

## RESEARCH ARTICLE



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# The 1918 influenza pandemic did not accelerate tuberculosis mortality decline in early-20th century Newfoundland: Investigating historical and social explanations

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**Abstract**

**Objectives:** The selective mortality hypothesis of tuberculosis after the 1918 influenza pandemic, laid out by Noymer and colleagues, suggests that acute exposure or pre-existing infection with tuberculosis (TB) increased the probability of pneumonia and influenza (P&I) mortality during the 1918 influenza pandemic, leading to a hastened decline of TB mortality in post-pandemic years. This study describes cultural determinants of the post-pandemic TB mortality patterns in Newfoundland and evaluates whether there is support for this observation.

**Materials and methods:** Death records and historical documents from the Provincial Archives of Newfoundland and Labrador were used to calculate age-standardized island-wide and sex-based TB mortality, as well as region-level TB mortality, for 1900–1939. The Joinpoint Regression Program (version 4.8.0.1) was used to estimate statistically significant changes in mortality rates.

**Results:** Island-wide, females had consistently higher TB mortality for the duration of the study period and a significant shift to lower TB mortality beginning in 1928. There was no similar predicted significant decline for males. On the regional level, no models predicted a significant decline after the 1918 influenza pandemic, except for the West, where significant decline was predicted in the late-1930s.

**Discussion:** Although there was no significant decline in TB mortality observed immediately post-pandemic, as has been shown for other Western nations, the female post-pandemic pattern suggests a decline much later. The general lack of significant decrease in TB mortality rate is likely due to Newfoundland's poor nutrition and lack of centralized healthcare rather than a biological interaction between P&I and TB.

**KEYWORDS**

1918 influenza pandemic, historical demography, Newfoundland, selective mortality, tuberculosis

## 1 | INTRODUCTION

The 1918 influenza pandemic significantly impacted nearly every population it touched, amounting to 50–100 million deaths worldwide (Johnson & Mueller, 2002). One phenomenon associated with this

event is a decline of tuberculosis (TB) mortality in the ensuing decades (Noymer, 2009, 2011). In the United States, for example, TB mortality declined from 20 deaths per 10,000 individuals in 1900 to nearly zero by 1940 (Noymer, 2009; Noymer & Garenne, 2000), raising questions about whether there was an association between the two respiratory

diseases in heavily afflicted populations during the pandemic and subsequent years. There has been little quantitative research investigating the post-pandemic TB decline in populations outside the United States, however. This paper seeks to describe the TB mortality decline in Newfoundland, a pre-industrial, and pre-demographic and pre-epidemiologic transition population, and to assess cultural and historical factors that may have contributed to those patterns.

The general pattern of increased TB mortality during the influenza pandemic itself, immediately followed by a steep downward trend of mortality, was first observed by Abbott (1922) after the 1918 influenza pandemic during investigation of United States TB mortality trends in the first half of the 20th century, but it has since been more thoroughly described as selective mortality of TB (Noymer, 2009, 2011; Noymer & Garenne, 2000). The selective mortality hypothesis suggests that the high frequency of TB deaths during the 1918 pandemic was the turning point for TB prevalence in the United States, in that mortality was already on the decline through the beginning of the twentieth century, but after the end of the influenza pandemic in 1920, the decline accelerated. Cutler and Miller (2005) suggest that the rapid late-19th and early-20th century TB decline in the United States was driven primarily by public health improvements, the elimination of the urban mortality penalty, and the role of water sanitation and chlorination. McKinlay and McKinlay (1977) also cast doubt on biomedicine's role in the decline of TB, noting that the most dramatic decline in mortality had already passed. Tuberculosis sanatoria, first established in the United States in 1875 and growing to 656 facilities across the country by 1923, are also given substantial credit for their role in the TB mortality decline (House, 1981; Murray et al., 2015). While these public health advancements and the sanatorium network undoubtedly contributed to the decline of TB in the United States in the early-20th century, the *immediate* decline of TB mortality after the 1918 influenza pandemic raises questions specifically about the role of the pandemic. This effect was likely supplementary to, not independent of, other public health measures that were already facilitating the decline.

Noymer (2009) suggested that this immediate post-pandemic TB decline was due to either “active” or “passive” selection, the former of which assumes that pathogenic co-infection is the precise determinant of increased risk, the latter of which assumes the overlap of the at-risk age categories led to increased mortality. An observed increase in TB mortality during the pandemic itself could have occurred because the contraction of TB in early life made individuals frailer and at higher risk for mortality from influenza during the pandemic. Noymer (2009) proposed that these frail individuals may have been disproportionately represented among individuals aged 20–44, since this age group experienced unprecedented excess influenza mortality. There are, additionally, several other theories regarding the susceptibility of this age group during the 1918 pandemic including but not limited to the previous acquisition of immunity to similar influenza viruses such as the 1889–90 Russian influenza (Gagnon et al., 2013; van Wijhe et al., 2018; Wilson et al., 2014) and the overactive immune response characterized by the cytokine storm (Gagnon et al., 2013; Loo & Gale, 2007; Osterholm, 2005), with some indication that

women of this age are at particular risk of this problem when infected with influenza, especially when pregnant (Gabriel & Arck, 2014). These theories lend credence to passive selection, whereby the age overlap and not necessarily the direct interaction of the disease processes of TB and P&I infection led to increased observed TB mortality during the pandemic.

Noymer (2011) showed that age-standardized death rates from TB for US females and males were between 12.5 and 20.0 deaths per 10,000 individuals, respectively, until the year 1918, after which there was a dramatic decline every year until they reached ~4.0 deaths per 10,000 by the end of the 1940s. Hopewell (2018) made the same observations of TB mortality for the United States and noted a further decline of overall mortality to nearly zero by 1960, but attributed the decline primarily to the effects of the First World War on disease spread and health and only acknowledged the 1918 influenza as a potential “confounder.” Analyses of mortality in other locations in the West, including Switzerland (Holloway et al., 2013), Germany (Loddenkemper & Konietzko, 2018), Austria (Wolf & Junker, 2018), the United Kingdom (Davies & Trafford, 2018), and the Netherlands (van Cleef et al., 2018), show a similar decrease in TB mortality. There are a few locations in which mortality did not experience such a decrease, including Malta (Tripp & Sawchuk, 2017), Japan (Mori & Ishikawa, 2018), and South Africa (Beyers & Gie, 2018). Noymer (2011) argued that the lack of acknowledgment of the role of the 1918 influenza pandemic in accelerating the decline of TB mortality is an oversight that must be corrected.

## 1.1 | Pathogenic co-morbidities and cultural determinants

The well-known interactions between influenza and TB may provide some support for the selective mortality hypothesis. Accelerated declines in TB mortality could have been a consequence of the chronic nature of the disease and associated immunosuppression, resulting in excess deaths of TB-infected individuals who were co-infected with the flu virus itself and/or with secondary bacterial infections, most commonly pneumonia (Brundage & Shanks, 2008; Mamelund & Dimka, 2019; Morens et al., 2008; Walaza et al., 2015, 2020). TB resulting from infection decades prior can become re-activated due to the suppression of immune function brought on by co-infection with another pathogen or immune suppression brought on by chronic or acute malnutrition (Elo & Preston, 1992; Jaganath & Mupere, 2012). The recognition that malnutrition, a social condition with biological consequences, can activate and accelerate TB disease makes the emphasis on social and cultural realities critical for a holistic understanding of the disease.

Noymer (2011) called for more research into co-morbidities with influenza during the 1918 pandemic and associated mortality outcomes during post-pandemic years. It is standard practice to categorize influenza and pneumonia (P&I) as inextricable causes of death—although extreme values of the proportion of P&I deaths accounted for by influenza can be associated with uncharacteristically high

influenza mortality and high volumes of media coverage (as during a flu season), they are considered a single cause of death (Noymer & Nguyen, 2013; WHO, 2019). Further, it is becoming more common to approach the study of infectious diseases and their outcomes on human health holistically by placing a high value on how human behavior and culture become embodied as health, rather than approaching infectious diseases and their biological impacts as individual and mutually exclusive (Goodman & Leatherman, 1998; Herring & Swedlund, 2010; Zuckerman & Martin, 2016). Anthropologically, this is referred to as the biocultural synthesis, which calls specifically for the investigation of how political-economic and social processes affect human biology, and vice versa (Goodman, 2013; Goodman & Leatherman, 1998; Hoke & Schell, 2020; Leatherman & Goodman, 2020; Wiley & Cullin, 2016). Even over two decades after Goodman and Leatherman's (1998) foundational text, there is an absence of engagement with the role of history (Leatherman & Goodman, 2020). This is an important approach when considering the past environments and behaviors of people that may have contributed to infection with TB decades before their death, as well as the ultimate reasons behind deaths attributed to TB.

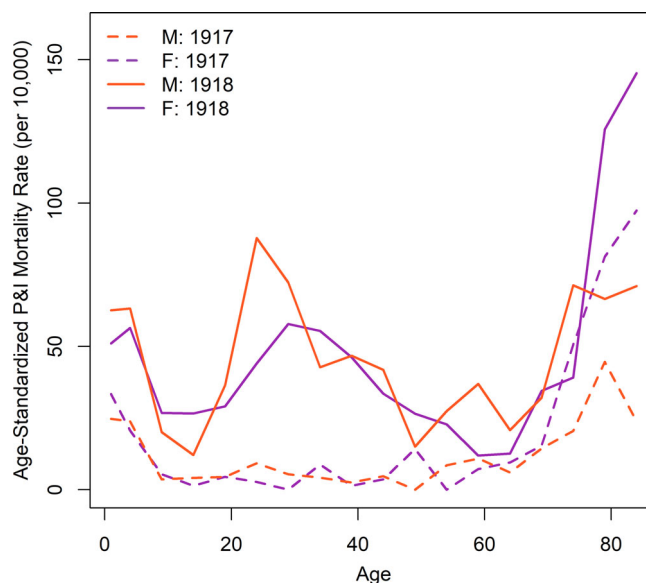
## 1.2 | Newfoundland: A special case of tuberculosis mortality

Suitable archival and demographic data that can be used to answer questions about selective mortality of TB in post-1918 influenza pandemic years are available from the island of Newfoundland, which, during the 1918 pandemic and the two subsequent decades, was a pre-industrial population and independent Dominion of the British Empire. Historical studies of Newfoundland often focus on the tremendous burden of TB on the island since well before the beginning of the 20th century, and the disease was consistently referred to as the "Constant Invader" (House, 1981). The mortality rate from all forms of TB (acute respiratory, extra-pulmonary, and newly active latent forms) at the end of the nineteenth century was 30.9 deaths per 10,000 individuals and it peaked in 1906 at 43.4 deaths per 10,000 individuals (House, 1981). TB mortality rates in other Western cities such as New York City (30.0 per 10,000), London (20.4 per 10,000), Berlin (40.8 per 10,000), and Vienna (40.8 per 10,000) in 1900 were comparable to Newfoundland's in the same year (Provincial Archives of Newfoundland & Labrador [PANL], 1907, File GN 8.47). These rates are not age-standardized and the data to perform direct standardization are not immediately available, but the crude mortality rates suggest that peak TB mortality in Newfoundland was one of the highest in the Western world at the time.

Further, the horrors of TB were not lost on the people of Newfoundland. In February 1908, the Association for the Prevention of Consumption was formed to generate island-wide awareness of the dangers of the disease (Knowing, 1996). Despite widespread approval of the organization, its efforts contributed little to actual medical knowledge and rather emphasized health measures that could curb transmission (Knowing, 1996). Following this initial attempt, the

Registrar General reported in 1910 that TB caused more than 1 in 5 of all deaths, while other epidemic diseases caused less than 1 in 15 of all deaths (PANL File GN 8.47). A report on the state of consumption from 1911 stated that every year, TB cost Newfoundland 400 lives, 3500 cases of sickness, and no less than \$1.2 million, unadjusted for inflation (PANL File GN 8.47).

In addition to the prolific burden of TB, Newfoundland's burden of influenza during the 1918 pandemic makes it an ideal population to study post-pandemic TB mortality. The pandemic hit Newfoundland hard between fall 1918 and spring 1920 with a total mortality rate of 74.5 deaths per 10,000 (Sattenspiel, 2011), and sex-specific mortality rates of 71.1 and 77.1 deaths per 10,000 for males and females, respectively (Paskoff & Sattenspiel, 2019), all figures calculated as the total number of deaths for pandemic years (1918–1920) per 1918 population estimate. Figure 1 shows the difference in sex-based mortality between pre-pandemic year 1917 and 1918, the deadliest pandemic year. The deaths represented in these data include all Newfoundland & Labrador death records with any form of influenza or pneumonia recorded. This figure clearly shows the extreme excess younger adult mortality, specifically of those aged 18–44, for both sexes compared to the otherwise low to nonexistent mortality in 1917, which is assumed to be a typical flu year. In 1917, the total age-standardized influenza mortality rates were 8.9 and 9.9 deaths per 10,000 for males and females respectively, while the 1918 total age-standardized mortality rates were 43.0 and 39.0 deaths per 10,000 for males and females, respectively. Given Newfoundland's high burden of both respiratory diseases and the observed strong selection pressures of this co-morbidity in the younger adult age classes, investigation of post-pandemic age patterns of mortality may hold more answers for overall post-pandemic TB mortality patterns.



**FIGURE 1** Age-standardized influenza mortality rates (per 10,000) for males and females in 1917 (dashed lines) and 1918 (solid lines) illustrating the U-shaped age pattern for a standard flu season and the W-shaped age pattern for the 1918 pandemic

It is important to acknowledge that early-twentieth century Newfoundland had undergone neither the demographic nor the epidemiologic transition that characterized most Western populations of the time (Schmidt & Sattenspiel, 2017). Epidemiologic transition theory, as proposed initially by Omran (1971, 1977) for late nineteenth century Western Europe and the US, highlights the mortality component of the demographic transition, by which high infectious disease and proportionately low chronic disease mortality transitions into low infectious disease mortality and proportionately high chronic disease mortality. McKeown (1976) argues that this transition was propelled more by the adoption of advanced sanitation procedures and superior nutrition than by almost any medical advancement, although this has been debated extensively over the last several decades, as many believe he placed too much emphasis on nutrition and not enough on other demographic and social determinants (Ostry & Frank, 2010; Preston, 2015; Szreter, 1988).

The causes and consequences of the transition on which Omran and McKeown focus remain fiercely debated, as is its relevance to the rest of the world (see, e.g., Alter, 2004; Colgrove, 2002; Mercer, 2018; Ostry & Frank, 2010; Szreter, 2002) but a full discussion of this issue is beyond the scope of this paper. Nonetheless, Omran's (1971, 1977) and McKeown's (1976) ideas about this transition are important to Newfoundland's experience for two reasons: (a) we know Newfoundland's post-pandemic TB mortality pattern was not influenced by factors that characterize typical Western post-demographic and epidemiologic transition populations, and (b) Newfoundland's pattern of mortality can be directly compared with its Western neighbors, which can illuminate important differences in population structure and behavior between pre- and post-transition populations.

This paper uses both quantitative death records and historical documents available for early twentieth century Newfoundland to investigate how infectious co-morbidities and social practices may have influenced post-pandemic TB mortality in a population that was similar to other Western nations in its age-specific pattern of influenza and TB mortality during the 1918 influenza pandemic but exhibited different trajectories of TB mortality in the following decades. This is critical to how we understand long-term mortality patterns that are influenced by epidemic events in populations of differing levels of development.

## 2 | MATERIALS AND METHODS

### 2.1 | The data

The Newfoundland mortality data consist of individual death records collected from the Provincial Archives of Newfoundland & Labrador ("The Rooms"). Accurate and comprehensive death records are available between 1900 and 1939, after which they are very sparse; they cease by 1942. These data include individual records for name, age, sex, cause of death, place of birth, place of death, place of internment (location of burial), and rarely, occupation. A database of 26,565

deaths from any type of TB was compiled, and includes 1789 records attributed to an extra-pulmonary cause of TB (Pott's disease, abdominal, cervical glandular, or consumption of bowels, brain, stomach, throat, kidneys, larynx, bladder, heart, and meninges). Population sizes were obtained from the 1901, 1911, 1921, and 1935 Censuses of Newfoundland & Labrador, and population sizes for intercensal years were estimated by linear interpolation.

With these data, yearly age-standardized mortality rates for the total population, males, and females were calculated for 1900–1939 to discern general patterns of decline. Yearly age-standardized mortality rates were also calculated for each of the four regions of Newfoundland (Avalon, North, South, and West). Further, island-wide age-standardized TB mortality rates for males and females for the four decades of the study period (1900–1909, 1910–1919, 1920–1929, 1930–1939) were calculated to assess the change in average age-specific mortality by decade. Direct age-standardization is a demographic method that ensures the comparability of populations by removing the effects of demographic structure. Any changes year-to-year in the demographic structure of the population during or as a consequence of the First World War or due to 1918 influenza mortality are accounted for using this standardization method. In addition, there is no *a priori* reason to assume that the effects of the First World War had any major consequences for the demographic structure of Newfoundland, as most individuals were turned away from enlistment due to poor health or other issues and very few of the Newfoundland Regiment even went to Europe (Sharpe, 1988).

One of the primary challenges of historical demography and epidemiology is how to use the available data to answer nuanced questions such as those pertaining to early life health and the effects of co-morbidities on the probability of mortality. To contextualize the quantitative results of all analyses in this paper, other documents housed in The Rooms such as reports on public health and reports on the status of tuberculosis (PANL File GN 8.47) were also referenced. These documents hold important information about the epidemiology of the disease at specific points in time, regulations on food quality, and attitudes of the government toward the disease that may have influenced public policy. Good mortality data, with well-recorded causes of death, can be useful when they can be supported with qualitative data detailing both the nutritional and socioeconomic realities.

### 2.2 | Statistical analyses

To determine if there were significant post-1918 pandemic TB mortality declines, joinpoint regression was performed using the Joinpoint Regression Program (version 4.8.0.1) (2020) built by the National Institutes of Health National Cancer Institute. Although this regression method was originally applied to determining significant changes in cancer incidence trends (Kim et al., 2001), it has since seen a wide range of application in other realms, such as identifying changes in trends of colorectal cancer mortality (Ilic & Ilic, 2016), suicide rates in

Denmark (Dyvesether, Nordentoft, Forman, & Erlangsen, 2018), and TB incidence in Iran (Marvi et al., 2017).

The overarching strength, and primary purpose, of this type of regression is in modeling significant changes in rates. The Joinpoint Regression Program (2020) analyzes data with the intent to identify points at which the trend, or slope, of a fitted model changes significantly for observations  $(x_1, y_1), \dots, (x_n, y_n)$  using the general model described by Kim et al. (2001):

$$y_i = \beta_0 + \beta_1 x_1 + \delta_1 (x - \tau_1)^+ + \dots + \delta_k (x - \tau_k)^+ + \varepsilon \quad (1)$$

where  $\beta_0$  is the y-intercept term,  $\beta_1$  is the slope estimate before any joinpoints are identified,  $\delta_k$  is a slope between two estimated joinpoints,  $\tau_k$  is an unknown joinpoint,  $(x - \tau_k)^+$  is  $x - \tau_k$  for  $x_i > \tau_k$  and zero for  $x_i < \tau_k$  (in other words, once a joinpoint is estimated, a new point cannot be added at a lower value of  $x$ ), and  $\varepsilon$  is the model error.

While this type of regression model is often also referred to as segmented or piecewise regression, it has two substantial benefits over them: (a) the program analyzes the data and statistically estimates the points at which there is significant change in data trends without pre-determined input of the location of those points, and (b) the coefficient estimates produced by the model are in the form of annual percent change (APC) in the slopes between each joinpoint calculated (Kim et al., 2001; Rea et al., 2017). If the APC estimate is determined significant by the model at the  $\alpha = 0.05$  level, there is a statistically significant change in the rate (in the case of this study, the TB mortality rate) at the estimated point in time. These analyses were performed both on age-standardized mortality rates for the whole population and on male and female age-standardized TB mortality rates. Joinpoint regression was then performed for age-standardized TB mortality in each of the four regions of the island to identify differences in trends between the region in which the island's urban center was located (the Avalon Peninsula) and the remaining three rural regions. Four models were produced for each of these analyses: zero joinpoints (a straight line) and one through three joinpoints to determine best fit for trends in mortality rates for each subpopulation.

### 3 | RESULTS

The age-standardized TB mortality rates calculated for the whole island and for males and females separately are presented in Table 1 and Figure 2. The yearly age-standardized mortality rates show that there seems to be a general decline in TB mortality through 1939. In Newfoundland, the highest TB mortality rates in the total population, males, and females were 39.9, 35.1, and 47.3 deaths per 10,000, respectively in 1906, but declined to post-pandemic minima of 14.5, 12.4, and 20.6 deaths per 10,000 in 1939. Yearly mortality rates are variable; generalizations about trends in TB mortality beyond the end of the study period cannot be made with confidence.

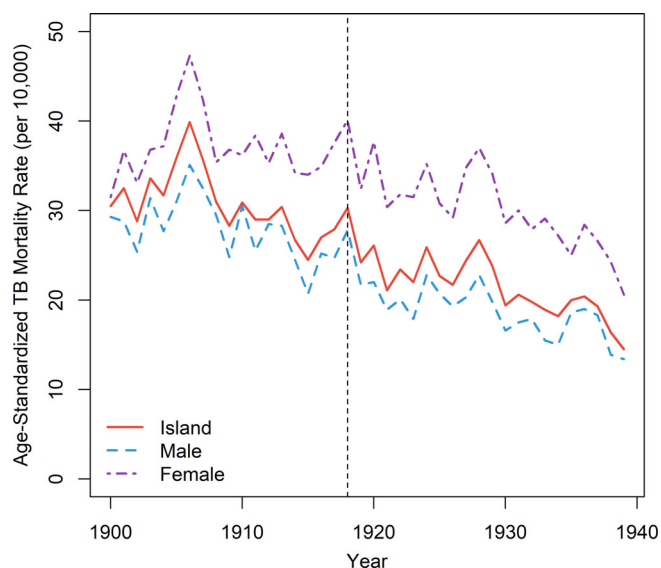
Average age-standardized and sex-based TB mortality rates per decade were calculated and plotted (Figure 3). These results show

**TABLE 1** Yearly age-standardized mortality rates for the whole island of Newfoundland (additionally, males and females), and for each of the four regions

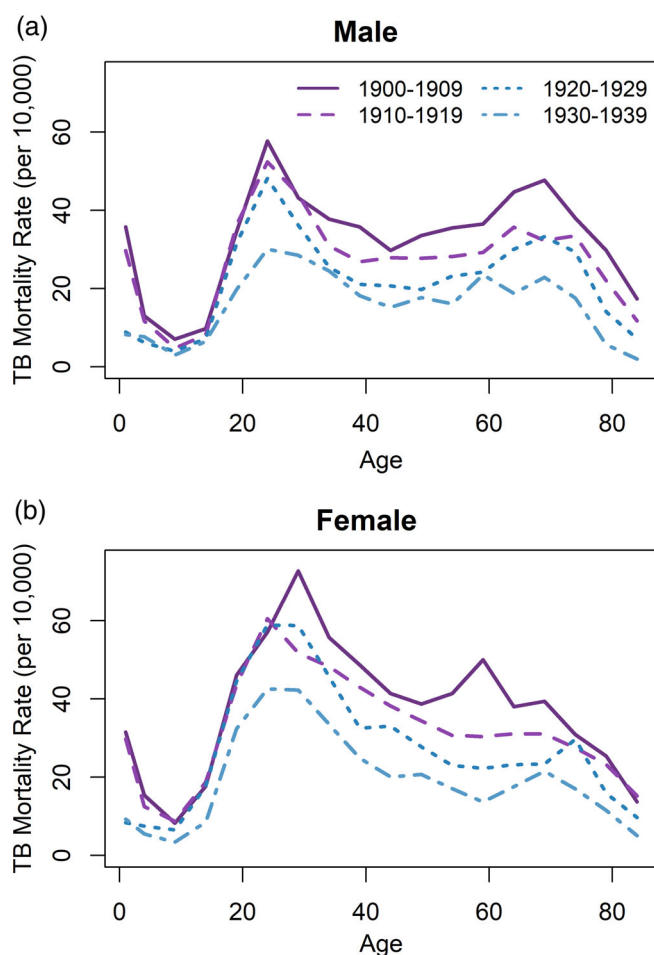
Year	Tuberculosis mortality rate (per 10,000)				
	Island (M, F)	Avalon	North	South	West
1900	30.5 (29.3, 31.5)	34.8	32.6	24.5	15.6
1901	32.5 (28.8, 36.7)	33.6	31.4	31.2	32.2
1902	28.8 (25.4, 33.1)	29.3	31.9	26.6	20.8
1903	33.6 (31.4, 36.8)	38.2	33.4	30.1	21.6
1904	31.7 (27.7, 37.2)	34.7	30.2	25.2	24.8
1905	35.9 (31.0, 42.8)	36.2	32.0	44.3	32.8
1906	39.9 (35.1, 47.3)	42.2	40.5	41.2	28.0
1907	35.7 (32.5, 42.4)	31.3	40.0	40.4	33.0
1908	31.0 (29.5, 35.4)	37.1	23.8	35.3	23.4
1909	28.3 (24.8, 36.8)	35.1	22.6	36.9	20.6
1910	30.9 (30.5, 36.2)	32.2	35.8	33.9	24.5
1911	29.0 (25.5, 38.4)	29.9	32.3	32.5	24.5
1912	29.0 (28.5, 35.3)	29.7	31.3	40.5	21.4
1913	30.4 (28.3, 38.6)	28.7	35.8	36.2	29.7
1914	26.7 (24.5, 34.2)	27.2	30.6	25.2	26.7
1915	24.5 (20.7, 34.0)	26.2	27.3	26.7	21.0
1916	27.0 (25.2, 34.9)	23.4	28.9	41.8	27.7
1917	27.9 (24.7, 37.6)	27.4	31.5	35.4	23.8
1918	30.3 (27.8, 40.1)	31.9	30.2	40.3	29.2
1919	24.2 (21.7, 32.4)	23.9	25.1	34.9	22.7
1920	26.1 (22.0, 37.7)	26.4	30.0	32.2	23.0
1921	21.1 (18.9, 30.4)	19.6	20.5	28.9	21.4
1922	23.4 (20.1, 31.8)	24.6	21.7	28.9	21.5
1923	22.0 (17.9, 31.5)	20.9	24.1	25.4	17.9
1924	25.9 (22.8, 35.2)	26.3	27.4	26.1	24.4
1925	22.7 (20.7, 30.8)	23.3	23.2	26.1	20.1
1926	21.7 (19.3, 29.2)	17.6	20.3	30.2	28.6
1927	24.4 (20.3, 34.8)	23.8	25.8	22.8	26.7
1928	26.7 (22.8, 37.0)	27.3	26.2	20.0	23.4
1929	23.8 (19.8, 34.1)	19.3	24.7	33.2	23.8
1930	19.4 (16.6, 28.6)	18.5	17.7	25.6	22.0
1931	20.6 (17.5, 30.0)	17.8	21.8	21.2	26.7
1932	19.8 (17.9, 27.9)	17.0	20.0	25.3	22.7
1933	18.9 (15.5, 29.1)	15.4	20.8	22.0	22.9
1934	18.2 (15.0, 27.2)	12.3	19.0	23.4	24.1
1935	20.0 (18.6, 25.0)	15.6	18.7	25.7	29.9
1936	20.4 (19.0, 28.4)	17.3	21.5	24.7	21.8
1937	19.3 (18.3, 26.6)	24.0	13.4	21.3	17.5
1938	16.4 (13.9, 24.3)	25.7	16.7	18.6	12.4
1939	14.5 (13.4, 20.6)	14.2	14.2	16.3	12.6

that there was indeed a decline in TB mortality for males and females in each decade. Further, there is clearly higher mortality in adults aged 20–44 than any other age group, although males aged 60+ had





**FIGURE 2** Age-standardized all-cause TB mortality rates (per 10,000) for the total population, males, and females from 1900 through 1939. The year 1918 is indicated by a dashed vertical line



**FIGURE 3** Standardized age-based TB mortality (per 10,000) for (a) males and (b) females for the four decades of the study period: 1900–1909, 1910–1919, 1920–1929, and 1930–1939

comparable mortality rates to the younger adults. This analysis affirms that, as described in other populations, adults aged 20–44 disproportionately contributed to the TB mortality experience in Newfoundland in the early twentieth century, specifically as seen in the 1910–1919 decade for both sexes.

The results of the joinpoint regression analyses for island-wide and sex-based TB mortality can be found in Table 2. Significant changes in slope, or yearly TB mortality rate, are noted in the APC columns (<sup>†</sup>); for example, for males, Model 2 predicts one joinpoint at 1906, which shows there is a significant change in slope for 1906–1939 compared to 1900–1906. The most important result to draw from these analyses is that no model identified a significant decline in TB mortality rates immediately after the 1918 influenza pandemic, as the selective mortality hypothesis suggests there would be. The APCs for Model 4 of the female TB mortality data do estimate a significant decrease in mortality rate in 1928, but this is an entire decade after the majority of the 1918 P&I mortality occurred. It cannot be attributed with confidence to selection driven by the 1918 pandemic. The models rather suggest linear declines beginning about a decade before the 1918 pandemic through the end of the study period, as shown by joinpoint predictions in 1902, 1906, and 1909 for males and 1905, 1906, and 1909 for the whole island. Figure 4 shows the observed TB mortality rates and model fits (two joinpoints for the island, two joinpoints for males, and three joinpoints for females to show 1928–1939 decline; see Supplementary Figure 1 for all model fits). According to the regression estimates and corresponding plots (Figures 2 and 3), island-wide female age-standardized TB mortality was higher than that of males and remained so throughout the study period.

Regression analyses at the regional level reported in Table 3 exhibit the same essential result: no model predicted a joinpoint shortly after the 1918 influenza pandemic that would indicate there was a significant decline in TB mortality as a direct consequence of the pandemic. Each of the regions clearly suffered the highest mortality in 1906, but in general, TB mortality rates decreased linearly from the middle to end of the first decade through the end of the study period. Plots of model fits for the four regions can be found in Figure 5.

There are two exceptions to the generalization that there was linear change. First, Model 4 in the South predicted a significant APC of  $-0.73$  for 1917–1939 ( $p < 0.001$ ). While 1917 is before the nominal pandemic flu year, it is possible that high 1918 influenza mortality in the South was such that it was indeed the turning point in TB mortality decrease in that region. The South did experience some of the highest standardized pandemic mortality of all four regions (Sattenspiel, 2011), but given the nature of the highly insignificant APC estimates for the two preceding joinpoints predicted by this model, this result could be due to overfitting the data rather than truly significant decline or association with the 1918 pandemic. Second, Model 4 in the West predicted a significant APC of  $-3.34$  for the years 1935–1939 ( $p = 0.048$ ). Models 2–3 in the West also predict a similarly rapid decline, but they are only significant on the  $\alpha = 0.10$  level ( $p = 0.075$  and  $0.052$ , respectively).

**TABLE 2** Joinpoint regression analyses for males, females, and total island TB mortality rates (per 10,000 individuals) for the years 1900–1939

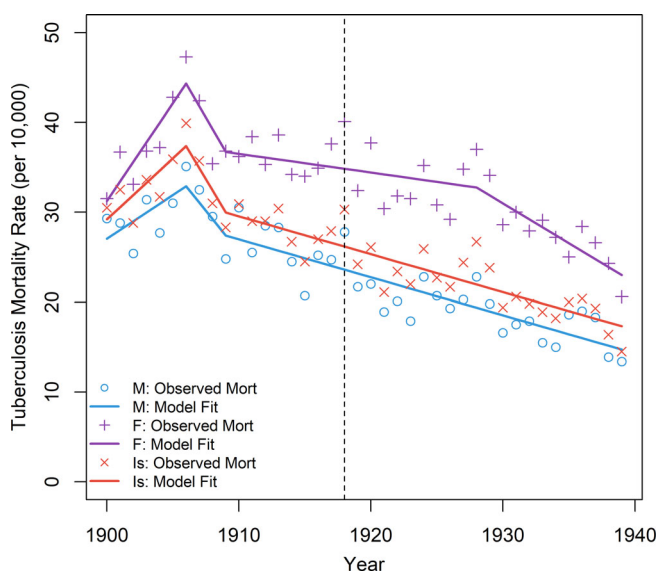
Male			Female			Total Island		
Slope (year range)	APC (SE)	p-value	Slope (year range)	APC (SE)	p-value	Slope (year range)	APC (SE)	p-value
<i>Model 1: Zero joinpoints</i>			<i>Model 1: Zero joinpoints</i>			<i>Model 1: Zero joinpoints</i>		
1900–1939	−0.42 (0.04) <sup>a</sup>	<0.001***	1900–1939	−0.45 (0.04) <sup>a</sup>	<0.001***	1900–1939	−0.44 (0.04) <sup>a</sup>	<0.001***
<i>Model 2: One joinpoint</i>			<i>Model 2: One joinpoint</i>			<i>Model 2: One joinpoint</i>		
1900–1906	0.30 (0.56)	0.596	1900–1905	1.87 (0.93)	0.053	1900–1905	0.64 (0.77)	0.414
1906–1939	−0.48 (0.04) <sup>a</sup>	<0.001***	1905–1939	−0.46 (0.05) <sup>a</sup>	<0.001***	1905–1939	−0.51 (0.04) <sup>a</sup>	<0.001***
<i>Model 3: Two joinpoints</i>			<i>Model 3: Two joinpoints</i>			<i>Model 3: Two joinpoints</i>		
1900–1906	0.97 (0.55)	0.084	1900–1906	2.12 (0.65) <sup>a</sup>	0.002**	1900–1906	1.36 (0.49) <sup>a</sup>	0.009**
1906–1909	−1.83 (3.23)	0.575	1906–1909	−1.91 (3.86)	0.623	1906–1909	−2.47 (2.90)	0.402
1909–1939	−0.42 (0.05) <sup>a</sup>	<0.001***	1909–1939	−0.41 (0.06) <sup>a</sup>	<0.001***	1909–1939	−0.42 (0.04) <sup>a</sup>	<0.001***
<i>Model 4: Three joinpoints</i>			<i>Model 4: Three joinpoints</i>			<i>Model 4: Three joinpoints</i>		
1900–1902	−1.61 (3.24)	0.625	1900–1906	2.18 (0.57) <sup>a</sup>	<0.001***	1900–1902	−0.85 (2.90)	0.772
1902–1906	1.91 (1.62)	0.249	1906–1909	−2.54 (3.39)	0.459	1902–1906	2.16 (1.46)	0.148
1906–1909	−2.25 (3.24)	0.493	1909–1928	−0.21 (0.11)	0.607	1906–1909	−2.83 (2.91)	0.339
1909–1939	−0.42 (0.05) <sup>a</sup>	<0.001***	1928–1939	−0.89 (0.23) <sup>a</sup>	<0.001***	1909–1939	−0.42 (0.04) <sup>a</sup>	<0.001***

<sup>a</sup>Indicates estimated annual percent changes (APC) that are statistically significant at the  $\alpha = 0.05$  level (Kim et al., 2001).

\* $p = 0.05$ ;

\*\* $p = 0.01$ ;

\*\*\* $p = <0.001$ .

**FIGURE 4** Best-fit joinpoint regression models for the total island population, males, and females for the duration of the study period. The year 1918 is indicated by a dashed vertical line (see Figure S1 for all tested model fits)

## 4 | DISCUSSION

In Newfoundland, it was well-known in the early twentieth century that there was a “lamentable” prevalence of TB throughout the island, but the available facilities and medical expertise island-wide were not

sufficient to gather the detailed information needed to develop comprehensive policy to address the issue. The peak in TB mortality in 1906 as seen in Figures 2, 4, and 5, may have been the turning point for formalizing the anti-TB campaign on the island; the Report on the Commission of Public Health in 1909 acknowledged the complexity of the problem and the large and expensive organization required to effectively combat the threat (PANL File GN 8.47). Even though the Commission of Public Health observed that Newfoundland had relatively low population density and had the advantage of “exceptionally pure and invigorating” air, they also acknowledged that while the mortality records and vital statistics were accurate, the true extent of the morbidity of TB on the island was unknown (PANL File GN 8.47). The Commission noted that countries such as the United States and Canada that were successful in their anti-tuberculosis campaigns required compulsory notification of the disease, saying “this has everywhere been deemed the first step towards combating the evil ... When the individual cases are not known it is of course impossible to deal with them” (PANL File GN 8.47).

Modulating the TB problem would take another few decades in Newfoundland. TB mortality remained high through the 1940s, with 11.4 deaths per 10,000 in 1945 and 10.1 deaths per 10,000 in 1946, after which the Department of Public Health began an island-wide case-finding campaign to attempt to reduce the burden further (Aykroyd et al., 1949; Lawson & Noseworthy, 2009).

According to medical surveys performed at the time, TB mortality in 1940 was about three times as high in Newfoundland as in the rest of Canada (4.1 deaths per 10,000 individuals) (Adamson et al., 1945). Further, historical accounts of TB in Newfoundland do not indicate a

**TABLE 3** Joinpoint regression analyses of TB mortality rates (per 10,000 individuals) for the four regions of the island: Avalon, north, south, and west for the years 1900–1939

Avalon			North		
Slope (year range)	APC (SE)	p-value	Slope (year range)	APC (SE)	p-value
<i>Model 1: Zero joinpoints</i>			<i>Model 1: Zero joinpoints</i>		
1900–1939	−0.54 (0.05) <sup>a</sup>	<0.001***	1900–1939	−0.47 (0.05) <sup>a</sup>	<0.001***
<i>Model 2: One joinpoint</i>			<i>Model 2: One joinpoint</i>		
1900–1934	−0.62 (0.06) <sup>a</sup>	<0.001***	1900–1906	0.51 (0.87)	0.056
1934–1939	0.89 (1.16)	0.449	1906–1939	−0.54 (0.07)	<0.001***
<i>Model 3: Two joinpoints</i>			<i>Model 3: Two joinpoints</i>		
1900–1905	0.57 (1.15)	0.625	1900–1906	0.45 (0.87)	0.611
1905–1934	−0.70 (0.08) <sup>a</sup>	<0.001***	1906–1936	−0.51 (0.08) <sup>a</sup>	<0.001***
1934–1939	1.10 (1.15)	0.343	1936–1939	−1.56 (2.59)	0.550
1900–1905	0.63 (1.04)	0.550	1900–1906	1.09 (0.65)	0.102
1905–1934	−0.72 (0.08)	<0.001***	1906–1909	−2.46 (3.82)	0.373
1934–1937	2.83 (4.67)	0.550	1909–1912	1.99 (3.82)	0.61
1937–1939	−3.35 (4.67)	0.480	1912–1939	−0.62 (0.07) <sup>a</sup>	<0.001***
South			West		
Slope (year range)	APC (SE)	p-value	Slope (year range)	APC	p-value
<i>Model 1: Zero joinpoints</i>			<i>Model 1: Zero joinpoints</i>		
1900–1939	−0.37 (0.08) <sup>a</sup>	<0.001***	1900–1939	−0.14 (0.06) <sup>a</sup>	0.035*
<i>Model 2: One joinpoint</i>			<i>Model 2: One joinpoint</i>		
1900–1906	2.48 (1.09) <sup>a</sup>	0.029*	1900–1935	−0.03 (0.07)	0.697
1906–1939	−0.59 (0.08) <sup>a</sup>	<0.001***	1935–1939	−3.21 (1.76)	0.075
<i>Model 3: Two joinpoints</i>			<i>Model 3: Two joinpoints</i>		
1900–1903	0.66 (2.99)	0.827	1900–1905	1.00 (1.18)	0.401
1903–1906	3.61 (5.99)	0.552	1905–1935	−0.09 (0.08)	0.274
1906–1939	−0.60 (0.08) <sup>a</sup>	<0.001***	1935–1939	−2.98 (1.67)	0.083
<i>Model 4: Three joinpoints</i>			<i>Model 4: Three joinpoints</i>		
1900–1906	2.71 (0.99) <sup>a</sup>	0.010*	1900–1906	1.75 (0.87)	0.052
1906–1914	−1.14 (0.78)	0.157	1906–1909	−2.32 (5.12)	0.655
1914–1917	1.23 (5.85)	0.835	1909–1935	0.03 (0.10)	0.785
1917–1939	−0.73 (0.14) <sup>a</sup>	<0.001***	1935–1939	−3.34 (1.62) <sup>a</sup>	0.048*

<sup>a</sup>Indicates estimated annual percent changes (APC) that are statistically significant at the  $\alpha = 0.05$  level (Kim et al., 2001).

\* $p = 0.05$ ;

\*\* $p = 0.01$ ;

\*\*\* $p = <0.001$ .

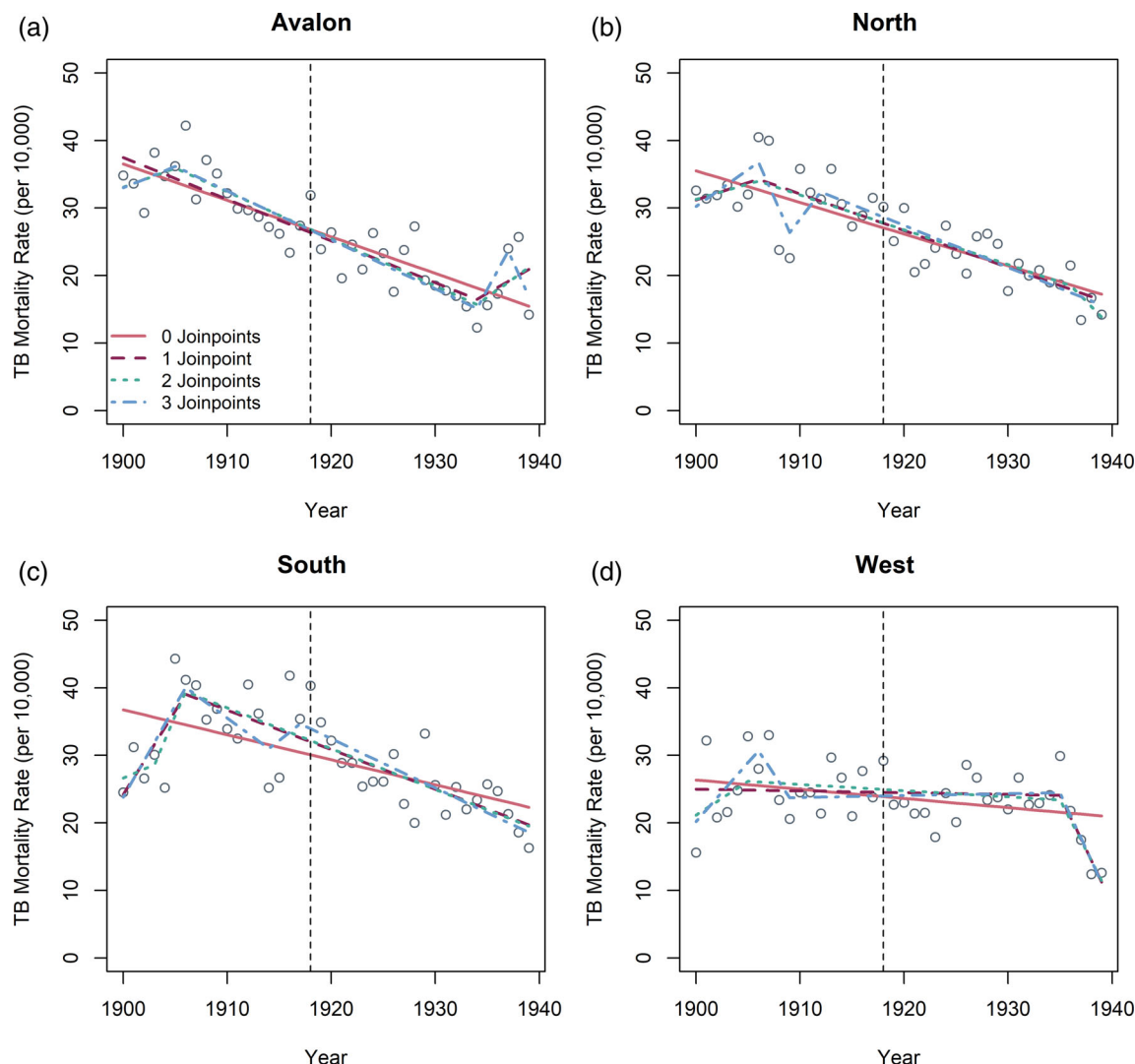
simultaneous decrease in morbidity through the same time period; rather, they suggest consistently high morbidity, and no real turning point until the 1970s (House, 1981). This raises two questions for future research: what are the patterns and variations in post-pandemic TB mortality decline in other populations, and what population-specific factors have the strongest influence on the magnitude of the decline?

As the results of the total island and sex-based TB mortality indicate (Figure 2), there was a general decrease in mortality rates through the end of 1939, but these rates were still three to four times higher than those reported by Noymer (2009) for the United States

by the end of the same time period. In the late 1930s, a sanatorium doctor estimated the total incidence of the disease was about 4% of the island's population, suggesting 12,000 new cases in 1938–1940 alone (House, 1981). Further, Newfoundland had been in considerable debt since the end of the 1918 influenza pandemic and the First World War, and by the time anti-TB drugs were made available in the United States around the end of the Second World War, the island could not easily supply the new antibiotics to patients who needed them (Hopewell, 2018; House, 1981).

The sex-based differences in TB mortality during the study period also suggest interesting differences between Newfoundland and the





**FIGURE 5** Joinpoint regression models for each of the four regions of the island of Newfoundland: (a) Avalon, (b) north, (c) south, and (d) west. The year 1918 is indicated by a dashed vertical line

United States, where males are consistently observed to have higher mortality from TB for every year from 1900 through 1940 (Noymer, 2009; Noymer & Garenne, 2000). In Newfoundland, age-standardized mortality rates from the beginning of the twentieth century through 1939 clearly indicate higher female TB mortality rates (Figure 2).

Paskoff and Sattenspiel (2019) showed that rates of P&I mortality by sex during the 1918 pandemic could be used to predict mortality among the four different regions, especially for the South, in which females were more likely to die than males. Results of this study also showed that substantial differences in P&I mortality between males and females occurred only in the South and West (Paskoff & Sattenspiel, 2019). At the very least, in these regions, higher female TB mortality during the pandemic may have been driven by the corresponding higher female P&I mortality. It is likely that, as was observed by Paskoff and Sattenspiel (2019) for influenza, differing levels of socioeconomic status, geographic isolation, and lack of

medical resources, especially in the rural South, contributed to the observed pattern of TB mortality in the current study.

No clear rapid reduction in TB mortality rates for the two decades beyond the end of the 1918 pandemic (1920–29 and 1930–39) is observed to suggest increased selection against the least healthy individuals in 1918, but rather there is an incremental decrease that resembles that of the two preceding decades before the 1918 pandemic (Figure 3). The results of the change in mortality by decade (Figure 3) indicate that mortality rates peaked in infants, adults aged 20–44, and adults aged 60+, a pattern consistent with TB mortality observed elsewhere (Grigg, 1958; Noymer, 2011; Tripp & Sawchuk, 2017; Zürcher et al., 2016). Unlike the post-pandemic decline in young adult mortality observed by Noymer (2011), however, in Newfoundland both males and females aged 20–44 had the highest TB mortality rates throughout the four-decade study period. This suggests substantial, persistent population-level risk for adults aged 20–44 in Newfoundland during the early twentieth century that

prevented a significant decline in TB mortality rates after the 1918 pandemic. To fully understand these effects, it is important to consider how history, culture, and behavior contribute to differential population-level disease and mortality risks, not simply the biological interactions of the pathogens and disease processes.

Physicians who performed nutritional surveys in rural regions of Newfoundland, such as the West and South, hypothesized that poor nutritional status had a strong influence on the high prevalence and severity of TB throughout the island. Nutrition was so poor in rural regions that even by the mid- to late-1940s, common physical pathologies in both children and adults included severe chronic lesions of the mouth, tooth loss, dental caries, scurvy, severely low levels of vitamin C, low body weight, atrophied and wrinkled skin, low muscular development, and mental and physical lethargy (Adamson et al., 1945; Aykroyd et al., 1949). The offending diets primarily consisted of white flour, cod, and a noticeable lack of fresh fruits and vegetables; Newfoundland's Department of Agriculture estimated that only 1% of the island's land was suitable for "agriculture," a generous term for what ultimately amounted to small-scale gardening (Adamson et al., 1945). Widespread malnutrition was observed until at least the mid-20th century, but one of the earliest identifications of extremely poor health was the observation that in the West and South, 53% and 56%, respectively of eligible men recruited for the Newfoundland Regiment in 1916 during the First World War were sent home because they were too physically weak (Sharpe, 1988).

Poor nutrition goes hand-in-hand with another form of TB infection that was present in early-20th century Newfoundland: extrapulmonary tuberculosis (x-TB), the primary origin of which was milk and meat of tuberculous cattle. Even though these products were consumed in low amounts throughout the island, from 1900 to 1939, in the death records there were 1789 deaths attributed to some form of x-TB out of 26,565 total TB deaths. There are complications that emerge with diagnostic criteria over four decades, but this was enough to warrant the concern of public health officials at the time (PANL File GN 8.47). The pathogen responsible for the observed prevalence of x-TB was likely *M. bovis*, the causative agent of bovine TB and an occasional causative agent of TB in humans that infects the GI tract primarily through infected milk and meat (Donoghue, 2009; O'Reilly & Dabor, 1995; Pérez-Lago et al., 2014). Due to its ease of transmission, *M. bovis* is still considered a major public health problem today, especially in the global south (O'Reilly & Dabor, 1995; Pérez-Lago et al., 2014).

Newfoundland officials estimated that at the beginning of the 20th century, at least 30% of cattle in England (the primary origin of imported beef) were somewhat tuberculous (PANL File GN 8.47). Further, as a matter of policy, contaminated meat was identified from visible lesions in the tissue; if these were not present, the meat could be imported and sold. If lesions were identified, criteria were in place that removed only contaminated organs (if the infection did not involve the lungs) and let the rest of the animal be imported (PANL File GN 8.47). The causative agent of x-TB infection, therefore, was allowed to enter the diets of the people of Newfoundland through their primary meat source.

Food sourcing and nutrition practices contributed to widespread general malnutrition and frailty that likely left populations more vulnerable to co-circulating diseases like TB, pneumonia, and influenza. Poor general health of the population for at least the first half of the 20th century may have prevented opportunities for significant declines in TB mortality rates. Despite a quantifiable slow decline in mortality rate from all forms of TB, the number of cases of individuals living with the disease remained high, which is not indicative of a population whose health is improving. This is substantiated by the fact that Newfoundland was a few decades away from TB control that included significant reductions in incidence, prevalence, and mortality (House, 1981). The regression analyses in the current study, for which all but one of the good fit models (island-wide female mortality) failed to predict a significant decrease in TB mortality rate immediately post-1918 pandemic, also support the conclusion that despite gradual linear decline from around 1906, there was no public health intervention or epidemic event that led to selection that could be associated with improvements in population health.

The single exception could be the Western region, for which the two- and three-joinpoint models predicted declines at the  $\alpha = 0.10$  level, and the four-joinpoint model predicted a significant decline at the  $\alpha = 0.05$  level, all for years 1935–1939. The APCs predicted in these models are some of the steepest predicted declines in the entire study, but they all have a slope of near zero for 1909–1935, suggesting that the TB mortality rate remained unchanged for a large portion of the early-20th century before dropping off quickly. An explanation for the observed differences between the West and other regions is the presence of the Grenfell Mission, a hospital established in 1892 in the northernmost corner of the island. As part of its mission, the hospital specialized in the care of TB patients, and it was well-funded and well-known for its success in helping ill patients regain their health (House, 1981). Throughout the first four decades of the twentieth century, this hospital was also the only centralized healthcare location outside of the Avalon region (Lawson & Noseworthy, 2009). This is likely a major reason the West's TB mortality rate started off much lower, and stayed low compared to the other three regions, for the entire study period (Figure 5). It is possible, therefore, that the rapid decline in TB mortality rate in the West at the end of the 1930s predicted by these models represents a true decline, but this decline cannot be confidently associated with the 1918 flu mortality event that happened nearly 20 years earlier.

The lack of support for the relationship between observed TB mortality decline and the 1918 pandemic is not entirely surprising, as Newfoundland was a pre-epidemiologic transition population at the time of study, meaning infectious disease mortality was proportionately higher than any other form of mortality (Omran, 1971; Schmidt & Sattenspiel, 2017). The United States, on the other hand, had been transitioning to a state of proportionately lower infectious disease mortality for almost 70 years by 1918, a transition that was upheld by infrastructural improvements in medical procedure, water sanitation, and nutrition needed to sustain a larger and longer-lived population (McKeown, 1976; Omran, 1977). Newfoundland's demographic and epidemiologic transition showed its first signs of beginning only by

the 1930s, and changes in life expectancy and cause of death indicative of the epidemiologic transition were observed at that time only for the capital region on the Avalon Peninsula (Schmidt & Sattenspiel, 2017). The widespread inability to control the incidence, prevalence, and mortality of all forms of TB in Newfoundland may in fact have been a primary factor in delaying the epidemiologic transition throughout the island.

The current study of Newfoundland did not identify any statistically significant decline in TB mortality immediately after the 1918 influenza pandemic, but rather a sustained, linear decline beginning around 1906 through the end of the study period in 1939. These results do not support a selective mortality hypothesis that strong selection against the frailest individuals during the pandemic years left a relatively more robust population and an accelerated decline in TB mortality in the following decades. Rather, vital and historical records suggest that the general health of Newfoundland populations was poor far beyond the end of 1939. These results, however, should not and do not negate the significance of the work on selective TB mortality done in the United States, and this paper does not seek to fundamentally reframe the observations initially made by Abbott (1922) and expanded upon by Noymer and Garenne (2000) and Noymer (2009, 2010, 2011). Instead, we seek to acknowledge variation in these post-pandemic patterns for populations at different stages of transitioning to lower infectious disease mortality levels, which is critical to modern-day applications of anthropology, demography, and epidemiology.

As outlined previously, there appear to be two distinct groups that emerge in the discussion of post-1918 influenza pandemic TB mortality patterns: one characterized by large decreases in TB mortality over the following decades as observed in Switzerland (Holloway et al., 2013), Germany (Loddenkemper & Konietzko, 2018), Austria (Wolf & Junker, 2018), the UK (Davies & Trafford, 2018), and the Netherlands (van Cleef et al., 2018), and a second that did not have observable significant decreases (Malta [Tripp & Sawchuk, 2017], Japan [Mori & Ishikawa, 2018], and South Africa [Beyers & Gie, 2018]). Newfoundland, ultimately, aligns most closely with this second group. Questions remain about the common demographic and cultural characteristics, if any, that would determine these populations' similar post-1918 pandemic TB mortality trajectories. Further research is needed, both with macro- and microdata, to glean more insights into determinants of the post-1918 influenza pandemic TB decline in variable populations to identify common characteristics that influence overall population health.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to report.

## AUTHOR CONTRIBUTIONS

**Taylor van Doren:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; software; writing—original draft; writing—review & editing. **Lisa Sattenspiel:** Conceptualization; data curation; formal analysis; funding acquisition; methodology; supervision; writing—original draft; writing—review & editing.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available on the Newfoundland's Grand Banks website at <http://ngb.chebucto.org>. Any other data is available upon request.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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