

# Injection Drug Users at High Risk for Incident *M. Tuberculosis* Infection in Tijuana, MX

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## Abstract

**Background:** Estimates of *M. tuberculosis* (*Mtb*) infection are sparse. **Methods:** IDUs in Tijuana, Mexico, who were negative by QuantiFERON® TB Gold In-Tube (QFT) assay at baseline underwent re-testing for QFT seroconversion and behavioral assessments over 18 months. Weighted multivariable logistic regression was performed to identify risk factors for QFT seroconversion.

**Results:** Of 129 baseline *Mtb* negative IDUs who completed repeat testing, QFT seroconversion was observed among 67 (51.9%, 95% CI: 43.3%-60.5%). Homelessness (OR=27.8, p<0.001), lifetime residence in Tijuana (OR=7.46, p=0.002), age ≥50 years old (OR=9.61, p=0.023), and daily marijuana smoking (OR=9.64, p=0.025) were independently associated with seroconversion. IDUs who perceived at baseline that they were likely to become HIV-infected had lower risk for seroconversion (OR=0.26, p=0.023).

**Conclusions:** Tijuana's IDUs are at great risk for new *Mtb* infection. While most infections will remain latent, IDUs are at increased risk for HIV co-infection and subsequent progression to active TB. These findings highlight the need for routine HIV and TB screening for IDUs and prophylactic treatment of latent TB infection. Educating IDUs on TB awareness and care-seeking when symptoms arise is also needed.

## Introduction

Illicit Drug use has increased in Mexico over the past decade, especially in US-Mexico border cities.<sup>1</sup> Recent studies in Tijuana show the annual incidence of HIV to be 2% among IDUs<sup>2</sup> and 12% among female sex workers who also inject drugs<sup>3</sup> providing evidence that Tijuana is in the early phase of a growing HIV epidemic.<sup>4</sup> Furthermore, 67% of IDUs in Tijuana were found to have latent TB infection (LTBI).<sup>5</sup> While only 10% of persons infected with *M. tuberculosis* will develop active TB in their lifetime, the yearly risk among persons with HIV co-infection is 10%.<sup>6</sup> TB incidence estimates among IDUs in Tijuana are lacking. Such estimates are needed to know how this epidemic is evolving and to provide a baseline for evaluating prevention efforts.

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## Objectives

To estimate the incidence and identify risk factors for *M. tuberculosis* infection among IDUs in Tijuana, Mexico.

## Methods

### Study Population

IDUs were recruited between April 2006 and April 2007 using Respondent Driven Sampling (RDS) for *Proyecto El Cuete*, a longitudinal cohort study to describe the prevalence, incidence and risk factors for HIV, TB and syphilis in a community based sample of IDUs in Tijuana, Mexico.

#### • Eligibility criteria:

- Age ≥ 18 years,
- Illicit drug injection in the past month confirmed by visible injection stigmata ("track marks"),
- Spanish or English speaking,
- Intention to reside in Tijuana over the next 18 months
- Ability to provide written informed consent

#### • This analysis only included IDUs who tested QFT-negative at baseline.

### Data Collection

• Interviews took place at baseline and 6-, 12-, and 18-month follow-up visits. TB testing was done at baseline and 18 months only.

• Face-to-face interviews were conducted in private settings using computer-assisted personal interviewing (CAPI) technology to assess socio-demographic, behavioral and contextual factors related to TB, HIV and syphilis.

• TB-like illness was assessed via symptom questions. IDUs with hemoptysis, or cough lasting >3 weeks plus one other symptom, were considered to have possible active TB and referred to a health clinic for diagnosis and treatment.

### Laboratory Testing

• TB infection was detected using the QuantiFERON®-TB Gold in-tube (QFT) assay according to the manufacturer's instructions.

• HIV antibodies were detected on site using the Determine rapid test and reactive samples were confirmed using HIV-1 ELISA and IFA assays.

### Statistical Analysis

Statistical analysis focused on identifying factors associated with seroconversion to QFT-positive during follow-up. Categorical data were compared using Fisher's exact test and continuous data were compared using Wilcoxon rank sum tests. Univariate analysis of factors associated with QFT seroconversion used logistic regression via generalized estimating equations (GEE) with robust variance estimation. All associations with a p<0.20 were considered in multivariable analysis to calculate adjusted odds ratios controlling for potential confounding using weighted logistic regression via GEE. To correct for bias introduced by the RDS sampling process, the models were RDS-adjusted.<sup>2,7</sup>

## Results

Table 1. Characteristics<sup>a</sup> of Injection Drug Users by Incident *M. Tuberculosis* Infection Status

	QFT-positive (N=67) n (%) <sup>c</sup>	QFT-negative (N=62) n (%) <sup>c</sup>	Total (N=129) n (%) <sup>c</sup>	P-value <sup>b</sup>
<b>Socio-demographics</b>				
Age (Years)				
Median (25th, 75th percentiles)	36.5 (32,49)	38.(32,43)	37.7 (32,43)	0.83
Mean (standard deviation)	38.2 (9.4)	37.5 (6.7)	37.9 (8.2)	
Age ≥50 years	10 (14.9%)	1 ( 1.6%)	11 ( 8.5%)	0.01
Male gender	57 (85.1%)	50 (80.6%)	107 (82.9%)	0.64
Speaks some English	37 (55.2%)	40 (64.5%)	77 (59.7%)	0.37
Homeless	10 (14.9%)	3 ( 4.8%)	13 (10.1%)	0.08
Lived in household with ≥3 persons (18 mth visit)	41 (61.2%)	24 (38.7%)	65 (50.4%)	0.01
Monthly income <3000 pesos at (18 mth visit)	60 (89.6%)	44 (71.0%)	104 (80.6%)	0.01
<b>Travel History</b>				
Born in Baja California, Mexico	25 (37.3%)	17 (27.4%)	42 (32.6%)	0.26
Lived entire life in Tijuana	19 (28.4%)	8 (12.9%)	27 (20.9%)	0.05
Years lived in Tijuana				
Median (25th, 75th percentiles)	10.0 (4.0,32.5)	7.5(3.0,23.0)	8.0 (3.5,30.0)	0.21
Mean (standard deviation)	18.5 (16.9)	14.5 (14.7)	16.6 (16.0)	
Ever traveled to the US	53 (79.1%)	52 (83.9%)	105 (81.4%)	0.51
<b>Health History</b>				
Tested HIV-positive	3 (4.5%)	5 (8.1%)	8 (6.2%)	0.48
Visible BCG scar	52 (77.6%)	46 (76.7%)	98 (77.2%)	0.99
Any symptoms suggestive of active TB (any visit)	0 ( 0.0%)	1 ( 1.6%)	1 ( 0.8%)	0.48
Drank unpasteurized milk in past 6 mths	2 ( 3.0%)	1 ( 1.6%)	3 ( 2.3%)	1.00
Ever lived/worked around cattle	6 ( 9.0%)	7 (11.3%)	13 (10.1%)	0.77
Known someone with TB	22 (33.3%)	17 (27.4%)	39 (30.5%)	0.57
<b>Behavioral Risk History</b>				
No. Years of injection drug use at baseline				
Median (25th, 75th percentiles)	13.5 (8.0,21.8)	14.8 (7.1,22.3)	14.2 (7.4,21.9)	0.83
Mean (standard deviation)	15.9 (10.7)	14.7 (8.6)	15.3 (9.7)	
Injected daily in past 6 months	67 (100%)	58 (93.5%)	125 (96.9%)	0.05
Smoked marijuana ≥once per day in past 6 mths	6 (9.0%)	1 (1.6%)	7 ( 5.4%)	0.12
Smoked methamphetamine ever (any visit)	38 (56.7%)	45 (72.6%)	83 (64.3%)	0.07
Traded sex for money/drug/goods in past 6 mths	21 (32.3%)	13 (21.0%)	34 (26.8%)	0.17
Self-perceived to be at high risk for HIV	20 (29.9%)	33 (53.2%)	53 (41.1%)	0.01

<sup>a</sup> Characteristics were assessed at the baseline visit unless otherwise specified in parentheses.

<sup>b</sup> P-values for comparing patient characteristics between QFT(+) and QFT(-) subjects are from Wilcoxon rank sum test for continuous variables or Fisher's exact test for categorical variables

<sup>c</sup> n (%) unless indicated otherwise.

## Results (cont.)

Table 2. Univariate Analysis of Risk Factors for Incident *M. Tuberculosis* Infection

	OR <sup>a</sup>	95% CI <sup>a</sup>	P-value <sup>a</sup>
<b>Socio-demographics</b>			
Age ≥50 years	10.70	(1.33, 86.3)	0.03
Homeless	3.45	(0.90, 13.20)	0.07
Lived in household with ≥3 persons (18 mth visit)	2.50	(1.23, 5.07)	0.01
Monthly income <3000 pesos at (18 mth visit)	3.51	(1.35, 9.12)	0.01
<b>Travel History</b>			
Lived entire life in Tijuana	2.67	(1.07, 6.66)	0.03
<b>Behavioral Risk History</b>			
Injected daily in past 6 months	10.38	(0.55, 196.95)	0.03 <sup>b</sup>
Smoked marijuana ≥once per day in past 6 mths	6.00	(0.70, 51.3)	0.10
Smoked methamphetamine ever (any visit)	0.50	(0.24, 1.04)	0.06
Traded sex for money/drug/goods in past 6 mths	1.80	(0.81, 4.01)	0.15
Self-perceived to be at high risk for HIV	0.37	(0.18, 0.77)	0.01

Abbreviations: OR=odds ratio; CI=confidence intervals

<sup>a</sup> OR, CI and p-value are from univariate logistic regression using generalized estimating equations (GEE) with robust variance estimation.

<sup>b</sup> Estimates obtained using Mantel-Haenszel method because one empty cell precluded calculation using logistic regression.

Table 3. Multivariable Analysis of Risk Factors for Incident *M. Tuberculosis* Infection

	Adjusted OR <sup>a</sup>	95% CI <sup>a</sup>	P-value <sup>a</sup>
Homeless	27.85	(4.08,190.21)	0.001
Lived entire life in Tijuana	7.46	(2.08, 26.77)	0.002
Age ≥50 years old (ref. age <50 years old)	9.61	(1.37, 67.39)	0.023
Used marijuana ≥daily in 6 months before follow-up	9.64	(1.33, 69.97)	0.025
Self-perceived to be at high risk for HIV at baseline	0.26	(0.08, 0.83)	0.023

Abbreviations: OR=odds ratio; CI=confidence interval

<sup>a</sup> Adjusted OR, CI and P-value are from multivariable logistic regression adjusting for all other variables in the model.

## Summary

Of 354 baseline QFT-negative IDUs, 153 (43.2%) completed repeat testing at 18 months; 24 (15.7%) tested indeterminate and were excluded leaving 129 (36.4%) IDUs for this analysis. **Overall, 67 (51.9%, 95% CI: 43.3%-60.5%) IDUs seroconverted to QFT-positive.**

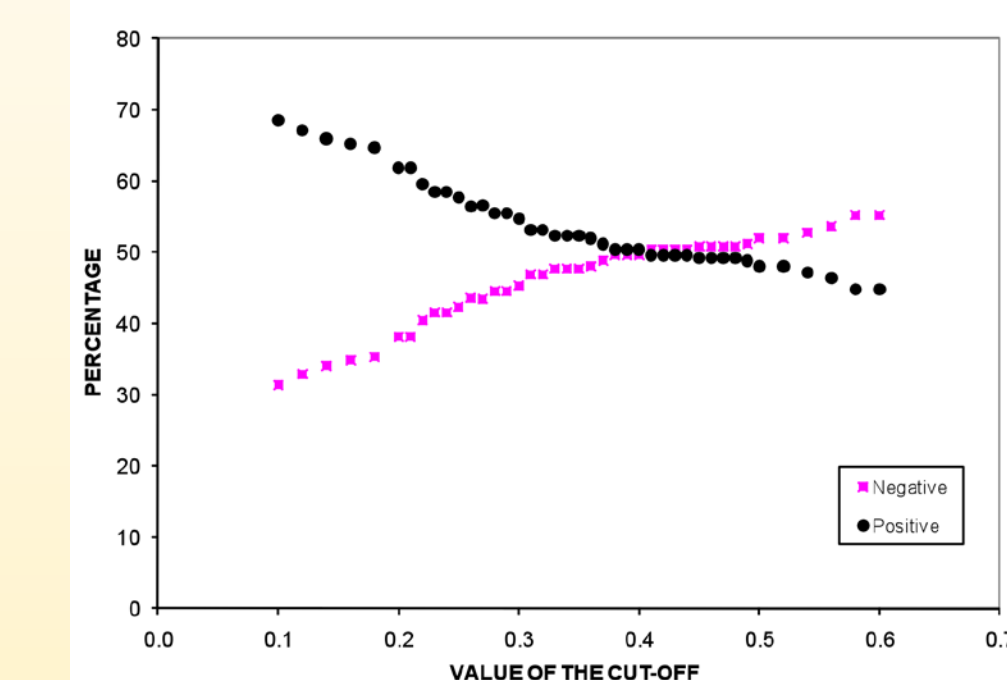
Seroconversion to QFT-positive was independently associated with homelessness, lifetime residence in Tijuana, age ≥50 years old, and daily marijuana smoking in the past 6 months. IDUs who thought at baseline that they were at high risk for HIV infection through injection drug use were at lower risk for QFT seroconversion.

Time to follow-up did not differ between QFT(+) and QFT(-) IDUs (mean [SD]: 1.59 [0.26] vs. 1.54 [0.20] years). No symptoms suggestive of active TB were reported by seroconverters at any follow-up visit.

## Limitations

• Given the 18-month interval between QFT tests, the exact time of infection is unknown; thus, factors associated with seroconversion may be correlated with rather than predictive of seroconversion.

• QFT results slightly above the cutoff (0.35 IU/ml) for this qualitative assay could produce false positive results. However, using a more stringent cutoff of >0.5 IU/ml reduced the number of seroconversions by only 10% (see figure).



**Figure** Distribution of interferon-gamma (IFN-γ) levels by QuantiFERON TB Gold In-Tube assay from 129 participants retested 18 months after an initially seronegative test result. Based on the manufacturer's recommended cutoff of 0.35 IU/mL, 67 (52%) would be considered to have incident *M. tuberculosis* infection. Using a more conservative cutoff of 0.50 IU/mL would yield 60 (48%) incident infections; only a 7% reduction in sensitivity.

## Conclusion

Injection drug users in Tijuana are at very high risk for incident *Mtb* infection. Marijuana smoking, homelessness, and lower perceived risk of becoming HIV infected were associated with greater risk of *Mtb* infection. Older age and lifetime residence in Tijuana were also associated with greater risk of infection, although unmeasured network factors might account for these findings, and future studies are needed to confirm these results. These findings suggest that IDUs in Tijuana require screening for HIV infection and active TB and support recommendations that HIV-infected persons be screened for TB and offered prophylactic treatment for LTBI. Interventions that educate IDUs to recognize symptoms of TB, to seek medical care if symptoms occur, and to understand TB transmission are needed to reduce the spread of TB among IDUs and their non-IDU contacts.

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