.93-1.74)	0.133
Age (years)	1.04 (1.03-1.05)	<0.001	1.03 (1.02-1.04)	**<0.001**
Waist Circumference (cm)	1.93 (1.74-2.13)	<0.001	1.61 (1.45-1.79)	**<0.001**
Living with HIV	0.37 (0.29-0.47)	<0.001	0.55 (0.42-0.74)	**<0.001**
Ever smoker	0.16 (0.08-0.32)	<0.001	0.50 (0.24-1.03)	0.063
Consumes alcohol	0.23 (0.14-0.38)	<0.001	0.49 (0.28-0.86)	**0.013**
Socioeconomic status	1.10 (1.03-1.16)	0.001	1.07 (1.00-1.13)	**0.035**

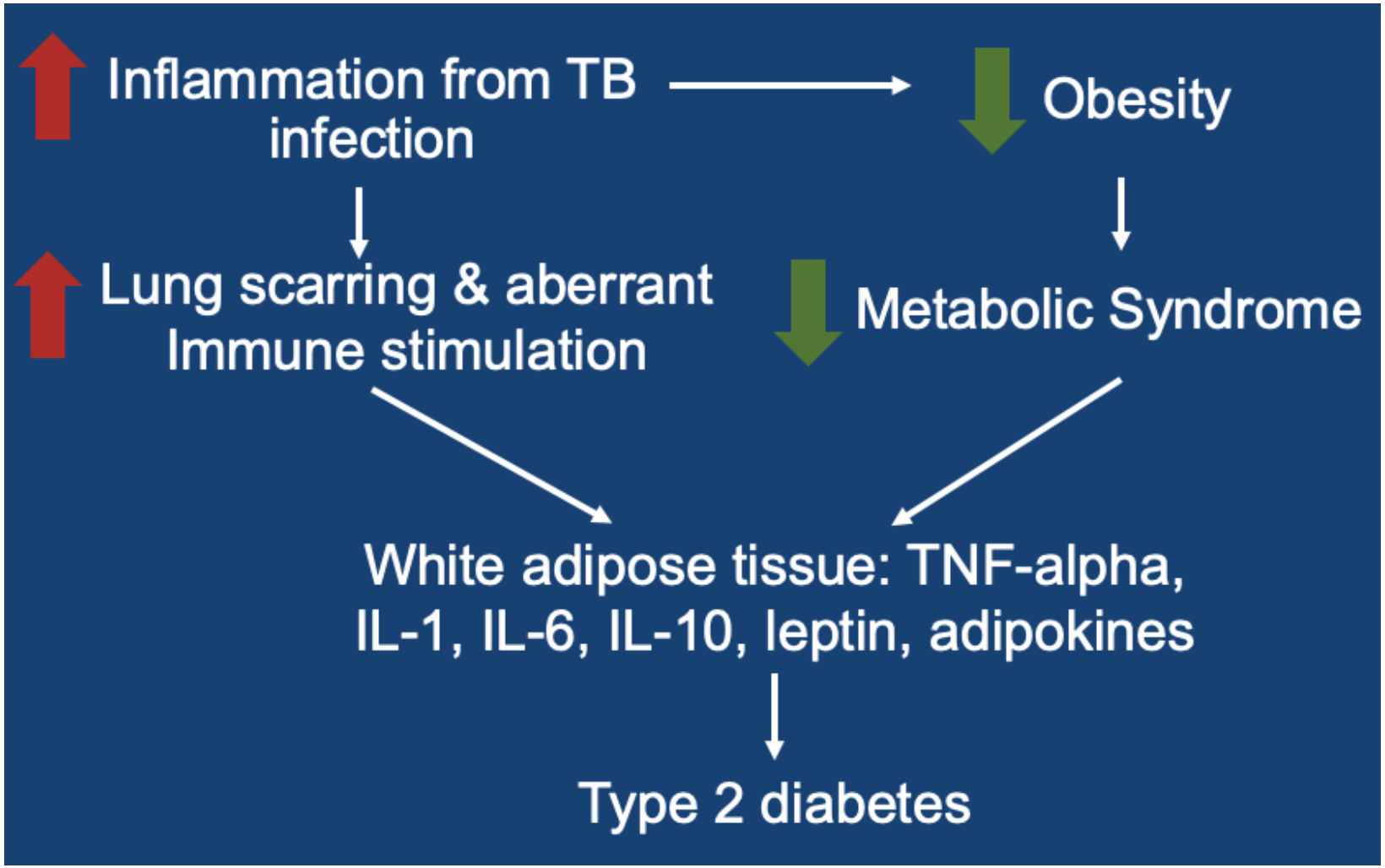
For every 10-unit increase in CXR scores, there was a 4% reduction in the odds of having diabetes, *among people without TB*

Characteristic	Unadjusted Odds Ratio (95%CI)	p value	Adjusted Odds Ratio (95% CI)	p value
Model: Non-TB comparator group (n=13,998)				
CAD4TB scores	**1.11 (1.09-1.13)**	**<0.001**	**0.96 (0.94-0.99)**	**0.013**
Female sex	2.40 (2.07-2.78)	<0.001	0.99 (0.83-1.19)	0.941
Age (years)	1.06 (1.05-1.06)	<0.001	1.04 (1.04-1.05)	**<0.001**
Waist Circumference (cm)	2.18 (2.07-2.31)	<0.001	1.66 (1.56-1.77)	**<0.001**
Living with HIV	0.54 (0.47-0.62)	<0.001	0.70 (0.59-0.82)	**<0.001**
Ever smoker	0.40 (0.29-0.55)	<0.001	0.98 (0.66-1.44)	0.901
Consumes alcohol	0.26 (0.19-0.35)	<0.001	0.44 (0.31-0.62)	**<0.001**
Socioeconomic status	1.11 (1.07-1.14)	<0.001	1.05 (1.01-1.08)	**0.009**

Study Limitations

- Survival Bias
- Cross-sectional study design prevents causal inference or directionality
- Chest radiography cannot distinguish former TB from other processes such as malignancy, environmental exposures, or other infections.

Revised conceptual framework



Conclusions

Among people with prior TB, pulmonary abnormalities on digital chest X-rays are associated with a **lower odds of prevalent diabetes**.

The presence or severity of radiographic post-TB lung disease **does not** appear to be a correlate of diabetes in this South African population.

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