Published in final edited form as:
Int J Tuberc Lung Dis. 2013 April ; 17(4): 486–492. doi:10.5588/ijtld.12.0133.

Non-adherence and drug-related interruptions are risk factors for delays in completion of treatment for tuberculosis

A. C. Pettit[*], **J. Cummins**[†], **L. A. Kaltenbach**[‡], **T. R. Sterling**[*,§], and **J. V. Warkentin**[†]

[*]Division of Infectious Diseases, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

[†]Tennessee Department of Health, Nashville, Tennessee

[‡]Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, North Carolina

[§]Center for Health Services Research, Vanderbilt University School of Medicine, Nashville, Tennessee, USA

SUMMARY

SETTING—A key program performance objective established by the Centers for Disease Control and Prevention (CDC) is that ≥93% of tuberculosis (TB) cases complete treatment within 12 months.

OBJECTIVE—To determine the rate of and risk factors for delay in anti-tuberculosis treatment completion.

DESIGN—Nested case-control study among TB cases reported to the Tennessee Department of Health between 1 January 2000 and 31 December 2010. Time to complete treatment was calculated using treatment start and stop dates documented in the Tuberculosis Information Management System (TIMS).

RESULTS—Of 2627 cases, 261 (9.9%) required >12 months to complete treatment. In adjusted conditional logistic regression analyses, cavitary disease and positive cultures after 2 months of therapy (OR 5.85, 95%CI 1.98–17.32, $P = 0.001$), non-adherence (OR 4.13, 95%CI 1.76–9.72, $P < 0.001$), and interruptions in treatment due to drug-related issues (OR 6.91, 95%CI 3.76–12.70, $P < 0.001$) were independently associated with delay in completion of TB treatment.

CONCLUSION—From 2000 to 2010, the proportion of TB cases completing treatment within 12 months increased from 84.6% to 94.9%, and remained above the CDC target during 2009–2010. Efforts to improve patient adherence and reduce interruptions in treatment due to anti-tuberculosis drug-related issues could improve the proportion of TB cases completing treatment within 12 months.

Keywords

Mycobacterium tuberculosis; treatment completion delay; treatment recommendations; program evaluation; program objective

Correspondence to: April C Pettit, Vanderbilt University Medical Center, 1161 21st Avenue South, A2200 Medical Center North, Nashville, TN 37232-2582, USA. april.pettit@vanderbilt.edu.

TUBERCULOSIS (TB) remains an important public health problem in the United States. The development of effective treatment has led to a dramatic reduction in TB disease. However, failure to complete treatment in a timely manner leads to a potentially preventable excess in TB morbidity and mortality, and *Mycobacterium tuberculosis* transmission.

In 2006, a TB program performance objective established by the Centers for Disease Control and Prevention (CDC) was, for patients with newly diagnosed TB for whom ≤12 months of treatment is indicated, to increase the proportion of patients who complete treatment within 12 months to 93.0%.[1] In 2009, the CDC launched the National Tuberculosis Indicator Project (NTIP), a secure web-based system intended to monitor program progress toward this objective.[2] During 1993–2006, the national treatment completion indicator increased from 64% to 84%. Risk factors for delays in treatment completion included extra-pulmonary disease, human immunodeficiency virus (HIV) infection, previous TB diagnosis, positive sputum cultures, homelessness, residence in a correctional facility and self-administered therapy (SAT),[3] During 2008, the completion of treatment indicator was reported by the CDC to be 84.6% nationwide and 86.7% in Tennessee.[4]

Current guidelines from the American Thoracic Society (ATS), CDC, and Infectious Diseases Society of American (IDSA) recommend a 6-month rifamycin-based regimen for drug-susceptible TB. Treatment is extended to 9 months in patients with cavitary disease and positive cultures following 2 months of treatment or silicotuberculosis. Twelve or more months of treatment are recommended for patients who cannot take isoniazid (H, INH) and pyrazinamide (Z, PZA), patients who cannot take rifampin (R, RMP), multi-drug-resistant TB (MDR-TB) cases and patients with central nervous system (CNS) disease.[5]

Recent programmatic data from the United States on the rates of TB treatment completion at 12 months are lacking.[2,3] Furthermore, previous studies have not assessed adherence, drug-related interruptions in treatment or other potential risk factors for delays in treatment completion available only by chart review. We report recent data from Tennessee on the duration of anti-tuberculosis treatment and compare these results with the CDC objectives. We also examine risk factors for delays in treatment completion to identify targets for intervention and to achieve the objectives of the CDC program.

METHODS

Patient population

We conducted a nested case-control study among drug-susceptible TB cases reported to the Tennessee Department of Health (TDOH) from 1 January 2000 to 31 December 2010. Directly observed therapy (DOT) is mandated in Tennessee, although patients on daily DOT can self-administer weekend doses after they are no longer isolated. Self-administration of doses apart from the above are not considered DOT. Patients were excluded if they were dead at diagnosis or died during treatment, did not initiate treatment with ≥1 anti-tuberculosis drug, had RMP resistance, had CNS disease, or were aged <15 years with miliary disease or a positive blood culture for *M. tuberculosis*.

As Vanderbilt University and TDOH Institutional Review Boards determined this study to be a public health program evaluation and that it did not constitute human subjects research, ethical approval was not required.

Study definitions

TB cases were defined according to CDC guidelines[6] and identified using the Tuberculosis Information Management System (TIMS), a case management and surveillance software

program used by TB control programs in the United States until 1 January 2011. TB cases were laboratory-confirmed (isolation of *M. tuberculosis*, demonstration of *M. tuberculosis* by polymerase chain reaction [PCR] or demonstration of acid-fast bacilli [AFB] when a culture has not been or cannot be obtained), clinical (positive tuberculin skin test [TST], other signs and symptoms compatible with TB or clinical evidence of current disease, treatment with ≥2 anti-tuberculosis medications, and a completed diagnostic evaluation), or provider verified (meets all criteria for a clinical case except for a positive TST).

Time to complete treatment was calculated using treatment start and stop dates documented in the TIMS. Treatment completion delay was defined as taking >366 days to complete treatment. Treatment was considered complete if the reason for stopping treatment recorded in the TIMS was due to successful completion of the prescribed course of treatment. Patients with missing stop dates were classified as having treatment completion delay (n = 3).

One control per case was randomly selected from those without treatment completion delay and individually matched by diagnosis date (before/after 20 June 2003 to reflect changes in treatment guidelines),[5] age (± 10 years) and health department region.[7] Demographic and laboratory data were obtained via TIMS. Charts were reviewed using a standardized abstraction form to gather data not available in the TIMS (height, weight, adherence, tobacco use and drug-related interruptions). Non-adherence was defined as missing >10% of planned doses. Tobacco use was defined as any cigarette smoking at the time of TB diagnosis.

Therapeutic drug monitoring (TDM) is not routinely performed among all patients in Tennessee. In the United States, TDM is currently recommended for 1) patients with an inadequate response to an appropriate anti-tuberculosis regimen delivered by DOT and in whom non-adherence and drug resistance have been ruled out, and 2) patients with severe gastrointestinal or metabolic abnormalities.[3] For some patients meeting these criteria, serum drug concentrations were obtained at 2 h and, if necessary, 6 h following dose administration to differentiate delayed absorption from malabsorption.[8] Drug malabsorption was identified if serum levels were low at 2 h and 6 h post dose.[8]

Suspected drug-induced hepatitis was noted if the aspartate transaminase (AST) level was ≥3 × the upper limit of normal (ULN) with symptoms or ≥5 × ULN without symptoms.[9] Drug intolerance or allergy was noted if a reaction caused an interruption in treatment or permanent discontinuation of the drug.

Information on medical comorbidities was collected by chart review. A patient was noted to have chronic lung disease (CLD) if records reported a diagnosis of chronic obstructive pulmonary disease, bronchiolitis obliterans or lung carcinoma. Viral hepatitis was defined as a positive hepatitis C antibody or polymerase chain reaction (PCR) result or a positive hepatitis B surface antigen or PCR result. Renal disease was defined as chronic dialysis, renal transplantation or chronic renal insufficiency (estimated glomerular filtration rate <60 ml/min/1.73 m^2 of >3 months' duration[10]). Diabetes mellitus (DM) was noted if records reported a diagnosis of any type of DM or if the patient was taking diabetes medications.

Laboratory methods

Drug susceptibility testing for first-line medications (including INH, RMP, PZA, ethambutol [E, EMB] and streptomycin) was performed at the TDOH Laboratory Services (Nashville, TN, USA) for all patients with positive cultures. Drug concentrations were measured by high performance liquid chromatography and interpreted at the National Jewish Medical and Research Center (Denver, CO, USA).[8,11]

Statistical analysis

Statistical analyses were conducted using STATA IC, version 10.1 (Stata Corp, College Station, TX, USA). Fisher's exact and Wilcoxon rank-sum tests compared categorical and continuous variables, respectively. The odds ratio (OR) for treatment completion delay was determined using conditional logistic regression. All *P* values were two-sided and were considered statistically significant if <0.05. Variables were chosen for the adjusted analysis if they were significant in the unadjusted analysis, significant in previous studies or clinically important. An interaction term between substance use and non-adherence as well as cavitary disease with positive cultures after 2 months of treatment and extra-pulmonary disease were included in the adjusted model.

Multiple imputation was used to impute missing height (*n* = 175) and tobacco use (*n* = 53).[12] Height was imputed using sex, age, weight and an interaction term between sex and weight. Tobacco use was imputed using all the variables for height plus HIV infection status, homelessness and CLD.

RESULTS

Baseline characteristics of study population

A total of 3068 TB cases were reported to the TDOH from 1 January 2000 to 31 December 2010. Patients were excluded if they were dead at diagnosis or died during treatment (*n* = 372), did not initiate treatment with ≥1 anti-tuberculosis drug (*n* = 96), had RMP resistance (*n* = 19), had CNS disease (*n* = 60) or were aged <15 years with miliary disease or a positive blood culture for *M. tuberculosis* (*n* = 1). The baseline demographic and clinical characteristics of the study population are listed in Table 1.

The characteristics of persons with missing and available HIV status are listed in Table 2. Rates of missing HIV status decreased during the study period from 34.6% to 4.4%. There were no differences in results when HIV status unknown persons were included as non-HIV-infected or excluded (results not shown). For the purposes of this study, persons with unknown HIV results were therefore considered to be non-HIV-infected.

Cohort results

Treatment completion delay occurred among 261 of 2627 eligible TB cases (9.9%, 95% confidence interval [CI] 8.8–11.1). Among these, the median time to treatment completion was 58.7 weeks (interquartile range [IQR] 53.9–70). Persons with treatment delay were more likely to be Black, US-born, HIV-infected, reside in a correctional facility, use excess alcohol, receive a combination of DOT and SAT (vs. exclusively DOT) and have extra-pulmonary, cavitary, smear-positive and culture-positive disease; they were less likely to receive exclusively DOT. The proportion of cases with confirmed relapse was higher among persons with treatment delay than those without (4/261, 1.5%, 95%CI 0.6–3.9 vs. 22/2366, 0.9%, 95%CI 0.6–1.4; Table 1). Rates of completion of treatment within 12 months increased during the study period, from 84.6% to 94.9%, *P* = 0.001 (Table 3).

Case-control results

Each case was matched with one control, except for eight cases for which the chart could not be located. In the unadjusted models, having other medical comorbidities increased the risk of TB treatment completion delay. In unadjusted and adjusted analyses, cavitary disease and culture positivity after 2 months of treatment, non-adherence to treatment, and drug-related interruptions in treatment, increased the risk of TB treatment delay. In the adjusted model, there was a trend toward an increased risk of TB treatment delay with extra-pulmonary disease (Table 4).

Results of the findings on drug-related interruptions in treatment, including drug malabsorption, drug-induced hepatitis and drug intolerance or allergy, are shown respectively in Tables 5–7.

DISCUSSION

Of 2627 eligible TB cases, 261 (9.9%, 95%CI 8.8–11.1) required >12 months to complete treatment. From 2000 to 2010, the treatment completion indicator increased from 84.6% to 94.9%, and remained above the CDC target during 2009–2010 (Table 3). During 2008, we found that 92.4% of eligible TB cases in Tennessee completed treatment within 12 months. This proportion likely differs from that reported by the CDC for Tennessee (86.7%)[4] due to data collected from charts which led to ineligibility for completion of treatment within 12 months or re-classification of cases to controls. Five cases of CNS disease were not captured in the TIMS, and there were six cases in which a recurrent TB case was included as a single entry in the TIMS. Furthermore, there were six cases with a missing treatment start or stop date obtained via chart review.

Despite the high proportion of patients who received at least partial DOT (2544/2627, 96.84%, 95%CI 96.1–97.7), non-adherence was still a risk factor for delays in treatment completion (OR 4.13, 95%CI 1.76–9.72, $P = 0.001$). Persons receiving exclusively DOT were more likely to complete treatment in <12 months compared to those with delayed treatment completion (69.0% vs. 59.0%, $P = 0.001$); those receiving combination DOT and SAT were more likely to have delayed treatment completion (34.5% vs. 28.2%, $P = 0.03$). There were no differences among those on exclusively SAT, although the numbers on exclusively SAT were small (2.1%). A systematic review of DOT among clinical trials concluded that there was no evidence that DOT improved TB treatment completion.[13] However, our findings support the use of exclusive DOT, in addition to individualized case management, to identify factors that may improve adherence, such as utilization of incentives or enablers.[14–17]

Drug-related interruptions in treatment were also a risk factor for delays in treatment completion (OR 6.91, 95%CI 3.76–12.70, $P < 0.001$). Many states, including Tennessee, have guidelines to assist clinicians in the timely identification and appropriate management of malabsorption, hepatitis and other adverse events.[18] It is important to ensure that clinicians are aware of these guidelines as a resource for the management of drug-related issues.

There was a trend towards an increased odds of treatment delay among persons with extra-pulmonary disease (OR 1.75, 95%CI 1.00–3.05, $P = 0.05$). This may be due to a tendency to treat extra-pulmonary disease for >12 months. Clinicians should be made aware that extra-pulmonary disease, excluding CNS disease, does not require extended treatment.

The proportion of matched cases and controls with drug malabsorption was 8.3% (95%CI 6.2–11.0). Programmatic data on TDM during anti-tuberculosis treatment are limited. In a study of TDM among slow responders in a Virginia TB control program, malabsorption was detected among 59% for INH, 52% for RMP and 33% for both medications. Among patients with TDM for PZA, all had levels within the expected range.[19] This is consistent with our findings of similar numbers of patients with malabsorption of INH and RMP, and lower numbers with malabsorption of PZA (Table 5).

The proportion of matched cases and controls with drug-induced hepatitis was 10.1% (95%CI 7.6–13.0). This rate is consistent with a previous review on the topic which reported an incidence of drug-induced hepatitis during multidrug anti-tuberculosis treatment of 2–

28%.[20] There is an urgent need to evaluate new drugs and drug regimens that are efficacious and less toxic. Administration of less hepatotoxic drugs could increase the proportion of cases who complete treatment within 12 months.

TB recurrence occurred in 4 of 261 patients (1.5%, 95%CI 0.6–3.9) who took >12 months to complete treatment compared to 22/2366 (0.9%, 95 %CI 0.6–1.4) who took <12 months. While the low recurrence rates do not provide enough power to detect significant differences, it is important to note that the proportion who recurred was almost twice as high among those with delayed treatment completion. Additional studies in larger populations are needed to determine whether delayed TB treatment completion is a risk factor for recurrence.

One limitation of this study is that TDM was not available for all case and control patients. Drug levels were more likely to be drawn for patients failing treatment and those without expected clinical improvement. It is possible that patients doing well—particularly patients with HIV infection—may also have had low serum drug levels that would have led to extension of treatment.[21,22] However, guidelines currently do not recommend TDM for HIV-infected patients.[5] Additional prospective studies are needed to determine the utility of TDM in HIV-infected persons and other populations at risk for malabsorption, such as patients with DM.[11]

Another possible limitation of the study is that some cases of TB may have been missed. However, this is unlikely given that TB is a reportable disease in Tennessee. Previous studies have detected that 0.5–6.0% of TB cases may not be reported to public health clinics.[23–25] If some cases were unreported, it is unlikely that these were cases with treatment completion delay, as physicians are more likely to seek public health expertise when treating complicated cases.

In conclusion, the proportion of TB cases completing treatment within 12 months increased from 84.6% to 94.9%, and remained above the CDC target during 2009–2010. Our findings support the use of DOT in the treatment of TB whenever possible, but highlight the fact that DOT should be used in conjunction with individualized case management. The findings also emphasize the importance of continued evaluation of new anti-tuberculosis drugs and drug combinations with improved absorption and tolerability, which could lead to fewer interruptions in treatment and a higher proportion of patients completing treatment within 12 months.

Acknowledgments

The authors thank the anonymous reviewers whose thoughtful comments significantly strengthened the manuscript. This research was supported by the National Institutes of Health: NIH 2 T32 AI07474-13 (ACP) and K24 AI065298 (TRS). These results were presented in part at the 2010 National TB Conference, 21–24 June 2010, Atlanta, GA, USA, and at the American Thoracic Society International Conference, 18–23 May 2012, San Francisco, CA, USA; Abstract #A3314.

Disclosures: TRS reports receiving research grant funding from Bristol-Myers Squibb and Pfizer for HIV observational studies. He is also a member of a data safety monitoring board for Otsuka.

References

1. Centers for Disease Control and Prevention. National TB program objectives and performance targets 2015. Atlanta, GA, USA: US Department of Health and Human Services, CDC; 2009. http://www.cdc.gov/tb/programs/evaluation/indicators/default.htm [Accessed December 2012]

2. Centers for Disease Control and Prevention. Monitoring tuberculosis programs—National Tuberculosis Indicator Project, United States, 2002–2008. MMWR Morb Mortal Wkly Rep. 2010; 59:295–298. [PubMed: 20300056]
3. Mitruka K, Winston CA, Navin TR. Predictors of failure in timely tuberculosis treatment completion, United States. Int J Tuberc Lung Dis. 2012; 16:1075–1082. [PubMed: 22668774]
4. Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2010. Atlanta, GA, USA: US Department of Health and Human Services, CDC; 2011. http://www.cdc.gov/tb/statistics/reports/2010/pdf/report2010.pdf [Accessed December 2012]
5. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America. Treatment of tuberculosis. MMWR Recomm Rep. 2003; 52(RR-11):1–77.
6. Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. MMWR Recomm Rep. 1997; 46(RR-10):1–55.
7. Bergstralh, EKJ. Locally written SAS macros. Rochester, MN, USA: Mayo Clinic Division of Biomedical Statistics and Informatics; 2003. http://mayoresearch.mayo.edu/mayo/research/biostat/sasmacros.cfm [Accessed April 2011]
8. Peloquin CA. Therapeutic drug monitoring in the treatment of tuberculosis. Drugs. 2002; 62:2169–2183. [PubMed: 12381217]
9. Ormerod LP, Skinner C, Wales J. Hepatotoxicity of anti-tuberculosis drugs. Thorax. 1996; 51:111–113. [PubMed: 8711637]
10. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003; 139:137–147. [PubMed: 12859163]
11. Peloquin CA. Using therapeutic drug monitoring to dose the antimycobacterial drugs. Clin Chest Med. 1997; 18:79–87. [PubMed: 9098612]
12. van Buren S, Boshuizen HC, Knook DL. Multiple imputation of missing blood pressure covariates in survival analysis. Stat Med. 1999; 18:681–694. [PubMed: 10204197]
13. Volmink J, Garner P. Directly observed therapy for treating tuberculosis. Cochrane Database Syst Rev. 2007; (4):CD003343. [PubMed: 17943789]
14. Chaulk CP, Kazandjian VA. Directly observed therapy for treatment completion of pulmonary tuberculosis: Consensus Statement of the Public Health Tuberculosis Guidelines Panel. JAMA. 1998; 279:943–948. [PubMed: 9544769]
15. Schluger N, Ciotoli C, Cohen D, et al. Comprehensive tuberculosis control for patients at high risk for noncompliance. Am J Respir Crit Care Med. 1995; 151:1486–1490. [PubMed: 7735604]
16. Sumartojo E. When tuberculosis treatment fails. A social behavioral account of patient adherence. Am Rev Respir Dis. 1993; 147:1311–1320. [PubMed: 8484650]
17. Davidson H, Schluger NW, Feldman PH, et al. The effects of increasing incentives on adherence to tuberculosis directly observed therapy. Int J Tuberc Lung Dis. 2000; 4:860–865. [PubMed: 10985655]
18. Tuberculosis elimination guidelines. Nashville, TN, USA: Tennessee Department of Health Communicable and Environmental Disease Services; 2004. Tuberculosis Elimination Program, Tennessee Department of Health Communicable and Environmental Disease Services. http://health.state.tn.us/DownIoads/TB_ProgramsEliminationGuidelinesTN.pdf [Accessed June 7, 2011]
19. Heysell SK, Moore JL, Keller SJ, et al. Therapeutic drug monitoring for slow response to tuberculosis treatment in a state control program, Virginia, USA. Emerg Infect Dis. 2010; 16:1546–1553. [PubMed: 20875279]
20. Tostmann A, Boeree MJ, Aarnoutse RE, et al. Anti-tuberculosis drug-induced hepatotoxicity: concise up-to-date review. J Gastroenterol Hepatol. 2008; 23:192–202. [PubMed: 17995946]
21. Peloquin CA, Nitta AT, Burman WJ, et al. Low anti-tuberculosis drug concentrations in patients with AIDS. Ann Pharmacother. 1996; 30:919–925. [PubMed: 8876848]
22. Sahai J, Gallicano K, Swick I, et al. Reduced plasma concentrations of anti-tuberculous drugs in patients with HIV infection. Ann Intern Med. 1997; 127:289–293. [PubMed: 9265429]
23. Curtis AB, McCray E, McKenna M, et al. Completeness and timeliness of tuberculosis case reporting. A multistate study. Am J Prev Med. 2001; 20:108–112. [PubMed: 11165451]

24. Trepka MJ, Beyer TO, Proctor ME, et al. An evaluation of the completeness of tuberculosis case reporting using hospital billing and laboratory data; Wisconsin, 1995. Ann Epidemiol. 1999; 9:419–423. [PubMed: 10501409]

25. Yokoe DS, Coon SW, Dokholyan R, et al. Pharmacy data for tuberculosis surveillance and assessment of patient management. Emerg Infect Dis. 2004; 10:1426–1431. [PubMed: 15496244]

Table 1

Baseline demographic and clinical characteristics of the study population

Characteristic	Persons who took >12 months to complete treatment (*n* = 261) *n* (%)	Persons who took <12 months to complete treatment (*n* = 2366) *n* (%)	*P* value*
Age at report date, years, median [IQR]	44 [31–59]	45 [30–61]	1.00
Male sex	184 (70.5)	1552 (65.6)	0.11
Black, non-Hispanic race	133 (51.0)	978 (41.3)	0.004
US-born	217 (83.1)	1769 (79)	0.002
Homeless	30 (11.5)	205 (8.7)	0.14
Correctional facility	21 (8.0)	102 (4.3)	0.01
Long-term care facility	7 (2.7)	55 (2.3)	0.67
HIV infection	31 (11.9)	194 (8.2)	0.04
Alcohol use	67 (25.7)	453 (19.1)	0.01
IDU	5 (1.9)	41 (1.7)	0.80
Non-IDU	36 (13.8)	263 (11.1)	0.22
Extra-pulmonary disease	73 (28.0)	510 (21.6)	0.02
Cavitary disease	92 (35.2)	639 (27.0)	0.006
Smear-positive	181 (69.3)	1157 (48.9)	<0.0001
Culture-positive	225 (86.2)	1710 (72.3)	<0.0001
Type of treatment			
Exclusively DOT	154 (59.0)	1632 (69.0)	0.001
DOT/SAT combination	91 (34.5)	667 (28.2)	0.03
Exclusively SAT	10 (3.8)	46 (1.9)	0.06
Subsequent TB recurrence	4 (1.5)	22 (0.9)	0.32
Time to completion of treatment, weeks, median [IQR]	58.7 [53.8–70.0]	29.8 [26.6–39.6]	<0.0001

* Fisher's exact and Wilcoxon's rank sum tests were used to compare categorical and continuous variables, respectively.

IQR = interquartile range; HIV = human immunodeficiency virus; IDU = injection drug use; DOT = directly observed therapy; SAT = self-administered therapy.

Table 2

Characteristics of persons with available and missing HIV status

Characteristic	HIV result available (*n* = 2190) *n* (%)	HIV result missing (*n* = 437) *n* (%)	*P* value*
Male sex	1491 (68.1)	245 (56.0)	<0.001
Black, non-Hispanic race	954 (43.6)	157 (35.9)	0.004
Age at report date, years, median [IQR]	44 [30–58]	56 [29–75]	<0.001
Us-born	1606 (73.3)	380 (87.0)	<0.001
Homeless	219 (10)	16 (3.7)	<0.001
IDU	45 (2.0)	1 (0.2)	0.005
Non IDU	293 (13.4)	6 (1.4)	<0.001
Alcohol use	477 (21.8)	43 (9.8)	<0.001

*Fisher's exact and Wilcoxon's rank sum tests were used to compare categorical and continuous variables, respectively.

HIV = human immunodeficiency virus; IQR = interquartile range; IDU = injection drug use.

Table 3

Percentage of eligible tuberculosis cases who completed treatment within 12 months by study year

Report year	Eligible patients	Patients completing treatment within 12 months *n*	Proportion of eligible patients completing treatment within 12 months* %	Yearly change, percentage points
2000	324	274	84.6	
2001	265	230	86.8	+2.2
2002	273	240	87.9	+1.1
2003	234	210	89.7	+1.8
2004	235	215	91.5	+1.8
2005	265	244	92.1	+1.4
2006	242	217	89.7	−0.6
2007	203	185	91.1	+1.4
2008	249	230	92.4	+1.3
2009	179	171	95.5	+3.1
2010	158	150	94.9	−0.6

* $P = 0.001$ for trend.

Table 4

Conditional logistic regression model for delays in completion of anti-tuberculosis treatment

Characteristic	Cases (*n* = 253) *n* (%)	Controls (*n* = 253) *n* (%)	Unadjusted OR (95%CI)	*P* value	Adjusted OR (95%CI)	*P* value
Male sex	178 (70.4)	170 (67.2)	1.16 (0.80–1.68)	0.45	1.25 (0.73–2.11)	0.41
Black, non-Hispanic race	230 (90.9)	226 (89.3)	1.24 (0.65–2.34)	0.52	0.76 (0.27–2.09)	0.60
US-born	211 (83.4)	195 (77.1)	1.57 (0.98–2.52)	0.06	1.23 (0.54–2.79)	0.63
Homeless	30 (11.9)	22 (8.7)	1.42 (0.79–2.56)	0.24	1.58 (0.70–3.77)	0.31
Correctional facility	21 (8.3)	14 (5.5)	1.78 (0.79–4.02)	0.17	1.78 (0.65–4.86)	0.26
HIV infection	31 (12.2)	19 (7.5)	1.80 (0.96–3.38)	0.07	2.10 (0.85–5.22)	0.11
Substance use (alcohol and/or illicit drugs)	78 (30.8)	78 (30.8)	1.00 (0.65–1.53)	1.00	0.36 (0.15–0.90)*	0.03*
Tobacco use	146 (57.7)	136 (53.7)	1.20 (0.82–1.73)	0.34	0.71 (0.39–1.29)	0.26
Extra-pulmonary disease	72 (28.5)	61 (21.1)	1.27 (0.84–1.93)	0.25	1.75 (1.00–3.05)	0.05
Cavitary disease and culture-positive at 2 months	35 (13.8)	11 (4.3)	4.00 (1.84–8.68)*	<0.001*	5.85 (1.98–17.32)*	0.001*
Any SAT	98 (38.7)	98 (38.7)	1.00 (0.60–1.67)	1.00	0.65 (0.33–1.30)	0.22
Non-adherent	91 (36.0)	36 (14.2)	4.06 (2.42–6.79)*	<0.001*	4.13 (1.76–9.72)*	0.001*
Drug-related treatment interruptions	115 (45.4)	29 (11.5)	6.09 (3.63–10.12)*	<0.001*	6.91 (3.76–12.70)*	<0.001*
Medical comorbidities	104 (41.1)	74 (29.2)	1.86 (1.23–2.80)*	0.003*	1.24 (0.71–2.17)	0.45

*Statistically significant.

OR = odds ratio; CI = confidence interval; HIV = human immunodeficiency virus; SAT = self-administered therapy.

Table 5

Drug malabsorption

Drug malabsorption	All patients (*n* = 506)	Cases: persons who took >12 months to complete treatment (*n* = 253)	Controls: persons who took <12 months to complete treatment (*n* = 253)
Isoniazid	25	20	4
Rifampin	34	29	4
Pyrazinamide	11	9	2
Any drug, *n* (%)	42 (8.3)	37 (14.6)	5 (2.00)

* Some patients had malabsorption of more than one drug. See Peloquin[8] for normal ranges of anti-tuberculosis drug levels.

Table 6

Drug-induced hepatitis

Drug	All patients (*n* = 506)	Cases: persons who took >12 months to complete treatment (*n* = 253)	Controls: persons who took <12 months to complete treatment (*n* = 253)
Isoniazid	37	34	5
Rifampin	11	10	1
Pyrazinamide	25	19	6
Any drug, *n*(%)	51 (10.8)	44 (17.4)	7 (2.8)

* Some patients had drug-induced hepatitis attributed to more than one drug.

Table 7

Drug intolerance/allergy

Intolerance/ allergy	All patients (*n* = 506)				Cases: persons who took >12 months to complete treatment (*n* = 253)				Controls: persons who took <12 months to complete treatment (*n* = 253)			
	INH	**R**	**PZA**	**Any drug**	**INH**	**R**	**PZA**	**Any drug**	**INH**	**R**	**PZA**	**Any drug**
Fever/chills	4	4	2	10	4	2		6				
Gl upset	2	10	9	21	2	2	7	11			2	2
Pruritus/rash	8		4	12	6		4	10	2		1	3
Neurologic	4		1	5	2			2	2		1	3
Arthralgias			5	5			3	3			2	2
Flushing			2	2			2	2				
Cytopenias		9		9		9		9				
Renal failure		2		2		1		1		1		1
Pregnancy			3	3			1	1			2	2
Anaphylaxis	1	3	1	5	1	3	1	5				
Any, *n* (%)	18 (3.6)	35 (6.9)	35 (6.9)	51 (12.1)	13 (5.1)	33 (13.0)	23 (9.1)	44 (17.4)	5 (2.0)	2 (0.8)	12 (4.7)	7 (2.8)

* Seven patients were intolerant to both INH and PZA; 5 patients were intolerant to both INH and RMP.

INH = isoniazid; R = rifamycin; PZA = pyrazinamide; GI = gastrointestinal.