

Online Appendix for “The Programmatic Benefits and Costs of Using MTD Nucleic Acid Amplification Testing to Diagnose Tuberculosis Disease in the U.S.”

Additional Description of Methods

Description of Patient Evaluation and MTD

Clinicians generally defined patients suspected of having pulmonary TB as persons who exhibited symptoms of respiratory TB disease or, if asymptomatic, had clinical and radiologic findings consistent with pulmonary TB (e.g., SP, abnormal chest radiograph, MTD positive) or were at moderate/high clinical suspicion for TB disease because of exposure and inclusion in a risk group (HIV infected, homeless, incarcerated, etc.). However, individual providers, hospitals, and laboratories use their own judgment in ordering or performing diagnostic tests. The State public laboratories in Georgia, Maryland, and Massachusetts all had protocols to conduct MTD on all smear-positive specimens. The study included only patients suspected of TB who were reported to the public health system from the project catchment areas of each participating site. Only sites that had full capture of AFB-smear and *Mycobacterium-tuberculosis*-culture results were eligible to participate in the evaluation study. Since data on patients suspected of TB are not reported to CDC, each site conducted specific procedures to obtain data, as described below.

Georgia collaborated with the epidemiology department at Grady Memorial Hospital, a public health hospital that cares for most TB patients in Fulton and DeKalb counties and sees a highly HIV-prevalent population, to obtain data on persons suspected of TB. MTDs are conducted at Grady on all SP respiratory specimens to help exclude TB and on high suspicion SN specimens to consider TB. For patients suspected of TB but not identified by Grady

Hospital, Georgia collaborated with the Georgia Department of Human Resources to obtain data.

In Hawaii, in accordance with Hawaii law, all persons suspected of TB, including those seen in the private sector, are reported to the Hawaii Department of Health (DOH) TB Branch within 24 hours. The majority (70%) of persons suspected of TB are reported to the DOH by the DOH TB Clinic, which also houses the TB Registry. Patients suspected of having TB by the DOH are identified through administrative screening, evaluation of recent immigrants, TB contact investigation, or through referrals to the DOH TB Clinic from private doctors. Clinical data of patients suspected of TB were abstracted from the DOH TB Clinic charts and/or electronic tracking system. Most specimens were analyzed for *M. tuberculosis* by one private commercial laboratory, which along with other laboratories sent specimen results to the DOH TB Registry.

In Massachusetts, the state laboratory conducted most MTD, with the remainder performed by individual hospitals or by commercial laboratories. Once a suspect was reported to the public health system, Massachusetts reviewed daily reports and gathered needed information by contacting multiple providers and laboratories.

Maryland officially defined persons suspected of TB as having a lab-confirmed AFB-positive smear or biopsy report consistent with active TB disease, an abnormal chest radiograph suggestive of active TB, or having initiated \geq two anti-TB medications. Persons suspected of TB were immediately reported to the Maryland DOH and materials submitted. However, the

timing of suspect reporting varied according to clinician discretion and whether state or private laboratories were used. If private laboratories were used, the suspect was referred to the local DOH TB clinic where the provider collected new specimens if the patient had been treated for less than seven days and sent them to the Maryland State Laboratory for AFB testing followed by MTD on all SP specimens and decided whether to start anti-TB treatment. If the MTD was positive, then the suspect was reported; if the MTD was negative, then the clinician determined whether to report the patient as a suspect. Other activities (contact investigation, isolation, etc.) were started depending on clinical data and symptoms. Maryland had access to Maryland State Laboratory data; all DOH TB clinics used the State Laboratory, as well as some hospitals and private doctors.

Analysis

The following outcomes were analyzed: AFB smear result (positive or negative), MTD conducted and result (positive or negative), *Mycobacterium tuberculosis* culture result (positive or negative), MTD and no MTD positive predictive value (PPV), MTD and no MTD negative predictive value (NPV), MTD and no MTD sensitivity, and MTD and no MTD specificity, non-tuberculous mycobacterial disease diagnosis, TB-related hospitalization, and TB-related death.

To assess statistically significant associations at $p < 0.05$ with dichotomous outcomes (MTD use, CP, NTM diagnosis), we used multivariable log-binomial regression (SAS Version 9.2, 9.3) including patient demographics and sites for final model determination. We defined substance abuse as a history of injection or non-injection illicit drug use or excess alcohol use within one year of suspect assessment. Patient demographics were: age groups 25-44, 45-64,

≥ 65 versus age < 25 as the referent; race/ethnicity Hispanic, black/African American (henceforth referred to as “black”), Asian, American Indian/Alaskan Native (AIAN), Native Hawaiian/Other Pacific Islander (NHPI) versus white; foreign-born versus US-born; HIV-infected versus HIV-uninfected; homelessness within the past year versus none; substance abuse within the past year versus none. Suspects missing any of the above characteristics were deleted from the models.

Outpatient days for patients never hospitalized were calculated as the product of the number of non-hospitalized patients and the average days to TB determination. For hospitalized patients, outpatient days were the product of the total number of persons hospitalized times the average outpatient days prior to determination. Contact investigation days were calculated as the average days of contact investigation per contact (average number of contact investigation days prior to TB determination per suspect divided by the average number of contacts per suspect) times the total number of contacts tested (average number of contacts per suspect times the number of suspects having contacts tested for latent TB infection).

Standard unit costs (presented in Table S2) were estimated as follows. The fee for the MTD (CPT Code 83898) was obtained from the Physicians’ Fee and Coding Guide¹ and converted to a cost using the 0.5 cost-to-charge ratio for the pulmonary diagnostic group.² Cost per person per day of TB-related hospitalization was obtained from a multisite U.S. study of TB hospitalization.³ To that cost, we added in physician fees for initial hospital care for level 2 (CPT Code 99222),¹ converted to a cost (multiplied by 0.5).² Medicare reimbursements were used to estimate costs for respiratory isolation (CPT Code 94662), intensive care (CPT Code 99292),

mechanical ventilation (CPT Code 94003).⁴ To estimate the costs per day of outpatient management of a patient suspected of TB, we used an average daily personnel cost at health departments from a study at three U.S. sites,⁵ averaged after adjusting each site's costs to a U.S. basis using Medicare Geographic Adjustment Factors (1.08 for New York City and Massachusetts and 0.94 for Texas),⁶ and updating the cost to 2010 dollars using the change in the U.S. Bureau of Labor Statistics average hourly earnings ratio (19.07/14.02).⁷ Medication costs of \$3/dose (from unpublished citations of public health HRSA 340B Program negotiated TB medication costs) were added. The cost per person per day of contact investigation were obtained from a multisite U.S. study of contact investigation:⁸ costs of \$180/contact in 1999 dollars from the study, divided by 130 for 6 months of 5-day weeks, to obtain a daily estimate, updated to 2010 dollars using the change in the medical care CPI.⁹ Productivity loss per day was estimated at \$165 in 2000 dollars,¹⁰ updated to 2010 dollars by the change in average hourly earnings ratio.

Figure S1. Cohort Description

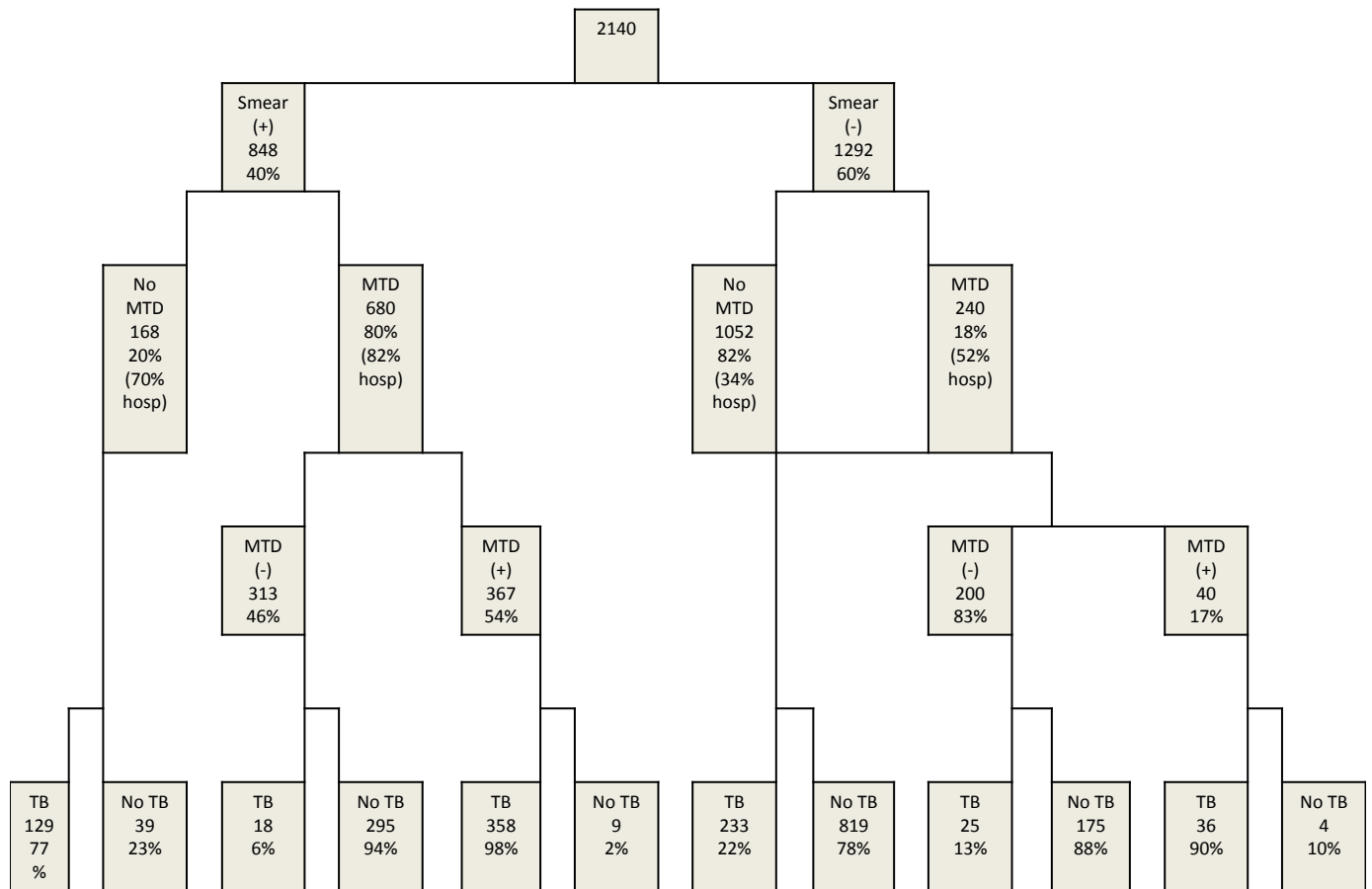


Figure S2. Analysis Methods

$$\text{Person days for service} = \text{Total number of persons receiving service} \times \text{Average number of days while TB suspect for service}$$

$$\text{Outpatient days for hospitalized suspects} = \text{Total number of persons hospitalized} \times \text{Average outpatient days prior to TB determination}$$

$$\text{Outpatient days for non-hospitalized suspects} = \text{Total number of non-hospitalized suspects receiving TB treatment} \times \text{Average number of days to TB determination}$$

$$\text{Contact investigation days} = \text{Average days of contact investigation per contact}^* \times \text{Total number of contacts tested}^{**}$$

$$* \quad \text{Average days of contact investigation per contact} = \frac{\text{Average number of contact investigation days prior to TB determination per suspect}}{\text{Average number of contacts per suspect}}$$

$$** \quad \text{Total number of contacts tested} = \text{Average number of contacts per suspect} \times \text{Number of suspects having contacts tested for LTBI}$$

Table S1. Average Days from TB Suspicion to TB Treatment

Average Days from Initial TB Suspicion to Treatment :				
		Started	%	Days to Treatment
	N	Treatment	Started	Start
SP/MTD(+)	367	355	97%*	5
SP/MTD(-)	313	73	23%*	12
SP/No MTD	168	147	88%	7
SN/MTD(-)	200	107	54%*	7
SN/MTD(+)	40	40	100%*	9
SN/No MTD	1052	439	42%	12
Total	2140	1161	54%	

Table S2. Cost Inputs, 2010 U.S. Dollars

CPT Code	Cost Per Person Per Day	Source
83898	\$ 50	Reference #1: 2009 Physician Fee and Coding Guide value, converted to a cost
	\$ 1,355	Reference #3: CDC 1996 TB Hospitalization Study average cost; added in physician fees converted to a cost, updated to 2010 dollars
94662	\$ 36	Reference #4
99292	\$ 114	Reference #4
94003	\$ 65	Reference #4
	\$ 33	Reference #5: TB suspect study average personnel costs per suspect for the 3 sites, cost-of-living adjusted to a US basis, divided by 40 days (8 weeks), updated 2010 dollars, plus estimated TB medication costs
	\$ 2	Reference #8: CDC 1999 Outcomes of Contact Investigation Study \$180/contact in 1999 dollars, updated to 2010 dollars, divided by 130 for 6 months of 5-day weeks
	\$ 224	Reference #10: Value of a lost day of work of \$165 in 2000 dollars, updated to 2010 dollars by the change in the average hourly earnings ratio

References

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- ¹ 2009 Physicians' Fee & Coding Guide. MAG Mutual Healthcare Solutions, Inc. Duluth, GA. 2008.
- ² The DRG Handbook: Comparative Clinical and Financial Standards. Ernst & Young LLP. 1998:21.
- ³ Taylor Z, Marks S, Ríos NB, Weis SE, Miller B, Stricoff RL. Causes and Costs of Hospitalization of Tuberculosis Patients. *The International Journal of TB and Lung Disease*. 2000; 4(10):931-939.
- ⁴ American Medical Association website (<https://ocm.ama-assn.org/OCM/CPTRelativeValueSearch.do>) listing for Medicare reimbursement by CPT Code.
- ⁵ Manangan LP, Moore M, Macaraig M, et al. Health Department Costs of Managing Persons with Suspected and Noncounted Tuberculosis in New York City, Three Texas Counties, and Massachusetts. *Journal of Public Health Management and Practice*. 2006; 12(3):248-253.
- ⁶ Centers for Medicare and Medicaid. Medicare FY2005 Prospective Payment System Impact File. FY2005 Geographic Adjustment Factors.
- ⁷ Bureau of Labor Statistics. Average Hourly Earnings of Production and Nonsupervisory Employees. Series ID CEU0500000008.
- ⁸ Outcomes of Contact Investigations of Infectious Tuberculosis Patients. *American Journal of Respiratory and Critical Care Medicine*. 2000; 162(6):2033-2038.
- ⁹ Bureau of Labor Statistics. Consumer Price Index Medical Care—All Urban Consumers. Series ID CUUR0000SAM.
- ¹⁰ Grosse S, appendix Table I.1a in *Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation*, Second Edition. 2003. Oxford University Press.