Determinants of the prevalence and severity of influenza infection in Indigenous populations in Canada

Introduction

Influenza is a highly contagious respiratory illness that results in approximately 3500 deaths each year in Canada (Public Health Agency of Canada [PHAC], 2014). In recognition of the impact of influenza on the health of Canadians, in 2013 the six National Collaborating Centres for Public Health (NCCs) initiated a two-year project on Influenza and Influenza-Like Illness (ILI). The collaborative project leverages the expertise of all the NCCs to address recognized knowledge gaps and needs of public health and primary care professionals who work in influenza prevention and control. A national consultation with public health experts and the NCCs resulted in the identification of a number of priority issues, including improving estimates of the burden of influenza and surveillance methods, the effectiveness of vaccines and of primary prevention strategies, and equitable delivery of services, among others.[1] This literature review is one in a series of knowledge products developed as part of the Influenza and ILI Project. It focuses on one vulnerable population, Indigenous peoples,[2] who have been shown to be especially vulnerable to severe outcomes of influenza, the evidence for which has largely come from pandemic events like the 1918-19 and 2009 A/H1N1 influenza pandemics (Ahillen, 2006; Kelm, 1999; Sattenspiel & Herring, 2003; Public Health Agency of Canada [PHAC] & Health Canada [HC], 2010). Such events underscore the many challenges Indigenous people face to achieving optimal health and well-being.

The purpose of this literature review is to examine the factors that may contribute to the prevalence and severity of influenza infection among Indigenous peoples. Zarychanski et al. (2010) note that "[p]redicting disease and mitigating hazard in at-risk populations is an important aim of public health epidemiology, and in preparation for future waves of pandemic … influenza, determining correlates of the severity of disease may be very important" (p. 258). Knowing why Indigenous people may be vulnerable to severe outcomes from large scale outbreaks of influenza like the 2009 H1N1 influenza pandemic is important not only for informing pandemic planning for future outbreaks, but also for developing policies and programs to address deeply rooted socio-economic, political and health services inequities. In addition, since many of the factors that may contribute to Indigenous peoples' vulnerability to influenza infection may also affect other Canadians, the findings from this review may be more broadly generalizable.

[1] For more information on the 2013 consultation and the NCCs collaborative project, see http://www.nccph-ccnsp.ca/330/Influenza.ccnsp

[2] For this paper, the term 'Indigenous peoples' will be used to represent all First Nations, Inuit, and Métis peoples inclusively. However, since some of the literature identified in this search focused on Indigenous populations inclusively (First Nations, Inuit and Métis) while the majority focused on First Nations populations specifically, the reader is advised to interpret the term as emphasizing an over-representation of First Nations people. Where researchers have clearly distinguished between First Nations, Inuit or Métis populations, these more specific terms will be used in this paper.

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Methodology

This review draws on peer and non-peer reviewed literature primarily identified through the use of three academic literature databases (PubMed, Medline, and Google Scholar) up to June 2015. Additional literature was identified from the bibliographies of relevant publications. The search strategy combined one of the terms 'Aboriginal', 'First Nations', 'Inuit', 'Metis' or 'Métis', with either 'influenza' or 'H1N1.' Publications were selected for review if they were:

- focused exclusively on Indigenous peoples (First Nations, Inuit and/or Métis) and their experiences with influenza;
- focused on the general population but included Indigenous ethnicity as a variable and undertook some analysis at this level;
- were case studies involving primarily Indigenous patients; and
- included discussion of one or more factors that may contribute to the prevalence or severity of influenza infection.

A total of 54 publications met the search criteria. Of these, most publications focused on the 2009 influenza A(H1N1) pandemic[3] (67%; n=36), fewer on the 1918-1919 pandemic (22%; n=12), and the remainder on other strains of influenza (n=7).[4] Factors identified as contributing to the prevalence or severity of influenza infection on First Nations, Inuit or Métis peoples were grouped into seven categories: geographic factors, demographic factors, socio-economic disparities and living conditions, cultural factors, health status, health behaviours, and genetic susceptibility.

Determinants of influenza prevalence and severity

The literature identified a wide range of possible factors that may explain the prevalence or severity of influenza infection. Some of these could influence the vulnerability of any individual during a pandemic regardless of ethnicity, while others could be considered unique to Indigenous populations.

Geographic Factors

One factor that has commonly been associated with the spread of infectious diseases is geography. Geography can impact access to health services, the level of government responsible for the provision of health care services, the quality of living conditions that may affect general health, the level of immunity that community members may have to infectious diseases, and the speed at which an infectious disease can spread.

The research indicates that during severe outbreaks like the 1918-1919 and the 2009 influenza pandemics, individuals living in rural and remote communities are at greater risk of becoming ill and developing severe outcomes compared to those living in urban areas (Fanella, et al., 2011; Mamelund, 2011; Morrison et al., 2013, 2014; Mostaço-Guidolin et al., 2011, 2012, 2013; Pollock, Sagan, Oakley, Fontaine, & Poffenroth, 2012; Spence & White, 2010). A greater proportion of First Nations, Inuit and Métis peoples live in rural and remote locales than do non-Indigenous people. While 80.9% of non-Indigenous people live in urban areas, approximately 69.4% of Métis, 44.7% of First Nations, and 37.6% of Inuit do so (Statistics Canada, 2006).[5]

Transportation between communities is slower in rural and isolated parts of Canada and geography can initially act as a barrier to influenza transmission.[6] However, once a community has been exposed, a range of intersecting conditions can facilitate the rapid spread of influenza (Charania & Tsuji, 2013). These conditions may include overcrowding and extreme poverty, inadequate access to many basic amenities like running water, limited access to federal government programs and services, limited transportation of required supplies and resources, continuous shortages of health care personnel, a high proportion of

[3] Hereafter referred to as the 2009 influenza pandemic.

[4] Numbers will not add to 100% because one publication had two separate sections – one on H1N1 and one on another strain of influenza.

[5] The 2006 Census data was used here because publically available data tables for the 2011 National Household Survey do not yet provide information on rural/urban residence. Given the increasing trend towards urbanization over the past few census enumerations, it is highly likely that a greater proportion of First Nations, Inuit and Métis people now live in urban areas than is presented here, but also equally likely that proportionately, more of them live in rural regions than the general population.

[6] Geographic distance from Norway House during the 1918-19 pandemic certainly appeared to act as a barrier to the transmission of influenza to the communities of Oxford House and God's Lake, which remained relatively immune to infection while Norway House was ravaged (see Ahillen, 2006; Sattenspiel & Herring, 1998, 2003; Herring, 1993; Herring & Sattenspiel, 2007; O'Neil & Sattenspiel, 2010; Sattenspiel, Mobarry & Herring, 2000).

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Additionally, rural and remote locations have differential access to health care. Because population sizes are small in these places, access to health infrastructure and availability of health care professionals may be severely limited.

immunocompromised individuals, and a tight social networking system (Charania & Tsuji, 2011a, 2012; Mamelund, 2011; Mostaço-Guidolin et al., 2011, 2013; Richardson, Driedger, Pizzi, Wu, & Moghadas, 2012; Morrison et al., 2013, 2014; Spence & White, 2010). Some of these conditions (such as living in crowded conditions and lack of running water) allow viruses to spread more rapidly; some weaken an individual's general health (such as poverty), leaving him/her more vulnerable to severe outcomes; and some prevent an effective and coordinated public health response in pandemic crises (such as limitations in critical infrastructure). In rural and isolated communities where there has been no past exposure to particular strains of influenza, individuals may not be protected through any prior immunity, which can result in higher viral multiplication, burden and transmitted dose, as well as increased virulence (Mamelund, 2011; Mathews et al., 2009 as cited in Spence & White, 2010, p. 7).

In the case of Indigenous peoples, geography also affects who has responsibility for responding to a public health emergency and in what way. The geographic isolation of First Nation communities, for example, can pose significant challenges during pandemic outbreaks because fragmented health care delivery can complicate decision-making and action. Multiple levels of government are responsible for providing health services to Indigenous peoples, particularly to First Nations on-reserve. Charania and Tsuji (2011b) highlighted a number of challenges during the emergency response to the 2009 H1N1 pandemic, including the presence of multiple pandemic plans which led to confusion over roles and responsibilities; contradictory guidelines; misleading, inconsistent or contradictory information; and lack of information sharing. They argue that these types of challenges can prevent the implementation of a swift and effective response to influenza outbreaks, resulting in a greater burden of illness.

Additionally, rural and remote locations have differential access to health care. Because population sizes are small in these places, access to health infrastructure and availability of health care professionals may be severely limited. Richardson et al. (2012), for example, attributed the lack of adherence to, or inadequate level of compliance with, some regulations in Inuit communities during the H1N1 pandemic to the inability to recruit and retain public health staff, cross-cultural barriers between health care professionals and residents, and the absence of people trained in enforcing regulations enacted to protect public health. Structural prejudice and racism, and the resultant lack of trust, can further complicate the delivery of appropriate care, preventing Indigenous people from seeking the care they need (Driedger, Maier, Sanguins, Carter, & Bartlett, 2014; Loppie, Reading, & de Leeuw, 2014). As a result, treatment may be delayed, resulting in a more severe manifestation of the illness.

Demographic Factors

Demographic factors can influence the spread of influenza in several ways. First, it is hypothesized that some individuals may have developed some level of immunity to particular strains of influenza through exposure to similar strains earlier in life. For example, it is known that there was some level of prior immunity to the 2009 influenza virus among the elderly resulting from their previous exposure to H-1 like viruses (Fisman et al., 2009; Laskowski, Mostaço-Guidolin, Greer, Wu, & Moghadas et al., 2011; Tuite, et al., 2010, Xu et al., 2010). In addition, contact and hygiene patterns of children and young adults can increase susceptibility to influenza infection (Mostaço-Guidolin et al., 2012). These two factors likely explain why younger adults were disproportionately represented in 2009 influenza cases (Mostaço-Guidolin et al., 2012; Kumar et al., 2009). In fact, increased susceptibility to infection in younger individuals is a common characteristic of influenza pandemics (Miller et al., 2008). It has also been noted that since children are key transmitters of influenza, women, who tend to have more intimate contact with children, may be over-represented in cases of influenza, at least during the initial phases of an outbreak when herd immunity has not yet been developed (Campbell et al., 2010; Thompson et al., 2012). This appears to have been the case during the 2009 influenza pandemic where women were over-represented during the first wave, whereas men were slightly over-represented during the second wave (Helferty et al., 2010).

The demographic profile of the Indigenous population, which is much younger than the general Canadian population, is suggested as a factor which contributed to the higher incidence of 2009 influenza among Indigenous people, having a larger proportion of the population with higher susceptibility (Mostaco-Guidolin et al., 2012, 2013; Pollock et al., 2012). Mostaco-Guidolin et al. (2012) point out, for example, that the average age in northern Manitoba and Nunavut, two regions that were particularly affected during the first wave of the 2009 pandemic, was 24 and 23 respectively compared with an average age of 38.7 in Winnipeg. They suggest, therefore, that the higher transmission rates of pH1N1 in these rural and remote areas are, at least in part, the result of higher rates of infectious contacts among schoolchildren and young adults resulting from differences in cross-protective innate or acquired immunity, as well as contact and hygiene patterns.

To investigate the role that demographic variables may play in determining the outcomes of an influenza epidemic in remote Indigenous communities, Laskowski and colleagues (2011, 2013) used an agent-based model[7] to demonstrate that "both age profiles and household compositions played an important role in the transmission of [2009] influenza within a remote and isolated community" (2011, p. 5). When housing conditions are overcrowded and the population is relatively young, as it is in many Indigenous communities, the effect of having older individuals with prior immunity on reducing disease transmission will be minimal because there are so few of them in the population to have a significant impact. In contrast, in conditions of low housing density and an older population, there are more individuals with prior immunity which can significantly slow the spread of influenza. Their modeling results provide evidence for the over-representation of 2009 influenza cases among Indigenous people from remote and isolated communities. According to the authors, the implications of these findings are that children below age 17 should be prioritized for vaccination in such communities to increase their cross-reactive protection levels and mitigate the potential for epidemic spread (Laskowski et al., 2013).

Socio-economic disparities and living conditions

O'Sullivan and Bourgoin (2010) conducted a review of literature and found evidence of a "social gradient of risk" of vulnerability during influenza pandemics (p. 2); the greater the socio-economic disadvantage, the greater the risk of infection and severe outcomes. First Nations, Inuit and Métis people experience significant socio-economic inequities including lower education, higher rates of unemployment, poverty, and

[7] An agent-based model is a powerful simulation modeling technique which consists of "a system of agents and the relationships between them" (Bonabeau, 2002, p. 7280). This involves identifying the active agents (people, companies, projects, assets, etc.), defining their behavior, putting them in a certain environment, establishing connections, and running the simulation to determine how the interactions of the individual behaviours affect global behavior (AnyLogic, n.d.).

substandard housing[8] which may contribute to the spread of infectious illnesses like influenza. Some of these factors can directly assist in spreading influenza more widely (e.g. crowded or poor quality housing, lack of running water, lack of education), while others, (e.g. inability to afford nutritious food) can lead to poorer general health which may increase vulnerability to more severe influenza outcomes (Silva et al., 2010). However, there is not yet strong research evidence that describes the association between socio-economic conditions in Indigenous communities and severe influenza outcomes.

Only one study could be identified that focused specifically on the impact of socio-economic disparities on the burden of influenza in Indigenous populations (Charland et al., 2011a). This study found that the rate of influenza-related outpatient and emergency-department visits in Kahna wá:ke was 58% greater than in neighbouring regions despite the First Nations residents having comparable socio-economic conditions, as determined by average income and percentage of car ownership. The factors underlying this difference are never explored, again highlighting the dearth of research in this area specific to Indigenous peoples.

Several studies among the general population provide some evidence that socio-economic factors may be associated with the higher transmission rates of influenza. Thompson et al. (2012) explored associations between seropositivity for pH1N1 and socio-economic determinants of infection among a convenience sample of adults (65% of which identified as Indigenous) from three inner city clinics in Winnipeg. They found that the marginalized, inner city populations (those living in areas with the lowest income and education levels, often in overcrowded and/or inadequate housing conditions) may be at increased risk of influenza infection and are less likely to have had the recommended levels of vaccination. In their exploration of the effects of social determinants of health on pH1N1 severity in a case-controlled study in Ontario, Lowcock, Rosella, Foisy, McGeer and Crowcroft (2012) found that hospitalized individuals were significantly more likely to reside in the most materially deprived neighbourhoods and that health outcomes were more severe for socio-economically disadvantaged individuals. However, Crighton, Elliott, Moineddin, Kanaroglou, and Upshur (2007) found that there was no significant association between low income with pneumonia and influenza (P&I) hospitalizations for all age groups and both sexes in Ontario between 1992 and 2001; however low levels of education were strongly associated. Crighton and colleagues were unsure whether this relationship was a direct one or mediated through other lifestyle, socio-economic, environmental or health care factors, but posited that low levels of education affected health seeking behaviours as well as adherence with medical regimes, resulting in higher rates of hospitalization.

Poor living conditions, including overcrowded housing, exposure to indoor air pollutants, and lack of access to clean running water, are factors identified in the literature as likely contributing to the incidence and severity of the 2009 H1N1 influenza infection among Indigenous populations (Janjua et al., 2012; Pollock et al., 2012; Silva et al., 2010).

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[8] For further information on the impact of social determinants on Indigenous peoples' health, please refer to the NCCAH's fact sheet series on social determinants and Reading & Wien (2009).

Poor living conditions, including overcrowded housing, exposure to indoor air pollutants, and lack of access to clean running water, are factors identified in the literature as likely contributing to the incidence and severity of the 2009 H1N1 influenza infection among Indigenous populations (Janjua et al., 2012; Pollock et al., 2012; Silva et al., 2010). First Nations living on reserve and Inuit are more likely to live in overcrowded or inadequate housing conditions (NCCAH, 2009), placing them at greater risk of infection because of their greater exposure to circulating influenza (Thompson et al., 2012). Janjua et al. (2012), in their study comparing H1N1 infection rates between on-reserve First Nations with off-reserve Indigenous and non-Indigenous people, found that despite having similar levels of access to health care services, the rates of influenza were reported to be higher among on-reserve First Nations. What distinguished on-reserve residents from the other groups in their sample was that a greater proportion of on-reserve First Nations lived in higher density housing. Likewise, Mostaço-Guidolin et al. (2012) noted that higher density housing in Nunavut and northern Manitoba (3.8 and 3.6 people per household respectively) compared to the City of Winnipeg (2.5 per household) likely accounted for the higher rate of secondary household transmission of the 2009 H1N1 influenza in rural and remote communities within these two regions. In rural and remote areas, communities may not have access to clean running water which may impede the implementation of non-pharmaceutical interventions such as handwashing as a strategy for mitigating the spread of infection (Mostaço-Guidolin et al., 2013).

There were few studies that could isolate which socio-economic factors increase transmission and severity of influenza infection among Indigenous people. Crighton et al. (2007) note, for example, that while they found no significant association between low income with P & I hospitalization rates in their sample, studies in other populations have both supported (Stelianides et al., 1999; Vrbova et al., 2005) and contradicted (Harrison et al., 2000; Morris & Munasinghe, 1994: Wood, Sallar, Schechter, & Hogg, 1999) this association (p. 1647). Many Indigenous people continue to experience socio-economic disadvantage and marginalization, living in poor quality housing and in rural and remote areas where access to clean running water may be lacking (NCCAH, 2012; Reading & Halseth, 2013). Given the mixed results of these studies, further research is warranted on this topic, especially research which considers how the various living conditions intersect to create greater vulnerability and how socio-economic inequities can be addressed in influenza mitigation strategies in vulnerable Indigenous communities.

Cultural Factors

Cultural factors have also been identified in the research as contributing to the spread of influenza in Indigenous communities. Researchers have suggested that pandemic influenzas will spread more rapidly in Indigenous communities because of their strong social ties (Mostaço-Guidolin et al., 2011), where individuals often live in multigenerational households and interactions among them are frequent, and because ceremonial

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gatherings are very important in Indigenous culture (Mousseau, 2013). As a result of these social and cultural norms, implementing non-pharmaceutical interventions like social distancing may be less effective in Indigenous communities. Most of the research in this area involves agent-based modelling of the spread of the 1918-19 influenza pandemic; none could be identified within the context of the 2009 pandemic. While specific findings from these studies may not be generalizable in a contemporary context, general findings related to cultural factors and their influence on levels of social contact among individuals within communities and among communities continue to have relevance today.

A large body of work undertaken on the 1918-19 influenza pandemic in three predominantly Indigenous communities in Manitoba indicates that the impact of illness varied in each community depending on the levels of social contact among individuals within the community and between communities. This social contact was affected, in turn, by a variety of factors

including settlement patterns, seasonal activities, and population movement. Sattenspiel and Herring (1998, 2003) argue that contact between individuals within a community had greater importance in determining the impact of the epidemic than movement between communities. In 1998, they argued that the key to understanding the effects of the epidemic in this region lie in the domain of social structure and community organization. For example, in 2003, they illustrated how quarantine measures implemented in Norway House curtailed movement between outlying communities. When coupled with the difficulty of winter travel and patterns of movement associated with trade in the region, these measures had the effect of sparing the communities of Oxford House and God's Lake while worsening the situation in Norway House, where restrictions were placed only on the ill, not on those who were not yet ill but were entering the homes of those who were ill.

Cultural factors such as settlement patterns, seasonal activities, and population movement were shown to affect the timing of the 1918-1919 pandemic in Labrador (Mamelund, Sattenspiel, & Dimka, 2013) and in northern Manitoba (Ahillen, 2006; Carpenter, 2004; Carpenter, & Sattenspiel, 2009; Herring, 1993; Herring & Sattenspiel, 2007; O'Neil & Sattenspiel, 2010; Sattenspiel, Mobarry, & Herring, 2000). Ahillen (2006) applied an agent-based model to a winter and summer scenario for the pandemic in three northern Indigenous communities and found that most of the observed differences between the two scenarios derived from seasonal differences in settlement patterns rather than from seasonal differences in mobility rates. Had the pandemic struck these communities in the summer, when extended Cree and Métis family bands gathered at the posts, the impact of the pandemic would likely have been shorter and more severe than it was, and it would have more likely reached the outlying communities as well. Instead, the spread of infection was more limited due to the dispersal of people into hunting camps scattered at a distance from the posts (Carpenter, 2004). While these cultural factors influenced the timing of the epidemic and increased the vulnerability of some communities compared to others, it only minimally affected the number of cases within a community (Sattenspiel, Mobarry & Herring, 2000).

The body of work undertaken by Sattenspiel, Herring and colleagues clearly demonstrates that socio-cultural factors, such as settlement patterns, seasonal activities and population movement, can change the course of an influenza epidemic in a human population. While there have been improvements in transportation which have impacted the ease with which individuals can engage in social contacts within and among communities, there are still some Indigenous communities which are relatively remote or isolated, and in which seasonal hunting and gathering activities may still affect patterns of mobility and contact. As a result, this agent-based model could be adapted to provide useful guidance on the timing and impact of future influenza epidemics (Carpenter & Sattenspiel, 2009).

Health status

There is a considerable gap in the health status of Indigenous people compared with other Canadians. Indigenous people have much higher rates of tuberculosis, HIV and AIDS, diabetes, hypertension, cardiovascular disease, and obesity (Waldram, Herring, & Kue Young, 2006; NCCAH, 2009, 2012; PHAC, 2015; Earle, 2010). Individuals with poor health are generally less able to resist influenza infections and are more likely to have severe outcomes. This is especially evidenced in research emerging after the 2009 influenza pandemic which shows strong associations between pre-existing health conditions such as chronic pulmonary disease, heart disease, and diabetes and influenza incidence and severity. Additionally, nutritional deficiencies have been posited as a factor that can affect an individual's resilience to influenza infection (Mamelund, Sattenspiel, & Dimka, 2013; Herring & Sattenspiel, 2007); and early-life exposure to tuberculosis (TB) has been posited as a factor which can exacerbate the severity of influenza outcomes (Stone, 1989 as cited in Herring & Sattenspiel, 2007). Nevertheless, the research on how these health factors affect influenza incidence and severity remains limited within the context of First Nations, Inuit and Métis peoples.

A number of studies emerging after the 2009 influenza pandemic supported a strong correlation between predisposing health conditions and incidence and severity of infection (Bettinger et al., 2010; Helferty et al., 2010; Janjua et al., 2010, 2012; Jouvet et al., 2010; Mostaço-Guidolin et al.,

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2013; Zarychanski et al., 2010; Silva et al., 2010; Morrison et al., 2014). Most of this research focused on the general Canadian population, though a few studies focused on First Nations populations within a specific community or region. For example, Helferty et al. (2010), drawing from data on laboratory-confirmed cases of pandemic H1N1 influenza across Canada, found that during the first wave of the pandemic, 47.5% of patients admitted to the hospital, 60.2% of those admitted to ICU, and 73% of fatalities had one or more pre-existing conditions (including chronic pulmonary disease, heart disease, renal disease, immunosuppression, and diabetes). There is also some evidence that obesity may be associated with pH1N1 severity and may increase the length of stay for patients given mechanical ventilation (Akinnusi, Pineda, & El Solh, 2008; Centers for Disease Control & Prevention, 2009). Since Indigenous peoples have higher rates of chronic diseases like obesity and diabetes, it is reasonable to assume that these rates would lead to greater vulnerability to H1N1 influenza among Indigenous populations. This highlights the need for holistic approaches aimed at improving general health and well-being as an essential component of pandemic prevention strategies in Indigenous communities.

Another area of research relates to the interaction of other pathogens like TB with influenza. A small body of research attributes some of the excess mortality experienced during the 1918-19 influenza pandemic to high rates of TB among Indigenous populations (Herring & Sattenspiel, 2007; Kelm, 1999). Tuberculosis had become epidemic within First Nations, Inuit and Métis populations during the early twentieth century, resulting in death rates that were ten to twenty times higher than for non-Indigenous people (Stewart, 1936, p. 675, as cited in Waldram, Herring & Kue Young, 2006, p. 69). Over 100 people died of influenza over the July 1918-19 period in Norway House, a predominantly Cree and Métis community in northern Manitoba (Sattenspiel & Herring, 2003), while other more remote communities were left virtually unscathed (Herring & Sattenspiel, 2007). In fact, the mortality rate in Norway House was about 18% compared to 3% of all Indigenous people in Canada thought to have died from influenza (Ibid.) One of the characteristics which distinguishes Norway House from other remote communities was the high rate of TB within the community (Herring & Sattenspiel, 2007). Several studies within the general population have shown statistically significant associations between having tuberculosis and dying from influenza in 1918 (Noymer, 2009; Noymer and Gareene, 2003). While rates of TB have declined significantly over the past 50 years, they still remain disproportionately high among First Nations, Inuit and Métis populations. In 2013, Indigenous people represented 4% of the total Canadian population but 19% of all tuberculosis cases (Public Health Agency of Canada, 2015). It is thus vitally important that any synergies between TB and influenza outcomes be identified and that the paucity of research in this area be addressed.

Health Behaviours

Certain health behaviours have the potential to affect the spread or severity of influenza. Some behaviours may be harmful to an individual's overall health and thus reduce his/her ability to resist infections; others may prevent individuals from taking preventative measures (e.g. vaccinations) to avoid becoming ill in the first place or seeking timely medical care when they do become ill. Current research investigating Indigenous peoples' health behaviours and the incidence or severity of influenza is at present sparse; only one study was identified that explored these links.

Crighton et al. (2007) examined the role of several behavioural factors on hospitalizations for pneumonia and influenza (P & I) in Ontario between 1992 and 2001. They found that Indigenous status, daily smoking, and heavy drinking, were all associated with hospitalizations in different age and sex-specific models. However, no comparisons were drawn between Indigenous and non-Indigenous people with respect to each of these variables, and thus we are unable to determine whether Indigenous people are at increased risk of hospitalization

due to these health behaviours. One additional study points to a strong likelihood that high rates of smoking may have played a major role in the spread of influenza in Indigenous communities. Charland and colleagues (2011a) suggest that higher rates of smoking were likely the cause of elevated rates of seasonal influenza-related outpatient and emergency department visits among First Nations residents of a Mohawk community compared with neighouring non-First Nations residents, since they had comparable socio-economic status, access to health care services, and chronic disease prevalence. Other research has shown that smoking is a major risk for severe influenza in other populations (Kark, Lebuish, & Rannon, 1982; Huttunen, Heikkinen, & Syrjänen, 2010; Ward, Spokes, & McAnulty, 2011; Dai et al., 2010). Given that smoking rates are considerably higher among Indigenous peoples compared to the general population (Reading & Halseth, 2013; NCCAH, 2012), Charland et al.'s suggestion seems a reasonable one. This is an important public health issue that requires further research given its potential implications for influenza pandemic prevention within Indigenous communities.

The willingness or ability of individuals to take precautions to avoid becoming ill may also affect the burden of influenza in populations (Quach et al., 2012), although once again, the research in this area is fairly sparse. Quach et al. (2012) used data from the 2003 and 2009 Canadian Community Health Survey (CCHS) to determine whether there were differences in influenza vaccination coverage across 12 ethnic groups in Canada. They found that after adjusting for socio-demographic characteristics, Indigenous people[9] were more likely to receive an influenza vaccine compared to white Canadians. Likewise, Xiao and Moghadas (2015) found that in Manitoba, individuals with First Nations identity were over 2.8 times more likely to be vaccinated for the 2009 influenza H1N1 pandemic compared with non-First Nations individuals, and those living on reserve were 5.15 times more likely to be vaccinated compared to those living off-reserve. However, it must be remembered that the federal government implemented a strategy for prioritizing vaccination among Indigenous populations to respond to the disproportionate impact of the 2009 influenza pandemic in Indigenous communities, especially on reserves and in remote and isolated locations (PHAC & HC, 2010).[10] As a result, no inferences can be drawn from this study regarding willingness or ability of Indigenous people to be immunized for influenza.

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[9] The data excluded First Nations people living on reserve.
[10] Please see the review in this series on the epidemiology of the 2009 H1N1 influenza among Indigenous peoples in Canada for further information.

Three studies found that Indigenous/First Nations people living on-reserve and/or in remote areas experienced longer delays from the onset of symptoms to seeking medical care compared with those living off-reserve or in urban areas ...

Several studies examined the effectiveness of giving priority to Indigenous people for vaccination during the 2009 influenza pandemic. Charania and Tsuji (2011a) reported generally positive perceptions about the mass immunization campaign in three northern Ontario First Nations communities, with study participants indicating they felt there were enough doses of vaccine and that uptake rates were good in their communities. Nevertheless, the effectiveness of the vaccination campaign appears to have varied widely within First Nations communities, with uptake rates ranging from 59% to 111%[11] (Boggild, Yuan, Low, & McGeer, 2011; PHAC & HC, 2010), while Thompson and colleagues (2012) reported that only one-third of urban Indigenous people in Winnipeg received the H1N1 vaccine. Driedger, Cooper, Jardine, Furgal, and Bartlett (2013) put forward one possible theory that may explain why some communities had lower uptake rates. They investigated how risk was communicated to First Nations and Métis during the 2009 influenza pandemic and found perceptions among some First Nations that they were being treated like guinea pigs for a new vaccine. Such perceptions can perpetuate feelings of fear and mistrust that many Indigenous people have in regards to mainstream health care systems which can keep them from seeking out health care when they need it (Browne & Fiske, 2001; Loppie, Reading, & de Leeuw, 2014; Towle, Godolphin, & Alexander, 2005).

Delaying seeking medical care is a health behaviour that can influence the severity of influenza illness. Three studies found that Indigenous/First Nations people living on-reserve and/or in remote areas experienced longer delays from the onset of symptoms to seeking medical care compared with those living off-reserve or in urban areas; two in Manitoba (Morrison et al., 2013, 2014) and one in BC (Janjua et al., 2012). In all three studies, the lack of access to health care services did not seem to fully explain this delay within the sample populations and no other reasons for the delay were made clear. There were likely a range of other factors which may have contributed to this delay, including a lack of trust in western health practitioners; the ways in which the H1N1 illness can manifest and progress within individual patients; greater availability of home supports during the early phases of illness which can lead to staying home longer; or testing whether home remedies will be effective before seeking out medical care, among others. Since delays in seeking medical care were found to be associated with a risk of severe outcomes during the 2009 influenza pandemic (Campbell et al., 2010; Daghofer, 2012; Morrison et al., 2014), the lack of knowledge

[11] Off-reserve residents returning to their communities for immunization accounted for the proportion exceeding 100%.

about the reasons for this delay must be addressed so that there can be a much more effective public health response to influenza pandemics in vulnerable Indigenous communities in the future.

One additional study examined knowledge, risk perceptions and attitudes regarding the avian influenza virus (AIV) among First Nations subsistence hunters (Charania, Martin, Liberda, Meldrum, & Tsuji, 2014). This study found that only a small percentage of hunters who could be exposed to avian influenza took any of the recommended protective measures, highlighting the need for more culturally-relevant education in this area to prevent the potential spread of avian influenza among this population. Given global concerns about AIV infections in humans and the increased potential exposure to this virus among subsistence hunters, Charania et al. argued that First Nations subsistence hunters should be considered an avian risk group and that future pandemic plans should include special considerations for AIV.

There is generally a lack of research exploring the factors which contribute to or impede Indigenous people from taking measures to avoid becoming ill from influenza. Overcoming any barriers that might impede such preventative measures will be important to mitigating the spread and severity of influenzas among this vulnerable population.

Genetic Susceptibility

A final factor identified as possibly being associated with pandemic H1N1 influenza is that of genetics. Some have posited that there may be immunogenetic determinants of severe H1N1 illness. Keynan, Malik, and Fowke (2013) and Juno, Fowke and Keynan (2012) undertook reviews of the literature on immunogenetic factors associated with severe respiratory illness associated with H1N1 illness. They identified several lines of evidence that lend some support to the theory that "different populations have disparate degrees of susceptibility to pH1N1 and that host variation in key genes associated with the appropriate immune response could play an important role in determining the outcome of infection" (p. 14). They note for example, several studies in other populations which suggest that excessive inflammation and release of cytokines are associated with severe cases of respiratory illness. However, these studies have a number of limitations including small sample size and no specific focus on immunogenetic determinants of H1N1 influenza A prevalence and severity in Indigenous populations.

Only one study could be identified that examined immunogenetic associations with H1N1 influenza A in Indigenous populations in Canada. La et al. (2011) compared 102 patients (40 Indigenous and 62 non-Indigenous) admitted to ICU with 2009 influenza virus with 105 H1N1-negative subjects from St. Theresa Point, a First Nations reserve in Manitoba, to assess killer cell[12] dysfunction in overactive immune responses to H1N1 infection. Though their sample size was small, their study showed that the enrichment of specific allotypes[13] (such as 3DL1*00101, 3DL1*01502, and 3DL1*029) in Indigenous patients and a "disproportional distribution of cognate HLA [human leukocyte antigen] class I ligands are likely factors that mediated NK cell dysfunction and lead to the development of severe responses to H1N1/09 in ICU patients" (p. 5). Zarychanski et al. (2010) notes, however, that Australian Aboriginals and Torres Strait Islanders were similarly over-represented in 2009 influenza cases, yet they do not share a common ancestry with Indigenous peoples in Canada. Instead, they share a common history of colonization and social inequities that have led to significant health disparities. Taken together, these studies provide several lines of evidence to suggest there may be genetic susceptibilities to several intracellular pathogens; however, at present these susceptibilities are generally not broadly racially based, and there is very little data that supports the hypothesis that "genetic factors explain the over-representation of complicated influenza infection among indigenous populations in general, or Canadian Indigenous peoples in particular" (Boggild et al., 2011, p. 347).

[12] A type of white blood cell and a component of the innate immune system (Wikipedia, 2015a).
[13] Allotype is the allele (one of a number of alternative forms of the same gene) of the antibody chains found in the individual (Wikipedia, 2015b).

Conclusion

No single characteristic likely explains the disproportionate burden of infection experienced by Indigenous peoples to either the 1918-19 or 2009 influenza pandemics. Instead, the explanation is likely that compounding effects of multiple determinants make this population more vulnerable relative to non-Indigenous Canadians, including a younger age structure, higher rates of smoking, higher rates of pre-existing chronic conditions, poverty, overcrowded and inadequate housing conditions, lack of access to clean water, lower levels of education, inadequate access to quality health care, and living in isolated locations, among others. While there is a fairly large body of literature on the influence of geographic remoteness and isolation, demographics, and pre-existing chronic conditions on the burden of influenza in First Nations, Inuit and Métis populations, there are numerous gaps that warrant further investigation, including:

- whether there are any associations between socio-economic determinants (income, employment, education) and influenza prevalence and severity;
- whether there are any associations between environmental determinants (overcrowded housing, poor quality housing, indoor air quality) and influenza prevalence and severity;
- the impact of health behaviours like smoking and drinking on susceptibility or resistance to infection;
- the impact of nutritional deficiencies on resistance to influenza infection;
- determinants of preventive, health, and health care seeking behaviours among Indigenous people;
- synergies between pathogens of previous illnesses in the population, like TB with influenza; and
- whether there is any genetic susceptibility that places Indigenous people at risk of severe outcomes from influenza pandemics.

Collectively, these determinants highlight the need for a holistic framework for pandemic planning that not only enacts measures that allow Indigenous communities to more effectively respond to public health emergencies in the future, but also aim to improve inequities in socio-economic status (ie. education, income) and living conditions (housing, clean running water), and improve health generally (ie. smoking cessation) within Indigenous communities. Without addressing such inequities, the burden of influenza illness will likely continue to be heavy in Indigenous communities.

In 2013 the six National Collaborating Centres for Public Health initiated a two-year project on Influenza and Influenza-Like Illness (ILI). As part of this collaborative project, the NCCAH produced three reports in order to understand how influenza, such as the 2009 H1N1 pandemic, is particularly experienced by Indigenous populations in Canada; the knowledge gaps in the epidemiological research related to influenza and Indigenous peoples; and how public health responses can be better tailored to the unique needs and characteristics of Indigenous peoples and communities. The three papers in this series include:

1. The 2009 H1N1 influenza pandemic among First Nations, Inuit and Métis peoples in Canada: Epidemiology and gaps in knowledge
2. Determinants of the prevalence and severity of influenza infection in Indigenous populations in Canada
3. Pandemic planning in Indigenous communities: Lessons learned from the 2009 H1N1 influenza pandemic in Canada

Additional NCC documents in this series are available at: http://nccid.ca/collection/influenza/

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How to use this fact sheet

REFLECT

Talk to others in your community, reflect on the content of this fact sheet, and contemplate how you could make a difference in the health and well-being for yourself, your family or your community.

ENGAGE

Find local friendship centers, community organizations or groups where you can volunteer or participate in healthy positive actions. You too can share knowledge and make a difference in the health and well-being of First Nations, Inuit, and Métis Peoples' of Canada.

sharing knowledge · making a difference
partager les connaissances · faire une différence
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