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Original Article

Transmissibility of the 1918 pandemic influenza in Montreal and Winnipeg of Canada

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Background The threat of 2009 pandemic influenza A (H1N1) is still causing widespread public concern. A comprehensive understanding of the epidemiology of 1918 pandemic influenza commonly referred to as the Spanish flu may be helpful in offering insight into control strategies for the new pandemic.

Objective We explore how the preparedness for a pandemic at the community and individual level impacts the spread of the virus by comparing the transmissibility of the 1918 Spanish flu in two Canadian cities: Montreal and Winnipeg, bearing in mind that each pandemic is unique and the current one may not follow the pattern of the 1918 outbreak.

Methods The historical epidemiological data obtained for Montreal and Winnipeg in Canada is analyzed to estimate the basic reproduction number which is the most important summary measure of transmission potential of the pandemic.

Results The transmissibility of the 1918 pandemic influenza virus in Winnipeg in the fall of 1918 was found to be much lower than in Montreal based on the estimated reproduction number obtained assuming different serial intervals which are the time between onsets of symptoms in an index case and a secondary case.

Conclusion The early preparedness and public health control measures could suggest an explanation for the fact that the number of secondary cases generated by a primary case was significantly reduced in Winnipeg comparing to it in Montreal.

Keywords 1918 Spanish flu, 2009 pandemic influenza, public health, transmissibility of flu virus.

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Introduction

The 1918–1919 pandemic influenza, commonly referred to as the 1918 Spanish flu, killed about 50 million people world wide.[10,15,26] There have been many studies of the transmissibility of the 1918 Spanish flu virus. Many analyses have involved fitting transmission models to the observed epidemic curves based on data from cities in Europe or in United States.[2,24,5] The transmissibility of the disease in Canada will be discussed in this article. It was reported that the 1918 pandemic influenza had been brought to Canada by American soldiers in Quebec City.[27] During the period of 3 months from the middle of September to the middle of December of 1918, 19% of troops in Canada were reported to be infected.[11] There were 117 deaths due to the pandemic influenza per 10 000 people for the period of 3 months in various military districts in Canada.[11] It was happened in some military districts that 76 deaths per 100 troops who were infected by the disease.[11] With mortality rate being estimated as 61 deaths per 10 000 people due to the 1918 Spanish flu (all waves) in Canada,[15] about 50 000 Canadians died of the influenza and its complications during the pandemic. It was shown that the Spanish flu spread more or less in three distinct waves during about 12 month period in 1918–1919 simultaneously in Europe, Asia, and United States.[29] A more fatal pandemic influenza wave occurred in Canada in the fall and early winter of 1918–1919. Because influenza was not a nationally reportable disease in Canada in 1918 and diagnostic criteria for influenza and pneumonia were vague, the historical and epidemiologic data which we have obtained are inadequate to identify the first pandemic influenza wave in Canada. The fall wave in Canada began in Quebec City on 9 September 1918 carried by a party of

soldiers coming from different parts of the United States. Among 600 participants, nine soldiers were killed by the disease.[27] The pandemic claimed its first victim of the Ottawa area on 26 September 1918. The people lived near main three stations of railroad were the first to become infected.[3] The influenza virus made its appearance in Montreal in late September 1918.[6] The flu then hit the prairies as the troop trains headed west. Soldiers brought the disease home to their towns, villages and farms. It was in the first week of October 1918, the cases of the pandemic influenza were reported in Winnipeg.[7] The pandemic influenza began to appear in Edmonton around 11 October 1918.[33] One month after the disease appeared in Quebec, Branford, Ontario reported 2500 cases by 9 October 1918.[21] It was seen that the virus transmitted at the same rate as the existing means of intercommunication in 1918 in Canada.

Historical data analysis and non-pharmaceutical interventions

People are concerned about the spread of the novel 2009 pandemic influenza A (H1N1) virus and public policy makers have accelerated their efforts to update the pandemic influenza plan for responding the pandemic. Antiviral prophylaxis and vaccines have been considered most important measures for control outbreaks of the pandemic influenza. However, it is already obvious that pre-seasonal vaccine for 2008/2009 season has no protective effect on disease from the novel influenza A (H1N1) strain among the population.[18] The rapid development of resistance of antiviral drugs and their side-effects become problems in reducing influenza complications and stopping spread of the disease.[20,28] For the 2009 pandemic influenza A (H1N1), it will take time to produce large quantities of the vaccine. Moreover, once vaccine production begins, it will not be possible to make enough new vaccine to protect everyone in the early stages.[30] When there would be a lack of antivirus drugs and effective pandemic vaccine at the outset of the pandemic, people would hope that all the other public health measures which have been employed in past infectious disease epidemics could make a difference. These measures are based on changing individual and community-based behavior to avoid exposure to the infectious agent during the outbreak of the epidemic. These measures often include voluntary quarantine of infected households, closure of schools, bans on public gatherings, and other tools, which are referred as non-pharmaceutical interventions (NPIs).[12] However, people are concerned the efficacy of NPIs in reducing either morbidity or mortality in an influenza pandemic,[13,14,4] because of an absence of systematic studies evaluating public health actions and their impact. Therefore, it is necessary to examine the impact of such interventions in the 1918 pandemic by analyzing the historical data. To understand the impact of non-pharmaceutical interventions and vaccination in the 1918 pandemic influenza, many quantities such as death rate or the rate of increase in the epidemic curve have been used in studies. The mortality rate due to the 1918 pandemic influenza for the first 3 months varied widely among Canadian cities [21] (see Figure 1). Especially, the death rate at the first 3 months in Montreal which was 489 per 100 000 people was much higher than one in Winnipeg which was 211 per 100 000 people.[21] However, it may be better to access epidemic transmissibility by reproduction number, denoted by R, which is the average number of secondary cases generated by a primary infectious case in a given population. The reproduction number is the key epidemiological determinant that characterizes the transmission potential of a disease.[1]

Transmissibility of pandemic influenza in Montreal and Winnipeg

A measure of transmissibility and of the stringency of control measures required to stop an epidemic is determined

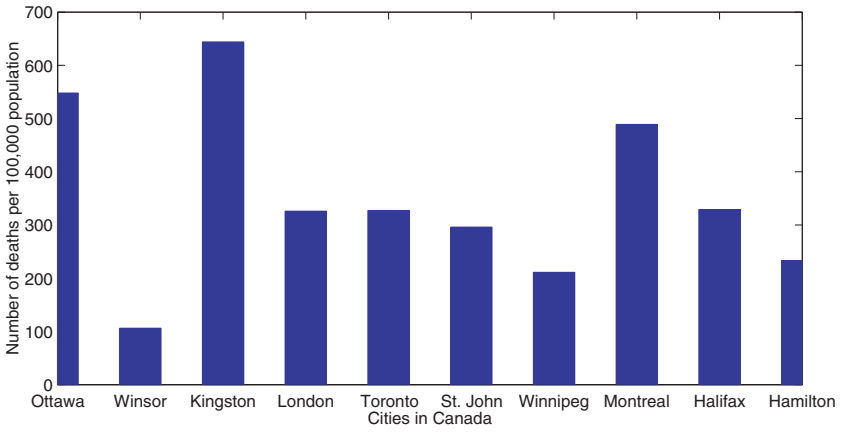

Figure 1. Death rates due to influenza and its complications, chiefly pneumonia from September to December of 1918 Spanish flu in some cities of Canada [21].

by the magnitude of the reproductive number R.[1] Estimates of R for 1918 pandemic influenza vary widely from city to city,[8,22] because R depends on not only the duration of the latent and infectious periods but also the infectious agent and the host population; for example, estimates for measles vary between rural and urban populations.[1] The median estimated R for 1918 Spanish flu in 45 US cities was 2·7 with interquartile range (2·3, 3·4),[22] based on the serial interval of 6 days.[19] The estimation of R could be affected by assumption of the serial interval. There are different results for estimation of the serial interval of human influenza infection. A recent study using a small sample of pairs of infector/infectee estimated a mean of the serial interval 3·6 days with a 95% confidence interval (2·9, 4·3).[9] Also, a serial interval of 5 days was used to estimate the transmissibility of 2009 pandemic influenza A (H1N1).[25] There are few results for estimating R for the 1918 pandemic influenza in any city of Canada. The historical data obtained from the reports [6,7] for the 1918 pandemic influenza in Montreal and Winnipeg are not sufficient to validate a detailed model for the transmission of influenza, because the individual parameters are not available from the data. The time series plots for the data obtained from these reports are shown in Figure 2.

To estimate the reproduction number, the analysis procedures rely on methods with broader model assumptions which can be applied to such data. The R is estimated by a formula based on a deterministic SEIR model fitting by assuming distributions of infectiousness consistent with previous studies and with viral shedding data. [19,31,23] First,

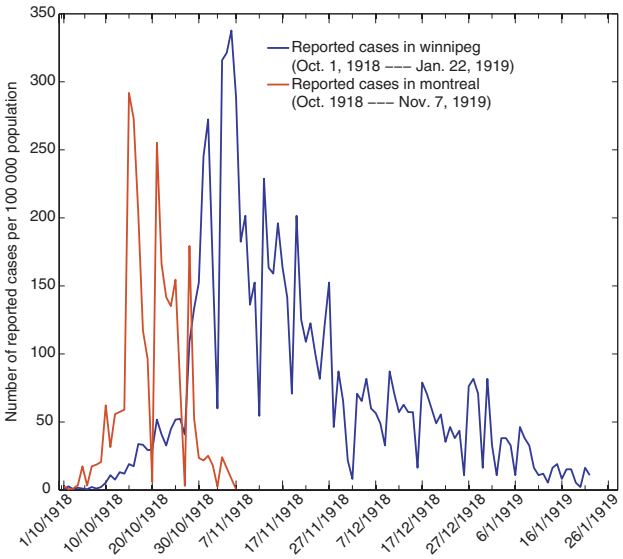

Figure 2. Reported cases of the 1918 Spanish flu in Montreal (Oct. 1–Nov. 7, 1918) (Source: Ref. 6) and Winnipeg (Oct.1 1918–Jan. 22 1919) (Source: Ref. 7).

it has to show that the incident cases increase exponentially in the early phase of the pandemic influenza. In fact, let $y(t)$ be the numbers of reported cases in the tth day during the grow phases of the pandemic influenza. Then, the log $y(t)$ can be modeled as $log\ y(t) = \beta_0 + \beta t + \varepsilon$ where β_0 and β are parameters which can be estimated from the data; the ε has normal distribution with mean 0. It is observed that the reported cases in Montreal had an exponential growth with rate 0·35 in the grow phase of the fall wave of the pandemic influenza. However, the reported cases in Winnipeg grew exponentially with rate 0·14 in the first month of the fall wave of the pandemic influenza. The residual case order plots (the case order error bar plots of 95% confidence intervals on residuals) (see Figures 3 and 4) show the simple model can capture the character of the increase of the number of reported cases during their growth phases of the 1918 pandemic influenza in Winnipeg and Montreal, respectively.

Now, the reproduction number during the early phase of an epidemic can be estimated by the following formula:[31] $1 + \hat{\beta}/\gamma$, where the reciprocal of γ is the serial interval and $\hat{\beta}$ is the estimated exponential growth rate of the incident cases during the early phase of the pandemic. Based on different serial intervals, the estimated effective reproduction numbers R in the initial growth phase of the 1918 Spanish flu in Montreal and Winnipeg are shown in Table 1.

Discussion

It is noted that outcomes appear to have correlated with the quality and timing of the public health response. The contrast of reproduction number between Montreal and Winnipeg is particularly striking: based on a serial interval of 5 days, it was 2·75 (95% CI: [2·32, 3·27]) in Montreal and it was 1·68 with the range 1·58–1·77 in Winnipeg. The 1918 Spanish flu made its appearance in Montreal in September of 1918, but Board of Health for the city composed of physicians for dealing with outbreak of the disease was set up after more than 2 weeks later of the outbreak.[6] The call for "the immediate closing of all places of public meeting, such as schools, theatres, dance halls, moving picture houses, concert halls, etc." was not adopted until 8 October 1918. It was pointed out "at the very beginning of the epidemic, steps had been taken to provide an emergency hospital for influenza patients too poor or friendless to be treated at home or unable to get a place in the general hospitals."[6] In contrast, On 30 September 1918, 23 soldiers suspected of having the "flu" in Winnipeg were quarantined at a military hospital;[16] on 3 October 1918, the Winnipeg health department authorities warned people "keep away from crowds and keep your mouth shut".[17] After the first cases of disease in Winnipeg were reported in the first week of October 1918, authorities moved rapidly to introduce a broad series of measures

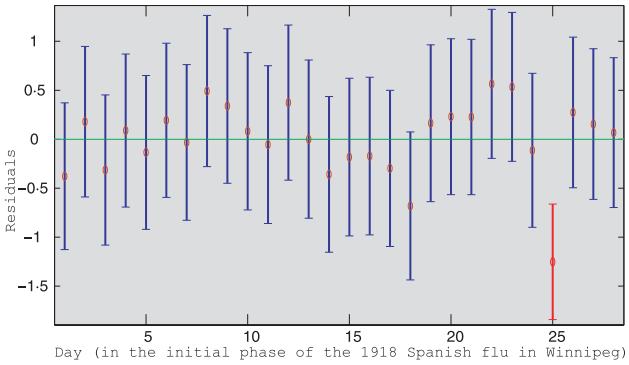

Figure 3. The residual case order plot of estimating growth rate in the initial phase of the 1918 Spanish flu in Winnipeg.

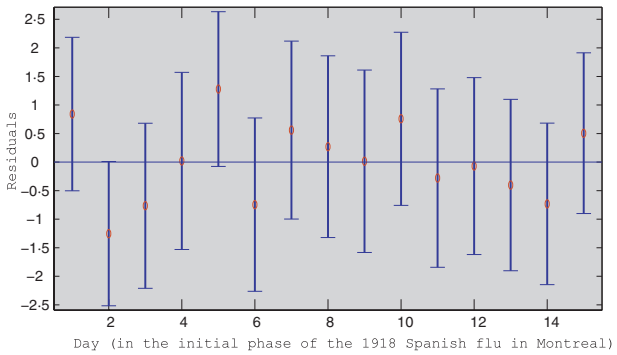

Figure 4. The residual case order plot of estimating growth rate in the initial phase of the 1918 Spanish flu in Montreal.

designed to promote social distancing: quarantine was placed on the army bases following the ban on public gatherings in the city.[7] The ban remained in place for 6 weeks until 27 November 1918.[17] A vaccine prepared from micro-organisms infecting the respiratory tract of those suffering from the disease was to be used as a prophylactic to raise the immunity of those inoculated against respiratory infection in Winnipeg [7,32] It was reported that in a sample of 528 soldiers admitted to a Winnipeg hospital in the 1918 pandemic influenza, no soldier who had taken two doses of the vaccine died.[7] Winnipeg had lower number of secondary cases for a primary case than Montreal during the initial phase of the pandemic, which may be due to the difference in response times and methods between the two cities.

Table 1. Estimated reproduction number and its 95% Confidence interval in the early phase of the 1918 Spanish flu

Serial interval	Montreal		Winnipeg	
5 days	2·75	(2·32, 3·27)	1·68	(1·58, 1·77)
3·6 days	2·26	(1·95,2·63)	1·49	(1·42, 1·55)
6 days	3·10	(2·58,3·72)	1·81	(1·71, 1·93)

The limitation of using historical data is that the number of reported cases may be not accurate. For example, during the 1918 pandemic, many physicians in Montreal sent their reports for Sunday by mail on the following Monday. Therefore, high figures of the Mondays in the data could be partly allotted to the preceding Sunday.[6] The original sources of the data being analyzed in this article could be administrative authority [7] or newspapers.[6] The variances are reflected in the estimation of the growth rate and reproduction number in the initial exponential growth phase of the pandemic. It is seen that the variances of the estimates of the growth rate and reproduction number for Montreal are bigger than ones for Winnipeg. There are several different methods for estimating the reproduction number based on number of reported cases.[8] Also, it is obvious that the assumption about the latent and infectious periods of the 1918 pandemic influenza affect the estimation of the reproduction number.[34] However, it is the fact that the growth rate in the initial phase of the 1918 pandemic influenza in Winnipeg is much smaller than one in Montreal. Therefore, the transmissibility of the 1918 pandemic influenza virus in Winnipeg is lower than one in Montreal whatever the assumption about latent and infectious period could be made, based on our method of estimation. The lower transmissibility of the virus in Winnipeg could lead to the lower mortality rate due to 1918 Spanish influenza pandemic in Winnipeg than in Montreal.[21] The relatively low transmissibility of the 1918 pandemic influenza virus in the Winnipeg may be due to early preparedness and control measures.

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References

1 Anderson RM, May RM. Infectious Diseases of Humans: Dynamics and Control. UK: Oxford University Press, 1991.
2 Andreasen V, Viboud C, Simonsen L. Epidemiologic characterization of the 1918 influenza pandemic summer wave in Copenhagen: implications for pandemic control strategies. J Infect Dis 2008; 197:270–278.
3 Bacic J. The Influenza Epidemic of 1918 in Ottawa. By town Pamphlet Series 63. Ottawa: The historical Society of Ottawa, 1988.
4 Barry JM. Comments on the non-pharmaceutical interventions in New York City and Chicago during the 1918 flu pandemic. J Transl Med 2007; 5:65. doi: 10.1186/1479–5876–5–65.
5 Bootsma MCJ, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. Proc Natl Acad Sci USA 2007; 104:7588–7593.

6 Boucher S. The epidemic of influenza. Can Med Assoc J 1918; 8:1087–1092.

7 Cadham FT. The use of a vaccine in the recent epidemic of influenza. Can Med Assoc J 1919; 9:519–527.

8 Chowell G, Nishiura H, Bettencourt LMA. Comparative estimation of the reproduction number for pandemic influenza from daily case notification data. J R Soc Interface 2007; 4:155–166.

9 Cowling BJ, Fang VJ, Riley S, Leung GM. Estimation of the serial interval of influenza. Epidemiology 2009; 20:344–347.

10 Crosby A. America's Forgotten Pandemic: The Influenza of 1918, 2nd edn. Cambridge: Cambridge Univ. Press, 2003.

11 Editorial. Official report on influenza epidemic, 1918. Can Med Assoc J 1919; 9:351–354.

12 Ferguson NM, Cummings DAT, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. Nature 2006; 442:448–452.

13 Group WW. Nonpharmaceutical interventions for pandemic influenza, national and community measures. Emerg Infect Dis 2006; 12:88–94.

14 Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. Proc Natl Acad Sci USA 2007; 104:7582–7587.

15 Johnson NP, Mueller J. Updating the accounts: global mortality of the 1918–1920 Spanish influenza pandemic. Bull Hist Med 2002; 76:105–115.

16 Jones EW. Co-operation in all human endeavour: quarantine and immigrant disease vectors in the 1918–1919 influenza pandemic in Winnipeg. Can Bull Med Hist 2005; 22:57–82.

17 Jones EW. Influenza 1918: Disease, Death and Struggle in Winnipeg. Toronto: University of Toronto Press, 2007.

18 National Institute of Infectious Diseases, Kobe Institute of Health, Japan. 2009. Interim report on clinical presentation of the novel influenza A (H1N1) cases reported from Kobe City. http://idsc.nih.go.jp/disease/swine influenza e/idsc e2009. Accessed 26 July 2009.

19 Longini IJ, Halloran ME, Nizam A, Yang Y. Containing pandemic influenza with antiviral agents. Am J Epidemiol 2004; 159:623–633.

20 McCaw JM, Wood JG, McCaw CT, McVernon J. Impact of emerging antiviral drug resistance on influenza containment and spread. PLoS ONE 2008; 3:e2362. doi:10.1371/journal.pone.0002362.

21 McCullough JWS. The control of influenza in Ontario. Can Med Assoc J 1918; 8:1084–1086.

22 Mills CE, Robins JM, Lipsitch M. Transmissibility of 1918 pandemic influenza. Nature 2004; 432:904–906.

23 Nicholson K, Webster RG, Hay AJ. Textbook of Influenza. Malden, MA: Blackwell Science, 1998.

24 Nishiura H. Time variations in the transmissibility of pandemic influenza in Prussia, Germany, from 1918–1919. Theor Biol Med Model 2007; 4:20. doi: 10.1186/1742-4682-4-20.

25 Paterson B 2009. Transmission rate of influenza A (H1N1) 2009 infection calculated from a school-based outbreak. Influenza A (H1N1) - worldwide (51): dynamics. Posted on http://www.promedmail.org. Accessed 29 May 2009.

26 Patterson KD, Pyle GF. The geography and mortality of the 1918 influenza pandemic. Bull Hist Med 1991; 65:4–21.

27 Robertson EA. Clinical notes on the influenza epidemic occurring in the Quebec garrison. Can Med Assoc J 1919; 9:155–159.

28 Shun-Shin M, Thompson M, Heneghan C, Perera R, Harnden A, Mant D. Neuraminidase inhibitors for treatment and prophylaxis of influenza in children: systematic review and meta-analysis of randomised controlled trials. BMJ 2009; 339:b3172.

29 Taubenberger JK, Morens DM. 1918 influenza: the mother of all pandemics. Emerg Infect Dis 2006; 12:15–22.

30 US Government. 2009. Guidance on allocating and targeting pandemic influenza vaccine. http://www.flu.gov/individualfamily/vaccination/allocationguidance.pdf (Accessed 18 Nov 2009).

31 Wearing HJ, Rhani P, Keeling MJ. Appropriate models for the management of infectious diseases. PLoS Med 2005; 2:23–41.

32 Wetmore FH. Treatment of influenza. Can Med Assoc J 1919; 9:1075–1080.

33 Whitelaw TH. The practical aspects of quarantine for influenza. Can Med Assoc J 1919; 9:1070–1074.

34 Yan P. Separate roles of the latent and infectious periods in shaping the relation between the basic reproduction number and the intrinsic growth rate of infectious disease outbreaks. J Theor Biol 2008; 251:238–252.