Annals of Epidemiology xxx (2017) 1–6

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

Individual- and neighborhood-level contextual factors are associated with *Mycobacterium tuberculosis* transmission: genotypic clustering of cases in Michigan, 2004–2012

Grace A. Noppert PhD [a,*,1], Zhenhua Yang MD, PhD [a], Philippa Clarke PhD [a,b], Wen Ye PhD [c], Peter Davidson PhD [d], Mark L. Wilson ScD [a]

[a] Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor
[b] Institute for Social Research, University of Michigan, Ann Arbor
[c] Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor
[d] Michigan Department of Health and Human Services, Lansing, MI

ARTICLE INFO

Article history:
Received 3 October 2016
Accepted 5 May 2017
Available online xxx

Keywords:
Communicable diseases
Social determinants of health
Health status disparities
Tuberculosis
Socioeconomic factors

ABSTRACT

Purpose: Using genotyping data of *Mycobacterium tuberculosis* isolates from new cases reported to the tuberculosis (TB) surveillance program, we evaluated risk factors for recent TB transmission at both the individual- and neighborhood- levels among U.S.-born and foreign-born populations.
Methods: TB cases ($N = 1236$) reported in Michigan during 2004 to 2012 were analyzed using multivariable Poisson regression models to examine risk factors for recent transmission cross-sectionally for U.S.-born and foreign-born populations separately. Recent transmission was defined based on spoligotype and 12-locus-mycobacterial interspersed repetitive unit–variable number tandem repeat typing matches of bacteria from cases that were diagnosed within 1 year of each other. Four classes of predictor variables were examined: demographic factors, known TB risk factors, clinical characteristics, and neighborhood-level factors.
Results: Overall, 22% of the foreign-born cases resulted from recent transmission. Among the foreign-born, race and being a contact of an infectious TB case were significant predictors of recent transmission. More than half (52%) of U.S.-born cases resulted from recent transmission. Among the U.S.-born, recent transmission was predicted by both individual- and neighborhood-level sociodemographic characteristics.
Conclusions: Interventions aimed at reducing TB incidence among foreign-born should focus on reducing reactivation of latent infection. However, reducing TB incidence among the U.S.-born will require decreasing transmission among socially disadvantaged groups at the individual- and neighborhood-levels. This report fills an important knowledge gap regarding the contemporary social context of TB in the United States, thereby providing a foundation for future studies of public health policies that can lead to the development of more targeted, effective TB control.

Introduction

Although the overall incidence of tuberculosis (TB) has been declining in the United States, stark disparities persist in the distribution of disease, particularly by race and nativity. Asian and Pacific Islanders (AI/PI) continue to have the highest incidence of TB in the United States and show no evidence of closing the gap with whites, whose incidence is lowest [1,2]. Moreover, the rate of decline in TB incidence has recently begun to stagnate [3], particularly among foreign-born populations [4], and in both urban and rural populations [5,6].

From a clinical perspective, measures of individual immune status and infectiousness are key to predicting transmission of *Mycobacterium tuberculosis (MTB)* [7]: individuals with underlying comorbidities, those with a positive sputum-smear, and those with abnormal chest radiography results are more likely to be associated with recent transmission. However, previous studies have also found both individual-level and neighborhood-level sociodemographic factors to be predictors of recent TB transmission. Individual-level sociodemographic characteristics such as younger age [8–10], minority race/ethnicity status [8,11], male sex [9,10],

* Corresponding author. Department of Epidemiology, University of Michigan School of Public Health, 1415 Washington Heights, Ann Arbor, MI 48109.
E-mail address: grace.noppert@duke.edu (G.A. Noppert).
[1] Present affiliation: Center for the Study of Aging and Human Development, Duke University, 201 Trent Dr. Durham, NC 27710; email: grace.noppert@duke.edu.

http://dx.doi.org/10.1016/j.annepidem.2017.05.009
1047-2797/

and being native-born [8,11–13] have been associated with recent TB transmission. In addition, "known TB risk factors" as defined by the Centers for Disease Control and Prevention (CDC) surveillance forms [14], such as homelessness [8,9,13], incarceration [8], and drug use [13] have also been linked to recent transmission. Neighborhood-level studies have demonstrated that area-based measures of disadvantage are associated with increased incidence and transmission of TB, a finding particularly pronounced for those who are U.S.-born [15]. Several studies have also suggested the predictors of recent transmission are different for foreign-born and U.S.-born populations [16], highlighting the importance of investigating these two groups separately.

In 2012, Michigan had an annual incidence rate of 1.28 TB cases per 100,000 [17], notably lower than the U.S. national average incidence of 3.2 per 100,000 [4]. Despite Michigan's lower incidence, there is evidence of persistent disparities in TB risk, particularly by race and nativity [17]. Using TB surveillance data collected by the Michigan Department of Health and Human Services (MDHHS), we evaluated risk factors for recent transmission at both the individual- and neighborhood-levels among U.S.-born and foreign-born populations separately.

Methods

Study population and data collection

Our study subsample included only those cases with complete genotype data, both spacer oligonucleotide (spoligotype) and 12-locus-mycobacterial interspersed repetitive unit–variable number tandem repeat typing (MIRU-VNTR) results, and address information. The genotyping data are part of the CDC-based National Tuberculosis Genotyping Service [18]. Cases were excluded if they had incomplete genotyping data and/or were missing address information. The state of Michigan employs universal genotyping such that greater than 90% of TB cases reported to the state of Michigan were genotyped. At the state level, genotyping was done on the first isolate of a given episode. Isolates from subsequent episodes that were at least 12 months apart were subjected to the same criteria for determining genotypic clusters as described in the following.

Demographic characteristics, risk factor information, and clinical characteristics of each case, as well as residential address, were drawn from TB surveillance data collected by MDHHS using the "Report of a Verified Case of TB" form developed by the CDC [14]. Thus, the variables included were defined on the basis of the CDC classifications.

Addresses were geocoded and linked with block group–level characteristics derived from the American Community Survey, 5-year estimates for 2012 [19]. The unit of analysis for neighborhood effects was the block group, which serves as a useful proxy for both household-level features such as degradation and vacancy, as well as access to neighborhood resources, both of which are dimensions likely to affect TB transmission. In addition to neighborhood population density and age composition, neighborhood socioeconomic disadvantage was captured using a mean index of six census indicators at the block group level: percent black, percent with less than a high school education, percent unemployed, percent using public assistance, percent of vacant properties, and percent with an income-to-poverty level ratio below 2 (The U.S. Census defines an income-to-poverty ratio below 2 as being "poor or struggling." Thus, we used 2.0 as our cut point to determine the proportion of the block group with an income-to-poverty ratio below 2.0; factor loadings ranged from 0.55 to 0.83, alpha reliability = 0.82). We also sought to examine county-level differences in urban and rural status; however, 94% of cases were identified in a metropolitan region, and thus, we did not include county-level urban/rural status in our investigations.

Genotypic cluster definition

Following previously established methods, genotypically clustered cases were considered a proxy for recently transmitted infections, as defined by those sharing an identical spoligotype and 12-locus-MIRU-VNTR result with at least one other case in the sample, and having a count date within 1 year of one another [5,20]. We used the count date as a proxy for date of diagnosis. Unique ("nonclustered") cases were those that either did not share an identical spoligotype and 12-locus-MIRU-VNTR result or did not have a count date within the 1-year time period and were considered a proxy for reactivation of latent TB infection (LTBI). Genotypic clusters could span more than 1 year if the cluster involved two cases with identical genotypes that had at least one other matching case within a 1-year time frame. Genotypically clustered cases defined as such do not necessarily occur in spatial clusters.

Statistical analysis

We analyzed individual- and neighborhood-level predictors of recent transmission in relation to variables of four types: demographic factors, known TB risk factors (as defined by the CDC [14]), clinical factors, and neighborhood characteristics at the block group level. Demographic factors included nativity, race/ethnicity, age, and gender. Known TB risk factors included HIV status, alcohol use, diabetes, injecting drug use, noninjecting drug use, long-term care facility stay, and homelessness. Clinical risk factors included immunosuppression, sputum-smear status, sputum-culture status, site of TB disease, and initial chest radiography results. Block-group characteristics included population density, proportion of the population over 64 years of age, and the neighborhood disadvantage index, all of which were modeled in quartiles. See Appendix A for details on how each variable was measured.

Univariate, modified Poisson regression models were used to examine the influence of each risk factor individually on recent transmission. For data reduction, we then used stepwise regression to determine which variables, when considered together, were the most significant predictors of recent transmission. Finally, we constructed a final set of multivariable modified Poisson models that included the variables determined to be significant based on the stepwise regression model as well as a priori knowledge.

Modified multivariate Poisson regression models were estimated using generalized estimating equations to account for nesting of cases within block groups [21]. Such models allow for accurate parameter estimation and robust variance estimates by accounting for the correlated observations existing among cases in the same block group. The prevalence ratio of recent transmission and corresponding 95% confidence intervals were calculated using a Poisson regression model with a log-link function.

Because previous research has suggested that the factors influencing transmission are different for U.S.-born and foreign-born populations [9,15,22], models were stratified by nativity, and results for U.S.-born and foreign-born persons are reported separately. For final analyses, a two-tailed alpha level of 0.05 was considered statistically significant. For the stepwise regression, we used alpha = 0.2 to select variables for inclusion in the model, and alpha = 0.05 for retention in the final stepwise regression model. Analyses were undertaken using SAS (version 9.4), Cary, NC.

This study was approved by the University of Michigan Institutional Review Board for Social and Behavioral Sciences and by the MDHHS Institutional Review Board.