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Full Length Research Paper

A cost effectiveness analysis of the H1N1 vaccine strategy for Ontario, Canada

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In Ontario, Canada, a mass vaccination strategy was developed and implemented to mitigate the effects of the 2009 pandemic influenza A (pH1N1). This study investigated its cost-effectiveness, mirroring actual events in Ontario, compared to no vaccine strategy. From a societal perspective, 1,780,491 cases and 154 deaths were averted through vaccine administration; the incremental cost effectiveness ratio predicted that the vaccination program saved $117 per case avoided, or $1.35 million per death averted, for total savings of $208.3 million. From a government perspective (Ontario Ministry of Health and Long Term Care) this strategy required an expenditure of $28 per case averted and $0.33 million per death averted, for a total cost of $252.4 million.

Key words: Cost effectiveness, H1N1, Ontario, pandemic influenza, vaccine

INTRODUCTION

On June 11, 2009, the World Health Organization (WHO) declared phase six influenza pandemic: Pandemic (H1N1) 2009 (pH1N1) was underway (World Health Organization (WHO, 2009). While some infections were severe and thousands resulted in death, pH1N1 was often associated with mild or subclinical symptoms. Characterized by a positively skewed distribution, most cases of pH1N1 occurred in populations below 25 years (Ministry of Health and Long Term care [MOHLTC], 2010a).

Vaccination is the principal strategy to reduce the transmission of influenza and to prevent or attenuate illness severity (Medlock et al., 2009). The Canadian government's pandemic influenza emergency plan included the purchase of 50.4 million doses of vaccine -- more than required for the Canadian population of roughly 33.2 million (one vaccine dose was required per person).

Due to the limited availability of vaccine at the outset of the outbreak, and the inability to vaccinate the entire population simultaneously, the Public Health Agency of Canada (PHAC) (PHAC, 2009a) developed a sequencing strategy that identified priority groups – patients at high risk to transmit the virus or for severe reactions. Decisions about vaccine distribution were further complicated by the varied demographic characteristics of the large Ontario population (13 million) (Khazeni et al., 2009).

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Abbreviations: CDC, Centers for Disease Control; C_{GV}, provincial government costs for vaccine scenario; $\mathbf{C_{GNV}}$, provincial government costs for scenario with no vaccine; $\mathbf{C_{SV}}$, societal costs for vaccine scenario; $\mathbf{C_{SNV}}$, societal costs for scenario with no vaccine; **ED**, emergency department; **GBS**, Guillain-Barré Syndrome; **ICER,** incremental cost effectiveness ratio; ICU, intensive care unit; **ILI**, influenza like illness; **MOHLTC**, Ministry of Health and Long-term Care; **OCCI,** Ontario Case Costing Initiative; **PCP**, primary care practitioner; **PHAC**, Public Health Agency of Canada; **pH1N1**, Pandemic **H1N1**; **SA**, sensitivity analysis; **WHO**, World Health Organization; **HCR**: health care resources.

Following the pandemic, public attention has focused on the cost effectiveness of the implemented mitigation strategy. The present study estimated the cost effectiveness of:

(1) Having no vaccination available, versus
(2) Vaccinating 65% of priority groups over the first three weeks followed by vaccination of 25% of the general population.

The cost effectiveness was assessed from both a societal and governmental perspective; specifically, the perspective of the Ontario Ministry of Health and Long-Term Care (MOHLTC). Accordingly this economic evaluation will have public health implications for the general population, and policy makers in Ontario and similar populations.

METHODS

This study assessed the course of pH1N1 and the associated cost-effectiveness of the Ontario vaccination strategy from societal and MOHLTC perspectives using a life-time time horizon. Present analyses adopted the provincial government perspective (that is, MOHLTC) because of their jurisdiction over healthcare delivery in Canada; accordingly, each province is responsible for developing and carrying out a mitigation strategy.

Simulations involving a cohort of individuals with demographic characteristics of the Ontario population exposed to an outbreak of pH1N1 from June 11, 2009 to June 10, 2010 were used to generate the expected number of cases and deaths. Outcomes were defined as the number of cases and deaths averted. These outcomes were used to establish incremental cost effectiveness ratios (ICERs). A 5% discount rate was used in accordance with Canadian Coordinating Office for Health Technology Assessment (1997) guidelines. Microsoft Excel (Microsoft, Redmond, WA) and TreeAge Pro (TreeAge, Williamstown, MA) software were used. A one-way sensitivity analysis was conducted in order to test the stability of the study results, and to identify the main cost-driving parameters.

Scenarios and simulation model

Two scenarios of possible responses to a pH1N1 outbreak in Ontario were modeled. In the first (baseline) scenario, no vaccines were available. The second scenario involved a three-stage vaccination effort. During the first stage (June 11, 2009 to October 25, 2009), there was no vaccine available in Ontario. The second stage involved the vaccination for 65% of individuals in priority groups, over a 21-day period (October 26, 2009 to November 15, 2009) (Kumar et al., 2009). The third stage (November 16, 2009 to December 31, 2009) involved immunization of the rest of the population, with a vaccine uptake rate of 25%. Reported results are based on a simulation that mimicked events for one-year June 11, 2009 to June 10, 2010. This total population rate (38%) was consistent with the reported overall population uptake rate in Ontario (King, 2010). Priority groups included: people under 65 with chronic health conditions (asthma or diabetes only); pregnant women; children aged six months to five years of age; and health care workers ($n_{priority}$ =3.4 million). The age distribution of priority groups was determined from statistics Canada.

The model used was a non-homogeneous agent-based simulation model that incorporates behavioral patterns that mirror real-life events (Aleman et al., 2009a, b). A compartmental model (S-I-R, Susceptible-Infectious-Removed) generated the expected number of cases and deaths for each of the two scenarios. For more model details, (Appendix A). Vaccine efficacy in this model was determined from a clinical trial (Health Canada, 2009) for an adjuvanted vaccine with the same antigen contents as the Canadian vaccine. The initial number of cases was based on the number of cases documented in Ontario on June 11, 2009 ($n_{initial}$ = 2,206) (Frenzen, 2008) To account for subclinical infections, this number of cases was divided by 0.30 (the average percentage of symptomatic cases that seek medical care for influenza like illness [ILI]; (Appendix B) for terminology definitions). Accordingly, the total initial number of cases in the model was 7,317.

Parameters and cost component

This study assessed costs related to health care use for influenza like illness (ILI) including primary care use, prescription sales, laboratory testing, emergency department (ED) visits, and hospitalization (Table 1). Additional costs are described below including lost productivity, vaccination, and side effects related to vaccination.

The prescription sales assessed include antiviral medications (Tamiflu® (oseltamivir) and Relenza® (zanamivir)). Only costs related to the treatment of symptoms were included in accordance with the treatment guidelines in this flu season (MOHLTC, 2009a). The rate of medication use was inferred from previous influenza season (2008 to 2009), but was likely underestimated due to the high treatment proportion in this pandemic. Drug mark-up costs were not included because it was unknown if mark-up fees were paid for the government stock pile. Given that the economic perspective adopted in this study was that of the provincial government, only 40% of the total prescription costs were included in these analyses because they were paid for by the provincial government. The remaining 60% of the prescription costs were paid by the federal government, and accordingly were not included in the present analysis (MOHLTC, 2010b, 2009b).

The human capital approach was used to determine lost productivity due to premature mortality and morbidity related to pH1N1. Age and sex specific estimates were used for average wages, labour force participation rates and average life expectancy (Statistics Canada, 2009b, c). Lost productivity calculations included caregiver costs for infected adolescents who were 15 years or younger (Table 2). The proportion of cases that required parents to miss work, the mean duration of work missed by caregivers, and the average time of work missed by adults due to illness were estimated from Canadian influenza studies (Hibbert et al., 2006). The average lost productivity time for vaccine administration was two hours per person, assuming one hour of wait time and one hour of transportation.

The per capita vaccine cost (excluding administration costs) was $7.93 per dose, given that the federal government paid $403 million for 50.4 million doses (MOHLTC, 2010b). The cost of the vaccine was calculated from the number of doses used in this study with an additional 1% allocated to wasted doses. The combined cost to purchase and deliver the vaccine in Canada was used to estimate the per person cost of vaccine administration at $22.07. This value was calculated using the per-person cost of vaccine purchase and administration ($30.00) subtracted by per capita vaccine cost ($7.93). Cost estimates from the MOHLTC perspective were reduced because the Canadian federal government paid for 60% of the vaccine, amounting to $241.8 million.

Mild or moderate side effects may require over-the-counter medications such as ibuprofen or acetaminophen to alleviate symptoms such as pain or fever. These medications were available at the vaccination clinics, and hence were included in administration costs. Two severe side effects associated with seasonal influenza vaccines were included in the present study: Guillain-Barré Syndrome (GBS) and anaphylactic reactions. An Ontario study estimated the risk of GBS, in the period after seasonal influenza

Table 1. Determination of quantity and cost for health care resources due to influenza like illnesses.

Health care item	Quantity and cost derivation
Primary care visits	**Quantity:** The rate of consultations for influenza- like-illness (ILI) by primary care practitioners was determined from Ontario and British studies (Sander et al., 2009) that estimated the number of PCP visits attributable to each case during influenza pandemics (Sander et al., 2009). **Cost:** The unit cost of each visit to a PCP for ILI was based on a Canadian study on immunization of seasonal influenza and an Ontario study on the pH1N1 vaccine (Sander et al., 2009)
Prescription sales	**Quantity:** Surveillance of antiviral pharmacy sales in Ontario from June 2009 until September 2009 was used to determine the percentage of antiviral medications sold that were child doses and adult doses as well as the ratio of Tamiflu® to Relenza® sales. Centre for Disease Control (CDC) guidelines dictate that in most cases, antiviral medications should be used within two days after symptom onset (Centre for Disease Control [CDC], 2009). To estimate antiviral medication use, we multiplied the likelihood that a person would present to a PCP within two days of symptom onset by the probability that these persons would be prescribed antiviral medication. **Cost:** The cost of both adult and child doses of Tamiflu® and the cost of Relenza® were estimated based on list prices from a commercial pharmacy pricing database (Distribution Logistic Services, 2009). The average dispensing fee for pharmacies in Ontario in 2010 was used.
Laboratory testing	**Quantity:** To estimate the number of lab tests, the total number of symptomatic cases was multiplied by the probability of presenting to a health care provider. **Cost:** Costs for laboratory testing were determined from a study on testing influenza samples in a Canadian laboratory (Church et al., 2002). Costs associated with non-symptomatic individuals who wanted to be tested were not included in the analysis.
ED visits	**Quantity:** ED rates were determined from a Canadian study (MOHLTC, 2009b) on excess health care use during peak influenza seasons. The relationship between hospitalization and ED rates was used to calculate excess ED rates based on observed pH1N1 hospitalization rates in Ontario. **Cost :** Cost of visiting the ED was from Canadian studies (Sander et al., 2009; Skowronski et al., 2006).
Hospitalizations	**Quantity:** The probability of hospitalization for pH1N1 was determined from the combined probability of factors leading to hospitalization. These factors include the probability that an individual would be symptomatic (MOHLTC, 2010) that s/he would visit a PCP and/or ED, and the likelihood that that individual would require inpatient hospitalization following hospital visit (MOHLTC, 2010a) (Figure 1). The presumed duration of infectiousness was taken from the MOHLTC clinical guidelines (MOHLTC, 2009d). **Cost:** The cost of these precautions was determined from a study that assessed costs associated with SARS at a Toronto hospital (Achonu et al., 2005). Hospital staff who interact with infected persons adopt additional pandemic control strategies which include the purchase of infection control supplies including gowns, gloves, N95 respirators, and goggles. Given that the rates of severe reactions to pH1N1 were lower and there were fewer hospital precautions than SARS a conservative estimate of one tenth of the SARS cost was used in the analysis. This was because SARS was transmitted predominantly in the health care settings, with a case fatality rate greater than 10%. Accordingly, SARS was amenable to individual-based control measures. In contrast, influenza viruses are characterized by shorter incubation periods, pre-clinical virus shedding and peak infectiousness shortly after illness onset (Longini et al., 2009) the 2009 pH1N1 contributed to a larger proportion of mild infections and a lower case fatality than SARS. Therefore, it required less costly in-hospital mitigation measures (Pourbohloul et al., 2009).
ICU	**Quantity:** Ontario surveillance data indicate that 20% of hospitalizations require an average of 10 days of ICU care. The remaining 80% require an average of six days of non-ICU (medical ward) hospitalized care (Khazeni et al., 2009; MOHLTC, 2010a) . Of hospitalized pH1N1 cases in Ontario 10.3% require mechanical ventilation. **Cost:** The costs of stays in an intensive care unit (ICU) and in a hospital medical ward for respiratory illness were determined from the Ontario Case Costing Initiative (OCCI) (Health Data Branch and Long Term Care, 2009).

Table 2. Parameters and data source.

Variable	Baseline	Source
Population (n)	13,077,256	Statistics Canada (2009a)
Population age range (years)	0 - 100	Statistics Canada (2009a)
Labour force participation rates (% average, M / F)		
15 to 24	67.8 / 67	Statistics Canada (2009b)
25 to 44	92.4 / 82.1	Statistics Canada (2009b)
45 to 64	81.6 / 72.2	Statistics Canada (2009b)
65 years and over	14.2 / 6.8	Statistics Canada (2009b)
Probability of symptomatic infection (%)	67	Khazeni et al. (2009)
Probability of using health care resources if symptomatic (%)	45.6	Rust et al.(2008)
Probability of visiting PCP if symptomatic (%)	28	Skowronski et al.(2006)
Probability of visiting ER if symptomatic (%)	0.5	Hibbert et al. (2007)
Average time missed from work for symptomatic adults (no hospitalization, (%)	4	Skowronski et al. (2006)
Proportion of infected children (0-15 years of age) requiring a parent to miss work (%)	61.4	Sandler et al. (2009)
Mean duration of work missed by caregivers (days)	3.2	Skowronski et al. (2006)
Probability of patient being prescribed antiviral (%)	9.5	Muennig et al. (2001)
Proportion of symptomatic patients that require inpatient care (%)	3.3	Khazeni et al. (2009)
Proportion of hospitalized patient admitted to a medical ward (%)	80	OAHPP (2009)
Mean duration of ICU stay (days)	10	OAHPP (2009)
Proportion of hospitalized patients requiring ICU care (no ventilation, %)	10.3	Khazeni et al. (2009)
Mean duration of ICU stays (days)	10	OAHPP (2009)
Proportion of hospitalized patients requiring mechanical ventilation (%)	10.3	Khazeni et al. (2009)
Case fatality (%)	0.01	Brouwer et al. (2009)
Susceptible to re-infection after recovery (%)	0	Health Canada (2009)
Vaccinated for high risk group (%)	60	user specified
Vaccinated for general population (%)	30.21	user specified
Adjuvanted vaccine effectiveness (%)	90	Health Canada (2009)
Time to develop immunity (days)	20	Health Canada (2009)
Probability of developing Guillain-Barre Syndrome	0.0001	PHAC (2009a)
Probability of developing anaphylactic reaction	0.00004	Hibbert et al. (2006)
Probability of death	0	PHAC (2009a)
Average time missed from work due to vaccine administration (hours)	1	Crowcroft (2009)

vaccination, as one case per one million vaccinations (Juurlink et al., 2006) GBS lifetime treatment costs exceed $318,966 (Frenzen, 2008). Second, an anaphylactic reaction is associated with a treatment cost of $3,489 (Prosser et al., 2006).

RESULTS

Population demographics similar to the Ontario population were accounted for by the simulation model. A total of 13,060,000 individuals (53% female) with an age range of zero to 100 years were assumed (Statistics Canada, 2009a). High priority groups represented roughly 26.15% of the study population (Table 2). The total number of persons vaccinated was 5,230,902 (40.01%). Possible outcomes and associated probabilities for individuals exposed to pH1N1 are presented in Figures 1 and 2 in addition to costing data in Table 3. In comparison to the no vaccine scenario, the vaccine strategy avoided 1,780,491 cases of pH1N1, 89 male deaths, and 65 female deaths (Table 4). From a societal perspective, the total cost associated with the no vaccine scenario was $1.10 billion while the cost of the vaccine program was $888.18 million (Table 5). Consequently, the vaccine program ICERs were negative indicating cost savings ($117.01 saved for each case averted; approximately $1.35 million saved for each death averted). In contrast, from a MOHLTC perspective, the total cost of the no vaccine scenario was $201.2 million, while the cost of the vaccine program was $252.4 million. These ICERs were positive, indicating that the vaccine program was not cost saving (that is, the MOHLTC spent $28.78 for each case averted and $0.33 million for each death averted). The positive ICERs indicate that the vaccine program scenario cost more but provided greater health benefit (that is, prevented cases and deaths) compared to the no vaccine scenario, from the MOHLTC perspective.

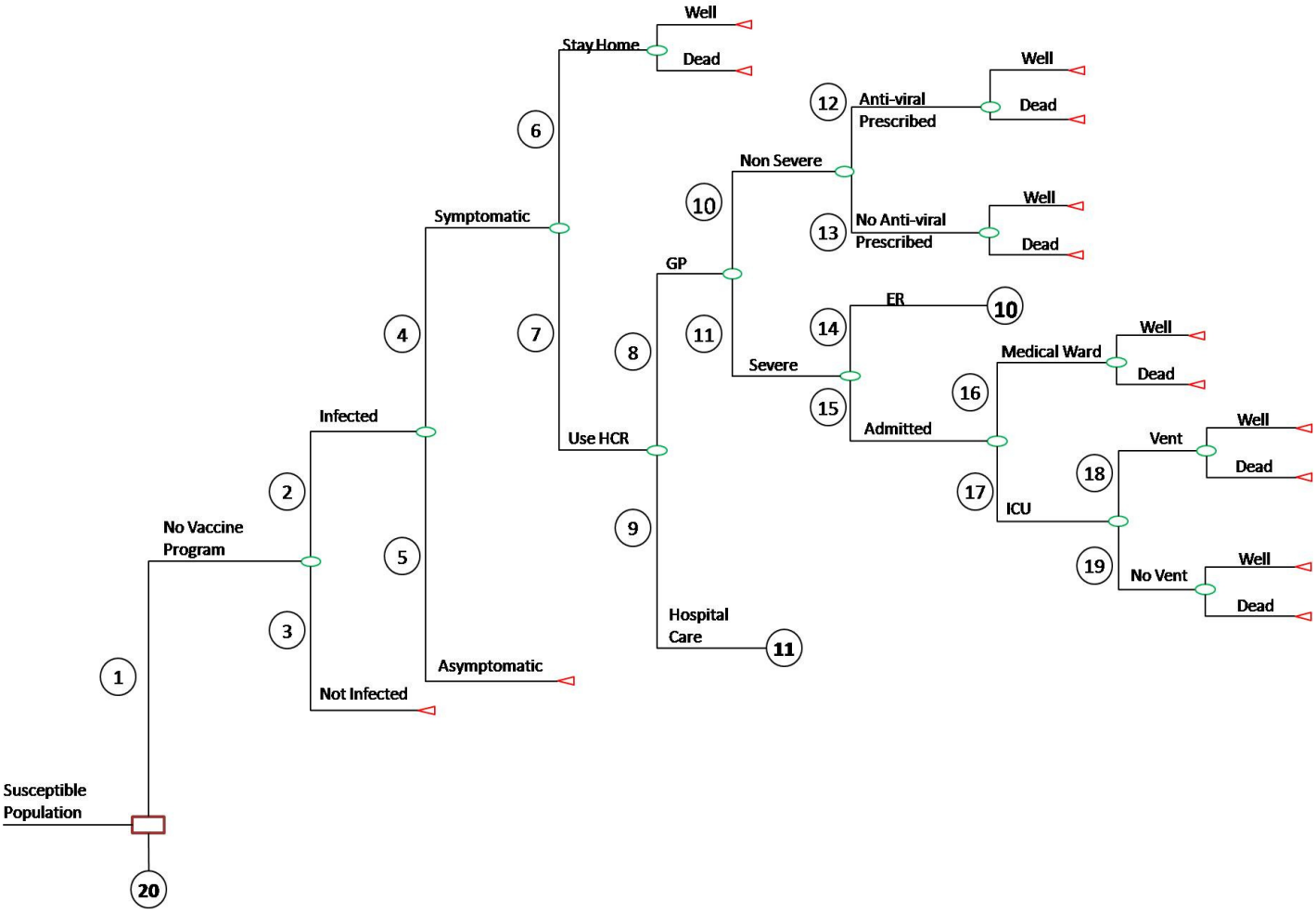

Figure 1. Probable events for susceptible population, no-vaccine strategy.

From a societal perspective, vaccine purchase, administration, and health care use represented the largest proportions of direct costs. Among healthcare costs, ICU admissions were the largest component despite the relatively low number of admissions. The main costs averted in the vaccine scenario compared to no vaccine were lost workdays and deaths avoided, which in aggregate amounted to over $373 million (42% of the total society savings). Large costs incurred in the vaccine scenario were attributable to vaccine administration and vaccine promotion, which totaled over $152 million (17% of the total cost of the vaccine program).

The following parameters were identified as the main cost drivers from both societal and governmental perspectives: Vaccine purchase and administration in the vaccine scenario, and PCP visits and hospitalization costs in both scenarios.

The government perspective did not account for costs associated with lost workdays for deceased and non-deceased persons. Accordingly, the vaccine strategy ICERs for cases averted and for deaths averted represented the expenditure of costs rather than cost savings.

The parameters subject to the sensitivity analysis included: probability of infection, vaccine cost, vaccine administration costs, patient wait time for vaccine administration, and discount rate. One-way sensitivity analyses identified vaccine cost and patient wait time as influential cost components, which was consistent with other cost-effectiveness studies of seasonal influenza vaccine strategies or pH1N1 vaccine programs (Nichol et al., 1995). When the vaccine purchase cost was increased from $7.93 per vaccine, that is, reflecting only those vaccines actually administered, to the total cost for all 19.4 million doses, the unit cost per vaccine increased 38.3 times to $39.30. From a societal perspective, this increase in cost per vaccine did not reverse the estimated cost saving attributable to the vaccine program. Excluding the ICER derived for an increase in patient waiting time (waiting

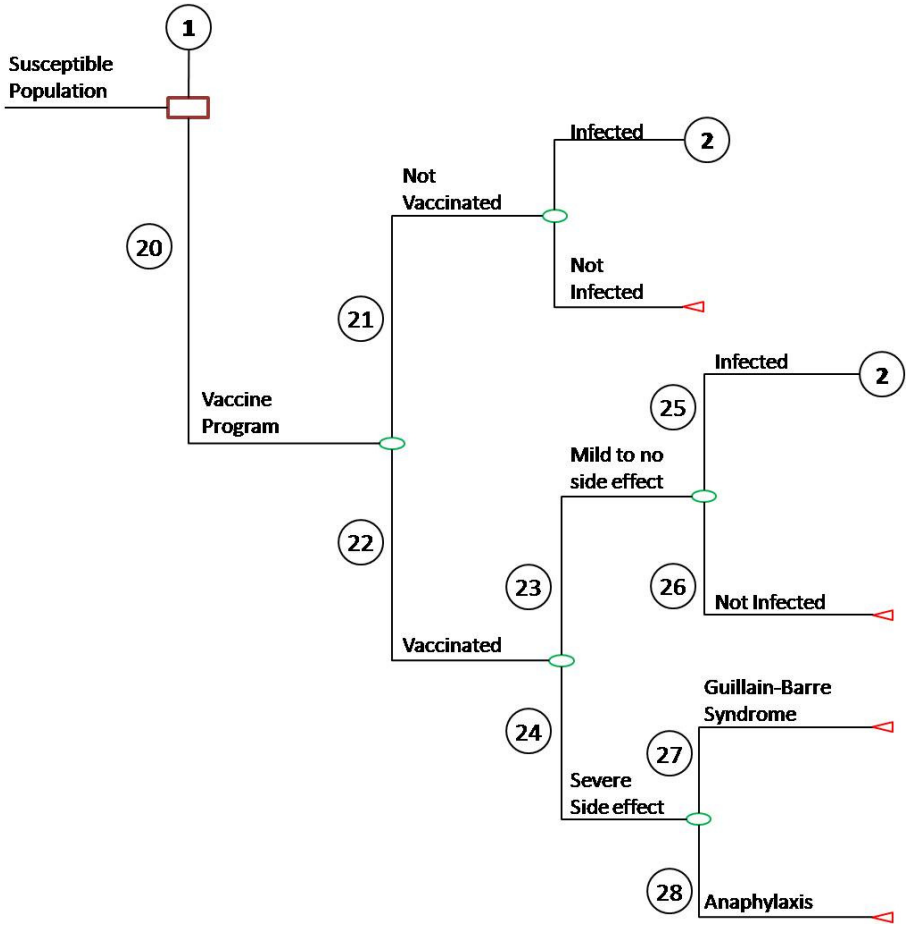

Figure 2. Probable events for susceptible population, vaccine strategy.

Table 3. Costs components

Item		Value	Source
HCR use ($/patient)	ED visit	220.00	Menec et al. (2003)
	Hospitalized non-ICU	4265.00	Ministry of Health (2008)
	ICU no mech. ventilator	32,344.00	Ministry of Health (2008)
	ICU with mech. ventilator	63,518.00	Ministry of Health (2008)
	PCP Visits	34.00	Skowronski et al. (2006)
	Lab Testing	26.00	Church et al. (2002)
Average wage, age group ($/hr)	15 to 24	13.00	Government of Canada (2009)
	25 to 44	25.00	Government of Canada (2009)
	45 to 64	24.00	Government of Canada (2009)
Vaccine cost ($)	Per dose (incl. administration)	30.00	Derived
	Promotion	2,600,000.00	Erie St Clair LHIN (2009
Prescription ($/patient)	Relenza®	49.54	Distribution Logistics Services(2006)
	Tamiflu® adult	49.50	Distribution Logistics Services(2006)
	Tamiflu® children	52.30	Distribution Logistics Services(2006)
Side effect treatment ($/patient)	Treatment for GBS	318,966.00	Hibbert et al. (2007)
	Anaphylaxis treatment	3,489.00	Prosser et al. (2006)

Table 4. Baseline results showing total number for each parameter and the difference between the two strategies in nominal number and in percentage. Differences were obtained by subtracting vaccine strategy results from the no-vaccine strategy results. Positive differences indicate there was greater cost in the no-vaccine scenario.

Parameter	Vaccine strategy	No vaccine strategy	Difference
Cases	2,598,704	4,379,195	1,780,491
Lab tests (n)	39,766	67,012	27,246
Prescriptions for Tamiflu®, child	58,646	98,827	40,181
Prescriptions for Tamiflu®, adult	19,549	32,942	13,394
Prescriptions for Relenza®	1,201	2,024	823
PCP visits	778,077	1,311,173	533,096
ED visits	14,314	24,122	9,807
Hospitalizations (non ICU)	5,206	8,773	3,567
ICU patients (without mechanical ventilator)	1,066	1,797	731
ICU patients (with mechanical ventilator)	129	218	89
Male deaths	110	200	90
Female deaths	80	144	64
Lost workdays	2,046,648	3,448,900	1,402,252
GBS cases	5	0	-5
Anaphylactic reactions	2	0	-2

Table 5. Cost analysis from both societal and governmental perspectives. The numbers in brackets and red mean the cost incurred by vaccine strategy is larger than the cost incurred by no-vaccine strategy. The bracketed red ICERs indicate money being spent to avert one case of infection or death.

Cost component	Costs from societal perspective			Costs from governmental perspective		
	Vaccine Csv*	No vaccine Csnv†	Difference Csnv – Csv	Vaccine Cgv‡	No vaccine Cgnv§	Difference Cgnv – Cgv
Lab tests	6,640,538.12	11,190,274.59	(4,549,736.47)	6,640,538.12	11,190,274.59	(4,549,736.47)
Tamiflu®, child	3.067,174.67	5,168,636.35	(2,101,461.69)	3,067,174.67	5,168,636.35	(2,101,461.69)
Tamiflu®, adult	967,655.49	1,630,640.53	(662.985.04)	967,655.49	1,630,640.53	(662.985.04)
Relenza®	59,496.51	100,260.30	(40,763.78)	59,496.51	100,260.30	(40,763.78)
PCP visits	26,088,919.30	43,963,631.47	(17,874,712.17)	26,088,919.30	43,963,631.47	(17,874,712.17)
ED visits	3,149,131.38	5,306,745.36	(2,157,613.98)	3,149,131.38	5,306,745.36	(2,157,613.98)
Hospitalizations (non ICU)	22,203,461.17	37,416,068.22	(15,212,607.05)	22,203,461.17	37,416,068.22	(15,212,607.05)
ICU (no ventilator)	34,487,856.38	58,117,064.59	(23,629,208.21)	34,487,856.38	58,117,064.59	(23,629,208.21)
ICU (with ventilator)	8,207,059.59	13,830,091,59	(5,623,032.00)	8,207,059.59	13,830,091,59	(5,623,032.00)
Fixed hospital costs	14,517,867.39	24,464,722.52	(9,946,855.13)	14,517,867.39	24,464,722.52	(9,946,855.13)
Deaths	105,025,247.62	190,150,974.64	(85,125,727.02)	-	-	-
Lost workdays	418,468,383.90	705,180,218.46	(286,711,834.56)	-	-	-
Vaccine purchase	40,693,873.76	-	40,693,873.76	16,277,549.50	-	16,277,549.50
Vaccine administration	112,559,693.42	-	112,559,693.42	112,559,693.42	-	112,559,693.42
Vaccine promotion	2,600,000	-	2,600,000	2,600,000	-	2,600,000
Person time lost	87,845,505.52	-	87,845,505.52	-	-	-
GBS	1,594,830.00	-	1,594,830.00	1,594,830.00	-	1,594,830.00
Anaphylactic reactions	6,978.00	-	6,978.00	6,978.00	-	6,978.00
Total	888,183,672.22	1,096,519,328.63	(208,335,656.41)	252,428,210.93	201.188.135.52	51,240,075.41
ICER ($/case averted)			(117.01)			28.78
ICER ($/death averted)			(1,352,828.94)			332,727.76

*CSV – Societal costs for vaccine scenario.† CSNV – Societal costs for scenario with no vaccine.‡ CGV – Provincial government costs for vaccine scenario.§ CGNV – Provincial government costs for scenario with no vaccine.

increased from the baseline of 1 h to 4 h) all ICERs calculated in the sensitivity analysis were cost saving from a societal point of view. The ICERs calculated using a waiting time of four hours were $31.00 spent per case averted (considerably higher than the baseline estimate of $117.01 saved per case averted) and $358,447.14 spent per death prevented (again higher than the baseline $1,352,828.94 saved per death prevented).

DISCUSSION

This paper examined the cost effectiveness of the vaccination strategy developed to mitigate the burden of the pH1N1 outbreak in Ontario, Canada. This study suggested that vaccinating 30.21% of the general population and 60% of priority group members could avert a large number of deaths, illnesses, and use of health care resources. This study is distinguished from similar studies because the events in the vaccine scenario mirror the real course of events in Ontario, namely that priority group members received the vaccine earlier and had higher vaccine uptake percentages than the general population. External validity may be limited to areas where the population differs substantially from the Ontario population in terms of demographic characteristic and geographic dispersion.

Chief model limitations are the limited availability of data on the disease and the population. The study finding is that the pH1N1 vaccine is cost effective from a societal viewpoint which is consistent with findings of Canadian (Sander et al., 2009) and American studies (Khazeni et al., 2009). From a governmental perspective the economic benefit is difficult to estimate due to limited knowledge surrounding willingness-to-pay from the MOHLTC perspective. This suggests that the health benefits associated with a vaccine strategy may outweigh the incurred costs.

Conclusion

This study assessed the cost-effectiveness of mass pH1N1 vaccination strategy that mirrored the real life initiatives executed in Ontario, from June 2009 to June 2010. Relative to no vaccine strategy, the strategy employed in Ontario was cost saving from a societal perspective. Despite the lack of savings from a governmental perspective, the vaccine strategy may still be beneficial relative to other health care interventions.

This study makes a contribution to the extant literature on pandemic influenza because of its basis in real events -- mirroring the Ontario timeline of events; the vaccine uptake percentage for the total population; considering a wide range of costs; and the simulation of disease patterns. In comparison to traditional homogeneous mixing model for influenza transmission, the present simulation reflects more realistic disease transmission patterns using using a non-homogeneous agent-based simulation model.

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APPENDICES

SIMULATION MODEL

Excerpt from Aleman et al. (2009b)

The disease transmission dynamics in the population are determined by the behavior of its individual members. This study employed an agent-based simulation to simulate each member of a population thereby providing a means by which to consider unique individual characteristics that affect transmission and infection probabilities including the type and length of contact between two individuals. An agent-based model can also account for the possibility of infected individuals recovering and becoming immune or possibly dying.

Each individual is an object in the simulation with various characteristics including age, vaccination status, home location, work location and household membership. Household membership indicates which members of the population live in the same dwelling. In addition, once infected, each individual will be contagious for a randomly generated number of days, which is calculated as a function of age. Transportation routes used for daily commutes area so assigned to individuals.

In order to establish contact leading to disease transmission between individuals, contact networks are used. Each individual in the population has a certain level of contact with every other member of the population (the level of contact may be nothing). The time and type of contact between two individuals can vary. In a contact network, each person is represented as a node, and contacts between individuals are arcs. For visualization, one may imagine millions of nodes with differently colored arcs connecting every node to many other nodes; the color of the arcs indicates the type and level of contact. Using this concept, the uniform reproduction number was replaced by the individualized probabilities for each person j transitioning from a susceptible state (S) to an infected state (I) in time period n:

$$Pr_j^n(S,I) = \sum_{i \in I}\left(t_{ij}^n b_{ij}^n + c_{ij}^n\right) \quad \forall j \in S \qquad (1)$$

where $S \subseteq N$ is the set of susceptible individuals in population N; $I \subseteq N$ is the set of infected individuals in population N; t_{ij}^n is the time of contact between person i and person j in time period n; b_{ij}^n is the probability of disease transmission from person i to person j per unit time in time period n; and c_{ij}^n indicates the probability of transmission from person i to j by means other than direct contact in time period n. Values for t_{ij}^n and b_{ij}^n for contact under social situations (not including contact while on public transportation) can be found in Del Valle et al. (2007) and Haber et al. (2007).

Different levels of contact can be created for any conceivable relationship between two individuals, thereby allowing unlimited flexibility in modeling daily interactions. In the simulation, one day is simulated for a particular individual by randomly selecting individuals who have the same public transportation route, school, etc. with whom to have contact.

In the simulation, one day is simulated for a particular individual by randomly selecting individuals who have the same public transportation route, school, etc. with whom to have contact. Members from the same household are pre-assigned fixed contact times for each day. Those people selected for contact who are infected are included in the calculation of $Pr_j^n(S,I)$. This calculation of $Pr_j^n(S,I)$ is repeated for all individuals. At the conclusion of a simulated day, a random number is generated to indicate whether each susceptible person transits to infected according to $Pr_j^n(S,I)$. Infected individuals transfer to a recovered/removed state after a pre-determined number of days if they survive the infection. Each day, infected individuals have a pre-determined probability of dying and transitioning to the recovered/remove state.

INFECTIOUS DISEASES TERMINOLOGY

Suspected case

Defined as “the acute onset of respiratory illness with fever (may not be present in the elderly or young children) and cough and one or more of the following: sore throat, arthralgia, myalgia, or prostration” (Haber et al., 2007).

Confirmed case

Defined as the laboratory confirmation of H1N1 virus infection, with or without clinical symptoms, by reverse transcriptase polymerase chain reaction (RT-PCR), viral culture or a four-fold rise in H1N1 virus specific neutralizing antibodies (Haber et al., 2007)

Influenza like illness (ILI)

Defined as the acute onset of respiratory illness with fever and cough, and with one or more of the following: sore throat, arthralgia, myalgia, or prostration which could be due to influenza virus. In children under 5, gastrointestinal symptoms may also be present. Inpatients under 5 or 65 years and older, fever may not be present (OAHPP, 2009).

Adjuvant

Adjuvants are compounds that boost the immune response to the vaccine, allowing lower doses to be used. Pregnant women did not receive the adjuvanted H1N1 vaccine due to limited research on the negative effects for this population (PHAC, 2009b).