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The Impact of HIV Infection on TB disparities among U.S.-born Black and White Tuberculosis Patients in the United States

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Abstract

Background/Objectives—U.S.-born non-Hispanic black (blacks) persons (12% of U.S. population) accounted for 41% of HIV diagnoses during 2008–2014. HIV significantly increases TB and TB-related mortality. TB rate ratios were 6–7 times as high in blacks versus U.S.-born non-Hispanic whites (whites) during 2013–2016. We analyzed a sample of black and white TB patients to assess the impact of HIV on TB racial disparities.

Methods—552 black and white TB patients with known HIV status were recruited from 10 U.S. sites in 2009–2010. We abstracted data from the National TB Surveillance System, medical records, and death certificates, and interviewed 477 patients. We estimated adjusted odds ratios (AOR) with 95% confidence intervals (CI) for associations of with HIV infection, late HIV diagnosis (≤ 3 months before or any time after TB diagnosis), and mortality during TB treatment.

Results—Twenty-one percent of the sample had HIV. Blacks (AOR=3.4, CI=1.7–6.8), and persons with recent homelessness (AOR=2.5, CI=1.5–4.3) had greater odds of HIV than others. The majority of HIV/TB patients were diagnosed with HIV ≤ 3 months before (57%) or after (4%) TB diagnosis. Among HIV/TB patients, blacks had similar percentages to whites (61% versus 57%) of late HIV diagnosis. Twenty-five percent of HIV/TB patients died, 38% prior to TB diagnosis and 62% during TB treatment. Blacks did not have significantly greater odds of TB-related mortality than whites (AOR=1.1, CI=.6–2.1).

Conclusions—Black TB patients had greater HIV prevalence than whites. While mortality was associated with HIV, it was not significantly associated with black or white race.

40-Word Summary:

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

U.S.-born non-Hispanic black TB patients had greater HIV prevalence than whites. Sixty percent of study patients were diagnosed with HIV near the time of TB diagnosis. While mortality was associated with HIV, it was not significantly associated with black race.

Keywords

Tuberculosis; HIV; disparities; race

While the United States reduced tuberculosis (TB) rates among nearly all demographic groups in the United States, disparities still exist. Among 4,331 U.S.-born cases in 2010, (39% of TB cases reported to the U.S. Centers for Disease Control and Prevention's [CDC] National TB Surveillance System [NTSS]), non-Hispanic black or African Americans (blacks) had the greatest TB burden: blacks accounted for 41% of U.S.-born TB cases, followed by 33% for non-Hispanic whites (whites).[1] While this percentage dropped to 37% in 2016, TB black/white rate ratios were consistently six to seven times as high from 2013–2016; in 2016, TB incidence was 3.0 cases per 100,000 blacks, compared with 0.5 per 100,000 whites.[2]

Blacks are also disproportionately affected by HIV infection, which significantly increases the risk for progression to TB after TB exposure and for TB-related mortality.[3] During 2008–2014, U.S.-born blacks accounted for approximately 41% of HIV diagnoses,[4,5] and, during 2008–2014 (excluding California and Vermont, which didn't report HIV/TB data to the NTSS during the period) made up 73% of U.S.-born TB cases with reported HIV.[6] HIV testing of TB patients is recommended practice, with HIV status reported for 77% of all TB cases during 2008–2014, and for 84% of TB cases aged 25–44 years.[1] As a percentage of U.S.-born TB cases during 2008–2014, 16% of blacks, but only 7% of Hispanics, 4% of whites, 3% of American Indian/Alaskan Natives, and 1% of Asians had HIV infection.[6] Figure 1 shows the percentage of reported HIV comorbidity among U.S.-born non-Hispanic whites and blacks with TB during 1994–2016. Although rates of concomitant HIV and TB among U.S.-born persons have dropped dramatically among blacks over the past two decades, they were more than 17 times as high in 2016 as those of whites (See Supplemental file).

One hypothesis is that delays in TB diagnosis and treatment during the infectious period among blacks could explain the TB disparity. This hypothesis was rejected, since a study evaluating delayed time to TB diagnosis as a risk factor for transmission of *Mycobacterium tuberculosis (Mtb)* from U.S.-born non-Hispanic black and white TB patients to their contacts found that whites actually had longer times to diagnosis than blacks.[7] However, the same study found that persons having close contact to black TB patients were twice as likely to have latent TB infection as contacts to white patients.[7] While reasons for this finding were not examined, blacks could have had greater prevalence of TB infection because of greater immunosuppression that makes such persons more susceptible to acquiring TB infection, or because of greater past TB exposure.[8,9]

We analyzed the above-mentioned sample to assess the impact of HIV on TB racial disparities. We describe characteristics of TB patients with and without HIV. Then, we

analyze the effect of race on timing of TB diagnosis in relation to HIV diagnosis and on TB-related mortality.

Methods

CDC's Division of TB Elimination funded 20 sites to participate in the Tuberculosis Epidemiologic Studies Consortium (TBESC-1).[10] Our analysis is a sub-study of a primary study to assess determinants of early diagnosis, prevention and treatment of TB in U.S.-born, non-Hispanic blacks and whites. Investigators performed two-stage sequential stratified sampling of reported TB cases, with seven TBESC and three collaborating sites having high percentages of black TB patients selected first, then black and white TB patients aged ≥15 reported to the NTSS from August 2009 through December 2010 selected until the site's recruitment goals were reached or until the recruitment period ended, whichever came first. Study sites were the District of Columbia, Georgia, Maryland, New Jersey, New York City, North Carolina, Pennsylvania, Tennessee, Texas, and Virginia.[7] Data sources included structured interviews with consenting patients (from December 2009 to March 2011), the NTSS, medical records, and death certificates (matched during and after TB treatment); all data were abstracted onto standardized forms. HIV infection at the time of TB diagnosis, from testing or by self-report, was obtained from the NTSS, medical records, and interviews; we used any source that indicated HIV infection or AIDS. Patients with unknown HIV status were not analyzed in this sub-study. Patient interviews assessed existence and timing of TB symptoms, date of HIV diagnosis, and HIV antiretroviral medication use. Other data included age, sex, education, residence in a long-term care facility, chronic illness (defined as diabetes, high blood pressure, kidney disease, asthma, sickle cell disease, heart disease, chronic obstructive pulmonary disease, cancer, rheumatoid arthritis, or silicosis), and recent (within the year prior to TB diagnosis) history of injecting or non-injecting substance use, of incarceration, and of homelessness within the past year.

Our current study further analyzed the above-mentioned sample to describe characteristics of TB patients with HIV, rapid TB diagnosis (using a nucleic acid amplification test, i.e., NAAT), late HIV diagnosis (defined as within 3 months before TB diagnosis [an AIDS defining illness] or any time after TB diagnosis),[5] and TB-associated mortality (prior to TB diagnosis or during TB treatment). Mortality prior to TB diagnosis can occur when specimens are collected or chest radiographs conducted while the patient is alive, but results are obtained and the TB diagnosis is made after the patient has died. Since we hypothesized that black race was associated with the outcomes of HIV among the TB patients, late HIV diagnosis, and TB-associated mortality, we identified potential confounding variables associated with those outcomes and with race and entered them into multivariable logistic regression models. We used backwards selection to derive final models and estimate adjusted odds ratios (AOR) with 95% confidence intervals (CI) using SAS (version 9.4, Cary, NC, USA). We calculated the days from HIV to TB diagnosis among patients reporting their HIV diagnosis date during the interviews.

This current study is a secondary analysis of de-identified data. For the original study, the institutional review boards at CDC and at the local sites provided approval and patients provided informed consent.

Results

At the selected sites, NTSS and medical record data were obtained for 552 U.S.-born TB patients having known HIV status for analysis in this study, including 426 black and 126 white patients, and 118 persons with HIV infection. Of the 552 TB patients, death certificate data were found for 67 black and 21 white patients. The project team interviewed 477 patients, including 91 with HIV infection. Some patients were interviewed prior to their subsequent death during TB treatment.

Characteristics of TB patients with HIV

Twenty-one percent of the sample had HIV. Blacks (AOR=3.4, CI=1.7–6.8), and persons with recent homelessness (AOR=2.5, CI=1.5–4.3) had greater odds, and persons aged 65 or older had less odds (AOR=.3, CI=.1-.6) of HIV than TB patients without the given characteristic (Table 1).

For the 86% of HIV/TB patients who had a tuberculin skin test (TST) or interferon gamma release assay (IGRA) that was documented in their medical charts, the test was less likely to be positive than for HIV-negative patients (OR=0.5, CI=0.3–0.8)(Table 2).

HIV patients with TB had 2.5 times the odds of having a prior episode of TB compared to those without HIV (OR=2.5, CI=1.1–5.6). HIV/TB patients with pulmonary disease showed less cavitation on chest radiography (OR=.4, CI=.3-.7) (Table 2). HIV/TB patients were more likely to have both pulmonary and non-pulmonary sites of TB disease (OR=3.5, CI=2.0–5.8) (Table 2).

Compared to HIV-negative patients, more patients with HIV/TB had reported symptoms of swollen lymph nodes (OR=2.8, CI=1.7–4.6), weight loss (OR=1.9, CI=1.1–3.3), or any TB symptom (OR=3.2, CI=1.1–9.2) (Table 2).

While 77% of HIV/TB patients were diagnosed with TB through a positive culture for *Mtb* compared with 83% of TB patients without HIV, this difference was not statistically significant (OR=.7, CI=.4–1.2). TB patients with HIV were no more likely to have had a NAAT for rapid diagnosis of TB disease than TB patients without HIV; 44% of patients with HIV and 48% of patients without HIV had a NAAT recorded (OR=.9, CI=.6–1.3) (Table 2). This was also true among 450 *Mtb* culture-positive patients only; overall, 52% received a NAAT, 49% of HIV/TB patients and 52% of TB patients without HIV (OR=.9, CI=.6–1.4).

Of HIV/TB patients who were interviewed (n=91), 63% stated they were on one or more HIV anti-retroviral medications at TB diagnosis, and 40% were on three or more HIV medications, including combination medications counted separately. There was no significant difference in HIV care by race (OR=1.7, CI=.4–7.2). The median CD4 count at the time of TB diagnosis, which was available for 102 HIV/TB patients, was 76 cells/μL, with an interquartile range (IQR) of 26–199 cells/μL. By race, the median was 62 cells/μL for blacks and 134 for whites, with nearly identical interquartile ranges. While not statistically different, 45% of blacks had CD4 counts less than 50, compared with 33% of whites (OR=1.7, CI=.4–7.0).

Timing of the TB/HIV diagnoses

For over 60% of the 81 TB patients with date of HIV diagnosis, the TB diagnosis occurred near the time of or before their HIV diagnosis. The majority of HIV/TB patients were diagnosed with HIV 3 months before (57%) or after (4%) TB diagnosis. Sixty-one percent of HIV-positive blacks had a late HIV diagnosis compared to 57% of whites; however, this difference was not statistically significant (OR=1.2, CI=.2–5.6). No characteristics were found to be significantly associated with a late HIV diagnosis (see Supplement).

TB-related mortality

Sixteen percent of the sample died; 16% of blacks and 17% of whites. Forty percent of deaths occurred prior to TB diagnosis, while 60% occurred during TB treatment. Twenty-five percent of patients with HIV died, compared with 14% of persons without HIV. Among the 29 HIV/TB patients who died, 38% were diagnosed with TB after death, and 62% were alive at the time of TB diagnosis, but died in a median 38 (IQR=10–89) days after starting TB treatment.

Patients with HIV had greater odds of TB-associated mortality than patients without HIV (AOR=4.2, CI=2.2–8.1) (see Supplement). Greater odds of TB-associated mortality, from greatest to least, were also found for: persons with chronic illness (AOR=4.0, CI=1.5–10.6-), and for persons aged 65 or older (AOR=2.9, CI=1.6–5.3) (see Supplement).

Discussion

We conducted this study to assess the impact of HIV on black/white TB disparities among a sample of U.S.-born non-Hispanic TB patients. The sample had approximately a two-fold higher rate of HIV co-morbidity than among all U.S. TB patients, and consequently a greater mortality rate, which limit generalizability of study findings to the sites that were sampled: ten Eastern and Southern U.S. sites. We documented that a significantly higher proportion of black TB patients had HIV than of white TB patients. We also found that it was common for blacks as well as whites to receive their HIV diagnosis at a time that was too late for them to have benefitted from HIV treatment that could have prevented their TB; 61% of blacks and 57% of whites received such “late” HIV diagnoses (a difference that was not statistically significant). While this is a secondary analysis of data collected in 2009 – 2010, it is the only known large multisite study to examine timing of HIV and TB diagnoses and immunosuppression, which are critical to understanding the risk of TB incidence and HIV/TB mortality. However a study specifically in California during the same period had similar findings.[11] Since the NTSS does not include date of HIV diagnosis, CD4 counts or viral loads, or HIV antiretroviral treatment, studies such as this one are needed to assess disparities in HIV/TB and should be repeated, especially as HIV care increases with improved insurance coverage.[12] HIV diagnosis and HIV treatment prior to exposure to TB can help prevent TB disease.[13, 14, 15] The median CD4 count at TB diagnosis among persons with HIV in our study was less than 80 cells/μL, and only 40% of the HIV/TB patients were on three or more anti-retroviral medications (for an unknown length of time), both indicating that HIV was poorly managed in this population.

We documented that tests for TB infection (i.e., TST or IGRA) were less likely to be positive for TB patients with HIV than for those without HIV, which is consistent with the literature.[16] As continued evaluation for TB disease is recommended for HIV-positive patients despite negative TB infection results, knowledge of HIV status prior to TB screening is imperative for early diagnosis of TB disease.[3]

Nearly all the HIV/TB patients reported one or more TB symptoms, which could raise provider suspicion of TB disease and prompt additional testing for TB, resulting in more detected and treated TB cases. Typically, the next diagnostic test ordered when a patient reports pulmonary TB symptoms is a chest radiograph. However, pulmonary TB patients with HIV have reduced likelihood of cavitation on chest radiography,[17] which was also documented in this study. NAATs can aid in rapidly diagnosing TB, but only 47% of TB patients in this study received a NAAT. CDC initially recommended NAAT in 1996 for use on (preferably) the first collected acid-fast-bacilli smear-positive specimen, and in January 2009 for all (including smear-negative) specimens when TB disease is suspected.[18] The use of NAAT is determined by providers, hospitals, and laboratories and must specifically be requested. NAAT has been recommended by the Infectious Diseases Society of America since at least 2004 for persons with HIV suspected of TB, because of the increased risk of TB transmission among a highly vulnerable population and of mortality from undiagnosed TB.[3] In 2016, 62% of all reported U.S. TB cases had documentation of a NAAT, so there is still room for improvement.[1]

We also documented that HIV infection was independently associated with greater TB-associated mortality. If blacks have greater odds of having HIV infection, and persons with HIV have greater odds of death, then prevention of mortality among blacks with HIV will depend on early access to HIV diagnosis and care. The largest proportion of blacks and the largest proportion of blacks with HIV in the United States reside in the South.[5] Many states in the South have not expanded Medicaid eligibility, which likely affects access to healthcare for many. Insurance coverage for persons with HIV has been most affected by their exclusion for pre-existing conditions, high premiums, and by ineligibility for Medicaid.[12] In a study comparing insurance coverage of persons with HIV in 2012 prior to implementation of the Affordable Care Act (ACA), with coverage in 2014 after ACA implementation, Medicaid coverage increased by 13% for whites and 11% for blacks in sampled states that expanded Medicaid, but did not increase significantly in sampled states that did not expand Medicaid.[12] As of November 2017, five of the jurisdictions in this study have expanded Medicaid (Maryland, New Jersey, Pennsylvania, New York City and the District of Columbia) and five have not (Georgia, Tennessee, Texas, North Carolina, and Virginia).[19] Among blacks with known HIV infection in the United States, levels of HIV care and viral suppression are lower than for whites; in 2014, 68% of blacks received any HIV care, versus 74% of whites.[20]

Limitations of our study include data collection and analysis at sites in the Eastern United States, which might not be representative of other locations. It is also possible that the black and white study participants who were interviewed might not be representative of all black and white TB patients at the study sites. However, a previous publication of study data reported that the 3:1 ratio of black to white study enrollees was maintained among

interviewees.[21] Another limitation is that cause of death was not specifically ascertained from medical records; however a recent publication documented that 72% of deaths with TB are TB-related.[22] While the study data are a bit old, the study required significant time to abstract data from multiple sources and to interview patients, study procedures which are not likely to be repeated in the near future.

Along with early HIV diagnosis and effective antiretroviral treatment, TB disease can be prevented by testing and treatment for TB infection.[3,23] Testing for TB infection is recommended at HIV diagnosis and annually for persons who are at risk for TB exposure.[3] For persons with HIV, recommended treatment for latent TB infection (LTBI) is 9 months of isoniazid.[3] For those on efavirenz or raltegravir-based HIV antiretroviral regimens, 4 months of rifampin or rifabutin, or 3 months of high-dose isoniazid and rifapentine (3HP) are alternative regimen choices.[3,24] A large population-based study in 2010–2012 revealed that more than 30% of HIV-infected patients had never been tested for TB infection, so there is potential room for improvement.[25]

Conclusions

U.S.-born non-Hispanic black TB patients had a greater HIV prevalence than whites. While TB-associated mortality was associated with HIV, it was not significantly associated with black or white race. Most HIV/TB patients in this study were severely immunosuppressed (median CD4=75.5 cells/μL) and were not diagnosed with HIV until near the time that they were diagnosed with TB. Appropriate management of HIV infection through effective antiretroviral therapy results in a more immunocompetent patient who is less susceptible to progressing to TB disease. Improvements in HIV diagnosis and care, treatment for latent TB infection, and rapid TB diagnosis are all needed to reduce TB incidence and mortality in persons with HIV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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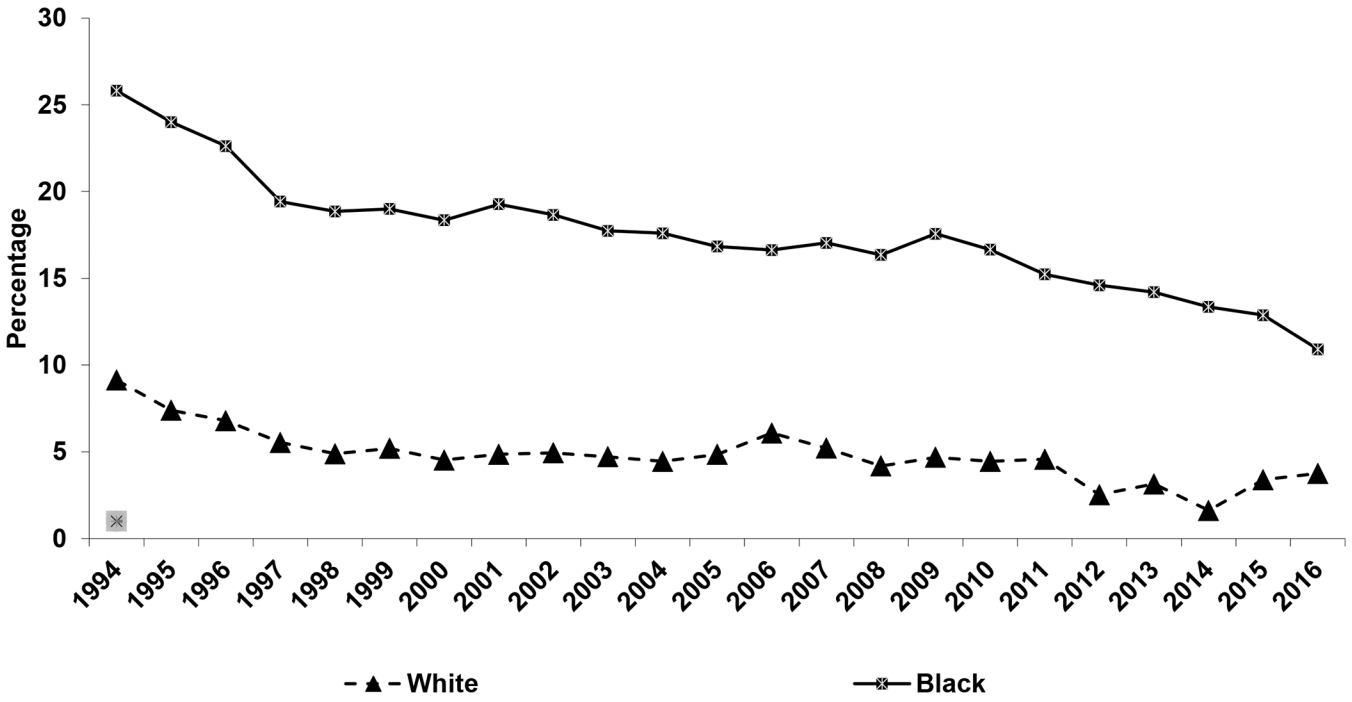

Figure 1.

Percentage of Reported US-born TB Cases with HIV, Non-Hispanic Whites and Blacks, 1994–2016*

*Data provided by CDC/DTBE Surveillance, Epidemiology, and Outbreak Investigations Branch, 12/19/2017. The numerator and denominator exclude all California cases from 1993 – 2016, which only reported AIDS/TB case registry match data from 1993–2003 and did not report HIV/TB until 2011, and Rhode Island cases from 1993 – 1997 and Vermont cases from 2007 – 2010, neither of which reported HIV/TB to CDC during those periods.

Table 1.

Characteristics of Study TB Patients With and Without HIV, 2009–2010, N=552

Characteristic	With HIV		Without HIV		Unadjusted		Adjusted[+]	
	n	Row %	n	Row %	Odds Ratio	95% Confidence Interval (CI)	Odds Ratio	95% Confidence Interval (CI)
	118	21	434	79				
Black[*]	108	25	318	75	3.9	2.0–7.8[*]	3.4	1.7–6.8[*]
White	10	8	116	92				
Male	85	22	298	78	1.2	.7–1.8		
Female	33	20	136	80				
Age > 65[*]	7	6	109	94	0.2	.1–.4[*]	0.3	.1–.6[*]
Age < 65	111	25	325	74				
< High School Education[*]	50	25	154	75	1.4	.9–2.2		
> High School Education	61	19	266	81				
Unknown	7		14					
Homeless[*]	34	37	59	63	2.6	1.6–4.2[*]	2.5	1.5–4.3[*]
Not homeless	83	18	375	82				
Unknown	1							
Inmate[*]	8	29	20	71	1.5	.7–3.6		
Not an inmate	102	21	395	79				
Unknown	8		19					
Long-term care resident[*]	2	12	15	88	0.5	.1–2.3		
Not a long-term care resident	105	21	399	79				
Unknown	11		20					
Substance use[*]	53	31	116	69	2.3	1.5–3.5[*]		
No substance use	62	17	307	83				
Unknown	3		11					

[*] Significant at 95% confidence level

[+] Variables statistically significant at the 95% confidence level from backwards selection. The initial model included race, sex, age, education, homelessness, incarceration, long-term care residence, and substance use

Table 2.

Clinical Characteristics of Study TB Patients With and Without HIV, 2009–2010, N=552

Characteristic	With HIV		Without HIV		Unadjusted		Adjusted[+]	
	n	Column %	n	Column %	Odds Ratio	95% CI	Odds Ratio	95% CI
Chronic illness	87	75	333	78	0.9	.5–1.4		
No chronic illness	29	25	95	22				
Unknown	2		6					
Prior TB disease	11	10	17	4	2.5	1.1–5.6[*]	2.8	1.0–7.6[*]
No prior TB	104	90	406	96				
Unknown	3		11					
Symptoms								
Hemoptysis	16	15	61	15	1.0	.6–1.8		
No hemoptysis	88	85	339	85				
Unknown	14		34					
Chest pain	48	47	193	48	1.0	.6–1.5		
No chest pain	54	53	209	52				
Unknown	16		32					
Shortness of breath	63	62	218	54	1.3	.9–2.1		
No shortness of breath	39	38	182	46				
Unknown	16		34					
Cough	76	73	265	65	1.5	.9–2.4		
No cough	28	27	143	35				
Unknown	14		26					
Fever	62	60	183	45	0.6	.4–.9[*]		
No fever	42	40	225	55				
Unknown	14		26					
Night sweats	61	60	217	54	1.3	.8–2.0		
No night sweats	41	40	183	46				
Unknown	16		34					
Weight loss	77	81	257	69	1.9	1.1–3.3[*]		
No weight loss	18	19	114	31				
Unknown	23		63					
Swollen lymph nodes	34	35	64	16	2.8	1.7–4.6[*]	2.4	1.4–4.2[*]
No swollen lymph nodes	62	65	329	84				
Unknown	22		41					

Characteristic	With HIV		Without HIV		Unadjusted		Adjusted[+]	
	n	Column %	n	Column %	Odds Ratio	95% CI	Odds Ratio	95% CI
Fatigue	63	64	216	55	1.4	.9–2.3		
No fatigue	36	36	177	45				
Unknown	19		41					
Any symptom	111	97	385	90	3.2	1.1–9.2*		
No symptom	4	3	45	10				
Unknown	3		4					
Diagnostics								
Ever had a tuberculin skin test (TST) or interferon gamma release assay (IGRA)	101	86	395	91	0.6	.3–1.1		
No TST history	17	14	39	9				
Ever had a positive TST, of those who had a TST or IGRA	71	70	327	83	0.5	.3–.8*		
No positive TST	30	30	68	17				
Ever had a chest radiograph (CXR)	117	99	434	100	0.0			
No CXR	1	1	0	0				
Abnormal CXR, among those having a CXR	111	96	411	95	1.2	.5–3.6		
No abnormal	5	4	22	5				
Unknown	1		1					
Cavitation on CXR, among those with pulmonary TB	26	27	168	47	0.4	.3–.7*		
No cavitation	71	73	191	53				
	7		13					
Ever had a nucleic acid amplification test (NAAT)	52	44	208	48	0.9	.6–1.3		
No NAAT	66	56	226	52				
Sites of disease								
Pulmonary only	75	64	332	76	0.5	.3–.8*		
Extrapulmonary only	10	8	56	13	0.6	.3–1.3		
Both pulmonary and extrapulmonary	31	26	41	9	3.5	2.0–5.8*		
Unknown	2	2	5	1				
Outcome								
Died, any non-accidental cause	29	25	59	14	2.1	1.3–3.4*		
Alive	89	75	375	86				

*Significant at 95% confidence level

[+]Variables statistically significant at the 95% confidence level from backwards selection. The initial model included chronic illness, prior TB, and all symptoms