Results of the Implementation of a Pilot Model for the Bidirectional Screening and Joint Management of Patients with Pulmonary Tuberculosis and Diabetes Mellitus in Mexico

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Abstract

**Background:** Recently, the World Health Organisation and the International Union Against Tuberculosis and Lung Disease published a Collaborative Framework for the Care and Control of Tuberculosis (TB) and Diabetes (DM) (CFTB/DM) proposing bidirectional screening and joint management.

**Objective:** To evaluate the feasibility and effectiveness of the CFTB/DM in Mexico. **Design.** Prospective observational cohort. **Setting.** 15 primary care units in 5 states in Mexico. **Participants:** Patients aged ≥20 years diagnosed with DM or pulmonary TB who sought care at participating clinics. **Intervention:** The WHO/Union CFTB/DM was adapted and implemented according to official Mexican guidelines. We recruited participants from July 2012 to April 2013 and followed up until March 2014. Bidirectional screening was performed. Patients diagnosed with TB and DM were invited to receive TB treatment under joint management. **Main outcome measures.** Diagnoses of TB among DM, of DM among TB, and treatment outcomes among patients with DM and TB.

**Results:** Of 783 DM patients, 11 (1.4%) were unaware of their TB. Of 361 TB patients, 16 (4.4%) were unaware of their DM. 95 TB/DM patients accepted to be treated under joint management, of whom 85 (89.5%) successfully completed treatment. Multiple linear regression analysis with change in HbA1c and random capillary glucose as dependent variables revealed significant decrease with time (regression coefficients (β) = −0.660, (95% confidence interval (CI), −0.96 to −0.35); and β = −1.889 (95% CI, −2.77 to −1.01, respectively)) adjusting by sex, age and having been treated for a previous TB episode. Patients treated under joint management were more likely to experience treatment success than patients treated under routine DM and TB programs as compared to historical (adjusted OR (aOR), 2.8, 95%CI 1.28–6.13) and same period (aOR 2.37, 95% CI 1.13–4.96) comparison groups.

**Conclusions:** Joint management of TB and DM is feasible and appears to improve clinical outcomes.

Citation: Castellanos-Joya M, Delgado-Sánchez G, Ferreyra-Reyes L, Cruz-Hervert P, Ferreira-Guerrero E, et al. (2014) Results of the Implementation of a Pilot Model for the Bidirectional Screening and Joint Management of Patients with Pulmonary Tuberculosis and Diabetes Mellitus in Mexico. PLoS ONE 9(9): e106961. doi:10.1371/journal.pone.0106961

Editor: Jen-Hsiang Chuang, Centers for Disease Control, Taiwan

Received June 3, 2014; Accepted August 3, 2014; Published September 17, 2014

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Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and its Supporting Information files.

Funding: The authors received no specific funding for this work.

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Tuberculosis (TB) remains a major cause of morbidity and mortality in low- and middle-income countries, where the numbers of individuals with type 2 diabetes mellitus (DM) are also increasing rapidly. [1,2] Many studies have explored the relationship between DM and TB, including a recent systematic review in which the risk of TB in DM patients was shown to be three-fold higher than that of individuals without DM. [3] Moreover, the available evidence indicates that DM comorbidity worsens the clinical outcomes of TB patients. [4,5]

Recently, the World Health Organisation (WHO) and the International Union against Tuberculosis and Lung Disease (Union) recognised the need for international guidelines regarding the joint management of TB and DM and published a provisional Collaborative Framework for the Care and Control (CFTB/DM) of both diseases. [6] This framework emphasized establishment of mechanisms of collaboration between national programs of TB and DM, bidirectional screening of TB and DM, and integration of TB and DM management. Integration of services in low and middle resource settings has long been debated. A recent systematic review found limited evidence of its effectiveness in improving health outcomes, and some evidence to suggest that it may improve efficiency but may not be appropriate in all circumstances. [7] Bidirectional screening of TB and DM has recently been reviewed. [8] Results showed that TB prevalence among patients with DM is high, ranging from 1.7% to 36%, and increasing with rising TB prevalence in the underlying population as well as with DM severity. Screening patients with TB for DM also yielded high prevalence of DM ranging from 1.9% to 35%. More recently, the WHO/Union framework has been tested in pilot experiences which demonstrated the feasibility of bidirectional screening. [9,10] To our knowledge, there is no published literature on integration of diabetes and tuberculosis management.

We have previously documented that the high prevalence of DM in Mexico results in a considerable proportion of TB cases that are attributable to this disease. [11] Thereby, we conducted this study in order to evaluate the feasibility and effectiveness of bidirectional screening and joint management of TB and DM as recommended by WHO/Union.

Methods

We conducted an observational cohort study recruiting participants from July 2012 to April 2013. Patients diagnosed with DM and TB were followed up until March 2014. We adapted the CFTB/DM, proposed by WHO and Union, according to the current official Mexican standards for the management of TB and DM. [6,12,13] Joint management focused to link DM and TB programs at the level of service delivery. It aimed: 1) to bring together TB and DM screening and health services through evaluation and testing of TB and DM among patients with DM and TB respectively, conducted by trained nurses to consenting patients and 2) periodical monitoring of glucose levels, provision of referral to specialised outpatient clinics in case of difficult control and counselling sessions to patients and their families by nurses providing directly observed tuberculosis therapy (DOTS). No additional staff was recruited. The program differed from the usual practice in that neither screening of TB was offered to DM patients nor screening of DM was offered to TB patients. Patients with DM and TB had their glucose level monitored monthly while under TB treatment. To implement the joint management program we conducted the following: 1) invitation of the federal TB and DM programs to state and local levels to participate; 2) establishment of mechanisms for inter-programmatic collabora-
DM treatment regimens, daily physical exercise program, attention to diet and importance of family involvement.

Mycobacteriology
Sputum samples were processed for acid fast bacilli smears and M. tuberculosis culture and drug susceptibility tests according to standardised procedures. [13] The Institute of Diagnosis and Epidemiological Reference performed quality control analyses for all participating laboratories.

Diagnosis of DM
The diagnosis of DM among TB patients was based on the following criteria: a) fasting glucose level $\geq 126$ mg/dL and b) HbA1c level $\geq 6.5\%$. [16]

Statistical Analysis
The primary outcomes were TB testing rate amongst new and prevalent DM clients, DM testing among new TB patients and treatment outcomes amongst patients treated under joint management. Laboratory and data processing personnel were blinded to the study. We used WHO definitions of treatment outcomes except default which was defined according to the Mexican official guidelines. [12,17] Briefly, failure was defined when AFB microscopies or cultures were positive at five months or later during treatment. Cure was defined when treatment was completed with the disappearance of signs and symptoms with two or more acid-fast bacilli smears or cultures with negative results at the end of therapy. Treatment completion was defined when a patient completed treatment but did not meet the criteria to be classified as a cure or a failure. Death was defined when a patient died of any cause during therapy. Treatment success was defined by the the sum of patients who were cured and those who had completed treatment. Mexican guidelines have defined default when a patient interrupts treatment for 30 days or more rather than 60 days defined by WHO so as to be able to timely prevent that patients drop out from treatment. Incomplete and inaccurate case report forms (including missing patient identifiers, missing or inconsistent testing information or missing or inconsistent treatment outcomes) were queried and corrected by clinic staff through checking clinical and laboratory records. The sociodemographic, epidemiological and clinical data of patients who were screened for DM and TB were analysed according to the screening results. Among patients with both DM and TB, characteristics were compared between patients with treatment success versus those who defaulted, failed, died or were transferred out.

Using robust random effects linear regression for longitudinal data, we estimated regression coefficients ($b$ and 95% confidence intervals (CI), to determine if HbA1c, serum glucose and random capillary glucose changed significantly during treatment adjusting for sex, age, and previous TB treatments. The variables included in the models were those with $p$-values $\leq 0.20$ in bivariate analysis or with biological plausibility. Covariates were arrived to by using hierarchical backward elimination approach. We tested the models with Hausman and Breusch-Pagan tests.

We used two comparison groups to evaluate whether joint management was associated to improved outcomes. These control groups were extracted from the National Register of Cases of Tuberculosis in Mexico—where all diagnosed cases in the country are mandatorily reported according to the current official guidelines [18]. The first comparison group was a historical control which included 139 patients with TB and DM diagnosed and treated in the same primary care units during the 36 months previous to the present study from a total of 653 pulmonary tuberculosis patients $\geq 20$ years of age. We also compared treatment outcomes of our study group with a same-period control group which included 232 patients with TB and DM diagnosed and treated in the same municipalities but in different primary care units as our study group from a total of 1058 pulmonary tuberculosis patients $\geq 20$ years of age. The demographic, clinical and treatment outcomes of patients with TB and DM from both groups were compared with those of our study population. With 95 subjects in the joint management group and 139 in the comparison group, the study would be able to show an increase of 15% in success rate from an estimated 75% registered for participating health jurisdictions in 2010, with 80% power, at a 5% significance level. The association between treatment success and study group was evaluated using logistic regression analysis after adjusting for sex, age and previous TB treatment. The logistic regression models were validated by evaluating the goodness of fit, model specificity and multicollinearity. As with regression models, variables included in the models were those with $p$-values $\leq 0.20$ in bivariate analysis or with biological plausibility and covariates were arrived to using hierarchical backward elimination approach. All analyses were performed using the STATA 13.0 statistical software package (StataCorp LP, College Station, TX, USA).

Ethical approval
This study was approved by the Ethical Commission of the Instituto Nacional de Salud Pública (approval number 422). Participants gave written informed consent before taking part. All patients were referred to health facilities to receive treatment in accordance with the stipulations of the National Program for the Prevention and Control of TB and the National Program for the Prevention and Control of DM.

Results
TB screening tests were performed in 783 (10.1%) of the 7,763 subjects with previous DM diagnoses who were listed during the study period at the primary care units. A large proportion of patients were not screened since DM care providers referred that they were too busy to conduct TB symptom screen for all DM cases. Among screened patients, TB was diagnosed in 38 (4.9%), of whom 11 (28.9%) had been unaware of their TB statuses. DM screening was performed in 361 (40.8%) of the 885 patients with recorded bacteriological TB diagnoses at the same clinics during the study period. TB clinic overload and lack of reagents to perform glucose tests explains why not all TB patients were screened for DM. Among these patients, DM was diagnosed in 70 (19.4%), of whom 16 (22.9%) had been unaware of their DM statuses (Figure 1). When we compared TB patients who were screened with those that were not, we found that screened patients were younger (median 38 years [interquartile range, IQR 28–50] versus 41 years [IQR 29.5–55], p = 0.006) but similar regarding the proportion of men and women (males, 64.5% [233/361] versus 70.4% [369/524], p = 0.065).

TB screening in DM patients
Table 1 shows the characteristics of DM patients in whom pulmonary TB was diagnosed in comparison to those in whom a TB diagnosis was ruled out. Patients who were diagnosed with TB were more likely to be male, thinner, receive treatment with insulin (and less likely to be treated with oral hypoglycaemic agents), have had a previous episode of TB and have had contact with a TB patient. The most frequent symptom was cough with phlegm. Six of 38 patients who did not refer this symptom were patients who had already been diagnosed with TB and were under...
treatment. Municipalities varied in the proportion of patients detected with TB.

**DM screening in TB patients**

Table 2 lists the characteristics of TB patients in whom DM was diagnosed in comparison to those who were not diagnosed with DM. Patients diagnosed with DM were more likely to be older; have parents with DM; have polydipsia or polyuria and although heavier, were more likely to have recently experienced weight loss. Municipalities varied in the proportion of patients detected with DM.

**Patients with TB and DM who received TB treatment**

Of the 108 patients diagnosed with TB/DM, 87.9% (95/108) agreed to receive treatment under joint management conditions. Table 3 lists the sociodemographic and clinical characteristics of these patients. Eighty one patients (85.26%) were cured; 4 (4.21%) completed treatment; 2 (2.11%) defaulted; 5 (5.26%) failed; 3 (3.2%) died; and none were transferred out (Table 3). By bivariate analyses, patients who successfully completed treatment were more likely to have access to social security (Table 3). Seventy nine patients (81.4%); 65 (67%) and 54 (55.6%) maintained their scheduled appointments for measurement of random capillary glucose, fasting glucose, and HbA1c respectively. As the TB treatment progressed, the levels of HbA1c and random capillary glucose showed a significant decreasing trend, ($p<0.001$; Figure 2). Multiple linear regression analysis with change in HbA1c and random capillary glucose as dependent variables revealed significant decrease with time ($p<0.001$) adjusting by sex, age and having had treatment for a previous TB episode (Table 4).

One hundred thirty nine patients were diagnosed and treated between June 2009 and June 2012 in participating clinics and 232 patients were treated between July 2012 and April 2013 in the same municipalities but different clinics. Patients under joint management were more likely to cure and less likely to complete treatment without showing evidence of treatment failure and without negative bacteriology and to default as compared to both control groups. No statistically significant differences were observed between the study group and the control groups regarding sex, age and previous TB treatment (Table 5).

As shown in Tables 5 and 6, by bivariate and multivariate analyses, patients who were treated according to the pilot model of joint management were more likely to experience treatment success than were those who had been treated in the same clinical units during the previous 36 months or those treated in the same municipalities but in different clinics during the same period as the study group after adjusting for sex, age and the previous TB treatment history.

**Discussion**

Our study demonstrates the feasibility of implementing a joint management model for the TB-DM association in Mexico and provides preliminary evidence of its effectiveness to improve treatment outcomes. Among the screenings conducted in DM patients, 11 (1.38%) had been previously unaware of their TB status, whereas in screenings conducted in TB patients, 16 (4.4%) had been unaware of their DM status, thus demonstrating the benefit of the strategy in this setting. Accordingly, 71 people with DM would need to undergo screening to detect a new case of TB, whereas only 22 people with TB would need to undergo screening to detect a new case of DM. On the other hand, the glucose measurements were found to significantly decrease during treatment in 95 recruited patients with both comorbidities. Finally, the proportion of patients who successfully completed treatment under the joint management model was higher than the success rate achieved at the same units during the previous 36 months and at different primary care clinics in the same municipalities during the same study period.

Prevalence of TB among patients with DM in a recent systematic review ranged from 1,995 to 36,206 per 100,000 individuals with DM. [8] TB prevalence among DM patients in our study (4,853 per 100,000 DM patients) is comparable to some of these studies (e.g. Tripathy in India in 1984) although higher than reports of recent screenings conducted in India and China.

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**Figure 1. Flowchart of the bidirectional screening for TB and DM (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico, 2013).**

doi:10.1371/journal.pone.0106961.g001
TB prevalence among DM patients was 147-fold higher than WHO reported prevalence for general population in Mexico, (33 (2.5th and 97.5th centiles, 16–57) per 100,000 inhabitants in 2012. [1] This notoriously higher TB prevalence among DM patients suggests that TB transmission may be occurring in health care settings in Mexico. This is supported by previous reports on TB transmission to health workers. [20] Moreover, usage of molecular tools has

| Table 1. Characteristics of the DM patients who were screened for TB (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico, 2013). |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Total           | Patients with TB | Patients without TB | p-value*
| Number/Total (%)| Number/Total (%)| Number/Total (%)|
| Male            | 205/783         | 20/38           | 185/745         | <0.001          |
| Age (years) [median (IQR)] | 45               | 46               | 49             | 0.555**         |
| Municipality    |                 |                 |                 |                 |
| Tijuana         | 90/783          | 1/38            | 89/745          | 0.026           |
| Ciudad Juarez   | 349/783         | 23/38           | 326/745         |                 |
| Reynosa         | 49/783          | 1/38            | 48/745          |                 |
| Guadalupe       | 94/783          | 8/38            | 86/745          |                 |
| Zapopan         | 201/783         | 5/38            | 196/745         |                 |
| Oral hypoglycaemic agents | 568/764          | 17/37           | 551/727         | <0.001          |
| Insulin         | 48/746          | 12/37           | 36/709          | <0.001          |
| TB history      |                 |                 |                 |                 |
| History of a previous TB episode | 25/782          | 6/38            | 19/744          | <0.001          |
| Contact with a TB patient | 55/779          | 8/38            | 47/741          | 0.001           |
| Signs and symptoms of TB |                 |                 |                 |                 |
| Fever           | 57/781          | 20/37           | 37/744          | <0.001          |
| Cough with phlegm | 148/782         | 32/38           | 116/744         | <0.001          |
| Weight loss     | 74/779          | 21/38           | 53/741          | <0.001          |
| Night sweats    | 109/783         | 23/38           | 86/745          | <0.001          |
| Anthropometric measures |                 |                 |                 |                 |
| BMI (m/kg²) [median (IQR)] | 29.3            | 24.8            | 29.6           | <0.001**        |
| Waist circumference (cm) [median (IQR)] | 99              | 88              | 99             | <0.001**        |
| Abdominal obesity | 573/777         | 17/37           | 556/740         | <0.001          |

*Chi-squared test;  **U Mann-Whitney test; TB, Tuberculosis; DM, Diabetes mellitus; IQR, interquartile range; BMI, Body mass index.

doi:10.1371/journal.pone.0106961.t001

(705 and 774 per 100, 000 DM patients). [10,19] TB prevalence among DM patients was 147-fold higher than WHO reported prevalence for general population in Mexico, (33 (2.5th and 97.5th centiles, 16–57) per 100,000 inhabitants in 2012. [1] This notably higher TB prevalence among DM patients suggests that TB transmission may be occurring in health care settings in Mexico. This is supported by previous reports on TB transmission to health workers. [20] Moreover, usage of molecular tools has
previously documented the occurrence of exogenous reinfection in one-fifth of the DM patients in a study conducted in Southern Mexico, suggesting that nosocomial TB transmission might be occurring as a result of DM patients attending clinics where there is a high prevalence of diagnosed and undiagnosed TB. [5] Lack of compliance to international guidelines (inadequate design or renovation of health units and insufficient administrative and environmental controls) to prevent TB transmission in both primary care centres and specialised units would favour this transmission. [21]

Table 2. Characteristics of TB patients who were screened for DM (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico, 2013).

| Characteristic | Total | Patients with DM | Patients without DM | p-value* |
|----------------|-------|------------------|---------------------|----------|
|                | Number/Total | Number/Total | Number/Total |          |
|                | (%) | (%) | (%) |          |
| Male           | 233/361 | 39/70 | 194/291 | 0.085    |
|                | (64.5) | (55.7) | (66.7) |          |
| Age (years) [median (IQR)] | 38 | 45 | 36 | <0.001** |
|                | (28–50) | (35–55) | (26–48) |          |
| Municipality   |       |       |       |          |
| Tijuana        | 39/361 | 16/70 | 23/291 | <0.001  |
|                | (10.8) | (22.9) | (7.9) |          |
| Ciudad Juarez  | 118/361 | 3/70 | 115/291 |          |
|                | (32.7) | (4.3) | (39.5) |          |
| Reynosa        | 76/361 | 40/70 | 36/291 |          |
|                | (21.1) | (57.1) | (12.4) |          |
| Guadalupe      | 107/361 | 8/70 | 99/291 |          |
|                | (29.6) | (11.4) | (34.0) |          |
| Zapopan        | 21/361 | 3/70 | 18/291 |          |
|                | (5.8) | (4.3) | (6.2) |          |
| History and risk factors for DM |       |       |       |          |
| Siblings with DM | 89/353 | 17/66 | 72/287 | 0.91     |
|                | (25.2) | (25.8) | (25.1) |          |
| Parents with DM | 131/354 | 38/66 | 93/288 | <0.001  |
|                | (37.0) | (57.6) | (32.3) |          |
| Women with children weighing ≤4 kg at birth | 40/127 | 12/32 | 28/95 | 0.398    |
|                | (31.5) | (37.5) | (29.5) |          |
| Signs and symptoms of DM |       |       |       |          |
| Polyuria       | 130/356 | 37/68 | 93/288 | 0.001    |
|                | (36.5) | (54.4) | (32.3) |          |
| Polydipsia     | 137/357 | 44/68 | 93/289 | <0.001   |
|                | (38.4) | (64.7) | (32.2) |          |
| Polyphagia     | 138/354 | 27/67 | 111/287 | 0.806   |
|                | (39.0) | (40.3) | (38.7) |          |
| Weight loss in the last 2 months | 188/355 | 54/68 | 134/287 | <0.001  |
|                | (53.0) | (79.4) | (46.7) |          |
| Anthropometric measures |       |       |       |          |
| BMI (m/kg²) [median (IQR)] | 21.9 | 23.8 | 21.5 | 0.002** |
|                | (19.9–25.1) | (20.5–26.1) | (18.9–24.6) |          |
| Waist circumference (cm) [median (IQR)] | 71 | 73 | 70 | 0.123** |
|                | (80–88) | (83–91) | (80–87) |          |
| Abdominal obesity | 102/358 | 26/69 | 76/289 | 0.06     |
|                | (28.5) | (37.7) | (26.3) |          |

* Chi-squared test;
**U Mann-Whitney test; TB, Tuberculosis; DM, Diabetes mellitus; IQR, interquartile range; BMI, Body mass index.

doi:10.1371/journal.pone.0106961.t002

Bidirectional Screening and Joint Management of TB and DM

The number of individuals with diabetes who would need to undergo screening to detect a new TB case has ranged from four...
in Sweden in 1961 to 442 in Korea in 1995, and 236 to 1036 in China and India in 2012; [8–10,19,22] therefore, the number detected in our study (n = 71) confirms that the number of individuals largely depends on the prevalence of both diseases in the region studied.

Prevalence of DM among patients with TB in our study (19.4%) was intermediate as compared to Jeon and colleagues’ recent study.

### Table 3. Characteristics of patients with TB and DM (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico, 2013).

| Characteristics | Total | Treatment success | Death, Failure or Default | p-value |
|-----------------|-------|-------------------|---------------------------|---------|
|                 | Number/Total (%) | Number/Total (%) | Number/Total (%)         |         |
| Male            | 49/95 (51.6) | 41/85 (42.2) | 8/10 (80.0) | 0.057   |
| Age (years) [median (IQR)] | 50 (39–58) | 50 (39–58) | 50.5 (41–65) | 0.836   |
| Municipality    |       |                   |                           |         |
| Tijuana         | 13/95 (13.7) | 8/85 (9.4) | 5/10 (50.0) | 0.007   |
| Ciudad Juarez   | 26/95 (27.4) | 23/85 (27.1) | 3/10 (30.0) |         |
| Reynosa         | 36/95 (37.9) | 34/85 (40.0) | 2/10 (20.0) |         |
| Guadalupe       | 16/95 (16.8) | 16/85 (18.8) | 0/10 (0.0) |         |
| Zapopan         | 4/95 (4.2) | 4/85 (4.7) | 0/10 (0.0) |         |
| Social Security | 80/95 (84.2) | 74/85 (87.1) | 6/10 (60.0) | 0.026   |
| <6 years of schooling | 48/91 (52.7) | 42/81 (51.9) | 6/10 (60.0) | 0.626   |
| >10 drinks per week | 6/95 (6.3) | 5/85 (5.9) | 1/10 (10.0) | 0.613   |
| >10 cigarettes per week | 3/95 (3.2) | 3/85 (3.5) | 0/10 (0.0) | 0.546   |
| Time since DM diagnosis, (years) [median (IQR)]; n = 95 | 3 (0–12) | 3 (0–11) | 4.5 (2–17) | 0.196   |
| At least 1 complication of diabetes | 21/95 (22.1) | 19/85 (22.4) | 2/10 (20.0) | 0.865   |
| Comorbidities   | 3/95 (3.2) | 3/85 (3.5) | 0/10 (0.0) | 0.546   |
| Resistance to isoniazid and rifampicin | 1/87 (1.1) | 1/79 (1.3) | 0/8 (0.0) | 0.749   |
| Previous TB treatment | 13/94 (13.83) | 10/84 (11.90) | 3/10 (30.00) | 0.117   |
| Haemoptysis     | 28/92 (30.4) | 26/84 (31.0) | 2/8 (25.0) | 0.727   |
| Fever           | 56/90 (62.2) | 50/82 (61.0) | 6/8 (75.0) | 0.435   |
| BMI (kg/m²) [median (IQR)] | 24.33 (21.51–27.81) | 24.71 (21.51–27.81) | 23.05 (22.13–26.15) | 0.459   |

1Chi-squared test.

2At least one of the following complications: retinopathy, hypertension, renal disease, renal failure, diabetic foot, obesity, neuropathy (mono or polynuropathy), visceral neuropathy (diarrhoea, erectile dysfunction, etc.), urinary albumin, chest pain or other.

3Mann–Whitney test. TB, Tuberculosis; DM, Diabetes mellitus; IQR, interquartile range; BMI, Body mass index.

doi:10.1371/journal.pone.0106961.t003
systematic review (3.5% to 35.2%) [8]. The DM frequency among TB patients was two-fold higher than self-reported DM prevalence (9.17%, 95% confidence interval, 8.79%–9.54%) reported for Mexican individuals 20 years of age in 2012 by a probabilistic, cluster household survey interviewing 46,303 individuals >20 years old conducted by the Mexican Secretariat of Health [23], although this figure could be higher due to the proportion of adults who are unaware of their condition. Our results indicate that only 23 DM patients would need to undergo screening to detect a new case of TB. This finding is similar to those of recent studies in India, where it was found that 6–34 TB patients would need to undergo screening to detect new cases of DM. [9,22,24–26]

**Table 4.** Robust random effects linear regression for longitudinal data with change in HbA1c, fasting serum glucose and random capillary glucose as dependent variable among patients with TB and DM (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico, 2013).

| Characteristics | HbA1c (%) | Fasting serum glucose (mg/dL) | Random capillary glucose (mg/dL) |
|-----------------|----------|------------------------------|---------------------------------|
|                 | Beta regression coefficients | Beta regression coefficients | Beta regression coefficients |
| IC95%            |          |                              |                                 |
| Time to treatment completion |          |                              |                                 |
| All patients     | −0.660**| −0.711**                     | −3.510*                         | −1.889**                       | −1.942**                       |
| Treatment success| 0.165    | 0.147                        | −17.73                         | −16.72                         | −6.728                         | −11.13                         |
| Age (years)      | −0.0321  | −0.033                       | −1.192*                        | 0.059                          | −0.255                         |
| Previous TB treatment | 0.413    | 0.362                        | 16.06                          | 27.51                          | 14.35                          | 23.62                          |

TB = Tuberculosis; DM = Diabetes mellitus; 95% CI = 95% Confidence interval; *p<0.05; **p<0.001.
doi:10.1371/journal.pone.0106961.t004

The present study had several limitations. The design of this observational study did not allow the randomisation of participating or control primary care clinics. Therefore, treatment results of this study were compared with those observed at the same clinics while still transmissible.
during the previous 36 months and at different primary care clinics in the same municipalities during the same study period. Consequently, organisational and human factors unrelated to the joint management of both diseases might partially explain the differences in the cure rates observed in our study. Outcomes are also dependent on DM disease characteristics such as duration of diabetes, glucose control, or type of treatment. This information was not available among our comparison groups; therefore we were unable to compare these parameters with our study population. Diagnoses of TB were based on sputum smears that are recognized with a low sensitivity. [33] Most of the clinics included in the study did not have chest X ray facilities; therefore it would not have been feasible to conduct chest X rays to improve detection rates. TB patients who were screened for DM were found to be younger that patients who were not screened, therefore the frequency of DM among TB patients may be underestimated. A proportion of our patients might have suffered from glucose intolerance, given that some of the patients received

Figure 2. Medians +95% Confidence intervals of measures of glycaemia at each visit among patients with TB and DM during TB treatment (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico, 2012–2013. Panel A, HbA1c (%); Panel B, Fasting serum glucose (mg/dL); Panel C, Capillary random blood glucose (mg/dL). As TB treatment progressed, the levels of HbA1c and random capillary glucose showed a significant decreasing trend, (regression coefficients $\beta$ = $-0.660$, (95% confidence interval (CI), $-0.96$ to $-0.35$); and $\beta = -1.889$ (95% CI $-2.77$ to $-1.01$, respectively) adjusting by sex, age and having had treatment for a previous TB episode.

doi:10.1371/journal.pone.0106961.g002
### Table 5. Comparison of the sociodemographic characteristics and treatment outcome of patients with TB/DM diagnosed and treated in the same clinics from June 2009 to June 2012 (historical control) and in the same municipalities but different clinics from July 2012 to April 2013 (same period control), as compared to study population (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico).

| Variable               | Study population | Historical control | Same period control |
|------------------------|------------------|--------------------|---------------------|
|                        | Number/Total     | Number/Total       | Number/Total        |
|                        | (%)              | (%)                | (%)                 |
| **n = 95**             |                  |                    |                     |
| Male                   | 49/95 (51.58)    | 86/139 (61.87)     | 142/232 (61.21)     |
| Age (years) [median (IQR)] | 50 (39-58)       | 52 (41-58)         | 52 (41-61)          |
| Previous TB treatment  | 13/94 (13.83)    | 26/139 (18.71)     | 28/232 (12.07)      |
| Treatment success      | 85/95 (89.47)    | 98/132 (74.24)     | 179/228 (78.51)     |
| Cure                   | 81/95 (85.26)    | 78/132 (59.09)     | 128/228 (56.14)     |
| Treatment completion   | 4/95 (4.21)      | 20/132 (15.15)     | 51/228 (22.37)      |
| Default                | 2/95 (2.11)      | 22/132 (16.67)     | 17/228 (7.46)       |
| Failure                | 5/95 (5.26)      | 4/132 (3.03)       | 9/228 (4.57)        |
| Death                  | 3/95 (3.16)      | 6/132 (4.55)       | 21/228 (9.21)       |
| Transfer out           | 0/95 (0.00)      | 2/132 (1.52)       | 2/228 (0.88)        |

*Pearson’s chi-squared test; **Binomial test; ^Mann-Whitney U test; ~As compared to study population. TB = Tuberculosis; DM = Diabetes mellitus; IQR = Interquartile range.
doi:10.1371/journal.pone.0106961.t005

### Table 6. Variables associated with treatment success in patients with TB/DM who were treated via joint management in the same clinics from June 2009 to June 2012 (historical control, Model 1) and in the same municipalities but different clinics from July 2012 to April 2013 (same period control, Model 2), as compared to study population (Tijuana, Ciudad Juarez, Reynosa, Guadalupe and Zapopan, Mexico).

| Variables                                | Model 1 | P value* | Model 2 | P value* |
|------------------------------------------|---------|----------|---------|----------|
|                                          | aOR     | (95% CI) | aOR     | (95% CI) |
|                                          |         |          |         |          |
| **n = 226**                              |         |          | **n = 322** |          |
| Patients treated under the joint management model versus patients in control group | 2.80    | 0.010    | 2.37    | 0.022    |
|                                          | (1.28–6.13) |        | (1.13–4.96) |        |
| Age (years)                              | 1.01    | 0.235    | 1.00    | 0.808    |
|                                          | (0.98–1.04) |        | (0.98–1.02) |        |
| Male                                     | 0.56    | 0.130    | 0.95    | 0.877    |
|                                          | (0.26–1.18) |        | (0.52–1.74) |        |
| Previous TB treatment                    | 0.31    | 0.005    | 0.40    | 0.020    |
|                                          | (0.13–0.70) |        | (0.18–0.86) |        |

*Logistic regression analysis TB = Tuberculosis; DM = Diabetes mellitus; aOR = Adjusted Odds ratio; 95% CI = 95% confidence interval.
doi:10.1371/journal.pone.0106961.t006
a simultaneous diagnosis of both diseases. Finally we did not measure client satisfaction nor assessed cost-effectiveness.

Conclusions

This report provides preliminary evidence suggesting that bidirectional screening and joint management in primary care settings is feasible. Treatment success of patients jointly managed compared favourably with outcomes achieved under routine DM and TB management during the previous 36 months at the same primary care clinics and in different clinics in the same municipalities during the same period. Given the growing global epidemic of DM, it is necessary to incorporate bidirectional screening and joint management in order to control TB and DM and to evaluate the effectiveness of this approach in controlled trials. The concurrence of both diseases represents a risk to the possible spread of TB worldwide as well as serious implications for TB control and the achievement of the Millennium Development Goals [34].

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