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Identification of spatial and cohort clustering of tuberculosis using surveillance data from British Columbia, Canada, 1990–2013

David Roth [a], Michael Otterstatter [a, b], Jason Wong [a, b], Victoria Cook [a, c], James Johnston [a, c], Sunny Mak [a, *]

[a] British Columbia Centre for Disease Control, 655 West 12th Avenue, Vancouver, British Columbia V5Z 4R4, Canada
[b] School of Population and Public Health, University of British Columbia, 2206 East Mall, Vancouver, British Columbia V6T 1Z3, Canada
[c] Department of Medicine, University of British Columbia, 2775 Laurel Street, 10th Floor, Vancouver, British Columbia V5Z 1M9, Canada

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ABSTRACT

Since 2000, the global incidence of tuberculosis (TB) has decreased by 1.5% per year, becoming increasingly clustered in key subpopulations in low incidence settings. TB clustering can manifest spatially from recent transmission, or in non-spatial cohort clusters resulting from reactivation of latent infection in populations with shared risk factors. Identifying and interrupting disease clusters is required to eliminate TB in low incidence countries. Here we demonstrate an analytical approach for detecting both spatial and cohort clustering of TB among population subgroups, and describe the value in differentiating these forms of clustering. TB cases in British Columbia meeting the Canadian case definition were geocoded and mapped using Geographic Information Systems (GIS). Incidence rates were calculated for three periods (1990–1997, n = 2556; 1998–2005, n = 2488; 2006–2013, n = 2225) among Canadian born (CB) and foreign-born (FB) populations using denominator data from the Canadian Census. Spatial clusters were identified using a scanning window statistic (SaTScan) and overlaid on provincial incidence maps. Country of birth (cohort) clustering in the FB was identified using Lorenz curves and Gini coefficients. TB incidence in the CB population was generally low, but punctuated with few areas of high incidence; the spatial clusters identified in the CB match previously identified clusters. TB incidence in the FB did not show spatially localized clusters. However, Lorenz curves revealed substantial, and increasing, cohort clustering in the FB in semi-urban and rural regions of British Columbia, and less pronounced, and decreasing, clustering in urban regions. In general, the TB incidence in groups defined by country of birth shifted over time to become increasingly uniform across regions. Our approach, based on spatial analysis and the application of Lorenz curves revealed a complex coexistence of spatial and cohort clustering. Spatial and cohort clusters require differing public health responses, and differentiating types of clustering can inform TB prevention programs.

1. Introduction

Tuberculosis (TB) is an airborne disease caused by the bacterial organism *Mycobacterium tuberculosis*. TB typically infects the lungs, but can affect other parts of the body. In 2014, there were 9.6 million incident cases of active TB disease globally, with 1.5 million TB related deaths, making TB the leading global infectious disease killer (World Health Organization, 2015). Worldwide, TB incidence has decreased slowly – by roughly 1.5% per year since 2000 (World Health Organization, 2015). The World Health Organization (WHO) aims to accelerate this decline in TB incidence with the WHO 2015 Global Tuberculosis 'EndTB' Strategy. The goal of this global strategy is to reduce TB incidence by 90% between 2015 and 2035, and in low TB incidence regions the WHO has set an ambitious target of reducing TB incidence to less than one case per million population by 2050 – or full elimination of the disease (World Health Organization, 2014).

Accelerating declines in low TB incidence regions has proven difficult over the past two decades as TB has become increasingly clustered in certain high-risk and marginalized populations (World Health Organization, 2015). With continued declines in TB incidence, we can expect clustering to become an increasingly

* Corresponding author.
E-mail address: sunny.mak@bccdc.ca (S. Mak).

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important driver of TB epidemiology in low incidence regions (Colijn et al., 2007). Identifying and understanding TB clusters in high-risk populations will be essential to developing new strategies for TB prevention and to achieving the goal of TB elimination in low incidence regions.

Traditionally, clustering of TB cases is thought to be the result of person-to-person TB transmission within a population. Endogenous transmission in a low incidence region often results in spatially localized TB outbreaks and hotspots (Alland et al., 1994; Colijn et al., 2007; Haase et al., 2007). Evaluation of such spatial TB clusters has been performed in many regions (Alvarez-Hernandez et al., 2010; Areias et al., 2015; Bastida et al., 2012; Gomez-Barroso et al., 2013; Liu et al., 2012; Maciel et al., 2010; Roza et al., 2012; Tiwari et al., 2006; Touray et al., 2010; Wang et al., 2012; Yakam et al., 2014; Zaragoza Bastida et al., 2012), with many of these pockets of high incidence associated with crowding, poverty and other socioeconomic determinants (Alvarez-Hernandez et al., 2010; Maciel et al., 2010; Munch et al., 2003; Roza et al., 2012; Woldeyohannes and Abera, 2015; Yakam et al., 2014).

However, it is important to note that clustering may also occur non-spatially among high-risk subgroups due to shared characteristics, rather than a shared transmission network. This phenomenon is known as *cohort clustering* (Bownson and Petitti, 1998). Cohort clustering occurs when TB disease aggregates in high-risk groups due to shared patterns of historic exposure or social determinants of health (Lonnroth et al., 2009; Lönnroth et al., 2015; World Health Organization, 2014) and is often referred to as simultaneous reactivation. This can occur in populations with a large historic pool of latent TB infection and a common driver (e.g., poverty) of reactivation. Foreign-born populations in particular tend to exhibit cohort clustering with TB. Migrants from high TB incidence regions often develop TB as a result of reactivation of latent tuberculosis infection (LTBI). A person with LTBI, a condition in which an individual is infected by the TB bacteria but is not growing or grows very slowly, can remain asymptomatic for years or decades and reactivate to active TB after migration (Long, 2013). With an estimated one-third of the world's populations infected with *M. tuberculosis*, and increasing global mobility, TB in migrant populations is emerging as a major barrier to TB elimination in low incidence regions. Addressing cohort clustering in migrant populations will be essential to TB elimination strategies in low incidence regions.

Given that endogenous TB transmission and LTBI reactivation can both contribute to TB clustering (van Deutekom et al., 2004), a combination of geographic and cohort clustering may also be expected in some regions. Indeed, spatial clustering and cohort clustering will co-occur if high risk groups converge in particular areas such as urban population centres. Such gathering creates environments of common socioeconomic, demographic and co-morbid risk factors that are conducive for reactivation of LTBI and subsequent person-to-person transmission (Barnes et al., 1997; de Vries et al., 2007; Lonnroth et al., 2009). An outbreak in British Columbia, Canada, for example, was linked to the combined effects of recent person-to-person transmission and the reactivation of historic infections promoted by the spread of crack cocaine use (Gardy et al., 2011). Hence, understanding patterns of TB incidence requires detailed analysis of spatial clustering and cohort clustering together.

In the province of British Columbia (population 4.6 million), Canada, overall TB incidence has declined from >100 per 100,000 during the early 1950s to a current rate of 5.6 per 100,000 in 2013 (British Columbia Centre for Disease Control, 2015). However, after a decade of stagnant TB incidence, there is a need to reconsider the provincial public health response to this disease (British Columbia Communicable Disease Policy Advisory Committee, 2012). With increasing immigration to British Columbia from high incidence countries, there is a growing population with LTBI population at risk of developing active TB (Greenaway et al., 2011; Langlois-Klassen et al., 2011) and roughly 70% of active cases currently occur in the foreign-born population (British Columbia Centre for Disease Control, 2015). However, the province has also experienced several spatially localized TB outbreaks in the domestic-born population (Cheng et al., 2015; Gardy et al., 2011). Understanding patterns of TB in British Columbia, in terms of the contributions of geographic and cohort clustering, would aid in developing appropriate actions to further reduce incidence.

In this study, we analyze TB surveillance data from British Columbia, 1990–2013, with the specific aim of contrasting spatial and cohort clustering. Furthermore, we show how explicitly differentiating cohort and spatial clustering may help clarify the public health response to TB, while also arguing for the importance of placing equal emphasis on simultaneous reactivation driven outbreaks that is currently given to active transmission. This approach uses standard surveillance data and freely available analytical software that can be used by public health practitioners to inform programs and interventions.

2. Methods

2.1. Data preparation

This study includes all active TB cases reported to the national authority (Public Health Agency of Canada (2015)) from British Columbia from 1990 to 2013. Provincial cases failing to meet the national case definition were excluded. British Columbia was selected as the study area because it has a relatively high foreign-born population (29.4%), and a good mix of population distribution in urban metropolitan, medium and smaller sized urban, and rural communities. In addition, British Columbia has had several well studied TB outbreaks in the last 10 years which allow for retrospective validation of the proposed methods. Finally, TB data management for active cases in British Columbia is centrally managed, resulting in a high quality dataset built on standardized reporting and data entry practices. All cases were geocoded using the 3 digit postal code (Forward Sortation Area, FSA) of client residence to enable geographic mapping and analysis. The FSA geographical unit was used in this analysis because there is a sufficient number of FSAs in British Columbia ($n = 189$) to enable small scale geographical analysis, and this is the most granular geographic location information available to us for mapping and spatial analysis that protects patient confidentiality. The FSA geographical unit is large enough to prevent re-identification of individuals by location, yet small enough to illustrate unique patterns of TB incidence. Furthermore, the FSA geographical unit has from the Census of Canada demographic and socioeconomic profile information such as place of birth which we use in the cohort clustering analysis. The use of jurisdictional boundaries as the unit of aggregation for cluster detection is not uncommon in the TB literature (Liu et al., 2012; Maciel et al., 2010; Munch et al., 2003; Roza et al., 2012; Yakam et al., 2014).

2.2. Geographic and demographic comparisons

Patterns of clustering were compared within Canadian-born (CB) and foreign-born (FB) given hypotheses regarding differences in TB epidemiology between these two groups, e.g., preponderance of reactivation of latent TB among FB cases due to pre-landing exposure in their country of origin and the development of comorbidities with age, versus the importance of social conditions