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ASSOCIATION BETWEEN TUBERCULOSIS AND DIABETES IN THE MEXICAN BORDER AND NON-BORDER REGIONS OF TEXAS

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Abstract. The association between tuberculosis and underlying risk factors was evaluated in Texas patients hospitalized in the 15 counties along the Mexico border within the remaining non-border counties. A case control analysis of the hospital discharge dataset from the Texas Health Care Information Council was performed for the years 1999–2001. A discharge diagnosis of tuberculosis identified cases (N = 4,915). Deep venous thrombosis, pulmonary embolism, and acute appendicitis conditions identified controls (N = 70,808). Risk factors associated with tuberculosis were identified by logistic regression. Diabetes patients were almost twice as likely to have tuberculosis after adjusting by sex, age, and race/ethnicity. The association was strong for the population in the Texas border region, where there are higher incidence rates of tuberculosis (odds ratio $[OR]_{adj}$ = 1.82; 95% CI = 1.57–2.12) compared with non-border counties (OR_{adj} = 1.51; 95% CI = 1.36–1.67).

INTRODUCTION

The positive association between diabetes and tuberculosis has been previously reported, especially in populations with low socio-economic status and high incidence rates for both diseases.[1–6] Diabetes and tuberculosis are highly prevalent in Texas, and both are major public health problems.[7,8] Furthermore, the population from 14 of the Texas-Mexico border counties are among the poorest in the United States (http://www.dshs.state.tx.us/commissioner/speeches/HRSA120204.shtm). Tuberculosis incidence and diabetes prevalence are simultaneously very high in border counties in Texas.[8–10]

While tuberculosis incidence rates are at a record low in the United States (5.6/100,000 for 2002), immigration poses challenges for its control.[11] During 2002, 51.6% of the tuberculosis cases were United States born, 24.6% were from Mexico, and 17.8% were from other countries.[12] In states like Texas, Arizona, and California, the incidence rates of tuberculosis are higher, possibly because of their shared borders with Mexico (10.1/100,000).[13]

Consider Texas, which has an overall incidence rate of 7.2/100,000 in 2002, ranking it fifth among all states.[12] Tuberculosis prevalence is higher in the 15 counties contiguous with Mexico (13.1/100,000) in comparison with non-border counties of Texas (6.6/100,000).[9] One of the border regions is the Lower Rio Grande Valley (LRGV), which is located in the southern-most tip of Texas. It contains two cities with high cross-border migration and high incidence rates of tuberculosis: McAllen and Brownsville (tuberculosis incidence 12.8 and 17.4/100,000 in 2002, respectively), adjacent to the Mexican sister cities of Reynosa and Matamoros (tuberculosis incidence 43.9 and 70.3/100,000 for 1999, respectively).[9,10,14]

In this paper, we consider the association between tuberculosis, socio-economic status, diabetes, and other comorbidities. We explicitly addressed whether areas with higher incidence rates of tuberculosis (border counties) and therefore higher risk of exposure to the bacteria may bias upward the association between diabetes and tuberculosis. For this, we explored the factors associated with tuberculosis and compared the effects of living in the 15 counties contiguous with the Texas-Mexico border where incidence rates of tuberculosis are higher versus the non-border counties of Texas with lower rates of this disease.

MATERIALS AND METHODS

Study population. A case-control analysis was performed with cross-sectional data using the Texas hospital discharge database from the years 1999–2001 (most recent data up to 2004). The data were obtained from the Texas Health Care Information Council (THCIC).[15] Two areas were defined: the 15 Texas counties along the Mexico border (Brewster, Cameron, El Paso, Hidalgo, Hudspeth, Jeff Davis, Kinney, Maverick, Presidio, Starr, Terrell, Val Verde, Webb, Willacy, and Zapata) and the 239 remaining counties (Figure 1).[16] Henceforth, the 15 border counties are referred to as the border and the remaining part of Texas as non-border. To determine whether the patients were from border or non-border, we used three variables to classify those discharges: the patient zip code, county code, or state code.

Case/control definitions and other covariables. Cases were all patients with a discharge diagnosis of tuberculosis using the ninth version of the International Classification of Diseases (ICD-9) codes 010–018 (N = 4,915).[17] There are often multiple ICD-9 diagnoses codes per patient; therefore, the reason for hospitalization was not necessarily limited to tuberculosis for all cases. Tuberculosis codes were sought in the admitting diagnosis, principal diagnosis, and eight other variables with diagnosis codes. We were unable to identify multiple admissions for a given person; therefore, each admission was considered a different patient. We selected the same control group defined previously by Pablos et al.,[1] which included discharge diagnosis of deep venous thrombosis, pulmonary embolism, or acute appendicitis (ICD-9 codes 451.1, 451.2, 451.9, 415.1, 540, and 541; N = 70,808). We restricted our analysis to patients 15 years old or older.

Factors potentially associated with tuberculosis were extracted from the database. Demographic characteristics of the population included age, sex, race/ethnicity, and insurance type. Race and ethnicity variables were combined as one co-

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FIGURE 1. Map of Texas-Mexico border and non-border counties.

variable: white, Hispanic, African American, and other. Insurance type/status was categorized as uninsured, Medicare (Federal government insurance for the retired, 65 years old or more, widowers and the disabled), Medicaid (state government insurance for the poor), private (i.e., Blue Cross and commercial sources), and other (e.g., worker's compensation, other federal programs, Champus). Co-morbidity factors included diabetes (ICD-9 code 250), chronic renal failure (ICD-9 codes 585 and 586), alcohol-related conditions (ICD-9 codes 291, 305, 303, 535.3, and 571–571.3), drug use (ICD-9 codes 304.2, 304, 305.6, 305.5, and 304.9), any type of cancer (ICD-9 codes 140–239), and nutritional deficit (defined by the physicians ICD-9 codes 260–269). HIV patients were excluded from analysis because age and sex are suppressed for this population in the THCIC data and because HIV is less prevalent in the Texas-Mexico border than in the rest of the United States (http://www.tdh.state.tx.us/hivstd/stats/reports_2003/2003_HIV.htm).

Income and education were not reported in the THCIC data. Therefore, we extracted this data from the Census 2000. Census data included the percentage of high school or college graduates (associate degree and higher) for the zip code area of residence of cases or controls.[18] We also extracted the 1999 median household income by zip code area to adjust for socio-economic status.

Data management and statistical analysis. Data management and analysis were carried out using SAS Version 8.2. Missing/illogical data were checked. No hospital identifiers were included in the analysis files. Descriptive analysis was performed using standard centrality and variability measures as proportions, interquartile range, etc., as appropriate. We report mean of median zip code income. Because of the skewness of educational variables by zip code, the medians of the zip code percentage of high school graduates as well as the median of the zip code percentage of college graduates were used in the analysis. Unconditional multiple logistic regression analysis was used to evaluate the relationship between tuberculosis and the factors defined above.[19] Crude (OR) and adjusted (OR_{adj}) odds ratios (ORs) with corresponding 95% confidence intervals (CIs) are reported. Before evaluating the data for confounders, we evaluated location in border and non-border areas as an effect modifier using the log-likelihood ratio test.

Human participant protection. Institutional review board approval was obtained from The University of Texas Health Science Center at Houston committee for the protection of human subjects HSC-SPH-03-020.

RESULTS

During 1999–2001, there were 1,244 and 3,671 tuberculosis hospital discharge cases in the border and non-border Texas areas, respectively. Demographic, economic, and clinical characteristics of hospital discharge subjects for cases and controls for border and non-border Texas are summarized in Table 1. Table 2 shows the demographic, economic, and clinical characteristics of control subjects by race/ethnicity by regions. Table 3 presents the adjusted ORs of significant potential risk factors for tuberculosis for border and non-border Texas. The three most common reasons for hospitalization of the cases included primary tuberculosis infection (62.3%), pneumonia of unspecified etiology (2.8%), and care involving use of rehabilitation procedures (1.5%). The three most common reasons for hospitalization of the controls included acute appendicitis (51.5%), acute pulmonary heart disease (18.7%), and phlebitis and thombophlebitis (3.1%).

Demographics. Compared with controls, hospitalized tuberculosis cases were more likely to be Hispanic men ≥ 45 years of age (Table 1). In the border region, the control group was comprised by younger (< 45 years old) Hispanics, whereas the non-border controls were older and had a higher proportion of African Americans (Table 2).

Socio-economic status. The distribution of cases and controls by insurance type/status was dissimilar among border and non-border regions ($P < 0.001$; Table 1). Having Medicare (OR = 0.57; 95% CI: 0.52–0.62) or private insurance (OR = 0.21; 95% CI: 0.19–0.23) is associated with lower risk of having tuberculosis in non-border Texas compared with the uninsured (self-pay). Similarly, in the Texas border region, Medicaid (OR = 0.80; 95% CI = 0.65–0.99) and private insurance (OR = 0.24; 95% CI = 0.20–0.29) were associated with lower risk of having tuberculosis. The other insurance category, which includes federal insurance such as worker's compensation, Veterans Affairs (VA), and military, was a risk factor for tuberculosis in the non-border region of Texas. Medicare and private insurance were associated with lower risk of having tuberculosis in both regions after adjusting for sex, age, and race/ethnicity (Table 3). Medicaid (OR_{adj} = 1.22; 95% CI = 1.06–1.41) and the other insurance category were risk factors for having tuberculosis in non-border Texas after adjusting for sex, age, and race/ethnicity (Table 3).

Based on zip code estimates, tuberculosis patients were more likely to come from neighborhoods with lower median incomes in all regions of Texas ($P < 0.0001$; Table 1). Tuberculosis was less likely to be located in zip code areas that had higher percentage of high school graduates or college graduates for border and non-border Texas. These effects were consistent after adjusting by age, sex, and race/ethnicity within the border and non-border regions (Table 3). The association between tuberculosis and zip code percentage of high school graduates was similar to that for zip code per-

TABLE 1
Demographic, economic, and clinical characteristics of hospital discharge subjects in two areas in Texas from 1999 to 2001

	Border				Non-border				
	Cases (n = 1,244)		Controls (n = 12,563)		Cases (n = 3,671)		Controls (n = 58,245)		
Variable	No.	Percent	No.	Percent	No.	Percent	No.	Percent	P*
Sex									
Male	725	61.28	6,104	48.90	1,947	61.71	28,506	49.86	
Female	458	38.72	6,379	51.10	1,208	38.29	28,668	50.14	0.0001
Age									
15–24	83	7.00	2,566	20.55	239	7.57	9,944	17.39	
25–44	242	20.42	3,747	30.01	879	27.85	17,934	31.36	
45–64	326	27.51	2,651	21.23	1,049	33.24	13,511	23.63	
65+	534	45.06	3,521	28.20	989	31.34	15,794	27.62	0.0001
Race/ethnicity									
White	147	11.99	4,448	35.87	1,190	32.90	37,997	65.65	
Hispanic	1,028	83.85	7,132	57.51	1,057	29.22	10,215	17.65	
African American	11	0.90	330	2.66	980	27.09	6,557	11.33	
Other	40	3.26	491	3.96	390	10.78	3,108	5.37	0.0001
Insurance type/status									
Uninsured (self-pay)	223	17.94	1,532	12.27	918	25.07	7,681	13.23	
Medicare	560	45.05	3,630	29.07	1,077	29.41	15,933	27.45	
Medicaid	175	14.08	1,507	12.07	413	11.28	3,045	5.25	
Private	179	14.40	5,150	41.24	709	19.36	28,282	48.73	
Other	106	8.53	668	5.35	545	14.88	3,100	5.34	0.0001
Diabetes									
No	888	71.38	11,094	88.31	3,063	83.44	53,146	91.25	
Yes	356	28.62	1,469	11.69	608	16.56	5,099	8.75	0.0001
Chronic renal failure									
No	1,218	97.91	12,507	99.55	3,622	98.67	57,993	99.57	0.0000
Yes	26	2.09	56	0.45	49	1.33	252	0.43	0.0001
Any type of cancer									
No	1,150	92.44	11,526	91.75	3,408	92.84	53,079	91.13	
Yes	94	7.56	1,037	8.25	263	7.16	5,166	8.87	0.0001
Alcohol									
No	1,221	98.15	12,541	99.82	3,467	94.44	57,907	99.42	
Yes	23	1.85	22	0.18	204	5.56	338	0.58	0.0001
Nutrition deficit									
No	1,110	89.23	12,382	98.56	3,341	91.01	57,375	98.51	
Yes	134	10.77	181	1.44	330	8.99	870	1.49	0.0001
	(n = 1,089)		(n = 12,228)		(n = 2,830)		(n = 55,170)		
Mean of median zip code income (SD)	26,855.84 (8,673.74)		33,195.52 (12,717.59)		36,992.00 (13,760.48)		43,757.08 (17,136.78)		0.0001
					(n = 2,838)		(n = 55,333)		
Median of the zip code percentage of high school graduates (IQR)	52.44 (18.02)		64.32 (31.28)		69.99 (18.38)		76.85 (19.04)		0.0002
Median of the zip code percentage of college graduates (IQR)	13.90 (9.71)		17.74 (17.09)		18.91 (16.13)		28.87 (22.74)		0.0001

Missing values for each characteristic can be derived from the difference between the total number of individuals and the sum of the frequencies within that characteristic.
IQR, interquartile range.
*P value calculated from multivariate logistic regression analysis for area (border and nonborder Texas) adjusting for the variable in the row.

centage of college graduates. Because these two variables were highly correlated (Spearman correlation = 0.81; P < 0.0001), we kept the zip code percentage of high school graduates as a measure of education for further analyses.

Among the control groups, Hispanics discharged on the border differed from those living in non-border areas (Table 2). Border Hispanics were more likely to have Medicare or any type of medical insurance (P < 0.001), they lived in zip code areas with lower median incomes (P < 0.0001), and they had a lower percentage of high school graduates (P < 0.0001).

Comorbidities. Tuberculosis patients were > 10 times as likely to be alcohol users compared with controls (Table 1). Because alcohol users had missing information for sex and age, adjusted ORs could not be established. After controlling for sex, age, and race/ethnicity, tuberculosis patients from the border area were more likely to be diabetic (OR_{adj} = 1.82; 95% CI = 1.57–2.12), have chronic renal failure (OR_{adj} = 3.09; 95% CI = 1.87–5.09), or have a nutritional deficit (OR_{adj} = 5.81; 95% CI = 4.46–7.57). Tuberculosis patients from the border were less likely to have cancer than controls (OR_{adj} = 0.65; 95% CI = 0.52–0.83; Table 3). Although similar findings were observed in non-border Texas, the strength of the association for these four comorbidities was statistically different between the border and non-border regions of Texas (Table 3). None of the hospital discharges were identified as illegal drug users.

Given the differences in the strength of the association between tuberculosis and other comorbidities in the border versus non-border regions of Texas, we evaluated further the potential effect of living in the border region (Table 4). As

TABLE 2
Demographic, economic, and clinical characteristics of control subjects discharged in two areas in Texas during 1999–2001 by race/ethnicity

	Border Texas				Non-border Texas			
Variable	Hispanics (n = 7,132)	Whites (n = 4,448)	African Americans (n = 330)	Other (n = 491)	Hispanics (n = 10,215)	Whites (n = 37,997)	African Americans (n = 6,557)	Other (n = 3,108)
Sex (%)								
Male	50.08	47.81	37.99	48.78	60.31	47.96	43.59	52.08
Female	49.92	52.19	62.01	51.22	39.69	52.04	56.41	47.92
Age (%)								
15–24	25.71	13.39	12.16	14.26	31.50	13.81	15.31	18.63
25–44	33.88	24.32	26.14	25.87	44.92	27.37	30.42	38.23
45–64	19.45	23.89	23.71	21.18	14.85	25.87	25.14	22.27
65+	20.96	38.41	37.99	38.70	8.74	32.96	29.13	20.87
Insurance type (%)								
Uninsured (self-pay)	14.71	8.14	11.11	8.37	32.64	7.97	12.72	15.17
Medicare	22.62	38.14	45.06	37.55	9.46	32.07	32.22	19.49
Medicaid	17.51	4.33	8.95	6.33	10.03	3.15	9.89	5.03
Private	39.92	44.76	28.40	42.24	38.29	52.94	38.72	53.53
Other	5.24	4.63	6.48	5.51	9.58	3.88	6.45	6.78
Chronic renal failure (%)	0.52	0.40	0.30		0.23	0.36	1.20	0.35
Diabetes (%)	13.24	9.02	17.58	10.18	7.07	8.18	15.62	7.18
Alcohol (%)	0.21	0.13			0.68	0.56	0.67	0.39
Any type of cancer (%)	6.63	10.09	16.06	9.78	3.67	9.97	11.99	6.44
Nutrition deficit (%)	1.21	1.71	2.42	2.04	0.55	1.63	2.26	1.35
	(n = 6,926)	(n = 4,340)	(n = 327)	(n = 476)	(n = 9,670)	(n = 36,005)	(n = 6,187)	(n = 2,980)
Mean of median zip code income (SD)	29,379.22 (9,907..28)	39,030.99 (14,252.73)	32,354.10 (11,847.27)	36,057.91 (14,305.27)	38,396.81 (13,184.03)	46,475.25 (17,704.29)	35,166.80 (13,151.28)	46,834.92 (18,894.33)
					(n = 9,728)	(n = 36,062)	(n = 6,222)	(n = 2,982)
Median of the zip code percentage of high school graduates (IQR)	57.02 (22.26)	80.29 (24.61)	68.93 (32.97)	70.57 (31.29)	69.04 (23.41)	81.11 (17.72)	70.49 (18.10)	81.22 (21.19)
Median of the zip code percentage of college graduates (IQR)	13.90 (12.09)	27.05 (22.25)	15.73 (20.32)	20.57 (20.98)	19.48 (18.84)	26.44 (24.97)	18.08 (17.71)	30.10 (28.64)

IQR, interquartile range.

described before, we controlled for demographic variables, socio-economic status, and co-morbidity covariates. Model 1 contains the interaction effect of being diabetic and living in the border region. Model 2 excludes the interaction (data not shown). The log-likelihood ratio (LLR) test of the significance of the border residence with diabetes in the relationship of tuberculosis was 10.07 (Model 2 [minus] Model 1; P = 0.0015). This indicated that living in the border region modi-

TABLE 3
Adjusted odds ratios (OR_{adj}) and 95% confidence intervals (CI) of significant potential risk factors for tuberculosis in two areas of Texas from 1999–2001

	Border Texas			Non-border Texas			
		95% CI			95% CI		
Variable	OR_{adj}	Lower	Upper	OR_{adj}	Lower	Upper	P*
Insurance type/status							
Uninsured (self-pay)	1.00			1.00			
Medicare	0.62	0.48	0.80	0.54	0.46	0.63	
Medicaid	0.81	0.65	1.03	1.22	1.06	1.41	
Private	0.25	0.20	0.31	0.26	0.23	0.29	
Other	1.10	0.84	1.45	1.23	1.08	1.41	0.0001
Diabetes	1.82	1.57	2.12	1.51	1.36	1.67	0.0200
Chronic renal failure	3.09	1.87	5.09	2.02	1.44	2.83	0.0074
Any type of cancer	0.65	0.52	0.83	0.71	0.62	0.81	0.0058
Nutrition deficit	5.98	4.60	7.76	4.91	4.18	5.76	0.0163
Median zip code income	1.00	1.00	1.00	1.00	1.00	1.00	0.4483
Zip code percentage of high school graduates	0.98	0.97	0.98	0.98	0.98	0.98	0.7022
Zip code percentage of college graduates	0.98	0.97	0.99	0.98	0.98	0.99	0.0725

* Associated P value calculated from multivariate logistic regression analysis for area (border and non-border Texas) for each characteristic.
Each variable adjusted by sex, age and race/ethnicity.

fied the strength of the association between diabetes and tuberculosis. As in Model 1, we evaluated the interaction effect of having nutritional deficit and living in the border region ($P = 0.05$) as well as the interaction effect of having chronic renal failure and living in the border region ($P = 0.06$). These models are not shown but they are available on request from the authors.

The details of the interaction effects of being diabetic are presented in Table 5. In the border region, patients with diabetes had more than twice the risk of tuberculosis compared with patients without diabetes, and in non-border counties, patients with diabetes had > 1.5 times the risk of tuberculosis as patients without diabetes. Any diabetic living in the border region had 1.3 times the risk of tuberculosis compared with patients with diabetes living in non-border counties (OR_{adj} = 1.27; 95% CI = 1.05–1.53). Non-diabetics in the border region had a lower risk for tuberculosis, but it was not statistically significant. The overall interaction effect indicated that patients with diabetes living in the border had almost twice the risk of having tuberculosis compared with patients without diabetes living in non-border counties (OR_{adj} = 1.93; 95% CI = 1.59–2.35).

Finally, we evaluated the interaction effect in Hispanics only, a population that has previously shown a higher association between tuberculosis and diabetes. Model 1 also fits for Hispanics, and the results are presented in Table 4 (LLR, $P < 0.005$; data no shown). The details of the interaction effects for Hispanics are presented in Table 5. Regardless of living in border or non-border counties, Hispanic patients with diabetes had over twice the risk of tuberculosis as patients without diabetes.

TABLE 4

Adjusted odds ratios obtained from multivariate logistic regression model analyses adjusted for all variables in the model (OR_{adj}), 95% confidence intervals (CI), and minus two log-likelihood (−2LL) for the model with intercept and covariates

Variable	Model 1. All races Cases = 3,847 Controls = 66,714 OR_{adj} (95% CI)	Hispanic Cases = 1,656 Controls = 16,536 OR_{adj} (95% CI)
Sex		
Male	1.00	1.00
Female	0.59 (0.55–0.63)	0.62 (0.56–0.70)
Age (years)		
15–17	1.00	1.00
18–44	2.37 (2.07–2.72)	1.99 (1.65–2.40)
45–64	4.67 (4.05–5.37)	4.77 (3.92–5.82)
65+	4.66 (3.91–5.55)	5.91 (4.58–7.64)
Race/ethnicity		
White	1.00	
Hispanic	2.82 (2.55–3.11)	
African American	3.03 (2.72–3.36)	
Other	4.14 (3.64–4.70)	
Insurance type/status		
Uninsured (self-pay)	1.00	1.00
Medicare	0.63 (0.54–0.72)	0.69 (0.55–0.86)
Medicaid	1.12 (0.98–1.27)	0.95 (0.79–1.15)
Private	0.35 (0.32–0.39)	0.41 (0.35–0.49)
Other	1.42 (1.25–1.62)	1.48 (1.22–1.79)
Any type of cancer	0.74 (0.65–0.84)	0.68 (0.54–0.85)
Chronic renal failure	1.99 (1.48–2.67)	2.89 (1.79–4.66)
Nutrition deficit	5.41 (4.70–6.23)	7.40 (5.69–9.63)
Mean of median zip code income	1.00 (1.00–1.00)	1.00 (1.00–1.00)
Median of the zip code percentage of high school graduates	0.99 (0.98–0.99)	0.99 (0.99–1.00)
Diabetes	1.53 (1.37–1.70)	2.66 (2.18–3.23)
Border	0.94 (0.85–1.04)	1.06 (0.92–1.22)
Diabetes × border	1.35 (1.14–1.62)	0.77 (0.60–0.997)
−2LL	25,380.55	9,430.55

TABLE 5

Tuberculosis adjusted odds ratios (OR_{adj}) and 95% confidence interval (CI) evaluating the interaction of Texas area and diabetes obtained from multivariate logistic regression analyses adjusted for all variables in Model 1

	All races			Hispanics		
		95% CI			95% CI	
Variable	OR_{adj}	Lower	Upper	OR_{adj}	Lower	Upper
Border						
Non-diabetic	1.00			1.00		
Diabetic	2.05	1.71	2.47	2.04	1.70	2.45
Non-border						
Non-diabetic	1.00			1.00		
Diabetic	1.53	1.37	1.70	2.66	2.38	2.96
Diabetic						
Non-border	1.00			1.00		
Border	1.27	1.05	1.53	0.81	0.67	0.98
Non-diabetic						
Non-border	1.00			1.00		
Border	0.94	0.85	1.04	1.06	0.96	1.17
Diabetic and border						
Non-border/non-diabetic	1.00			1.00		
Border/diabetic	1.93	1.59	2.35	2.16	1.77	2.63

DISCUSSION

Using the THCIC data set for hospital discharge from the years 1999–2001, we confirmed that diabetes is a risk factor for tuberculosis. The result holds after adjusting for sociodemographic, health insurance, medical risk factors, and Texas border area, which is a proxy for either higher exposure to *M. tuberculosis* or higher rates of individuals with a latent tuberculosis infection. This result also held true for all races combined and for Hispanics alone. This finding is consistent with previous reports and confirms the importance of developing public health measures specifically designed for the growing number of patients with diabetes in the United States.[1–3,20]

When evaluating differences in the strength of the association between diabetes and tuberculosis based on either living in the border or non-border regions of Texas, we found that for all races combined, living in the border counties increased the strength of the association. However, an opposite effect was observed for Hispanics only: diabetic Hispanics living in non-border Texas were 23% more likely to develop tuberculosis compared with those living on the border (OR_{adj} 2.66 versus 2.16). This intriguing finding may be caused by the fact that, regardless of their place of residence within the United States, most Hispanics are immigrants from tuberculosis-endemic countries and are likely to have a latent tuberculosis infection with higher probability of reactivation on development of diabetes. This possibly suggests that there are unobserved differences between border and non-border Hispanics with diabetes. These unobserved differences may affect the risk of development of active tuberculosis. Our overall data suggest that the strength of the association between tuberculosis and diabetes will vary between populations, being moderately overstated in regions or groups of individuals who have a higher exposure to *M. tuberculosis*. Our results also show that, in the absence of diabetes or other risk factors for tuberculosis, living in the border region does not increase the chances of developing active tuberculosis.

The higher incidence of tuberculosis in the border region is likely caused by increased risk of exposure to *M. tuberculosis*. Subsequent progression of a latent tuberculosis infection to active tuberculosis disease is dependent on host factors, including host genetics and/or a medical condition compromising an effective immunity against *M. tuberculosis*.[21,22] Accordingly, the unadjusted risk for contracting tuberculosis infection is increased when an individual is in an endemic region for the disease, such as the Texas-Mexico border.[10] However, our adjusted estimates show that the Texas border area is not a risk factor for tuberculosis in itself, after controlling for socio-economic, demographic, insurance status, education, and medical risks. This somewhat surprising result indicates that diabetes and/or non-insured persons exposed to tuberculosis have a greater risk of tuberculosis than those only with exposure.

We confirm that diabetes is an important factor for having tuberculosis, but we have no evidence to distinguish between activation of a latent tuberculosis infection or primary disease. Our findings are important given the growing number of patients with diabetes in the United States and other parts of the world and the complications associated with this patient population.[20,23,24] Several studies suggest that diabetes modifies the presentation of tuberculosis disease in several ways. That is, these patients have 1) an increased proportion of cases with cavitary disease, a radiologic finding associated with higher infectivity caused by release of abundant number of bacilli in sputum; 2) increased risk of mortality (adjusted hazard ratio = 6.7; 95% CI = 1.6–29.3); and 3) association with multi-drug resistant tuberculosis, (resistant to the two first-line medications, rifampicin and isoniazid), the most serious and life-threatening form of tuberculosis.[25–29]

Another medical condition identified as a risk factor for tuberculosis was nutritional deficit. This condition can lead to diminished immune surveillance, increasing the risk for tuberculosis, or alternatively, it may be a consequence of the cachexia characterizing advanced stages of *M. tuberculosis* infection.[22,30,31] Nutritional deficit may be associated with homelessness and low socio-economic status, two risks factor for tuberculosis controlled in Model 1.

It is important to conduct future re-evaluation of our results when updated data are available for the United States because the prevalence of diabetes is expected to grow. This research could also be expanded to include the entire U.S.-Mexico region to understand the complete magnitude between different border areas and between border states. The former will require obtaining hospital discharge data from the states of New Mexico, Arizona, and California.

Although we would like to have performed a multilevel analysis, incorporating estimation of variance estimates in random slope models, it would not be feasible using this data. We needed to guarantee enough sample size at each one of the zip code area of residence. There were many zip codes and many non-border counties with very few individuals. Our enthusiasm to conduct this analysis was diminished by the number of additional constraints to make it feasible.

There are limitations to our data. 1) The THCIC data set is confined to discharge records from hospitalized patients lacking information on non-hospitalized tuberculosis cases. Our inpatient tuberculosis population may represent the most severe cases with complicated and advanced tuberculosis or other comorbidities. 2) Disease coding may have mistakes, despite a previous study with a large electronic data set using the ICD9 codes that showed that diabetes is generally well coded.[32] 3) Multiple admissions of the same patient could not be identified and excluded and may lead to overestimation of our analysis. In fact, the Texas Department of State and Health Services reported 4,798 cases of tuberculosis in the years 1999–2001, suggesting we may indeed have used rehospitalized cases.[10] 4) This database does not allow differentiation between patients with diabetes patients type I versus type II or well and poorly controlled diabetes. These are conditions that influence the ability to mount an adequate immune response against *M. tuberculosis*.[33] 5) Hispanics with tuberculosis may not use hospitals in Texas at the same rate as other race/ethnic groups do. This is especially true in the border region, where surveys show that Hispanics are least likely to have insurance in the state of Texas.[16] Uninsured border residents may use Mexican physicians because of language and cultural barriers. In fact, the Border Epidemiologic Study on Aging (BESA) provides some evidence on the use of Mexican physicians by U.S. residents on the Texas border. The BESA is a population-based study of community-dwelling Mexican Americans ⩾45 years of age residing in the Texas U.S./Mexico border and includes extensive socioeconomic, demographic, and health information on a sample of 1,089 respondents. Only 3 of 939 respondents in Wave 3 (2000-2001) of BESA reported using hospitals in Mexico (personal communication). In contrast, many respondents in the sample used Mexican dentist services, Mexican doctor services, and Mexican pharmacies (http://www.utexas.edu/lbj/news/spring2005/aging_conf.html). Therefore, whereas our sample does not include out-patient tuberculosis cases, it is representative of the hospitalized tuberculosis population in Texas. 6) Income and educational variables were only available by zip code area, limiting our ability to adjust for confounding factors. Zip code areas on the border are broad and heterogeneous, which partially obscures some of the protective effect of education. 7) A cause-and-effect relationship between tuberculosis and medical conditions cannot be established from this case-control analysis of cross-sectional data.

From a policy standpoint, the results from this study indicate a need for a better understanding of the underlying factors leading to the association between tuberculosis and diabetes, especially in regions where both diseases are highly prevalent. The profile of patients with diabetes at high risk of developing tuberculosis must be established with more precision in prospective studies. These criteria should be adopted by the local health departments so patients are promptly identified and offered chemoprophylaxis before the development of symptoms, or diagnosed at the early stages of disease before development of advanced, cavitary, and contagious forms of the infection. Establishing the level of diabetes control may also be particularly important, because patients with high glucose levels are likely to be more prone to the most complicated forms of tuberculosis, including multi-drug resistant tuberculosis.[28,33]

Increasing access to health insurance may be important for tuberculosis control. Patients with health insurance may report to the physician earlier and begin prompt control of the infection, preventing development of advanced forms of the disease that may require hospitalization. This study supports the importance of reinforcing tuberculosis control on the Mexican side of the border with programs such as the Center for Disease Control and Prevention–funded bi-national project "Grupo Sin Fronteras" (http://www.r11.tdh.state.tx.us/services/tb_bi-national.html), with focus on controlling multidrug resistant tuberculosis, to prevent further spread to Mexico and into the United States. In summary, further understanding of the underlying factors explaining the association between tuberculosis and diabetes are essential as tuberculosis morbidity and mortality rates are high worldwide, and there is a threatening growth in the number of diabetes that is making populations more vulnerable to this infection.

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