

Treatment Practices, Outcomes, and Costs of Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis, United States, 2005–2007

Technical Appendix

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Additional Methods

Sampling

Each participating site identified MDR-TB and XDR-TB patients reported to CDC during 2005–2007. All XDR-TB patients were selected for participation in the study. From the sampling

frame of MDR-TB patients, a simple random sample of 75% was selected from California and New York and of 50% from Texas. In one instance in New York, a randomly selected patient whose records were unavailable was replaced with another randomly selected patient.

Data Collection

Data were abstracted onto standardized data collection forms, one for TB clinic records and one for each hospitalization, which were entered into separate databases. Separate Excel spreadsheets were used for direct entry of abstracted data on specimens, chest radiography/CT exams, and medications. All databases were converted to SAS for analysis.

Data Analysis

From the originally collected variables, we created the following new variables:

- First date of a positive specimen
- First and last date of positive specimen culture
- Sputum-culture-conversion date: the first date (at least 7 days after the date of last sputum-culture positivity) of 2 consecutive negative sputum-culture results, with 3 categories of exceptions:
 - If there were not 2 consecutive negative culture results 7 days after the last positive, used the available date 7 days after (3 patients).
 - If there were 2 consecutive negative culture results, but the 2nd result was more than a month after the first and the first is not quite 7 days from the last positive, use the first even though it is not quite 7 days after (1 patient)
 - If there were at least 2 negative culture results after the last positive, but none met the 7 day criteria, use the last one available (otherwise the patient would have qualified as no culture conversion) (1 patient)
- First date and duration of TB medications
- First date of diagnosis: earliest of report date, first medication, first positive specimen
- First date and duration of symptoms: from various documented symptoms
- First date and duration of respiratory isolation, intensive care unit, mechanical ventilation
- Days hospitalized: sum of days hospitalized over all TB-related hospitalizations
- Any resistance to each medication
- Initial resistance to each medication within 30 days of TB treatment start
- Acquired resistance to any medication: any resistant result after a susceptible result
- Five mutually exclusive categories of drug resistance: INH/RIF/RBT-only, INH/RIF/RBT-plus, First-line, Pre-XDR, XDR
- Milligrams per medication per week per patient: dose*frequency per week*weeks
- Days to culture conversion: date of culture conversion minus date of TB medications start
- Medication duration: days on each individual medication before and after culture conversion
- Effective medication duration: days on each individual medication to which the isolate was never resistant
- Start and duration of a 5-drug regimen: the date the patient started taking at least 5 medications (including an INJ and FQ) to which their TB isolate was never resistant
- Days infectious: number of days 12 weeks prior to first symptom or, if asymptomatic, prior to initial diagnosis through culture conversion or medications stop
- Number of outpatient DOT visits per patient: DOT regimen*frequency per week*weeks

- Total number of chest radiographs and CTs per patient
- Disseminated disease: TB in ≥ 2 noncontiguous sites at any time during treatment
- Died during treatment: if the reason for treatment stop was died, or hospital disposition was died
- History of TB: if there was a history of TB from either clinic or hospital records or patient self-report
- History of latent TB infection: if there was a history of LTBI from either clinic or hospital records or patient self-report
- Homeless: if in a homeless living situation within the year prior to TB treatment or hospitalization, or if homeless at TB diagnosis or during TB treatment
- Prison/jail inmate: if incarcerated within the year prior to TB treatment or hospitalization, or if an inmate at TB diagnosis or during treatment
- Unemployed: if primary occupation within the year prior to TB treatment was “unemployed”
- Uninsured: if no health insurance during TB treatment, separately for clinic and hospitalization
- Smoker: if patient smoked at least once within the year prior to clinic intake or hospitalization
- Long-term-care facility resident: if the patient was a resident of a long-term-care facility at TB diagnosis or within 3 months prior to TB treatment start

The following data analyses were performed:

- Compared the representativeness of study data with National TB Surveillance System (NTSS) data¹
- Examined homelessness prior to TB, during TB treatment, housing assistance
- Examined unemployment prior to TB, because of TB
- Summarized DST testing by medication, initial resistance, ever resistance, and acquired resistance
- Calculated the median number of DSTs on medications, median number of medications having resistance
- Assessed associations with pre-XDR and XDR combined vs. other MDR patients
- Examined resistance patterns by country of birth, compared with NTSS all-TB data by country of birth
- Identified medications to which resistance was acquired during treatment
- Identified factors associated with any acquired resistance
- Calculated the percentage of patients diagnosed while hospitalized
- Assessed symptoms
- Calculated the median days to initial diagnosis
- Calculated the median months of infectiousness
- Calculated the percentage of patients on each medication at any time during treatment
- Calculated the medication changes per patient, reasons
- Examined whether patients were hospitalized, the number of hospitalizations, and reasons for hospitalization
- Calculated the outpatient DOT use per medication
- Calculated the number of medications taken prior to culture conversion to which the patient’s isolate was never resistant

- Calculated the median days from medications start to 5-drug regimen start, 5-drug regimen to culture conversion, any regimen to culture conversion, 5-drug regimen to treatment stop, by drug resistance pattern
- Calculated the median treatment length and by resistance pattern and 5-drug regimen
- Identified factors associated with treatment longer than 2 years after culture conversion
- Assessed culture conversion by resistance pattern and by number of effective medications prior to culture conversion
- Analyzed treatment outcomes by resistance pattern, comparison with US MDR/XDR and U.S. drug-susceptible cases
- Calculated the number of days to TB-related death, by 5-drug regimen and for HIV+ by highly active antiretroviral treatment (HAART)
- Calculated the median days on effective medications before and after culture conversion by resistance pattern
- Identified characteristics associated with death during treatment
- Calculated the median and average number of adverse events by resistance pattern and association with individual and combined medications
- Calculated the median days of inpatient (inpatient days, respiratory isolation) and outpatient care (total outpatient, DOT days, outpatient isolation)
- Measured the number of outpatient procedures: chest radiographs, smears, cultures
- Assessed receipt of expert consultation, associations with expert consultation
- Calculated case management usage types and frequency
- Assessed use of interpreters by non-English speaking patients
- Analyzed impairment during treatment

Cost Analysis: Inpatient Cost Estimation

From total charges per TB-related hospitalization that were collected, inpatient costs were calculated by:

- Converting all charges to 2010 inflation-adjusted dollars using the Consumer Price Index for Medical Care²
- Converted charges to costs by multiplying the charges by each hospital's cost-to-charge ratio³
 - If a specific hospital's cost-to-charge ratio was unavailable, we used operating-cost-to-charge ratio average for the state (CA=0.32, NY=0.46, TX=0.40)
- Converted site-specific costs, using Medicare Geographic Adjustment Factors⁴ as the cost-of-living adjustment factor, to a US basis for aggregation (CA=1.13, NY=1.08, TX=0.94)
- Added in physician costs for each hospitalization day from the 2009 Physicians' Fee and Coding Guide of \$238.50 for the first day of hospitalization at Level 2,⁵ converted to a cost by multiplying by the average cost-to-charge ratio for pulmonary diseases 0.502,⁶ updated to 2010 dollars using the Medical Care CPI,² for a value of \$123.81. The remaining hospitalization days were calculated similarly from a 2009 charge of \$131 to a cost of \$68/day.
- For 17 patients for whom we were not able to obtain detailed hospital data, the length of stay (which was obtained for all patients) was multiplied by an average cost per day (\$1419) for hospitalizations for which we did have data

Cost Analysis: Outpatient Cost Estimation

Outpatient costs were estimated as follows:

- Computed the number of outpatient days of treatment
- Estimated outpatient diagnosis costs, using numbers of chest radiographs (2 views \$30.97), computed tomographies (\$308.99), AFB smears (\$7.70), *M.tuberculosis* cultures (\$15.48), DSTs (\$8.10), and other diagnostic tests, and applied Centers for Medicare and Medicaid Lab Schedule Fees⁷
- Often, DOT visits were not specified as taking place at the clinic or at home, so we estimated that 11% of DOT visits occurred in the clinic (5 days/week for 6 weeks=30 visits, plus 25 visits for the remaining 490 work days of a 2-year period of 520 work days), and the remaining 89% of DOT visits occurred in the patient's home. Costs for a home DOT visit (\$32.70) were estimated using the 2001 Physicians' Fee and Coding Guide Medicare Allowable Charge for a home DOT visit by a nurse (\$49)⁸ and updating it to 2010 dollars using the change in home health care average weekly earnings² and converting it to a cost by multiplying by 50.2%, the average cost to charge ratio for pulmonary diagnostic related group (DRG)⁶: $(49 * (484.58 / 364.51) * .502)$). Costs for clinic DOT visits (\$38.63) were estimated using the 2009 Physicians' Fee and Coding Guide average outpatient physician visit charge for an established level 2 patient (\$58.67 for Level 2 patient⁵), then updated to 2010 dollars using the CPI/MC, converted to a cost by multiplying by 0.502, plus 15 minutes of a nurse based on the cost of an outpatient DOT visit: $(58.67 * (388.436 / 375.613) * .502) + (.25 * (49 * (484.58 / 364.51) * .502))$.
- Estimated outpatient medication costs by multiplying the total outpatient mg. of each medication by its Red Book average wholesale price per mg.⁹ Added therapeutic monitoring costs (CBC \$11.14, LFT \$11.70), according to the Drug-Resistant Tuberculosis Survival Guide for Clinicians,¹⁰ for those on CYC, AMK, CAP, KAN.

Costs per mg by medication were:

- o INH=(0.000517778)
- o RIF=(0.006702778)
- o RBT=(0.102664)
- o RPT=(0.02765)
- o PZA=(0.002381)
- o EMB=(0.004448)
- o SM=(0.00432)
- o CAP=(0.175)
- o KAN=(0.006041667)
- o AMK=(0.06771)
- o CIP=(0.0026254)
- o LEV=(0.0385332)
- o MOX=(0.048954167)
- o GAT=(0.10723)
- o ETH=(0.0168836)
- o PAS=(0.000934417)
- o CYC=(0.024)
- o CLO=(0.2022)
- o LIN=(0.194871667)
- o CLR=(0.008477)

- o AZI=(0.04242)
- Estimated, using Centers for Medicare and Medicaid Lab Schedule Fees,⁷ outpatient lab tests for baseline tests (CBC with WBC differential [\$11.14], comprehensive metabolic panel \$15.14, LFT [\$11.70], HIV EIA initial [\$19.65] and follow-up Western Blot test [\$38.35] if positive, TSH [\$24.06] if on CYC or ETH, and 6 drug levels [\$21.59] for those on CAP, KAN, AMK, SM, or CYC). Estimated ongoing lab tests, based on the MDR-TB Survival Guide,¹⁰ for those on treatment longer than one week (monthly CBC, monthly LFT, monthly comprehensive metabolic panel for those on CAP, KAN, AMK, SM, monthly audiometry [\$34.38] if on AMK, CAP, KAN, SM, monthly visual function screening [\$3.06] if on EMB, CLO, RBT, LIN, quarterly TSH for those on CYC, ETH, PAS)
- Estimated case management costs, based on the frequency of each type of case management.
 - o Transportation costs were estimated at \$20/week in LA, \$29/week in NYC, \$17.50/week in TX.
 - o Housing costs were estimated at \$31/day in CA, \$37/day in NY, \$19/day in TX.¹¹
 - o Social worker costs were estimated at \$23.95 for 2 days consultation.¹²
 - o Interpreters were estimated at \$21.73/hour¹²
- Calculated outpatient direct costs as the sum of outpatient diagnosis, outpatient DOT, outpatient medication, outpatient lab, and case management costs.

Cost Analysis: Total Direct Cost Estimation

Estimated total direct costs as the sum of outpatient direct costs and inpatient direct costs.

Cost Analysis: Productivity Loss Estimation

Estimated productivity losses as follows:

- o Calculated a disability adjustment based on responses to Adverse Events variable on the clinic form, 100% divided into 6 segments (100%, 83%, 67%, 50%, 33%, 17%)
- o Estimated inpatient productivity losses as follows: Applied a value of work plus home production, updated to 2010 dollars using the change in average hourly earnings,¹³ at \$224/day for employed patients, and just home production (\$40) for non-employed to each day hospitalized¹⁴
- o Estimated outpatient productivity losses as follows: ½ day for each DOT day, a full day if in outpatient isolation, times the disability adjustment factor for all remaining outpatient days
- o Estimated one year of productivity losses for one year after treatment for one person who had documentation, at 50% disability, and discounted it using a 3% social discount rate.
- o For TB-related deaths (9/13 deaths), applied a value of remaining lifetime productivity, updated to 2010 dollars using the change in average hourly earnings,¹⁵ based on the age at death¹⁴
- o Estimated total productivity loss as the sum of inpatient productivity loss, outpatient productivity loss, after treatment productivity loss, and productivity loss due to premature death.

Cost Analyses

- Estimated 3 illness severity categories similar to analysis done in the previous TB hospitalization study:
 - o Category 1= those who died from TB-related causes
 - o Category 2= any comorbidities, pregnancy, disseminated or extensive disease
 - o Category 3= all remaining cases
- Calculated average costs by resistance pattern, by illness severity, and for each cost category
- Identified characteristics associated with high direct and societal costs
- Estimated U.S. MDR/XDR direct and direct-plus-productivity-loss costs during 2005-2007 by applying average costs per study patient to the U.S. cohort of cases during the period.
- Assessed who paid the costs by public sector/private sector insurance

Study Definitions

Initial diagnosis: earliest of TB medication start, collection of first positive specimen (AFB-smear, M. tuberculosis culture, PCR, HPLC, or NAA), or report date (date the health department first suspected a patient had TB)

First-line TB Medications: isoniazid (INH), rifampin (RIF), rifabutin (RBT), pyrazinamide (PZA), ethambutol (EMB), streptomycin (SM),

Second-line TB Medications: capreomycin (CAP), kanamycin (KAN), amikacin (AMK), any second-line injectable (INJ), ciprofloxacin (CIP), ofloxacin (OFL), levofloxacin (LEV), moxifloxacin (MOX), gatifloxacin (GAT), any fluoroquinolone (FQ), ethionamide (ETH), para-aminosalicylic acid (PAS), cycloserine (CYC),

Third-line TB Medications: clofazimine (CLO), linezolid (LIN), clarithromycin (CLR), azithromycin (AZI)

MDR TB: resistance to at least INH and RIF

Initial resistance: any resistance found on the initial TB isolate cultured within 30 days of specimen collection in the U.S.

Acquired resistance: any resistance found after a documented prior susceptible culture

Resistance patterns, mutually exclusive:

- INH/RIF/RBT-only
- INH/RIF/RBT-plus other resistance to any of the following: PZA, EMB, SM, PAS, ETH, or CYC (excluding total first-line resistance)
- Total First-line: resistance to INH, RIF, PZA, and EMB
- Pre-XDR: MDR TB plus resistance to a FQ or an INJ
- XDR: MDR TB plus resistance to both a FQ and a INJ

5-drug-regimen: an INJ, a FQ, and ≥ 3 other medications to which M. tuberculosis was never resistant

Infectious period: began 12 weeks before earliest of first symptom, first medication, first positive specimen collection, or report date; ended at culture conversion, or, if no culture conversion, censored at medications stop

Date of culture conversion: After the last positive-sputum-culture, the first date (≥ 7 days after last positive) of 2 consecutive negative-sputum-culture results

Disseminated disease: ≥ 2 non-contiguous sites of disease

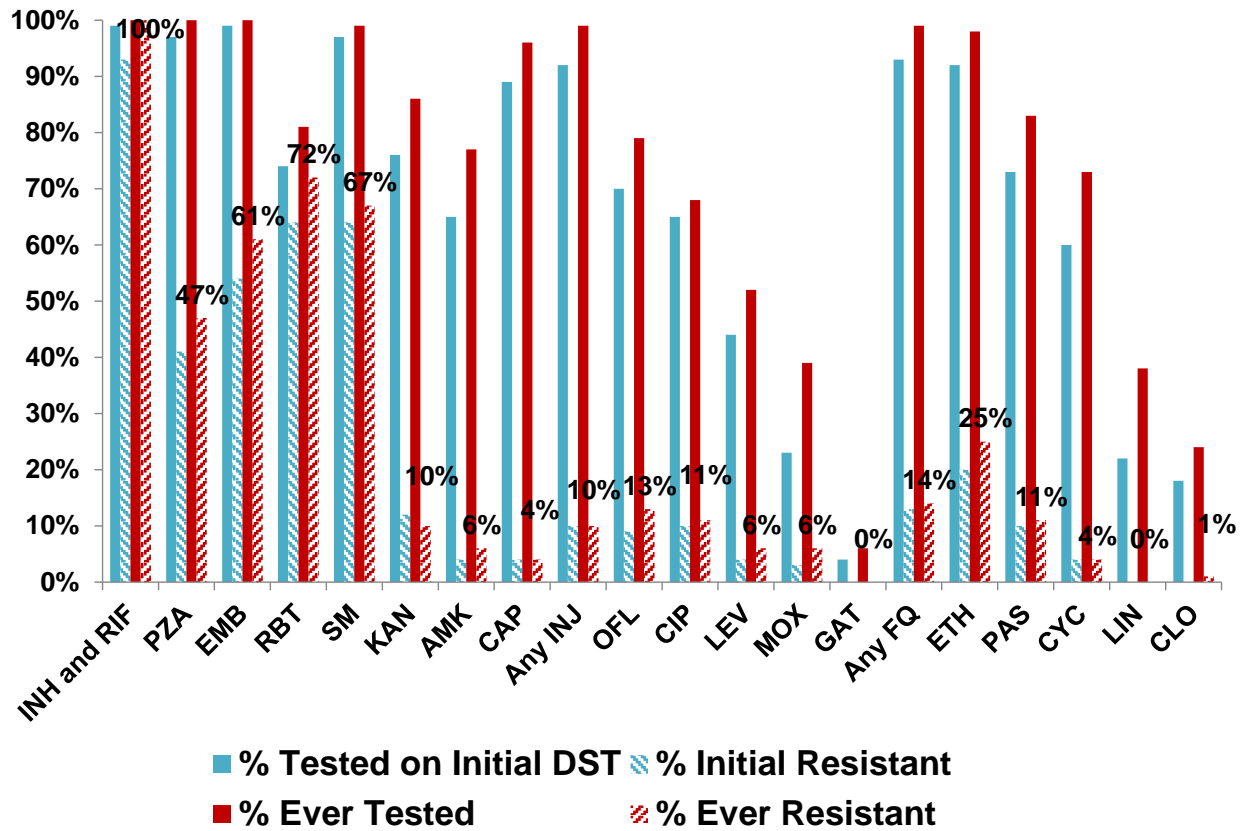
Extensive disease: incapacitating, preventing normal everyday activities

Moderate disease: sufficiently discomforting to interfere with normal everyday activities

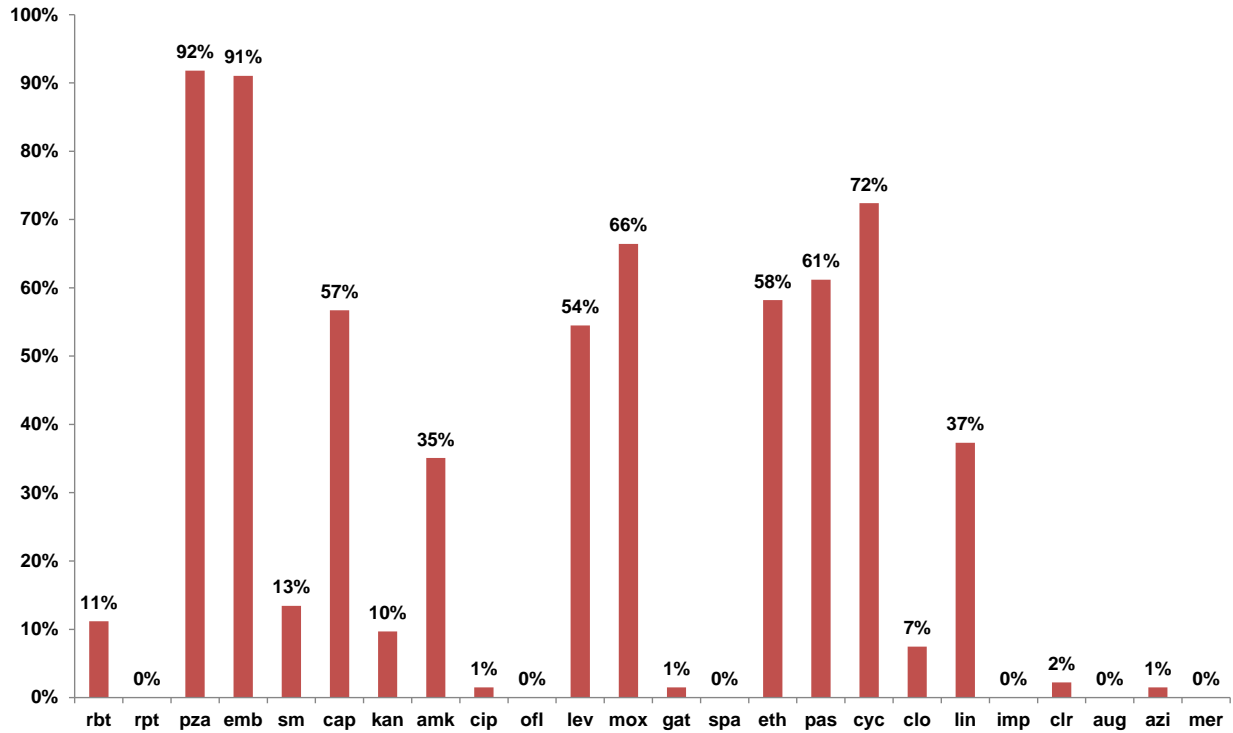
Minimal disease: causing minimal discomfort, easily tolerated, not interfering with everyday activities

Additional Results

Percent of Patients Having Isolates Tested within 30 days of Medications Start and Resistance to Medications, N=134

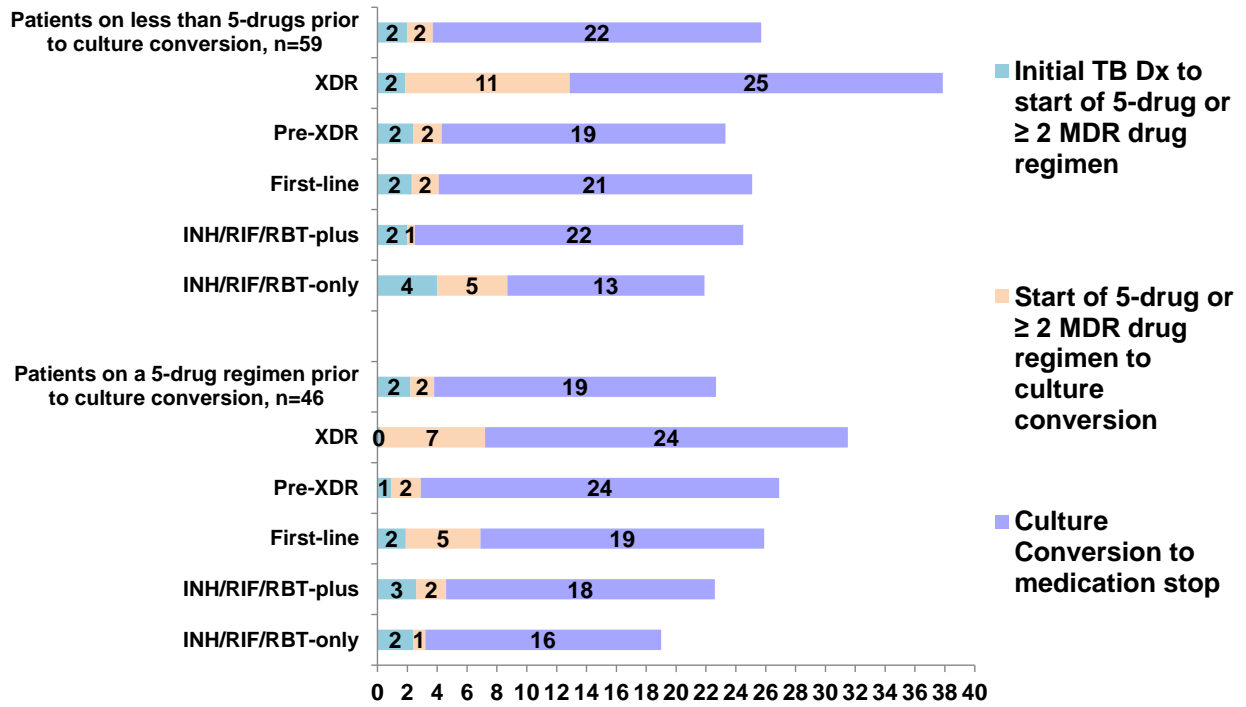


**Percentage of Patients on Various Medications at Any Time During Treatment
(N= 134 patients)***



* 1 patient was diagnosed at death and was not started on medications

Median Months to Event



Acquired Resistance Multivariate Models

Variable	Initial	Initial	Initial	Pr > ChiSq	Final	Final	Final	Final	
	95%	95%	95%		95%	95%	95%	95%	
	Odds Ratio	Confidence	Confidence		Odds Ratio	Confidence	Confidence	Odds Ratio	
Estimate	Lower Limit	Upper Limit	Estimate	Lower Limit	Upper Limit	Estimate	Lower Limit	Upper Limit	Pr > ChiSq
Age 65 or over	<0.001	<0.001	>999.999	0.973					
Black race	33.19	0.80	>999.999	0.065	4.07	1.08	15.37	0.039	
Recent homelessness	18.76	0.93	377.71	0.056	5.81	1.17	28.86	0.031	
Pre-XDR or XDR TB	8.78	2.31	33.42	0.001	5.15	1.86	14.21	0.002	
AFB smear positive	5.34	0.86	33.22	0.072					
Age 25-44 years	4.83	0.65	36.03	0.124					
Hispanic ethnicity	4.83	0.11	216.20	0.417					
≥ 4 effective medications	3.46	0.41	29.47	0.256					
Age 45-64 years	3.41	0.39	30.21	0.271					
Asian race	3.35	0.07	151.32	0.534					
Disseminated TB disease	2.28	0.21	24.20	0.495					
Foreign born	2.10	0.15	28.64	0.577					
Recent cigarette smoker	1.96	0.41	9.31	0.397					
Recent excess alcohol use	0.99	0.13	7.65	0.988					
TB clinic outpatient management	0.98	0.18	5.35	0.980					
Recent unemployment	0.97	0.24	3.93	0.964					
Cavitary disease	0.77	0.21	2.84	0.694					
Diabetes	0.76	0.16	3.70	0.732					
History of TB disease	0.44	0.12	1.59	0.208					
HIV infection	0.39	0.03	4.92	0.463					
Recent injecting-drug or non-injecting-drug use	0.15	0.00	5.08	0.291					
Model Fit Statistics									
	Initial Model	Final Model							
	Intercept	Intercept							
	and	and							
Criterion	Covariates	Covariates							
AIC	136.392	116.619							
SC	198.964	127.996							
-2 Log L	92.392	108.619							

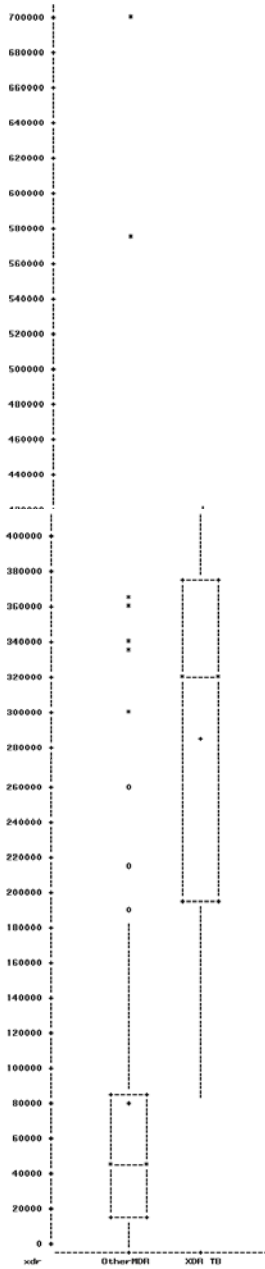
Death During TB Treatment Multivariate Model A

Death During Treatment Model A		Initial	Initial			Final	Final	
	Initial	95%	95%		Final	95%	95%	
	Odds Ratio	Confidence	Confidence	Initial	Odds Ratio	Confidence	Confidence	Final
Variable	Estimate	Lower Limit	Upper Limit	Pr > ChiSq	Estimate	Lower Limit	Upper Limit	Pr > ChiSq
Recent cigarette smoker	>999.999	2.60	>999.999	0.023	6.39	1.04	39.41	0.046
Age 45-64 years	>999.999	<0.001	>999.999	0.924				
Age 25-44 years	>999.999	<0.001	>999.999	0.947				
Age 65 or over	>999.999	<0.001	>999.999	0.890	20.21	2.26	180.98	0.007
Recent excess alcohol use	690.52	0.16	>999.999	0.126				
Foreign born	303.05	0.10	>999.999	0.164				
HIV infection	99.82	0.09	>999.999	0.201	6.31	1.05	37.73	0.044
TB clinic outpatient management	17.19	0.13	>999.999	0.251				
Hispanic ethnicity	17.14	0.00	>999.999	0.567				
Black race	14.02	0.00	>999.999	0.565				
Asian race	6.00	0.00	>999.999	0.682				
Disseminated TB disease	2.23	0.01	852.99	0.792				
Recent unemployment	0.83	0.05	14.21	0.900				
Recent homelessness	0.48	0.00	82.71	0.777				
Pre-XDR or XDR TB	0.36	0.01	16.56	0.598				
History of TB disease	0.26	0.01	6.02	0.401				
Diabetes	0.04	<0.001	12.94	0.268				
Male	0.02	<0.001	2.40	0.107				
Recent injecting-drug or non-injecting-drug use	0.01	<0.001	12.50	0.186				
Pregnant	0.00	<0.001	>999.999	0.990				
Correctional inmate	<0.001	<0.001	>999.999	0.971				
Model Fit Statistics								
	Initial Model	Final Model						
	Intercept	Intercept						
	and	and						
Criterion	Covariates	Covariates						
AIC	72.127	56.51						
SC	135.88	68.101						
-2 Log L	28.127	48.51						

Death During TB Treatment Multivariate Model B

Variable	Initial	Initial Pr > ChiSq	Final	Final	Final	Final
	Odds Ratio Estimate		Odds Ratio Estimate	Confidence Lower Limit	Confidence Upper Limit	Confidence 95%
Age ≥65	0.00	0.9774	61.926	3.099	>999.999	0.0069
Age ≥65*Excess alcohol	1.00
Age ≥65*Black race	1.00
Age ≥65*effluorom	1.00
Age ≥65*effective INJ med	>1000	0.9983
Age ≥65*Foreign born	1.00
Age ≥65*HIV-infection	1.00
Age ≥65*Homeless	1.00
Age ≥65*Hispanic	1.00
Age ≥65*IDU or NIDU	1.00
Age ≥65*Smoker	>1000	0.9984
Age ≥65*TB clinic	>1000	0.9791
Age ≥65*TB history	0.00	0.9774
Excess alcohol	0.00	0.9986
Excess alcohol*effective FQ med	1.00
Excess alcohol*effective INJ med	1.00
Excess alcohol*Smoker	>1000	0.9986
Excess alcohol*TB clinic	1.00
Excess alcohol*TB history	1.00
Black race	0.02	0.9959
Black race*Excess alcohol	1.00
Black race*effective FQ med	1.00
Black race*effective INJ med	0.00	0.9996
Black race*Foreign born	>1000	0.9994
Black race*HIV-infection	>1000	0.9996
Black race*Homeless	0.00	0.9968
Black race*IDU or NIDU	1.00
Black race*Smoker	>1000	0.9994
Black race*TB clinic	1.32	0.9992
Black race*TB history	1.00
effective FQ med	0.00	0.9792
effective INJ med	0.00	0.9629	0.017	0.002	0.176	0.0006
effective INJ med*effective FQ med	>1000	0.976
Foreign born	1.26	0.9997
Foreign born*Excess alcohol	0.05	0.9964
Foreign born*effective FQ med	1.00
Foreign born*effective INJ med	1.00
Foreign born*HIV-infection	>1000	0.9996
Foreign born*Homeless	1.00
Foreign born*IDU or NIDU	>1000	0.9983
Foreign born*Smoker	1.71	0.9991
Foreign born*TB clinic	4.60	0.998
Foreign born*TB history	1.00
HIV-infection	0.00	0.9995
HIV-infection*Excess alcohol	>1000	0.9983
HIV-infection*effective FQ med	1.00
HIV-infection*effective INJ med	1.00
HIV-infection*Homeless	>1000	0.9972
HIV-infection*IDU or NIDU	0.00	0.9976
HIV-infection*Smoker	0.05	0.9965
HIV-infection*TB clinic	1.00
HIV-infection*TB history	>1000	0.9982
Homeless	>1000	0.9969
Homeless*Excess alcohol	>1000	0.9982
Homeless*effective FQ med	1.00
Homeless*effective INJ med	1.00
Homeless*IDU or NIDU	1.00
Homeless*Smoker	>1000	0.9996
Homeless*TB clinic	1.00
Homeless*TB history	1.00
Hispanic	6.79	0.9978
Hispanic*Excess alcohol	>1000	0.9984
Hispanic*Black race	1.00
Hispanic*effective FQ med	0.01	0.9905
Hispanic*effective INJ med	71.72	0.9907
Hispanic*Foreign born	0.14	0.9975
Hispanic*HIV-infection	56.90	0.9965
Hispanic*Homeless	0.00	0.9969
Hispanic*IDU or NIDU	0.00	0.999
Hispanic*Smoker	0.52	0.9978
Hispanic*TB clinic	1.39	0.9984
Hispanic*TB history	2.03	0.9956
IDU or NIDU	>1000	0.9991
IDU or NIDU*Excess alcohol	0.00	0.9977
IDU or NIDU*effective FQ med	1.00
IDU or NIDU*effective INJ med	1.00
IDU or NIDU*Smoker	1.00
IDU or NIDU*TB clinic	1.00
IDU or NIDU*TB history	1.00
male	0.00	0.9755
male*Age ≥65	0.00	0.9994
male*Excess alcohol	10.85	0.996
male*Black race	1.68	0.9985
male*effective FQ med	>1000	0.9742
male*effective INJ med	42.97	0.9916
male*Foreign born	0.46	0.9989
male*HIV-infection	65.29	0.9963
male*Homeless	0.00	0.998
male*Hispanic	2.69	0.9937
male*IDU or NIDU	>1000	0.9982
male*Smoker	0.46	0.9984
male*TB clinic	1.17	0.9992
male*TB history	2.74	0.9934
Smoker	1.73	0.999	19.387	2.727	137.817	0.0031
Smoker*effective FQ med	1.00
Smoker*effective INJ med	1.00
Smoker*TB clinic	1.12	0.9997
Smoker*TB history	0.53	0.9979
TB clinic	0.22	0.9981
TB clinic*effluorome	0.14	0.9911
TB clinic*effective INJ med	5.50	0.9957
TB history	0.07	0.9948
TB history*effective FQ med	0.27	0.9939
TB history*effective INJ med	36.59	0.9924
TB history*TB clinic	1.05	0.9997
Model Fit Statistics						
	Initial Model	Final Model				
Criterion	Intercept and Covariates	Intercept and Covariates				
AIC	140.006	40.932				
SC	342.855	82.524				
-2 Log L	0.006	32.932				

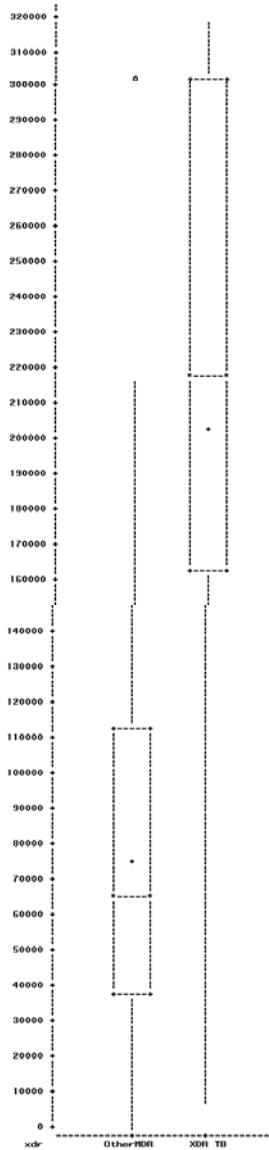
Inpatient Direct Costs



Standard error of the mean:

Other MDR	12,200
XDR	70,829

Outpatient Direct Costs

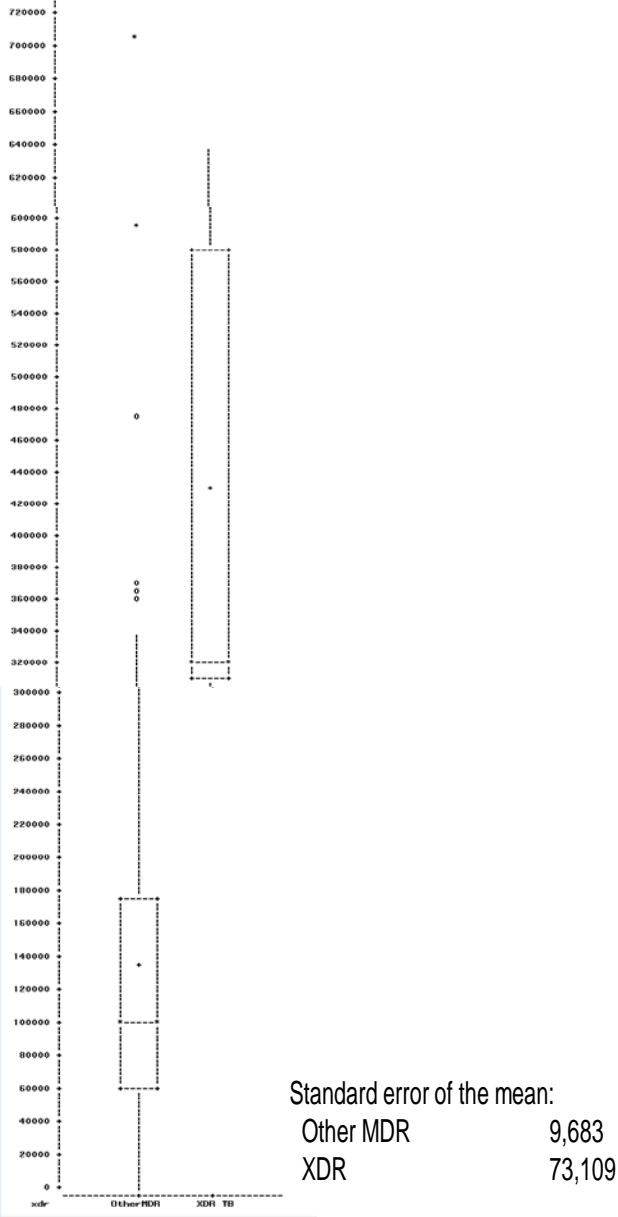


Standard error of the mean:

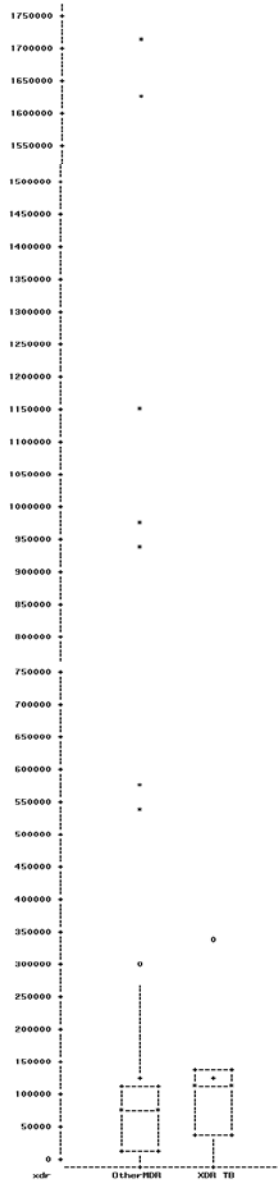
Other MDR 4,991

XDR 56,374

Total Direct Costs

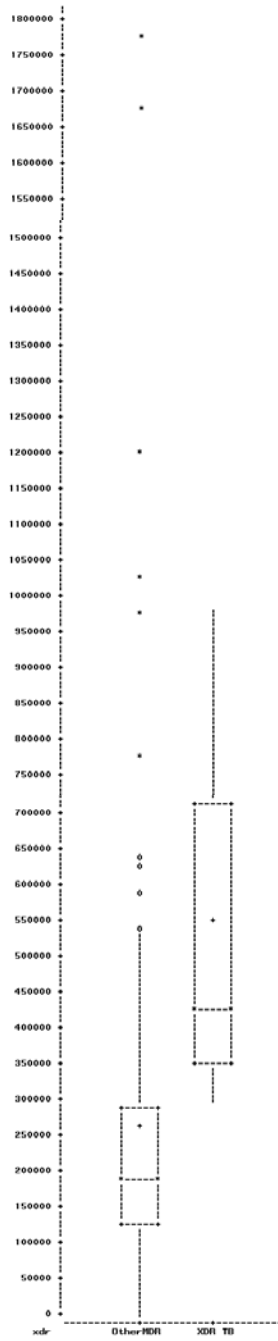


Productivity Losses



Standard error of the mean:
 Other MDR 22,520
 XDR 59,594

Direct Costs and Productivity Losses



Standard error of the mean:

Other MDR 23,212

XDR 127,707

MDR-TB Direct Costs Multivariate Model

Variable	Initial	Initial Pr > F	Final	Final	Final F Value	Final Pr > F
	Parameter Estimate		Parameter Estimate	Standard Error		
Intercept	29,310	0.559	80,807	11,139	52.620	<.0001
XDR TB	242,811	<.0001	219,438	42,494	26.670	<.0001
Long-term care facility resident	208,619	0.003	182,545	64,022	8.130	0.005
Recent non-injecting-drug use	119,934	0.065	112,203	42,984	6.810	0.010
Black race	86,395	0.054				
HIV infection	58,745	0.135	69,368	33,234	4.360	0.039
Asian race	54,566	0.238				
Recent homelessness	44,402	0.314				
Public insurance	43,185	0.053	57,221	17,052	11.260	0.001
Hispanic ethnicity	41,324	0.371				
Total firstline resistance	28,626	0.196				
Foreign born	11,142	0.747				
Male	9,828	0.606				
Pre-XDR TB	9,263	0.712				
Diabetes	3,845	0.889				
No. of days hospitalized	451	<.0001	426	60	50.540	<.0001
Recent injecting-drug use	-324,397	0.000	-315,716	70,089	20.290	<.0001
Recent excess alcohol use	-78,044	0.033	-74,682	33,009	5.120	0.026
Age 45-64 years	-34,156	0.240				
Age 65 or over	-30,517	0.487				
Correctional inmate	-24,708	0.632				
Recent unemployment	-14,145	0.535				
Age 25-44 years	-14,492	0.568				
Native Hawaiian/Other Pacific Islander	-1,829	0.986				
Model Statistics	Adj R-Square=.52		Adj R-Square = 0.55			
Analysis of Variance						
Source	Degrees of freedom		Sum of Squares	Mean Square	F Value	Pr > F
Model	8		1,160,877,000,000	145,109,600,000	18.84	<.0001
Error	111		854,750,200,000	7,700,452,335		
Corrected	119		2,015,627,000,000			

MDR-TB Direct Costs and Productivity Losses Multivariate Model

	Initial		Final	Final		
Variable	Parameter	Initial	Parameter	Standard	Final	Final
	Estimate	Pr > F	Estimate	Error	F Value	Pr > F
Intercept	41,006	0.688	175,161	27,059	41.900	<.0001
Died	837,849	<.0001	810,082	82,887	95.520	<.0001
XDR TB	322,504	0.001	315,817	91,413	11.940	0.001
Recent non-injecting-drug use	188,405	0.158	240,819	93,512	6.630	0.011
Hispanic ethnicity	151,102	0.112				
HIV infection	144,532	0.084	151,514	71,251	4.520	0.036
Asian race	137,699	0.154				
Native Hawaiian/Other Pacific Islander	104,329	0.628				
Diabetes	83,578	0.140	123,628	47,944	6.650	0.011
Male	63,478	0.104	65,679	35,964	3.340	0.071
Recent injecting-drug use	91,371	0.588				
Black race	52,318	0.566				
Public insurance	57,079	0.209				
Total firstline resistance	24,606	0.584				
Age 25-44 years	37,381	0.470				
No. of days hospitalized	525	0.000	424	128	11.020	0.001
Age 65 or over	-379,300	0.000	-428,817	80,756	28.200	<.0001
Long-term care facility resident	-357,057	0.020	-280,788	137,546	4.170	0.044
Correctional inmate	-158,124	0.134	-180,258	91,947	3.840	0.053
Recent excess alcohol use	-149,285	0.049	-179,858	67,536	7.090	0.009
Age 45-64 years	-67,604	0.253	-123,917	39,748	9.720	0.002
Recent unemployment	-68,354	0.146				
Pre-XDR TB	-50,252	0.328				
Foreign born	-35,118	0.627				
Recent homelessness	5,003	0.956				
Model Statistics	Adj R-Square=.64		Adj R-Square = 0.66			
Analysis of Variance						
Source	Degrees of freedom		Sum of Squares	Mean Square	F Value	Pr > F
Model	12		7,719,364,000,000	643,280,300,000	19.91	<.0001
Error	107		3,456,381,000,000	32,302,623,791		
Corrected	119		11,175,740,000,000			

Estimate of the Average Cost of Non-MDR TB, 2010 U.S. Dollars									
Site	Avg hospitalization length	1998\$ avg cost per patient hospitalized*	2010\$ avg cost per patient hospitalized**	2010\$ hospital physician cost***	2010\$ avg total hospitalization cost per patient	Weight	2010\$ weighted avg cost per pt. hospitalized	2010\$ outpatient cost per patient****	2010\$ avg cost per TB patient*****
1	17	\$11,987	\$19,233	\$1,290	\$20,523	6.2	\$127,485	\$3,419	
2	37	\$22,518	\$36,130	\$2,605	\$38,735	12.2	\$473,212	\$3,419	
3	35	\$12,231	\$19,623	\$2,474	\$22,097	7.1	\$157,255	\$3,419	
4	15	\$13,631	\$21,871	\$1,159	\$23,030	10.8	\$248,245	\$3,419	
5	22	\$15,114	\$24,250	\$1,619	\$25,869	5.5	\$141,508	\$3,419	
6	20	\$17,651	\$28,320	\$1,487	\$29,808	13.6	\$404,616	\$3,419	
7	24	\$17,009	\$27,290	\$1,751	\$29,040	14.1	\$409,356	\$3,419	
8	36	\$22,316	\$35,806	\$2,540	\$38,345	17.9	\$685,538	\$3,419	
9	23	\$10,438	\$16,746	\$1,685	\$18,431	13.8	\$254,907	\$3,419	
10	16	\$11,970	\$19,205	\$1,224	\$20,429	14.7	\$299,492	\$3,419	
Total						115.8	\$3,201,614		
Average							\$27,640	\$3,419	\$16,963
* From reference 16: 49% of TB patients were hospitalized; included MDR TB costs for 13/733 hospitalized patients									
** Converted from 1998 dollars to 2010 dollars using the consumer price index for medical care (388.436/242.1) reference 2									
*** Average of lower and upper physician fees (reference 5) for one day of initial hospital care (\$206,\$271)=\$238, and remaining days at Level 2 subsequent care (\$113,\$149)=\$131, converted to a cost using the cost-to-charge ratio for the respiratory Diagnostic Related Group (reference 6), multiplied by 0.502									
**** From reference 17, \$2985 from Nashville, TN, adjusted to a US basis using the Census Bureau Cost of Living Index 87.3 (reference 18)									
***** (Weighted average hospitalization cost X 49% of patients hospitalized)+average outpatient cost									

References

- Centers for Disease Control and Prevention. Online TB Information System (OTIS 2009, wonder.cdc.gov/TB-v2009.html), accessed March 2012.
- Bureau of Labor Statistics. Consumer Price Index—all urban consumers, medical care. Series ID CUUR0000SAM. [cited February 21, 2012] <http://data.bls.gov/cgi-bin/srgate>
- Centers for Medicare and Medicaid Services. 2005 Operating cost to charge ratios (OPCCR). FY2005 Impact file (inpatient prospective payment system) [cited May 12, 2010]. <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PCPricer/index.html?redirect=/pcpricer>
- Centers for Medicare and Medicaid Services. 2005 Medicare geographic adjustment factors. [cited May 12, 2010] http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Geographic-Variation/GV_PUF.html
- Mag Mutual Healthcare Solutions, Inc. 2009 Physicians' fee & coding guide. Duluth (GA). 2008.
- The Diagnosis-Related Group Handbook. comparative clinical and financial standards. Ernst & Young LLP. Washington, DC. 1998:21.

7. Centers for Medicare and Medicaid Services. Clinical laboratory fee schedule [cited February 9, 2012].
www.cms.gov/Medicare/Medicare-Fee-For-Service-Payment/Clinicallabfeesched/index.html
8. Health Care Consultants of America, Inc. 2001 Physicians Fee and Coding Guide. Augusta, Georgia. 2002.
9. Red Book Online. Thompson and Reuters Red Book. Average wholesale prices [cited 2012 Mar].
www.micromedexsolutions.com
10. Francis J. Curry National Tuberculosis Center and California Department of Public Health. Drug-Resistant Tuberculosis: A Survival Guide for Clinicians. 2nd ed.; 2008.
11. US Department of Housing and Urban Development. Fair Market Rents.
<http://www.huduser.org/portal/datasets/fmr.html>
12. US. Department of Labor. Wages, earnings, and benefits [cited 2012 Feb].
<http://www.dol.gov/dol/topic/statistics/wagesearnings.htm>
13. Bureau of Labor Statistics. Average Hourly Earnings of Production and Nonsupervisory Employees; Series CEU0500000008.
14. Grosse SD. Appendix I: productivity loss tables. In Haddix AC, Teutsch SM, Corso PS, editors. Prevention effectiveness: a guide to decision analysis and economic evaluation. 2nd ed. Oxford University Press; New York, New York. 2003:245-257.
15. Taylor Z, Marks SM, Rios Burrows NM, Weis SE, Stricof RL, Miller B. Causes and Costs of hospitalization of tuberculosis patients in the United States. *Int J Tuberc Lung Dis.* 2000;4:931–9.
[PubMed](#)
16. Shepardson D, Marks SM, Chesson H, Kerrigan A, Holland DP, Scott N, et al. Cost-effectiveness of a 12-dose regimen for treating latent tuberculosis infection in the United States. *Int J Tuberc Lung Dis.* 2013;17:1531–7. [PubMed](#) <http://dx.doi.org/10.5588/ijtld.13.0423>
17. ACCRA Cost of Living Index. Annual Average 2010 via U.S. Census Bureau
http://www.census.gov/compendia/statab/cats/prices/consumer_price_indexes_cost_of_living_index.html accessed 02/05/2014.