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Flight related tuberculosis contact investigations in the United States: Comparative risk and economic analysis of alternate protocols

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Summary *Background:* In-flight transmission risk of *Mycobacterium tuberculosis* is not well defined, although studies suggest it is low. The impact of flight-related tuberculosis (TB) contact investigations (TBCIs) on TB prevention and control is not well established, and they compete for resources with activities with established benefits. We sought to determine the risks and cost–benefits of using more restrictive criteria in comparison to the Centers for Disease Control and Prevention (CDC) 2008 protocol for TBCIs.
Methods: The risk-benefits of a modified CDC protocol were analyzed in comparison to the 2008 CDC protocol using data from flight-related TBCIs conducted in the United States from 2007 through 2009. We predicted the numbers and characteristics of case-travelers that would be identified using each protocol's criteria, and results of the associated passenger-contacts' TB screening tests. The economic analysis compared the costs of TBCIs to avoided costs of TB treatment and mortality using a Return on Investment model.
Results: The estimated in-flight transmission risk using a modified CDC protocol was 1.4%–19% versus 1.1%–24% for the 2008 protocol. Numbers of TBCIs and immediate costs to health departments were reduced by half. Long-term cost–benefits were comparable.
Conclusions: CDC's modified protocol appears to be a feasible alternative that will conserve public health resources without jeopardizing the public's health.
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Introduction

Investigating contacts of persons with infectious tuberculosis (TB) to identify cases of TB disease and latent TB infection (LTBI) is the foundation of TB control and elimination efforts in the United States and in many other low prevalence countries [1—4]. In the United States, 32—36% of household, community, social, and work contacts of TB patients have LTBI, and 1.3—4% have TB disease at the time of investigation [3,5]. The risk of transmission of *Mycobacterium tuberculosis* is higher from patients with sputum smears that are positive for acid-fast bacilli (AFB) or cavitary lesions on chest radiograph (CXR), and is highest when both conditions are present [1,3,5]. Risk for progression from LTBI to TB disease is greatest within 2 years of infection, when approximately half of the 5—10% lifetime risk occurs [1,6].

There are few estimates of the in-flight transmission risk of *M. tuberculosis*. Modeling suggests risk of transmission from a highly infectious passenger on an 8.7 h commercial flight as 1/1000 for all passengers, with higher risk to those seated closer to the infectious passenger [7]. Transmission during air travel is uncommon, but has been documented. A review of 13 studies that assessed risks of in-flight transmission found two studies that reported reliable evidence of transmission on long-haul flights [8]. Both index patients were considered highly infectious at the time of the flights as they were sputum smear-positive and had cavitation on CXR [9,10]. Other studies found no evidence of transmission among passengers or were inconclusive [8,11,12]. No documented TB disease resulting from exposure during air travel has been reported [8,11,12]. However, given the long latency period between exposure and disease such cases are unlikely to be detected.

The 2006 World Health Organization (WHO) guidelines for prevention and control of TB during air travel provided recommendations for conducting flight-related TB contact investigations (TBCIs); these guidelines were updated in 2008. [13,14] Several countries, including the United States, have used the WHO guidelines as a foundation for development of their own national policies [11—16].

The US Centers for Disease Control and Prevention (CDC) flight-related TBCI protocol, initially developed in 2005 and updated in 2008, was developed by the Division of Global Migration and Quarantine (DGMQ) in collaboration with the Division of TB Elimination. To facilitate TBCIs in the United States, after verifying that the case-traveler meets CDC criteria, DGMQ obtains passengers' information from airlines and US Customs and Border Protection, and provides it to state-based public health departments (HDs) for contact tracing. HDs voluntarily report outcomes to DGMQ. Information on foreign nationals without US contact information is provided to foreign public health authorities [11,12].

A comprehensive analysis of the epidemiology and outcomes of CDC-led flight-related TBCIs conducted in the United States from January 2007—June 2008 involved 131 case-travelers and 4550 passenger-contacts [11]. Of the 3375 (74%) passenger-contacts whose information was provided to US HDs for contact tracing, TB evaluation results were reported to DGMQ for 861 (26%), of whom 103 (12%) had a previous history of a positive TB screening test (tuberculin skin test [TST] or interferon-gamma release assay [IGRA] test) result or treatment for LTBI or TB disease and were not re-tested. Of the remaining 758 passenger-contacts, 24% were test positive. Of these, 71% had risk factors for prior infection, such as having been born or lived in a country with high TB prevalence; 7% were reported as having no risk factors; and risk factors were unknown or not addressed for 22% [11]. Although passenger-contacts with risk factors were more likely to have pre-existing LTBI, it was not possible to exclude the possibility that infection was acquired during the flight. Furthermore, because outcomes data of varying quality and completeness were reported for only 26% of passenger contacts forwarded to US health departments (19% of all passenger contacts) the authors concluded that precise determination of in-flight transmission risk of *M. tuberculosis* was not feasible, although the risk appeared to be low. And that despite the expenditure of substantial resources by local, state, federal, and international public health authorities, the contribution of flight-related TBCIs to TB control was also likely low. Despite hundreds of flight-related TBCIs, their impact on TB prevention and control is not well-established [1,8,11,12]. Nonetheless, because the precedent for conducting air travel-related TBCIs had been set for several years, changing current national policy without strong supportive evidence was not acceptable. Obtaining that evidence would require comprehensive cohort studies with national and international commitment, collaboration, and funding, and were deemed unlikely given global economic status.

Allocation of increasingly limited public health resources to flight-related contact investigations competes with efforts with known impacts on TB prevention and control, such as targeted screening and treatment of foreign-born US residents from high TB-prevalence countries [17,18]. Therefore, because the benefits of these investigations must be balanced against the limited resources, in their 2010 article, the authors suggested evaluating the cost-effectiveness of contact investigations for preventing TB disease secondary to exposure during air travel to inform possible policy revisions [11]. In this study we identified three alternative protocols with more restrictive criteria than our 2008 CDC protocol. We selected one of those for which risk-benefit analyses in comparison to the 2008 CDC protocol were achievable. Our goal was to determine the feasibility of a more restrictive protocol that would result in fewer flight-related TBCIs and reduce public health expenditures without negatively impacting TB prevention and control.

Methods

Contact investigation protocol alternatives

We did a literature review of *M. tuberculosis* transmission and conveyance-associated disease epidemiology, using the key search words tuberculosis, air travel, tuberculosis transmission, contact tracing, tuberculosis guidelines, air-travel related illness [8,11,12,19—28], reviewed published national and international guidelines for flight-related TBCIs [1,14—16,29] and unpublished data on TBCIs from the DGMQ database to identify potential alternative protocols to the 2008 CDC protocol for conducting flight-