National Collaborating Centre for Infectious Diseases

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Purple Paper

Optimal Treatment Strategies for Remote and Isolated Communities

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1. Introduction

This report summarizes the outcomes of a research project on "Optimal Treatment Strategies for Remote and Isolated Communities" to mitigate the impact of novel influenza viruses with pandemic potential. Mathematical modelling, simulations, and statistical analysis were used to conduct this research. Model recommendations for effective use of antiviral drugs in terms of both treatment and prophylaxis are provided.

2. Background

Early outbreaks of the 2009 H1N1 influenza pandemic displayed variable degrees of incidence, with higher transmissibility and more severe disease outcomes (e.g., hospitalization and ICU admission) in several remote and isolated communities in Canada (1,2,3,4,5). The mechanisms underlying the differential incidence and outcomes in these Canadian communities are not well identified, but could be related to the effectiveness of available disease control programs (e.g., antiviral treatment), environmental factors including the prevalence of low-quality housing and crowded living conditions (6), exposure to indoor air pollutants, lack of access to critical infrastructure, and the prevalence of predisposing health conditions and co-morbidity.

Evidence is accumulating for the correlation between the speed with which antiviral treatment is initiated after the onset of clinical symptoms and the degree of disease severity and outcomes in critically ill patients of influenza (4,5). In the spring wave of the 2009 pandemic, Canada's northern Aboriginal communities were disproportionately affected, with severe outcomes often necessitating hospitalization and ICU admission (3,4,5). Previous analysis of the age-distribution of the 2009 H1N1 cases in the province of Manitoba, Canada, indicates significantly higher rates of infection and hospitalization amongst First Nations compared to non-First Nations populations. These rates were as much as 12 times (for infection) and 22 times (for hospitalization) higher in First Nations young children, aged 0-4, compared to the same age group in non-First Nations populations (3). Our research on the effect of antiviral treatment indicates that early initiation of antiviral treatment is more critical for lowering the overall attack rate (i.e., the cumulative incidence of clinical infection with symptoms during the entire course of the outbreak) in a remote setting with a low population-average age compared to an urban population.

3. New Evidence and Models

Our research evaluated cumulative and relative age-specific attack rates in the populations. We considered four main age groups in the demographics of a remote community simulated in our research. These include pre-school children (0 to 5 years of age); school-aged children (6 to 18 years of age); adults (19 to 49 years of age); and older adults (50+ years of age). Simulation results indicate that school-aged children have considerably higher attack rates in all the simulated scenarios regardless of how early clinical patients are treated (after the onset of symptoms). The older adults' age group has the lowest attack rates in all scenarios. We observed that increasing the treatment coverage (the fraction of patients receiving treatment) has a marginal effect on reducing cumulative age-specific attack rates (the ratio of infections in the specific age group to the total number of infections) for the older adults age group, but the delay in start of treatment has virtually no impact on the magnitude of this reduction. However, increasing the treatment coverage can have a relatively modest effect on reducing cumulative attack rates in other age groups, especially in adults.

Comparing the simulated scenarios with similar strategies in an urban population, we observed that the lowest attack rates are associated with the pre-school children, while the attack rates for the group aged 50 years and older remain in the same range

as in a remote population. Importantly, in contrast to the remote community, the attack rate for adults is higher than for school-aged children at relatively low treatment levels. However, at high treatment levels in an urban population, these rates decrease and become lesser than or equal to those for school-aged children. Overall, the reduction in age-specific attack rates is comparable in the corresponding scenarios for both remote communities and urban populations.

When considering the relative attack rates (the fraction of infected individuals in each age group) for all the scenarios discussed above, we found that the highest attack rates occur in the school-aged children in both remote and urban populations.

We considered the impact of targeted antiviral prophylaxis of close contacts (post-exposure prophylaxis). For conservative treatment levels in the range of 10% to 40%, our results indicate that targeted prophylaxis of close contacts has little impact on reducing overall and age-specific attack rates. This range of treatment level (10% - 40%) is highly plausible and may result from several factors, including diagnosis uncertainties for influenza cases, treatment guidelines for use of antiviral drugs, familiarity with antiviral agents, access to drug stockpiles, or knowledge of the potential severity and outcomes of infection (6,7).

4. Implications for Public Health

Our findings show that maintaining a significant public health response that focuses on following up close contacts of index cases for the provision of antiviral prophylaxis in the community leads to a large drug wastage. Prophylaxis strategy at the community level (regardless of the size of community) contributes to a significant workload in an already overburdened healthcare system during an outbreak. Within an antiviral strategy, early treatment of index cases (clinically ill patients) is significantly more crucial to the effectiveness of drugs than targeted prophylaxis. Within plausible ranges of antiviral treatment, our findings do not provide any convincing evidence for the implementation of community-wide targeted prophylaxis of close contacts.

Evidence suggests that delay in start of treatment is strongly correlated with the degree of severe outcomes. Our results show a significant delay in start of treatment after the onset of symptoms for treated cases of H1N1 in several remote communities (e.g., the Burntwood health region in northern Manitoba), with an average of 3.5 days delay for treatment initiation post symptoms onset. While we observed a similar delay in start of treatment for an urban population (e.g., the Winnipeg health region), the differential outcomes of infection in remote communities attest to the fact that other factors may influence rates of disease burden, including health disparities and the prevalence of co-morbid and immuno-compromised conditions.

5. Conclusion

Model outcome: Wider availability (higher coverage) and timely distribution of antiviral drugs for treatment of clinically ill individuals is a key to reducing the illness burden in remote communities. Drug wastage could be significantly high for a prophylaxis strategy.

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