

# Refugees with diabetes mellitus have higher prevalence of latent tuberculosis infection

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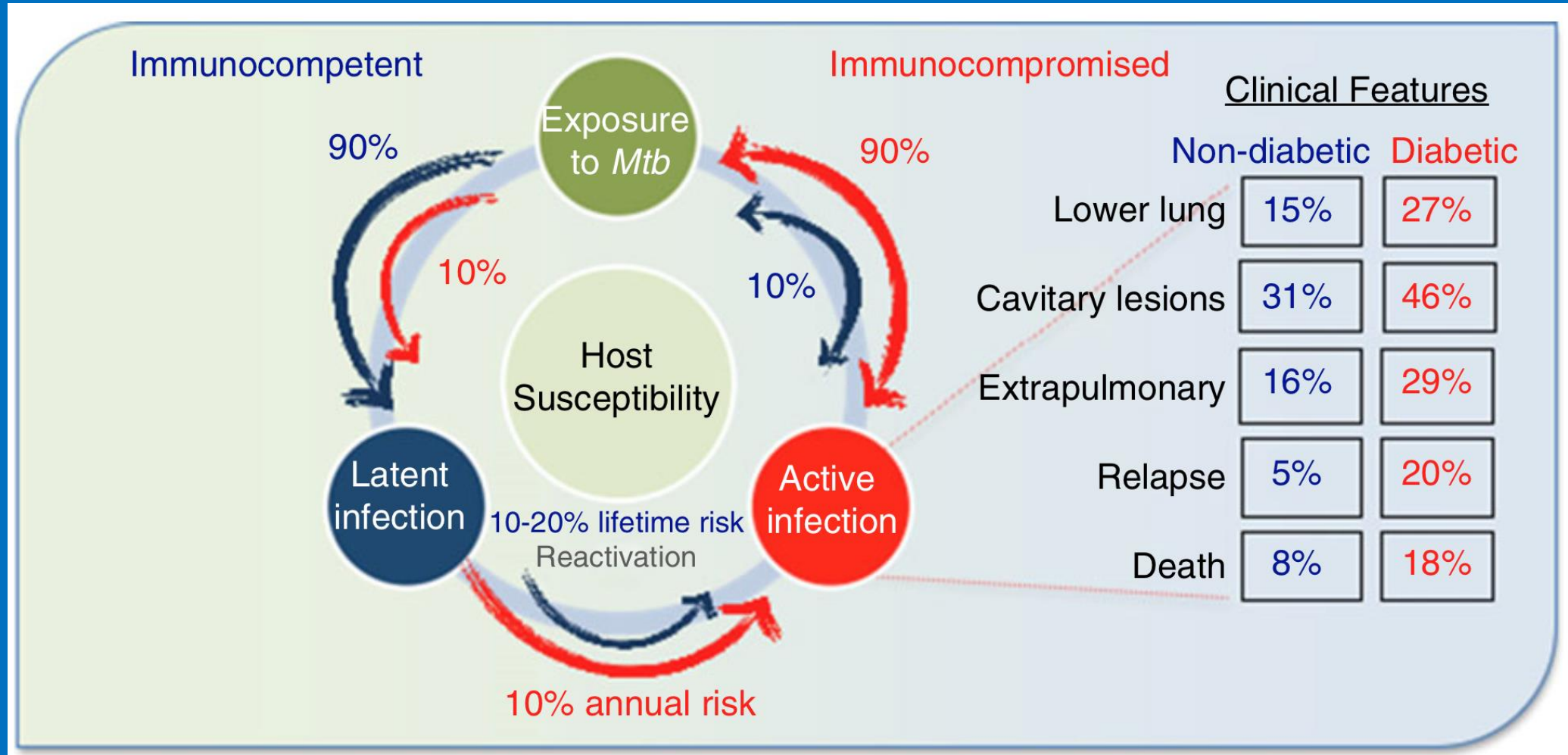
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# Background

- Diabetes mellitus is an established risk factor for active TB disease
- Estimated risk of active TB in persons with diabetes is approximately 3-times the risk of the general population
- Currently unknown:
  - Does diabetes increase the risk of progression from latent TB infection to active TB disease?
  - Does diabetes increase the risk of latent TB infection?

# Background



Hodgson K et al. Immunological mechanisms contributing to the double burden of diabetes and intracellular bacterial infections. *Immunology* 2015 Feb; 144 (2)

# Study Aims

1. Estimate the association between diabetes, pre-diabetes, and prevalent latent TB infection.
1. Determine if the effect of diabetes on latent TB infection is modified by levels of vitamin D.

# Study Design

- Cross-sectional study
- DeKalb County Board of Health Refugee Clinic, Oct 2013-Aug 2014
- Eligibility criteria:
  - Adult ( $\geq 21$  years) patients
  - New patient screening during the study period
  - No active TB

# Study Design

- Primary Exposure: Diabetes status
  - **HbA1c**: No diabetes ( $\leq 5.6\%$ ), Pre-diabetes ( $\geq 5.7-6.4\%$ ), and diabetes ( $\geq 6.5\%$ )
- Primary Outcome: Latent TB infection
  - **QuantiFERON-TB Gold In-Tube (QFT)**: Negative/Positive
- Interaction covaritate: Plasma vitamin D level
  - 25-hydroxyvitamin D concentration  $< 20$  ng/ml was defined as deficient

# Results

- 702 patients from 54 countries were included in the study
  - 695 had HbA1c results, 694 had QFT results, 681 had both
- 7.8% (54/695) had diabetes and 235/695 (34%) had pre-diabetes
  - Median HbA1c among patients with diabetes 7.2% (IQR 6.6-9.8)
  - 55.6% (30/54) were newly diagnosed with diabetes
- 31.8% (221/694) had latent TB infection by QFT
- 42.4% (292/688) were vitamin D deficient

# Results

Table 1. Patient characteristics and prevalent latent TB infection

Patient Characteristics	Latent TB infection N=221 (32%)	No latent TB N=473 (68%)	P-value*
Age, median years (IQR)	35 (27-46)	32 (26-41)	<0.01
Male, N (%)	127 (59)	254 (54)	<0.01
High burden TB country of birth#, N (%)	70 (32)	160 (34)	0.48
Plasma vitamin D, median ng/ml (IQR)	21 (16-27)	20 (15-27)	0.42

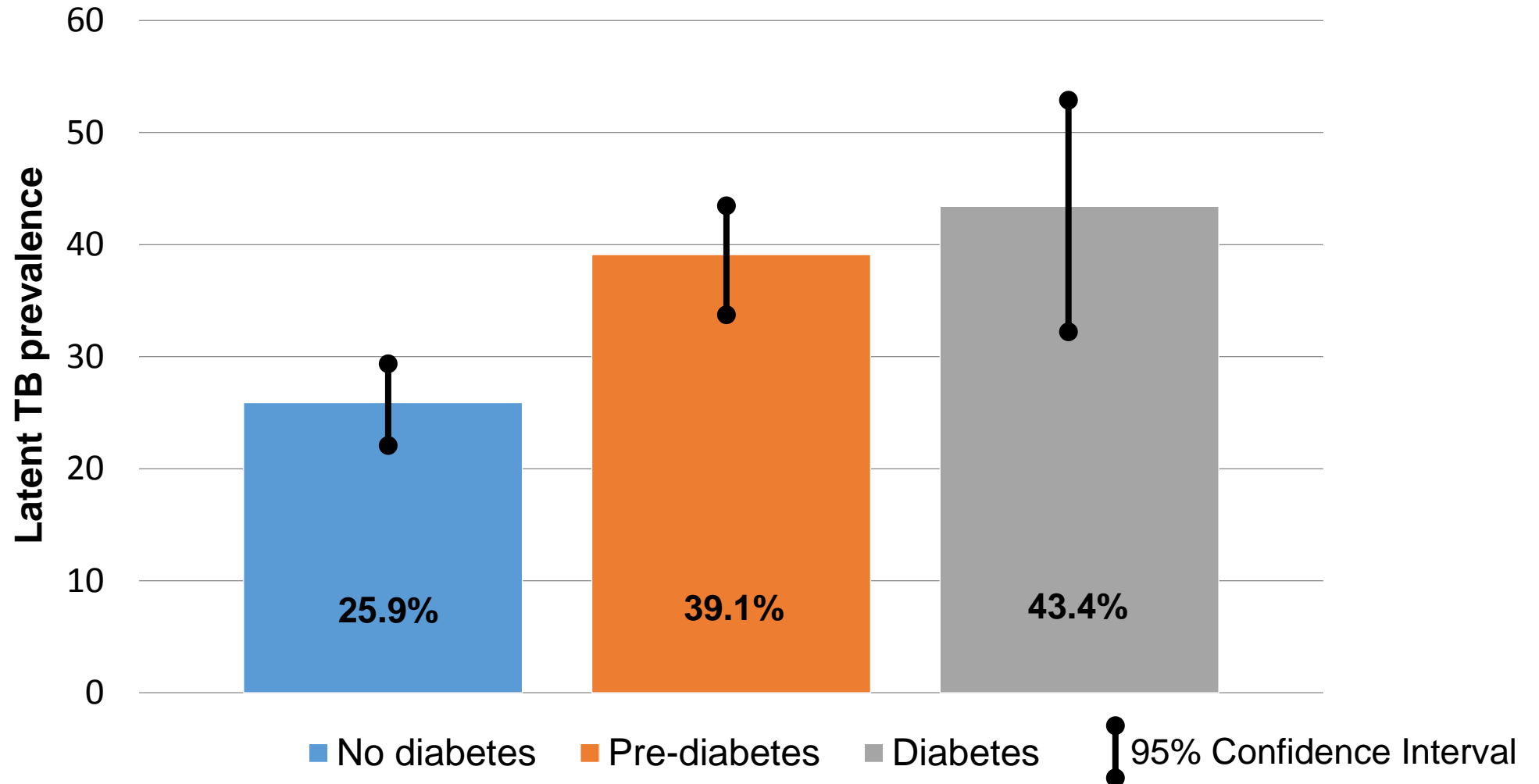
\*Chi-square or Wilcoxon Rank sum two-sided p-value

#Defined by WHO 2014 Global TB Report



# Results

Figure 1. Latent TB infection and diabetes status



# Results

Table 2. Diabetes status and prevalence of latent TB infection

Diabetes status	Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*
No diabetes	1.00	1.00
Pre-diabetes	1.83 (1.30, 2.58)	1.68 (1.16, 2.43)
Diabetes	2.19 (1.22, 3.94)	2.40 (1.22, 4.71)

\*Multivariable logistic regression; adjusted for age, sex, body mass index, smoking status, vitamin D level, and TB incidence in country of origin

# Results

Table 3. Interaction between diabetes status and vitamin D level with prevalence of latent TB infection

Vitamin D level <sup>#</sup>	Diabetes status	Odds ratio (95% CI)	Adjusted odds ratio (95% CI) <sup>*</sup>
Normal Vitamin D ≥ 20 ng/ml	No diabetes	1.00	1.00
	Pre-diabetes	1.35 (0.86, 2.10)	1.25 (0.78, 2.01)
	Diabetes	1.14 (0.49, 2.68)	1.21 (0.48, 3.04)
Low Vitamin D < 20 ng/ml	No diabetes	1.00	1.00
	Pre-diabetes	2.89 (1.64, 5.10)	3.14 (1.80, 5.49)
	Diabetes	4.79 (2.05, 11.21)	5.10 (2.00, 12.99)

<sup>#</sup>Likelihood ratio p-value for vitamin D-diabetes interaction terms <0.01

<sup>\*</sup>Multivariable logistic regression; adjusted for age, sex, body mass index, smoking status, and TB incidence in country of origin

# Limitations

- Cross sectional design
  - Does latent TB infection increase the risk of diabetes?
  - One-time point measure of diabetes and latent TB
- Imperfect adjustment for exposure to *Mycobacterium tuberculosis*
- Unable to measure previous active TB

# Conclusions

- Based on HbA1c screening, we found 7.8% of adult refugees had diabetes and 33.8% had pre-diabetes
- Among refugees with low vitamin D, the prevalence of latent TB was 5 times greater in those with diabetes compared to no diabetes
- Diabetes may increase the risk of latent TB infection
- Findings need replication with prospective study designs
- Patients with diabetes should be targeted for latent TB screening and subsequent treatment

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