

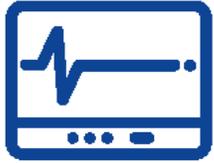
Hospitalization and diagnosis of TB: an opportunity to prevent transmission

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TB disrupts lives



Death

- 1 in 6 die within five years of diagnosis
- 10% do not survive treatment



Disability

- After treatment, impaired lung function and shorter life expectancy
- >80% of children with CNS TB die or permanently disabled



Hospitalization

- 50% of TB patients are hospitalized
- 2x as expensive and 4x longer than hospitalizations for other conditions



Cost

- Catastrophic costs to patients and families
- >\$180 million in direct and societal costs in California in 2020

Questions

1. How often are TB patients hospitalized in CA and what is the length of stay and cost?
2. What isolation criteria are promoted by guidelines and can NAAT add value for decisions on treatment and isolation?
3. Has NAAT been adopted for routine use in TB detection?

How often are TB patients hospitalized?

The International Journal of Tuberculosis and Lung Disease: Readhead et al. Hospitalizations with TB, California, 2009-2017

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Hospitalizations with TB, California, 2009–2017

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SUMMARY

BACKGROUND: Hospitalization is a costly event that affects more than half of all TB patients in the United States. State-level hospitalization data are crucial in estimating the cost of TB disease and the financial impact of preventing TB.

were more likely to be male, of working age, and Asian/Pacific Islander. The median cost for TB hospitalizations was US\$22,807 vs. US\$11,568 for other hospitalizations. The median length of stay for TB hospitalizations was 12 days compared to 3 days for other hospitaliza-

Study purpose:

- 1) to characterize TB hospitalizations
- 2) compare with non-TB hospitalizations

Study Methods

Data source: 2009-2017 California hospital discharge data

Definitions: TB hospitalization defined as hospitalization with a TB ICD-9/10 code as primary diagnosis

Estimated hospitalization cost in 2017 dollars using reported charges and cost-to-charge ratios

Readhead Results 1: Frequency and length of TB hospitalizations

- In 2017, 1,159 hospitalizations had TB as a primary diagnosis
- Roughly **half of TB patients** in 2017 were **hospitalized**
- The **median length of stay** for TB hospitalizations was **12 days** vs. 3 days for other conditions

Readhead Results 2: Who is hospitalized for TB?

- In comparison to persons hospitalized for other conditions, persons hospitalized for TB in 2017 were more likely to be male, of working age, and Hispanic or Asian Pacific Islander
- In contrast to 14% of non-TB hospitalizations, ~ 23% of TB hospitalizations occurred among persons residing in zip code areas in the lowest quartile by household income
- 69% of TB hospitalizations had a complication or comorbidity compared to 51% of other hospitalizations suggesting clinical severity

Readhead Results 3: Costs

- The **median charge** for TB hospitalizations was US \$102,695 – twice the median charge for other hospitalizations US \$50,946
- The **median cost** for TB hospitalizations was US \$22,807 vs US \$11,568 for other hospitalizations
- Most costs were **borne by public payers**
- **Medicaid** was payer for half of all TB hospitalizations totaling \$US 21,438,208 in 2017

Readhead Conclusions

- This study reveals the disruption TB disease causes for patients and communities in the form of hospitalization and hospitalization costs
- It updates the high cost of of TB care and underscores the costs that would be averted if TB cases are prevented

“Respiratory isolation of inpatients during evaluation for TB is a slow and costly process in low burden settings”

Millman et al., 2013

What criteria for isolation are promoted by current guidelines?

CDC/ATS/IDSA: nucleic acid amplification test recommendations for TB diagnosis

A task force supported by the supported by the American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America suggest:

Performing a diagnostic nucleic acid amplification test (NAAT), rather than not performing a NAAT, on the initial respiratory specimen from patients suspected of having pulmonary TB (conditional recommendation, low-quality evidence).

- In AFB smear-positive patients, a negative NAAT makes TB disease unlikely.
- In AFB smear-negative patients with an intermediate to high level of suspicion for disease, a positive NAAT can be used as presumptive evidence of TB disease, but a negative NAAT cannot be used to exclude pulmonary TB.

CDPH/CTCA Joint Guidelines for the Assessment of TB Patient Infectiousness and Placement into High and Lower Risk Settings, 2017

Purpose: To reduce the risk of TB transmission, the guideline promotes statewide practices and criteria for determining infectiousness and placement into high and low risk settings, criteria for discharge/transfer and for home isolation

Table 1. Criteria for Evaluating Placement in a HIGH RISK SETTING^B

Category	Lab Criteria ^{h,i}	Treatment Criteria ^j
TB suspected	AFB smear negative x 3 OR NAAT negative x 2 ^h OR AFB smear positive AND NAAT negative x 2 (ideally done on the same specimens) ^h	No minimum number of days of TB treatment required
TB suspected or known <ul style="list-style-type: none"> • AFB smear negative OR NAAT negative x 2 (without smear results) OR AFB smear negative AND NAAT positive • No MDR TB risk factors 	AFB smear negative x 3 Obtain direct genetic test, if available and not already done, for rifampin resistance	≥5 daily doses of appropriate TB treatment taken and tolerated AND Clinical improvement
TB suspected or known <ul style="list-style-type: none"> • AFB smear positive AND NAAT positive OR NAAT positive (without smear results) • No MDR TB risk factors 	AFB smear negative x 3 Obtain direct genetic test, if available and not already done, for rifampin resistance	≥14 daily doses of appropriate treatment for TB, preferably by directly observed therapy (DOT), taken and tolerated AND Clinical improvement.

Summary: guidelines and criteria in use

- National guidelines support NAAT use for TB detection
- Criteria and decision-making depend on individual and setting characteristics

Does NAAT add value for TB detection, isolation decisions, and time to treatment start?

PloS One Journal: Millman et al. Rapid Molecular Testing for TB to Guide Respiratory Isolation in the US – A Cost-benefit Analysis, 2013

Study purpose:

to examine the costs of molecular testing as a replacement for smear microscopy in an urban public hospital setting in the US

Methods:

- Conducted an incremental cost-benefit analysis comparing use of a single negative Xpert versus two negative sputum smears to release consecutive adult inpatients with presumed TB from respiratory isolation.
- Estimated all health-system costs and patient outcomes related to Xpert implementation, diagnostic evaluation, isolation hospitalization and treatment
- Performed sensitivity and probabilistic uncertainty analysis to determine at what threshold the Xpert strategy would become cost-saving

Millman et al. Results

- Of 234 patients undergoing TB evaluation annually in a hypothetical cohort , 6.4% had culture-positive TB
- Compared to smear microscopy, Xpert reduced isolation bed utilization from an average of 2.7 to 1.4 days per patient with
- 48% reduction in total annual isolation bed usage from 632 to 328 bed-days
- Xpert saved an average of \$2,278 per admission or \$533,320 per year compared with smear microscopy

Conclusions

- Molecular testing for TB could provide substantial savings to hospitals in high income countries by reducing respiratory isolation usage and overall length of stay

Clinical Infectious Diseases Journal: Lowenthal et al. Evaluation of the Impact of a Sequencing Assay for the Detection of Drug Resistance on the Clinical Management of Tuberculosis, 2019

Clinical Infectious Diseases

MAJOR ARTICLE



Evaluation of the Impact of a Sequencing Assay for Detection of Drug Resistance on the Clinical Management of Tuberculosis

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Background. In 2012, the California Department of Public Health began using pyrosequencing (PSQ) to detect mutations associated with resistance to isoniazid, rifampin, quinolones and injectable drugs in *Mycobacterium tuberculosis* complex. We evaluated the impact of the PSQ assay on the clinical management of tuberculosis (TB) in California.

Methods. TB surveillance and laboratory data for specimens submitted 1 August 2012 through 31 December 2016 were analyzed to determine time to effective treatment initiation. A survey of clinicians was used to assess how PSQ results influenced clinical decision making.

Results: Patients with MDR-TB initiated effective treatment **5 weeks earlier** when PSQ was used compared to those without PSQ

PSQ shortens time to MDR treatment

California Aug 2012-Dec 2016

	Days to start MDR regimen	
	PSQ done (n=72) median	PSQ not done (n=38) median
All	21.5	51.0
PSQ on isolate (n=33)	57.0	n/a
PSQ on sputum (n=39)	12.0	n/a

Assay turnaround time from specimen receipt = 1 day

Journal of clinical microbiology: Banerjee et al. Use of the Molecular Beacon Assay reduced the time to detection and treatment of MDR-TB in California, 2010.

- Assessed the clinical impact of a molecular beacon assay that detects MDR TB
- Investigated 127 MDR-TB cases with and without molecular beacon testing , California, 2004-2007
- Results: the use of molecular Beacon assay reduced the time to detection and treatment of MDR TB

Is NAAT being used in California for diagnosis?

California use of NAAT

During 2016-2020,

- 76% of smear positive TB cases in California had NAAT and
- 46% of smear negative cases

Summary

- TB hospitalizations are common, lengthy, and costly
- Use of rapid molecular tests can facilitate TB detection, impact isolation decisions and shorten time to effective treatment
- Additional actions for consideration could be alternative isolation sites outside hospital for those who no longer need inpatient care

Considerations for isolation decisions may include:

- Suspicion level, test results, and risk of destination setting
- Effective therapy initiation
- Suspected/confirmed drug resistance

Stay tuned for:

- A survey developed by NTCA/Canada/NYC/California/Oregon to assess practices in the US and in Canada on the use of NAAT in isolation decision-making and access to NAAT for TB detection

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Pennan Barry MD MPH

CDPH TB registry