Age Related Incidence of Tuberculosis in Persons Vaccinated with BCG

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Aim
The aim of our study is to examine impact of three different BCG vaccination policies on incidence of TB in the South of Ireland over a 13-year period.

Data collection
Surveillance data from the regional TB laboratory was used to identify all Mycobacterium tuberculosis complex (MTC) isolates from 2003-2016. Data were collected over a 13-year period (01/03/2003 to 12/13/2016) for all reported cases of MTC. BCG cases were divided into Local Health Offices (LHO) within the South of Ireland (North, South, West, Cork, North Cork and Kerry). National incidence rate comparisons were with Health Service Executive (HSE) South rates using serum 2011 population keeping with Health Protection Surveillance Centre reports (Figure 1).

Methods, study design and population
Residential addresses for each MTB case were geocoded using the Open Maps API. Information about case locations were spatially linked to 2011 census population data at the small area level using QGIS (v.2.18.13). Spatial data were similarly linked to the coverage of the HSE Local Health Offices (LHO) for Kerry, West Cork, South Lee, North Cork, and North. The 13-year incidence of MTB was calculated assuming a steady-state population. Using SaTScan software, we identified up to 3 times higher than normal TB incidence at the small area level with the spatial scan statistic based on the discrete Poisson probability distribution.

Results
A total of 212 cases of MTB were identified during the study period. The median age was 43 years (range 0-84 years). 95% of the sample were older than 18 years of age. 327 (95%) cases were male with 357 (79%) Irish born. The incidence of MTB (Figure 2) was higher in the unvaccinated population, regions C, with an incidence 222/100,000 (95% confidence interval 95% CI 116-130). A single high-risk cluster of 138 cases within a population of 40,000 was identified in unvaccinated region C (relative risk 35.4). The year-on-year incidence rates in the 20 to 35-year age range suggested a decreasing risk consistent with a beneficial impact of vaccination policies (Figure 3).

Limitations
The unvaccinated group (region -C) was in an urban area. Although population density was high, the BCG proportion index was not. This needs to be considered as a confounding factor, as homelessless and lower socioeconomic factors are traditionally considered greater issues in urban areas.

Population rather than individual BCG vaccination coverage estimates were used. Use of vaccines in different policy areas was not represented. It was reported that several children where there was no BCG vaccination available (region -C) received the BCG vaccine in other jurisdictions due to parental concern following local outbreaks. Low numbers of cases resulted in lower power. In some age groups in West Cork (vaccinated region), few or no cases were reported.

Strengths
The cohort of unvaccinated children provides a reliable source of the incidence of childhood TB in a non-vaccinated Irish population and other high-income countries.

Conclusion
Prevention and treatment of TB remains a significant challenge worldwide. The incidence of MTB infection is higher in Southern Ireland compared to the general Irish population. Our study demonstrates significant differences in the incidence of Mycobacterium tuberculosis infection in demographically similar populations (based on BCG immunization policy). This is in accordance with previous studies which support the efficacy of BCG for prevention of tuberculosis infection.

References
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Background
Tuberculosis (TB) is the ninth leading cause of death worldwide and the leading cause of death among children. One in three people worldwide is infected with TB. In 2016 the World Health Organisation estimated that 10.4 million people were infected and that there had been 1.7 million TB related deaths. [1]

The discovery of the Bacille Calmette-Guerin (BCG) vaccine in the 1920s was a milestone in tuberculin control and in 1949 was introduced in Ireland by Dr. Dorothy Stephenson Price.

Despite its widespread use, it is controversial with known variations in BCG sub strains, vaccine efficacy, policies, and practices across the world. [2] The BCG vaccine has been subject to several trials which have estimated an overall protective efficacy of 60-80% against severe forms of pulmonary tuberculosis in children, particularly meningitis. Protection against pulmonary tuberculosis varies according to age of administration and geographical location. [3]

By the 1970s in pilot studies in Western Europe were emerging demonstrating the decline in risk of serious forms of tuberculosis in children, evidence of the weak protective effect of BCG in adults and lack of impact on the global incidence of tuberculosis. This resulted in a discontinuation of national BCG vaccination in several countries including former Czechoslovakia (1965–1972) and Sweden (1976/79). [4]

In Southern Ireland, a universal neonatal BCG vaccination was offered in Cork up to 1972. The vaccine was then discontinued for a variety of reasons including the relatively low TB rate in the area and concerns on positive Mantoux tests in the immunized population complicating a diagnosis of TB in the future. [5]

Elsewhere in Ireland, BCG vaccination remained in place as evidence continued to support its use in the Irish context. Moving from universal to selective BCG vaccination in Ireland was under evaluation in accordance with other European countries however in the interim, due to an ongoing global BCG vaccine shortage universal vaccination in Ireland has stopped and a no longer national policy as of 2016. [6]

In our study we analyse TB surveillance data in the South of Ireland over a thirteen-year period (2003 – 2016). This data is unique in that it compares three different BCG vaccination policies across bordering geographic regions. We extracted data on regional vaccination of children aged 10-12 years (vaccinated region-C) and no vaccination (unvaccinated region-C).