

Article details: 2016-0050	
Title	Trends in influenza vaccine coverage and vaccine hesitancy in Canada, 2006-07 to 2013-14: results from cross-sectional survey data
Authors	Sarah A. Buchan MSc, Jeffrey C. Kwong MD MSc
Reviewer 1	Wendy Vaudry
Institution	Division of Infectious Diseases, Department of Pediatrics, University of Alberta, Edmonton, Alta.
General comments (author response in bold)	<p>This is a well written paper summarizing and analyzing the results of the Canadian community health survey responses for influenza immunization in Canada over a recent 8 year period. Two minor comments:</p> <ol style="list-style-type: none"> 1. The observations about the uptake of influenza vaccine during the pandemic year could be analyzed further; although uptake was overall lower for seasonal influenza vaccine, it was higher than normal if all vaccine administered is taken together. (i.e. 48% overall) this could be pointed out and possible explanations explored. We have added further information regarding this point to the Interpretation section (Main findings, page 10). 2. Further discussion about the relative uptake within high risk groups would be helpful. It appears that the uptake in groups with chronic cardio/pulmonary conditions is close to 60% but uptake in the whole group is affected by the relatively low uptake of those reporting asthma. This is quite a large group (would be useful to have the breakdown of the sizes of each risk group) with relatively low immunization rates. Is this because asthmatics or their caregivers believe it is unnecessary? or because self-reported asthma isn't really asthma...? These could be described as limitations and highlighted as issues to be addressed Highlighting relative lower rates of immunization between the risk groups would be useful for programmatic implementation of interventions. We thank the Reviewer for this comment. Asthma made up a substantial portion of those with chronic conditions (the percentages have now been added to Table 1), with the lowest vaccine coverage attained by this group. In a sensitivity analysis with asthma removed, coverage for those with chronic conditions during the overall study period increased to 54%. This has been included as a footnote in Table 1. We have also added additional comments about this issue in the Interpretation section (page 10).
Reviewer 2	Dena Schanzer
Institution	Public Health Agency of Canada, Centre for Infectious Disease Prevention and Control, Ottawa, Ont.
General comments (author response in bold)	<p>This manuscript updates a previous publication of influenza vaccination rates in Canada. The manuscript is well written and I have only a few comments.</p> <ol style="list-style-type: none"> 1. The introduction discusses the importance of timing without any mention of the ideal timing, other than early? As we have had epidemics peaking as early as November (A/Fujian), waiting until November seems a little late. Can you comment further? Is there a public health recommendation? We understand that discussion about recommendations on timing would be beneficial, but we were unable to find Canadian guidelines. NACI recommends immunization before the season starts, noting that epidemics can start as early as November, but recognizes that precise timing may be different depending on setting, geographic area, and local epidemiologic factors; as such, they recommend that advice regarding timing should come from local public health agencies and this advice may change yearly to reflect the characteristics of that influenza season. Looking at some examples of provincial recommendations, British Columbia simply recommends one should get immunized "as soon as possible" and Ontario recommends to "get it early."^{2,3} Given the highly variable nature of influenza virus epidemics, we have refrained from postulating about best timing in this manuscript. 2. The survey question asks about flu 'shots'. What about live attenuated nasal spray? Do you have any information on the use of the mist product? When was this recommended by NACI? Unfortunately, there is no distinction in the survey regarding the type of influenza vaccine received, and we do not know if respondents would have made the distinction between injected influenza vaccines and the intranasal live-attenuated influenza vaccine (LAIV). LAIV was authorized for use in Canada in 2010 and was recommended by NACI as of the 2011-12 season for children aged 2-17 years. However, CCHS includes only those aged ≥12 years, so the majority of those receiving LAIV would not have been included in our study. 3. While I recognize the E and F flags from Stat Can survey results, the significance of a CV between 16-33% could be explained in more detail. As per the Editor's first comment, this information has been included in the footnotes to Tables 2 and S1. 4. What are the numbers in Table 3? Is there any way to include confidence intervals or CVs? The E flag is not sufficient if one wants to compare two numbers. Same for Tables 4

and 5. Are the differences statistically significant?

The data in Table 3 represented the distribution of influenza immunization by month. As per the Editor's suggestion, we have removed this table and have included this information in the text of the manuscript instead. We intentionally avoided adding confidence intervals for the former Tables 4 and 5 (now combined into a new Table 3) because the estimates are based on samples representing very large populations, leading to very narrow confidence intervals, and they added considerable clutter to the tables. However, we have included an alternative version of the new Table 3 below with the 95% confidence intervals (and an extra decimal place) included in case the Editor prefers that version.

Table 3: Reasons reported for not receiving influenza immunization during the 2006-07 to 2013-14 influenza seasons, by selected characteristics and province/territory of residence^a

Reason (%; 95%CI)	%	Unnecessary	Did not get around to it	Previous bad reaction	Fear	Doctor said unnecessary
Overall (N=336,105 ^b)	100.0	71.7 (71.4, 72.0)	15.3 (15.1, 15.5)	5.7 (5.6, 5.9)	4.2 (4.0, 4.3)	1.8 (1.7, 1.9)
Group						
Never immunized	62.4	82.8 (82.5, 83.1)	8.5 (8.3, 8.7)	1.7 (1.6, 1.8)	4.9 (4.8, 5.1)	2.0 (1.9, 2.1)
Ever immunized but not in last 12 months	37.6	53.2 (52.7, 53.7)	26.6 (26.1, 27.0)	12.5 (12.2, 12.8)	2.9 (2.7, 3.0)	1.6 (1.4, 1.7)
High-risk (aged ≥65 years)	7.8	68.7 (67.9, 69.4)	11.0 (10.5, 11.5)	11.3 (10.8, 11.7)	4.7 (4.4, 5.1)	3.5 (3.2, 3.8)
High-risk ≥65 with a chronic condition	3.2	63.1 (62.0, 64.3)	12.1 (11.2, 12.9)	14.0 (13.2, 14.8)	4.6 (4.1, 5.0)	4.3 (3.8, 4.9)
High-risk ≥65 without a chronic condition	4.6	72.5 (71.5, 73.4)	10.3 (9.6, 10.9)	9.4 (8.9, 10.0)	4.8 (4.4, 5.3)	3.0 (2.6, 3.4)
High-risk (aged 12-64 with a chronic condition)	13.6	64.3 (63.5, 65.1)	17.6 (16.9, 18.2)	8.3 (7.8, 8.8)	5.0 (4.7, 5.4)	2.5 (2.2, 2.7)
Low risk group	78.6	73.3 (73.0, 73.6)	15.3 (15.1, 15.6)	4.8 (4.6, 4.9)	3.9 (3.8, 4.1)	1.5 (1.4, 1.6)
Province/Territory	100.0					
Newfoundland & Labrador	1.6	74.9 (73.8, 76.0)	13.4 (12.5, 14.3)	4.5 (4.0, 5.1)	4.3 (3.6, 4.7)	1.9 (1.6, 2.2)
Prince Edward Island	0.4	67.2 (65.5, 68.9)	18.2 (16.7, 19.9)	5.9 (5.0, 6.8)	4.7 (4.0, 5.3)	2.0 (1.5, 2.6)
Nova Scotia	2.3	64.7 (63.4, 66.1)	20.1 (19.0, 21.2)	6.8 (6.1, 7.5)	5.3 (4.7, 6.0)	2.4 (2.0, 2.8)
New Brunswick	2.1	71.2 (70.0, 72.4)	14.5 (13.6, 15.4)	6.4 (5.8, 7.1)	4.9 (4.4, 5.4)	1.7 (1.4, 2.0)
Quebec	25.6	79.5 (79.0, 80.1)	9.4 (9.0, 9.8)	3.9 (3.7, 4.1)	2.7 (2.5, 2.9)	1.4 (1.3, 1.6)
Ontario	37.4	68.2 (67.7, 68.7)	17.7 (17.3, 18.1)	7.2 (7.0, 7.5)	5.2 (5.0, 5.5)	2.2 (2.0, 2.3)
Manitoba	3.5	70.5 (69.4, 71.7)	15.3 (14.4, 16.3)	5.2 (4.7, 5.8)	3.8 (3.3, 4.2)	1.9 (1.6, 2.2)
Saskatchewan	2.9	67.7 (66.6, 68.9)	18.8 (17.8, 19.8)	5.4 (4.9, 5.9)	3.9 (3.5, 4.3)	1.4 (1.2, 1.6)
Alberta	10.9	69.2 (68.4, 70.0)	17.9 (17.1, 18.6)	5.5 (5.1, 5.9)	3.5 (3.2, 3.8)	1.5 (1.3, 1.8)
British Columbia	13.1	70.8 (70.0, 71.5)	16.4 (15.7, 17.0)	5.4 (5.0, 5.7)	4.2 (3.9, 4.6)	1.8 (1.6, 2.1)
Territories	0.1	63.4 (61.8, 64.9)	21.0 (19.9, 22.2)	7.8 (6.8, 8.7)	4.9 (4.1, 5.7)	1.4 (1.1, 1.8)

^a Those who reported not receiving their influenza immunization in the last 12 months were asked why. Respondents could pick more than one reason. [†] Representing 19,049,608 Canadians.

5. Public Health messaging related to influenza vaccination seems to have waned recently. Do you have any information on this? Starting in 2006, a number of papers have been released suggesting that VE is much less than previously thought (from earlier estimate the influenza vaccination reduced annual all-cause mortality by 50% for 65+ to recent estimates of very low VE particularly in the elderly). The new high dose vaccine for seniors shows promise. Some context to the current situation could be included in the discussion. Unfortunately, we are unable to measure changes in Public Health messaging. Promotion of annual immunization has expanded in recent years beyond provincial governments, local public health departments, and physician offices to include pharmacies and pharmacist organizations in certain provinces, making it difficult to quantify changes over time. We are also unable to provide concrete evidence regarding the potential impact of messaging regarding lowered influenza vaccine effectiveness on coverage. Certain high-profile papers, such as Jackson et al.'s 2006 article regarding influenza vaccine effectiveness in older adults,⁴ challenged previously-accepted knowledge of the impact of influenza vaccines and has sparked conversation related to their benefit. It is unclear how these articles translated into the media and how they may have impacted vaccine coverage or belief in the necessity of immunization. However, communication and education were two types of interventions related to improving vaccination rates included in the review articles cited in the Interpretation section (page 11).

Reviewer 3

Norman A. Giesbrecht

Institution

Centre for Addiction and Mental Health, Social Prevention and Health Policy Research Department, Toronto, Ont.

General comments (author response in bold)

Thank you for the opportunity to review this manuscript. My comments and questions are provided below, organized by page number

1. 3 Top. How was the target of 80% set?

This target was set by consensus at a conference of Canadian immunization experts. Some targets had been originally established in 1993, with additional coverage recommendations put forward at a meeting in 2001; prior to this, no recommendations had existed. The 2001 targets included a goal of 80% coverage for those aged ≥65 years and those younger than 65 years with high-risk conditions. At the 2005 meeting, the task group decided to maintain these coverage targets; 89% of those at this consensus conference agreed to maintain these targets, 9% agreed with reservations, and only 2% disagreed.⁵ We have included additional information regarding this in the Introduction (page 3).

2. 3 Middle. Text refers to public funding as a factor in potentially stimulating greater coverage. What about MD training, or mass media promotional announcements? Are there any data or studies on how these might vary by province/territory? Also, any information on what % of physicians speak to their patients about immunization? What about accessibility to having this done at the work place - does it vary by province or over time?

Unfortunately, we are unable to measure changes in Public Health messaging. Promotion of annual immunization has expanded in recent years beyond provincial governments, local public health

departments, and physician offices to include pharmacies and pharmacist organizations in certain provinces, making it difficult to quantify changes over time. We were unable to find information related to the percentage of doctors in Canada who speak to their patients about immunization; however, we know this conversation is an important one. While we have provided some information in the text regarding the use of pharmacists in administering influenza vaccines, we are unable to comment on the number of workplaces providing immunization services as these data are not readily available.

3. 3 Bottom: "timing of immunization" What does that refer to?
We discussed timing of immunization as the month of vaccine receipt. We have clarified this language in the Introduction (page 3).

4. 4 Bottom: "institutionalized persons" please elaborate
According to Statistics Canada, this term includes persons living in hospitals, nursing homes, or facilities for those with a disability, as well as those in those in correctional facilities, shelters, or establishments for children and minors. This wording is standard for those using CCHS data.

5. 4 Bottom: Are there any estimates on how non-respondents differed from respondents using census data, by age, sex, etc.?
We are unaware of any data collected on those who chose not to respond and thus cannot compare them to respondents. However, use of the weights provided by Statistics Canada ensures that the results are representative of the Canadian population.

6. 5 Middle: What is the rationale for two different sets of age groups.
We categorized the data by age and risk group to better understand vaccine coverage in various policy-relevant populations and to be consistent with our previous publication (in order to facilitate comparisons over time). The risk groups were based on National Advisory Committee on Immunization (NACI) recommendations; all individuals aged ≥ 65 years and those younger than 65 years with chronic conditions are considered to be at high risk for serious complications from influenza infection.¹ Furthermore, we provided estimates by more finely stratified age groups. For example, among younger age groups we hypothesized that there might be behavioural differences between those aged 12-19 years (adolescents and young adults) and those aged 20-49 years (working age adults); we collapsed these groups due to the similarity in coverage attained, but also presented the more finely stratified groups as the estimates might be useful for some readers. We separated those aged 50-64 years from those aged 20-49 years because the prevalence of chronic conditions increases substantially in the former group. Despite the guidelines for those aged ≥ 65 years, we identified substantial heterogeneity within this age group, so we stratified older adults further to demonstrate the differences within this high-risk group. We provided a variety of age groups to address the disparate needs of different readers (e.g., clinicians, public health officials, researchers).

7. 6 Line 20: Would "past 12 months" be better than "previous year"
We have updated this language.

Results

8. Length of the tables is a bit overwhelming, giving the appearance of raw data being presented.
We have modified the tables as requested.

9. Authors should consider simplifying and also using bar graphs to highlight a few trends.
We have included Figure 1 to highlight temporal trends by age group.

10. Also, for the main variables showing trends, not necessarily the details, they may consider adding statistical tests as to the significance of the trends.
We thank the Reviewer for this comment. However, we have refrained from using statistical tests of significance and focused more on the results with clinical and/or public health significance. Given the large sample, many tests resulted in significant findings but may have no public health relevance. Consequently, we chose a change of 5 percentage points as meaningful and focused on those results, as opposed to statistical significance.

11. Table 3 might be deleted and the main findings summarized in a few sentences.
We have removed Table 3 and have summarized the findings in the text (Results section, page 9).

12. Reasons. In tables 4 and 5 I am assuming that respondents could only choose one reason. This might be clarified. Also, did the proportions choosing different reasons change over time.

Respondents who reported not receiving an influenza vaccine in the last 12 months were asked why, and were able to choose more than one reason. This has been clarified in the footnotes for the new Table 3.

Reasons were very consistent over time in all groups. Only one reason for one group changed as much as 5% during the study period: 49% reported thinking the vaccine unnecessary in 2006-07

and 54% reported this reason in 2013-14. This has been added to the Results section (page 9).

Interpretation

13. Are there any countries that have achieved or almost achieved their targets? If so what are the differences in accessibility, knowledge, role of MDs, media, etc. between that place(s) and Canada?

We have included information in the Interpretation section (page 11) and Table 4 (page 21) related to vaccine coverage for the 2013-14 influenza season for the Northern Hemisphere (2014 season for the Southern Hemisphere) in countries similar to Canada, including Australia, England and the United States. A European study found that between 2008-09 and 2010-11, only three countries, Northern Ireland, Scotland, and the Netherlands, met the European target of 75% in older adults;⁶ the Canadian target is set at 80%. We have included this information in the Interpretation section (page 11), although between-country comparisons are somewhat limited by differences in how coverage was measured.

We could speculate about the reasons for the similarities and differences. While these countries are similar to Canada in their universal healthcare systems, the system in the Netherlands has been ranked among the top globally, and their use of immunization registries to monitor vaccine coverage may explain some of the differences seen in Canadian coverage levels.

14. The interpretation section would benefit from a further discussion of what can be done to increase coverage. For example, how can the main reasons, as given by respondents, for not being immunized be addressed and effectively challenged?

We thank the Reviewer for this comment and have provided some additional information (Interpretation, page 11).

15. What % of doctors now speak to their patients about immunization? What steps might be taken to increase this?

We were unable to find information related to the percentage of doctors in Canada who speak to their patients about immunization; however, we know this conversation is an important one and efforts are needed to shift the dialogue to support the need for these patients to receive their immunization. We also know that patients may follow their physicians' example, and patients are more likely to get their immunization if their doctor also has.⁷ Improving uptake in healthcare workers and providing reminders to physicians to have the conversation each season and to provide patient-oriented resources to shift the dialogue may help to increase immunization coverage.⁸

16. Should some pilot intervention/study be undertaken - e.g. in one city or province --that would be dedicated to enhancing coverage? The authors might recommend this.

We thank the Reviewer for this comment. While the aim of this study was to describe recent trends in influenza immunization, we have included some information related to interventions identified in a recent Cochrane review that could be undertaken to address this issue (Interpretation, page 11).⁹

17. What are the main myths of the risks immunization and what might be done, or has been done elsewhere, to address them? What could be proposed for Canada?

Some of the main myths regarding influenza immunization include: the vaccine can give you "the flu;" if you are healthy you do not need to get it; influenza is not a serious disease; and the vaccine does not work.^{10,11} Public health workers at local, provincial, and federal levels are attempting to tackle these myths by increasing communication with the public, through bulletins published each year.¹²⁻¹⁴ There is also media coverage each influenza season with articles intended to separate fact from fiction when it comes to seasonal influenza vaccines.¹⁵ Given the large gap that remains to reaching the target coverage level, and the fact that coverage is decreasing in some groups, further efforts are needed. We have highlighted this last point in the manuscript and have presented the results for why people report not receiving the vaccine; we have refrained from hypothesizing about all the mechanisms behind these reasons but believe in the value of that future work.

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