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Residential urban tree canopy is associated with decreased mortality during tuberculosis treatment in California

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Abstract

Trees can sequester air pollutants, and air pollution is associated with poor tuberculosis outcomes. However, the health impacts of urban trees on tuberculosis patients are unknown. To elucidate the effects of urban tree canopy on mortality during tuberculosis treatment, we evaluated patients diagnosed with active tuberculosis in California from 2000 through 2012, obtaining patient data from the California tuberculosis registry. Our primary outcome was all-cause mortality during tuberculosis treatment. We determined percent tree cover using 1m resolution color infrared orthoimagery categorized into land cover classes, then linked tree cover to four circular buffer zones of 50–300m radii around patient residential addresses. We used the Kaplan-Meier method to estimate survival probabilities and Cox regression models to determine mortality hazard ratios, adjusting for demographic, socioeconomic, and clinical covariates. Our cohort included 33,962 tuberculosis patients of median age 47, 59% male, 51% unemployed, and 4.9% HIV positive. Tuberculosis was microbiologically confirmed in 79%, and 1.17% were multi-drug resistant (MDR). Median tree cover was 7.9% (50m buffer). Patients were followed for 23,280 person-years with 2,370 deaths during tuberculosis treatment resulting in a crude mortality rate of 1,018 deaths per 10,000 person-years. Increasing tree cover quintiles were associated with decreasing mortality risk during tuberculosis treatment in all buffers, and the magnitude of association decreased incrementally with increasing buffer radius: In the 50m buffer, patients living in neighborhoods with the highest quintile tree cover experienced a 22% reduction in mortality (HR 0.78, 95%CI

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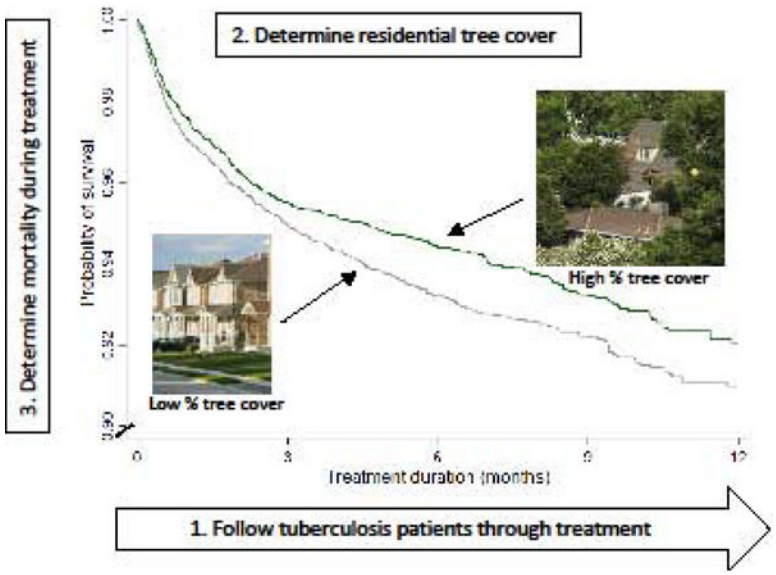
0.68 – 0.90) compared to those living in lowest quintile tree cover; whereas for 100, 200, and 300m buffers, a 21%, 13%, and 11% mortality risk reduction was evident. In conclusion urban tree canopy was associated with decreased mortality during tuberculosis treatment even after adjusting for multiple demographic, socioeconomic, and clinical factors, suggesting that trees might play a role in improving tuberculosis outcomes.

Graphical Abstract



Keywords

green space; urban tree canopy; air pollution; tuberculosis treatment outcomes; mortality; health impacts

1. Introduction

Tuberculosis (TB) is the leading cause of infection-related death worldwide with more than 1 million TB-related deaths per year (WHO 2018). Mortality is high despite the widespread availability of adequate treatment (Fielder et al. 2002; Pascopella et al. 2014), and evidence suggests that inhaled toxicants such as cigarette smoke (Jee et al. 2009; Lin et al. 2007) and ambient air pollution (Blount et al. 2017; Peng et al. 2016) may increase mortality during TB treatment. TB treatment requires several months of multidrug therapy and mortality is elevated in patients with impaired host immune responses to *Mycobacterium tuberculosis* (Mtb), the causative organism (Nahid et al. 2016). Air pollution may impair host immunity to Mtb at multiple levels: airway epithelial innate immune responses (Rivas-Santiago et al. 2015), monocyte/macrophage activation (Sarkar et al. 2012), and T-cell responses (Torres et al. 2019).

The urban tree canopy can act as an air pollution sink, decreasing ambient concentrations of particulate and gaseous pollutants (Nowak et al. 2006; Yli-Pelkonen et al. 2017). Large particles adhere to foliage and bark while submicron particles and gases can be respired into

plant tissue via leaf stomata, microscopic pores located in the epidermis of leaves and responsible for plant gas exchange (Ejidike and Onianwa 2015; Lovett 1994; Odabasi et al. 2016; Song et al. 2015). The potential health impacts of tree-mediated sequestration of air pollution have been mathematically modelled (Nowak et al. 2014), and a few cross-sectional and ecological studies have shown associations between trees and cardiovascular and pulmonary health (Donovan et al. 2013; Donovan et al. 2015). However, prospective cohort studies evaluating the health effects of urban tree canopy are limited (Franchini and Mannucci 2018).

Based on these observations that trees sequester air pollution and that air pollution, possibly through impairing host immunity, has detrimental effects on TB treatment outcomes, we hypothesized that high percent tree cover would be associated with decreased all-cause mortality, our primary outcome, during the treatment of patients with TB, and that the effects on mortality would be greatest for trees nearest to patients' residences. We also hypothesized that tree cover would be associated with a greater reduction in cause-specific mortality from diseases known to be exacerbated by air pollution—cardiovascular, pulmonary, and TB-related diseases—compared to death from other causes. Finally, we hypothesized that the decreased risk of all-cause mortality would be mediated through reduced mycobacterial burden of disease, as indicated by fewer TB patients with detectable acid-fast bacilli (AFB) in their sputa. AFB is a standard staining method for microscopically diagnosing TB and determining mycobacterial burden in the lungs. To test these hypotheses, we analyzed TB surveillance data from a large cohort of Californians with active TB. California experiences both high TB incidence and poor air quality: Nearly a quarter of all TB cases diagnosed in the U.S. occur in California (Stewart et al. 2018); of the 10 most ozone-polluted counties in the U.S., all 10 were in California; and of the 10 most particulate-polluted (annual $PM_{2.5}$) U.S. counties, 8 were in California (ALA 2019).

2. Materials and methods

2.1 Study cohort

We have described cohort selection and TB data collection elsewhere (Blount et al. 2017). California mandates that all TB cases are reported, from both private and public health care systems in the state. All patients with active TB reported to the California Department of Public Health between January 1, 2000 and December 31, 2012 were eligible for inclusion (Figure 1). Active TB cases were determined using microbiological diagnostic criteria (positive culture or nucleic acid amplification testing for *Mycobacterium tuberculosis*) and clinical criteria (patient symptoms, physical exam, radiographic findings, and an appropriate response to TB treatment). Exclusion criteria were: inability to determine the longitudes and latitudes of residential addresses to street-level resolution, residence outside the urban tree canopy map coverage area, death or migration out of California before treatment initiation, or unavailable treatment dates. Health professionals at 61 local TB control programs across California collected demographic, socioeconomic, and clinical data during routine patient treatment and entered these data into a CDC-developed and validated data collection form (the Report of a Verified Case of TB (RVCT)). We obtained our primary outcome data, all-cause mortality during TB treatment, as well as covariate data, from the RVCT.

2.2 Exposure assessment

The California Department of Forestry and Fire Protection provided land-use data. Source data included aerial digital 1m resolution color infrared orthoimagery performed during the spring and summer of 2012 by the U.S. Department of Agriculture National Agriculture Imagery Program. Seven land-use categories (trees, shrubs, herbaceous, water, impervious, bare, and shadows) were assigned using a hybrid machine classification approach which combined both Geographic Object-Based Image Analysis (GEOBIA) and Classification and Regression Trees (CART) methods. Horizontal accuracy was confirmed using human visual assessments of a subset of points to verify machine classification, with 94.8% of points falling within 6 meters of true ground. Land-use areas classified as trees were extracted and clipped to California urban areas, thus creating a dichotomous tree cover variable for each 1m of urban surface area in California. We included all areas in California (Supplemental Excel File) defined as urban clusters (population: 2,500 to 50,000) and urbanized areas (population ≥ 50,000) according to the 2010 U.S. Census (U.S. Census Bureau 2012).

We obtained patient residential addresses at the time of TB diagnosis and matched addresses to geographic coordinates using Tele Atlas®, Navteq®, and Tiger® reference datasets as previously described (Blount et al. 2017). We then linked urban tree canopy rasters to circular buffers of 50, 100, 200, and 300m radii around patient residential addresses using ArcGIS 10.4 (Environmental Systems Research Institute, Redlands, California, USA) (Figures 2 and 3). We calculated percent tree cover by adding the number of 1m tree pixels in each buffer, dividing this by the buffer's total surface area, and multiplying by 100 (Figure 3). We calculated traffic density (sum of length-adjusted road segment traffic counts in each buffer per hour (vh·km/h) using California Department of Transportation (Caltrans) data and California Environmental Health Tracking Program Traffic Spatial Linkage Service software (CDPH, Richmond, California, USA) as previously described (Blount et al. 2017). Traffic density was available for 100, 200, and 300m buffers but not for the 50m buffer. We obtained annual median household income estimates at the block group level from the 2006–2010 American Community Survey (ACS) (U.S. Census Bureau 2016). The ACS includes income data from all individuals ≥ 15 residing in the household, including nonfamily members and marginally housed individuals living in not traditional living structures such as RVs and tents. However, the ACS does not include those living in group quarters such as community shelters, in their determination of median household income.

In secondary analyses to explore linkages between tree cover and specific causes of death, deaths from our cohort were matched with the California Death Registry, accepting only perfect matches for name, date of birth, and residential address. Deaths were then grouped into three categories using ICD-10 coding: TB-related; cardiovascular and pulmonary deaths (including lung cancer and excluding TB-related deaths); and "other deaths" not included in the first two categories.

2.3 Ethics approval

This study was approved by the institutional review boards at the University of California San Francisco, the University of Iowa, and the California Department of Public Health.

2.4 Statistical analyses

Student's t-tests and chi-squared tests were used to describe baseline characteristics. TB patient follow-up time started on the date of treatment initiation and ended on the date of death or was right-censored on the date of: adequate completion of TB therapy, migration out of state, lost to follow-up, refusal to continue treatment, drug toxicity, or the end of the study—whichever occurred first. To test our primary hypothesis that percent tree cover is associated with increased all-cause mortality during TB treatment, we fit multivariable Cox proportional hazards regression models with time to all-cause mortality as our predetermined primary outcome and percent tree cover in 50, 100, 200, and 300m buffer zones around residential addresses as our primary environmental predictor. Percent tree cover was skewed to the right and to better adhere to hazard function assumptions we categorized tree cover into quintiles of equal number participants. The first quintile represented the lowest range of tree cover (from 0 – 3.00% in the 50m buffer) and served as the referent quintile in Cox models, whereas the fifth quintile represented the highest residential tree cover (15.9 – 99.9% in the 50m buffer) also with the widest spread. We tested for linear trends across quintiles using Wald tests with *p*-values reported as *p*-trends. We selected demographic, socioeconomic, and clinical variables as potential confounders *a priori* based the biological plausibility of such associations in directed acyclic graph (DAG) modelling guided by literature review: Age, sex, race, ethnicity, non-U.S.-birth, recent immigration (within one year prior to diagnosis), household income, employment status, substance abuse (excessive alcohol and/or recreational drugs within one year prior to diagnosis), homelessness, and HIV infection were included as covariates. All covariates were fixed in time obviating the need for time-dependent covariates in Cox analyses. We used the Kaplan-Meier method to construct survival curves by tree cover quintile and to determine the unadjusted probabilities of survival (with associated 95% confidence intervals) for 6- and 12-month treatment durations. We tested for effect modification by fitting a multivariable Cox model with each interaction term between dichotomous tree exposure and effect modifier of interest: age, sex, race/ethnicity, traffic density, household income, climate zone (U.S. Department of Energy 2015), and season (spring, summer, fall, or winter) in which the patient was diagnosed.

To test our tertiary hypothesis that percent tree cover is associated with increased cardiovascular and pulmonary mortality, increased TB-related mortality, but not an increase in other causes of death, we fit multivariable Cox models with time to specific cause of death as the outcome and tree cover in quintiles as the exposure.

To test our secondary hypothesis that the effects of trees on mortality are mediated through mycobacterial burden (AFB sputum smear positivity), we first fit multivariable logistic regression models with AFB sputum smear positivity as the dichotomous outcome and tree cover quintiles in each buffer as predictors. Secondly, we fit a multivariable Cox model with time to all-cause mortality as outcome and AFB smear positivity as predictor. We adjusted both models for the same covariates as in our primary Cox models mentioned above. Our criteria for classifying AFB smear positivity as an intermediate variable were: 1) Tree cover is associated with decreased AFB smear positivity ($p<0.05$); and 2) AFB smear positivity is

associated with increased all-cause mortality ($p<0.05$). Statistical analyses were performed using Stata/SE 15.1 (StataCorp).

3. Results

3.1 Study population characteristics

We included 33,962 participants out of 36,511 total patients (93%) with active TB reported in California during 2000 – 2012 (Figure 1). We excluded the remaining 2,549 (7%) of TB patients for the following reasons: incomplete address such that accurate street-level geocoding was not possible (n=736, 2.0%), residence outside the tree-map area (n=686, 1.9%), death (n=739, 2.0%) or migration out of California (n=64, 0.18%) before treatment initiation, or incomplete treatment dates (324, 0.89%). Median age at the time of TB diagnosis was 46.9 years; 59.4% were male; most participants were either Asian (44.4%) or Hispanic (37.6%); and 76.9% had emigrated from another country (Table 1). More than half of patients resided in Southern California (56.5%) and nearly a quarter of patients resided in the San Francisco Bay Area (24.0%) at the time of diagnosis. Unemployment was common (51.0%), 5.62% were homeless, and 12.3% abused drugs or alcohol within one year prior to diagnosis. Most TB cases were microbiologically confirmed (n=26,732, 78.7%), 80% of patients were diagnosed with pulmonary TB, and 396 (1.17%) of cases were multi-drug resistant (MDR).

In sensitivity analyses we compared those included in the study (n=33,962) with those excluded (n=2,549) (Table S1). Those excluded were more likely to be older, male, Hispanic or white, living in the North Coast/Mountain or Central Valley regions, living in a less densely populated area, homeless, abusing drugs/alcohol, or HIV infected; and less likely to be Asian, non-U.S.-born, a recent immigrant, living in the San Francisco Bay Area, or receiving directly observed therapy for all doses.

A total of 2,370 out of 33,962 study participants died during TB treatment (7.0%). Total follow-up time was 23,280 person-years and the crude mortality rate was 1,018 deaths per 10,000 person-years. A specific cause of death was determined for 1,569 TB patients: cardiovascular and pulmonary (n=522, 33%), TB-related (n=516, 33%), and other causes (n=531, 34%).

3.2 Exposure characteristics

We constructed a 1 m^2 resolution urban tree canopy map of California composed of 59 urbanized areas and 151 urban clusters covering a total area of 1.22×10^{10} m^2 (Supplemental Excel File). Tree cover ranged from 0 to 99.9% with a mean percent tree cover of 10.3%, 10.4%, 10.5%, and 10.5%; and a median percent tree cover of 7.93%, 8.36%, 8.57%, and 8.66% in the 50m, 100m, 200m, and 300m buffers, reflecting a right-skewed distribution (Table 2).

3.3 Associations between urban tree canopy and mortality

Higher percentages of tree cover were associated with decreased all-cause mortality during the TB treatment of Californian patients in multivariable Cox models adjusted for

demographic, socioeconomic, and clinical potential confounders (Table 3). As tree cover increased, mortality risk decreased, with statistically significant *p*-trends in all buffers. Considering the 50m residential buffer, TB patients living in neighborhoods with the most tree cover (5th quintile) experienced a 22% decreased risk of mortality during TB treatment (HR 0.78; 95%CI 0.68, 0.90) compared to patients living in neighborhoods with the lowest quintile of tree cover; whereas those living in 4th, 3rd, and 2nd quintiles of tree cover experienced a 14%, 12%, and 7% decreased risk of mortality compared to those living in neighborhoods with the lowest tree cover quintile. Additionally, both the magnitude of association and level of significance decreased as buffer radius increased. For instance, patients living in the 5th quintile vs. 1st quintile of tree cover in the 50m buffer experienced a 22% reduction in mortality risk: whereas for 100, 200, and 300m buffers, a 21%, 13%, and 11% mortality risk reduction was evident (Figure 4).

Using Kaplan-Meier estimates, we determined the probability of surviving TB treatment by tree cover quintile. Patients living in neighborhoods with the highest quintile tree cover were more likely to survive TB treatment compared to those living in neighborhoods with the lowest quintile tree cover, findings that were consistent throughout treatment (Figure 5).

Specific cause of death was ascertained by death registry for only 66.2% of total patients who died during TB treatment. In this subgroup analysis, high percent tree cover in the 5th quintile was associated (though not statistically significant) with decreased cardiovascular and pulmonary mortality (HR 0.75; 95%CI 0.55, 1.01) and decreased TB-related mortality (HR 0.73; 95%CI 0.54, 0.99), whereas no association was evident between tree cover and other causes of mortality (Figure 6). A statistically significant dose response, with increasing tree cover associated with decreasing mortality, was found for cardiovascular and pulmonary mortality (*p*-trend 0.03) but not for TB-related mortality. This intriguing preliminary finding requires a more comprehensive investigation of the effects of tree canopy on cause-specific mortality.

Of potential confounders included in final models, age, race and ethnicity, non-U.S.-birth, and recent immigration augmented the effect of tree cover on decreased mortality risk; whereas sex, employment status, substance abuse, and HIV infection attenuated the effect in Cox models (Table S2). Household income and homelessness did not significantly augment or attenuate the effect. Collectively, addition of these potential confounders to the model did not alter the direction or statistical significance of the association between tree cover and decreased mortality.

Our results suggest that the effects of tree cover on decreased all-cause mortality were mediated through mycobacterial burden of disease. Increasing tree cover quintiles were associated with decreasing odds of AFB smear positivity, with statistically significant *p*-trends in all buffers tested (Table 4); and AFB smear positivity was associated with increased mortality risk (HR 1.42; 95%CI 1.30, 1.56).

Among interactions tested, high percent tree cover compared to low percent tree cover appeared to be more protective in younger participants, those with drug-susceptible TB, and those who did not exclusively receive directly observed therapy, although *p*-interactions

were not statistically significant in all buffers (Table S3). Race exhibited variable effect modification, while significant interactions were not seen for other variables tested. Traffic density did not significantly augment or attenuate mortality hazards when considered as a potential confounder (Table S4) and was not a statistically significant effect modifier (Table S5).

4. Discussion

In a large cohort of 33,962 TB patients with 23,280 person-years of follow-up, we found that urban tree cover was associated with decreased mortality during TB treatment in all buffers evaluated, with the greatest effect for trees closest to the patient's residence. The beneficial effects of trees appeared to be mediated through decreased mycobacterial burden measured by AFB sputum smear positivity.

The association between tree canopy and decreased mortality is strengthened by evidence of a dose-response: Increasing percent tree cover and tree proximity were associated with incremental decreases in mortality risk. Within the smallest buffer around patients' residences, the dose-response was most significant, with incremental decreases in mortality hazards with each increasing quintile of tree cover. As buffer size increased representing wider exposure areas around residences, the dose-response became less statistically significant and the magnitude of association decreased. Dose-response relationships between tree canopy and improvements in health outcomes such as reductions in mortality and emotional stress have been observed in other studies (Donovan et al. 2013; Jiang et al. 2014b; Mitchell and Popham 2008).

The urban tree canopy could improve human health through a number of postulated mechanisms: air pollution sequestration (Ejidike and Onianwa 2015; Lovett 1994; Odabasi et al. 2016; Song et al. 2015), emotional stress reduction (Jiang et al. 2014a; Ward Thompson et al. 2012), noise reduction (Fan et al. 2010; Fang and Ling 2003), increased physical activity (Almanza et al. 2012; Giles-Corti et al. 2005), resilience to adverse life events (van den Berg et al. 2010), decreased crime, and increased socializing (Branas et al. 2018). We hypothesized that if the health benefits of tree canopy were operative through air pollution sequestration, trees would be associated with decreased risk for specific causes of deaths thought to be increased by air pollution—cardiovascular, pulmonary (Dockery et al. 1993), and TB-related (Blount et al. 2017)—but not for other causes of death. Prior studies have found associations between tree canopy and cause-specific mortality. For instance, Donovan et al., found that the Emerald Ash Borer destruction of tree canopy was associated with elevated risk for lower-respiratory and cardiovascular mortality (Donovan et al. 2013; Donovan et al. 2016). Our findings also support this hypothesis, yet firm conclusions cannot be drawn from our observations because 1) specific cause of death was only known for a subset of our cohort and 2) the accuracy of death registry data is limited (Beavers et al. 2018). To further test the validity of the sequestration mechanistic pathway, prospective cohort studies are needed to investigate the effects of tree cover and pollutant sequestration into plant tissue on neighborhood ambient air pollutant concentrations and health outcomes.

We further hypothesized that the effects of tree cover on reduced mortality risk would be mediated through decreased mycobacterial burden. We found that 1) tree cover was associated with decreased AFB sputum smear positivity and 2) AFB sputum smear positivity was associated with increased mortality. These findings support a possible mechanism in which trees lessen the mycobacterial burden of disease to improve TB treatment outcomes, perhaps through the sequestration of immunosuppressing air pollutants as seen in prior studies (Lovett 1994; Song et al. 2015),.

We evaluated potential confounding from socioeconomic and traffic density variables. Although a modest positive correlation between tree cover and block group household income was evident, inclusion of this potential confounder, as well as other indicators of socioeconomic status—unemployment and homelessness—did not significantly attenuate our findings, demonstrating that the effect of tree cover on decreased mortality was independent of these included socioeconomic variables. However, data on individual-level household income and education were not available, and residual confounding through socioeconomic status remains a possibility. We further investigated if percent tree cover was simply an indicator for less traffic in neighborhoods. Although tree canopy was moderately inversely correlated with traffic density, inclusion of traffic density in Cox models did not significantly alter mortality hazards.

The study has several strengths: a large sample size of nearly 34,000 participants with close follow-up (often daily with directly observed therapy) throughout the course of treatment over several months, a definable primary outcome (all-cause mortality), enough outcomes to adequately test the main hypothesis, high resolution of tree canopy data, and ample exposure contrast between high and low percent tree cover.

Several limitations should be considered. This was an observational study and intrinsic to this design there is potential for unmeasured confounding. Tree cover was determined at the end of the cohort period in 2012 rather than reassessing tree cover throughout the study. This likely introduced random exposure measurement inaccuracies expected to bias results toward the null. Urban tree canopy has been found to be relatively temporally stable, with small net losses seen (−1.7 to −3.3% over 5 years depending on the neighborhood studied) (Chuang et al. 2017). Those excluded were significantly different from participants in several baseline characteristics thus introducing the potential for selection bias, though the number excluded remained small. The role of health seeking behavior as a potential confounder in the relationship between tree canopy and treatment mortality was not measured or analyzed. Specific cause of death was determined through death registry, with exact matches in only two-thirds of total deaths, also introducing possible selection bias into those analyses. Rural residences were not included in urban tree mapping, such that the study cannot be generalized to TB patients residing in rural areas. Tree cover was only determined for residential and not school and work addresses, limiting our ability to fully characterize cohort tree exposures. However, it has been shown that North Americans spend the majority of their time at their home address, such that residential tree canopy is a reasonable surrogate for total tree canopy exposure (Klepeis et al. 2001; Leech et al. 2002; Leech and Smith-Doiron 2006). Finally, due to the large number of tree species located

throughout California, we were unable to analyze a differential health effect for specific tree species.

5. Conclusions

Tuberculosis patients living in neighborhoods with high percent tree cover were at decreased risk for all-cause mortality during treatment. This association remained after controlling for key factors that may impact risk of mortality, including demographic, socioeconomic, and clinical factors. Our findings suggest that urban trees may provide health benefits for TB patients undergoing TB treatment. However, conclusions should be drawn with caution given the possible role of unmeasured socioeconomic confounders in this observational study, and these findings should be confirmed with additional prospective and interventional studies quantifying air pollutant sequestration properties of tree canopy in relation to health benefits.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosures

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Highlights

- Tuberculosis is the leading cause of death from infection worldwide
- It is unknown if trees could mitigate the harmful effects of air pollution on tuberculosis patients
- Using Kaplan-Meier and Cox survival analyses, we determined the effects of trees on tuberculosis patient mortality
- Those living in neighborhoods with high percent tree cover were less likely to die during treatment
- Trees may provide health benefits to patients undergoing tuberculosis treatment

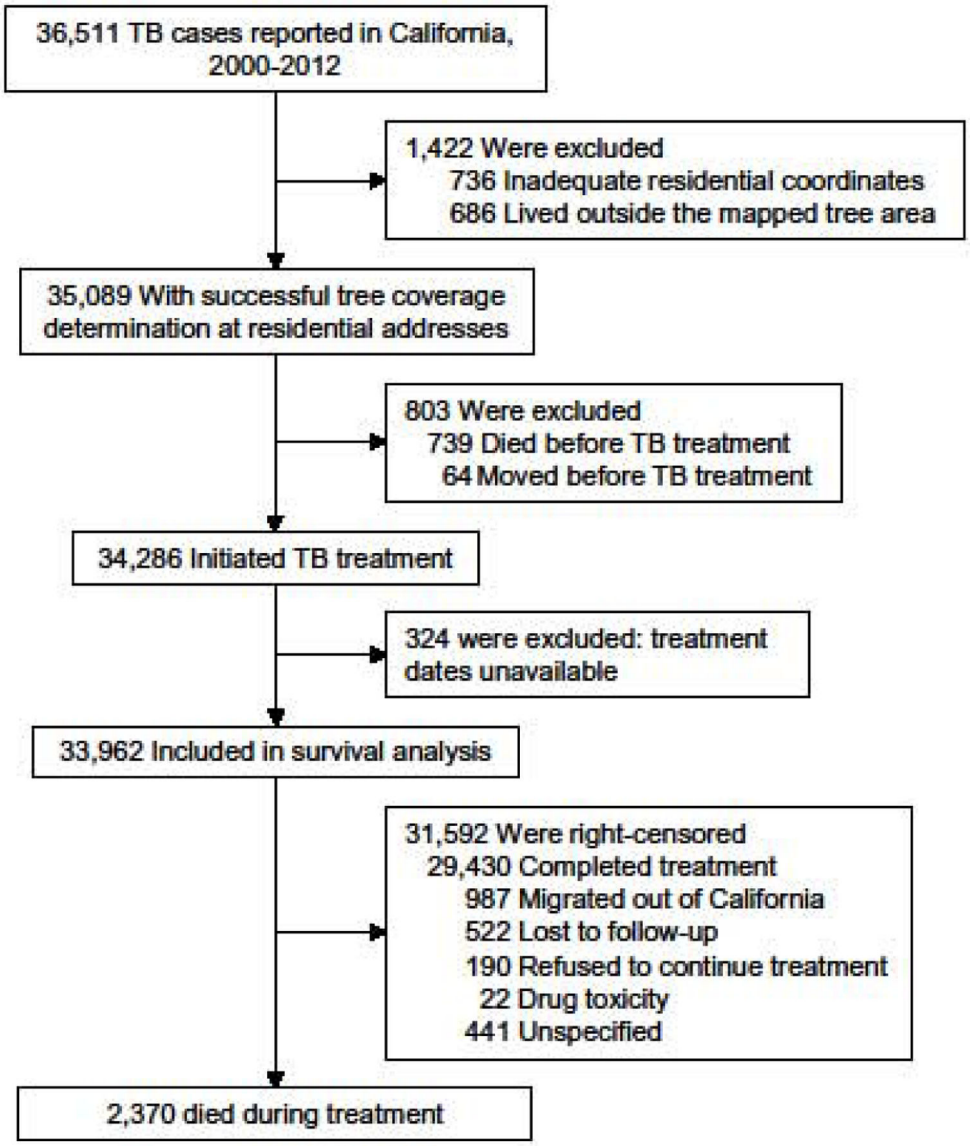

Figure 1.
TB patient enrollment flow chart.

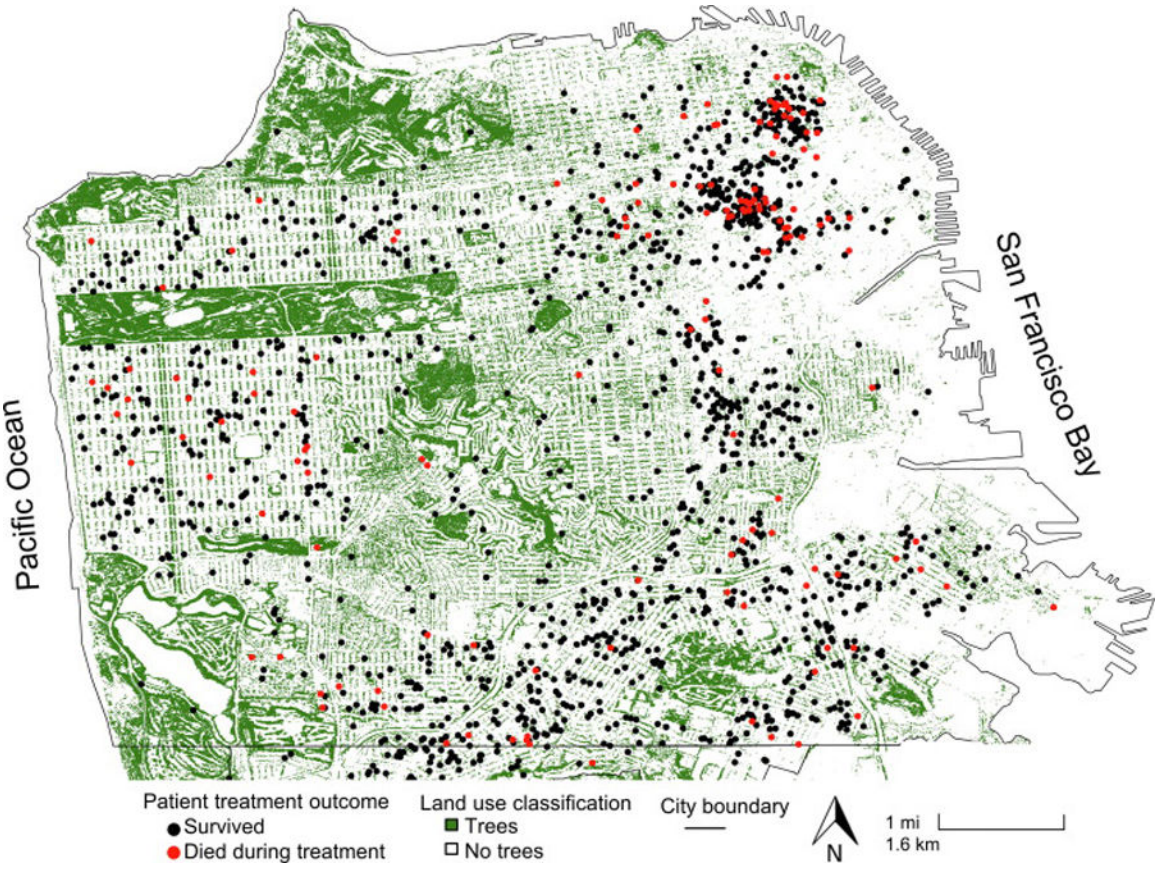

Figure 2.

TB patient residences and treatment outcomes in San Francisco, years 2000–2012. Points were randomly offset (jiggered) to protect patient identity. Data from the entire State of California could not be shown in this figure due to size and resolution limitations.

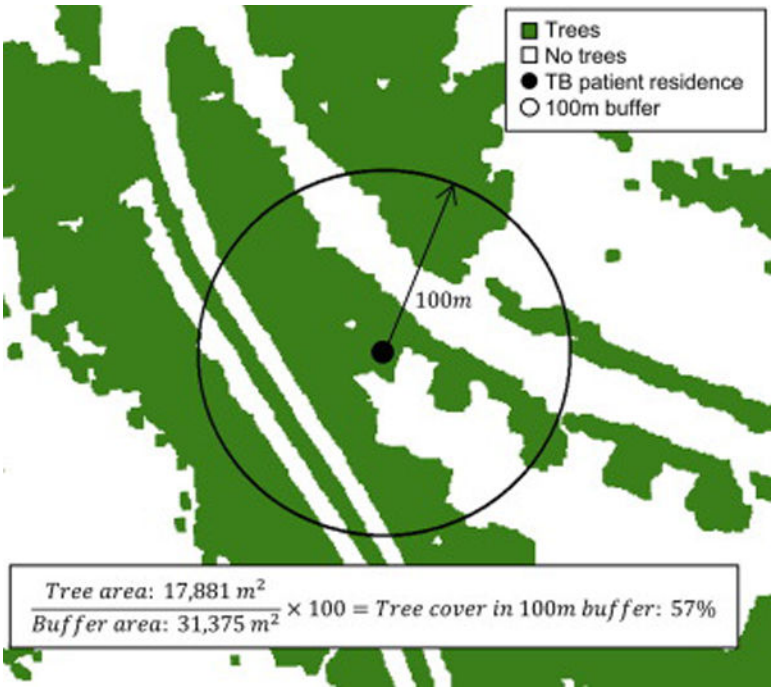

Figure 3.
Sample calculation: percent tree cover within a 100m radius buffer around a patient's residence.

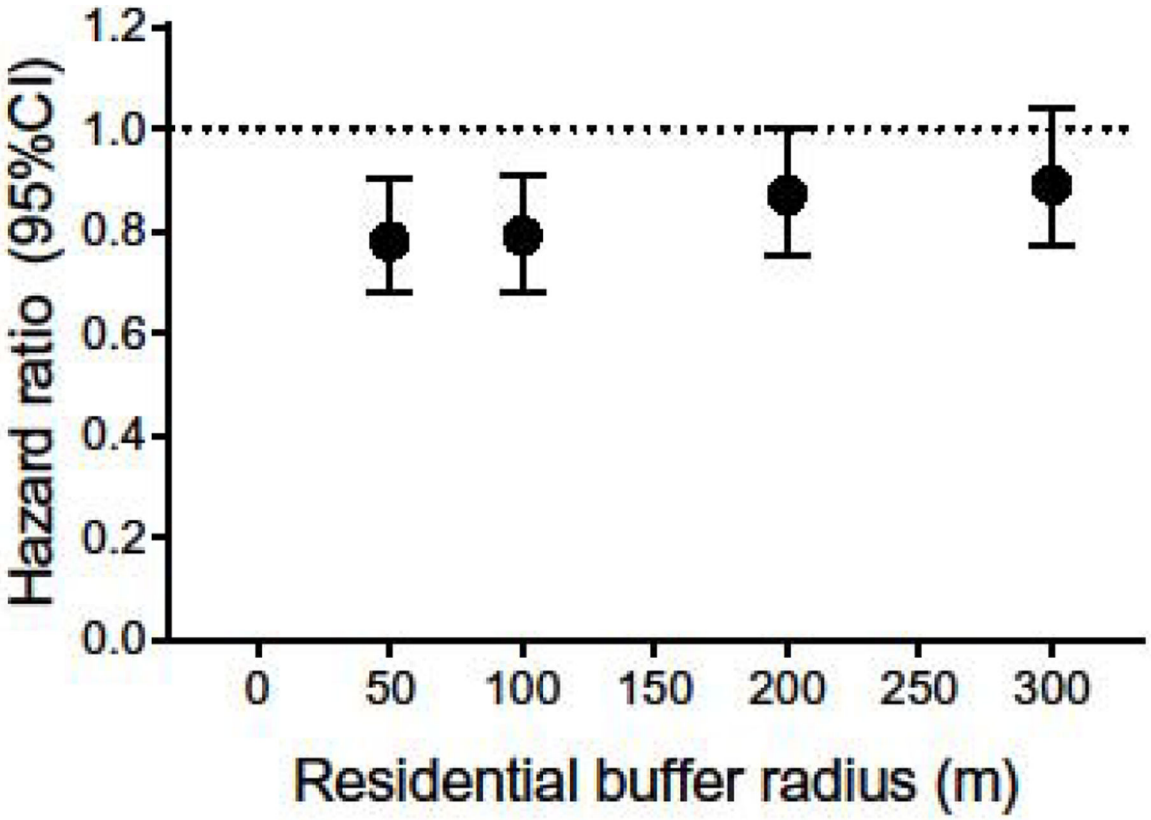

Figure 4.

Adjusted cumulative hazard of all-cause mortality for 5th quintile compared to 1st quintile tree cover by buffer. Buffers are expressed in radius (m) around each patient's residence. 5th quintile represents the most heavily forested quintile and 1st quintile represents the least forested referent quintile. Hazard ratios were determined using Cox proportional hazards models, adjusting for age, sex, race, ethnicity, non-U.S.-birth, recent immigration, household income, employment status, substance abuse, homelessness, and HIV infection.

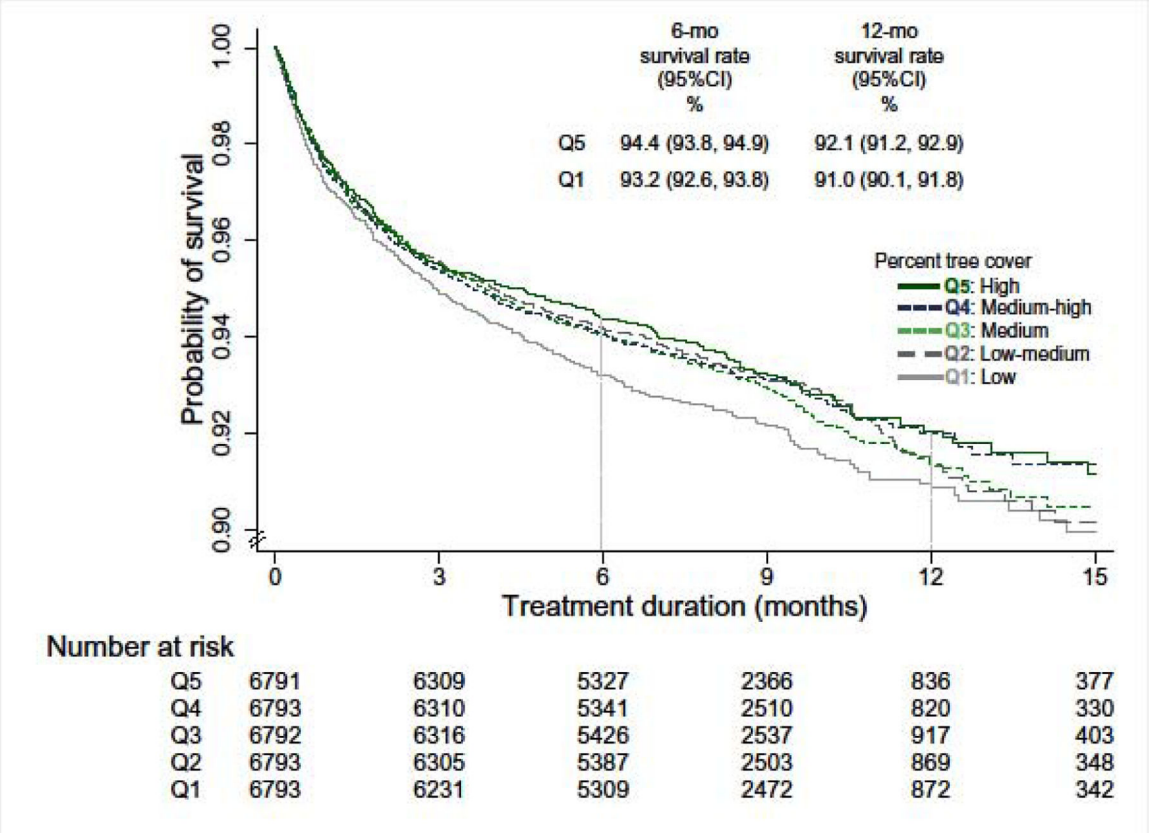

Figure 5.

Kaplan-Meier estimates of survival by tree cover quintile in the 50m buffer around patient residences. Q5–1 represent 5th through 1st quintiles of tree cover, with 5th quintile representing the most heavily forested quintile and 1st quintile representing the least forested.

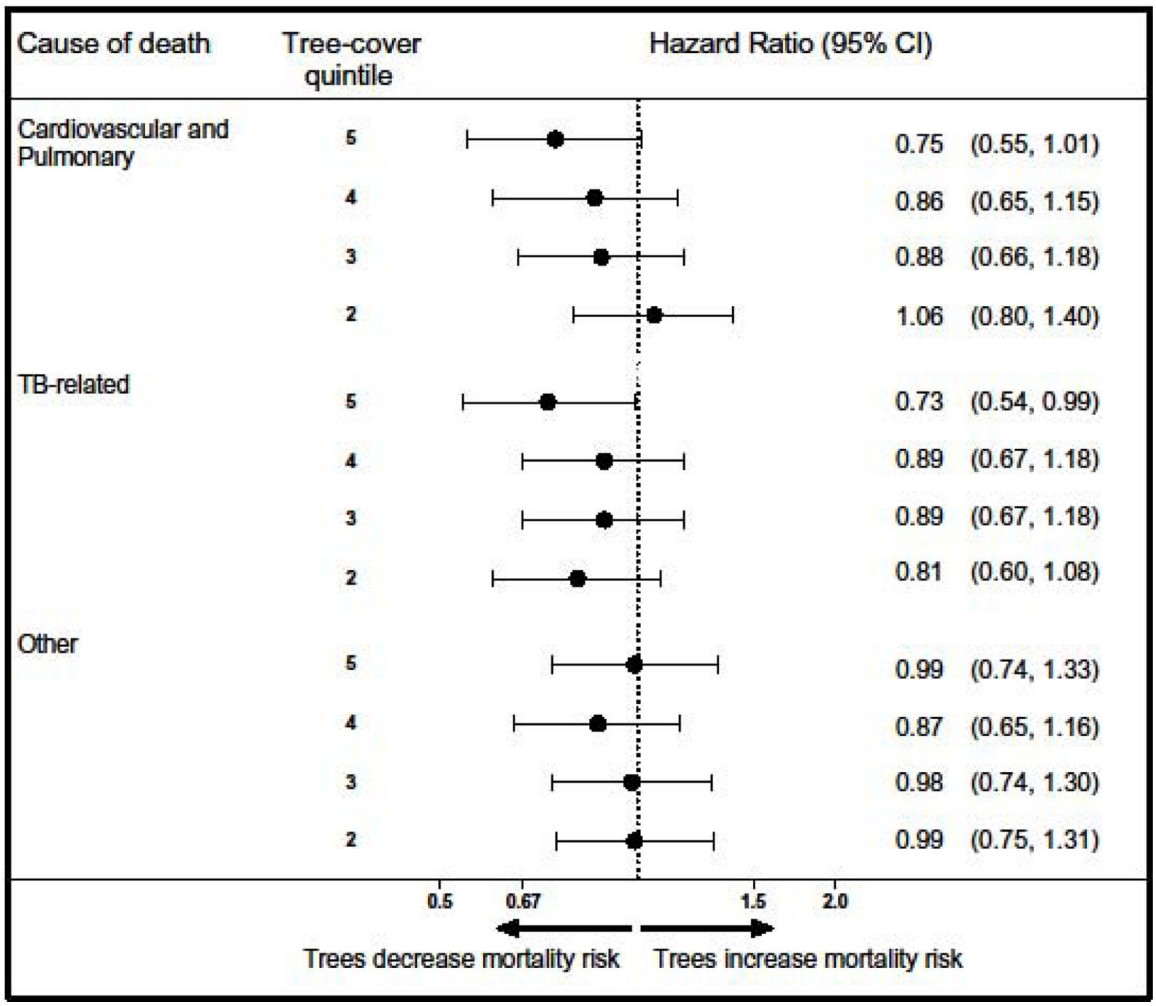

Figure 6.

Adjusted cumulative hazard of cause-specific mortality by tree cover quintiles, 50m buffer around patient residences, with 5th quintile representing the most heavily forested quintile and 1st quintile representing the least forested referent quintile (not shown). Hazard ratios were determined using Cox proportional hazards models, adjusting for age, sex, race, ethnicity, non-U.S.-birth, recent immigration, household income, employment status, substance abuse, homelessness, and HIV infection.

Table 1.

Patient characteristics by percent tree cover, 100m buffer, n=33,962

Characteristic	% Tree cover[a]		
	Total	Low	High[c]
n (%)[b]	33,962 (100)	16,986 (50.0)	16,976 (50.0)
Age at diagnosis, median (IQR), y	46.9 (30.7–63.5)	45.9 (30.4–61.5)	48.0 (30.9–65.6)
Male sex	20,163 (59.4)	10,450 (61.5)	9,713 (59.2)
Race and ethnicity			
Asian	15,086 (44.4)	6,777 (39.9)	8,309 (49.0)
Hispanic	12,777 (37.6)	7,245 (42.7)	5,532 (32.6)
White[d]	3,091 (9.10)	1,234 (7.26)	1,857 (10.9)
Black[d]	2,658 (7.83)	1,590 (9.36)	1,068 (6.29)
Other	350 (1.03)	140 (0.82)	210 (1.24)
Non-U.S.-born	26,099 (76.9)	12,833 (75.6)	13,266 (78.2)
Recent immigrant	8,340 (24.6)	4,027 (23.7)	4,313 (25.4)
Region			
Southern California	19,193 (56.5)	11,419 (67.2)	7,774 (45.8)
Central Valley	4,600 (13.5)	1,271 (7.48)	3,329 (19.6)
North Coast and Mountain	572 (1.68)	78 (0.46)	494 (2.91)
San Francisco Bay Area	8,138 (24.0)	3,244 (19.1)	4,894 (28.8)
Central Coast	1,459 (4.30)	974 (5.73)	485 (2.86)
Population density, mean ± SD, persons/km^2 [e]	5,570 (6,130)	6,790 (7,688)	4,349 (3,614)
Annual household income, median (IQR), USD[e]	50,682 (35,046–71,759)	43,893 (31,429–62,417)	57,841 (40,811–80,417)
Unemployed	17,328 (51.0)	8,884 (52.3)	8,444 (49.7)
Homeless	1,908 (5.62)	1,347 (7.93)	561 (3.30)
Substance abuse[f]	4,192 (12.3)	2,590 (15.3)	1,602 (9.44)
HIV-infected	1,657 (4.88)	1,029 (6.06)	628 (3.70)
TB characteristic			
Microbiologically confirmed	26,732 (78.7)	13,474 (79.3)	13.258 (78.1)
Pulmonary	27,016 (80.0)	13,712 (80.7)	13,304 (78.4)
Extrapulmonary	10,009 (29.5)	4,864 (28.6)	5,145 (30.3)
Cavitary	6,553 (19.3)	3,395 (20.0)	3,158 (18.6)
Both pulmonary & extrapulmonary	3,067 (9.03)	1,591 (9.37)	1,476 (8.69)
Miliary	585 (1.72)	294 (1.73)	291 (1.71)
Multi-drug resistant (MDR)	396 (1.17)	159 (0.94)	237 (1.40)
DOT for all doses	19,513 (57.5)	10,683 (62.9)	8,830 (52.0)
Treatment duration,[g] median (IQR), days	245 (189–301)	250 (190–303)	240 (188–300)

Abbreviations: USD, US Dollars; MDR, Multi-drug resistant TB (resistant to both isoniazid and rifampicin); DOT, directly observed therapy

Missing data are listed below in the following format—characteristic (number of missing observations for the "Low" tree cover group, number of missing observations for the "High" tree cover group): Age (1, 0); Male sex (1, 0); Non-U.S.-born (37, 63); Recent immigration (37, 63); Population density (4, 0); Annual household income (64, 23); Unemployed (430, 595); Homeless (105, 62); Substance abuse (212, 221); Microbiologically confirmed (5, 10); Cavitary (11, 21); DOT (101, 94)

[a] Median cut-off point for percent tree cover was used: Low <8.36%; High ≥ 8.36%

[b] Column values represent "n (%)" unless otherwise indicated.

[c] Differences in characteristic by tree cover are all statistically significant ($p<0.05$) except for "miliary TB".

[d] Non-Hispanic white, non-Hispanic black

[e] Obtained from American Community Survey 2006–2010 census block group data

[f] Excess alcohol and/or recreational drug use (oral, inhaled, or injected) within one year prior to TB diagnosis

[g] Treatment duration among those who completed treatment

Table 2.

Tree distribution by tree cover quintile and buffer around patient residences

Tree cover quintile	Buffer; Median (range) tree cover[a]				
	N	50m	100m	200m	300m
Q1	6,793	1.39 (0–3.00)	2.62 (0–4.10)	3.31 (0–4.67)	3.54 (0–4.89)
Q2	6,793	4.60 (3.00–6.24)	5.48 (4.10–6.86)	5.90 (4.67–7.19)	6.09 (4.89–7.31)
Q3	6,792	7.93 (6.24–9.93)	8.36 (6.86–10.1)	8.57 (7.19–10.2)	8.66 (7.31–10.2)
Q4	6,793	12.5 (9.93–15.9)	12.2 (10.1–15.2)	12.1 (10.2–14.9)	12.0 (10.2–14.7)
Q5	6,791	21.9 (15.9–99.9)	20.5 (15.2–99.1)	19.8 (14.9–95.5)	19.4 (14.7–95.0)
All Quintiles	33,962	7.93 (0–99.9)	8.36 (0–99.1)	8.57 (0–95.5)	8.66 (0–95)

Abbreviations: Q1 – Q5, Quintiles of percent tree cover, from low to high

[a]Tree cover was calculated as the buffer area covered by the tree canopy divided by the total buffer area around a patient's residence and multiplied by 100; all reported values are percentages (%).

Table 3.

Adjusted mortality hazard ratios[a] (95%CI) by tree cover quintiles and residential buffers

Tree cover[b] quintile	Buffer radius around patients' residences			
	50m	100m	200m	300m
Q1	1.00	1.00	1.00	1.00
Q2	0.93 (0.82,1.06)	0.96 (0.84,1.09)	1.03 (0.90, 1.18)	1.08 (0.95, 1.24)
Q3	0.88 (0.77, 1.00)	0.87 (0.76, 1.00)	0.98 (0.85, 1.12)	1.01 (0.88, 1.16)
Q4	0.86 (0.75, 0.98)	0.92 (0.81, 1.06)	0.92 (0.80, 1.06)	0.93 (0.81, 1.07)
Q5	0.78 (0.68, 0.90)	0.79 (0.68, 0.91)	0.87 (0.75, 1.00)	0.89 (0.77, 1.04)
P-trend	0.0003	0.002	0.02	0.03

Abbreviations: Q1 – Q5, Quintiles of percent tree cover, from low to high

[a]We determined hazard ratios by fitting Cox proportion hazards models with events defined as all-cause mortality during TB treatment; time defined by treatment initiation to termination; and adjusting for age, sex, race, ethnicity, non-U.S.-birth, recent immigration, household income, employment status, substance abuse, homelessness, and HIV infection.

[b]Tree cover was calculated as the buffer area covered by the tree canopy divided by the total buffer area around a patient's residence and multiplied by 100.

Table 4.

Association of tree cover[a] with AFB sputum smear positivity by residential buffer, OR (95%CI).[b]

Tree cover quintile[a]	Buffer radius around patients' residences			
	50m	100m	200m	300m
Q1	1.00	1.00	1.00	1.00
Q2	1.04 (0.96, 1.12)	1.00 (0.93, 1.08)	0.93 (0.86, 1.00)	0.96 (0.89, 1.03)
Q3	1.00 (0.93, 1.08)	0.96 (0.89, 1.04)	0.99 (0.92, 1.07)	0.97 (0.90, 1.05)
Q4	0.98 (0.91, 1.06)	0.93 (0.86, 1.01)	0.90 (0.83, 0.97)	0.92 (0.85, 0.99)
Q5	0.93 (0.86, 1.01)	0.89 (0.82, 0.96)	0.86 (0.79, 0.93)	0.88 (0.81, 0.96)
P-trend	0.02	0.001	0.0002	0.002

Abbreviations: AFB, Acid Fast Bacilli, a stain used to microscopically detect *Mycobacterium tuberculosis;* Q1 – Q5, Quintiles of percent tree cover, from low to high

[a]Tree cover is calculated as the buffer area covered by the tree canopy divided by the total buffer area around a patient's residence and multiplied by 100.

[b]We determined odds ratios by fitting logistic regression models with outcome defined as a positive result for AFB sputum smear at the time of diagnosis and with predictor defined as percent tree cover categorized into quintiles, adjusting for age, sex, race, ethnicity, non-U.S.-birth, recent immigration, household income, employment status, substance abuse, homelessness, and HIV infection.