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Doomed to Die?: An Examination of Demographics and Comorbidity During the 1918 Influenza Pandemic in Milwaukee, Wisconsin

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Abstract: The 1918 influenza pandemic is estimated to have killed 20 to 50 million people worldwide, with over half a million American casualties both at home and abroad. Despite the devastating effects, the 1918 outbreak of the Spanish Flu is often overlooked. This is possibly due to the United States victory in World War I, which ended shortly after the influenza pandemic began, or to a lack of adequate medical understanding of the disease, highlighting the elusive nature of the virus' transmission. Comparatively lower mortality rates in Wisconsin are a reflection of lower population densities throughout the state, as well as active government and civic prevention efforts. With an understanding of the incredible virulence of the 1918 influenza outbreak, I investigated comorbid tuberculosis (TB) as a cause of potency and the patterns of selective mortality within a Midwestern population. This project employs documentary data from Milwaukee County, Wisconsin, to assess the patterns of selection for age and sex, as well as investigate the selective force of TB during the 1918 influenza epidemic in Milwaukee. Results indicate a W-shaped mortality curve with the highest death rates occurring within the young and middle adult cohorts. A selective bias towards males is observed, providing evidence for TB-influenza interaction. Additionally, the confluence of influenza and TB was noted on individual death certificates. This comorbidity of TB and influenza facilitated lasting social change for women's rights and may have important implications for the understanding, treatment and prevention of future outbreaks.

Keywords: influenza, historic archaeology, paleodemography

Introduction

The 1918 influenza pandemic is estimated to have killed 20 to 50 million people worldwide (Ahmed, Oldstone and Palese

2007; Mills, Robbins and Lipsitch 2004; Taubenberger and Morens 2006; Tumpey et al. 2005). This viral outbreak became known as the Spanish Influenza due to the uncensored press reports broadcasting the impacts of the virus from within the county of Spain, giving the illusion that Spain was singularly devastated by the epidemic (Barry 2004). Also called "La Grippe", the 1918 influenza pandemic is currently recognized as the worst epidemic in recorded history, killing more people than all wars of the twentieth century combined (Quinn 1999). Despite the high mortality rates in Europe and the United States, little information is evident in the mass media outlets of the time (Quinn 1999). This lack of attention could be related to the Allied victory in World War I, which was contemporaneous and highly publicized, or to a lack of adequate medical understanding of the disease (Quinn 1999). Although it is unknown why the 1918 influenza pandemic is "the 20th century's most readily forgotten global disaster" (Brown 1992), evidence of the virulence and selectivity of this outbreak can be estimated from examination of individual death records.

From the beginning of the outbreak in September 1918, to the following fall of 1919, over half a million Americans perished from influenza (Quinn 1999). During the three-month period from September to December of 1918, at least 103,000 people were infected in Wisconsin alone (Burg 2000; Quinn 1999). The death toll from influenza or influenza-related pneumonia in Wisconsin at the end of 1918, reached over 18,000, an approximate 19% increase from the influenza and pneumonia mortality rates from the entirety of 1917 (Annual Report 1918; Burg 2000; Quinn 1999; Wisconsin Blue Book, 1919).

Many unanswered questions surround the origin and epidemiology of the 1918 influenza virus. It has been theorized that undetected tuberculosis (TB) may have been the driver behind this virulent flu outbreak (Broxmeyer 2006; Morens, Taubenberger and Fauci 2008; Noymer 2008, 2011, 2012; Oei and Nishiura 2012; Taubenberger and Morens 2006; Wanatabe et al. 2014). An examination of the current TB epidemic revealed that the American Midwest would have been highly vulnerable to this disease during the time of the 1918 influenza outbreak (Broxmeyer 2006). "In 1917, it was estimated that 25% of deaths from tuberculosis in adult humans were caused by animal tuberculosis" (Broxmeyer 2006:1008). Autopsies of a sample of the thousands of pigs that died in Kansas in the fall of 1918, indicated

that avian TB was to blame (Broxmeyer 2006). It was hypothesized that pigs in the Midwestern United States became unwitting petri-dishes where avian and human TB genetically combined through mycobacteriophage mutation (Broxmeyer 2006). Mycobacteriophage refers to the infection of one TB virus by another virus, in this case, the infection of human TB by avian TB, or vice versa (Broxmeyer 2006). Shortly after the influenza epidemic in the rural swine populations of Haskell County, Kansas, the mutated strain of influenza began to affect the servicemen at Camp Funston a few hundred miles away, followed swiftly by reports from Fort Devens, Massachusetts by September of 1918 (Broxmeyer 2006). Other research suggested that the 1918 influenza strain is a subtype of the H1N1 swine flu virus that caused a pandemic in 2009 (Broxmeyer 2006; Morens, Taubenberger and Fauci 2008; Wanatabe et al. 2014).

It is hypothesized that this mutated, deadly strain of influenza evolved within the swine populations of the United States and was spread across the globe via servicemen who fought overseas during World War I (Burg 2000; Morens, Taubenberger and Fauci 2008). The first documented case of the Spanish flu in the United States was reported in Boston on September 14th, 1918 (Burg 2000). The earliest signs of the Spanish Influenza in Wisconsin occurred during the week of September 11th, 1918, at the Great Lakes Training Facility, located approximately 50 miles south of Milwaukee (Burg 2000; Quinn, 1999). Within the first seven days, approximately 2,600 servicemen were hospitalized, and by the third week in September, 100 deaths were reported at the training facility (Burg 2000; Quinn 1999). The death rates in Wisconsin were high (Figure 1), but despite its virulence, Wisconsin had the fourth lowest mortality rates within the United States (Acuna-Soto et al. 2011; Burg 2000; Shors and McFadden 2009).

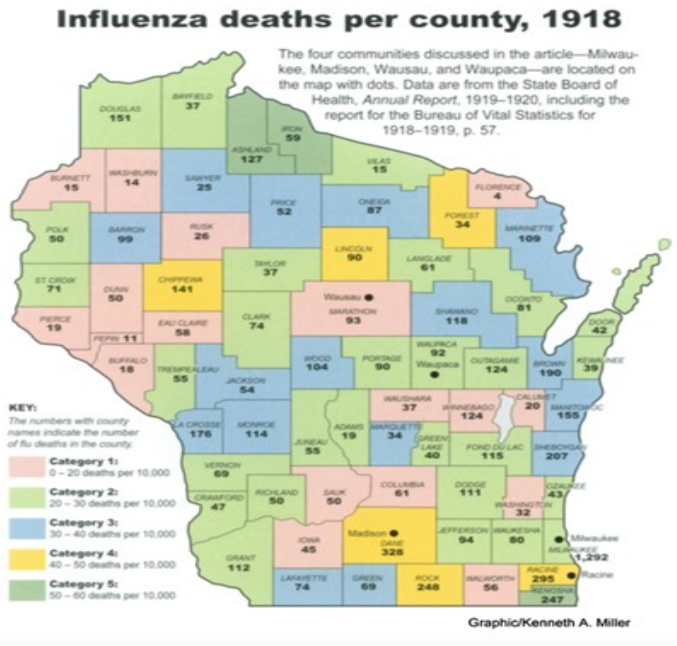

Figure 1. Death rates during the 1918 Spanish Flu in Wisconsin, per county (adapted from Burg, 2000).

The lower mortality rates in Wisconsin are a reflection of lower population densities throughout the state, as well as active government and civic prevention efforts (Bootsma and Ferguson 2007; Burg 2000; Leavitt 1996; Markel et al. 2007; Quinn 1999; Report of the State Board of Health 1919; Wisconsin State Board of Health Bulletin 1918). On page 2 of the July-September, 1918, edition of the State of Wisconsin State Board of Health Bulletin, the importance of the influenza mask, as well as instructions for its creation, are used to emphasize the use of masks as an effective preventative agent against communicable diseases (Wisconsin State Board of Health Bulletin 1918). The Bulletin also mentions the use of vaccinations to prevent the Spanish flu virus, but the vaccines from this time were found to be ineffective (Wisconsin State Board of Health Bulletin 1918). Non-pharmaceutical interventions, such as school closure, cancellation of public events, and quarantine, were found to be highly effective in the prevention of the spread of Spanish flu in Milwaukee (Bootsma and Ferguson 2007; Burg 2000; Leavitt 1996; Markel et al. 2007; Quinn 1999).

In an effort to better understand the mechanisms of the 1918 outbreak, physicians were urged to attend the American Public Health Association annual meeting in December 1918, which held a special symposium on influenza (Wisconsin State Board of Health Bulletin 1918). At least half of the Health Bulletin from October-December 1918, focused on the facts of the Spanish flu, the reinvestigation of potential vaccines and methods of prevention (Wisconsin State Board of Health Bulletin 1918). "The death rate for 1918 is more than 3 per thousand population higher than any rate ever recorded in Wisconsin and is due entirely to the influenza epidemic which swept over the state during the months of October, November and December" (Wisconsin State Board of Health Bulletin 1918:17-18).

With an understanding of the incredible virulence of the 1918 influenza outbreak, I investigate comorbid TB as a cause of potency, and the patterns of selective mortality within a Midwestern population. Therefore, this project employs documentary data from Milwaukee County, Wisconsin, to assess the patterns of selection for age and sex, as well as investigate the selective force of TB during the 1918 influenza epidemic in Milwaukee.

Previous Research

Age-Based Mortality Patterns

During an outbreak of the common flu virus one would expect to see a U-shaped mortality pattern (Figure 2) (Ahmed, Oldstone and Palese 2007; Gagnon et al. 2013; Noymer 2011; Taubenberger and Morens 2006). Within the U-shaped pattern the highest death rates occur in very young and very old individuals, with the young and middle adult cohorts remaining less susceptible to infection (Ahmed, Oldstone and Palese 2007; Gagnon et al. 2013; Noymer 2011; Taubenberger and Morens 2006). However, during the 1918 influenza pandemic mortality patterns exhibited an uncharacteristic W-shape (see Figure 2) that has yet to be replicated by any other disease outbreak (Ahmed, Oldstone and Palese 2007; Gagnon et al. 2013; Noymer 2011; Noymer and Garenne 2000; Taubenberger and Morens 2006). What makes the W-shaped mortality pattern unique is the high rate of death in the young and middle adult population, typically those individuals from 20 to 40 years of age (Ahmed, Oldstone and Palese 2007;

Gagnon et al. 2013; Noymer 2011; Noymer and Garenne 2000; Taubenberger and Morens 2006).

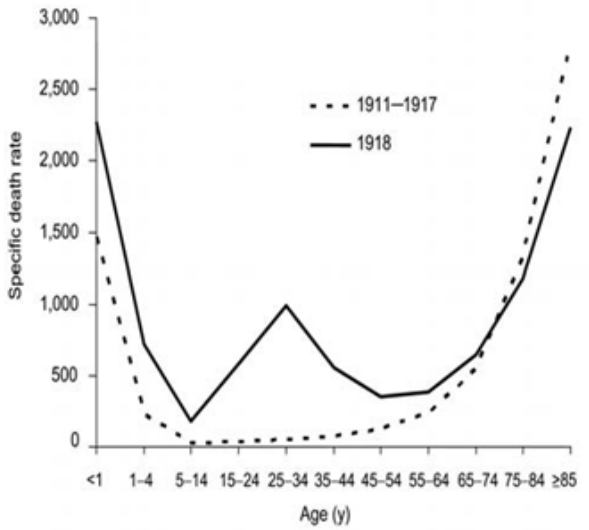

Figure 2. Mortality patterns for influenza and pneumonia in the United States, 1911-1918. (adapted from Taubenberger and Morens, 2006). *death rates per 100,000 in each age group.

Why was this strain of influenza so devastating to the young adult cohort? Ahmed, Oldstone and Palese (2007) and Taubenberger and Morens (2006) argue that immunological memory may be a factor. This means that individuals born before 1889, experienced previous exposure to a similar strain of the flu virus, causing their bodies to produce antibodies that would have made them less vulnerable to infection during the 1918 outbreak (Ahmed, Oldstone and Palese 2007; Taubenberger and Morens 2006). The prior exposure was likely a result of the Russian flu pandemic that occurred from 1889 to 1890, which was lethal and swift across the globe (Gagnon et al. 2013). Since young adults would not have been exposed to this virus prior to 1918, there is a corresponding spike in the mortality rates for this cohort (Ahmed, Oldstone and Palese 2007). Alternatively, it has been suggested that individuals born during or just prior to the 1889 pandemic may have been at an increased risk of lethal exposure during the 1918 outbreak (Gagnon et al. 2013). This would have been due to T-cell dysregulation, which meant that individuals exposed to the H3Nx strain of influenza in 1889, would have experienced a dysregulated cellular immune response, or decreased antigenic

production, if exposed to the H1N1 strain of 1918 (Gagnon et al. 2013). This decreased immune response would have made these young adult individuals more susceptible to secondary bacterial pneumonia, which was commonly fatal (Brundage and Shanks 2008; Chien, Klugman and Morens 2009; Gagnon et al. 2013; McAuley et al. 2007; Morens, Taubenberger and Fauci 2008). Another immunological theory, suggests that young adults experienced higher mortality rates due to an overactive immune response (i.e., cytokine storm) during the peak of immunocompetency (Gagnon et al. 2013). This theory has been tested by Kobasa et al. (2007) in a population of monkeys inoculated with the 1918 influenza strain. This study concluded that the monkey population experienced an overactive, yet ineffective antiviral response that caused a potent respiratory infection, and ultimately resulted in death (Kobasa et al. 2007). An overactive immune response could have occurred in young adults exposed to the 1918 virus, however, this does not account for probable exposure to previous influenza outbreaks (Gagnon et al. 2013). Lastly, this increased mortality pattern for young adult may have been caused by comorbitity with TB, which tended to effect young adult males (Gagnon et al. 2013; Noymer 2011). The likelihood and consequences of confluent TB and influenza infection during the 1918 pandemic will be discussed later in this paper in the section on comorbidity.

Sex-Based Mortality Patterns

In addition to its predominance among the young adult cohort, the 1918 Spanish flu frequently affected males (Noymer and Garenne 2000). According to Noymer and Garenne (2000), the 1918 outbreak exhibited "a difference between male and female age-standardized death rates of 174 per 100,000" (565), indicating greater vulnerability in males versus females in 1918. Although the exact cause of this increased vulnerability in males is still debated, Noymer and Garenne (2000) argue that the increased mortality in the male portion of the population is due to the presence of TB prior to and during the 1918 outbreak. Tuberculosis infection could have expressed itself with clinical symptoms or as a latent infection (Noymer and Garenne 2000). Regardless of its expression, the TB-influenza interaction caused much higher mortality rates in the male portion of the population

(Noymer and Garenne 2000). Males suffering from TB during the 1918 outbreak were more vulnerable to infection from influenza. The combination of these infections exacerbated many respiratory issues, of which secondary bacterial pneumonia was highly lethal (Brundage and Shanks 2008; Chien, Klugman and Morens 2009; Gagnon et al. 2013; Noymer and Garenne 2000; McAuley et al. 2007; Morens, Taubenberger and Fauci 2008).

In addition to the possibility of comorbid TB, wartime conditions also influenced the rate of infection. Military personnel, who were predominantly young males, were overcrowded in training camps, ships, trenches, and hospitals for long periods of time (Blackburn et al. 2018). "This proximity, combined with the stress of war and the malnutrition that sometimes accompanied it, created weakened immune systems in soldiers and allowed the virus to spread rapidly" (Blackburn et al. 2018). More soldiers died of the flu than from battle, and the constant transport of troops overseas contributed to the global transmission and virulence of the disease (Blackburn et al. 2018).

Despite a high incidence rate among soldiers, enlistment was not the sole factor for influenza infection. This is evidenced by a high domestic male mortality rate, specifically in those individuals who were never directly involved in the war effort (Blackburn et al. 2018; Noymer and Garenne 2000). This highlights the generalization that epidemics tend to kill more men than women (Blackburn et al. 2018; Noymer and Garenne 2000). In the years before the 1918 outbreak, females had a distinct advantage in mortality patterns and tended to exhibit longer life expectancy (Noymer and Garenne 2000). Noymer and Garenne (2000) hypothesized that the 1918 influenza caused a shift in sex-based mortality through selective bias, where males suffering from TB were wiped out by the influenza outbreak. This caused the male mortality rates from TB to decrease in the years following the Spanish flu (Noymer and Garenne 2000). As a result, males experienced a longer life expectancy, closer to that of their female counterparts (Noymer and Garenne 2000). Therefore, the 1918 Spanish flu effectively eradicated the previous female advantage, which would not be regained until the 1950's (Noymer and Garenne 2000).

Comorbidity

It has been suggested that TB played a pivotal role in the virulence and selectivity of the 1918 influenza virus. The mutation based origin of the 1918 strain within the swine population from Kansas, lends support to the theory of TB-influenza comorbidity (Broxmeyer 2006; Morens, Taubenberger and Fauci 2008; Noymer 2008, 2011, 2012; Oei and Nishiura 2012; Taubenberger and Morens 2006; Wanatabe et al. 2014). In addition to TB, influenza was commonly recorded with reference to pneumonia (Brundage and Shanks 2008; Chien, Klugman and Morens 2009; Gagnon et al. 2013; McAuley et al. 2007; Morens, Taubenberger and Fauci 2008). The high number of deaths from bacterial pneumonia could be an indicator of TB-influenza interaction, but these deaths could also result from influenza related pneumonia (Brundage and Shanks 2008; Chien, Klugman and Morens 2009; Gagnon et al. 2013; McAuley et al. 2007; Morens, Taubenberger and Fauci 2008). Antemortem lung biopsies from a number of patients from 1918, indicate that bacterial pneumonia was highly prevalent among both civilian and military personnel, with a portion of each population testing positive for an undetermined bacterial infection (Chien, Klugman and Morens 2009). It is plausible to conclude that the additional bacterial infection could have been TB or influenza related. Morens, Taubenberger and Fauci (2008) examined lung tissue from 58 victims of the 1918 Spanish flu, as well as copious autopsy documents, to create an experimental sample of 8,398 individual autopsy investigations. Within this sample they discovered that "the majority of deaths in the 1918-1919 influenza pandemic likely resulted directly from secondary bacterial pneumonia caused by common upper respiratory tract bacteria" (Morens, Taubenberger and Fauci 2008:198). The most important implication of this finding is the discovery that pandemic level influenza outbreaks may be an effect of viral-bacterial copathogenesis, which means that treatment and planning must address more than just the viral culprit (Morens, Taubenberger and Fauci 2008:198).

To this point, the most compelling evidence for the comorbidity of TB and influenza in 1918, was presented by Noymer (2011). Tuberculosis is a chronic infection of the lungs, where influenza is an acute respiratory infection, which commonly kills via secondary bacterial pneumonia (Noymer 2012). Figure 3 shows death rates for influenza and pneumonia as presented by Noymer (2011). In 1917, TB death rates for individuals from 20

to 35 years of age greatly exceed those for pneumonia and influenza (Noymer 2011). In 1918, the effects of the pandemic are clearly represented, with pneumonia and influenza death rates greatly exceeding those for TB (Noymer 2011). The overlap between TB and influenza mortality rates in 1918, suggests a predisposition within the tuberculous population to die from influenza (Noymer 2011). Although the selective mechanism behind it is unknown, evidence suggests that TB tended to effect young male individuals (Gagnon et al. 2013; Nhamoyebonde and Leslie 2014; Noymer and Garenne 2000; Oei and Nishiua 2012). In the years following the 1918 pandemic, there is a decrease in the amount of TB death rates in the United States (Noymer 2011). This suggests that the 1918 flu virus was selecting for members of the tuberculous population, effectively providing evidence for the comorbidity of these two diseases (Gagnon et al. 2013; Noymer 2011, 2012; Noymer and Garenne 2000; Oei and Nishiua 2012).

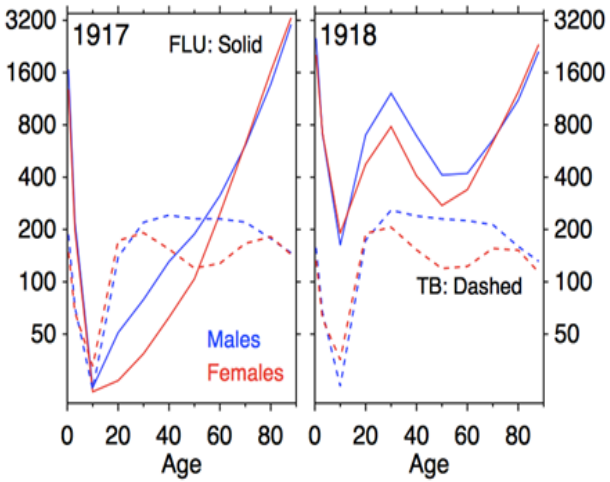

Figure 3. Death rates from tuberculosis (TB) and influenza and pneumonia (FLU), 1917-1918 (adapted from Noymer, 2011). *Death rates per 100,000.

Research Question

In order to investigate patterns of demographic and co-pathogenic selectivity during the 1918 Spanish flu in Milwaukee a theory based research question and hypotheses were developed. Based on previous research on age-based mortality patterns, I expect to observe a W-shaped mortality curve from 1918 to 1919,

with the highest mortality rates for influenza and TB occurring in the young and middle adult cohort (~20-40 years of age). Given information on sex-differentials during the 1918 outbreak, I expect to observe a selective bias towards males. Additionally, I expect to find evidence of comorbidity between TB and influenza, with lower rates of each disease present in 1919.

If the mortality patterns observed in the Milwaukee sample are in accordance with those demonstrated by previous research, then the following conclusions can be made about the virulence and selectivity of the Spanish flu in Milwaukee. First, it would be concluded that although Wisconsin experienced significantly lower mortality rates compared to the remainder of the United States, patterns of selectivity match those for areas that were more significantly impacted. Second, it would be concluded that young adult males were at the highest risk for infection during the 1918 pandemic. Third, evidence for the comorbidity of TB, and its effects on the young male population of 1918, would be highlighted.

Given the information gleaned from previous research in the United States, I believe that the patterns of mortality for age and sex during the 1918 pandemic in Milwaukee will be in accordance with those from previous research. Additionally, I hypothesize that there will be plausible evidence for the comorbidity of TB and influenza during the 1918 outbreak.

Materials and Methods

Experimental Sample

The experimental sample consisted of vital record data from 416 individuals from the Milwaukee County Poor Farm Cemetery (MCPFC) who died of influenza, pneumonia or TB related causes between January 1918 and December 1919. This skeletal sample is housed at the University of Wisconsin-Milwaukee and contains over 1,600 individuals (Charaus 2010; Richards et al. 2016). Specimens from this sample are associated with the Milwaukee County Poor Farm that was established in 1852 (Charaus 2010; Richards 1997; Richards et al. 2016). The cemetery was in official use from 1872 to 1974, with known interments during the 1918 influenza pandemic (Charaus 2010; Richards 1997; Richards et al. 2016).

Vital records data are available for the MCPFC sample, specifically in the form of death certificates. Since the MCPFC represents a small, institutionalized portion of the Milwaukee population, death records from Milwaukee County as a whole were also examined. Hard copies of these vital records data are housed at the Milwaukee County Courthouse. I was able to examine 11,000 death certificates from 1918 and 1919. From this examination a randomly selected sample of 500 individuals with influenza, pneumonia and TB related causes of death (COD) was created.

Methods

Age, sex and comorbidity were assessed via documentary examination. Demographic information, such as name, age, sex, and dates of birth and death were recorded in a Microsoft Excel spreadsheet. The location of death, place of burial, and the name and qualification of the physician issuing the death certificate were also recorded. The primary, secondary and tertiary causes of death were noted from individual death certificates. Each of these data points were used to compare the MCPFC cemetery sample with the Milwaukee County sample on the basis of age and sex related patterns of mortality, as well as comorbidity with TB. The MCPFC cemetery primarily served as a burial location for individuals that died while living in one of the Milwaukee County facilities (e.g. almshouse, hospital, children's home), those that were unidentified or unclaimed, or those whose families could not afford burial elsewhere (Richards 1997; Richards et al. 2016). Therefore, the MCPFC cemetery sample provided a unique view of mortality among a potentially poorer subset of the greater city population. By comparing the patterns of mortality and comorbidity for the MCPFC cemetery sample and the sample from the greater Milwaukee County area, we can gain a greater understanding of the selective mortality of the disease across various demographic boundaries.

Results

Previous research suggested that influenza and pneumonia are highly correlated (Brundage and Shanks 2008; Chien, Klugman and Morens 2009; Gagnon et al. 2013; McAuley et al. 2007;

Morens, Taubenberger and Fauci 2008). Within the Milwaukee County sample pneumonia and influenza were listed as comorbid causes of death for 95 individuals, with an additional 13 individuals categorized with COD's of influenzal pneumonia. Therefore, approximately 22% of the total sample was affected by comorbid influenza and pneumonia. With this in mind, pneumonia and influenza were combined for the comparative assessments of age, sex and comorbidity with TB.

Age-Based Mortality Patterns

Age categories were created to examine the impacts of influenza at different life stages (Table 1). These age categories were used to assess mortality patterns for age within the following causes of death: all respiratory deaths, which includes influenza, pneumonia and TB, all deaths involving pneumonia and influenza, all deaths solely resulting from influenza, and all deaths associated with TB. Each of the COD categories were broken down by year in order to observe pattern changes at the height and decline of influenza pandemic. The age-based mortality pattern for all respiratory deaths is illustrated in Figure 4. Figure 5 demonstrates the age-based mortality pattern for influenza and pneumonia related deaths. There were fewer deaths documented with a solitary, primary COD as influenza. The age-based mortality pattern for these influenza related deaths can be found in Figure 6. Lastly, the age-based mortality pattern for all deaths with a primary or secondary COD of TB were recorded in Figure 7. Figures 4-7 include data from both the Milwaukee County and MCPFC cemetery sample, making these graphs ideal for visual pattern comparison.

Table 1. Age categories for examination.

Category	*Age (in years)*
Infant/toddler	Birth to 2.49
Childhood/Pre-teen	2.5 to 12.9
Adolescent	13 to 19.9
Young Adult	20 to 34.9
Middle Adult	35 to 49.9
Old Adult	50+

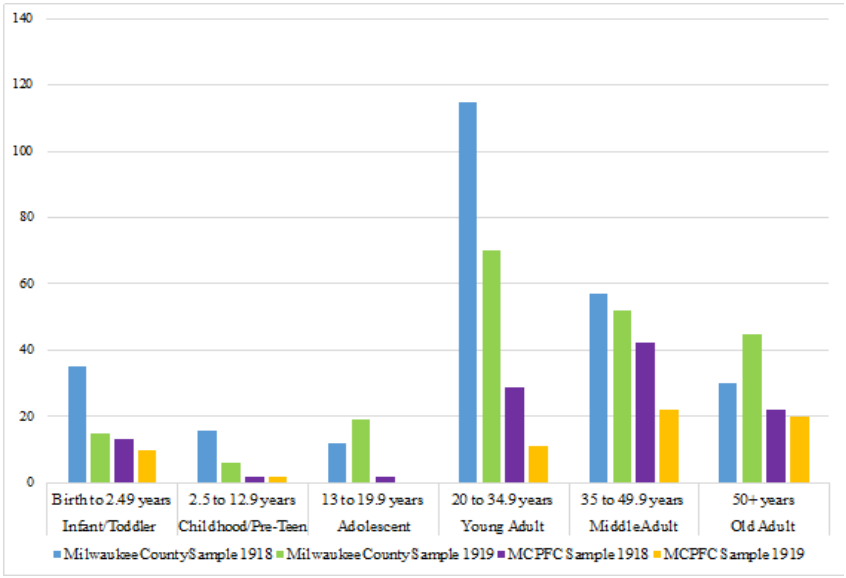

Figure 4. Age-based mortality patterns for all respiratory deaths in the Milwaukee County and MCPFC samples, 1918-1919.

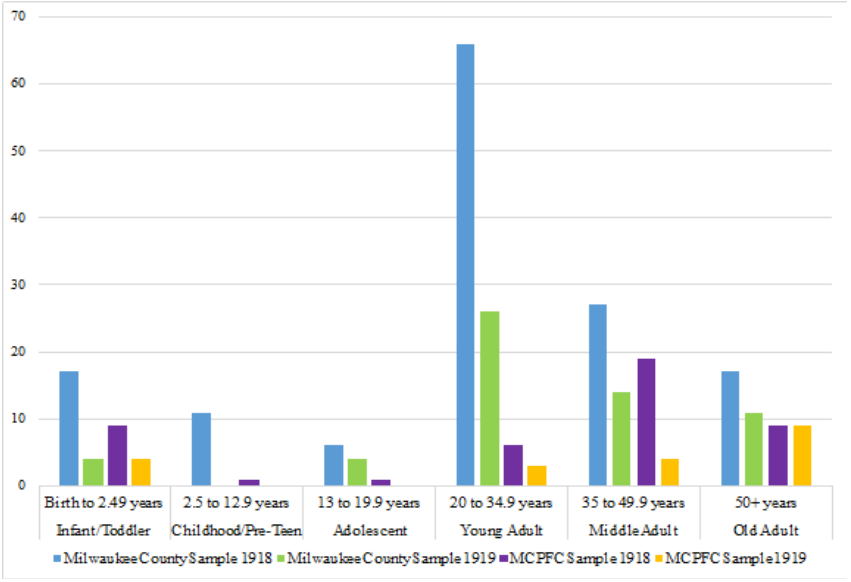

Figure 5. Age-based mortality patterns for influenza and pneumonia related deaths in the Milwaukee County and MCPFC samples, 1918-1919.

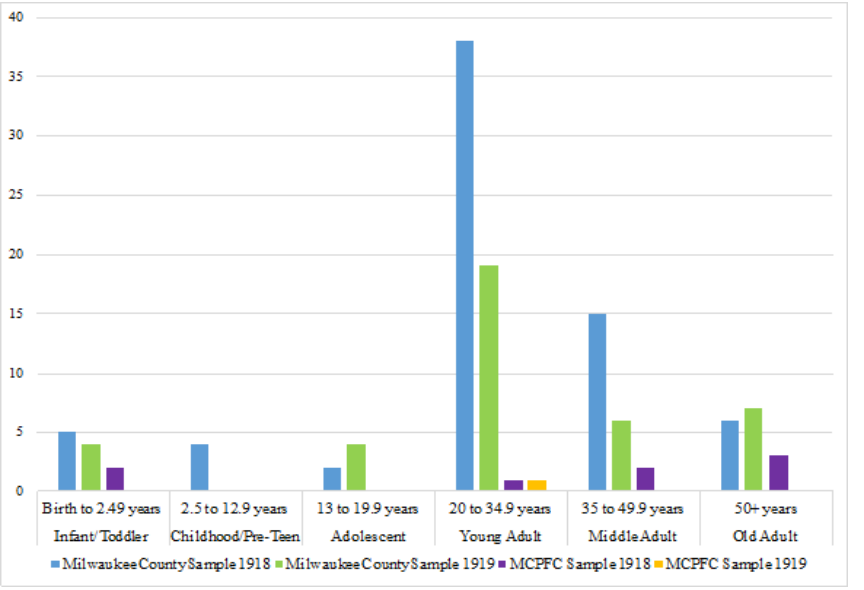

Figure 6. Age-based mortality patterns for influenza related deaths in the Milwaukee County and MCPFC samples, 1918-1919.

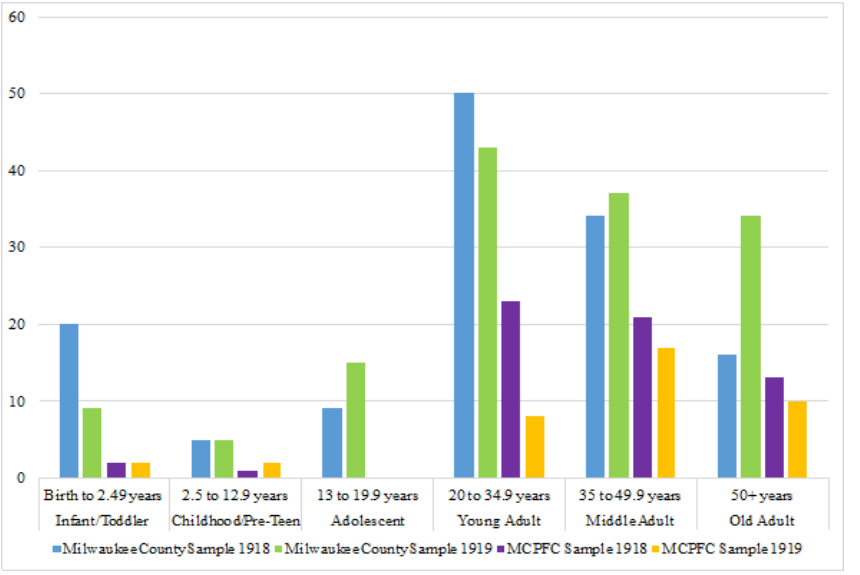

Figure 7. Age-based mortality patterns for tuberculosis related deaths in the Milwaukee County and MCPFC samples, 1918-1919.

Sex-Based Mortality Patterns

Sex-based mortality patterns were assessed using the same COD categories applied in the examination of age-based mortality. Each COD category was broken down by male and female, and also by year. For comparative purposes, the Milwaukee County sample and the MCPFC cemetery sample are both included in the graphical representation of this sex-based assessment. Therefore, Figure 8 includes the sex-based mortality patterns for TB, influenza and pneumonia related deaths in the Milwaukee County and MCPFC cemetery sample from 1918 and 1919.

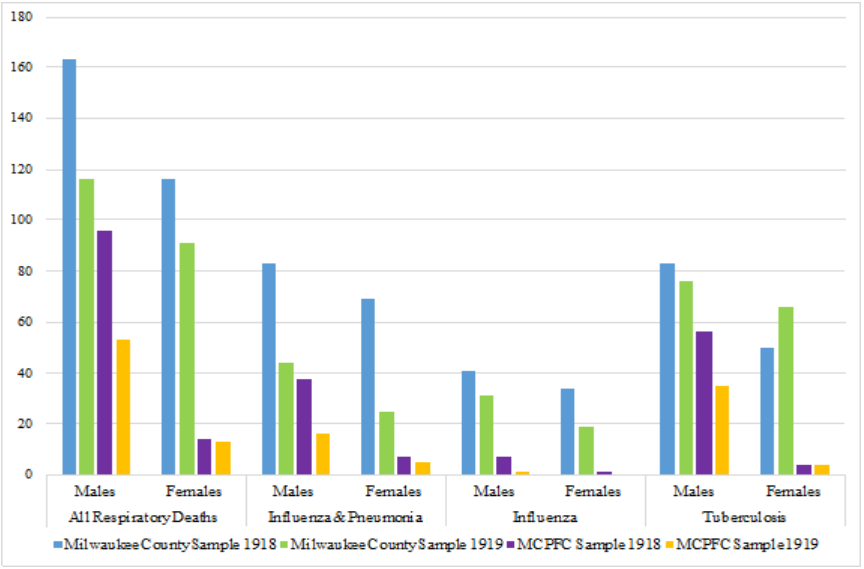

Figure 9. Frequency of documented causes of death (COD) for tuberculosis, influenza and pneumonia related deaths in the Milwaukee County and MCPFC samples, 1918-1919.

Discussion

Age-Based Mortality Patterns

The pattern created by the age categories in Figure 4 demonstrates the atypical W-shaped mortality curve that is highlighted in previous influenza research (Ahmed, Oldstone and Palese 2007; Gagnon et al. 2013; Noymer 2011; Noymer and Garenne 2000; Taubenberger and Morens 2006). As a result, we see higher mortality rates in the youngest age cohort, followed by a drop in mortality level in the following two age categories

(childhood/pre-teen and adolescent), and a large spike in mortality for the young adults, clearly exhibiting the highest mortality level of all the age cohorts. This young adult spike is followed by a significant, but gradual drop in mortality throughout the middle and adult age cohorts. This W-shaped mortality curve is what we would expect to see in this scenario, since all respiratory deaths, including TB, influenza and pneumonia are selected. Since this sub-sample includes all respiratory deaths, it will constitute the largest sample size of all the COD sub-samples being analyzed.

The same W-shaped mortality curve is observed in Figure 5. However, of note here, is the total lack of influenza and pneumonia related COD's in the childhood/pre-teen age cohort for 1919. The pattern is observed in both the Milwaukee County and MCPFC cemetery samples. In addition to the previous observation, we can also see a significant gap between the 1918 and 1919 levels within the infant/toddler, young adult and middle adult age cohorts. The pattern is observed within both the Milwaukee County and MCPFC cemetery samples. The most significant difference occurs in the young adult cohort from Milwaukee County, with a drop from 66 cases in 1918, to 26 cases in 1919. Within the MCPFC cemetery sample, the large discrepancy occurs in the middle adult cohort, with a shift from 19 cases in 1918 to 4 cases in 1919. Since the W-shaped mortality curve indicates that young and middle adult individuals have the highest mortality levels, the data from from the Milwaukee County and MCPFC cemetery samples is in accordance with findings from previous research (Ahmed, Oldstone and Palese 2007; Gagnon et al. 2013; Noymer 2011; Noymer and Garenne 2000; Taubenberger and Morens 2006). Lastly, the mortality levels for the MCPFC old adult cohort do not change from 1918 to 1919, with 9 cases in each year. Since the influenza pandemic of 1918 tended to target young and middle aged adults, it stands to reason that the older adult population might be over-represented in 1919. This could be due to delayed susceptibility, or greater immunity, which allowed individuals to live longer with the symptoms of pneumonia and influenza than their young adult counterparts. If the latter is the case, then this evidence might suggest that the immunological theory (i.e. overactive immune response in young adults) proposed by Gagnon et al. (2013) and Kobasa et al. (2007) is plausible.

Of the COD's that were recorded, influenza as the sole, primary COD was rarely observed. Rather than being documented

as the singular COD, influenza was more commonly observed as a primary or secondary COD to another respiratory or non-respiratory issue. Although the frequencies are much lower, the W-shaped mortality curve is still observed in the Milwaukee County sample. This pattern cannot be discerned in the MCPFC cemetery sample. There are very low frequencies of influenza in all age cohorts of the MCPFC sample, with the childhood/pre-teen and adolescent being non-existent for both 1918 and 1919. One individual is observed from 1919 in the MCPFC sample, belonging to the young adult cohort. Given the pattern observed within Figures 4 and 5, it is unlikely that the results presented in Figure 6 for the MCPFC cemetery sample are an accurate representation of the prevalence of influenza.

The atypical W-shaped mortality curve is observed in Figure 7 for the Milwaukee County sample from 1918 and 1919. However, a skewed W-shaped curve is also observed in the MCPFC sample. The levels for the infant/toddler and childhood/pre-teen age categories are low and similar, so we do not get the typical high mortality of the W-shaped curve. These low frequencies are followed by drop a to zero in the adolescent cohort, making the spike in the young adult category more intense. In the 1918 MCPFC sample, the largest frequency in observed in the young adult cohort, whereas in the 1919 MCPFC sample, the largest frequency is observed in the middle adult category. This could be due to the fact that many young and middle aged adults died of TB in 1918, which resulted in high mortality levels in 1919. The middle and old adult cohorts from the 1919 Milwaukee County sample even show higher TB mortality levels than were observed in 1918.

Throughout Figures 4-7, the atypical W-shaped mortality patterns associated with the 1918 influenza pandemic is commonly observed. This pattern shows the highest mortality levels in the young and middle adult cohorts, with the Milwaukee County sample having the highest levels in the former, young adult age cohort. The MCPFC cemetery sample had the highest mortality levels in the middle adult cohort for all respiratory deaths and all influenza and pneumonia deaths. However, the highest mortality rates for influenza deaths were observed in the old adult age category, and the highest mortality rates for TB related deaths were seen in the young adult cohort. Although there is some slight fluctuation within the MCPFC sample, the results for age-based pat-

terns of mortality appear in accordance with those discussed in previous research.

Sex-Based Mortality Patterns

As we would expect to see, the highest frequency of deaths seen in Figure 8, is in the category of all respiratory death since this COD category is all inclusive. In each death category breakdown, the males have higher frequencies than the females. In each of the male cases, the 1918 frequency is greater than the 1919 level. This increased male frequency could be due to comorbidity with TB, a disease which is selectively biased towards males (Noymer and Garenne 2000).

Females also tend to show higher frequencies in 1918, with the exception of TB related deaths. Females with TB related deaths tended to have higher mortality levels in 1919, than 1918, in the Milwaukee County sample. Within the MCPFC cemetery sample, the females with TB related COD's were found to have equal levels of mortality in 1918 and 1919. If TB is found to be comorbid with influenza during the 1918 outbreak, then many of the young and middle adult men would have died of TB related illness. The spike in the frequency of females with TB related COD's in 1919, could be an over-representation that is the result of the high mortality rates for males in 1918. It is also important to note that the mortality rates for TB in 1919, for males and females is similar. Compare this similarity to the large discrepancy between male and female patterns in 1918. Previous research indicated that in the years after the 1918 outbreak, male and female life expectancy became more similar due to the large number of males being wiped out by the pandemic (Noymer and Garenne 2000). It is plausible that the similarity in the TB levels for males and females in 1919 is beginning to reflect is change.

Comorbidity

From Figure 9, we can see that influenza and pneumonia are the most commonly listed COD of 1918, in the Milwaukee County sample. This is followed closely by tuberculosis. Within the 1919 Milwaukee County sample, tuberculosis is the most common COD, with all other primary and secondary COD's being at significantly lower levels. Within the Milwaukee County

sample for 1918, the primary COD of influenza is used approximately half the amount that influenza and pneumonia are used. Within the MCPFC cemetery sample, TB is listed as the primary COD most frequently, followed by influenza and pneumonia, and influenza. This pattern is illustrated in both 1918 and 1919.

In 1918 and 1919, influenza and pneumonia are listed as the secondary COD with the most frequency, followed by influenza and tuberculosis related deaths. This pattern can be observed in both the Milwaukee County and MCPFC cemetery samples. If TB and influenza are comorbid during the 1918 outbreak, then we would expect to see similar mortality patterns for both COD's. The frequency data in Figure 9 support this idea with the levels of influenza and pneumonia and the levels of TB as the primary COD being almost identical. The age-related mortality patterns presented in Figures 5 and 7 also show similar patterns for 1918 in the Milwaukee County and MCPFC cemetery sample. The 1919 data for both samples is also similar (see Figures 5 and 7).

The aforementioned results lend evidence towards the comorbidity of TB and influenza. If these diseases are comorbid, we would expect to see a decline in the frequency of TB in the years following the 1918 outbreak. During the height of the pandemic from August to December 1918, a total of 153 individuals died of primary or secondary TB within the Milwaukee County sample. By August to December 1919, the prevalence of TB as a primary or secondary COD within the Milwaukee County sample had decreased to 56. This constitutes an approximate 64% decrease in the prevalence of TB in the year after the influenza pandemic in Milwaukee. A similar pattern is observed in the MCPFC cemetery collection. From August to December 1918, 22 cases of primary or secondary TB were observed. One year later, a total of 8 TB cases were recorded. This pattern also represents a near 64% decrease in the prevalence of TB within this institutionalized population. This information coupled with the presence of 14% of the Milwaukee County sample and 3% of the MCPFC sample indicating documented comorbidity between TB and influenza, provides plausible evidence for the presence of TB comorbidity during the 1918 influenza outbreak in Milwaukee.

Patterns of Influenza

The fall and winter of 1918 are considered the height of

the influenza pandemic. During the short period from August to December 1918, casualty levels reached their peak. Within the Milwaukee County sample 287 individuals had documented COD's of influenza, pneumonia or TB. Of these 287 cases, 275 had primary COD's of influenza, pneumonia or TB. A total of 144 individuals had a primary COD of influenza or pneumonia. One-hundred and six individuals had primary COD's of influenza or influenzal pneumonia. Therefore, 21.2% of the total Milwaukee County sample died of influenza or influenza related pneumonia during the months of August to December 1918. From August to December 1919, 64 individuals had primary or secondary COD's related to influenza, pneumonia, or TB. Sixty-two of these cases listed these illnesses as the primary COD. A total of 8 individuals from August to December 1919, perished from influenza or influenzal pneumonia. This indicates a 92.5% decrease in the prevalence of influenza related deaths in the Milwaukee County sample just one year after the height of the influenza pandemic.

Within the MCPFC cemetery sample, 53 individuals died of influenza, pneumonia or TB related causes from August to December 1918. A total of 34 cases were observed with COD's of influenza or infleunzal pneumonia. During the height of influenza pandemic, 7.38% of the MCPFC cemetery sample perished from influenza or influenza related pneumonia. By August 1919, no deaths were documented with influenza or pneumonia as the primary COD. This is a 100% decrease from the death toll a year before.

These results indicate the swiftness and severity of the 1918 influenza outbreak. Within Milwaukee, the Spanish flu was short lived, but highly devastating. The similar frequency patterns observed in both the Milwaukee County and MCPFC samples, indicates that individuals from all walks of life were susceptible to the effects of influenza.

Conclusion

This research project identifies age and sex-based selectivity during the 1918 influenza outbreak in Milwaukee, and provides evidence for the comorbidity of TB during this time. Within both experimental samples from Milwaukee, mortality patterns for age-at-death in 1918 and 1919 show a W-shaped mortality curve. The highest mortality rates within this model are observed

within the young and middle adult cohort. Sex-based mortality patterns show a selective bias towards males. This selective bias could be due to the comorbidity with TB. Males, in general, are more susceptible to TB, and those males with TB were more likely to be infected and die from influenza (Noymer and Garenne 2000). The probable TB-influenza interaction caused much higher mortality rates in the male portion of the population (Noymer and Garenne 2000). Additionally, documented evidence was provided that described both influenza and TB as interacting COD's. This occurred to a higher degree in the Milwaukee County sample, but was also present in the MCPFC cemetery sample. Lastly, both sample populations experienced a significant decrease in the amount of TB and influenza related deaths from the height of the pandemic in the fall of 1918, to the following fall of 1919. The lower rates of these diseases following the influenza outbreak, coupled with the documented comorbidity provided by individual death certificates, offers plausible evidence for the comorbidity of TB and influenza during the 1918 pandemic in Milwaukee. Therefore, the findings from the Milwaukee County and MCPFC cemetery samples are in accordance with previous research findings on the subjects of age, sex and TB selectivity during the 1918 influenza pandemic.

Two main issues were encountered during the execution of this project. First, was the issue of categorization. Since death certificates are issued by different physicians, many respiratory COD's have different names, but refer to the same issue. The most common example of this within both Milwaukee-based samples was the use of broncho pneumonia. Broncho pneumonia is another term for TB, but is categorized on many death certificates as a form of pneumonia. Another common example was the use of influenza or pneumonia as the primary or secondary COD, versus influenzal pneumonia or pneumonia-influenzal type. It has been argued that the mortality levels from the influenza pandemic were under reported in the media due to a lack of medical knowledge or understanding (Quinn 1999). However, I suggest that this is not the case. During the height of the influenza outbreak and into the early months of 1919, the majority of Milwaukee County death certificates listed influenza as either a primary or secondary COD. This indicates that medical professionals were able to recognize not only the presence of influenza, but also the presence of other comorbid respiratory issues. This is perhaps

why influenza is listed as a singular, primary COD so infrequently in both samples from Milwaukee. The physicians recognized that many complications could arise from influenza, and that other respiratory issues could increase susceptibility to influenza infection.

The second issue that became apparent relates to sample size and random selectivity. The results presented in this paper provide a snapshot of two portions of the population of Milwaukee in 1918 and 1919. It is possible that the low numbers of respiratory deaths in the MCPFC sample reflect an abundance of more lethal, non-respiratory deaths within this population. Since tens of thousands of deaths occurred in Milwaukee County from 1918 and 1919, I was unable to collect data to represent all influenza related deaths within the entire population due to time constraints for data collection. However, I was able to gather a sample from the height and decline of the Spanish flu outbreak in Milwaukee, indicating that the population as a whole will likely exhibit mortality patterns similar to those presented above.

The most pertinent outcome of this project is the confirmed presence of comorbid factors during the 1918 Spanish flu. Although the etiology of the 1918 influenza is still debated, compelling evidence has been found to support the comorbidity of TB and influenza. This unique disease confluence, combined with wartime conditions, led to increased lethality in young adult males, which had an unexpected influence on American society. The combined efforts of World War I and the 1918 Spanish flu created a vast worker shortage, which allowed women access to the labor market (Blackburn et al. 2018). At the end of the war, the number of female employees had increased by 25 percent, and by 1920, 21 percent of the entire American workforce was female (Blackburn et al. 2018; U.S. Dept. of Labor 2018). While this change, which led to the ratification of the 19th amendment, is often described as a direct effect of World War I, the indispensable role of female laborers would have been far less prominent without the selective male bias of the 1918 Spanish flu (Blackburn et al. 2018).

In addition to its effect on social change, the confirmed comorbidity of TB and influenza can be used to investigate novel methods for the treatment and prevention of future outbreaks. In 2005, scientists from the Center for Disease Control (CDC)

successfully reconstructed the 1918 influenza strain using historic tissue samples from infected individuals (Tumpey et al. 2005). Since then, multiple studies have sought to determine the etiology and nuances of its swift and deadly force, which have been unmatched by subsequent influenza outbreaks across the globe (Ahmed, Oldstone and Palese 2007; Belser and Tumpey 2018; Broxmeyer 2006; Chien, Klugman and Morens 2009; Kobasa et al. 2007; McAuley et al. 2007; Mills, Robins and Lipstitch 2004; Morens, Taubenberger and Fauci 2008; Noymer 2008, 2011, 2012; Oei and Nishiura 2012; Tumpey et al. 2005; Watanabe et al. 2014).

Recently, there has been a marked increase in media coverage of the topic associated with the 100th anniversary of the 1918 pandemic (Belser and Tumpey 2018; CDC 2018; Nature 2018; PBS 2018). This increased attention is undoubtedly linked with the fact that influenza still circulates within the human population, causing seasonal epidemics worldwide. Continued research of past disease outbreaks can aid in modern vaccine development, as well as increased preparedness and methods of response. For instance, if influenza is confluent with TB, there is the potential for underlying mycobacterial disease in addition to the viral infection (De Paus et al. 2013; Reford et al. 2014). Therefore, a single treatment option, such as antiviral vaccinations or antibacterial drugs, will not be an effective method of prevention. Instead, future research should seek to address which methods of treatment and prevention are most effective in outbreaks with both viral and bacterial pathogenesis. By confirming the comorbidity of TB and influenza during the 1918 epidemic, the present study serves as a clear example of the link between historical research and its contemporary implications.

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