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The impact of geographical location of residence on disease outcomes among Canadian First Nations populations during the 2009 influenza A(H1N1) pandemic

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ABSTRACT

We sought to evaluate the effect of geographical location of residence on disease burden in Canadian First Nations (FN) populations during the 2009 pandemic influenza A(H1N1). Descriptive statistics and regression analysis of data for cases of pandemic A(H1N1) infection and hospitalization in the province of Manitoba, Canada, were conducted to estimate the odds of hospitalization and delay in time-to-hospitalization for on-reserve and off-reserve FN populations, while considering their geographical proximity to urban centers. We found that on-reserve FN individuals experienced a longer delay between infection and hospitalization compared to off-reserve FN individuals ($p < 0.001$). The average fraction of FN cases that experienced a delay longer than 4 days for hospitalization was 20% higher for on-reserve compared to off-reserve residence. The odds of hospitalization were twice as high for FN people living on-reserve as compared to off-reserve (odds ratio = 2.34; 95% CI: 1.16–4.73). Given the independent effect of on-reserve residency, higher disease burden among FN people cannot be attributed entirely to limited healthcare access due to remoteness from urban centers.

1. Introduction

Although infection with the pandemic 2009 influenza A(H1N1) virus generally resulted in mild illness with a global impact less than anticipated by many preparedness plans, Canadian indigenous populations, and particularly First Nations (FN) communities in northern regions, experienced disproportionately high rates of severe outcomes (Campbell et al., 2010; Zarychanski et al., 2010). A comparative analysis between FN and non-FN populations for the province of Manitoba, Canada, indicated that the age-specific rates of infection and hospitalization were significantly higher amongst individuals with FN identity, with a marked elevation in both infection and hospitalization among FN children younger than 5 years of age (Mostaço-Guidolin et al., 2013a, 2013b) The underlying reasons for higher rates of infection and severe illness in indigenous populations are poorly understood, but they likely include a high prevalence of predisposing health conditions, limited access to critical infrastructure and non-pharmaceutical interventions such as clean water for hand-washing, exposure to indoor air pollutants, crowding and low-quality housing, and limited access to healthcare services (Kermode-Scott, 2009; Zarychanski et al. 2010).

Using a range of methodologies, studies have described how place and environment can affect health in First Nations communities (Wilson and Rosenberg, 2002; Wilson, 2003; Frohlich et al., 2006). For example, Richmond and Ross (2009) interviewed community health representatives and used qualitative methods to determine that physical environment and culture are intimately connected in First Nations populations, and such connections to surroundings are determinants of health. In the context of A(H1N1) pandemic influenza, Driedger et al. (2013) discussed the complexities in communicating risks and intervention strategies (such as vaccine prioritization) aimed at First Nations individuals living in remote areas or on-reserves as opposed to individuals living off-reserve or in urban communities. First Nations individuals in Canada were indirectly prioritized to receive vaccination for pandemic influenza via a mandate that gave priority to those living in isolated communities, and individuals of Aboriginal ancestry were explicitly prioritized in the province of Manitoba (Manitoba Health, 2009, 2010; Sander et al., 2010). In summary, geography, place, environment, and culture all play a complex and nuanced role in the determinants of health in First Nations communities in Canada.

Geographical location of residence is one important factor in determining access to healthcare, with isolated and remote

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communities generally being the most underserved (Richardson et al., 2012). In Canada, members of these communities often belong to indigenous groups that have traditionally lived in the northern regions of provinces and territories both on and off reserves. Although FN people experienced higher rates of infection and hospitalization during the A(H1N1) pandemic (Kumar et al., 2009; Freed et al., 2010), the effect of their geographical location of residence on these outcomes has not been investigated.

We sought to evaluate the effect of geographical location of residence on hospitalization among FN people with A(H1N1) influenza infection who were living in different geographic regions in the province of Manitoba. We used clinical and epidemiological data collected during pandemic A(H1N1) in Manitoba to investigate the effect of geography on a delay in initiating hospitalized care. Our analysis compared distributions of time-to-hospitalization for on-reserve and off-reserve FN communities with the distributions of time-to-hospitalization for FN populations residing in urban and remote areas. Specifically, we assessed the effect of remoteness and delay in initiating critical care (considered as hospital admission) post-infection as possible reasons for differential rates of hospitalization in on-reserve FN populations and rural areas. We also assessed the likelihood of hospitalization with A(H1N1) infection for on-reserve and off-reserve FN individuals, while controlling for the location of residence as an urban, rural, or remote community.

2. Materials and methods

2.1. Study area

Manitoba is the easternmost prairie province of Canada, with a population size of approximately 1.27 million (Fig. 1). According to the 2011 census data, 61% of Manitoba's FN population with registry status resides on-reserve, described as a geographic area which is specified by the Indian Act as a “tract of land” (Department of Justice, 2009). The FN ethnic group with registry status constitutes approximately 11% of the total population, and refers to the Canadian Aboriginal peoples who are neither Inuit nor Métis (Richardson et al., 2012). Manitoba has 63 on-reserve

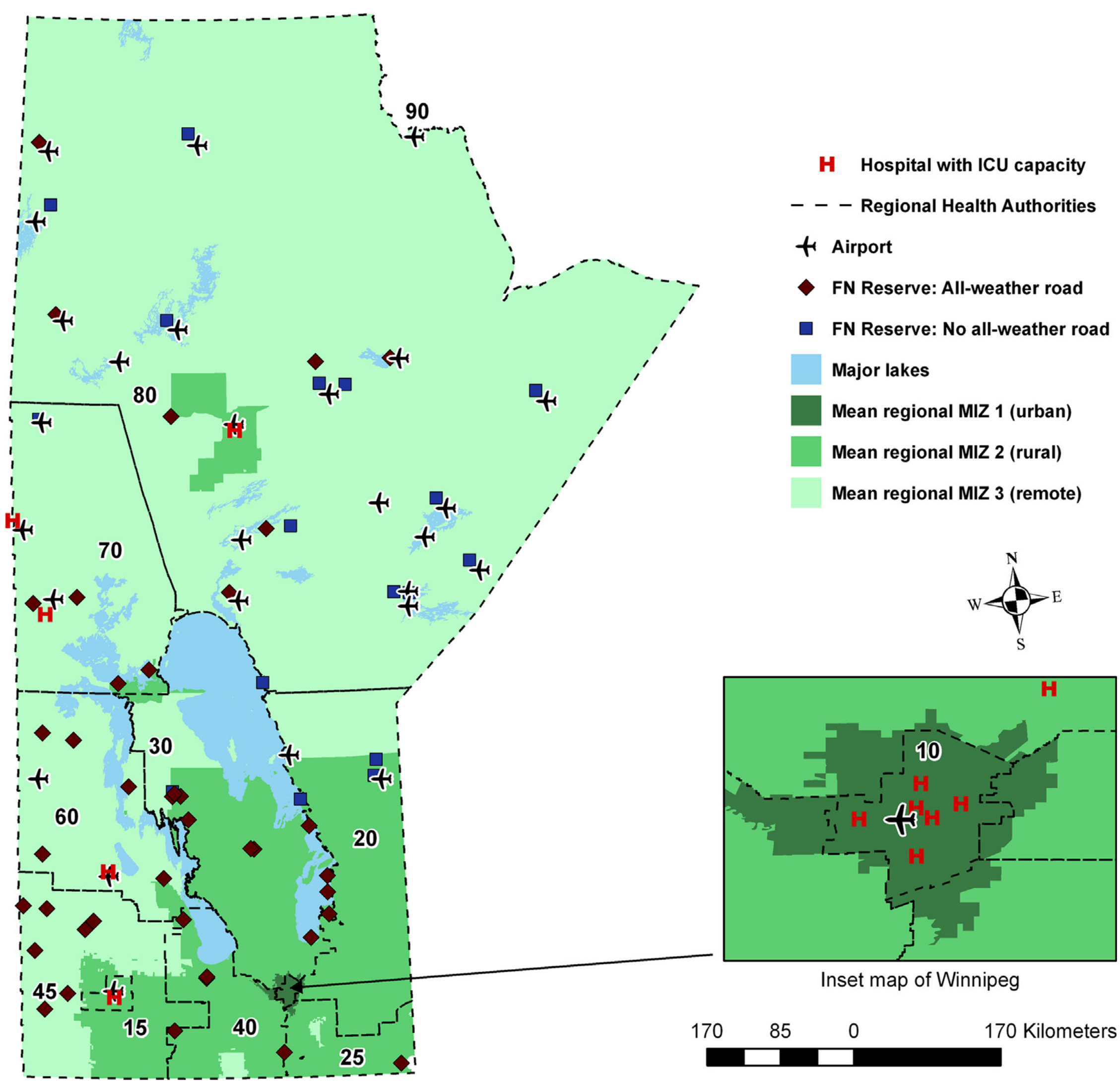

Fig. 1. Map of Manitoba with aggregated MIZ scores by Forward Sortation Area (FSA) and boundaries for regional health authorities (RHAs): Winnipeg (10), Brandon (15), North Eastman (20), South Eastman (25), Interlake (30), Central (40), Assiniboine (45), Parkland (60), Norman (70), Burntwood (80), Churchill (90).
Data sources include: (i) Health regions in Canada, 2011, Statistics Canada (http://www.statcan.gc.ca/pub/82–402-x/2011001/gui-eng.html); (ii) Geospatial data for location of lakes (http://www.empr.gov.bc.ca/Mining/Geoscience/MapPlace/GeoData/pages/default.aspx); (iii) Canadian Institute of Health Information for hospital location (http://www.cihi.ca/cihi-ext-portal/xlsx/internet/beds_staffed_2011-2012_en); (iv) BioDiaspora project for location of airports (http://www.biodiaspora.com); and (v) Aboriginal Affairs and Northern Development Canada for location of reserves (http://pse5-esd5.ainc-inac.gc.ca/FNP/Main/Index.aspx).

lands spread across different health regions in the entire province, 23 of which are not accessible by all-weather roads (Fig. 1). Manitoba is also the home for six of the 20 largest FN bands in Canada (Aboriginal Affairs and Northern Development Canada, 2013).

2.2. Data

We obtained data for laboratory confirmed cases of pandemic A (H1N1) infection in the province of Manitoba from May 2009 to January 2010, covering both spring and fall waves. A laboratory confirmed case was an individual with influenza-like symptoms or severe respiratory illness who tested positive for A(H1N1) influenza virus by viral culture or by real-time reverse-transcriptase PCR (RT-PCR). For each confirmed case, the identification date was recorded as the earliest of the dates associated with the onset of symptoms, specimen collection, hospital admission, and ICU admission. Data were stratified by age groups (available as 5-years intervals and aggregated into children: 0–4; youth: 5–19 years of age; adults: 20–49 years of age; and older adults: 50+ years of age), health region of patient residence, hospitalization and ICU admission, antiviral treatment, ethnicity (FN identity), dates associated with the initiation of critical care and antiviral use, and postal codes for residence of confirmed cases. Manitoba Health used the information provided through the case investigation form for each case to determine FN status, which was confirmed using the Indian Registry database from Indian and Northern Affairs Canada. We used postal codes and the Aboriginal Canada Portal database to determine the association of each FN confirmed case with an on-reserve or off-reserve residential area (Aboriginal Affairs and Northern Development Canada, 2012).

2.3. Geography and defining rurality

In Canada, postal codes are six-digit alphanumeric codes used for mail delivery and are defined across each province, representing a small spatial unit in urban areas. The first three digits of the postal code represent a geographic region referred to as the Forward Sortation Area (FSA), which corresponds to a large region of aggregated postal codes starting with the same three digits. In many databases, including the database used in this paper, six-digit postal codes are truncated to an FSA prior to releasing the data in order to preserve the confidentiality of residents of sparsely populated postal code areas. Census subdivisions are an alternative geographic unit, used to collect and disseminate census and survey data from Statistics Canada. The geographic boundaries of census regions and postal code regions do not exactly align, but data collected in census subdivisions can be aggregated into postal code regions using weighted averaging.

For each confirmed case, we measured rurality using the Statistics Canada definition referred to as Metropolitan Influence Zones (MIZs) (Statistics Canada, 2012). Each census subdivision in Canada is classified with an MIZ score of one or two if it is located within a metropolitan area. Regions outside of metropolitan areas are given an MIZ score between three and seven based on their characteristics, such as population density and proximity to the closest urban center (McNiven et al., 2000).

Using all seven MIZ scores to classify the cases in our study would result in small or empty cells for some levels of rurality. To enhance the stability of our estimates, we aggregated MIZ scores in a manner consistent with the Public Health Agency of Canada definition of remote and isolated areas in the context of the 2009 A (H1N1) pandemic (Public Health Agency of Canada, 2009). We considered three levels corresponding to scores from one to two (MIZ1); three to five (MIZ2); and six to seven (MIZ3). We applied these zones to characterize a region within an urban center by MIZ1; a moderately rural region by MIZ2; and a remote/isolated region by MIZ3. Fig. 1 shows a map of the average aggregated MIZ score for each Forward Sortation Area in the province of Manitoba, with overlaid location of each FN reserve in the province (Statistics Canada, 2006).

2.4. Time to hospitalization

We used the *U*-test (Tang and Tsui, 2007) to assess the statistical significance of the difference between the mean values of hospitalization for on-reserve and off-reserve FN populations, stratified by MIZ areas. This analysis was carried out for hospital admission within 1 day, within 2–4 days, and beyond 4 days post-infection. We also used the non-parametric Kolmogorov–Smirnov test (Massey, 1951) to compare the full distribution of delays for hospitalization between on-reserve and off-reserve FN populations and MIZ score areas. For both tests, we used a two-sided significance level of 0.05.

We identified 495 cases of A(H1N1) infection among FN individuals during both waves, of whom 142 were hospitalized (Table 1), and 26 of those hospitalized cases were admitted to ICU. Among hospitalized cases, 16 cases were reported with no hospital admission date. For the analysis of time to hospitalization, we first excluded these cases from the data and performed the descriptive analysis. We then imputed missing dates and replicated the descriptive statistics as described in the following sections. Results of this imputation are consistent with the results from an analysis of the reported data.

Table 1
Cases of A(H1N1) infection in FN populations with hospitalization counts in different geographic places.

Area	Age group	Hospitalized		Not hospitalized	
		Wave 1	Wave 2	Wave 1	Wave 2
On-reserve	0–4	38	1	35	17
	5–19	11	1	44	23
	20–49	24	5	30	30
	50+	6	2	7	2
	Subtotal	79	9	116	72
Off-reserve	0–4	8	2	6	12
	5–19	8	4	30	53
	20–49	16	9	15	44
	50+	4	3	2	3
	Subtotal	36	18	53	112
	Total	115	27	169	184
MIZ1	0–4	5	2	2	0
	5–19	7	4	19	15
	20–49	9	9	5	24
	50+	2	3	1	0
	Subtotal	23	18	27	39
MIZ2	0–4	20	0	8	6
	5–19	2	0	12	23
	20–49	10	0	12	16
	50+	1	1	1	3
	Subtotal	33	1	33	48
MIZ3	0–4	21	1	31	23
	5–19	10	1	43	38
	20–49	21	5	28	34
	50+	7	1	7	2
	Subtotal	59	8	109	97
	Total	115	27	169	184

2.5. Odds of hospitalization given infection

We used logistic regression to calculate the odds of hospitalization (given infection with the pandemic A(H1N1) virus) for on-reserve and off-reserve FN populations, and across different MIZ regions. For this analysis, we included demographic and geographic variables (i.e., rurality, reserve residency, age, and pandemic wave) to investigate the simultaneous effect of these factors on odds of hospitalization. We used a regression model in the form of

$$\begin{aligned}&\textbf{Log}-\textbf{odds}\,(\textbf{hospitalization}\mid\textbf{infection with A(H1N1)})\\&=\beta_0+\beta_1(\text{age, youth})+\beta_2(\text{age, adults})+\beta_3(\text{age, older adults})\\&+\beta_3(\text{MIZ2})+\beta_3(\text{MIZ3})+\beta_4(\text{residence, reserve})+\beta_5(\text{wave}),\end{aligned}$$

where β_is are the regression coefficients, the exponentiated values of which are odds ratios. Children (aged 0–4 years) and MIZ1 (urban area) were the baseline values in their respective categories and therefore have a fixed odds ratio of 1.0.

2.6. Imputing missing data

We computed the delays for hospitalization (the time interval from the date of symptom onset to the date of hospital admission), and used bootstrapping to estimate the missing dates of hospital admission for 16 cases. We first excluded cases with no hospital admission date from the reported data and adopted the method of bootstrap to generate 200 samples of the same size as the original data set for each geographic variable: on-reserve (85 cases), off-reserve (57 cases), MIZ1 (26 cases), MIZ2 (45 cases) and MIZ3 (71 cases). Comparing these samples with several standard distribution functions, we found that the probability distribution functions for delay in hospitalization follow the shape of a negative exponential function. We then used the least squares method to fit the negative exponential function $f(x)=ae^{-bx}$ to fit the samples and estimate a and b for each geographic area. We used the average values of a and b estimated from the fitting procedures for 500 samples associated with each area in the probability function for delays in hospitalization. Using the random generator ranging from 0 to 1, and the probability density function for delays in each area, we generated number of days for delay in hospitalization post-infection, and included in data set for cases with missing hospital admission dates. We ran simulations and generated 200 samples for dates of hospitalization in each area, and grouped each sample by hospital admission within 1 day, within 2–4 days, and beyond 4 days post-infection. We then performed descriptive analysis of the 200 samples and their mean values between different geographic areas using the non-parametric Kolmogorov–Smirnov test.

3. Results

3.1. Time-to-hospitalization

Comparing on-reserve and off-reserve populations (Kolmogorov–Smirnov test), we found a significant difference (p=0.022) between their respective full distributions of time-to-hospitalization post-infection. Using the non-parametric test (Kruskal–Wallis), we also found that on-reserve residents experienced longer delay (on-average) between infection and hospitalization compared to off-reserve residents ($p<0.001$). There was a significant difference between average time-to-hospitalization for MIZ regions, with a longer delay for residents of MIZ3 compared to MIZ2 ($p<0.001$). Similarly, residents of MIZ2 experienced a longer delay in time-to-hospitalization compared to residents of MIZ1 ($p<0.001$).

The average proportion of A(H1N1) cases hospitalized within 2–4 days was significantly (59%) smaller for individuals living on-reserve versus off-reserve. In contrast, the average proportion of hospitalized cases beyond 4 days was 22% larger for on-reserve compared to off-reserve residents. This average was significantly 94% (respectively, 62%) smaller for MIZ2 (respectively, MIZ3) compared to MIZ1 for hospitalization within 2–4 days. For time-to-hospitalization beyond 4 days, the average proportions of hospitalization in MIZ2 and MIZ3 areas were respectively 28% and 29% higher than that of MIZ1.

3.2. Odds of hospitalization given infection

The results of our regression analysis (Table 2) indicate that age, rurality, pandemic wave, and on-reserve residency all influenced the odds of hospitalization given A(H1N1) infection for FN populations in Manitoba. The significant effect of age on hospitalization (for youth aged 5–19 OR=0.219, 95% CI: 0.116–0.419), for adults aged 20–49 (OR = 0.80, 95% CI: 0.460–1.390), and for older adults (OR=1.830, 95% CI: 0.750–4.450), compared to baseline children aged 0–4, suggests that the very young and those over 50 were at an increased risk of hospitalization post-infection, while controlling for other variables. The odds of hospitalization were also significantly higher for FN populations living on-reserve (OR = 2.34; 95% CI: 1.16–4.73), even after controlling for the influence of rurality, pandemic wave, and age. When controlling for age, the effect of other variables on hospitalization was reduced. In contrast, rurality (living in a more rural or remote area) was associated with a decrease in odds of hospitalization when controlling for the other variables, including reserve residency. The pandemic wave was a significant variable in the model (OR = 0.194; 95% CI: 0.114–0.332), suggesting that the odds of hospitalization were higher in the first wave compared to the second, after controlling for covariates. We found no evidence of multiplicative interaction between on-reserve residency and rurality; when included as a product term in the regression model, the interaction terms were insignificant ($p>0.20$) and the magnitude or direction of the other terms did not substantially change.

3.3. Results of imputation

Using the results of our sampling analysis and the Kruskal–Wallis test, we found a significant difference ($p=0.022$) between the full distributions of time-to-hospitalization. Overall, on-reserve residents experienced longer delay for hospitalization compared to off-reserve residents ($p<0.001$). MIZ3 residency was associated with a longer delay for hospitalization post-infection compared to MIZ1 and MIZ2 residencies ($p<0.001$). We also calculated the fraction of hospitalized cases for different geographic areas and time-to-hospitalizations (Table 3), and

Table 2
Logistic regression parameters, odds ratios (OR), and 95% confidence intervals for OR.

Parameters	β_i	OR (95% CI)	p-Value
Intercept	0.990		0.00394
Age (0–4, baseline)	–	1.0	–
Age (5–19)	−1.520	0.219 (0.116, 0.415)	<0.001
Age (20–49)	−0.224	0.800 (0.460, 1.390)	0.428
Age (50+)	0.603	1.830 (0.750, 4.450)	0.185
MIZ1 (baseline)	–	1.0	–
MIZ2	−1.430	0.240 (0.111, 0.519)	<0.001
MIZ3	−1.990	0.137 (0.060, 0.311)	<0.001
Wave 2	−1.640	0.194 (0.114, 0.332)	<0.001
On-reserve	0.850	2.340 (1.160, 4.730)	0.0179

Table 3
Proportion of hospitalized cases in different geographic locations with time to hospitalization after imputation.

Area	Proportion of hospitalized cases (95% CI)		
	Within 1 day	Within 2–4 days	Beyond 4 days
On-reserve	0.221 (0.207, 0.253)	0.298 (0.253, 0.345)	0.481 (0.437, 0.517)
Off-reserve	0.185 (0.182, 0.200)	0.434 (0.418, 0.455)	0.381 (0.364, 0.400)
MIZ1	0.176 (0.171,0.195)	0.484 (0.463, 0.512)	0.340 (0.317,0.366)
MIZ2	0.262 (0.257,0.286)	0.256 (0.229,0.286)	0.481 (0.457,0.514)
MIZ3	0.198 (0.182,0.242)	0.313 (0.273,0.364)	0.489 (0.439,0.545)

obtained 95% confidence intervals. The results are consistent with those obtained before imputation.

4. Discussion

We investigated the effect of rurality and living on reserve with hospitalization for influenza among FN people in Manitoba, Canada. Our results show that hospitalization post-infection was associated with longer delay for on-reserve residence compared to off-reserve residence of FN populations. We also observed a significant difference in the time-to-hospitalization between remote and urban areas, with a delay to admission of at least 4 days post-infection for a significant fraction of hospitalized cases (Table 3). A longer delay to access medical care could translate to an increased risk of severe outcomes and ICU admission, and this may have contributed to high rates of hospitalization among FN populations. The highest age-specific hospitalization rates among FN populations were observed in young children, 0–4 years of age, with as much as 22 times higher rates of hospital admission when compared to the same age group in non-FN populations during the first wave of A(H1N1) pandemic (Mostaço-Guidolin et al., 2013a, 2013b). Our results indicate that the odds of hospitalization were higher for on-reserve FN populations, even after controlling for the influence of rurality. In contrast, we found that infected cases in rural areas (MIZ2 and MIZ3 as compared to MIZ1) had a lower odds of hospitalization when controlling for reserve residency and the other model variables. There are many plausible explanations for this finding, including differences in laboratory testing practices or differences in the use of antiviral medication for prophylaxis treatment. Unfortunately, the data necessary to explore this issue further are not available. Nonetheless, our findings indicate that the geographic location of residence with respect to urban proximity is not the sole factor influencing health outcomes in FN populations.

The impact of remoteness and rurality on health outcomes has been evaluated in several studies, particularly in relation to chronic diseases (Virnig et al., 2004; Tonelli et al., 2006, 2007; Smith et al., 2008; Bello et al., 2012). However, the effect of these factors in the context of the 2009 A(H1N1) pandemic has not been assessed. Given demographic and health disparities between many on-reserve and off-reserve FN populations, possible factors influencing disease outcomes may include crowded and multigenerational households on reserves, and lack of access to critical (Mostaço-Guidolin et al., 2011, 2012). Such disparities could relate to limited access to health services, particularly when some of Canada's constitutionally identified Aboriginal peoples have different levels of government responsible for the provision of healthcare. Furthermore, the differential prevalence of predisposing health conditions, including diabetes and morbid obesity, has received considerable attention as explicators of severe outcomes of A(H1N1) pandemic in rural communities in Canada (Zarychanski et al., 2010). In the context of pandemic A(H1N1) in Manitoba, asthma, diabetes, and chronic lung diseases were the most prevalent comorbidities among hospitalized and ICU-admitted cases (Mostaço-Guidolin et al., 2013a, 2013b). The high rates of hospitalization and ICU admission within these remote regions could also be linked to higher transmissibility of the disease compared to urban centers (Mostaço-Guidolin et al., 2012).

Canadian FN populations were more likely to be infected with A(H1N1) and hospitalized, and more likely to suffer severe outcomes due to infection when compared to non-FN populations (Zarychanski et al., 2010). The reasons underlying the differential outcomes are not well understood, but the geographic location may be considered a potential reason, since many FN populations are located in rural or remote areas without hospital infrastructure. During the first wave of the A(H1N1) pandemic, medevac services were used to transfer patients from northern communities without critical care capacity to hospitals in southern part of the province, mostly in the Winnipeg health region, which is the largest urban center in Manitoba. In addition to life-flight services that were used to transport critically ill patients, air ambulance services were required for transportation of 76 patients from northern communities. Surge capacity for ICU admission was seriously challenged due in part to the greater incidence of severe disease in northern communities and prolonged use of ventilators by critically ill A(H1N1) patients. The peak demand was on June 24, 2009, when use of ventilators by confirmed or probable A(H1N1) patients reached 50% of the province's capacity of the ventilator-capable beds. The entire MIZ3 area in Manitoba (Fig. 1) has four hospitals with ICU capacity, with only seven intensive care beds (CIHI, 2012). In the Burntwood health region, where most on-reserve FN communities without all-weather road access are located, there is only one hospital with three intensive care beds in the city of Thompson.

During the first wave, 40.3% of all hospitalized cases in Manitoba were residents of northern regions, where the majority of remote and isolated communities without year-round road access are located. The lack of access to the continuum primary care is one of the main challenges for these communities, and may explain higher rates of hospitalization in rural and northern areas as compared to urban settings (Mostaço-Guidolin et al., 2013a, 2013b). While on-reserve and off-reserve Aboriginal communities are covered by a single healthcare system in Manitoba, the challenges of community health are compounded by several regional factors, including the availability of healthcare services that varies across these communities with similar needs, due in large measure to the scarcity of health and human resources, distance and modes of transportation, and ambiguity regarding the responsibility for healthcare delivery due to jurisdictional overlap related to Aboriginal status at the provincial and federal levels. In the context of the influenza A(H1N1) pandemic, delayed treatment of clinically ill patients in northern communities appears to have contributed to a significant demand for hospitalized and intensive care, which are mainly available in more urban areas, necessitating patient transportation (Kumar et al., 2009; Zarychanski et al., 2010).

Our results show that location of residence does indeed play an important role in determining severe disease outcomes among FN individuals, with independent effects of reserve residency status and proximity to an urban center. Although the results are based on the analysis of a data set for a Canadian province, our findings are highly relevant to other countries that have large Aboriginal populations, and/or remote communities that are underserviced (in terms of access to healthcare resources) but over-burdened (in terms of disease), including the US and Australia.

Previous research on the geographic disparities in indigenous health often has used off-reserve residency as a proxy for “urban-dwelling”, and considered on-reserve populations as rural or remote communities (Brown et al., 2009; Place, 2012). However, many FN reserves are close to urban centers, and many FN populations reside off-reserve but in areas which are considered rural and remote communities (Public Health Agency of Canada, 2009). Reserve residency may therefore not be an accurate measure of proximity to an urban center. In this study, we considered the rurality of a region independently from reserve residency, by using an existing measure developed by Statistics Canada that accounts for both population density and proximity to the nearest urban center (Statistics Canada, 2012). This measure allowed us to simultaneously model rurality and reserve residency, and to investigate their independent influence on the odds of hospitalization from A(H1N1) infection.

The database used in this study contained information on laboratory-confirmed FN cases of pandemic A(H1N1) in the province of Manitoba, and while the sample size for the entire database was large (approximately 500), only a small number of individuals (27 cases) were admitted to intensive care. This small data set was inadequate to conduct a similar analysis for ICU admission as an independent health outcome. Although we explored variation in time between infection and hospitalization, evaluation of differences in the length of time prior to hospitalization for on-reserve FN populations who experienced severe outcomes merits further investigation. Such analysis, with the use of time-to-event modeling (possibly with a larger database) could be used to explore trends of health outcomes while controlling for rurality, age, and disease wave. Our analysis could also be expanded to apply spatially explicit modeling and investigate the impact of geography (location of each case) and the characteristics of distinct geographic regions on disease outcomes. These characteristics may differ between FN populations (both on-reserve and off-reserve), which may include different levels of access to healthcare (e.g., on-site nursing station or hospitalized facilities); modes of conduit to and from the communities (e.g., all-time roads, flights); the availability of critical infrastructure (e.g., clean water); quality of life (e.g., overcrowded households); and prevalence rates of comorbid conditions (e.g., asthma, diabetes (Zarychanski et al., 2010; Mostaço-Guidolin et al., 2011, 2012; Pollock et al., 2012)). While we have not included specific characteristics (including level of services) of each FN reserve in our analysis, we expect that these characteristics are highly correlated with remoteness as defined in our study. In the database used for this study, reported cases did not have consistent levels of geography (i.e., full versus partial postal code) and data were inadequate to develop a full spatial model. Using databases with a finer spatial scale, one could model counts of disease per region as a spatial Poisson process, capture the unique characteristics of each region as covariates (urban proximity, percent FN ethnicity), and directly estimate the risk of hospitalizations across space. Finally, since our analysis suggests that urban proximity and reserve residency have independent effects on the odds of hospitalizations, further research is needed to understand the reasons for high rates of severe outcomes amongst on-reserve FN populations. One very plausible explicator could be higher rates of predisposing comorbidities in FN populations living on-reserve, and this could be explored using surveillance databases with information on health condition of individuals at risk of infection.

5. Conclusions

Canadian FN populations experienced differential burden of the pandemic A(H1N1) compared to the general population. However, the reasons for these differential outcomes are not evident. While our analysis indicates that on-reserve (and rural) populations experienced longer time-to-hospitalization post-infection compared to off-reserve (and urban) populations, it is unclear whether the severe health outcomes from influenza are a direct result of limited healthcare access, or if the relationship is confounded by other issues such as a higher prevalence of preexisting comorbidities in remote and underserviced communities. The results, however, suggest that the risk of hospitalization was associated with age, with higher odds of hospitalization for children under 5 years. Furthermore, on-reserve residency was found to be associated with an increased risk of hospitalization, even when controlling for rurality. Our research suggests that severe outcomes (e.g., hospitalization) cannot be attributed entirely to limited healthcare access or underlying medical conditions, at least as measured by proximity to urban healthcare. The findings of this study suggest that geographic location of residence is an important factor in determinants of health and disease outcomes, and rurality should be considered in a broader context to revisit preparedness and mitigation strategies for future planning.

Authors' contributions

SM obtained the data; YX analyzed the data and performed the imputation and time-to-hospitalization analysis, and wrote the relevant sections. KM performed the spatial analysis to define the rurality measure, ran the logistic regression analysis, and wrote the majority of the first draft of the manuscript. DB and SM conceived the study and provided expert subject area knowledge and direction. All authors contributed to the final version of the manuscript and approved it.

Ethics

Data use was approved by the Human Research Ethics Board of the University of Manitoba (H2009:339), and Health Information Privacy Committee of Manitoba (2009/2010-40), Canada.

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