

Differences in Clinical Presentation among Persons with Pulmonary Tuberculosis: A Comparison of Documented and Undocumented Foreign-Born versus US-Born Persons

Jacqueline M. Achkar,^{1,3} Tsering Sherpa,³ Hillel W. Cohen,² and Robert S. Holzman³

Departments of ¹Medicine and Epidemiology and ²Population Health, Albert Einstein College of Medicine, Bronx, and ³Department of Medicine, New York University School of Medicine, New York, New York

(See the editorial commentary by Cain et al. on pages 1284–6)

Background. Most cases of tuberculosis (TB) in the United States are diagnosed in foreign-born persons, and undocumented foreign-born persons may face particular barriers to timely access to health care services. This study investigates whether differences in clinical presentations among persons with pulmonary TB are associated with foreign birth or documentation status.

Methods. In this cross-sectional study, we reviewed the medical records of patients who had received a diagnosis of microbiologically proven pulmonary TB at a New York City public hospital during the period April 1999 through March 2005. Three groups of patients with pulmonary TB (US-born persons, foreign-born persons with documents, and undocumented, foreign-born persons) were defined and compared at presentation. Odds ratios (ORs) for a symptom duration ≥ 8 weeks before hospital admission for each group were estimated using logistic regression.

Results. Among 194 subjects with newly diagnosed pulmonary TB, 61 (31%) were US born, 62 (32%) were documented foreign-born persons, and 71 (37%) were undocumented foreign-born persons. Undocumented foreign-born persons presented with significantly higher frequencies of cough ($P = .020$) and hemoptysis ($P = .012$) and had a significantly longer median duration of symptoms, compared with US-born persons (8 vs. 4 weeks; $P = .023$). No statistically significant differences between documented foreign-born and US-born persons were observed. Multivariate analysis revealed that undocumented status (compared with being US born; adjusted OR, 4.1; 95% confidence interval, 1.7–10.2; $P = .002$) and being unemployed (adjusted OR, 2.2; 95% CI, 1.1–4.5; $P = .023$) were independently associated with a prolonged symptom duration (i.e., ≥ 8 weeks).

Conclusions. Undocumented status was associated with an increased frequency of cough and hemoptysis and a longer duration of symptoms before medical evaluation for pulmonary TB. Whether reducing barriers to health services for undocumented foreign-born persons could enhance TB control deserves additional study.

Despite its decreasing incidence, tuberculosis (TB) continues to be a social, public health, and economic burden in urban areas of the United States. In fact, experts fear a resurgence of the disease resulting from decreased funding for TB elimination at the Centers for Disease Control and Prevention (Atlanta, GA) [1]. Further-

more, the increased incidence of multidrug-resistant TB worldwide and the occurrence of extensively drug-resistant TB highlight the necessity for better TB control [2]. In 2006, a total of 13,770 active TB cases were reported to the Centers for Disease Control and Prevention, representing a TB case rate of 4.6 cases per 100,000 population in the United States—a rate much higher than the Healthy People 2010 objective of 1.0 case per 100,000 population [3, 4].

The majority (57%) of TB cases nationwide are diagnosed in foreign-born persons. The TB case rate for foreign-born persons is almost 10 times as high as the case rate for US-born persons (22.0 vs. 2.3 cases per 100,000 population, respectively) [4]. New York City (NYC) has a high proportion of foreign-born residents,

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Reprints or correspondence: Dr. Jacqueline M. Achkar, Albert Einstein College of Medicine, 1300 Morris Park Ave., Mazer Bldg., Rm. 209, Bronx, NY 10461 (jachkar@aecom.yu.edu).

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and its TB case rate is 2.6 times higher than the national average [5]. Concomitant with a continuing decrease in annual TB case rates in NYC, the proportion of foreign-born persons among patients with reported TB cases increased from 18% in 1992 to >70% in 2006.

It is unknown whether differences in clinical presentations among persons with pulmonary TB (PTB) are associated with foreign birth or documentation status, compared with birth in the United States. Undocumented foreign-born persons may face particular barriers to timely access to health services, resulting in delayed hospital evaluation for suspected PTB, compared with US-born persons. We hypothesized that, among foreign-born persons with PTB, those with undocumented status would present with signs of more-advanced disease than would US-born persons. The objectives of this study were (1) to measure the extent of disease and the presence and duration of symptoms at the time of initial hospital evaluation for PTB and to compare the results for documented and undocumented foreign-born persons with results for US-born persons, and (2) to assess whether documentation status among foreign-born persons (relative to US-born persons) has an independent association with prolonged symptom duration before the initial hospital evaluation in persons with PTB, after adjustment for other risk factors.

METHODS

Design, setting, and study population. In this cross-sectional study, we reviewed the medical records of all identifiable patients (age, 18–99 years) who received a diagnosis of PTB during the period April 1999 through March 2005 at Bellevue Hospital Center (BHC; NYC). This 800-bed public hospital is part of the NYC Health and Hospitals Corporation, which is a public benefit corporation that serves 1.3 million New Yorkers and nearly 400,000 persons who are uninsured [6]. BHC is the largest Health and Hospitals Corporation hospital and is located in midtown Manhattan; thus, it evaluates most persons with suspected TB from that community. Over recent years—including the period of study—BHC and Elmhurst Hospital Center (a Health and Hospitals Corporation facility located in the borough of Queens) have reported the highest number of new TB cases among all facilities in NYC [7].

We screened the records of patients whose cases were reported to the NYC Department of Health as new, probably active TB, and we reviewed the records of patients with microbiologically proven, active TB. Patients whose diagnosis of PTB was confirmed by growth of *Mycobacterium tuberculosis* from a respiratory specimen culture were included in the analysis. Patients were excluded from analysis if they received a diagnosis of extrapulmonary TB without microbiologically proven pulmonary disease, if they had received a diagnosis of active PTB before hospital admission, or if information was

missing on outcome variables or documentation status. Patients who received a TB diagnosis before hospital admission were excluded from the study, because BHC is a referral hospital for patients with TB who have been detained by order of the NYC Department of Health for noncompliance with TB treatment. Inclusion of such patients could potentially skew results, because these patients have often received partial treatment for several months and come from outside the community, and information on outcome variables (e.g., symptom duration at the time of diagnosis) is frequently vague. Furthermore, these patients are often not reported by BHC as new cases of active TB and, thus, would not be detected by our screening method. Approval for human subjects' research was obtained from the institutional review boards of the New York University School of Medicine and BHC.

Measurements. Information on reported variables was extracted from the admitting physician's note, social worker's note, and diagnostic test reports in the patients' medical records. Our main variables of interest were location of birth and documentation status. The patients' self-reported information on location of birth was extracted from the physician's note, whereas self-reported information on documentation status was extracted from the social worker's note. Statements in the social worker's note such as "undocumented," "no legal papers," or "no visa" were considered indicative of an undocumented status. Subjects were categorized into 3 groups: US-born persons, documented foreign-born persons, and undocumented foreign-born persons. Persons born in Puerto Rico or the US Virgin Islands were considered to be US born. Additional recorded demographic factors included sex, age, race (on the basis of the physician's note), self-reported number of years in the United States (for foreign-born persons), health insurance and self-reported employment status, and homelessness.

Clinical characteristics included HIV status, results of other diagnostic tests regarding the establishment of PTB diagnosis, and self-reported symptoms. Chest radiograph findings were recorded as unilobar versus multilobar or miliary infiltrates, with separate scoring for the presence or absence of cavitory lesions. Sputum smears for acid-fast bacilli (AFB) were defined as positive if at least 1 of the initial 3 smears yielded positive results, regardless of quantity of AFB seen per microscopy slide. Furthermore, the degree of smear positivity was categorized as rare (1–10 AFB/slide), few (11–20 AFB/slide), and numerous (>20 AFB/slide). The presence of multilobar or miliary infiltrates, cavitory lesions, and/or smear positivity were considered to be potential signs of more-advanced disease. Because HIV-mediated immunosuppression can impair granuloma formation, resulting in both diminished formation of pulmonary cavities and atypical infiltrates [8], we performed univariate analyses that included and excluded HIV-infected subjects.

The patients' self-reported symptoms that were recorded as potentially suggestive of PTB included the presence of cough, hemoptysis, fever, night sweats, and weight loss >2 lbs (>0.9 kg). For each of these symptoms, the patients' self-reported duration was recorded as the number of weeks before hospital evaluation. The longest duration of any one of the symptoms suggestive of PTB, as listed above, was considered to be the symptom duration. For multivariate analysis, symptom duration was treated as a dichotomous outcome, with a cutoff of ≥ 8 weeks based on the median duration of 7 weeks for all subjects included in the analysis.

Statistical analysis. Statistical analysis was performed using Stata software, version 9.2 (StataCorp). A 2-tailed $\alpha < .05$ indicated statistical significance.

For univariate analysis, depending on distribution, we used Student's *t* test or the Mann-Whitney *U* test when comparing 2 groups, and we used 1-way analysis of variance or the Kruskal-Wallis test when comparing 3 groups. For categorical variables, we used the χ^2 test, without correction for continuity. In each case, a summary test was used to assess differences among the 3 groups; a significant or nearly significant summary test result was followed by pairwise contrasts between documented foreign-born persons and US-born persons and between undocumented foreign-born persons and US-born persons. For the pairwise contrasts, a Bonferroni-corrected 2-tailed $\alpha < .025$ was used as the criterion for statistical significance.

Multivariate logistic regression models were constructed to test whether there was an independent association between the dichotomous outcome variable (i.e., symptom duration, ≥ 8 weeks) and documented or undocumented foreign-born status, with US-born status as a reference. Variables for which the association with outcome had a *P* value $< .2$ in univariate analysis or which are known to have an impact on delayed PTB diagnosis were initially included in the model. Adequacy of the final model was assessed by the goodness-of-fit test.

RESULTS

We identified 244 patients who had received a diagnosis of active TB during the period April 1999 through March 2005. After some patients were excluded (figure 1), 194 patients with newly diagnosed, microbiologically proven PTB were included in the analysis. Among the 194 subjects evaluated, 61 (31%) were US born, 62 (32%) were documented foreign born, and 71 (37%) were undocumented foreign born. Table 1 shows the characteristics of these 3 groups and, apart from the number of years of residence in the United States, lists the summary *P* values for the 3-group comparison.

Comparison of characteristics. In pairwise contrast, documented foreign-born subjects were similar to US-born subjects with regard to sex, age, and health insurance status but differed significantly with regard to racial distribution ($P <$

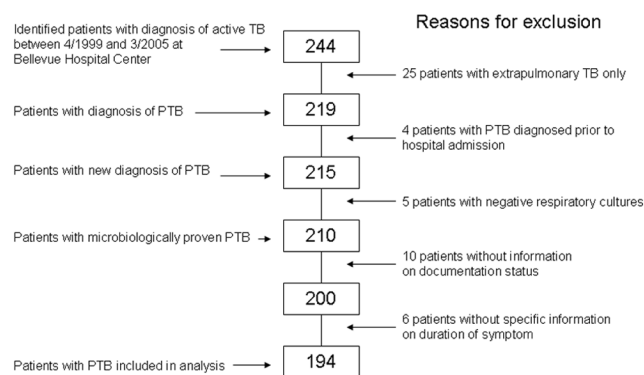


Figure 1. Reasons for exclusion of subjects from analysis. PTB, pulmonary tuberculosis; TB, tuberculosis.

.001). Among both documented and undocumented foreign-born persons, Asians represented the largest ethnic group, whereas the US-born group consisted mostly of black and Hispanic persons. According to frequency, the countries of origin among foreign-born Asians were as follows: China, 44 (51%) of 87 persons; Nepal, 11 persons (13%); Tibet, 10 persons (11%); The Philippines, 7 persons (8%). Fifteen (17%) were distributed among several other Asian countries with $< 5\%$ per country. Both documented and undocumented foreign-born persons were significantly less likely to be unemployed ($P < .001$) or HIV infected ($P < .001$ and $P = .008$, respectively) than were US-born persons. Undocumented foreign-born persons were significantly younger and less likely to have health insurance than were US-born persons ($P < .001$).

Comparison of diagnostic test results. No significant differences among the 3 groups were observed with regard to the presence of multilobar or miliary infiltrates or cavitary lesions or to positive sputum smear results (table 2). Furthermore, no significant differences among the 3 groups were observed with regard to the degree of smear positivity. This did not change when HIV-coinfected subjects were excluded from univariate analysis.

Presence of symptoms suggestive of PTB. Table 2 reports the presence of symptoms suggestive of PTB and the summary *P* values for the comparisons of the 3 groups. Because the difference among the 3 groups in the presence of cough was nearly significant ($P = .069$), pairwise contrast was performed. Presentation with cough was significantly more common among undocumented foreign-born persons than among US-born persons ($P = .02$), whereas there was no significant difference between documented foreign-born persons and US-born persons ($P = .297$). Similarly, for the presence of hemoptysis, for which there were significant differences in the 3-group comparison ($P = .018$), pairwise contrast revealed that hemoptysis was significantly more likely to be present among undocumented foreign-born persons than among US-born per-

Table 1. Characteristics of 194 subjects with pulmonary tuberculosis, by location of birth and documentation status.

Characteristic	US-born patients ^a (n = 61)	Foreign-born patients		P
		Documented status (n = 62)	Undocumented status (n = 71)	
Male sex	46 (75)	48 (77)	43 (61)	.063 ^b
Age, mean years \pm SD	45 \pm 12	42 \pm 12	33 \pm 10	<.001 ^c
Race				
Black	34 (56)	10 (16)	5 (7)	
Hispanic	22 (36)	11 (18)	12 (17)	<.001 ^b
Asian	2 (3)	37 (60)	50 (70)	
White	3 (5)	4 (6)	4 (6)	
Duration of residence in the United States, ^d median years (range)	NA	9 (1–37)	3 (1–13)	<.001 ^e
Has health insurance ^f	41 (68)	37 (61)	8 (11)	<.001 ^b
Unemployed	53 (87)	38 (61)	44 (62)	.002 ^b
Homelessness	15 (25)	8 (13)	2 (3)	.001 ^b
Proportion of HIV-infected persons ^g (%)	22/44 (50)	4/37 (11)	8/37 (22)	<.001 ^b

NOTE. Data are no. (%) of patients, unless otherwise indicated.

^a Includes Puerto Rico and US Virgin Islands.

^b Determined by the χ^2 for 3-group comparisons.

^c Determined by 1-way analysis of variance.

^d Information on duration of residence in the United States was available for 122 (92%) of 133 foreign-born persons.

^e Determined by the Mann-Whitney *U* test.

^f Health insurance information was available for 192 subjects (99%).

^g HIV-1 and/or HIV-2 serologic test results were available for 118 subjects (61%).

sons ($P = .012$), whereas there was no significant difference between documented foreign-born persons and US-born persons ($P = .653$). There was a trend of higher frequency for other symptoms suggestive of PTB (e.g., fever and night sweats) among undocumented foreign-born persons, compared with US-born persons, although this difference did not reach statistical significance.

Duration of symptoms suggestive of PTB. Univariate analysis revealed that the duration of symptoms before hospital evaluation for PTB was significantly different among the 3 groups ($P = .014$) (table 2). Undocumented foreign-born persons had a significantly longer median duration of symptoms (8 weeks) than did US-born persons (4 weeks; $P = .023$), whereas there was no statistically significant difference in the median duration between documented foreign-born persons and US-born persons.

Table 3 presents the adjusted ORs and 95% CIs for having a prolonged symptom duration of ≥ 8 weeks, according to place of birth and documentation status, relative to US birth. Multivariate analysis revealed that undocumented foreign-born status, compared with US-born status, was independently associated (adjusted OR, 4.1; 95% CI, 1.7–10.2; $P = .002$) with symptom duration ≥ 8 weeks. In addition, being unemployed (adjusted OR, 2.2; 95% CI, 1.1–4.5; $P = .023$) was independently associated with prolonged symptom duration. Neither lack of health insurance nor HIV infection was significantly

associated with prolonged symptom duration; neither were homelessness nor any of the other demographic variables. Race was removed from the model because of multicollinearity, due to the fact that foreign-born persons were predominantly Asian and the US-born persons were almost all black or Hispanic. To control for potential confounding by race, we constructed a logistic regression model for Asians alone—the largest ethnic group among the foreign-born persons with PTB. Table 4 shows the adjusted association between undocumented status, relative to documented status, with prolonged symptom duration for Asian persons who were born outside the United States (OR, 3.3; 95% CI, 1.0–10.6; $P = .045$).

DISCUSSION

To our knowledge, this is the first study that compared the clinical presentation of documented and undocumented foreign-born with US-born persons with PTB at the time of initial hospital evaluation. Contrary to hypothesized expectation, we found no statistically significant differences between undocumented and US-born persons regarding the presence of multilobar or miliary infiltrates, cavitory lesions, or smear positivity. However, being an undocumented foreign-born person was statistically significantly associated with an increased frequency of cough, hemoptysis, and symptom duration ≥ 8 weeks, compared with being born in the United States. In contrast, doc-

Table 2. Diagnostic test results for and symptoms in 194 subjects with pulmonary tuberculosis (PTB), by location of birth and documentation status.

Characteristic	US-born patients ^a (<i>n</i> = 61)	Foreign-born patients		<i>P</i>
		Documented status (<i>n</i> = 62)	Undocumented status (<i>n</i> = 71)	
Diagnostic test result				
Multilobar or miliary infiltrate(s)	41 (67)	44 (71)	44 (62)	.541 ^b
Presence of cavitory lesions	20 (33)	23 (37)	26 (37)	.886 ^b
Positive smear result ^c	38 (62)	35 (56)	47 (66)	.512 ^b
Presence of symptoms suggestive of active PTB ^d				
Cough	40 (66)	46 (74)	59 (83)	.069 ^b
Fever	32 (52)	32 (52)	46 (65)	.224 ^b
Night sweats	19 (31)	16 (26)	31 (44)	.081 ^b
Weight loss ^e	28 (46)	29 (47)	35 (49)	.920 ^b
Hemoptysis	9 (15)	11 (18)	24 (34)	.018 ^b
Symptom duration suggestive of active PTB, ^f median weeks (range)				
	4 (0–36)	4 (0–104)	8 (1–104)	.014 ^g

NOTE. Data are no. (%) of patients, unless otherwise indicated.

^a Includes Puerto Rico and US Virgin Islands.

^b Determined by the χ^2 for 3-group comparisons.

^c At least 1 of the initial 3 sputum smears tested positive for acid-fast bacilli, regardless of quantity of acid-fast bacilli.

^d Symptoms were self-reported by patients.

^e Defined as a self-reported weight loss of >2 lbs (>0.9 kg).

^f Longest duration of any single or several symptoms suggestive of PTB.

^g Determined by the Kruskal-Wallis test.

umented foreign-born persons did not differ from US-born persons in these respects.

The epidemiologic profile of our study population was largely similar to that reported for TB cases in NYC during the study period, although the proportions of homeless and HIV-infected subjects, as well as of Asians, was larger in our study population [9]. This is likely because our study site is a public hospital located in midtown Manhattan, close to homeless shelter facilities and Chinatown. Because HIV infection and homelessness are known risk factors for TB and might be associated with the clinical presentation of TB, we performed univariate analyses with inclusion and exclusion of HIV-infected subjects, and we adjusted for HIV infection and homelessness in the multivariate analysis and controlled for potential confounding by Asian race. In addition, our reported frequencies of positive smear results, cavitory lesions, and symptoms associated with PTB were similar to the frequencies found in other US studies [10–12], and the median reported duration of symptoms before hospital evaluation in our study population was similar to the average patient delay of 5–10 weeks before TB diagnosis reported in other US studies [11–14]. Therefore, we believe that our results may allow inferences toward other US urban areas with large immigrant populations.

It is well known that persons with smear-positive cavitory disease transmit TB more frequently than do those with most other forms of PTB [15]. Furthermore, studies have shown that a delay in TB diagnosis is associated with greater transmission

of infection to contacts [10, 15]. Asch et al. [12] found that, during the delay between symptom onset and TB diagnosis, a person exposes, on average, 8 contacts. Our findings suggest that the difference in time to presentation may not impact the course of disease in undocumented foreign-born persons but could, in addition to the higher frequency of cough, lead to an increased exposure of close contacts. Population-based molec-

Table 3. Adjusted association of birth location and documentation status with duration of symptoms ≥ 8 weeks in patients with pulmonary tuberculosis.

Variable	Adjusted OR (95% CI)	P
Birth location/documentation status		
US-born persons	Reference	
Documented foreign-born persons	1.01 (0.46–2.24)	.976
Undocumented foreign-born persons	4.14 (1.68–10.22)	.002
Has health insurance ^a	1.51 (0.73–3.10)	.240
Unemployed	2.24 (1.12–4.46)	.023
HIV status ^b		
Negative	Reference	
Positive	0.74 (0.31–1.81)	.511
Unknown	0.81 (0.41–1.57)	.525

NOTE. The logistic regression model included 192 observations.

^a Information on health insurance was available for 192 (99%) of 194 subjects.

^b HIV-1 and/or HIV-2 serologic test results were available for 118 subjects (61%).

Table 4. Adjusted association of documentation status with duration of symptoms ≥ 8 weeks in foreign-born Asians with pulmonary tuberculosis.

Variable	Adjusted OR (95% CI)	P
Documentation status		
Documented	Reference	
Undocumented	3.30 (1.03–10.61)	.045
Has health insurance ^a	1.13 (0.34–3.77)	.841
Unemployed	1.77 (0.69–4.53)	.233

NOTE. The logistic regression model included 86 observations.

^a Information on health insurance was available for 86 (99%) of 87 subjects.

ular epidemiologic studies performed in the United States and Europe have not demonstrated significant associations between strains isolated from foreign-born persons and evidence of recent TB transmission, but these studies have not specifically examined transmission among close contacts of undocumented foreign-born persons [16–20]. A detailed investigation would be needed to further investigate whether undocumented foreign-born persons—who, as our data suggest, may face different barriers to health care—transmit TB more than do documented foreign-born persons.

The underlying reason for the statistically significantly higher frequency of hemoptysis among undocumented foreign-born persons, compared with US-born persons, is not clear to us. The presence of hemoptysis is often associated with cavitary lesions and, therefore, could be considered to be a sign of advanced PTB [21]. However, the presence of cavitary lesions on chest radiographs in our study population was similar among the 3 groups, and detailed information on size of cavitary lesions was not available for most subjects. For the majority of persons, regardless of ethnic and cultural background, hemoptysis is an extremely worrisome symptom. It is conceivable that the occurrence of hemoptysis would lead undocumented foreign-born persons to overcome the potential barriers to seeking health care. Larger studies would be needed to further investigate whether the higher frequency of hemoptysis among undocumented foreign-born persons is associated with more-advanced disease at the time of hospital evaluation, with major health concerns that lead to immediate health care-seeking behavior, or both.

The significantly positive association between undocumented foreign-born status and prolonged symptom duration could be due to patient factors that have been shown to be associated with a delay in TB diagnosis. Among these are nonwhite race [10], primary language other than English [11], fear of immigration authorities [12], concern about costs [12], unemployment [12], and lower level of education [13]. Although undocumented immigrants in our study population were significantly less likely to have health insurance or to be white, we found that neither of these characteristics were significantly

associated with prolonged symptom duration. We did find an independent positive association between unemployment and prolonged symptom duration that was consistent with the results of previous studies [12]. A detailed analysis of factors that potentially contribute to the prolonged symptom duration of undocumented foreign-born persons was beyond the scope of this study and would require a larger, prospective investigation.

Our study was limited by the retrospective nature of the design, which did not permit us to evaluate factors such as English language-speaking ability, which was not described in detail in the records of most patients. Furthermore, we were not able to assess treatment outcomes for our study population, because part of our study population received TB treatment outside BHC; thus, this information was not available to us. BHC serves a predominantly poor and disadvantaged population; therefore, our results might not be generalizable to non-public institutions. The fact that lack of health care insurance was not significantly associated with outcome may reflect this limitation. Our study was further limited by the self-reported information on documentation status. It is conceivable that undocumented persons might report that they are documented out of fear of immigration authorities. However, this would create a bias toward smaller observed differences between documented and undocumented foreign-born persons.

Undocumented foreign-born persons have been the ongoing focus of intense policy debate over the past several years. A recent study, which analyzed data from the 2003 California Health Interview Survey, showed that undocumented Mexicans and other undocumented Latinos reported less use of health care services, compared with their US-born counterparts [22]. Our data showing significantly longer symptom duration prior to hospital evaluation for PTB in undocumented but not documented foreign-born compared with US-born persons is consistent with these findings. This raises the concern that current political developments with aggressive measures targeting undocumented foreign-born persons could further jeopardize timely access to health services in this disadvantaged population.

In conclusion, undocumented foreign-born status is associated with increased presentation of cough and hemoptysis and a longer duration of symptoms before hospital evaluation for PTB. Whether identifying and reducing barriers to health services for undocumented persons can enhance case finding and TB control deserves additional study.

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