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Incidence of influenza in Ontario following the Universal Influenza Immunization Campaign

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Abstract

The purpose of this study was to determine whether the incidence of influenza in Ontario, Canada has decreased following the introduction of the Universal Influenza Immunization Campaign (UIIC) in 2000. All laboratory-confirmed influenza cases in Ontario, from January 1990 to August 2005 were analyzed using multitaper time series analysis. We found that there has not been a decrease in the mean monthly influenza rate following the introduction of the UIIC (109.5 (S.D. 20) versus 160 (S.D. 50.3) $p < 0.1$). Despite increased vaccine distribution and financial resources towards promotion, the incidence of influenza in Ontario has not decreased following the introduction of the UIIC.

Keywords: Influenza; Universal immunization; Public health; Vaccination

1. Background

In Canada, influenza and pneumonia (as a complication of influenza) are responsible for approximately 75,000 hospitalizations each year [1] and 700–2500 deaths [2,3]. With roughly 40% of the population of Canada residing in Ontario, it could be extrapolated that in Ontario approximately 30,000 people are hospitalized annually due to influenza and pneumonia resulting in 280–1000 deaths. Previous research has examined causes of emergency department (ED) overcrowding [4–7], and the association between influenza and ED utilization [8,9].

The Canadian National Advisory Committee on Immunization (NACI) [10] recommends yearly influenza vaccination for persons at high risk for influenza-related complications, and in Ontario, persons in the high risk category have received publicly funded vaccinations since 1989.

In 1993, the publicly funded influenza immunization program was expanded in Ontario to include the vaccination of healthcare workers. In 1999, this program was expanded further to include all workers in long-term care facilities and hospitals, and all members of the regulated health professions. Thus, 'high risk' individuals were:

- Everyone 65 years of age or older.
- Anyone with a serious long-term health problem such as heart, kidney, or lung disease (including asthma).
- Anyone with diabetes or other metabolic disease, cancer, or blood disorder.
- Anyone whose immune system is weakened.
- Anyone aged 6 months to 18 years on long-term treatment with acetylsalicylic acid (ASA).
- Anyone who lives, works or volunteers in a nursing home, chronic care institution or retirement home.
- Healthcare workers and essential service workers (i.e., ambulance staff, fire and police).
- Anyone who volunteers in a hospital or other healthcare facility.
- Anyone who lives in the same household as people in any high risk group who are unable to get vaccinated.

In July 2000, the Ministry of Health and Long Term Care (MOHLTC) of Ontario announced a Universal Influenza

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Immunization Campaign (UIIC) for all residents of Ontario [11], extending coverage to include low risk adults and children. Through this program, all 12 million Ontarians were eligible to receive publicly funded influenza vaccine annually. Vaccination under the UIIC started in October 2000. The two stated objectives at the onset of the UIIC were to:

1. Ease emergency department pressures by decreasing the impact of influenza on emergency department visits and on other health facilities/providers during the influenza season.
2. Decrease the number and severity of cases of influenza in Ontario.

In June 2001, the MOHLTC announced a second year of the UIIC [12], promoting the low incidence of influenza in Ontario in 2000/2001 as an indicator of success of the program [12]. However, there is currently no published research on the incidence of influenza in Ontario following the UIIC.

2. Objective

The objective of this study was to compare the incidence of influenza in Ontario before and after the implementation of the UIIC to determine if there has been a decrease in influenza following the UIIC.

3. Methods

3.1. Study design

This is a population-based, retrospective study of laboratory-confirmed influenza cases as reported to Health Canada from 1 January 1990 to 31 August 2005.

3.2. Influenza data collection

Influenza is a reportable disease in Ontario and the reporting definition is the presence of the following three symptoms:

- Fever greater than 39 °C.
- Cough or sore throat.
- Myalgia, malaise and/or prostration.

In addition, to at least one of the following:

- A laboratory confirmation by detection or isolation of influenza virus in pharyngeal or nasal secretion.
- Demonstration of a four-fold or greater increase in haemagglutination antibody titers to influenza between acute and convalescent sera.

Confirmed influenza cases are reported to the Division of Disease Surveillance at the Centre for Infectious Diseases Prevention and Control (CIDPC), Canada, and information regarding the number of tests performed and the type of influenza viruses isolated is posted on the Health Canada website.

Provincial and national influenza data for 1996–2005 (the years for which it is available) were obtained from Health Canada's 'Flu Watch' website [13]. Influenza data for Ontario for the years 1990–1996 were obtained directly from Health Canada. While data on influenza-like illness are also collected and reported, this study used only the *laboratory-confirmed cases of influenza* reported to the CIDPC, as it may be a more reliable measure of clinical influenza [14].

4. Analysis

4.1. Descriptive statistics

All analyses, with the exception of the time series analysis, were performed using SPSS version 12 [15]. Monthly influenza counts were changed to rate per 100,000 population using annual Ontario population estimates from Statistics Canada [16]. The percent of influenza found in Ontario, with respect to the rest of Canada was compared using Mann–Whitney *U*-test for the years 1996–2005 (years for which Flu Watch data for the country as a whole were available).

It is possible that the rate of influenza in Ontario declined relative to other provinces, even if it did not decline within Ontario. In order to determine if the Ontario influenza rates differed significantly from those of other provinces and regions in Canada, the rate ratios (the ratio of the annual rate of influenza in Ontario over the annual rate of influenza in Quebec, British Columbia, the Prairie Provinces (Saskatchewan, Alberta and Manitoba) and the Maritime Provinces (Nova Scotia, New Brunswick and Newfoundland and Labrador)) were compared using the Mann–Whitney *U*-test.

Similarly, it is possible that an increase in the number of laboratory tests performed in Ontario following the introduction of the UIIC would result in an increase in the number of influenza cases detected. Therefore, the number of tests performed in Ontario was compared to other provinces and regions using a one-way analysis of variance (ANOVA) for the period surrounding and following the introduction of the UIIC, 1999–2005.

5. Time series analysis

Multitaper time series analysis [17,18] was used to compare the mean rate of influenza in Ontario prior to and following the introduction of the UIIC. As a preliminary check on the temporal structure of this data, the power spectrum was calculated using multitaper methods, supplemented by the harmonic *F*-test for periodic components. Multitaper analysis gives greater control over the resolution-bias-variance tradeoff, and spectra thus obtained can be used to estimate the

underlying system variance, previously affected by estimate errors. The multitaper estimate of amplitude at 0 frequency as an estimate of the process average, before and after 2000 was also used.

The multitaper method of extracting the periodic content is a frequency domain method alternative, similar to the commonly used ARIMA method, but requires fewer assumptions. The ARIMA method retains all periodic information, including harmonic content that is not statistically significant. The multitaper relies on an *F*-statistic to determine the statistical significance of individual harmonics leaving out statistically insignificant harmonics, thereby reducing spurious noise in the signal. By visualizing the log-spectrum, this estimate has the advantage over other methods, as it is easier to identify multiple periodicities in the data compared with the method of using the autocorrelation to identify periodic information.

5.1. Ethical considerations

This protocol has been approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

6. Results

Fig. 1 shows laboratory-confirmed influenza cases in Ontario per 100,000 population from 1 January 1990 to 31 August 2005.

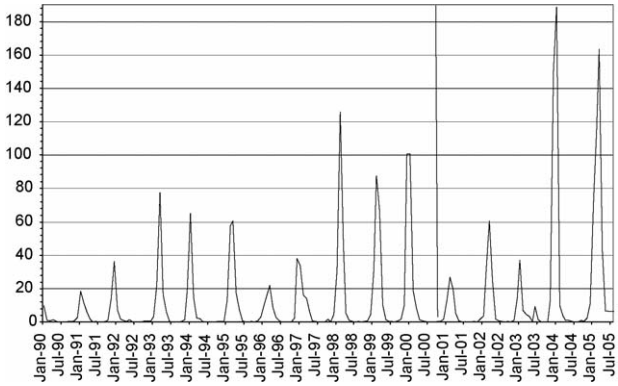

Fig. 1. Mean monthly influenza cases per 100,000 population in Ontario from 01/1990 to 08/2005. Vertical line shows introduction of the UIIC.

Table 1 shows the number of influenza cases in Ontario as a percent of the total number of cases in Canada before and after the introduction of the UIIC in 1999/2000. There is not a significant difference in the percent of influenza cases following the introduction of the UIIC ($p = 1.00$).

The ratio of the rate of influenza in Ontario, with respect to other regions in Canada is shown in Table 2. The difference in rate ratio before and after the introduction of the UIIC reveals a significant decrease in the rate ratio between Ontario and Quebec ($p = 0.016$), but no difference between Ontario and the Maritimes ($p = 0.690$), the Prairies ($p = 0.151$) or British Columbia ($p = 0.421$).

The number of laboratory tests for influenza performed in Ontario increased from 20,314 in 1999 to 37,345 in 2005. This increase was not significantly different from other provinces or regions except the Prairies ($p < 0.02$). There was no difference between Ontario and Quebec ($p = 0.22$), British Columbia ($p = 0.96$), or the Maritimes ($p = 0.96$).

Multitaper time series analysis shows that there has not been a decrease in mean monthly influenza cases per 100,000 population following the introduction of the UIIC (mean = 109.5, S.D. = 20 prior versus mean = 164, S.D. = 50.3 post). In addition, to the annual fluctuation in influenza rates, the analysis reveals a strong periodic component at ~4 cycles/year (~3.25 months) corresponding with a significant seasonal variation ($p < 0.01$), and a periodic component at 4.8 cycles/year significant at the $p < 0.05$ level.

Table 1
The number of influenza cases in Ontario as a percent of the total number of cases in Canada before and after the introduction of the UIIC in 2000

Year	1995–1996	1996–1997	1997–1998	1998–1999	1999–2000	**2000–2001**	**2001–2002**	**2002–2003**	**2003–2004**	**2004–2005**
Ontario	222	537	1466	1329	2899	**852**	**2249**	**936**	**4512**	**5135**
Canada	1075	1930	3802	4203	7027	**4154**	**6766**	**3480**	**11370**	**12879**
Percentage	20.7	27.8	38.6	31.6	41.2	**20.5**	**33.2**	**26.9**	**39.7**	**39.9**

Table 2
The ratio of annual influenza rates of Ontario and Quebec, the Prairie Provinces (Saskatchewan, Manitoba, and Alberta), the Maritime Provinces (Nova Scotia, Newfoundland and Labrador, and Prince Edward Island), and British Columbia

Year	1995/1996	1996/1997	1997/1998	1998/1999	1999/2000	2000/2001	2001/2002	2002/2003	2003/2004	2004/2005
Ratio										
Ontario:Quebec	0.82	1.15	1.16	0.92	1.16	0.56	0.61	0.69	0.92	0.75
Ontario:Prairies	0.18	0.34	0.79	0.37	0.71	0.24	0.61	0.36	0.75	1.20
Ontario:Maritimes	3.40	1.11	3.01	3.84	2.17	0.51	2.30	1.63	1.62	1.43
Ontario:British Columbia	0.69	0.76	1.26	1.74	2.82	0.91	2.70	0.85	1.76	2.85

7. Comment

The Universal Immunization Campaign was introduced in Ontario in July 2000 with two primary objectives: to reduce ED pressure in the winter and to reduce the incidence of influenza [11]. The present study was unable to find a significant reduction in the incidence of influenza in Ontario following the introduction of the UIIC. The ratio of influenza rates in Ontario to other regions of Canada and the number of tests performed was also examined and, in the majority of cases, there was no difference when comparing Ontario to other provinces or regions in Canada.

The implication of these findings relate most importantly to the cost of the program versus the ability or the UIIC to achieve its initial stated goals. According to MOHLTC press releases [11,12], approximately $200 million has been spent to date on vaccine purchase, distribution, and public awareness to provide free influenza immunization to the population not previously covered (see Table 3). This includes adults under the age of 65 at low risk for complications of influenza, and children over 6 months of age. While influenza vaccination has been shown repeatedly to be effective in reducing mortality and morbidity in populations at high risk for complications from influenza [19–25], the low risk population was the target of the UIIC. Available literature is divided regarding the benefit and cost effectiveness of vaccinating healthy, low risk individuals [26–32] and even healthy individuals over age 65 [33].

One review compiled for the Cochrane Library in 2004 [34] examined studies evaluating the effectiveness of vaccines in preventing cases of influenza in healthy adults (age 14–60) and concluded that "the recommended live aerosol vaccines reduced the number of cases of serologically confirmed influenza A by 48% (95% confidence interval 24–64%), whilst recommended inactivated parenteral vaccines had a vaccine efficacy of 68% (95% confidence interval 49–79%). The vaccines were less effective in reducing clinical influenza cases, with efficacies of 13% and 24%, respectively. Use of the vaccine significantly reduced time off work, but only by 0.4 days for each influenza episode (95% confidence interval 0.1–0.8 days)" [34].

The reviewers also reported that while hospital admissions were lower in the vaccinated group, this finding was not statistically significant, and there was little difference in complication rates between vaccinated and unvaccinated groups. The reviewers concluded "the results of this review seem to discourage the utilization of vaccination against influenza in healthy adults as a public health measure. Having healthy adults at low risk of complications due to respiratory disease, the use of the vaccine may be only advised as individual protection measure in very specific cases" [34].

One explanation for the lack of reduction in influenza rates in Ontario is the virulence of the virus in circulation. Research done in the United States shows influenza A viruses with the H3N2 subtype dominated most seasons of high excess mortality due to influenza, while seasons where influenza A H1N1 or B predominated were generally quite mild [35]. In Canada, the 2000/2001 and 2002/2003 seasons were dominated by the influenza A H1N1 and B serotypes, while the influenza A H3N2 predominated in 1999/2000, 2001/2002, 2003/2004, and again in 2004/2005 [13]. The 2000/2001 and 2002/2003 influenza seasons were considered mild, so it is possible that vaccination would not have had a large impact on such low rates.

The second factor to consider is the vaccine effectiveness is highest when the vaccine strain is identical to the wild-type strain [36]. Studies report anywhere between 40% and 70% vaccine effectiveness depending on the match [37]. Health Canada reports a good match between the circulating virus and the vaccine composition for 2000/2001, 2001/2002, 2002/2003, and 2004/2005 [13]. However, in 2003/2004, the vaccine was a poor match for the circulating virus with the predominant virus strain being A/Fujian H3N2, while the vaccine contained A/Panama H3N2 [13]. Studies looking at the cost versus the benefit of vaccination programs stress the need for good matches and high vaccination rates in order for programs to be cost effective [34].

Finally, it is also possible that an increased awareness of the signs and symptoms of influenza on the part of the general population may lead to an increase in visits to physicians and thus result in an increase in reported cases. However, the proportion of influenza cases in Ontario relative to the rest of Canada has not changed (see Table 1) and the relative increase in the number of tests performed is not significantly different from most other regions of the country.

Table 3
Vaccine distribution in Ontario by year

Fiscal year	Vaccine doses			Provincial government costs	
	Distributed (million)	Administered (million)	Coverage (%)	Vaccine (million $)	Total (million $)
1999/2000	2.10	1.90	16	3.97	7.41
2000/2001	7.90	5.76	44	17.3	40.2
2001/2002	6.00	4.90	42	18.5	~40
2002/2003	5.40	4.26	42	18.5	~40
2003/2004	6.01	5.52[a]	44[a]	22.5	~42

Reference: Dr. Karim Kurji, Associate Chief Medical Officer of Health National Influenza Vaccine Summit, Atlanta, U.S.A.; April 2004 [42].
[a] 2003/2004 data being analyzed.

8. Conclusion

The findings of this study do not show a reduction in the rate of influenza in Ontario following the introduction of the Universal Influenza Immunization Campaign. Given that the individuals at low risk for complications from influenza are less likely to seek medical attention and less likely to develop complications, it may be more cost effective to target high risk individuals [34]. In their 1993 paper, Duclos and Hatcher state: "from our findings, the most effective approach to increase the proportion of high risk Canadians protected against influenza would be to target healthcare providers" [38]. People at high risk for complications from influenza (the 'high risk' population) are also often the same people who visit the ED frequently [39]. It has been shown that providing influenza vaccinations in the ED targets the high risk population and may also be a more cost efficient method to reduce influenza rates in the segment of the population most likely to develop complications [40,41].

9. Limitations

Any assessment of the Universal Immunization Campaign will be affected by the lack of data on vaccine coverage in Ontario. No uniform baseline data on pre-UIIC vaccine coverage were collected, thus it is impossible to know how many low risk individuals received the influenza vaccination, or what their health outcomes were. Data on vaccine coverage is still not systematically collected, and although individual Health Units and physician offices may keep their own records regarding vaccinations that they have administered, these records are not linked to any central source, and there is presently no way to know the vaccination status of different segments of the population. Information regarding the health outcomes of those vaccinated is also not collected, so it is not possible to link vaccination status with clinical influenza cases, or with subsequent resource utilization. As systematic collection of vaccination status and patient outcome does not exist, any proposed evaluation of the UIIC will also be hampered by this lack of data.

While information regarding the health outcomes of individuals who were vaccinated is not collected, it is possible to get a general indication of vaccination coverage rates from the purchase and distribution information. In 2000, the MOHLTC administered 5.76 million doses of vaccine for a 44% coverage of the Ontario population, and this number decreased to 4.26 million doses in 2003 (42% coverage) [42]. Table 3 shows the number of vaccines purchased and distributed and the cost of the vaccine and the overall program cost (vaccine, distribution, promotion) [42].

It is assumed that the number of reported influenza cases is an underestimation of the true number of influenza cases in any given year. This is true because not all persons ill with influenza will seek medical attention, and even those who do may not be diagnosed with influenza. It is beyond the scope of this paper to elucidate the true error rate of influenza reporting in Canada or Ontario, however, the cases presented in this paper are from the only source of systematically collected confirmed influenza cases in Ontario and Canada, and numbers upon which past statements concerning the UIIC program and future policy decisions are made [43].

Table 4
Vaccination status for Canada and Ontario

Year	1990/1991[a]	1996/1997[b]	2000/2001[c]	2003[d]
Ontario (%)	64.6	59.5	72.5	68.7
Canada (%)	44.8	51.1	66.8	62.4

Percent of population age 65 or older vaccinated in the past 12 months.
[a] Duclos P, Hatcher J. Epidemiology of influenza vaccination in Canada. Can J Public Health 1993;84:311–5 [38].
[b] 1996/1997 National Population Health Survey.
[c] 2000/2001 Canadian Community Health Survey.
[d] 2003 Canadian Community Health Survey.

The only systematically collected information on vaccine coverage in Canada occurs through telephone surveys conducted by Health Canada. In 1991, a question regarding vaccine coverage was added to Statistics Canada General Social Survey, and revealed that 13.8% of the general population and 44.8% of the population 65 years and over received a flu shot in the winter of 1990/1991 [38]. In the 1996/1997 National Population Health Survey, a similar question showed that 18.4% of the general population and 59.5% of the population 65 years and over received a flu shot in the winter of 1996/1997 [44]. In May 2001, Health Canada performed a telephone survey and found that in the 2000–2001 influenza season 37.0% of the general population and 72.5% of persons over age 65 had been vaccinated against influenza [43] and in July 2003, the Canadian Community Health survey [45] reported 26.6% of the general population and 62.4% of persons over age 65 had been vaccinated in the previous 12 months (see Table 4).

In summary, this paper has examined the incidence of influenza in Ontario following the introduction of a Universal Influenza Immunization Campaign. The findings to date suggest that the UIIC has not led to a decrease in influenza rates in Ontario. It is recommended that the program be reevaluated, with respect to, its goals and cost. This would include examining other potentially more cost effective and efficient methods of immunizing people at high risk for complications from influenza, where research has shown the largest morbidity, resource utilization, and mortality to occur.

References

[1] Russell ML, Maxwell CJ. The prevalence and correlates of influenza vaccination among a home care population. Can J Public Health 2000;91:441–4.
[2] Health Canada. Population and Public Health Branch Influenza Information; November 2001. www.hc-sc.gc.ca/pphb-dgspsp/publicat/info/influ_e.html.
[3] Sibbald B. Estimates of flu-related deaths rise with new statistical models. CMAJ 2003;168:761.

[4] Chan BTB, Schull MJ, Schultz SE. Atlas report. Emergency departments in Ontario 1993–2000. Toronto, Ontario: Institute for Clinical Evaluative Sciences; 2001.
[5] Hospital Report Research Collaborative. Hospital Report 2001. Emergency Department Care. Ontario Hospital Association and the Government of Ontario. Toronto: Queen's Park; December 2001.
[6] Kelen GD, Scheulen JJ, Hill PM. Effect of an emergency department (ED) managed acute care unit on ED overcrowding and emergency medical services diversion. Acad Emerg Med 2001;8(11):1095–100.
[7] Baer RB, Pasternack JS, Zwemer Jr FL. Recently discharged inpatients as a source of emergency department overcrowding. Acad Emerg Med 2001;8(11):1091–104.
[8] Groll DL, Henry B. Can a universal influenza immunization program reduce emergency room volume? CJEM 2002;4(4):245–51.
[9] Schull MJ, Mamdani MM, Fang J. Influenza and emergency department utilization by elders. Acad Emerg Med 2005;12(4):338–44.
[10] Health Canada. National Advisory Committee on Immunization (NACI) Statement on influenza vaccination for the 2002–2003 season. Canada Communicable Disease Report. 1 August 2002;28:ACS-5.
[11] Government of Ontario Press Releases; 25 July 2000. http://ogov.newswire.ca/ontario/GPOE/2000/07/25/c6018.html?lmatch=&lang=_e.html [accessed 12 December 2005].
[12] Government of Ontario Press Releases; 27 June 2001. http://ogov.newswire.ca/ontario/GPOE/2001/06/27/c7833.html?lmatch=&lang=_e.html [accessed 12 December 2005.
[13] FluWatch. http://www.hc-sc.gc.ca/pphb-dgspsp/fluwatch.
[14] Navarro-Mari JM, Perez-Ruiz M, Cantudo-Munoz P, Petit-Gancedo C, Jimenez-Valera M, Rosa-Fraile M. Influenza Surveillance Network in Andalusia, Spain. Influenza-like illness criteria were poorly related to laboratory-confirmed influenza in a sentinel surveillance study. J Clin Epidemiol 2005;58(3):275–9.
[15] SPSS Inc. Chicago, Illinois.
[16] Statistics Canada. http://www.statcan.ca/.
[17] Thomson DJ. Multipaper analysis of nonstationary and nonlinear time series data. In: Fitzgerald W, Smith R, Walden A, Young P, editors. Nonlinear, nonstationary signal processing. Cambridge University Press; 2001. p. 317–94.
[18] Thomson DJ. Spectrum estimation and harmonic analysis. Proc IEEE 1982;70:1055–96.
[19] Carman WF, Elder AG, Wallace LA, McAulay K, Walker A, Murray GD, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomized controlled trial. Lancet 2000;355(9198):93–7.
[20] Gross PA, Hermogenes AW, Sacks HS, et al. The efficacy of influenza vaccine in elderly persons: a meta-analysis and review of the literature. Ann Intern Med 1995;123:518–27.
[21] Voordouw BC, van der Linden PD, Simonian S, van der Lei J, Sturkenboom MC, Stricker BH. Influenza vaccination in community-dwelling elderly: impact on mortality and influenza-associated morbidity. Arch Intern Med 2003;163(9):1089–94.
[22] Nichol KL, Nordin J, Mullooly J. Influence of clinical outcome and outcome period definitions on estimates of absolute clinical and economic benefits of influenza vaccination in community dwelling elderly persons. Vaccine; 18 October 2005 [Epub ahead of print].
[23] Mangtani P, Cumberland P, Hodgson CR, Roberts JA, Cutts FT, Hall AJ. A cohort study of the effectiveness of influenza vaccine in older people, performed using the United Kingdom general practice research database. J Infect Dis 2004;190(1):1–10.
[24] Govaert TM, Thijs CT, Masurel N, et al. The efficacy on influenza vaccination in elderly individuals: a randomized double-blind placebo-controlled trial. JAMA 1994;272:1661–5.
[25] Jefferson T, Smith S, Demichelli V, Harnden A, Rivetti A, Di Pietrantonj C. Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. Lancet 2005;365:773–80.
[26] Schabas RE. Mass vaccination in Ontario: a sensible move. CMAJ 2001;164(1):36–7.
[27] Demicheli V. Mass influenza vaccination in Ontario: is it worthwhile? CMAJ 2001;164(1):38–9.
[28] Buxton Bridges C, Thompson WW, Meltzer MI, et al. Effectiveness and cost–benefit of influenza vaccination of healthy working adults—a randomized controlled trial. JAMA 2000;284:1655–63.
[29] Nichol KL, Lind A, Margolis KL, et al. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. NEJM 1994;331:778–84.
[30] Demicheli V, Jefferson T, Rivetti D, Deeks J. Prevention and early treatment of influenza in healthy adults. Vaccine 2000;18:957–1030.
[31] Muennig PA, Khan K. Cost-effectiveness of vaccination versus treatment of influenza in healthy adolescents and adults. Clin Infect Dis 2001;33:1879–85.
[32] Monto AS. Preventing influenza in healthy adults—the evolving story. JAMA 2000;284:1699–700.
[33] Allsup S, Haycox A, Regan M, Gosney M. Is influenza vaccination cost effective for healthy people between ages 65 and 74 years? A randomised controlled trial. Vaccine 2004;23:639–45.
[34] Demicheli V, Rivetti D, Deeks JJ, Jefferson TO. Vaccines for preventing influenza in healthy adults (Cochrane review). The Cochrane Library, Issue 3; 2004.
[35] Klimov A, Simonsen L, Fukuda K, Cox N. Surveillance and impact of influenza in the United States. Vaccine 1999;17:S42–6.
[36] Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. Lancet 2005;366(9492):1165–74.
[37] Carrat F, Tachet A, Rouzioux C, Housset B, Valleron A-J. Field investigation of influenza vaccine effectiveness on morbidity. Vaccine 1998;16:893–8.
[38] Duclos P, Hatcher J. Epidemiology of influenza vaccination in Canada. Can J Public Health 1993;84:311–5.
[39] Statistics Canada. The Daily; 19 October 2004.
[40] Kapur AK, Tenenbein M. Vaccination of emergency department patients at high risk for influenza. Acad Emerg Med 2000;7(4):354–8.
[41] Pappano D, Humiston S, Goepp J. Efficacy of a pediatric emergency department-based influenza vaccination program. Arch Pediatr Adolesc Med 2004;158(11):1077–83.
[42] Dr. Karim Kurji, National Influenza Vaccine Summit, Atlanta, U.S.A.; April 2004. www.ama-assn.org/ama1/pub/upload/mm/36/2004_flu_kurji.pdf.
[43] Progress towards Canadian target coverage rates for influenza and pneumococcal immunizations. Canada Communicable Report, vol. 27, no. 10; 15 May 2001.
[44] Statistics Canada Health Reports, vol. 15, no. 2; March 2004.
[45] Health Canada. The Canadian Community Health Survey 2003. http://www.statcan.ca/english/freepub/82-576-XIE/82-576-XIE2005001.htm.