Tuberculosis in the Inner City: Impact of a Continuing Epidemic in the 1990s

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Tuberculosis cases have recently declined in the United States, renewing interest in disease elimination. We examined the epidemiology of tuberculosis from 1991 through 1997 at an inner-city public hospital and assessed population-based tuberculosis rates by ZIP code in the 8 metropolitan Atlanta counties. During the 7 years, 1378 new patients had tuberculosis diagnosed at our hospital (mean, 197 patients/year), accounting for 25% of tuberculosis cases in Georgia. Coinfection with human immunodeficiency virus (HIV) was common, but a significant decrease in the proportion of HIV-infected patients with tuberculosis was noted over time. Most patients were members of a minority group (93%) and were born in the United States (96%). Two inner-city ZIP code areas had annual tuberculosis rates >120 cases per 100,000 persons, and 8 ZIP code areas had annual rates of 47–88 cases per 100,000 persons between 1993 and 1997, compared with the annual national average of 8.7 cases per 100,000 persons. Our hospital continues to care for large numbers of tuberculosis patients, and rates of tuberculosis remain high in the inner city. These data mandate a concentration of efforts and resources in urban locations if tuberculosis control and elimination is to be achieved in the United States.

Tuberculosis is a major public health problem worldwide and the leading cause of deaths due to infectious disease [1–3]. Initially regarded as a disease that could be eliminated in the United States, tuberculosis in this country increased in incidence by 20% between 1985 and 1992. This was, in large part, due to the epidemic of human immunodeficiency virus (HIV) infection, the decline of the public health infrastructure as a result of underfunding, and increases in the homeless population in US cities [4–11].

Because of enhanced public health interventions, increased funding for tuberculosis control efforts, implementation of directly observed therapy, and prevention of nosocomial transmission of tuberculosis, the incidence of tuberculosis in the United States declined 26% between 1992 and 1997 [6, 12, 13]. In 1997, the tuberculosis case rate in the United States was 7.4 cases per 100,000 persons, the lowest ever reported [12, 14]. The decreasing incidence has again raised discussion about the feasibility of the goal of the US Public Health Service to eliminate tuberculosis in the United States by 2010 [4].

Over the past 2 decades, tuberculosis has impacted urban areas [5, 10, 15–17]. The city of Atlanta had high rates of tuberculosis in the early 1990s. In 1991 and 1992 it had the highest incidence of tuberculosis among US cities [6]. The large majority of persons with tuberculosis in Atlanta receive care at Grady Memorial Hospital, a 1000-bed inner-city, university-affiliated public hospital in downtown Atlanta. In this study, we (1) examined the epidemiology of tuberculosis at Grady Memorial Hospital over a 7-year period, from 1991 through 1997, and (2) assessed population-based rates of tuberculosis disease in ZIP code areas in the 8 metropolitan Atlanta counties from 1993 to 1997 and determined associations between these tuberculosis incidence rates and ZIP code area demographic and socioeconomic variables.

Methods

Patients with tuberculosis at Grady Memorial Hospital: All patients with tuberculosis disease diagnosed at Grady Memorial Hospital between 1 January 1991 and 31 December 1997 were included in the study. Demographic data, including race, sex, age, county of residence, HIV serological status, and CD4 cell count, were collected for all patients and were analyzed by use of Epi Info software, version 6.1 (Centers for Disease Control and Prevention [CDC], Atlanta, GA). Country of birth was obtained during the period of 1993–1997 from the Georgia Department of Human Resources, Division of Public Health; this information was not available during the years 1991 and 1992. Odds ratios (ORs), χ2 tests, and Cornfield 95% confidence intervals (CIs) were used for analyses of variables.

Smears for acid-fast bacilli were performed at the Grady clinical microbiology laboratory by means of a fluorochrome method on
concentrated clinical specimens [18]. All specimens submitted for culture for acid-fast bacilli were processed by a radiometric broth method (Bactec 460 Tuberculosis; Becton Dickinson Microbiology Systems, Sparks, MD) as well as with a solid medium (Lowenstein-Jensen medium). A diagnosis of tuberculosis disease was determined by (1) a positive culture for Mycobacterium tuberculosis or (2), beginning in 1994, clinically, on the basis of the case definition criteria of the CDC and a physician’s decision to treat the patient for tuberculosis disease despite a negative culture for M. tuberculosis [19].

Susceptibility testing of M. tuberculosis isolates was performed against isoniazid, rifampin, and ethambutol by the Georgia Public Health Laboratory, by use of a broth radiometric method [17]. If resistance to any of these 3 drugs was found, the isolate was forwarded to the CDC, where susceptibility testing was performed for confirmation of resistance, and other antituberculosis drugs were tested by means of the proportion method [20]. Routine susceptibility testing of all M. tuberculosis isolates recovered from patients at Grady Memorial Hospital was initiated in July 1991.

Molecular typing of rifampin-resistant M. tuberculosis isolates was performed with IS6110 restriction fragment length polymorphism (RFLP) analysis, as previously described [21–23].

## Rates of tuberculosis by metropolitan Atlanta ZIP code areas.

The number of tuberculosis cases by ZIP code area from 1993 through 1997 was obtained from the Georgia Department of Human Resources, Division of Public Health, for the 8 metropolitan Atlanta counties (Fulton, DeKalb, Clayton, Rockdale, Cobb, Gwinnett, Douglas, and Newton). Total population data for ZIP code areas obtained from the US Bureau of the Census (1990 census) were used to determine tuberculosis rates for ZIP code areas. Additional demographic and socioeconomic census variables for ZIP code areas were obtained from the US Bureau of the Census.

Poisson regression modeling by means of SAS software (SAS Institute, Cary, NC) was used to perform a multivariate analysis to determine associations between census variables and tuberculosis incidence for ZIP code areas.

### Results

#### Tuberculosis disease at Grady Memorial Hospital.

Between 1 January 1991 and 31 December 1997, a total of 1378 different patients were diagnosed with tuberculosis disease at Grady Memorial Hospital (mean, 197 patients per year) (table 1). If Grady Hospital were a state, it would rank 28th in the number of tuberculosis patients reported from 1991 through 1997 (table 2) [12, 14, 24, 25]. During the 7 years, 24.7% of all tuberculosis cases in Georgia (1378 of 5586) were reported from Grady Memorial Hospital (table 2). The highest number of new patients (255) was seen in 1991, and the lowest number (157) was seen in 1995 (table 1). Between 1991 and 1994, there was a 35.6% decrease in the number of culture-confirmed cases. However, unlike national trends, the total number of tuberculosis patients seen at Grady Memorial Hospital between 1994 and 1997 remained relatively stable, and between 1995 and 1997, the number of culture-confirmed cases increased (table 1). During the 7-year period, there was a total of 1536 tuberculosis-related admissions (an average of 219 per year).

Demographic information for patients who had tuberculosis diagnosed is shown in table 1. Most patients (93.2%) were members of a minority group, and 96.1% were born in the United States. There was little variation in the sex, race, or age of patients between 1991 and 1997. A significant trend over time was observed for the proportion of foreign-born patients, which increased from 1% in 1993 to 6% in both 1996 and 1997 (P =.01). Ninety-six percent of patients resided in either Fulton

### Table 1. Demographic data for patients with tuberculosis at Grady Memorial Hospital, Atlanta, 1991–1997.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients with indicated characteristic, no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of different patients</td>
<td>1378 255 244 193 179 157 175 175</td>
</tr>
<tr>
<td>Tuberculosis diagnosis</td>
<td></td>
</tr>
<tr>
<td>Culture-confirmed</td>
<td>1282 (93.0) 255 (100) 244 (100) 193 (100) 164 (96.1) 133 (84.7) 158 (89.3) 135 (77)</td>
</tr>
<tr>
<td>Clinical</td>
<td>96 (7.0) NC NC NC 15 (8.4) 24 (15.3) 17 (9.7) 40 (23)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1015 (73.7) 187 (73.3) 175 (71.7) 142 (73.6) 146 (81.6) 114 (72.6) 125 (71.4) 126 (72)</td>
</tr>
<tr>
<td>Female</td>
<td>363 (26.3) 68 (26.7) 69 (28.3) 51 (26.4) 33 (18.4) 43 (27.4) 50 (28.6) 49 (28)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1211 (87.9) 225 (88.2) 216 (88.5) 172 (89.1) 152 (84.9) 140 (89.2) 146 (83.4) 160 (91.4)</td>
</tr>
<tr>
<td>White</td>
<td>94 (6.8) 23 (9.0) 12 (4.9) 16 (8.3) 16 (8.9) 9 (5.7) 14 (8.0) 4 (2.3)</td>
</tr>
<tr>
<td>Other</td>
<td>73 (5.3) 7 (2.8) 16 (6.6) 5 (2.6) 11 (6.2) 8 (5.1) 15 (8.6) 11 (6.3)</td>
</tr>
<tr>
<td>Age in years, mean (median)</td>
<td>40.5 (39) 39.5 (38) 40 (39) 40.3 (39) 40.9 (40) 40.7 (39) 39.9 (38) 42.5 (38)</td>
</tr>
<tr>
<td>HIV statusa</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>536 (38.9) 104 (40.8) 102 (41.8) 83 (43.0) 80 (44.7) 58 (36.9) 66 (37.7) 43 (24.6)</td>
</tr>
<tr>
<td>Negative</td>
<td>632 (45.9) 105 (40.8) 93 (38.1) 89 (46.1) 82 (45.8) 80 (51.0) 80 (45.7) 103 (58.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>210 (15.2) 46 (18.4) 49 (20.1) 21 (10.9) 17 (9.5) 19 (12.1) 29 (16.6) 29 (16.5)</td>
</tr>
<tr>
<td>Birth country (n = 879)b</td>
<td></td>
</tr>
<tr>
<td>Foreign</td>
<td>34 (3.9) NA NA 2 (1.1) 7 (3.9) 5 (3.2) 10 (6.0) 10 (5.7)</td>
</tr>
<tr>
<td>United States</td>
<td>845 (96.1) NA NA 191 (98.9) 172 (96.1) 152 (96.8) 165 (94.0) 165 (94.3)</td>
</tr>
</tbody>
</table>

**NOTE.** HIV, human immunodeficiency virus; NA, not available; NC, not collected/no surveillance.

a HIV-seropositive and HIV-seronegative patients compared for trend over time, P < .001.

or DeKalb county, the 2 most urban counties in the metropolitan Atlanta area.

Of 1378 patients with tuberculosis, 536 (38.9%) were HIV-seropositive, 632 (45.9%) were HIV-seronegative, and 210 (15.2%) did not have HIV serological testing performed. The proportion of HIV-seropositive patients was highest in 1994 (80 of 179 [44.7%]) and lowest in 1997 (43 of 175 [24.6%]; table 1). A significant trend toward a decrease in the proportion of HIV-seropositive tuberculosis patients was found when HIV-seropositive and -seronegative patients were compared over time (P < .001). The mean and median CD4 cell counts for HIV-seropositive patients with tuberculosis were 167 cells/mL and 86 cells/mL, respectively. HIV-seronegative patients were more likely to have smear-positive pulmonary tuberculosis than were HIV-infected patients (472 [81.5%] of 579 vs. 335 [69.5%] of 482; OR, 1.94; 95% CI, 1.44–2.60).

Susceptibility testing was performed on M. tuberculosis isolates from 1170 (91.3%) of 1282 patients. Ninety-one percent (1066 of 1170) were fully susceptible to first-line antituberculosis antibiotics. Isolates from 65 patients (5.6%) were resistant to isoniazid only; isolates from 16 (1.4%) were resistant to rifampin only, isolates from 14 (1.2%) were resistant to both isoniazid and rifampin (multidrug resistance), and isolates from 9 (0.8%) were resistant to ≥2 drugs but not both isoniazid and rifampin. During the 7-year period, there was a significant increase over time in the monoresistance to isoniazid (P = .03) (table 3). Primary resistance was seen in 61 (93.8%) of 65 patients from whom isoniazid-resistant isolates were recovered.

There was no significant association between HIV serological status and the resistance of isolates to isoniazid (OR, 1.2; 95% CI, 0.7–2.1; P = .47) or multidrug resistance (OR, 1.9; 95% CI, 0.6–6.8; P = .24). However, single-drug resistance to rifampin was strongly associated with HIV coinfection (OR, 8.5; 95% CI, 1.8–54.1), as 14 of 16 patients whose isolates were resistant only to rifampin were HIV-seropositive. Seven (43.8%) of these 16 patients developed secondary resistance to rifampin after initially having susceptible isolates; all were HIV-coinfected, with a mean CD4 cell count of 18.4/mm³ (range, 7–44 mm³).

IS6110 RFLP analysis of available rifampin-resistant M. tuberculosis revealed that isolates from nine of 12 patients had different banding patterns. In addition, when susceptible and resistant paired isolates from 5 patients who developed rifampin-only resistance were examined, the later banding pattern was identical to the earlier banding pattern in all cases, confirming the development of resistance in the original M. tuberculosis strain rather than infection and disease with a new strain.

### Rates of tuberculosis by metropolitan Atlanta ZIP code areas.

The annual tuberculosis incidence rate in the eight-county metropolitan Atlanta area (census population, 2,524,637) was 14.1 cases per 100,000 persons between 1993 and 1997. Inner-city ZIP code areas, including those near Grady Memorial Hospital, had the highest rates of tuberculosis, and incidence rates decreased with distance from the inner city (figure 1). Two inner-city ZIP code areas had annual tuberculosis case rates higher than 120 cases per 100,000 persons between 1993 and 1997, and 8 ZIP code areas had annual rates between 47.0 and 87.5 cases per 100,000 persons during the same 5-year period (figure 1).

In addition, 23 other ZIP code areas (primarily in urban locations of Fulton and DeKalb counties) had annual rates >10 cases per 100,000 persons. The remaining 78 ZIP code areas (70%) had annual rates of <10 cases per 100,000 persons; 17 of these ZIP code areas reported no cases of tuberculosis between 1993 and 1997.

Poisson regression modeling of ZIP code-specific data determined significant associations between higher tuberculosis incidence and higher percentage of minority-race residents (P < .001), higher percentage of male residents (P < .001), higher median age (P < .001), lower per capita income (P = .001), smaller household size (P < .001), higher percentage of foreign-born residents (P < .001), and lower percentage of high school graduates (P < .001). Significant associations were not found between tuberculosis incidence and percentage of residents unemployed (P = .825) or percentage of residents below the poverty level (P = .332).

### Discussion

The impact of tuberculosis on urban areas and inner-city institutions that serve a predominantly indigent population is

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**Table 3.** Drug resistance patterns at Grady Memorial Hospital, Atlanta, 1992–1997.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of new isolates tested</th>
<th>Isoniazid (%)</th>
<th>Rifampin (%)</th>
<th>Isoniazid and rifampin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td>242</td>
<td>14 (5.8)</td>
<td>4 (1.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>1993</td>
<td>193</td>
<td>6 (3.1)</td>
<td>3 (1.7)</td>
<td>6 (3.1)</td>
</tr>
<tr>
<td>1994</td>
<td>164</td>
<td>5 (3.7)</td>
<td>4 (2.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>1995</td>
<td>133</td>
<td>2 (1.5)</td>
<td>1 (0.8)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>1996</td>
<td>158</td>
<td>12 (7.6)</td>
<td>2 (1.3)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>1997</td>
<td>134</td>
<td>15 (11.2)</td>
<td>0 (0.0)</td>
<td>2 (1.5)</td>
</tr>
</tbody>
</table>

χ² test for trend: P = .03 for Isoniazid, P = .20 for Rifampin, P = .81

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**NOTE.** Isolates from 1991, first year of study period, were excluded because routine susceptibility testing was not performed on all Mycobacterium tuberculosis isolates until July 1991.
highlighted by our study. Tuberculosis in the United States is no longer an “equal opportunity” disease and has become focused in urban areas [17]. Our public inner-city hospital in Atlanta cared for an average of nearly 200 patients with tuberculosis per year over the 7-year study period, which was more cases than the number reported from nearly half of the states in the United States. In fact, if Grady Hospital were a state, it would have ranked 28th in reported number of cases of tuberculosis (1378) between 1991 and 1997, placing it well above Oregon and just under Hawaii [12, 14, 24].

In stark contrast to national trends in the United States, where the number of tuberculosis cases continued to decline at a rate of ~7% per year between 1994 and 1997 [25], the total number of tuberculosis cases at our urban hospital remained stable over these years. Our data demonstrate that tuberculosis remains at a high rate of endemicity in the inner city. The continuing impact of tuberculosis in the inner city is also reflected by the fact that in 1997, our public urban hospital cared for more patients with tuberculosis than it did in 1980 [15], during a time when the rate of tuberculosis in the United States was 40% higher [25].

The rate of HIV coinfection among patients with tuberculosis who were cared for at our hospital during the study was striking (~46% among those who had HIV serological testing performed). This rate is similar to the ~40% rate of HIV coinfection among patients with tuberculosis in a number of developing countries in Africa [3, 26, 27]. Tuberculosis-related mortality appears to be high among the HIV-coinfected inner-city residents cared for at our institution. Nearly 20% of these patients seen in 1994 died with active disease [28], which is similar to the 1-year mortality among HIV-coinfected individuals with tuberculosis reported from countries such as the Ivory Coast, Uganda, and Zaire [29].

During the study there was a significant decrease over time
in the proportion of patients with tuberculosis who were HIV-coinfected. This was most pronounced in 1997, when 25% of patients were HIV-seropositive and 60% were HIV-seronegative. The reasons for the decrease in HIV coinfection among patients with tuberculosis who are served by our hospital are unclear. However, it is unlikely that this trend is due to a decline in HIV infection in the patient population served by Grady Memorial Hospital, since, unlike other institutions, our hospital has not experienced a significant decline in the number of HIV-infected patients admitted in recent years [30]. The introduction of highly active antiretroviral therapy, including protease inhibitors, for HIV-infected patients is one possible explanation for this trend. The shift toward proportionally more HIV-negative and fewer HIV-positive TB cases in our patient population may also be due to a combination of increased infection control efforts designed to prevent nosocomial spread of tuberculosis [31, 32] and the expanded use of directly observed therapy; the percentage of patients with tuberculosis receiving directly observed therapy increased from 13% to 90% between 1991 and 1995 in the Atlanta/Fulton County area [33].

The low median CD4 cell count (86 cells/mL) among HIV-infected patients with tuberculosis at our institution suggests that many of those patients with tuberculosis and HIV coinfection have advanced HIV disease and probably were recently infected with *M. tuberculosis* prior to developing active disease. Molecular-typing data are consistent with this, indicating a high degree of IS6110 RFLP clustering (>50%) among banding patterns for *M. tuberculosis* isolates recovered from patients cared for at our hospital [34].

The large number of patients with tuberculosis cared for at our urban hospital reflects the high rates of tuberculosis in inner-city neighborhoods served by the hospital. Tuberculosis is not evenly distributed throughout the population, as demonstrated by assessment of case rates by ZIP code area in metropolitan Atlanta for 1993–1997. The overall yearly incidence rate of 14.1 cases per 100,000 persons per year in metropolitan Atlanta was higher than the average for the United States of 8.7 cases per 100,000 persons per year during 1993–1997 [25]. The mean rate in the city of Atlanta, which includes most of the inner-city neighborhoods in the metropolitan Atlanta area, was 54.6 cases per 100,000 persons per year during the study period (Georgia Department of Human Resources, Division of Public Health), more than 6× the national tuberculosis case rate.

Rates of tuberculosis in 2 inner-city ZIP code areas served by our institution were >120 cases per 100,000 population per year, similar to those reported for developing countries and >10× the national average in the United States [3, 25]. Of the 33 ZIP code areas where tuberculosis rates were higher than the national average, most were in either Fulton or DeKalb county, the 2 most urban counties that contain most of the city of Atlanta. This indicates the continued concentration of tuberculosis in the inner city, with little presence in the surrounding affluent metropolitan suburbs. These findings are similar to those reported nearly 25 years ago from a study of tuberculosis incidence in the Central Harlem district of New York City, which revealed an annual incidence of 131.8 cases per 100,000 persons, a rate 14× higher than that in several of New York City’s more affluent areas [35].

Multivariate modeling of several demographic and socioeconomic census variables revealed significant associations between higher rates of tuberculosis and higher median age and lower per capita income; higher percentages of minority-race, male, and foreign-born residents; and lower percentage of residents who graduated from high school. These data are consistent with the epidemiology of tuberculosis in the United States, where rates are traditionally higher among minorities in lower-income areas and among the foreign-born [9, 12, 16, 36, 37]. A recent study by Cantwell et al. [37] suggests that socioeconomic status accounts for a sizable proportion of the increased risk of tuberculosis in the United States previously associated with race/ethnicity.

In our study, a higher rate of tuberculosis was also significantly associated with smaller household size, a finding that appears contradictory to the fact that crowding is an important factor in increased incidence of tuberculosis [9, 37]. Reasons for this finding are unclear, but it may be partly explained by the facts that homeless populations and those with transient housing may not be well represented in the census data and that household size may not accurately represent crowding within a particular ZIP code area. Although a significant increase in the proportion of cases of tuberculosis among foreign-born patients was seen at our institution (and in the metropolitan Atlanta area) during the study period, the impact of imported tuberculosis is relatively minor in our area in comparison with that in the United States as a whole; tuberculosis in foreign-born patients now accounts for ~40% of all cases in the United States [25].

Despite a high degree of HIV coinfection, overall drug resistance among *M. tuberculosis* isolates recovered from patients at our institution was relatively low, especially in terms of the proportion of patients with multidrug-resistant tuberculosis. This is in contrast to cities such as New York and Miami, which had high rates of multidrug-resistant tuberculosis in the late 1980s and 1990s [38]. Single-drug resistance to rifampin was strongly associated with HIV coinfection; 14 of 16 patients with such resistance were coinfected with HIV, and nearly half of the 16 patients acquired the resistance after initial susceptibility.

Molecular typing studies demonstrated that most rifampin-resistant strains were unique and that isolates from patients with secondary resistance had persistence of the same RFLP pattern, suggesting the emergence of rifampin resistance among multiple strains rather than transmission of a single resistant clone. Our findings are consistent with those of recently published reports that associate rifampin-only resistance and HIV coinfection [39–41]. Two of these reports also suggested non-
adherence to treatment as a potential risk factor for patients infected with strains resistant only to rifampin [39, 40]. Although a case-control study would be required to investigate whether nonadherence was a risk factor for the emergence of rifampin resistance in our patients, it is suggested by the fact that all 7 patients with acquired single-drug resistance to rifampin had a history of nonadherence to therapy. Malabsorption of rifampin in HIV-infected patients with severe immunosuppression has been proposed as a possible mechanism leading to the development of rifampin resistance [39–43], and all of our patients whose M. tuberculosis strains developed rifampin resistance had advanced HIV disease, with CD4 cell counts <50 cells/mL.

Our data indicate that, despite declines in tuberculosis case rates in the United States since 1992, tuberculosis remains a serious problem in urban areas and greatly impacts inner-city institutions such as our public inner-city hospital. Over the final 4 years of the study (1994–1997), the number of patients with tuberculosis cared for at our institution remained fairly constant, despite a significant decrease in the proportion of patients with HIV coinfection. This is in sharp contrast to the continuing decrease in tuberculosis incidence in the United States [25].

Tuberculosis case rates in inner-city Atlanta and the proportion of patients with HIV coinfection are similar to those seen in developing countries. In addition, mortality rates among our patients with tuberculosis and HIV coinfection appear to be similar to those reported from developing countries [28, 29]. The large number of patients with tuberculosis cared for at our institution reflects the high incidence of disease in the community we serve. Our data mandate a concentration of efforts and resources on inner-city locations if the goal of tuberculosis elimination and control [4] is to be achieved in the United States.

References


