Title Page

Title: Assessing influenza vaccine uptake among older Canadian adults and identifying factors associated with low uptake

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Abstract

Background

Those with chronic medical conditions (CMC) and those aged ≥65 years are at high risk of severe outcomes from influenza. Caregivers who interact with care recipients at high risk of severe outcomes are at risk to transmit influenza. Influenza vaccination can reduce disease severity and prevent transmission. Further research is necessary to estimate the prevalence and characteristics of unvaccinated individuals. The Canadian Longitudinal Study on Aging (CLSA) is a large national cohort study and presents a unique opportunity to identify factors associated with influenza non-vaccination.

Objectives

The objectives of this thesis research are to 1) estimate the prevalence of influenza non-vaccination by assessing self-reported vaccine uptake in the past 12 months among a) adults at high risk of severe outcomes (i.e. adults aged ≥65 and adults aged 45-64 with at least 1 CMC) and b) among caregivers (i.e. adults aged ≥45 who report caregiving) and care recipients (i.e. adults aged ≥65 who report receiving any type of care) and 2) identify factors associated with non-vaccination in each group.

Methods

This study is an analysis of participants from the CLSA follow-up 1 survey (2015-2018). Covariates assessed in these analyses were identified *a priori*. We assessed lack of influenza vaccine uptake and factors associated with non-vaccination in 2 groups at high risk of severe outcomes (adults aged ≥65 and adults aged 45-64 with CMC) and in 2 groups who have close contact and a high risk of transmission (caregivers aged ≥45 and care recipients aged ≥65). We estimated group-specific non-vaccination prevalence. Adjusted odds ratios (aOR) with 95% confidence intervals from logistic regression models were used to identify factors associated with influenza non-vaccination for all groups.

Results

Nearly one-third (29.5%, 95% CI: 28.9%, 30.1%) of 23,226 participants aged ≥65, 49.9% (95% CI: 49.0%, 50.9%) of 10,685 participants aged 45-64 with CMC, 41.4% (95% CI: 40.8%,

42.0%) of 23,500 caregivers, and 24.8% (95% CI: 23.7%, 26.0%) of 5,559 care recipients reported NOT receiving influenza vaccination in the past 12 months. For the 2 lowest-coverage groups, those aged 45-64 with CMC and caregivers who had not visited a family doctor in the past 12 months had higher odds of reporting non-vaccination than those who had in each fully adjusted model.

Discussion

Influenza vaccination is a safe and effective approach to reduce the risk of severe outcomes of influenza disease and the risk of transmission. Of the 4 groups assessed in our analysis, those aged 45-64 with CMC and caregivers aged ≥45 had the highest overall reported influenza non-vaccination in the past 12 months. Vaccination campaigns that do not rely on physician visits could increase uptake among these groups.

Conclusion

From our analysis of CLSA follow-up 1 data (2015-2018), we found that new interventions are urgently needed to improve influenza vaccination coverage in Canada.

Résumé

Contexte

Les personnes vivant avec des maladies chroniques et celles âgées de 65 ans et plus ont un risque élevé de complications liées à la grippe. Les proches aidants qui interagissent avec un bénéficiaire de soins vulnérable aux complications sont à risque de transmettre la grippe. La vaccination antigrippale permet à la fois de réduire la sévérité de l'infection et d'en prévenir la transmission. Davantage de recherche est nécessaire pour estimer la prévalence des personnes non vaccinées et leurs caractéristiques. L'Étude longitudinale canadienne sur le vieillissement (ÉLCV), une grande étude de cohorte nationale, offre une occasion unique de cerner les facteurs associés à la non-vaccination contre la grippe.

Objectifs

Les objectifs de cette thèse de recherche sont 1) d'estimer la prévalence de la non-vaccination contre la grippe en évaluant la vaccination autodéclarée au cours des 12 derniers mois chez a) les adultes à risque élevé de complications graves (c'est-à-dire les adultes de 65 ans et plus et les adultes de 45 à 64 ans ayant au moins une maladie chronique) et chez b) les proches aidants (c'est-à-dire les adultes âgés de 45 ans et plus qui déclarent prodiguer des soins) et les bénéficiaires de soins (c'est-à-dire les adultes âgés de 65 ans et plus qui déclarent recevoir tout type de soins), puis 2) de cerner les facteurs associés à la non-vaccination dans chaque groupe.

Méthodes

Cette étude consiste à analyser les participants au premier suivi de l'ÉLCV (2015-2018). Les covariables examinées ont été déterminées précédemment. Nous avons évalué le taux de non-vaccination antigrippale et les facteurs associés à la non-vaccination dans deux groupes à risque élevé de complications graves (adultes âgés de 65 ans et plus et adultes âgés de 45 à 64 ans ayant une maladie chronique) et dans deux groupes qui ont des contacts étroits avec autrui et qui présentent un risque élevé de transmission (proches aidants âgés de 45 ans et plus et bénéficiaires de soins âgés de 65 ans et plus). Nous avons estimé la prévalence de la non-vaccination pour chacun des groupes étudiés. Des rapports de cotes ajustés (RCa) avec des intervalles de confiance à 95 % provenant de modèles de régression logistique ont été utilisés pour identifier les facteurs associés à la non-vaccination antigrippale pour tous les groupes.

Résultats

Près du tiers (29,5 %, IC à 95 % : 28,9 %, 30,1 %) des 23 226 participants âgés de plus de 65 ans, 49,9 % (IC à 95 % : 49,0 %, 50,9 %) des 10 685 participants âgés de 45 à 64 ans ayant une maladie chronique, 41,4 % (IC à 95 % : 40,8 %, 42,0 %) des 23 500 proches aidants et 24,8 % (IC à 95 % : 23,7 %, 26,0 %) des 5 559 bénéficiaires de soins ont déclaré ne PAS avoir reçu le vaccin antigrippal au cours des douze derniers mois. Dans les deux groupes ayant la couverture vaccinale la plus faible, les personnes âgées de 45 à 64 ans vivant avec une maladie chronique et les proches aidants, ceux qui n'avaient pas consulté de médecin de famille au cours des douze derniers mois étaient plus susceptibles de déclarer ne pas avoir été vaccinés que ceux qui en avaient consulté un, après ajustement complet de chaque modèle.

Discussion

La vaccination antigrippale est une approche sûre et efficace pour réduire le risque de complications graves liées à la grippe ainsi que le risque de transmission. Parmi les quatre groupes examinés dans notre analyse, les personnes âgées de 45 à 64 ans ayant une maladie chronique et les proches aidants âgés de plus de 45 ans avaient globalement le taux de non-vaccination antigrippale déclarée le plus élevé au cours des douze derniers mois. Des campagnes de vaccination qui ne dépendent pas d'une visite chez le médecin pourraient accroître la vaccination parmi ces groupes.

Conclusion

À partir de notre analyse des données du premier suivi de l'ÉLCV (2015-2018), nous avons constaté que de nouvelles interventions sont urgemment requises afin d'améliorer la couverture vaccinale contre la grippe au Canada.

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Contribution of Authors

This study is a part of a research concept that was originally proposed by Dr. Nicole Basta (my primary supervisor) with contributions from Dr. Christina Wolfson (my co-supervisor). I chose to study the influenza vaccination component of this project and specified my study objectives with advice from Dr. Nicole Basta. I conducted the literature search. For manuscript 1 and manuscript 2, I conceived of the analytic plan and study methodology, developed the statistical coding, independently conducted the statistical analyses, and provided the interpretation of results. I wrote and edited the initial and final drafts of the thesis text and the text of both manuscripts, and I am the primary author for both manuscripts. Drs. Nicole Basta and Christina Wolfson both provided feedback on the study methodology and guidance for the revision of the two manuscripts and the thesis.

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List of Abbreviations and Acronyms

Chronic medical condition (CMC)

National Advisory Committee on Immunization (NACI)

World Health Organization (WHO)

Canadian Longitudinal Study on Aging (CLSA)

Influenza-like illness (ILI)

Public Health Agency of Canada (PHAC)

Serious Outcomes Surveillance (SOS)

Network of the Canadian Immunization Research Network (CIRN)

Odds ratio (OR)

Chronic obstructive pulmonary disease (COPD)

Inactivated influenza vaccines (IIV)

High-dose (HD)

Adjusted odds ratio (aOR)

Canadian Community Health Survey (CCHS)

Follow-up 1 (FUP1)

Cerebrovascular accident (CVA)

Transient Ischemic Attack (TIA)

95% confidence interval (95% CI)

Canadian Institutes of Health Research (CIHR)

Chapter 1: Introduction

Vaccination remains one of the most effective ways to prevent infection with influenza, a disease caused by the influenza virus that leads to an estimated 12,200 hospitalizations and 3,500 deaths in Canada each year (Public Health Agency of Canada, 2021a; Buchan and Kwong, 2016). Several groups including all adults aged 65 years and older and adults under 65 years with at least one chronic medical condition (CMC), are at increased risk of influenza complications leading to severe outcomes (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2020). Therefore, Canada's National Advisory Committee on Immunization (NACI) strongly recommends vaccination for all individuals at high risk of severe influenza outcomes (Public Health Agency of Canada, 2021a; Zhao et al., 2019). The Canadian National Immunization Strategy objectives for 2016-2021 were established to adapt the coverage goals of the World Health Organization (WHO) to the Canadian context. As part of these objectives, the National Immunization Strategy set a target to achieve 80% vaccination coverage by 2025 among these two risk groups (adults aged 65 years and older and adults under 65 years with at least one CMC) (Government of Canada, 2021b). As this 2025 deadline approaches, influenza vaccination coverage still has not come close to reaching this target for many groups at high risk of severe outcomes. For example, based on data collected 2015-2020, an estimated 65% to 70.7% of adults 65 years of age and older received influenza vaccine and approximately 45% of adults aged 18-64 years with at least one CMC were estimated to receive influenza vaccine during this same time period (Public Health Agency of Canada, 2018; Public Health Agency of Canada, 2019a; Public Health Agency of Canada, 2020; Public Health Agency of Canada, 2021a; Okoli et al., 2020). In order to better understand why influenza vaccination targets have not yet been met and to plan for increasing influenza vaccination coverage, it is first necessary to identify who among these groups at high risk of severe influenza outcomes are not receiving recommended annual influenza vaccinations. Once we learn more about those most likely to remain unvaccinated among adults in Canada, this evidence can help inform future public health outreach and intervention efforts designed to improve uptake.

Influenza vaccination provides direct benefits by reducing the risk of disease and severe outcomes among those who are vaccinated and indirect benefits by reducing the risk of infection

and the possibility of transmission to others. Influenza vaccination is also recommended by NACI for household contacts of individuals at high risk of severe outcomes, as vaccinating these individuals reduces the risk that they will get ill and thus reduces the risk that they could transmit influenza to those at high risk given their close and prolonged contact (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2021). Immune responses to influenza vaccines among older adults are sub-optimal compared to younger adults due to age-related waning in immune system function (Borgey et al., 2019; Goronzy and Weyand, 2013; Langley et al., 2004). Thus, ensuring that both high-risk older adults and their household contacts are vaccinated is in an important approach to control the spread of influenza, limit exposure among groups at high risk of severe outcomes, and prevent hospitalizations and deaths (Schanzer et al., 2008a).

Household contacts are just one set of individuals who may have close contact with a person who is at high risk of severe influenza outcomes. Caregivers who provide some form of care or assistance to others are very similar to household contacts for individuals who require at-home care (formal or informal), as caregivers have close contact with and a high risk of influenza transmission to those they care for. Vaccination of caregivers therefore helps protect care recipients, which is particularly important among care recipients at high risk of severe outcomes, such as those aged 65 years and older. Along with the risk of transmission to their care recipients, caregivers are also at risk of becoming infected with influenza through contact with those to whom they provide care, which could limit the ability of caregivers to perform their necessary caregiving tasks. Caregivers themselves may also be at high risk of severe outcomes following infection (for example, a younger adult caregiver with CMC). Therefore, it is important to understand influenza vaccination coverage and associated factors in both caregivers and care recipients due to the potential for transmission between these groups, which may increase the overall incidence of severe outcomes from influenza infection. Once these factors are known, public health interventions can be specified for individuals within these populations in order to increase vaccination coverage. Increased coverage will mean lower overall chances of exposure to influenza, which is particularly important to those at high risk of severe outcomes.

However, despite the NACI vaccination recommendations for household contacts and the importance of vaccination in this group, vaccination coverage among those who provide informal assistance to those at high risk of severe outcomes in Canada has been largely unexamined. Many previous studies have focused on vaccination of healthcare workers or other formal caregivers in institutional settings. However, no studies examining influenza non-vaccination across informal and non-specialized types of caregivers in the Canadian context have been done. Because of the lack of knowledge about influenza vaccination among those who provide informal care to community-dwelling older adults, it is important to estimate non-vaccination prevalence and associated factors for non-vaccination in this group. Examining influenza uptake among this group will provide evidence that can be used to inform the design of future influenza vaccination programs so that vaccination is encouraged in this group to protect them AND their contacts from influenza.

Providing robust estimates of vaccination coverage in Canada among subpopulations at high risk of severe outcomes and understanding who is not being vaccinated despite the recommendations for these groups is key to improving coverage and reaching the 80% coverage goal by 2025. The Canadian Longitudinal Study on Aging (CLSA) provides a unique opportunity to assess vaccination coverage in specific groups and to investigate factors associated with influenza vaccination coverage. The CLSA is a national cohort study launched in 2009 of over 50,000 participants at baseline who provide a wide range of data on sociodemographic factors, physical health and clinical biomarkers, health status, health services utilization, lifestyle and health behaviors, psychological health, economic measures, and social characteristics across multiple follow up visits (Raina et al., 2009). Participants have been surveyed to assess whether they have received influenza vaccination in the 12 months prior to the study visit. Participant data includes information that can identify whether individuals are at high risk for influenza complications due to the presence of CMC or age, and whether individuals are serving as informal caregivers, a role that leads to close contact with high-risk individuals. In addition, individual-level data have been collected on a wide range of factors that may be associated with influenza vaccination. The CLSA offers many advantages as a source of data to estimate and examine influenza coverage because the complexity of the CLSA datasets allows researchers to study the role of many different characteristics (such as demographic factors, social characteristics, and health services

utilization) among a large sample of older adults. In addition, the CLSA included participants as young as 45 years of age at baseline, which also allows for the investigation of influenza vaccination among those with CMC in this age group, a group for which less research has been conducted compared to the frequently investigated population of adults aged 65 years and older (Raina et al., 2009). Investigating a broad range of covariates identified *a priori* to determine whether and to what degree these factors may be associated with failure to receive influenza vaccine is important so that we understand whether and to what degree factors beyond demographic characteristics are associated with non-vaccination. The CLSA has multiple advantages for this analysis given the breadth of data collected about individuals and the ability to investigate these questions among several of the groups that NACI recommends to receive annual influenza vaccine, specifically adults with chronic health conditions, adults aged 65 years and older, and household contacts of individuals at high risk. The CLSA allows for in-depth analysis and comparison by groups that have only rarely been investigated in adequately powered analyses (Raina et al., 2018). Analyzing the CLSA data will allow us to undertake a detailed assessment of who is not getting vaccinated among these groups recommended for vaccination and provide the research background for studies to begin to examine the reasons of those who do not vaccinate. This study is a first step that will help us understand trends in influenza vaccination in order to reach the goal of 80% coverage.

In this thesis research, we take advantage of data available from the CLSA follow-up 1 wave (2015-2018) to achieve the following objectives:

1) **Estimate prevalence of influenza non-vaccination among adults at increased risk of severe influenza outcomes** by assessing self-reported vaccine uptake in the 12 months prior to the survey among

1a) all adults aged 65 years and older,

1b) adults aged 45-64 years with at least 1 chronic medical condition (CMC)

2) **Estimate prevalence of influenza non-vaccination among caregivers who are at risk of transmitting to individuals at increased risk of severe outcomes and among high-risk care recipients** by assessing self-reported vaccine uptake in the 12 months prior to the survey among

2a) caregivers aged 45 years and older,

2b) care recipients aged 65 years and older

3) **Identify factors associated with low vaccination uptake** among the following groups:

3a) all adults aged 65 years and older,

3b) adults aged 45-64 years with at least 1 CMC,

3c) caregivers aged 45 years and older,

3d) care recipients aged 65 years and older

This thesis contains 6 chapters. In chapter 2, the literature review, I present a summary of the literature on the influenza virus, its transmission, and its impact; influenza surveillance and prevention in the Canadian context; and influenza vaccination, vaccination coverage and what is currently known about factors associated with vaccination in those at high risk of severe outcomes, as well as highlighting the knowledge gaps that still exist in this important area of public health research. In chapter 3, I present manuscript 1, entitled "*Influenza Vaccine Coverage and Factors Associated with Non-Vaccination Among High-Risk Adults in the Canadian Longitudinal Study on Aging*", which addresses objectives 1a, 1b, 3a, and 3b. Chapter 4 contains manuscript 2, entitled "*Influenza Vaccine Coverage and Factors Associated with Non-Vaccination Among Caregiving and Care-Receiving Adults in the Canadian Longitudinal Study on Aging*", which addresses objectives 2a, 2b, 3c, and 3d. The manuscripts in chapters 3 and 4 meet the formatting requirements of peer-reviewed submissions to the journal *Vaccine*. The tables for each manuscript are found at the end of their respective chapters. References for manuscript 1 are included in chapter 3 and references for manuscript 2 are included in chapter 4. Chapter 5 contains the discussion and Chapter 6 contains the conclusions that encompass both manuscripts 1 and 2. This thesis conforms to the guidelines and requirements for a manuscript-based thesis as established by McGill University.

Chapter 2: Literature Review

The Influenza Virus

The influenza virus is an enveloped single-stranded RNA virus of the family Orthomyxoviridae; of the 5 genera in this family, only influenza A and B have clinical relevance for humans (Arbeitskreis Blut, 2009; Neumann and Kawaoka, 2015). The surface of the virus contains the spike glycoproteins hemagglutinin and neuraminidase, which are respectively part of viral entry into uninfected cells and part of the process the virus uses to emerge from infected cells (Rossman and Lamb, 2011). Influenza viruses are also characterized by their rapid evolution: frequent point mutations lead to changes of the viral proteins (antigen drift), particularly in the surface antigens hemagglutinin and neuraminidase in influenza B and influenza A viruses (Arbeitskreis Blut, 2009). Influenza B has additional methods of genetic change such as insertions, while another cause of influenza A viral variability is antigen shift, where whole genome segments are exchanged between different influenza A viruses co-infecting the same host (Arbeitskreis Blut, 2009).

Influenza Transmission

Influenza viruses infect the human respiratory tract (Killingley and Nguyen-Van-Tam, 2013). Influenza viruses are transmitted from person to person primarily by aerosols: large droplets (>10 μm) expelled from an infected host through mechanisms such as coughing or sneezing which then enter the upper respiratory tract mucosae of uninfected individuals in close proximity (Arbeitskreis Blut, 2009; Killingley and Nguyen-Van-Tam, 2013). It has also been suggested that aerogenic transmission through smaller (<5 μm), inhaled droplets that remain in the air longer and can reach the lungs may be an important transmission pathway, particularly in poorly ventilated indoor conditions (Arbeitskreis Blut, 2009; Killingley and Nguyen-Van-Tam, 2013; Weber and Stilianakis, 2008). Influenza transmission can also occur through direct contact with an infected individual or via touching contaminated surfaces followed by mucosal contact, although the survival time of influenza viruses on surfaces depends on a wide variety of environmental factors such as temperature (Arbeitskreis Blut, 2009; Killingley and Nguyen-Van-Tam, 2013; Shaman and Kohn, 2009). Most outbreak studies suggest that the majority of influenza transmission occurs in close proximity to an infected individual (Brankston et al., 2007; Killingley and Nguyen-Van-Tam, 2013).

The likelihood of transmission from an infected individual to an uninfected household contact depends upon environmental factors such as the nature and duration of contact, characteristics of the infected individual such as the degree of viral shedding, and characteristics of the household contact, including their susceptibility to infection (Tsang et al., 2016). A review of studies that investigated secondary transmission within households found that the risk of PCR-confirmed influenza infection in household contacts ranged from 1% to 38% (Tsang et al., 2016).

Influenza Symptoms and Severe Outcomes

Influenza is a mild illness for the majority of healthy individuals who become infected, typically lasting for an average of 5-6 days with symptoms such as rapid onset of fever, nonproductive cough, and malaise (Nichol, 2005). Clinical features may differ between influenza B and subtypes of influenza A (Kaji et al., 2003). However, influenza infection can also lead to complications such as the worsening of underlying CMC and secondary bacterial infections such as pneumonia or otitis media (ear infection) (Meyer and Lum, 2017; Nichol, 2005). Along with hospitalizations due to pneumonia, influenza is also associated with hospitalizations for pulmonary and cardiovascular disease and neuromuscular complications (Rothberg et al., 2008). The most common severe types of influenza complications are pulmonary and include primary influenza pneumonia caused by the influenza virus and secondary bacterial pneumonia caused by pathogens such as *Streptococcus pneumoniae, Staphylococcus aureus,* and *Haemophilus influenza* (Rothberg et al., 2008). Additionally, a meta-analysis of the association between influenza and cardiovascular events from database inception through August 2014 found that influenza-like illness (ILI) was associated with a twofold increase in myocardial infarction across studies that evaluated the association between influenza and myocardial infarction (Kwok et al., 2015).

Global and National Impact of Influenza

Influenza occurs seasonally and remains a significant global public health issue. In the northern hemisphere, the influenza season typically occurs between November and April while in the southern hemisphere the influenza season typically occurs between June and October (Public Health Agency of Canada, 2021a; Barr et al., 2019; Huang et al., 2015). It is estimated that

influenza kills 250,000 to 500,000 people annually worldwide, with an additional 3 to 5 million cases of severe disease (Smetana et al., 2018). In Canada, estimates from 2016 suggest that there are an average of 3,500 influenza-related deaths and 12,200 influenza-related hospitalizations each year, and influenza and pneumonia remained in the top 10 causes of death in Canada for all ages as of 2020 (Public Health Agency of Canada, 2021a; Statistics Canada, 2022). Independently of vaccination, the number of hospitalizations varies based on the dominant influenza strain in circulation and the duration of the influenza season (Rothberg et al., 2008).

Influenza Surveillance in Canada

To begin to estimate influenza vaccination coverage and assess the impact of vaccination, it is necessary for multiple types of surveillance to be undertaken across Canada. Surveillance is also required to understand the burden of influenza among groups at high risk of severe outcomes. Canada's national influenza surveillance system, FluWatch, established by the Public Health Agency of Canada (PHAC), monitors and reports on the annual spread of influenza and ILI (Government of Canada, 2019). This influenza surveillance system encompasses both active and passive surveillance from a variety of sources, including outpatient sentinel surveillance, hospital-based active surveillance networks, provincial and territorial ministries of health, and clinical and laboratory-based reporting (Andrew and McNeil, 2021).

In the 2018/2019 influenza season (the most recent report available that does not include the disruptions to influenza epidemiology from the control measures implemented during the SARS-CoV-2 pandemic), the FluWatch annual report found that adults aged 65 years and older had the highest rate of hospitalizations (132 hospitalizations per 100,000); additionally, the highest proportion of deaths was reported in this age group (66% of the 224 deaths reported this season) (Government of Canada, 2021a). A review of influenza vaccination and recommendations for older Canadian adults including data from the 2011/2012 Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN) found that a considerable proportion of older adults experience catastrophic disability or are placed in long-term care after hospitalization for influenza (Andrew and McNeil, 2021; Godin et al., 2019).

For those with CMC, data on the burden of influenza are more limited, but asthma and heart disease are two of the most common medical conditions among adults hospitalized with influenza in the United States (Centers for Disease Control and Prevention and National Center for Immunization and Respiratory Diseases (NCIRD), 2021), and a systematic review and meta-analysis of those at high risk of severe outcomes from influenza up to March 2011 found that the presence of chronic lung disease and chronic obstructive pulmonary disease were both associated with a higher likelihood of receiving ventilator support, and chronic lung disease was also associated with a higher risk of hospitalization (odds ratio (OR): 2.38, 95% CI: 1.58, 3.57) and admission to an ICU (OR: 4.46, 95% CI: 1.34, 14.79) (Mertz et al., 2013). Additionally, asthma was associated with a higher risk of developing pneumonia (OR: 1.35, 95% CI: 1.12, 1.62) (Mertz et al., 2013). Diabetes mellitus was associated with a higher risk for hospital admission (OR: 9.91, 95%: 5.46, 17.99) (Mertz et al., 2013). Cardiovascular disease increased the risk of death (OR: 1.97, 95% CI: 1.06, 3.67), as well as the risk of pneumonia, hospitalization, and ventilator support (Mertz et al., 2013).

Prevention of Influenza Infection and Severe Outcomes in Individuals

Influenza vaccination is the primary approach to preventing influenza infection, severe influenza disease which can lead to hospitalization and death, and influenza transmission. Influenza vaccines were first developed in the 1940s and numerous studied have demonstrated that they are safe and effective at reducing the risk of influenza (Barberis et al., 2016; Nichol, 2008). Vaccination reduces the risk of influenza infection and associated negative outcomes such as hospitalization from ILI (Demicheli et al., 2018).

The rapid evolution of the influenza virus through the accumulation of mutations means that the vaccine formulation must be modified each influenza season so that the influenza strains used to develop the vaccine match the circulating strains as closely as possible so that the vaccine will produce a robust immune response to circulating strains (Harding and Heaton, 2018). The seasonal effectiveness of the influenza vaccine depends on this similarity between the vaccine and circulating strains (Gupta et al., 2006). Therefore, the annual process of updating vaccines means that vaccination against influenza must be repeated every year.

Influenza vaccination can reduce the risk of mortality for each group at high risk of severe outcomes, particularly if the vaccine is well-matched to the circulating influenza strain (Chan et al., 2015; Chen et al., 2007; Christenson and Lundbergh, 2002). For those with CMC at high risk of severe outcomes, influenza vaccination has been shown to reduce influenza-associated morbidity and mortality in those with pneumonia, diabetes, and chronic lung diseases such as chronic obstructive pulmonary disease (COPD): notably, one study of the 2001 mortality data of over 35,000 influenza-vaccinated older adults in Taiwan found that the vaccine efficacy of reducing mortality was 53% for pneumonia and 45% for COPD (Jimenez-Garcia et al., 2009; Wang et al., 2007). Influenza vaccination has also been associated with lower mortality risk from cardiovascular diseases (Jimenez-Garcia et al., 2010). A randomized clinical trial of 301 Argentinian patients with myocardial infarction found that the incidence of cardiovascular death at 1 year was significantly lower in the vaccinated group compared to the unvaccinated control group (Gurfinkel et al., 2004). Additionally, a randomized placebo-controlled study of 658 Polish patients with confirmed coronary artery disease between October 2004 and December 2005 found vaccinated patients had an estimated 0.63% 12-month cumulative rate of cardiovascular death compared to 0.76% of controls (Ciszewski et al., 2008). However, both studies were limited by their small sample sizes: the Gurfinkel et al. study was underpowered for further analyses of interest and the Ciszewski et al. study only identified a small number of cardiac events. A cohort study of 25,922 Ontario residents over age 65 covering 8 influenza seasons between 1996/1997 and 2006/2007 found a significant reduction in all-cause mortality associated with influenza vaccination during influenza seasons (hazard ratio: 0.61, 95% CI: 0.47, 0.79) (Campitelli et al., 2010). Influenza vaccination has also been associated with both reduced hospitalizations (including for secondary infections such as pneumonia) and mortality (Landi et al., 2005; Nichol, 2005). Vaccination has also been evaluated for safety among older adults; serious adverse events in this population are very rare (Smetana et al., 2018).

Efficacy Estimates of Influenza Vaccination

A 2008 study that calculated estimates of 4 measures of vaccine efficacy (susceptibility, symptomatic illness given infection, infection and illness, and infectiousness) from human challenge studies with a wild-type influenza strain (as opposed to a vaccine strain) found that influenza vaccines protect against influenza infection in seronegative adults (Basta et al., 2008).

The live attenuated and inactivated influenza vaccines (IIV) examined in the study provided similar protection against laboratory-confirmed influenza infection (absolute efficacy: 41%, 95% CI: 15, 66, and 43%, 95% CI: 8, 79, respectively). The absolute vaccine efficacy of symptomatic illness given infection was 67% (95% CI: 24, 100) for the live vaccine and 29% (95% CI: −19, 76) for the inactivated vaccine (Basta et al., 2008).

The influenza vaccines typically available in Canada include IIV3-SD, IIV3-Adj, IIV3-HD, IIV4-SD, IIV4-cc, IIV4-HD, LAIV3, and LAIV4 (Public Health Agency of Canada, 2021b). IIV3-SD, IIV3-Adj, and IIV3-HD are trivalent inactivated vaccines, while IIV4-SD, IIV4-cc, and IIV4-HD are inactivated quadrivalent vaccines. Trivalent vaccines contain 3 antigens, while quadrivalent vaccines contain 4 antigens (Public Health Agency of Canada, 2021b). The suffix -SD indicates standard-dose, unadjuvanted IIV vaccines, while -HD refers to an IIV with a higher antigen content than the standard dose; -Adj indicates an IIV with an adjuvant to promote immunogenicity; and -cc indicates an IIV grown in cell cultures instead of chicken eggs (Public Health Agency of Canada, 2021b). LAIV3 and LAIV4 are live attenuated nasal spray vaccines (Public Health Agency of Canada, 2021b).

These vaccines have differing levels of effectiveness, especially among older adults. NACI recommends the use of IIV-HD over IIV-SD in adults aged 65 and older as IIV-HD provides better protection (Public Health Agency of Canada, 2021b). Studies have shown that these high-dose (HD) vaccines induce a greater immune response in older adults, even in those with comorbidities or those older than 75, which increases vaccine efficacy against laboratory-confirmed influenza infection (Andrew et al., 2019a). The benefits of IIV-HD have been demonstrated across multiple settings. A 2017 systematic review and meta-analysis of 7 randomized trials of HD influenza vaccines in older adults found that patients who received a HD vaccine had a lower risk of developing laboratory-confirmed influenza infections compared to those who received a standard dose (relative risk: 0.76, 95% CI: 0.65, 0.90) (Wilkinson et al., 2017). A 2014 phase IIIb-IV randomized controlled trial that compared IIV3-HD to IIIV3-SD in adults aged 65 years and older in Canada and the United States found significantly higher seroprotection rates in the IIV3-HD group and estimated an absolute efficacy of influenza infection prevention of 62% for IIV3-HD in older adults (DiazGranados et al., 2014).

Like HD vaccines, adjuvants are also added to increase the immune response to vaccination. Adjuvanted vaccines have been found to be more effective than non-adjuvanted vaccines in preventing laboratory-confirmed influenza and hospitalizations due to pneumonia/influenza. A systematic review and meta-analysis of observational studies of MF59-adjuvanted IIV3 in older adults found that MF59-adjuvanted IIV3 had greater efficacy in preventing hospitalizations due to pneumonia/influenza (adjusted risk ratio: 0.75, 95% CI: 0.57, 0.98) and laboratory-confirmed influenza (adjusted odds ratio (aOR): 0.37, 95% CI: 0.14, 0.96) than non-adjuvanted vaccines (Domnich et al., 2017). A systematic review and meta-analysis of 39 studies evaluating new and potentially more effective seasonal influenza vaccines, which included HD, adjuvanted, and intradermal vaccines, found similar immunogenicity in older adults between all of these enhanced vaccine types (Ng et al., 2019).

However, it is important to note that validly measuring influenza vaccine effectiveness and efficacy estimates can be challenging. Effectiveness has been found to vary by age group, season, vaccination history, sex, and influenza strain (Kwong et al., 2020; Lewnard and Cobey, 2018). Many studies also have inherent limitations, as many are observational studies that cannot account for unmeasured confounding instead of randomized controlled trials; there may also be issues with vaccine misclassification or missing information about the influenza vaccines given, and limited generalizability of estimates (Kwong et al., 2020).

Despite the greater immunogenicity of the HD and adjuvanted vaccines, studies also show that the effectiveness of these vaccines are low. A study of vaccine effectiveness in Canadian older adults with physician-diagnosed COPD across 6 influenza seasons found that vaccination was associated with a 22-43% (accounting for vaccination misclassification) reduced risk of laboratory-confirmed influenza-associated hospitalization, indicating the need for more effective vaccines in this population (Gershon et al., 2020). Another study in Canadian adults over the 2011/2012 and 2013/2014 seasons that analyzed data from SOS CIRN found vaccine effectiveness in adults aged 65 years and older was 39.3% (95% CI: 29.4, 47.8%), compared to 48.0% (95% CI: 37.5, 56.7%) in adults aged under 65 years (Nichols et al., 2018). The low overall effectiveness of these vaccines, particularly in those at high risk of severe outcomes,

demonstrates why vaccination coverage needs to be as high as possible to prevent influenza transmission and severe outcomes.

Development of Provincial Influenza Vaccination Recommendations

These estimates of vaccine effectiveness are used to inform influenza vaccination programs in Canada. Annual recommendations on the use of influenza vaccines are provided by NACI. NACI develops their recommendations for new and existing influenza vaccines through targeted reviews of the available data generated by studies of influenza vaccine candidates, which also includes evaluating the quality of evidence and the strength of the resulting recommendations (Andrew and McNeil, 2021). Recommendations are given on an individual (for individual patient choices) or programmatic (for informing publicly funded influenza vaccination policies) basis, and follow an analytic framework developed to address the many components of immunization programs, such as cost-effectiveness and the burden of disease (Andrew and McNeil, 2021; Erickson et al., 2005). These recommendations are then passed on to PHAC for dissemination (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2018). For Quebec only, the *Comité sur l'immunisation du Québec* performs a parallel role in evaluating and recommending vaccines.

NACI also continually reviews the available evidence on the effectiveness/efficacy, safety, and feasibility of new and in-use vaccines to ensure that recommendations remain up to date. For example, a literature review update was published by NACI in 2018 to include efficacy and effectiveness data on IIV-HD (Fluzone® High-Dose) and IIV3-Adj (Fluad®) vaccines that had been published since the original literature review (National Advisory Committee on Immunization (NACI), 2018). The *Comité sur l'immunisation du Québec* also performs ongoing program monitoring and evaluation procedures (Gouvernement du Québec, 2022).

The State of Influenza Vaccination Recommendations in Canada

In Canada, influenza vaccines are usually available locally beginning in early-middle October through the end of the influenza season (Andrew et al., 2019b). Although the recommendations from NACI are made at the national level (with the exception of Quebec, which makes its own recommendations), there remains variation in the province-level vaccination programs (Andrew

and McNeil, 2021). All provinces except Quebec currently recommend and provide public funding for universal vaccination for all individuals aged at least 6 months who do not have any contraindications (Immunize Canada, 2021; Public Health Agency of Canada et al., 2020; Andrew et al., 2019b). All provinces recommend and fund influenza vaccination for those with chronic conditions that are severe enough to require regular medical or hospital care, such as diabetes and renal disease (Public Health Agency of Canada et al., 2020). As of 2018, only 3 provinces specifically funded vaccination for household contacts of those at high risk (British Columbia, New Brunswick, and Quebec) despite NACI recommendations that this group be vaccinated annually (National Institute on Ageing, 2018), which may impact perceptions of the need for vaccination.

At the provincial level, which influenza vaccine is recommended is primarily determined by age group, with 6 vaccines (IIV3-SD, IIV3-Adj, IIV3-HD, IIV4-SD, IIV4-HD, and IIV4-cc) authorized for use in those aged 65 years and older (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2021). All of these are inactivated influenza vaccines: IIV3-SD is a trivalent, unadjuvanted, standard dose vaccine, IIV3-Adj is trivalent adjuvanted, IIV3-HD is high-dose unadjuvanted, IIV4-SD is quadrivalent, standard dose, and unadjuvanted, IIV4-HD is high-dose quadrivalent, and IIV4-cc is a quadrivalent, unadjuvanted, standard dose, cell culture-based vaccine (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2021). All influenza vaccines are equally recommended for use in this group at the public health program level (vaccine programs that are publicly funded by provinces and territories) for the 2021/2022 season (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2021). However, public funding and availability of each of these vaccines differs between provinces, and vaccines that are not included in public programs may be available to individuals (Andrew and McNeil, 2021). There are no influenza vaccines specifically recommended for those with CMC or those in contact with individuals at high risk of severe outcomes; these individuals may receive any vaccine for which they are eligible (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2020).

Vaccination Recommendations for Those at High Risk of Influenza Complications

Factors including older age (typically defined as those aged 65 years and older) and the presence of 1 or more CMC are strongly associated with an increased risk of influenza complications (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2020; Mertz et al., 2013; Schanzer et al., 2008b; Walker et al., 2020). In Canada, NACI has identified those at increased risk of serious influenza complications to include those with cardiac or pulmonary disorders, diabetes mellitus and other metabolic conditions, cancer, renal disease, residents of chronic care facilities, and adults 65 years of age and older (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2020). Currently, individuals in these groups at high risk of severe outcomes (including those aged 65 years and older and those aged 18-64 years with certain CMC) are "*particularly* recommended" to receive a seasonal influenza vaccination by NACI; this recommendation was also given by NACI during the period relevant to our research (2015-2018) (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2020).

Influenza Vaccination in Contacts and Caregivers

Household contacts of individuals at high risk of influenza complications or hospitalization are also recommended to be vaccinated with influenza vaccine by NACI at the program level independently of whether the contact at high risk of severe outcomes has been vaccinated (An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI), 2020). Because this recommendation is put in place to help mitigate the spread of influenza between these high-risk groups, caregivers and care recipients have a similar reason to get vaccinated. Preventing transmission also reduces the risk that vulnerable individuals will be exposed to the virus.

It has been proposed that vaccination campaigns could also focus on those with the highest potential of *transmitting* influenza as well as those at greatest risk of influenza morbidity and mortality (Bansal et al., 2006). Influenza vaccination can also provide a community-wide benefit that results from the prevention of cases and reduced infectiousness, which makes individuals in highly vaccinated communities less likely to be exposed to influenza. This is an example of the

vaccination strategy known as cocooning, where vaccination of contacts is used to further reduce the risk of influenza exposure for those at high risk of severe outcomes (Rensink et al., 2021).

In addition to protecting individuals at high risk of severe outcomes, vaccination of contacts and caregivers has been recommended as a preventative measure against influenza, as well as to reduce the costs of influenza infection, which include direct costs such as treatment and indirect costs such as loss of productive time (Jit et al., 2013; Schanzer et al., 2008a). Studies have also found that for older adults, having vaccinated younger individuals in their social networks was a strong determinant of influenza vaccine uptake (Chan et al., 2015).

However, despite these benefits, influenza vaccination coverage of all types of caregivers (for example, expanding the focus beyond care home staff or live-in caregivers) and contacts of individuals at high risk of severe outcomes remains unknown in Canada. Several studies have evaluated the impact that contacts and caregivers who live with community-dwelling older adults have on influenza vaccination uptake in these older adults. A systematic review and meta-analysis of social determinants of influenza vaccine uptake for all age groups in Europe from inception to February 2016 found that not living alone was associated with 39% higher seasonal influenza vaccine uptake (Jain et al., 2017). Additionally, some studies included in the review also found that higher household density was associated with decreased influenza vaccine uptake, indicating that household makeup may influence vaccination uptake beyond whether an individual lives alone (Jain et al., 2017). Similarly, a secondary analysis of the Hong Kong government-run cross-sectional Thematic Household Survey data from October 2011 to January 2012 found that influenza vaccine uptake in household members aged under 65 years was strongly associated with the vaccination of older (aged ≥65 years) adults in the household (OR: 8.03, 95% CI: 5.79, 11.13), although the nature of this study meant that this could not be classified as a determinant (Chan et al., 2015).

Influenza Vaccine Hesitancy and Mechanisms that Lead to Vaccination

Understanding and identifying the characteristics of individuals who are not receiving influenza vaccines as recommended is only the first step to increasing uptake. Examining why individuals remain unvaccinated is also important. Vaccine hesitancy is one contributor to low vaccination

uptake. In Canada, vaccine hesitancy has been generally defined as "reluctance to receive recommended vaccination because of concerns and doubts about vaccines that may or may not lead to delayed vaccination or refusal of one, many or all vaccines" (Dube et al., 2016). Addressing vaccine hesitancy and the factors that lead to vaccination is a complex issue, and frameworks have been developed to encompass the wide variety of factors that contribute to hesitancy.

One such model is the 5C scale, which focuses on psychological predictors of vaccination: vaccine confidence (such as a lack of trust in vaccine efficacy), complacency (perceived risk of vaccine-preventable disease), constraints (perceived barriers to vaccination), calculation (level of engagement in vaccination-related research), and collective responsibility (willingness to protect others) are all thought to be related to vaccine hesitancy (Betsch et al., 2018). Another recent model based on behavioral science and adapted by the WHO posits that vaccination uptake arises from 3 components: what people think and feel, as determined by disease risk appraisal and confidence in vaccines; social processes, related to the spread of vaccination-related social norms and preferences through social networks; and direct behavior change, where vaccination is encouraged through removing barriers to vaccination or shaping behavior through efforts such as vaccination incentives (Brewer, 2021). Because there are so many contributing causes to vaccine hesitancy, strategies to address this issue should be similarly complex, involving proactive vaccine communication and promotion strategies that are tailored to the concerns of different population groups (Dube et al., 2016; Guay et al., 2019).

There are also many potential barriers to vaccination at a broader level that need to be considered. These many be physical barriers, such as cost or geographic accessibility (MacDonald and Hesitancy, 2015), or more intangible barriers such as a lack of trust in health officials (Dube et al., 2013). One model that tries to encompass these disparate factors is known as the "5A" model: this model covers access (ability to connect with recommended vaccines); affordability (financial and non-financial costs); awareness (knowledge of vaccination need, access, and benefits); acceptance; and activation (degree to which individuals are encouraged to get vaccinated) (Thomson et al., 2016).

The research presented in this thesis focuses on identifying the characteristics among those who are at high risk of severe influenza outcomes and/or transmission who remain unvaccinated despite national recommendations; the CLSA does not collect data to address the conceptual reasons behind non-vaccination. However, some contributing factors to influenza vaccination hesitancy in Canada have been previously identified. A study that analyzed data from the Canadian Community Health Survey (CCHS) from 2007 to 2014 found that the most frequently reported reason for not receiving a seasonal influenza vaccination across all study characteristics (including risk group) was perceiving it to be unnecessary; this was particularly true among those who had never received an influenza vaccine (Buchan and Kwong, 2016). The CCHS is a cross-sectional survey on health status, healthcare utilization, and determinants of health for the Canadian population that occurs every 2 years, beginning in 2001 (Statistics Canada, 2021). A similar study that looked at 2013/2014 CCHS data also found that the most frequently reported reason for non-vaccination was "respondent didn't think it was necessary", even in those aged 18-64 with CMC and adults aged 65 years and older (Roy et al., 2018). Variations on this reason for vaccine hesitancy have also been found at the provincial level: a study in Ontario found that the most common explanation for not receiving a seasonal influenza vaccine was related to low perceived vaccine importance (Meyer and Lum, 2017).

Factors influencing vaccine hesitancy among groups at high risk of severe outcomes have also been studied. For Canadian older adults, vaccine hesitancy may stem from misconceptions that the vaccine is ineffective or unnecessary, especially among those who do not typically receive annual influenza vaccinations (Andrew et al., 2019b; Pereira et al., 2019). For the 2016/2017 influenza season, the most frequent reason for non-vaccination was "Don't need it/not a person at high risk/not recommended for me" among both those aged 18-64 with CMC (46.7%) and those aged 65 years and older (47.7%) in a survey of 2,024 Canadian adults overseen by PHAC (Public Health Agency of Canada, 2018). For a similar survey of the 2017/2018 influenza season, the most frequent reason for influenza non-vaccination was "I do not believe the flu shot works/it's not effective" among those aged 18-64 with CMC (19.3%) and those aged 65 years and older (25.0%), followed by "I don't need the flu shot/it isn't necessary" (18.7 % and 21.8% respectively) (Public Health Agency of Canada, 2019a). Reasons for influenza non-vaccination were not reported for the 2015/2016 season (Public Health Agency of Canada, 2021a).

Characteristics Associated with Influenza Non-Vaccination

An individual's influenza vaccination status has been found to be associated with a wide range of social, demographic, and health characteristics. A study of 1,950 Canadian adults surveyed during the 2015-2016 Influenza Immunization Coverage Survey found that younger age was associated with non-vaccination for those aged 18-64 years both with and without CMC, as well as for those aged 65 and older (Farmanara et al., 2018). These results were also confirmed in a longitudinal study of nearly 4,000 adults across the European Union, where it was found that older age (aOR for those aged ≥85 years: 1.21, 95% CI: 1.01, 1.46) and comorbidity (aOR: 1.26, 95% CI: 1.08, 1.47) was associated with a higher probability of being vaccinated across the majority of countries (Landi et al., 2005), as well as in a prospective Swedish study of 7,836 adults aged 65 and older, which found a lower vaccination rate in those aged 65-69 (60%) compared to those aged 70 and older (67-72%) and a higher vaccination rate in those with underlying chronic disease (71%) compared to those without (Christenson and Lundbergh, 2002). The factors most often associated with vaccination are those that define groups at high risk of severe outcomes: primarily, older age and presence of CMC. Although the association between presence of CMC and receiving influenza vaccination often varies by type of CMC, the effect of multiple CMC is still widely unknown (Christenson and Lundbergh, 2002).

Other associated characteristics include sociodemographic factors. A scoping review of influenza vaccination uptake in older adults found that the impact of biological sex was variable: some studies report higher vaccination uptake rates in males and some in females (Roller-Wirnsberger et al., 2021). Additionally, a systematic review and meta-analysis of the determining factors for seasonal influenza vaccine uptake for community-dwelling older adults between 2000-2019 in previously published studies found that race/ethnicity may be associated with influenza vaccine uptake (Okoli et al., 2020). Household income and socioeconomic status were found to be among the most relevant determinants of vaccine uptake in these reviews; the Influenza Immunization Coverage Survey study also found that having lower income as compared to higher income was an independent predictor of non-vaccination (Farmanara et al., 2018; Okoli et al., 2020; Roller-Wirnsberger et al., 2021). Similarly, many studies have evaluated the impact of education on influenza vaccination uptake, and a study that analyzed the 2013/2014 CCHS data

found that having a lower level of education was associated with non-vaccination in groups at high risk of severe outcomes (those aged 18-64 with CMC and those aged 65 and older) and in healthy adults aged 18-64 (Roller-Wirnsberger et al., 2021; Roy et al., 2018). This study of CCHS data also found that the proportion of unvaccinated individuals varied significantly across provinces (Roy et al., 2018).

Another category of vaccination-associated factors includes those related to health and healthcare. The study of the 2013/2014 CCHS data found that not having a family doctor was significantly and independently related to non-vaccination (OR: 3.57, 95% Cl: 3.01, 4.24) (Roy et al., 2018). This association was also found for studies conducted in North American included in a systematic review and meta-analysis (Okoli et al., 2020). Negative health behaviors such as smoking and lack of exercise have also been associated with decreased vaccination uptake in multiple reviews and cross-sectional studies (Andrew et al., 2004; Chen et al., 2007; Okoli et al., 2020; Roller-Wirnsberger et al., 2021).

In contrast, a study of CCHS data of approximately 130,000 individuals who answered the question "Have you ever had a flu shot?" found that those with poor self-perceived health had a higher likelihood of vaccination (over three times greater for females and over two times greater for males) compared to those who reported their general health as "excellent", and hospital admission history was also associated with a 17% increase in the adjusted odds of vaccination (Chen et al., 2007). A similar national survey-based study in the United States also found a positive association between self-rated health and annual influenza vaccination for those who rated their health as "Fair" or "Poor" compared to "Excellent" (Watson and Oancea, 2020).

Vaccination Coverage and Targets

As noted previously, Canada has set a goal to achieve 80% influenza vaccination coverage by 2025 for groups at high risk for influenza complications by NACI (Public Health Agency of Canada, 2019b; Public Health Agency of Canada, 2021a). This is similar to the target set by the WHO, which suggested a global goal of 75% influenza vaccination coverage for those aged 65 years and older; similarly, this target has yet to be achieved by many countries (Roller-Wirnsberger et al., 2021). Influenza vaccination coverage in Canada decreased 9% in those aged

65 years and older between 2006 and 2014 (Smetana et al., 2018), potentially due to the multi-season impact of the 2009 A/H1N1 pandemic (Buchan and Kwong, 2016). Additionally, vaccination has stayed below 80% coverage across influenza seasons, even in groups at high risk of severe outcomes and their contacts (Public Health Agency of Canada, 2019a; Public Health Agency of Canada, 2021a; Public Health Agency of Canada, 2021c). According to reports by PHAC, while coverage is relatively high among adults 65 years of age and older (at 65%, 69%, and 70.7% during the 2015/2016, 2016/2017, and 2017/2018 influenza seasons respectively), adults aged 18-64 years with CMC still had coverage estimates that were well below Canada's vaccination target, with coverage measuring only 37% for the 2015/2016 and 2016/2017 seasons with a very slight increase to 39.4% for the 2017/2018 season (Public Health Agency of Canada, 2018; Public Health Agency of Canada, 2019a; Public Health Agency of Canada, 2021a). Similarly, during the 2019/2020 season, coverage in those aged 65 and older remained at 70%, although coverage increased to 44% for adults aged 18-64 years with CMC (Public Health Agency of Canada, 2020). The number of those who repeatedly get an influenza vaccination each year is also likely lower than these reported percentages which capture vaccination status in a single influenza season (Okoli et al., 2020). However, estimates of vaccination coverage among those who are household contacts or informal caregivers to individuals at high risk have not been reported.

Impact of COVID-19 on Influenza and Influenza Vaccination

Another factor that has recently affected the landscape of influenza vaccination is the SARS-CoV-2 pandemic. When the rapid global spread of SARS-CoV-2 overlapped with the 2020/2021 influenza season, the public health measures used to prevent the spread of SARS-CoV-2 caused a notable change in the incidence of influenza infections on a global scale, with very little influenza activity reported for both the southern and northern hemispheres, despite rigorous testing for influenza cases (Adlhoch et al., 2021). Canada's 2020/2021 influenza season followed a similar trend: Canada experienced no community circulation of influenza and had no laboratory-confirmed influenza outbreaks (Nwosu et al., 2021). There were also no influenza-associated severe outcomes (hospitalizations, intensive care unit admissions, or deaths) reported (Nwosu et al., 2021). These historically low rates occurred despite an increased number of influenza tests performed compared to previous influenza seasons (Pierce et al., 2021). Much of

this decline has been attributed to the use of non-pharmaceutical interventions, such as mask-wearing and school closures, to prevent COVID-19, which were in place during what would typically have been the 2020/2021 influenza season (Nwosu et al., 2021).

Despite the myriad of changes caused by the COVID-19 pandemic, influenza vaccination coverage during the 2020/2021 influenza season was not affected, even in groups at high risk of severe outcomes. According to estimates reported by PHAC, vaccination remained at 70% for those aged 65 and older, and for those adults under 65 with CMC, coverage was still only 40%; the estimates are very similar to the coverage estimates reported for the previous 3 seasons (including 70% for those aged 65 and older and 43% for adults under 65 with CMC during the 2018/2019 season and 70% for those aged 65 and older and 44% for adults under 65 with CMC during the 2019/2020 season) (Public Health Agency of Canada, 2019a; Public Health Agency of Canada, 2019b; Public Health Agency of Canada, 2020; Nwosu et al., 2021).

Because influenza vaccination coverage levels in groups at high risk of severe outcomes have plateaued below targeted levels and non-vaccination continues to be a persistent public health issue, it is important to examine which factors are associated with influenza non-vaccination among those in groups at high risk of severe outcomes in order to identify additional targets for vaccination campaigns to increase influenza vaccination coverage.

Increasing vaccination coverage is necessary to reduce the burden of influenza and prevent hospitalizations and deaths as well as to reduce influenza transmission in communities (Harrison et al., 2018; Papagiannis et al., 2020). As influenza-related healthcare visits have begun to rise again, high influenza vaccination coverage is especially important during the COVID-19 pandemic to reduce the number of vaccine-preventable hospitalizations and lessen the pressure on the health care system (Meyer and Lum, 2017; Roller-Wirnsberger et al., 2021).

Data Source Rationale

To identify characteristics that are associated with non-vaccination for those in groups at high risk of severe outcomes with the goal of targeting outreach efforts to these individuals to increase vaccine uptake, we quantified influenza vaccination coverage across Canada among several

groups. The data collected in the CLSA can be used to achieve this goal. The CLSA is a national study that follows over 50,000 participants from baseline in 2011-2015 with the objective of creating infrastructure for novel population-based research on aging (Kirkland et al., 2015).

Study Objectives

This study was designed to 1) estimate prevalence of influenza non-vaccination among adults at increased risk of severe influenza outcomes among 1a) all adults aged 65 years and older and 1b) adults aged 45-64 years with at least 1 CMC, 2) estimate prevalence of influenza non-vaccination among caregivers aged 45 years and older and among high-risk care recipients aged 65 years and older, and 3) identify factors associated with low vaccination uptake among each group. The next chapter includes manuscript 1, entitled "Influenza Vaccine Coverage and Factors Associated with Non-Vaccination Among High-Risk Adults in the Canadian Longitudinal Study on Aging", and presents the results of the analyses to estimate the prevalence of influenza non-vaccination for those at high risk of severe outcomes and identify factors associated with lack of vaccination among all adults aged 65 years and older and adults aged 45-64 years with at least 1 CMC.

Chapter 3: Manuscript 1

This chapter reports the results of my analysis of the prevalence of influenza non-vaccination and factors associated with non-vaccination among adults at high risk of influenza complications (objectives 1a, 1b, 3a, and 3b) using data from the CLSA first follow-up 1 (FUP1) with unvaccinated participants defined as those who reported that they had not been vaccinated within the previous 12 months at the time of the survey. In this analysis, I estimate the proportion of participants who reported that they had not been vaccinated within the previous 12 months at the time of the survey for adults aged 45-64 years with at least 1 CMC and for adults aged 65 years and older, and I assess the factors associated with non-vaccination for each of these 2 groups. This manuscript has been formatted according to the specifications of the journal *Vaccine*.

This manuscript goes beyond previously published work that evaluated factors associated with non-vaccination by examining a broad and comprehensive set of characteristics potentially associated with non-vaccination among a large sample of older adults participating in the CLSA to better understand influenza vaccine uptake. Most previous studies have been restricted to analyzing a limited number of covariates and small sample sizes, which limits opportunities to investigate the objectives outlined here. Because these analyses focus on influenza vaccination coverage and associated factors in those at high risk of severe outcomes, they will help inform public health outreach and interventions that could increase influenza vaccination uptake and ultimately prevent hospitalizations and deaths in these high-risk groups.

Influenza Vaccine Coverage and Factors Associated with Non-Vaccination Among High-Risk Adults in the Canadian Longitudinal Study on Aging

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Abstract

Background

Influenza vaccination is particularly recommended for those at high risk of severe outcomes. However, further research is needed to estimate the non-vaccination prevalence in these groups and identify the characteristics of the unvaccinated to increase coverage.

Objectives

The objectives of this study were to 1) estimate the prevalence of influenza non-vaccination and 2) assess factors associated with non-vaccination among adults at high risk of severe outcomes (i.e., adults aged ≥65 and adults aged 45-64 with at least one chronic medical condition (CMC).

Methods

This study is a secondary analysis of cross-sectional data collected from 2015-2018 among participants of the Canadian Longitudinal Study on Aging, a national cohort. For 2 groups at high risk of severe outcomes, we estimated group-specific non-vaccination prevalence and used logistic regression models to estimate adjusted odds ratios with 95% confidence intervals and identify factors associated with non-vaccination.

Results

In total, 29.5% (95% CI: 28.9%, 30.1%) of participants aged ≥65 and 49.9% (95% CI: 49.0%, 50.9%) of participants aged 45-64 with CMC reported NOT receiving an influenza vaccination in the past 12 months. For both groups, no recent contact with a family doctor and current smoking was strongly associated with non-vaccination after adjustment for multiple factors.

Discussion

Influenza vaccination is a proven strategy for preventing severe influenza outcomes. Non-vaccination prevalence was high in adults aged 45-64 with CMC, and those without family doctor contact had particularly high odds of non-vaccination. While successful efforts have

focused on healthcare personnel encouraging vaccination, campaigns to increase influenza vaccination among those without routine family doctor visits may improve coverage among those at high risk of severe outcomes in Canada.

Conclusion

Vaccination coverage among adults aged 45-64 with CMC and adults aged ≥65 remains suboptimal in Canada. Vaccination campaigns need alternate strategies to reach those at high risk of severe outcomes.

Keywords

Influenza, Vaccination, Canada, CMC, Older Adults, CLSA

Introduction

Although influenza is typically thought of as a mild illness, it leads to an estimated 3 to 5 million severe cases and up to 500,000 deaths worldwide each year.[1,2] Canada alone has an estimated 3,500 deaths and 12,200 hospitalizations annually, and the combined category of influenza and pneumonia remains in the top ten causes of death for Canada.[3,4]

Despite the provision of publicly funded influenza vaccines and the benefits of vaccination in groups at high risk of severe outcomes,[3,4] influenza vaccination coverage rates across Canada have remained suboptimal. For the 2015/2016 influenza season, vaccination in people 65 years and older was reported at 65%, followed by 69% during the 2016/2017 season and 70.7% during the 2017/2018 season.[3,5,6] The lack of coverage was especially pronounced for those aged under 65 with chronic medical conditions (CMC); this group had vaccination coverage of only 37% for the 2015/2016 and 2016/2017 influenza seasons, and only 39.4% during the 2017/2018 season.[3,5,6] More recently, during the 2019/2020 season, coverage in Canada increased to 44% in those aged under 65 with CMC, while coverage in those aged 65 and older stayed essentially stationary at 70%.[7] This lack of vaccination lead to the development of a vaccination coverage target of 80% by the Canadian government.[3] The identification of who is not getting their recommended seasonal vaccination within these groups at high risk of severe outcomes could help public health programs develop new vaccination campaign targets.

Annual influenza vaccination of groups at high risk of severe outcomes is routinely recommended as part of immunization services in Canada and many other countries where influenza vaccines are widely available. However, while the SARS-CoV-2 pandemic greatly disrupted the epidemiology of influenza, the pandemic did not have a notable impact on influenza vaccination trends in groups at high risk of severe outcomes, whose vaccination coverage was similar to that of the prior influenza season.[8] During the 2020/2021 influenza season, Canada had no community circulation of influenza,[8] and a markedly lower number of influenza cases were reported compared to previous seasons despite an increased number of influenza tests performed.[9] Despite this initial decrease in cases during the SARS-CoV-2 pandemic, in the 2021/2022 Canadian season, influenza activity and related healthcare visits have risen.[8,10] As the influenza seasons during the SARS-CoV-2 pandemic begin to regain their

typical severity and influenza vaccination has plateaued in groups at high risk of severe outcomes, it is still necessary to continue investigating who is not receiving influenza vaccinations among groups at high risk of severe outcomes despite recommendations to vaccinate. Because of the potential for vaccination to prevent hospitalizations and deaths, this knowledge will help us understand, track, and ideally intervene effectively to increase influenza vaccination uptake among those at high risk of severe outcomes.

There are multiple individual characteristics that increase the risk of complications from influenza infection. The National Advisory Committee on Immunization (NACI) includes adults with chronic medical conditions (CMC) and older adults (those aged 65 years and older) as individuals at high risk for influenza-related complications.[3] Individuals at greatest risk of influenza complications as noted by NACI include those with cardiac or pulmonary disorders (including asthma), diabetes mellitus, cancer, and renal disease.[11] Individuals in these groups are more likely to suffer hospitalizations and are at an increased risk of death following influenza infection compared to the general population.[11] Because of this, vaccination is "*particularly* recommended" by NACI for these individuals.

Many characteristics have been associated with missed influenza vaccination in a given season in Canadian adults. These include sociodemographic characteristics (such as younger age, lower education level, and residence in Quebec), health-related factors (such as smoking status, poor self-rated health, and the number of CMC), and healthcare utilization (such as lack of hospital admission history).[12-15] However, many studies focus on a limited set of covariates and do not account for the extensive range of characteristics that have been associated with vaccination in other settings or are of general public health importance, so it is difficult to assess their relative importance. These studies may also have insufficient power to detect significant differences within categories due to small sample sizes or may be subject to bias due to low response rates. At the national level, influenza vaccination coverage in Canada is primarily measured through the annual Seasonal Influenza Vaccination Coverage Survey.[16] These data include a breakdown of influenza vaccination by those at high risk of severe outcomes, age, and CMC (as well as sex in the report for the 2017/2018 influenza season), but the surveys also have response rates around 20%, only include about 2,000 adults each year, and are not designed to assess the broad range of

characteristics that may be associated with non-vaccination.[3,5,6] To reach the 80% vaccination coverage target, particularly for those within groups at high risk of severe outcomes, those most likely to remain unvaccinated need to be identified so that outreach efforts and resources can be allocated effectively to increase vaccination.

The Canadian Longitudinal Study on Aging (CLSA) provides a large dataset on the characteristics of its participants from the Comprehensive and Tracking cohorts collected during the first follow-up (FUP1) visit, with information on a wide range of factors including influenza vaccination status along with CMC (type and number), sociodemographic factors, healthcare utilization, and self-rated health and health behaviors.[17] These data can be used to address many of the limitations found in other surveys and similar studies.

The objectives of this study are to 1) estimate the prevalence of influenza non-vaccination in the 12 months prior and 2) assess factors associated with non-vaccination. We conducted this analysis for both adults aged 65 years and older and adults aged 45-64 years with at least 1 CMC, two groups at increased risk of severe influenza outcomes.

Materials and Methods

2.1 Data Source

The CLSA is a national study of 51,338 adults aged 45-85 at enrollment (2011-2015), recruited from all 10 Canadian provinces. The CLSA includes two cohorts that differ in type and intensity of data collection: the Comprehensive cohort (N=30,097 at baseline) and the Tracking cohort (N=21,241 at baseline). Data collection occurs every 3 years.[18] Participants were recruited using 3 sampling frames: the Canadian Community Health Survey (CCHS), random-digit dialing, and provincial health registries. Participants were randomly selected across 7 provinces in the Comprehensive cohort and across all 10 provinces in the Tracking cohort.[18]

Participants were not eligible to participate in the CLSA if they were a resident of a federal First Nations reserve or other First Nations settlement; a full-time member of the Canadian Armed Forces; a resident in the 3 territories; living in long-term care institutions; unable to respond in French or English; or cognitively impaired (as determined by interviewers). More information on

the CLSA study procedures and participant recruitment can be found elsewhere.[17-19] Additionally, the CLSA baseline and FUP1 protocol and other supporting documentation can be downloaded from the CLSA website (clsa-elcv.ca).

Approval to access the data was obtained from the CLSA (Application Number: 2006029) and ethics approval was obtained from the McGill University Institutional Research Board (Application Number: 21-02-048).

2.2 Analytic Sample

This study is a cross-sectional analysis of secondary data from respondents from both cohorts at FUP1— Comprehensive (N=27,765) and Tracking (N=17,050)— who had a valid response to the dependent variable and had reported whether or not they had received influenza vaccine in the past 12 months. From 2015 to 2018, data in the Tracking cohort were collected via phone interviews, while in the Comprehensive cohort data were collected via in-person interviews and site visits. We restricted our analyses to variables collected from participants within both cohorts.

2.3 Variables in Influenza Vaccination Coverage and Regression Analyses

The variables included in these analyses were those of potential public health interest for targeted vaccination campaigns and/or previously cited in the literature as potentially associated with influenza vaccination.[20-23] Variables were chosen prior to analysis. Data on race and education level were available for both cohorts from the CLSA baseline assessment and were also included in this analysis. The CLSA variables used in the analysis and variable categorizations can be found in the appendix (**Supplementary Table 1**).

Sociodemographic Variables

To identify additional individual factors associated with non-vaccination in those at high risk of severe outcomes, the independent variables of age, sex at birth, household income, province of residence, rural or urban classification, the number of people in the household (excluding the respondent), race, and education were evaluated. Age was categorized into 5 groups based on participant ages at FUP1: 45-54, 55-64, 65-74, 75-84, 85-94 years (the youngest participant was 46). Sex was male or female. Urban or rural categorization was binary; those classified as "Link

to DA" (individuals for whom there was insufficient postal code information for urban or rural categorization) were designated as missing due to the unspecified urban/rural mix in this category caused by insufficiently detailed postal code linkage.[24] Each of the 10 provinces were included in a categorical variable with Ontario as the reference category due to its early universal influenza vaccination program and higher vaccination coverage reported elsewhere. We categorized household income (less than $20000 CAD, 20000-<50000, ≥50000-<100000, ≥100000-<150000, and more than 150000) and number of people in household (0, 1, 2 or more). Race was dichotomized as "white" or "non-white". Education was categorized as an ordinal variable: less than secondary school graduation; secondary school graduation, no post-secondary education; some post-secondary education; and post-secondary degree/diploma.

Outcome

The outcome variable was self-reported influenza vaccination status within the past 12 months, based on the survey question "Have you had… Flu shot in the last 12 months". Respondents who answered "no" were categorized as not vaccinated and referred to as the non-vaccinated group throughout. Respondents who answered "yes" were categorized as vaccinated. Respondents who selected, "Don't Know/No Answer", who "Refused", or had a "Missing" response to this question were excluded from the analysis. The use of self-reported influenza vaccination status has been validated as a method with high sensitivity and moderate specificity compared to medical records for older adults.[25,26]

Chronic Medical Conditions

To evaluate non-vaccination in those with CMC, respondents who self-reported a physician diagnosis of any of the following conditions were considered to have at least one CMC. This set of conditions was selected based on NACI's definition of groups for whom influenza vaccination is particularly recommended, those with: heart disease, heart attack or myocardial infarction, high blood pressure or hypertension, lung problems, kidney disease or failure, asthma, diabetes, cancer, dementia or Alzheimer's disease, Parkinsonism or Parkinson's Disease, stroke or cerebrovascular accident (CVA), or ministroke or Transient Ischemic Attack (TIA).[11] Heart disease, lung problems, kidney disease or failure, asthma, diabetes, and cancer were considered separate binary variables. All other CMC listed (heart attack or myocardial infarction, high blood

pressure or hypertension, dementia or Alzheimer's disease, Parkinsonism or Parkinson's Disease, stroke or CVA, and ministroke or TIA) were combined into the variable "other CMC". The new variable "number of CMC" was derived by summing and categorizing the number of "yes" responses to each of the NACI CMC and "other CMC" variables for each participant (i.e., 0 CMC, 1 CMC, and 2 or more CMC in total).

Healthcare Utilization, Health Perception, and Health Behaviors

Healthcare utilization factors, hospitalization history, contact with a family doctor, and specialist contact, were also evaluated based on prior studies that identified these factors as potentially associated with influenza vaccination for individuals at high risk of severe outcomes, based on studies in Spain and Canada.[13,27-29] The association with healthcare utilization may be related to the participant being exposed to recommendations for influenza vaccination from health providers. Participant responses were dichotomized for each healthcare utilization variable: family doctor contact, specialist contact, and hospitalization history (**Supplementary Table 1**).

Since health status and the limitations and challenges associated with aging have been consistently identified as factors associated with influenza vaccination in Canada and the United States, including for those at high risk of severe outcomes,[12,30,31] we included self-rated health and self-rated healthy aging in our analyses. Self-rated health has been validated[32,33] as a way to measure health in general health surveys. In our analyses, self-rated health and self-rated healthy aging were included as ordinal variables with 5 categories: excellent (1), very good, good, fair, and poor (5). "Excellent" was used as the reference category for this variable as previous studies have found that older adults who self-report positive health were less likely to receive an influenza vaccination.[28,34]

The presence of limitations that lead to receiving care may impede the ability to receive influenza vaccination, particularly in older adults. Therefore, we wished to investigate this variable and we identified respondents who reported receiving professional or non-professional care in the past 12 months. Respondents were categorized as having received *non-professional* assistance based on the question "During the past 12 months, did you receive short-term or long-term assistance from family, friends, or neighbours because of a health condition or limitation

that affects your daily life, for any of the following activities?". Respondents were categorized as having received *professional* assistance based on the question "During the past 12 months, did you receive short-term or long-term professional assistance at home, because of a health condition or limitation that affects your daily life, for any of the following activities?". Participants who received both professional and non-professional care were included and analyzed in both care groups.

Participants were also asked about their current smoking behavior, alcohol consumption in the past 12 months, and exercise in the past 7 days (**Supplementary Table 1**), as these health behaviors were found to be associated with influenza vaccination in a 2004 study of the older (>65 years) adult Canadian population using data from the Canadian Study of Health and Aging.[12]

2.4 Statistical Analysis

To address our primary objectives, we assessed the level of influenza non-vaccination and factors associated with low vaccination uptake in groups at high risk of severe influenza outcomes: adults aged 65 years and older and adults aged 45-64 years with at least one CMC.

The analyses were conducted in R version 1.3.1073 using the "survey" package.

To accomplish objective 1 (estimate influenza non-vaccination prevalence among adults aged 65 and older and among adults aged 45-64 with CMC), we described the prevalence of self-reported influenza non-vaccination in the previous 12 months for each group overall and then within each group stratified according to the study categories of CMC, healthcare utilization, health perception, health behaviors, and sociodemographics.

To accomplish objective 2 (assess factors associated with a lack of vaccine uptake among those aged 65 and older and aged 45-64 with CMC), separate multivariable logistic regression models were used to estimate the association between the independent variables with influenza non-vaccination for each group of interest. We reported adjusted odds ratios (aOR) for the association

between each covariate included in each model and NOT having received influenza vaccine in the past 12 months, along with 95% confidence intervals (95% CIs).

In Model 1, we first estimated the associations between influenza non-vaccination and sociodemographic and type of CMC variables due to their consistent association with influenza vaccination across studies. Sociodemographic variables included age, province, sex, urban or rural classification, household income, education, and race; type of CMC variables included heart disease, lung problem, kidney disease, asthma, diabetes, cancer, and other CMC. In Model 2, we estimated the associations between influenza non-vaccination and direct measures of health (*number* of CMC, received professional care, received non-professional care, contact with family doctor, contact with medical specialist, hospitalization history) in addition to the sociodemographic and type of CMC variables included in Model 1. Finally, in Model 3, our full model, we estimated the associations between influenza non-vaccination and self-reported and/or indirect measures of health (self-rated health, self-rated healthy aging, exercise, smoking frequency, alcohol use) and the transmission-related number in household in addition to the covariates in Model 2. Using these nested models allowed us to investigate the independent association between a covariate and the outcome controlling for the effect of an increasingly comprehensive set of other variables. We report the results of our full model (Model 3) in the text and the results of all models in **Tables 3-4**.

Participants with missing values for one or more study variables were excluded in the analyses involving those variables. The highest percentage of missing values for a variable within each full dataset using this process was 15.1% (estimate of the total household income received by all household members, from all sources, before taxes and deductions, in the past 12 months). Responses of "Don't Know/No Answer", "Refused", "Missing", and "Did not complete a DCS visit" were considered as missing.

The CLSA uses complex sampling techniques and provides inflation and analytic weights for the baseline datasets to account for sample misrepresentation and to scale regression analyses for provincial and study site sizes, respectively. However, sampling weights were not used in these analyses as FUP1 weights were not available from the CLSA at the time of the analyses, and

CLSA baseline weights were not applicable for use with the FUP1 data. Despite the inability to use weights, we did stratify by age and included the variables sex and province in our analyses as recommended by the CLSA.[35] More information on the use of weights is available from the CLSA.[35]

Sensitivity analyses (two-sample tests of proportions) were performed to see if the time frame in which respondents were asked about influenza vaccination was associated with reporting being vaccinated. We compared the prevalence of vaccination by among participants surveyed during each of the typical Canadian influenza seasons in 2015-2018 (e.g., Nov. 1, 2015 to April 30, 2016) to those who were surveyed outside of each annual influenza season across all years combined (2015-2018).[3,36]

Results

3.1 Participant Demographics

The Comprehensive cohort included 27,765 participants, of which 0.31% (N=86) were excluded due to missing data for the outcome variable; the Tracking cohort included 17,050 participants, of which 2.09% (N=357) were similarly excluded. **Tables 1-2** present the demographic characteristics of each group by vaccination status. Information on the demographic characteristics by cohort for each group can be found in the appendix (**Supplementary Tables 2-3**). Data for both cohorts were collected between 2015 to 2018.

3.2 Influenza Vaccination in Adults Aged 65 Years and Older

The proportion of participants aged 65 years and older (N=23,226) who reported NOT receiving influenza vaccination in the past 12 months was 29.5% (95% CI: 28.9%, 30.1%) (**Table 3**). Vaccination prevalence was higher as self-rated health decreased; this trend was also true for self-reported perception of healthy aging. In terms of health behaviors, current daily smokers had a higher prevalence of non-vaccination (43.1%, 95% CI: 40.0%, 46.3%) than current non-smokers (28.8%, 95% CI: 28.2%, 29.4%). Nova Scotia residents had the lowest prevalence of non-vaccination (18.5%, 95% CI: 16.8%, 20.1%), while Quebec residents had the highest prevalence of non-vaccination (41.0%, 95% CI: 39.5%, 42.5%). All types of CMC had similar vaccination coverage.

Table 3 also presents the results of the logistic regression analyses for adults aged 65 years and older. For Model 3, our full model which included additional variables related to health behavior and status, as well as sociodemographic factors, type of CMC, and health-related factors from Models 1 and 2, currently "occasionally" smoking was strongly associated with non-vaccination (4.013, 95% CI: 1.431, 11.252) after controlling for all other variables in this model (**Table 3**). Residence in Newfoundland was associated with the highest odds of non-vaccination for any province (3.026, 95% CI: 1.671, 5.481) after controlling for all other variables. Those who identified as non-white had significantly higher odds of non-vaccination (2.021, 95% CI: 1.163, 3.513) than those who identified as white after controlling for all other variables. In contrast, those in the 85-94 age group had the lowest odds of remaining unvaccinated in this model (0.354, 95% CI: 0.204, 0.613) after controlling for all other variables. Those who had contact with a family doctor in the past 12 months had notably lower odds of remaining unvaccinated (0.375, 95% CI: 0.179, 0.786) than those without contact after controlling for all other variables. Having a post-secondary degree or diploma was significantly associated with lower odds of remaining unvaccinated (0.623, 95% CI: 0.429, 0.904) compared to those at the lowest education level after controlling for all other variables. Those in urban areas had lower odds of remaining unvaccinated compared to those in rural areas (0.641, 95% CI: 0.475, 0.865), and those who had contact with a medical specialist in the past 12 months had lower odds of remaining unvaccinated (0.755, 95% CI: 0.576, 0.988) than those without contact after controlling for all other variables.

3.3 Influenza Vaccination in Adults Aged 45-64 with CMC

In our second group of interest, who are also routinely recommended to receive annual influenza vaccination, adults aged 45-64 with CMC (N=10,685), 49.9% (95% CI: 49.0%, 50.9%) of participants reported NOT receiving influenza vaccination in the past 12 months (**Table 4**). The percentage of participants who reported not being vaccinated decreased as age increased. Quebec residents had the highest prevalence of non-vaccination (67.0%, 95% CI: 65.0%, 69.0%) among the provinces. A higher percentage of those who were current daily smokers reported not being vaccinated than those who currently did not smoke (60.8%, 95% CI: 57.6%, 64.0% vs 48.7%,

95% CI: 47.7%, 49.7%, respectively). Vaccination coverage did not notably differ across type of CMC, although groups with a higher number of CMC reported higher vaccination coverage.

Table 4 also presents the results of the logistic regression analysis for adults aged 45-64 years with CMC. For Model 3, which included additional variables related to health behavior and status, as well as adjusted for the sociodemographic, type of CMC, and health-related factors from Models 1 and 2, the odds of non-vaccination for Quebec residents compared to Ontario residents were largest (2.990, 95% CI: 1.864, 4.796) after controlling for all other variables in Model 3 (**Table 4**). Those who currently smoke daily had notably higher odds of non-vaccination than current non-smokers (1.892, 95% CI: 1.120, 3.194) after controlling for all other variables. A history of hospitalization was also strongly associated with non-vaccination (1.829, 95% CI: 1.150, 2.910) after controlling for all other variables. Contact with a family doctor in the past 12 months was associated with extremely low odds of remaining unvaccinated (0.203, 95% CI: 0.092, 0.448) after controlling for all other variables. Residence in urban areas was also associated with lower odds of remaining unvaccinated (0.611, 95% CI: 0.411, 0.911) compared to residence in rural areas after controlling for all other variables. Occasional drinkers had lower odds of remaining unvaccinated (0.618, 95% CI: 0.383, 0.997) than those who never drank after controlling for all other variables in this model. The only CMC to be significantly associated with lower odds of remaining unvaccinated compared to those without that CMC was cancer after controlling for all other variables (**Table 4**).

3.4 Sensitivity Analysis

For those aged 45-64 with CMC, the prevalence of influenza non-vaccination was not significantly different between individuals surveyed during the typical Canadian flu season (N=5,471), November-April, and individuals surveyed outside those months (N=5,214) for both cohorts (Comprehensive Cohort, p-value=0.715; Tracking Cohort, p-value=0.939). Having been surveyed during (N=11,704) or outside (N=11,522) the typical Canadian flu season was also insignificant for those aged 65 years and older for both cohorts (Comprehensive Cohort, p-value=0.485; Tracking Cohort, p-value=0.229).

Discussion

Despite the provision of publicly funded influenza vaccines for groups at high risk of severe outcomes across Canada and national recommendations for annual vaccination among these groups, vaccination coverage remains under the target of 80% coverage.[3,4] In this study, we describe the prevalence of influenza non-vaccination and identify factors associated with non-vaccination using the large and robust data available from the CLSA FUP1 (2015-2018). We found that the prevalence of non-vaccination was 29.5% (95% CI: 28.9%, 30.1%) among those aged 65 and older and 49.9% (95% CI: 49.0%, 50.9%) among those aged 45-64 who had at least one CMC. In the fully adjusted model, for both groups, contact with a family doctor, current non-smoking, and residence in urban areas were strongly associated with lower odds of remaining unvaccinated compared to those without contact, and non-vaccination prevalence and association with non-vaccination varied widely by province. For those with CMC, hospitalization in the past 12 months was also strongly associated with non-vaccination.

The vaccination coverage estimates from 2015-2018 in this study were somewhat similar to those reported in Canada by NACI during the period of CLSA data collection, although these data were cross-sectional and covered multiple influenza seasons during the data collection period, as well as only examining those with CMC aged 45-64. During the 2015/2016 influenza season, the Public Health Agency of Canada reported that those aged 18-64 with CMC had 37.2% coverage (95% CI: 31.9%, 42.5%) compared to a coverage rate of 64.6% (95% CI: 60.2%, 68.9%)in individuals 65 and older.[3] Those aged 65 and older had vaccination rates of 69% for the 2016/2017 influenza season and 70.7% for the 2017/2018 season, while coverage in those aged under 65 with CMC respectively remained at 37% and 39.4% for those influenza seasons.[5,6] We estimated that 29.5% (95% CI: 28.9%, 30.1%) of adults aged 65 and older and 49.9% (95% CI: 49.0%, 50.9%) of those aged 45-64 with CMC had missed receiving their recommended influenza vaccine in the previous 12 months for the study period covering 2015 to 2018. These results demonstrate the need to substantially increase vaccination uptake to meet the 80% coverage target.

We found doctor visits in the past 12 months to be associated with lower odds of remaining unvaccinated in each of the groups at high risk of severe outcomes examined in the fully adjusted model. This may indicate a similar pattern of groups at high risk of severe outcomes being more

exposed to medical care and therefore influenza vaccination recommendations. In contrast, hospitalization history in the past 12 months was significantly associated with higher odds of non-vaccination for those aged 45-64 with CMC in the fully adjusted model. The type of medical care received, the type of specialist visited, and the reason for hospitalization may play a role in determining whether an individual is directly and personally recommended to be vaccinated by a health care professional during a health care encounter: a survey of subspecialists in the United States who provide outpatient care to patients at high risk of severe outcomes aged 45-64 found that stocking and recommendation of the influenza vaccine varies.[37,38] In another Canadian study of influenza vaccination, researchers reported that presence of a CMC was associated with a lower risk of non-vaccination, possibly due to the contact with health professionals that accompanies the diagnosis of a chronic medical condition.[14]

This study adds additional evidence to the existing collection of factors associated with influenza vaccination. Despite several previous cross-sectional studies that have found low self-rated health to be associated with higher influenza vaccination rates for older adult participants, [13,28,37,39] we did not find significant associations between self-rated health and non-vaccination for any group in the fully adjusted model. Additionally, we found that non-vaccination prevalence and the odds of non-vaccination were highly variable by province of residence. Although all provinces publicly fund influenza vaccination for groups at high risk of severe outcomes, there may be differences in existing policies or vaccination barriers within each province, such as the ability of pharmacists to give seasonal influenza vaccines, a factor that has been shown to be associated with higher coverage.[40] Provinces with lower coverage may need additional support for their influenza vaccination programs.

Communicating the importance of vaccination needs to be applied toward those at high risk of severe outcomes, particularly those aged 45-64 with CMC, to improve vaccination coverage and reduce hospitalizations and deaths from influenza. One study found that higher influenza vaccine coverage among Swiss adults at high risk of severe outcomes could be achieved by having practitioners systematically propose vaccination to their patients.[41] A systematic review of methods of influenza vaccination distribution found that influenza coverage could be increased in healthcare settings through methods such as standing orders for influenza vaccination in

hospital and tertiary-care settings;[42] this finding could be adapted to address the lack of vaccination in those aged 45-64 with CMC and a history of hospitalization. In order to increase awareness of influenza vaccination recommendations among those who do not have contact with a family doctor, additional strategies that deliver recommendations more broadly, perhaps by expanding vaccination availability in alternative sites such as the use of pharmacists who can administer influenza vaccines,[43] could increase public communications and disseminate information about influenza vaccine safety, efficacy, and benefits in groups at high risk of severe outcomes.[37]

This study has multiple strengths, including the ability to precisely estimate vaccination coverage due to the large sample size, the provision of province-level vaccination estimates, and the wide range of available covariates across many vaccination-associated domains. This study, as with most observational studies, has several limitations. For one, our results apply only to community-dwelling adults since participants living in institutions were ineligible to participate in the CLSA.[44] Additionally, many of the variables used in this study are based on self-report, which may be less reliable compared to objective measures; however, the key outcome of interest, self-reported influenza vaccination, has been validated in previous studies.[25,26] Lastly, the datasets used in this study did not include information on participants' reasons for not receiving an influenza vaccine in the past 12 months; further research is needed to characterize the barriers to vaccination.

Conclusion

Influenza vaccination coverage in individuals at high risk of severe influenza remains below national targets in Canada, particularly among those with CMC aged 45-64 but also among those aged 65 years and older. For both groups, contact with a family doctor was strongly associated with lower odds of remaining unvaccinated, and vaccination uptake varied between provinces. This suggests that interventions to increase influenza vaccination among groups at high risk of severe outcomes should focus on finding ways to increase awareness about vaccination recommendations among the general population potentially via venues that older adults and those with CMC frequent, such as pharmacies, to improve overall vaccination rates, particularly in low-coverage provinces.

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Declaration of competing interest

The authors state that no conflicts of interest exist.

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Table 1. Demographic Characteristics by Influenza Vaccination: Participants Aged 65 Years and Older (N=23,226)

	Received Influenza Vaccination in Last 12 Months (N=16,373)	Did Not Receive Influenza Vaccination in Last 12 Months (N=6,853)
	N(%)	N(%)
Sociodemographics		
Age		
65-74	8591(52.5)	4606(67.2)
75-84	6378(39.0)	1888(27.5)
85-94	1404(8.6)	359(5.2)
Province of Residence		
Newfoundland	962(5.9)	500(7.3)
Prince Edward Island	386(2.4)	121(1.8)
Nova Scotia	1709(10.4)	387(5.6)
New Brunswick	405(2.5)	161(2.3)
Quebec	2546(15.5)	1770(25.8)
Ontario	3910(23.9)	1257(18.3)
Manitoba	1451(8.9)	592(8.6)
Saskatchewan	375(2.3)	169(2.5)
Alberta	1650(10.1)	593(8.7)
British Columbia	2975(18.2)	1298(18.9)
Sex		
Male	8241(50.3)	3331(48.6)
Female	8127(49.6)	3513(51.3)
Urban or Rural		
Urban	14160(86.5)	5707(83.3)
Rural	1533(9.4)	782(11.4)
Household Income		
< 20000	764(4.7)	537(7.8)
≥20000-<50000	4690(28.6)	2367(34.5)
≥50000-<100000	6266(38.3)	2293(33.5)
≥100000-<150000	2190(13.4)	674(9.8)
≥150000	1080(6.6)	370(5.4)
Education		
Less than secondary school graduation	1336(8.2)	653(9.5)
Secondary school graduation, no post-secondary education	1792(10.9)	850(12.4)
Some post-secondary education	1282(7.8)	569(8.3)
Post-secondary degree/diploma	11920(72.8)	4751(69.3)
Race		
White	15841(96.8)	6541(95.4)
Non-White	521(3.2)	298(4.3)

Table 2. Demographic Characteristics by Influenza Vaccination: Participants Aged 45-64 Years with at Least 1 CMC (N=10,685)

	Received Influenza Vaccination in Last 12 Months (N=5,350)	Did Not Receive Influenza Vaccination in Last 12 Months (N=5,335)
	N(%)	N(%)
Sociodemographics		
Age		
45-54	1153(21.6)	1502(28.2)
55-64	4197(78.4)	3833(71.8)
Province of Residence		
Newfoundland	355(6.6)	404(7.6)
Prince Edward Island	104(1.9)	84(1.6)
Nova Scotia	558(10.4)	286(5.4)
New Brunswick	136(2.5)	131(2.5)
Quebec	699(13.1)	1422(26.7)
Ontario	1310(24.5)	1079(20.2)
Manitoba	474(8.9)	441(8.3)
Saskatchewan	120(2.2)	121(2.3)
Alberta	660(12.3)	487(9.1)
British Columbia	932(17.4)	879(16.5)
Sex		
Male	2554(47.7)	2725(51.1)
Female	2793(52.2)	2607(48.9)
Urban or Rural		
Urban	4644(86.8)	4434(83.1)
Rural	501(9.4)	646(12.1)
Household Income		
< 20000	254(4.7)	268(5.0)
≥20000-<50000	729(13.6)	851(16.0)
≥50000-<100000	1674(31.3)	1724(32.3)
≥100000-<150000	1156(21.6)	1183(22.2)
≥150000	1292(24.1)	1057(19.8)
Education		
Less than secondary school graduation	180(3.4)	240(4.5)
Secondary school graduation, no post-secondary education	518(9.7)	591(11.1)
Some post-secondary education	404(7.6)	378(7.1)
Post-secondary degree/diploma	4240(79.3)	4120(77.2)
Race		
White	5046(94.3)	5016(94.0)
Non-White	298(5.6)	314(5.9)

Table 3. Factors Associated with Non-Vaccination Against Seasonal Influenza Among Participants Aged 65 Years and Older (N=23,226)

	Proportion Unvaccinated (95% CI)	Model 1[a] (N=4,207)	Model 2[a] (N=1,741)	Model 3[a] (N=1,724)
Total	0.295 (0.289, 0.301)			
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Age				
65-74	0.349 (0.341, 0.357)	Ref	Ref	Ref
75-84	0.228 (0.219, 0.237)	0.606 (0.515, 0.714)	0.602 (0.467, 0.778)	0.597 (0.458, 0.778)
85-94	0.204 (0.185, 0.222)	0.415 (0.283, 0.607)	0.380 (0.223, 0.649)	0.354 (0.204, 0.613)
Province of Residence				
Ontario	0.243 (0.232, 0.255)	Ref	Ref	Ref
Newfoundland	0.342 (0.318, 0.366)	2.010 (1.471, 2.746)	2.928 (1.665, 5.149)	3.026 (1.671, 5.481)
Prince Edward Island	0.239 (0.202, 0.276)	0.719 (0.380, 1.360)	0.638 (0.325, 1.252)	0.645 (0.326, 1.276)
Nova Scotia	0.185 (0.168, 0.201)	0.620 (0.440, 0.872)	0.725 (0.433, 1.214)	0.674 (0.395, 1.151)
New Brunswick	0.284 (0.247, 0.322)	1.090 (0.640, 1.858)	1.042 (0.586, 1.854)	1.037 (0.577, 1.863)
Quebec	0.410 (0.395, 0.425)	1.826 (1.460, 2.284)	1.632 (1.144, 2.328)	1.629 (1.137, 2.333)
Manitoba	0.290 (0.270, 0.309)	1.048 (0.761, 1.443)	1.076 (0.619,1.869)	1.129 (0.648, 1.969)
Saskatchewan	0.311 (0.272, 0.350)	1.056 (0.540, 2.066)	1.024 (0.506, 2.074)	0.984 (0.471, 2.058)
Alberta	0.264 (0.246, 0.283)	1.119 (0.826, 1.516)	1.372 (0.869, 2.166)	1.377 (0.866, 2.188)
British Columbia	0.304 (0.290, 0.318)	1.397 (1.117, 1.747)	1.348 (0.931, 1.951)	1.363 (0.938, 1.979)
Sex				
Male	0.288 (0.280, 0.296)	Ref	Ref	Ref
Female	0.302 (0.293, 0.310)	1.034 (0.886, 1.207)	1.083 (0.849, 1.382)	1.101 (0.851, 1.423)
Urban or Rural				
Rural	0.338 (0.319, 0.357)	Ref	Ref	Ref
Urban	0.287 (0.281, 0.294)	0.811 (0.640, 1.027)	0.650 (0.485, 0.872)	0.641 (0.475, 0.865)
Household Income				
< 20000	0.413 (0.386, 0.440)	Ref	Ref	Ref
≥20000-<50000	0.335 (0.324, 0.346)	0.914 (0.692, 1.208)	0.987 (0.653, 1.492)	0.997 (0.643, 1.546)
≥50000-<100000	0.268 (0.259, 0.277)	0.607 (0.453, 0.813)	0.653 (0.419, 1.019)	0.624 (0.385, 1.011)
≥100000-<150000	0.235 (0.220, 0.251)	0.545 (0.383, 0.775)	0.750 (0.433, 1.299)	0.721 (0.395, 1.315)
≥150000	0.255 (0.233, 0.278)	0.566 (0.367, 0.873)	0.507 (0.244, 1.054)	0.495 (0.228, 1.075)
Education				
Less than secondary school graduation	0.328 (0.308, 0.349)	Ref	Ref	Ref
Secondary school graduation, no post-secondary education	0.322 (0.304, 0.340)	1.135 (0.835, 1.544)	0.805 (0.521, 1.243)	0.836 (0.536, 1.304)
Some post-secondary education	0.307 (0.286, 0.328)	1.104 (0.789, 1.545)	0.793 (0.483, 1.302)	0.845 (0.509, 1.402)
Post-secondary degree/diploma	0.285 (0.278, 0.292)	0.841 (0.650, 1.088)	0.597 (0.416, 0.857)	0.623 (0.429, 0.904)

Race				
White	0.292 (0.286, 0.298)	Ref	Ref	Ref
Non-White	0.364 (0.331, 0.397)	1.773 (1.331, 2.363)	1.840 (1.087, 3.117)	2.021 (1.163, 3.513)
CMC by Type				
Heart Disease	0.237 (0.224, 0.250)	0.883 (0.739, 1.057)	0.925 (0.678, 1.262)	0.908 (0.659, 1.252)
Lung Problems	0.226 (0.208, 0.245)	0.674 (0.519, 0.876)	0.734 (0.489, 1.102)	0.670 (0.437, 1.028)
Kidney Disease or Failure	0.248 (0.221, 0.275)	0.727 (0.530, 0.995)	0.696 (0.429, 1.129)	0.663 (0.398, 1.103)
Asthma	0.228 (0.211, 0.244)	0.819 (0.652, 1.029)	1.192 (0.837, 1.697)	1.186 (0.827, 1.702)
Diabetes	0.242 (0.227, 0.257)	0.905 (0.776, 1.055)	1.322 (0.938, 1.864)	1.396 (0.980, 1.990)
Cancer	0.247 (0.236, 0.258)	0.695 (0.583, 0.829)	0.677 (0.497, 0.922)	0.694 (0.506, 0.952)
Other CMC	0.264 (0.256, 0.271)	0.735 (0.623, 0.867)	0.938 (0.645, 1.362)	0.999 (0.683, 1.460)
Number of CMC				
0	0.371 (0.359, 0.384)		Ref	Ref
1	0.307 (0.297, 0.318)		0.867 (0.481, 1.561)	0.801 (0.440, 1.457)
≥ 2	0.235 (0.227, 0.244)		0.545 (0.253, 1.175)	0.489 (0.222, 1.078)
Care or Assistance Received by Type				
Professional	0.229 (0.213, 0.245)		1.080 (0.772, 1.512)	1.120 (0.795, 1.576)
Non-Professional	0.254 (0.241, 0.267)		1.257 (0.916, 1.723)	1.247 (0.901, 1.726)
Healthcare Utilization by Type				
Family Doctor Contact	0.280 (0.274, 0.286)		0.384 (0.182, 0.811)	0.375 (0.179, 0.786)
Specialist Contact	0.263 (0.256, 0.270)		0.750 (0.576, 0.976)	0.755 (0.576, 0.988)
Hospitalization History	0.261 (0.245, 0.277)		0.978 (0.694, 1.378)	1.047 (0.738, 1.484)
Self-Rated Health				
Excellent	0.339 (0.324, 0.354)			Ref
Very Good	0.295 (0.286, 0.305)			0.969 (0.569, 1.652)
Good	0.283 (0.273, 0.294)			0.883 (0.507, 1.538)
Fair	0.273 (0.255, 0.290)			1.110 (0.592, 2.083)
Poor	0.229 (0.194, 0.263)			0.754 (0.300, 1.895)
Number in Household				
0	0.307 (0.297, 0.318)			Ref
1	0.281 (0.273, 0.288)			1.121 (0.845, 1.488)
≥ 2	0.339 (0.319, 0.359)			0.886 (0.560, 1.402)
Self-Rated Healthy Aging				
Excellent	0.331 (0.317, 0.345)			Ref
Very Good	0.288 (0.279, 0.297)			1.096 (0.714, 1.683)
Good	0.287 (0.277, 0.298)			0.863 (0.544, 1.367)
Fair	0.284 (0.263, 0.306)			1.124 (0.623, 2.026)
Poor	0.260 (0.213, 0.308)			0.865 (0.297, 2.517)
Exercise				

None or Seldom	0.295 (0.288, 0.301)			Ref
Sometimes or Often	0.298 (0.284, 0.311)			0.965 (0.677, 1.376)
Smoking				
Not at All	0.288 (0.282, 0.294)			Ref
Occasionally	0.376 (0.311, 0.442)			4.013 (1.431, 11.252)
Daily	0.431 (0.400, 0.463)			1.469 (0.908, 2.377)
Alcohol				
Never	0.316 (0.301, 0.331)			Ref
Occasionally	0.325 (0.309, 0.341)			1.008 (0.696, 1.460)
Regular	0.284 (0.277, 0.291)			0.994 (0.731, 1.351)

[a]Grey cells indicate variables that were not included in the model represented by that column.

Table 4. Factors Associated with Non-Vaccination Against Seasonal Influenza Among Participants Aged 45-64 Years with at Least 1 CMC (N=10,685)

	Proportion Unvaccinated (95% CI)	Model 1[a] (N=2,418)	Model 2[a] (N=935)	Model 3[a] (N=933)
Total	0.499 (0.490, 0.509)			
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Age				
45-54	0.566 (0.547, 0.585)	Ref	Ref	Ref
55-64	0.477 (0.466, 0.488)	0.646 (0.525, 0.796)	0.747 (0.520, 1.074)	0.813 (0.555, 1.191)
Province of Residence				
Ontario	0.452 (0.432, 0.472)	Ref	Ref	Ref
Newfoundland	0.532 (0.497, 0.568)	1.301 (0.921, 1.838)	1.326 (0.669, 2.630)	1.333 (0.684, 2.600)
Prince Edward Island	0.447 (0.376, 0.518)	1.148 (0.581, 2.269)	1.614 (0.755, 3.450)	1.618 (0.734, 3.570)
Nova Scotia	0.339 (0.307, 0.371)	0.512 (0.356, 0.736)	0.869 (0.482, 1.567)	0.909 (0.498, 1.659)
New Brunswick	0.491 (0.431, 0.551)	1.008 (0.609, 1.668)	1.322 (0.753, 2.321)	1.303 (0.732, 2.317)
Quebec	0.670 (0.650, 0.690)	2.117 (1.617, 2.772)	2.760 (1.745, 4.365)	2.990 (1.864, 4.796)
Manitoba	0.482 (0.450, 0.514)	1.043 (0.755, 1.442)	1.888 (0.956, 3.730)	2.009 (0.975, 4.137)
Saskatchewan	0.502 (0.439, 0.565)	1.493 (0.794, 2.809)	1.854 (0.934, 3.679)	1.916 (0.963, 3.812)
Alberta	0.425 (0.396, 0.453)	1.007 (0.733, 1.383)	1.872 (1.145, 3.060)	1.923 (1.172, 3.157)
British Columbia	0.485 (0.462, 0.508)	0.983 (0.761, 1.270)	1.583 (0.980, 2.557)	1.588 (0.965, 2.613)
Sex				
Male	0.516 (0.503, 0.530)	Ref	Ref	Ref
Female	0.483 (0.469, 0.496)	0.858 (0.722, 1.020)	0.875 (0.656, 1.166)	0.945 (0.699, 1.278)
Urban or Rural				
Rural	0.563 (0.535, 0.592)	Ref	Ref	Ref
Urban	0.488 (0.478, 0.499)	0.631 (0.473, 0.843)	0.635 (0.430, 0.939)	0.611 (0.411, 0.911)
Household Income				
< 20000	0.513 (0.471, 0.556)	Ref	Ref	Ref
≥20000-<50000	0.539 (0.514, 0.563)	1.195 (0.832, 1.717)	1.346 (0.743, 2.437)	1.553 (0.811, 2.970)
≥50000-<100000	0.507 (0.491, 0.524)	0.925 (0.657, 1.303)	1.045 (0.576, 1.897)	1.218 (0.626, 2.371)
≥100000-<150000	0.506 (0.486, 0.526)	0.901 (0.625, 1.298)	1.022 (0.535, 1.954)	1.112 (0.535, 2.311)
≥150000	0.450 (0.430, 0.470)	0.709 (0.487, 1.034)	0.816 (0.419, 1.590)	0.890 (0.420, 1.885)
Education				
Less than secondary school graduation	0.571 (0.524, 0.619)	Ref	Ref	Ref
Secondary school graduation, no post-secondary education	0.533 (0.504, 0.562)	1.228 (0.785, 1.921)	1.804 (0.939, 3.465)	1.618 (0.817, 3.204)
Some post-secondary education	0.483 (0.448, 0.518)	1.201 (0.761, 1.897)	1.501 (0.738, 3.054)	1.265 (0.610, 2.624)

Post-secondary degree/diploma	0.493 (0.482, 0.504)	1.060 (0.723, 1.556)	1.131 (0.649, 1.970)	1.011 (0.563, 1.815)
Race				
White	0.499 (0.489, 0.508)	Ref	Ref	Ref
Non-White	0.513 (0.473, 0.553)	1.147 (0.837, 1.571)	1.149 (0.624, 2.114)	1.166 (0.630, 2.161)
CMC by Type				
Heart Disease	0.468 (0.440, 0.497)	0.864 (0.671, 1.112)	0.755 (0.490, 1.163)	0.733 (0.467, 1.151)
Lung Problems	0.449 (0.419, 0.480)	0.852 (0.639, 1.136)	1.052 (0.652, 1.696)	1.022 (0.625, 1.671)
Kidney Disease or Failure	0.492 (0.446, 0.539)	0.642 (0.432, 0.954)	0.517 (0.259, 1.032)	0.524 (0.262, 1.050)
Asthma	0.466 (0.448, 0.483)	0.687 (0.556, 0.849)	0.686 (0.457, 1.030)	0.676 (0.443, 1.031)
Diabetes	0.438 (0.414, 0.461)	0.686 (0.574, 0.820)	0.840 (0.565, 1.247)	0.809 (0.541, 1.209)
Cancer	0.483 (0.463, 0.504)	0.947 (0.746, 1.202)	1.624 (1.084, 2.435)	1.655 (1.094, 2.505)
Other CMC	0.488 (0.475, 0.500)	0.770 (0.639, 0.927)	0.955 (0.618, 1.476)	0.897 (0.570, 1.412)
Number of CMC				
1	0.539 (0.527, 0.551)		Ref	Ref
≥ 2	0.432 (0.416, 0.447)		0.620 (0.375, 1.026)	0.640 (0.378, 1.084)
Care or Assistance Received by Type				
Professional	0.424 (0.382, 0.465)		0.830 (0.513, 1.343)	0.825 (0.500, 1.360)
Non-Professional	0.448 (0.424, 0.472)		0.969 (0.656, 1.430)	0.919 (0.620, 1.362)
Healthcare Utilization by Type				
Family Doctor Contact	0.484 (0.474, 0.494)		0.214 (0.101, 0.455)	0.203 (0.092, 0.448)
Specialist Contact	0.465 (0.453, 0.477)		0.837 (0.611, 1.146)	0.820 (0.596, 1.128)
Hospitalization History	0.473 (0.441, 0.506)		1.711 (1.097, 2.667)	1.829 (1.150, 2.910)
Self-Rated Health				
Excellent	0.512 (0.485, 0.539)			Ref
Very Good	0.511 (0.496, 0.527)			1.671 (0.602, 4.635)
Good	0.503 (0.487, 0.519)			2.137 (0.745, 6.136)
Fair	0.459 (0.432, 0.486)			1.918 (0.634, 5.802)
Poor	0.417 (0.363, 0.470)			2.564 (0.675, 9.742)
Number in Household				
0	0.514 (0.491, 0.536)			Ref
1	0.478 (0.464, 0.492)			0.949 (0.642, 1.402)
≥ 2	0.523 (0.507, 0.539)			1.378 (0.879, 2.161)
Self-Rated Healthy Aging				
Excellent	0.528 (0.503, 0.554)			Ref
Very Good	0.506 (0.491, 0.521)			0.782 (0.400, 1.528)
Good	0.493 (0.477, 0.509)			0.846 (0.422, 1.698)
Fair	0.466 (0.437, 0.496)			0.612 (0.278, 1.347)

Poor	0.456 (0.396, 0.516)			0.817 (0.295, 2.266)
Exercise				
None or Seldom	0.502 (0.491, 0.513)			Ref
Sometimes or Often	0.491 (0.471, 0.510)			1.068 (0.701, 1.627)
Smoking				
Not at All	0.487 (0.477, 0.497)			Ref
Occasionally	0.577 (0.511, 0.643)			1.783 (0.545, 5.828)
Daily	0.608 (0.576, 0.640)			1.892 (1.120, 3.194)
Alcohol				
Never	0.481 (0.454, 0.508)			Ref
Occasionally	0.467 (0.442, 0.493)			0.618 (0.383, 0.997)
Regular	0.508 (0.497, 0.519)			0.967 (0.637, 1.467)

[a]Grey cells indicate variables that were not included in the model represented by that column.

Supplementary Table 1: Variable Categorization

CLSA Question and Label	CLSA Participant Response → Variable Characterization for Models
Have you had… Flu shot in the last 12 months PHB_FLUV_COF1[a] PHB_FLUV_TRF1[a]	1 = Yes 2 = No 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Participant age at FU1 (in years) AGE_NMBR_COF1 AGE_NMBR_TRF1	45-54, 55-64, 65-74, 75-84, 85-94
Province of residence WGHTS_PROV_COF1 WGHTS_PROV_TRF1	Newfoundland, Prince Edward Island[b], Nova Scotia, New Brunswick[b], Quebec, Ontario, Manitoba, Saskatchewan[b], Alberta, British Columbia
What was your sex at birth? SDC_BTHSEX_COF1 SDC_BTHSEX_TRF1	1 = Male → 0 2 = Female → 1 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
Urban/ rural classification SDC_URBAN_RURAL_COF1 SDC_URBAN_RURAL_TRF1	0 = Rural area → Rural 1 = Urban core → Urban 2 = Urban fringe → Urban 3 = Rural fringe in CMA/CAs → Rural 4 = Urban Areas out CMA/CAs → Urban 5 = Rural fringe out CMA/CAs → Rural 6 = Secondary urban core → Urban 9 = Link to DA → NA -88888 = Missing → NA
What is your best estimate of the total household income received by all household members, from all sources, before taxes and deductions, in the past 12 months? INC_TOT_COF1 INC_TOT_TRF1	1 = Less than $20,000 2 = $20,000 or more, but less than $50,000 3 = $50,000 or more, but less than $100,000 4 = $100,000 or more, but less than $150,000 5 = $150,000 or more 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern
Highest Level of Education - Respondent, 4 Levels ED_UDR04_COM ED_UDR04_TRM	1 = Less than secondary school graduation 2 = Secondary school graduation, no post-secondary education 3 = Some post-secondary education 4 = Post-secondary degree/diploma

	9 = At least one required question was not answered → NA
Cultural / Racial Background SDC_DCGT_COM SDC_DCGT_TRM	1 = White only → White 2 = Black only → Non-White 3 = Korean only → Non-White 4 = Filipino only → Non-White 5 = Japanese only → Non-White 6 = Chinese only → Non-White 7 = South Asian only → Non-White 8 = Southeast Asian only → Non-White 9 = Arab only → Non-White 10 = West Asian only → Non-White 11 = Latin American only → Non-White 12 = Other racial or cultural origin (only) → Non-White 13 = Multiple racial or cultural origins → Non-White 99 = Required question was not answered → NA
Type of CMC Has a doctor ever told you that you have heart disease (including congestive heart failure or CHF)? CCC_HEART_COF1 CCT_HEART_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Type of CMC Has a doctor told you that you have/had any of the following: emphysema, chronic bronchitis, chronic obstructive pulmonary disease (COPD), or chronic changes in lungs due to smoking? CCC_COPD_COF1 CCT_COPD_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Has a doctor ever told you that you have kidney disease or kidney failure? CCC_KIDN_COF1 CCT_KIDN_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Has a doctor ever told you that you have asthma? CCC_ASTHM_COF1 CCT_ASTHM_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA

	-88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Were you diagnosed with? Type I, Type II, Neither [Type of Diabetes] DIA_TYPE_COF1 CCT_DIABTYPE_TRF1	1 = Type I → 1 2 = Type II → 1 3 = Neither → 0 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Type of CMC … Has a doctor ever told you that you had cancer? CCC_CANC_COF1 CCT_CANC_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Other CMC: **composite variable**[c] Has a doctor ever told you that you have had a heart attack or myocardial infarction?; Has a doctor ever told you that you have high blood pressure or hypertension?; Has a doctor ever told you that you have dementia or Alzheimer's disease?;. Has a doctor ever told you that you had Parkinsonism or Parkinson's Disease?; Has a doctor ever told you that you have experienced a Stroke or CVA (cerebrovascular accident)?; Has a doctor ever told you that you have experienced a ministroke or TIA (Transient Ischemic Attack)? CCC_AMI_COF1 and/or CCC_HBP_COF1 and/or CCC_ALZH_COF1 and/or CCC_PARK_COF1 and/or CCC_CVA_COF1 and/or CCC_TIA_COF1 and/or CCT_AMI_TRF1 and/or CCT_HBP_TRF1 and/or CCT_ALZH_TRF1 and/or PKD_PARK_TRF1 and/or CCT_CVA_TRF1 and/or CCT_TIA_TRF1	0 = No other CMC 1 = Other CMC
Number of CMC: **calculated variable**[d] Heart disease (Y = 1, N = 0) + lung problem (Y = 1, N = 0) + kidney disease (Y = 1, N = 0) + asthma (Y = 1, N = 0) + diabetes (Y = 1, N = 0) + cancer (Y = 1, N = 0) + other CMC (Y = 1, N = 0) = ∑Y = Total CMC	0 = 0 1 = 1 2-7 = ≥2
Received professional care in past 12 months: **composite variable**[c] During the past 12 months, did you receive short-term or long-term professional assistance at home, because of a health condition or limitation that affects your daily life, for any of the following activities?:	0 = 0 → No professional care received for any activity listed 1 = 1 → Professional care received for any activity listed

Received professional personal care; Received professional medical care; Received professional managing care; Received professional assistance with meal preparation or delivery; Received professional assistance with activities; Received professional assistance with transportation; Received professional physical therapy; Received professional training and adaptation assistance; Received other professional assistance CR1_PRO_PR_COF1 and/or CR1_PRO_MD_COF1 and/or CR1_PRO_MG_COF1 and/or CR1_PRO_MH_COF1 and/or CR1_PRO_WK_COF1 and/or CR1_PRO_TR_COF1 and/or CR1_PRO_PT_COF1 and/or CR1_PRO_TA_COF1 and/or CR1_PRO_OT_COF1 and/or CR1_PRO_PR_TRF1 and/or CR1_PRO_MD_TRF1 and/or CR1_PRO_MG_TRF1 and/or CR1_PRO_MH_TRF1 and/or CR1_PRO_WK_TRF1 and/or CR1_PRO_TR_TRF1 and/or CR1_PRO_PT_TRF1 and/or CR1_PRO_TA_TRF1 and/or CR1_PRO_OT_TRF1	
Received non-professional care in past 12 months: **composite variable**[c] Received non-professional personal care; Received non-professional medical care; Received non-professional managing care; Received non-professional assistance with activities; Received non-professional assistance with transportation; Received non-professional assistance with meal preparation; Received non-professional physical therapy; Received non-professional training and adaptation assistance; Received other non-professional assistance CR2_FAM_PR_COF1 and/or CR2_FAM_MD_COF1 and/or CR2_FAM_MG_COF1 and/or CR2_FAM_WK_COF1 and/or CR2_FAM_TR_COF1 and/or CR2_FAM_MH_COF1 and/or CR2_FAM_PT_COF1 and/or CR2_FAM_TA_COF1 and/or CR2_FAM_OT_COF1 and/or CR2_FAM_PR_TRF1 and/or CR2_FAM_MD_TRF1 and/or CR2_FAM_MG_TRF1 and/or CR2_FAM_WK_TRF1 and/or CR2_FAM_TR_TRF1 and/or CR2_FAM_MH_TRF1 and/or CR2_FAM_PT_TRF1 and/or CR2_FAM_TA_TRF1 and/or CR2_FAM_OT_TRF1	0 = 0 → No non-professional care received for any activity listed 1 = 1 → Non-professional care received for any activity listed
During the past 12 months, have you had contact with any of the following about your physical or mental health? Has had contact with: Family Doctor HCU_FAMPHY_COF1 HCU_FAMPHY_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA

	-88888 = Missing → NA -99999 = Skip Pattern → NA
Has had contact with: Medical specialist (such as a Cardiologist, Gynaecologist, Psychiatrist or Ophthalmologist) HCU_SPEC_COF1 HCU_SPEC_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Were you a patient in a hospital overnight during the past 12 months? HCU_HLOVRNT_COF1 HCU_HLOVRNT_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
In general, would you say your health is excellent, very good, good, fair, or poor? GEN_HLTH_COF1 GEN_HLTH_TRF1	1 = Excellent 2 = Very good 3 = Good 4 = Fair 5 = Poor 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
How many people, not including yourself, currently live in your household?: c**alculated variable**[d] SN_LIVH_NB_COF1 SN_LIVH_NB_TRF1	0 = 0 1 = 1 2-9 = ≥2 -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
In terms of your own healthy aging, would you say it is excellent, very good, good, fair, or poor? GEN_OWNAG_COF1 GEN_OWNAG_TRF1	1 = Excellent 2 = Very good 3 = Good 4 = Fair 5 = Poor 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
Over the past 7 days, how often did you engage in moderate sports or recreational activities such as ballroom dancing, hunting, skating, golf without a cart, softball or other similar activities?; Over the past 7 days, how often did you engage in strenuous sports or recreational activities such as jogging, swimming, snowshoeing, cycling, aerobics, skiing or other similar activities?: **composite variable**[c] PA2_MSPRT_COF1 and/or PA2_SSPRT_COF1 and/or PA2_MSPRT_TRF1 and/or PA2_SSPRT_TRF1	1 = Never → None or Seldom 2 = Seldom (1 to 2 days) → None or Seldom 3 = Sometimes (3 to 4 days) → Sometimes or Often 4 = Often (5 to 7 days) → Sometimes or Often 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA

At the present time, do you smoke cigarettes daily, occasionally or not at all? SMK_CURRCG_COF1 SMK_CURRCG_TRF1	1 = Daily (at least one cigarette every day for the past 30 days) 2 = Occasionally (at least one cigarette in the past 30 days, but not every day) 3 = Not at all (you did not smoke at all in the past 30 days) 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
Type of Drinker (Past 12 Months) ALC_TTM_COF1 ALC_TTM_TRF1	1 = Regular drinker (at least once a month) 2 = Occasional drinker 3 = Did not drink in the last 12 months -77771 = Inconclusive due to at least one missing item → NA

[a]COF1 indicates the Comprehensive cohort; TRF1 indicates the Tracking cohort
[b]There were no participants in the Comprehensive cohort in these provinces
[c]Respondents who responded "Y" or "1" to at least one of the multiple included variables were coded as "Y" or "sometimes or often" in the new composite variable
[d]Re-categorization of existing categories for single variable

Supplementary Table 2. Demographic Characteristics by Cohort: Participants Aged 65 Years and Older (N=23,226)

	Comprehensive Cohort (N=14,181)	Tracking Cohort (N=9,045)
	N(%)	N(%)
Outcome Variable		
Received influenza vaccination in last 12 months		
Yes	10087(71.1)	6286(69.5)
No	4094(28.9)	2759(30.5)
Sociodemographics		
Age		
65-74	8221(58.0)	4976(55.0)
75-84	5051(35.6)	3215(35.5)
85-94	909(6.4)	854(9.4)
Province of Residence		
Newfoundland	990(7.0)	472(5.2)
Prince Edward Island	N/A	507(5.6)
Nova Scotia	1432(10.1)	664(7.3)
New Brunswick	N/A	566(6.3)
Quebec	2814(19.8)	1502(16.6)
Ontario	3106(21.9)	2061(22.8)
Manitoba	1434(10.1)	609(6.7)
Saskatchewan	N/A	544(6.0)
Alberta	1357(9.6)	886(9.8)
British Columbia	3040(21.4)	1233(13.6)
Sex		
Male	7087(50.0)	4485(49.6)
Female	7093(50.0)	4547(50.3)
Urban or Rural		
Urban	13193(93.0)	6674(73.8)
Rural	744(5.2)	1571(17.4)
Household Income		
< 20000	763(5.4)	538(5.9)
≥20000-<50000	3976(28.0)	3081(34.1)
≥50000-<100000	5364(37.8)	3195(35.3)
≥100000-<150000	1906(13.4)	958(10.6)
≥150000	1000(7.1)	450(5.0)
Education		
Less than secondary school graduation	1060(7.5)	929(10.3)
Secondary school graduation, no post-secondary education	1455(10.3)	1187(13.1)
Some post-secondary education	1129(8.0)	722(8.0)
Post-secondary degree/diploma	10500(74.0)	6171(68.2)
Race		

White	13585(95.8)	8797(97.3)
Non-White	581(4.1)	238(2.6)

Supplementary Table 3. Demographic Characteristics by Cohort: Participants Aged 45-64 Years with at Least 1 CMC (N=10,685)

	Comprehensive Cohort (N=6,662)	Tracking Cohort (N=4,023)
	N(%)	N(%)
Outcome Variable		
Received influenza vaccination in last 12 months		
Yes	3337(50.1)	2013(50.0)
No	3325(49.9)	2010(50.0)
Sociodemographics		
Age		
45-54	1748(26.2)	907(22.5)
55-64	4914(73.8)	3116(77.5)
Province of Residence		
Newfoundland	518(7.8)	241(6.0)
Prince Edward Island	N/A	188(4.7)
Nova Scotia	562(8.4)	282(7.0)
New Brunswick	N/A	267(6.6)
Quebec	1393(20.9)	728(18.1)
Ontario	1494(22.4)	895(22.2)
Manitoba	659(9.9)	256(6.4)
Saskatchewan	N/A	241(6.0)
Alberta	696(10.4)	451(11.2)
British Columbia	1337(20.1)	474(11.8)
Sex		
Male	3312(49.7)	1967(48.9)
Female	3350(50.3)	2050(51.0)
Urban or Rural		
Urban	6134(92.1)	2944(73.2)
Rural	436(6.5)	711(17.7)
Household Income		
< 20000	323(4.8)	199(4.9)
≥20000-<50000	878(13.2)	702(17.4)
≥50000-<100000	2050(30.8)	1348(33.5)
≥100000-<150000	1494(22.4)	845(21.0)
≥150000	1633(24.5)	716(17.8)
Education		
Less than secondary school graduation	205(3.1)	215(5.3)
Secondary school graduation, no post-secondary education	564(8.5)	545(13.5)
Some post-secondary education	483(7.3)	299(7.4)
Post-secondary degree/diploma	5408(81.2)	2952(73.4)
Race		

White	6218(93.3)	3844(95.6)
Non-White	441(6.6)	171(4.3)

Chapter 4: Manuscript 2

In this chapter, I report on the prevalence of influenza non-vaccination and on factors associated with non-vaccination in the past year among those who report providing informal care as caregivers and care recipients at high risk of severe outcomes (objectives 2a, 2b, 3c, and 3d). This analysis was done to estimate influenza non-vaccination prevalence for caregivers aged 45 years and older and care recipients aged 65 years and older. Factors associated with lack of vaccination were also assessed for each of these groups. This manuscript has been formatted according to the specifications of the journal *Vaccine*.

Along with those at high risk of severe outcomes from influenza infection, as discussed in manuscript 1, caregivers are also an important population that should receive influenza vaccinations because vaccination would be a benefit to their own health, by reducing their risk of influenza and preventing them from becoming ill and being unable to provide care, and influenza vaccination can reduce their risk of transmitting influenza to the person that they care for who may be especially vulnerable to severe outcomes. Expanding influenza vaccination interventions to include those in contact with those at high risk of severe outcomes is important. Caregivers are recommended to receive influenza vaccine because they are in close contact with vulnerable individuals and vaccination can also prevent transmission.

This study is the most comprehensive assessment to date of non-vaccination prevalence and factors associated with non-vaccination among informal caregivers who provide care to individuals with a health condition or limitation who may or may not be within the same household. The CLSA cohort is an ideal setting to undertake this analysis because the large dataset allows for the examination of many characteristics that may be associated with influenza non-vaccination within many domains, using a robust sample size with many caregiver-specific covariates available that are not typically assessed. This study evaluates non-vaccination prevalence and factors associated with non-vaccination in caregivers and care recipients. Therefore, these findings can help identify new opportunities to increase vaccination to prevent both influenza exposure and severe outcomes from infection within these groups in Canada.

Influenza Vaccine Coverage and Factors Associated with Non-Vaccination Among Caregiving and Care-Receiving Adults in the Canadian Longitudinal Study on Aging

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Abstract

Background

Vaccination is recommended for those at increased risk of influenza complications and their household contacts. Vaccinating the contacts of those at high risk of severe outcomes can help reduce influenza exposure. However, influenza vaccination frequency in adult caregivers and care recipients remains largely unknown in Canada.

Objectives

The objectives of this study were to estimate the prevalence of non-vaccination and assess factors associated with non-vaccination among caregivers aged ≥45 years and among care recipients aged ≥65 years.

Methods

We conducted an analysis of cross-sectional data from the Canadian Longitudinal Study on Aging, a cohort study of 44,815 participants at follow-up 1. We estimated non-vaccination prevalence overall and stratified by covariates and we estimated adjusted odds ratios with 95% confidence intervals from logistic regression models to identify factors associated with non-vaccination in caregivers and care recipients.

Results

The percentage who reported NOT receiving influenza vaccine in the 12 months prior to the survey was 41.4% (95% CI: 40.8%, 42.0%) for caregivers and 24.8% (95% CI: 23.7%, 26.0%) for care recipients. For both groups, the odds of non-vaccination in the fully adjusted model were notably higher for those who had not visited a family doctor compared to those who had. Caregivers in Saskatchewan, Newfoundland, and Quebec had higher odds of non-vaccination, as did those who identified as non-white compared to those who identified as white.

Discussion

Understanding who is unvaccinated among those at risk of influenza transmission and severe outcomes can inform public health messaging. New strategies, such as disseminating messages through organizations that support caregivers, are needed to reach younger caregivers and care recipients to encourage influenza vaccination.

Conclusion

Caregivers benefit from influenza vaccination directly and their care recipients benefit indirectly because vaccination reduces the risk of illness and transmission. Influenza vaccination campaigns should target these groups to increase coverage.

Keywords
Influenza, Vaccination, Canada, CLSA, Older Adults

Introduction

Seasonal influenza remains an important public health problem in Canada, which has an annual average of 12,200 hospitalizations and 3,500 deaths related to influenza.[1] While both the 2020/2021 and 2021/2022 influenza seasons in Canada had no community circulation of influenza reported, likely due to the preventative measures taken to prevent the transmission of SARS-CoV-2, the 2021/2022 season has had a proportion of visits to healthcare professionals due to influenza-like illness (ILI) similar to expected pre-pandemic levels since the start of this surveillance season.[2,3] The prevention of influenza infection remains a public health priority.

Vaccination against influenza reduces the risk of influenza infection, transmission, and severe disease. Vaccination may benefit individuals directly by reducing their risk of disease by preventing influenza infection and associated negative outcomes such as hospitalization from ILI and both influenza-specific and all-cause mortality.[4-9]

The National Advisory Committee on Immunization (NACI) "*particularly*" recommends annual influenza vaccination for groups at increased risk of influenza complications, such as adults aged 65 years and older, to reduce the number of hospitalizations and deaths from influenza infection.[10] NACI also recommends influenza vaccination for household contacts of individuals at high risk of severe outcomes from influenza to prevent influenza illness and thus transmission by these contacts.[11] Like household contacts, close contacts may increase exposure to infection and have also been found to influence seasonal influenza vaccination decision-making;[12,13] therefore, contacts can impact both influenza transmission and vaccination for those at high risk of severe outcomes. Additionally, for care recipients, recovery from influenza may be a lengthy process and can increase the burden on their contacts who act as caregivers.[14] Vaccinating individuals to both provide direct protection by reducing their risk of illness and to provide indirect protection to their contacts is a strategy called cocooning, where the contacts of those at high risk of severe outcomes are vaccinated to prevent infection in themselves and to prevent the subsequent transmission of disease to their vulnerable contacts.[15]

Vaccination coverage in Canadian adults aged 65 years and older was 65% for the 2015/2016 influenza season, 69% for the 2016/2017 season, and 70.7% for the 2017/2018 season, as

reported by the Public Health Agency of Canada.[1,16,17] The period of data collection for these analyses included these influenza seasons. The percentage of informal caregivers and care-recipients who report receiving influenza vaccine in a given season remains unknown in Canada, as studies of influenza vaccination in those who provide or receive care often focus on formal settings such as hospitals or on influenza vaccination in children.[18-22]

In order to increase influenza vaccination coverage and inform vaccination programs in Canada, it is necessary to obtain precise estimates of vaccination coverage and to determine the characteristics of those least likely to receive an influenza vaccination within subpopulations at high risk of severe outcomes or of transmission of influenza. While previous studies have reported characteristics that may be associated with influenza vaccination in Canadian adults,[23-26] the Canadian Longitudinal Study on Aging (CLSA) is a large, national cross-sectional cohort study that includes information on influenza vaccination history along with a broad range of covariates that allow for the examination of associations with influenza non-vaccination in unique groups of interest across many different vaccination-related domains.[27]

The objectives of this study were to 1) estimate the prevalence of non-vaccination and assess factors associated with non-vaccination among caregivers aged 45 years and older and 2) estimate vaccination coverage and assess factors associated with non-vaccination among care recipients aged 65 years and older.

Materials and Methods

2.1 Data Source

The CLSA is a nationally representative study of adults aged 45-85 at enrollment. Baseline recruitment took place from 2011-2015 using 3 sampling frames (the Canadian Community Health Survey, random-digit dialing, and provincial health registries). The CLSA is made up of 2 cohorts: the Comprehensive cohort (N=30,097 at baseline) which included in-person study visits and provided biological samples along with survey data and the Tracking cohort (N=21,241 at baseline) which collected data via computer-assisted telephone interviews. Data collection takes place every 3 years and is ongoing.[28] Recruitment was done across 7 provinces in the Comprehensive cohort and across all 10 provinces in the Tracking cohort.[28] For the

Comprehensive cohort, participants were randomly selected within age and sex strata from 11 data collection site recruitment areas.

Exclusion criteria during CLSA recruitment include residence on a federal First Nations reserve or other First Nations settlement; being a full-time member of the Canadian Armed Forces; residence in the 3 territories; residence in long-term care institutions; inability to respond in French or English; or cognitive impairment as determined by interviewers. More information on the CLSA study procedures is available,[27-29] and the CLSA survey protocols and supporting documentation can be downloaded from the CLSA website (clsa-elcv.ca).

Approval to access the data was obtained from the CLSA (Application Number: 2006029). Ethics approval was obtained from the McGill University Institutional Research Board (Application Number: 21-02-048).

2.2 Analytic Sample

This study is a cross-sectional analysis of CLSA first follow up (FUP1) data collected from 2015-2018. Participants in the Comprehensive (N=27,765) and Tracking (N=17,050) cohorts who had a valid response to the outcome variable (self-reported influenza vaccination status within the past 12 months) were included in these analyses. Tracking cohort data were collected via phone interviews, while Comprehensive cohort data were collected via in-person interviews and CLSA site visits. Only variables collected from participants within both the Comprehensive and Tracking cohorts were included in these analyses.

2.3 Influenza Vaccination Status and Covariates of Interest

The variables included in these analyses were chosen *a priori* based on previously published studies that reported an association with influenza vaccination or potential interest when evaluating new opportunities for vaccination.[26,30-32] Data from the CLSA baseline assessment were used for race and education level. The CLSA variable coding used in the analyses can be found in **Supplementary Table 1**.

Outcome

The outcome variable we refer to as "influenza non-vaccination" was determined by the self-reported response to the question “Have you had… Flu shot in the last 12 months”. Participants who responded “no” were categorized as not vaccinated; participants who responded, “Don’t Know/No Answer”, who “Refused”, or had a “Missing” response were excluded from the analysis due to the small percentage of respondents in these categories for the outcome variable (0.3% in the Comprehensive cohort and 2.1% in the Tracking cohort). Self-reported influenza vaccination status as a dependent variable has been validated for older adults in the United States and Australia as having high sensitivity and moderate specificity compared to medical records.[33,34]

Sociodemographic Variables

We investigated the association of sociodemographic characteristics and influenza non-vaccination among caregivers and care recipients. Age was categorized into 5 groups based on the participant age at FUP1 (**Supplementary Table 1**). Sex at birth was male or female, and race was white or non-white. Urban or rural categorization was dichotomized; participants classified as “Link to DA”, which indicates the cases where postal codes are linked at an insufficiently detailed level to provide urban/rural information, were considered missing due to the unspecified urban/rural mix within this category.[35] Each of the 10 provinces were included in a categorical variable. For this variable, Ontario was selected as the reference category due to its history of providing universal influenza vaccination and historically higher vaccination coverage, including among those at high risk of severe outcomes.[36,37] Household income and number of people in household were categorized as ordinal variables (**Supplementary Table 1**). Education was categorized as an ordinal variable (**Supplementary Table 1**).

Chronic Medical Conditions

The type and number of chronic medical conditions (CMC) were also examined to evaluate the association between non-vaccination in those at high risk of severe outcomes and the presence of CMC. Participants were considered to have a CMC if they self-reported a physician diagnosis of any of the following conditions based on the NACI definition of groups for whom influenza vaccination is particularly recommended.[10] For the CMC that fit the NACI definition and were represented in the CLSA data, heart disease, lung problems, kidney disease or failure, asthma,

diabetes, and cancer were considered separate binary variables ("yes"/"no"), while the CMC of heart attack or myocardial infarction, high blood pressure or hypertension, dementia or Alzheimer's disease, Parkinsonism or Parkinson's Disease, stroke or cerebrovascular accident (CVA), and ministroke or Transient Ischemic Attack (TIA) were combined into the variable "other CMC". In addition, a variable "number of CMC" was derived by summing the number of the NACI CMC variables and the "other CMC" variable for each participant. This variable was classified as 0 CMC, 1 CMC, or ≥2 CMC.

Healthcare Utilization, Health Perception, and Health Behaviors

Healthcare utilization factors were also analyzed based on prior studies that identified the types of healthcare utilization that were associated with influenza vaccination in Spain and Canada.[38,39] Healthcare visits increase exposure to health providers who may make vaccination recommendations. Participant responses to the question "During the past 12 months, have you had contact with any of the following about your physical or mental health?... Has had contact with: Family Doctor" were dichotomized (yes, no). Similarly, dichotomous variables were created for the other healthcare utilization variables: contact with a specialist in the past 12 months and overnight hospitalization history in the past 12 months (**Supplementary Table 1**).

Self-rated health and self-rated healthy aging variables were used in our analyses to assess the association between self-perceived health and influenza vaccination. Prior studies in Canada and the United States have found that health status and older age limitations were associated with influenza vaccination in groups at high risk of severe outcomes.[7,9,36,40,41] In our analyses, self-rated health was assessed by the question "In general, would you say your health is excellent, very good, good, fair, or poor?". Self-rated healthy aging was assessed by the question "In terms of your own healthy aging, would you say it is excellent, very good, good, fair, or poor?". Both were included as ordinal variables with 5 categories: excellent (1), very good (2), good (3), fair (4), and poor (5). "Excellent" was used as the reference category for both variables. Self-rated health has been validated[42,43] as a measure of health in general health surveys.

To evaluate the impact of health-related behaviors that were previously identified as associated with influenza vaccination in older (>65) adult Canadians,[36] participants were also asked about

their current smoking behavior (daily, occasionally, not at all), alcohol consumption in the past 12 months (regular, occasionally, or never), and amount of exercise in the past 7 days (derived from self-reported levels of moderate or strenuous exercise: none or seldom, sometimes or often).

Caregiving

To evaluate influenza vaccination of individuals who act as caregivers, based on their response to the question "During the past 12 months, have you provided any of the following types of assistance to another person because of a health condition or limitation?", respondents were classified as caregivers ("yes") or not ("no"). Variables that elucidated the type of caregiving relationship were also examined to determine if an association between different caregiver-care recipient relationships and influenza vaccine uptake could be identified. The sex of the care recipient to whom the caregiver provided the most assistance (i.e., the primary care recipient) was male or female. The relationship to the primary care recipient was categorized as: spouse/partner, father/mother, child, sibling, non-immediate family that may be at increased risk of influenza transmission or severe outcomes (grandfather, grandmother, grandson, or granddaughter), other relative (father-, mother-, son-, daughter-in-law or other relative), and friend or neighbor.[44] The average number of hours per week of care given to the primary care recipient was an ordinal variable categorized as 1-20, 21-40, and 41+ hours. The number of care recipients was an ordinal variable of 1 or ≥2 recipients. Lastly, the dwelling location of the primary care recipient was a categorical variable comprised of: living in your household, living in another household, living in a health care institution, or now deceased.

Care or Assistance Received

A study that analyzed cross-sectional data from the 2009 Behavioral Risk Factor Surveillance System in the United States found that those with functional limitations were more likely to have received an influenza vaccination in the past 12 months and have a regular healthcare provider.[45] This may indicate a higher likelihood to seek care due to these limitations, leading to greater exposure to vaccination recommendations from providers. Limitations related to receiving care may also negatively impact the ability to receive influenza vaccination (such as reduced ability to reach a vaccination center due to difficulties with ambulation). Therefore, we identified

respondents who reported receiving at-home professional or non-professional care during the past 12 months.

Based on the responses to the question “During the past 12 months, did you receive short-term or long-term assistance from family, friends, or neighbours because of a health condition or limitation that affects your daily life, for any of the following activities?”, we categorized participants as having received *non-professional* care ("yes") or not having received non-professional care ("no"). Participants who responded "yes" to the question “During the past 12 months, did you receive short-term or long-term professional assistance at home, because of a health condition or limitation that affects your daily life, for any of the following activities?” were categorized as having received *professional* care (“yes”) or not (“no”) Participants who received both professional and non-professional care were included in both the non-professional and professional care groups for analysis.

2.4 Statistical Analysis

We assessed influenza non-vaccination prevalence and the factors associated with non-vaccination in adults who are at risk of transmitting influenza to individuals at increased risk of severe outcomes and care recipients.

These analyses were conducted in R (version 1.3.1073) using the “survey” package.

Participants with missing values for one or more study variables were excluded in the analyses involving those variables. Responses of “Don’t Know/No Answer”, “Refused”, “Missing”, and “Did not complete a DCS visit” were considered as missing.

To assess factors associated with non-vaccination for the care recipient group, we first estimated the associations between influenza non-vaccination and sociodemographic variables and type of CMC in Model 1. In Model 2, we added the objective healthcare-related variables of *number* of CMC, type of care received, and healthcare utilization variables to the covariates included in Model 1. Finally, in Model 3, we added variables also associated with health without direct medical background— self-rated health, household size, self-rated healthy aging, and health

behaviors— to the covariates included in Model 2. For the caregiver group, Model 1 included sociodemographic factors, type of CMC, and the transmission-associated variable of household size, while Model 2 included variables about the caregivers' relationship to their care recipient(s) as well as the Model 1 covariates. Model 3, the full model, included health-related variables (number of CMC, healthcare utilization, self-rated health, and health behaviors) along with the covariates in Model 2. We report the results of Model 3 in the text. Results for all models can be found in **Tables 3-4**.

To estimate influenza vaccination coverage among 1) caregivers aged 45 years and older and 2) care recipients aged 65 years and older, we calculated influenza non-vaccination prevalence in the previous 12 months for caregivers and care recipients by the presence of CMC, healthcare utilization history, health perception, health behaviors, and sociodemographic factors. The association between the independent variables and influenza non-vaccination was estimated using multivariable logistic regression. The adjusted odds ratios (aOR) along with 95% confidence intervals (95% CIs) were reported for the association between each covariate included in each model and NOT having received influenza vaccine in the past 12 months.

Due to the complex sampling techniques used by the CLSA, inflation and analytic weights are available for the baseline datasets to account for survey sample misrepresentation and to scale regression analyses by sample size of recruitment location. Sampling weights were not used in these analyses as CLSA baseline weights are not applicable for cross-sectional analyses of the FUP1 data and valid weights for FUP1 were not available at the time of the analyses. We stratified by age and included the variables of sex and province of residence in our analyses as recommended by the CLSA.[46]

Two-sample tests of proportions across 2015-2018 as a whole were performed as sensitivity analyses to determine if the prevalence of vaccination of individuals who were asked about their influenza vaccination history during each of the Canadian influenza seasons from November-April included in this dataset was significantly different compared to participants surveyed outside of each influenza season.[1]

Results

3.1 Participant demographics

At FUP1, the Comprehensive cohort included 27,765 participants, of which 0.31% (N=86) were excluded for an invalid response to the outcome variable; the Tracking cohort included 17,050 participants, of which 2.09% (N=357) were excluded. The distribution of demographic characteristics for the 23,500 caregivers aged 45 years and older and the 5,559 care recipients aged 65 years and older by vaccination status are reported (**Tables 1-2**). The demographic characteristics by cohort for each group can be found in **Supplementary Tables 2-3**.

3.2 Influenza Vaccination in Caregivers Aged 45 Years and Older

Of the 44,372 participants in this study sample with a valid response to the outcome variable, 23,500 were classified as caregivers. 41.4% (95% CI: 40.8%, 42.0%) of this group reported influenza non-vaccination in the past 12 months (**Table 3**). Those aged 45-54 and 55-64 had notably higher non-vaccination prevalence than those aged 65 and older. Quebec residents had the highest prevalence of non-vaccination (55.5%, 95% CI: 54.0%, 57.0%). Caregivers who cared for their father or mother had particularly high prevalence of non-vaccination (50.2%, 95% CI: 48.9%, 51.5%) compared to the prevalence for other care recipient relationships. Those who currently smoked daily or occasionally had notably low vaccination prevalence. Finally, as the number of CMC increased, the prevalence of vaccination was higher: those without CMC had a non-vaccination prevalence of 51.4% (95% CI: 50.3%, 52.4%) compared to 28.8% (95% CI: 27.7%, 29.9%) in those with ≥ 2 CMC.

Table 3 also presents the results of the logistic regression analyses for caregivers aged 45 years and older. Model 3 adjusted for number of CMC, healthcare utilization, self-rated health, and health behavior characteristics as well as the caregiving factors of Model 2 and the sociodemographic, CMC type, and household structure categories of Model 1. In Model 3, increasing age was associated with lower odds of remaining unvaccinated, particularly for those aged 65 years and older after controlling for all other variables in Model 3 (**Table 3**). Those who reported contact with a family doctor in the past 12 months had considerably lower odds of remaining unvaccinated (0.381, 95% CI: 0.264, 0.548) compared to those who did not have contact after controlling for all other variables in this model. Those who lived in urban areas had

lower odds of remaining unvaccinated than those who lived in rural areas (0.686, 95% CI: 0.531, 0.885) after controlling for all other variables in this model. Those who had contact with a specialist in the past 12 months had lower odds of remaining unvaccinated (0.706, 95% CI: 0.597, 0.834) than those without after controlling for all other variables in this model. In contrast, Quebec residents had notably higher odds of non-vaccination than Ontario residents (1.758, 95% CI: 1.377, 2.243) after controlling for all other variables in this model. Those with secondary school graduation and no post-secondary education also had higher odds of non-vaccination (1.519, 95% CI: 1.022, 2.259) than those who had less than secondary school graduation after controlling for all other variables in this model. Those who identified as non-white had higher odds of non-vaccination (1.445, 95% CI: 1.053, 1.983) compared to those who identified as white after controlling for all other variables in this model. No type of CMC was significantly associated with lower odds of remaining unvaccinated after controlling for all other variables in Model 3. None of the variables that defined the caregiver-care-recipient relationship (such as number of care recipients) were notably associated with non-vaccination (**Table 3**).

3.3 Influenza Vaccination in Care Recipients Aged 65 Years and Older

24.8% (95% CI: 23.7%, 26.0%) of this group (N=5,559) was unvaccinated in the past 12 months (**Table 4**). The 65-74 age group had notably higher prevalence of non-vaccination (30.6%, 95% CI: 28.7%, 32.5%) than the 75-84 (20.7%, 95% CI: 19.1%, 22.4%) and 85-84 (20.5%, 95% CI: 17.7%, 23.3%) age groups. Across Canada, Quebec residents had the highest prevalence of non-vaccination (33.5%, 95% CI: 30.6%, 36.3%). Non-vaccination prevalence was similar for all CMC types, and vaccine coverage did not notably differ by self-rated health.

Table 4 also presents the results of the logistic regression analyses for care recipients aged 65 years and older. For Model 3, which included additional variables related to health behavior and status, as well as adjusting for the sociodemographic, type of CMC, and health-related factors from Models 1 and 2, the odds of NOT receiving an influenza vaccine in the past 12 months were distinctly lower in those who reported contact with a family doctor (0.155, 95% CI: 0.027, 0.903) compared to those without contact after controlling for all other variables in Model 3 (**Table 4**). The odds of remaining unvaccinated were significantly lower for the 85-94 age group (0.446, 95% CI: 0.221, 0.900) compared to the 65-74 age group after controlling for all other

variables. Newfoundland residents had the largest association with non-vaccination in this model (5.793, 95% CI: 1.844, 18.199) after controlling for all other variables.

3.4 Sensitivity Analysis

For caregivers, the proportions of influenza non-vaccination by cohort were not significantly different between individuals surveyed during the typical Canadian flu season of November-April (N=11,896) and individuals surveyed outside those months (N=11,604) (Comprehensive Cohort, p-value=0.171; Tracking Cohort, p-value=0.330). For care recipients, the proportions of influenza non-vaccination by cohort were also not significantly different between individuals surveyed during the typical Canadian flu season (N=2,754) and individuals surveyed outside those months (N=2,805) (Comprehensive Cohort, p-value=0.930; Tracking Cohort, p-value=0.117).

Discussion

NACI recommends vaccination for groups at high risk of severe outcomes, as well as for their household contacts due to the risk of influenza transmission from close contacts, and the benefits of vaccination against influenza have been well-documented. Despite this, vaccination coverage in caregivers and care recipients remains largely unexplored outside of studies that focus on healthcare workers or children.[18-22] Our study of CLSA FUP1 data from 2015-2018 found that caregivers aged 45 years and older had a prevalence of influenza non-vaccination of 41.4% (95% CI: 40.8%, 42.0%), while care recipients aged 65 years and older had a prevalence of 24.8% (95% CI: 23.7%, 26.0%). Younger age was a consistent factor in lower vaccination coverage for both groups, particularly for caregivers aged 45-64; this age group made up a large proportion of the total caregiver group. The odds of non-vaccination for care recipients were notably lower if the respondent had seen a family doctor. Vaccination coverage was also highly variable between provinces.

As caregivers may have close, frequent, and sustained contact with those at high risk of severe outcomes due to their caregiving role, targeted educational campaigns to increase vaccination in caregivers could directly reduce the risk of influenza infection in this group and help prevent the spread of influenza to their vulnerable contacts through cocoon vaccination.[15] In contrast to the

relatively high vaccination coverage in care recipients, the prevalence of vaccination for caregivers was notably lower. Our findings on vaccination in caregivers highlight the importance of ensuring that caregivers are aware of the multiple direct and indirect benefits of influenza vaccination. Influenza transmission between caregivers and care recipients could be a significant issue for both groups: infected caregivers may be unable to provide the same level of care, while care recipients may experience a higher prevalence of morbidity and mortality. It is also important for caregivers to get vaccinated for their own well-being, something that is often overlooked for those with caregiving responsibilities. Influenza vaccination provides the dual benefit of protecting the health of caregivers as well as the health of their care recipients.

One notable finding of this study is that care recipients who have had contact with a family doctor during the past 12 months had distinctly lower odds of remaining unvaccinated (0.155, 95% CI: 0.027, 0.903) after controlling for all other variables in the fully adjusted model. Having a family doctor was shown to be associated with influenza vaccination in a 2009 study of Canadians with chronic respiratory disease.[39] Although hospitalization and specialist contact have also been found to be associated with influenza vaccination in other studies,[38,39] our findings did not support this for care recipients aged 65 years and older. This may be because studies have shown that subspecialists make up an important fraction of ambulatory care visits for those at risk of severe outcomes and that subspecialists may be less likely to recommend influenza vaccination or have the vaccine available.[47,48] Therefore, adults who primarily have contact with subspecialist physicians, such as those with CMC, may miss opportunities to be vaccinated against influenza. Ensuring that influenza vaccinations are strongly recommended independently of healthcare providers could help increase vaccination coverage further; this could include providing influenza vaccination information from a variety of sources, such as social media and targeted public announcements.

For both care recipients and caregivers, the number of CMC and lower self-rated health was not significantly associated with non-vaccination across categories in the fully adjusted model. This is in contrast to several previous studies in older adult Canadians which found that self-rated health and presence of CMC were associated with influenza vaccination.[8,24,26,36,38] Our findings may indicate that influenza vaccination in these groups is influenced by factors outside of self-

perceived health, such as public vaccination recommendations or risk awareness, which often center around age. Public health messaging and education needs to be tailored toward caregivers, particularly younger individuals, who may not think of influenza vaccination as a necessity for their own health and the health of their contacts.

Our study contributes new insight into factors that are associated with vaccination in caregivers and care recipients which can be used to identify new opportunities for public health programs to close the existing gaps in influenza vaccination coverage and prevent transmission within these groups. Provinces with low vaccination coverage may need to devote additional resources to increasing uptake. Care recipients without contact with a family doctor and caregivers who may be in contact with multiple care recipients or those at high risk of severe outcomes may be unaware of their recommendation to be vaccinated against influenza and the accompanying benefits: public health outreach efforts could be aimed at this important group for influenza prevention.

Although this study has several unique strengths compared to other observational studies, including its wide range of covariates and the large sample size that allows for precise estimation of non-vaccination prevalence and associations, it also has several limitations. Many variables, including the outcome variable, are based on self-report, although self-reported influenza vaccination has been validated in prior studies. The CLSA data collection methods may cause individuals with more severe disabilities to be under-represented in these data, as institutionalized individuals are excluded during baseline recruitment.[49] We did not have the information in this dataset to determine the reasons for non-vaccination; further investigation into the mechanisms behind non-vaccination is necessary. We also did not have the ability in this dataset to distinguish between paid and unpaid non-family caregivers; this dynamic may influence influenza vaccination in caregivers.

Conclusion

The prevalence of influenza non-vaccination in adult caregivers and older adult care recipients in Canada from 2015-2018 indicates that efforts are needed to increase uptake in these groups. For both groups, encouraging influenza vaccination in younger age groups (particularly those aged

under 65 for the caregiver group) is necessary to raise coverage, as is specifically targeting care recipients and caregivers to emphasize the important of vaccination. In order to prevent transmission between these two important populations, public health strategies to immunize and protect individuals in these groups against influenza need to be adapted.

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Declaration of competing interest

The authors state that no conflicts of interest exist.

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Table 1. Demographic Characteristics by Influenza Vaccination: Caregivers Aged 45 Years and Older (N=23,500)

	Received Influenza Vaccination in Last 12 Months (N=13,771)	Did Not Receive Influenza Vaccination in Last 12 Months (N=9,729)
	N(%)	N(%)
Sociodemographics		
Age		
45-54	1480(10.7)	2141(22.0)
55-64	4183(30.4)	4250(43.7)
65-74	4504(32.7)	2340(24.1)
75-84	3027(22.0)	869(8.9)
85-94	577(4.2)	129(1.3)
Province of Residence		
Newfoundland	707(5.1)	567(5.8)
Prince Edward Island	291(2.1)	153(1.6)
Nova Scotia	1389(10.1)	556(5.7)
New Brunswick	313(2.3)	183(1.9)
Quebec	1861(13.5)	2318(23.8)
Ontario	3255(23.6)	1944(20.0)
Manitoba	1233(9.0)	897(9.2)
Saskatchewan	346(2.5)	231(2.4)
Alberta	1590(11.5)	925(9.5)
British Columbia	2781(20.2)	1952(20.1)
Sex		
Male	6232(45.3)	4360(44.8)
Female	7534(54.7)	5363(55.1)
Urban or Rural		
Urban	11943(86.7)	8140(83.7)
Rural	1272(9.2)	1113(11.4)
Household Income		
< 20000	482(3.5)	447(4.6)
≥20000-<50000	2902(21.1)	2077(21.3)
≥50000-<100000	4987(36.2)	3213(33.0)
≥100000-<150000	2424(17.6)	1808(18.6)
≥150000	2122(15.4)	1653(17.0)
Education		
Less than secondary school graduation	669(4.9)	445(4.6)
Secondary school graduation, no post-secondary education	1310(9.5)	1025(10.5)
Some post-secondary education	1001(7.3)	742(7.6)
Post-secondary degree/diploma	10762(78.1)	7497(77.1)
Race		
White	13256(96.3)	9215(94.7)
Non-White	505(3.7)	501(5.1)

Table 2. Demographic Characteristics by Influenza Vaccination: Care Recipients Aged 65 Years and Older (N=5,559)

	Received Influenza Vaccination in Last 12 Months (N=4,178)	Did Not Receive Influenza Vaccination in Last 12 Months (N=1,381)
	N(%)	N(%)
Sociodemographics		
Age		
65-74	1617(38.7)	713(51.6)
75-84	1922(46.0)	503(36.4)
85-94	639(15.3)	165(11.9)
Province of Residence		
Newfoundland	178(4.3)	84(6.1)
Prince Edward Island	101(2.4)	23(1.7)
Nova Scotia	393(9.4)	72(5.2)
New Brunswick	102(2.4)	38(2.8)
Quebec	688(16.5)	346(25.1)
Ontario	937(22.4)	227(16.4)
Manitoba	368(8.8)	132(9.6)
Saskatchewan	97(2.3)	38(2.8)
Alberta	497(11.9)	125(9.1)
British Columbia	817(19.6)	295(21.4)
Sex		
Male	1716(41.1)	528(38.2)
Female	2458(58.8)	852(61.7)
Urban or Rural		
Urban	3651(87.4)	1167(84.5)
Rural	354(8.5)	143(10.4)
Household Income		
< 20000	307(7.3)	180(13.0)
≥20000-<50000	1360(32.6)	545(39.5)
≥50000-<100000	1381(33.1)	369(26.7)
≥100000-<150000	429(10.3)	85(6.2)
≥150000	228(5.5)	47(3.4)
Education		
Less than secondary school graduation	390(9.3)	160(11.6)
Secondary school graduation, no post-secondary education	483(11.6)	169(12.2)
Some post-secondary education	350(8.4)	131(9.5)
Post-secondary degree/diploma	2942(70.4)	912(66.0)
Race		
White	4063(97.2)	1316(95.3)
Non-White	113(2.7)	64(4.6)

Table 3. Proportion Unvaccinated and Factors Associated with Non-Vaccination Against Seasonal Influenza Among Caregivers Aged 45 Years and Older (N=23,500)

	Proportion Unvaccinated (95% CI)	Model 1 [a] (N=3,659)	Model 2[a] (N=3,494)	Model 3[a] (N=3,475)
Total	0.414 (0.408, 0.420)			
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Age				
45-54	0.591 (0.575, 0.607)	Ref	Ref	Ref
55-64	0.504 (0.493, 0.515)	0.645 (0.505, 0.824)	0.647 (0.505, 0.830)	0.660 (0.513, 0.851)
65-74	0.342 (0.331, 0.353)	0.322 (0.246, 0.420)	0.322 (0.244, 0.425)	0.356 (0.268, 0.473)
75-84	0.223 (0.210, 0.236)	0.190 (0.138, 0.261)	0.188 (0.134, 0.262)	0.210 (0.149, 0.296)
85-94	0.183 (0.154, 0.211)	0.096 (0.046, 0.201)	0.094 (0.043, 0.207)	0.109 (0.049, 0.239)
Province of Residence				
Ontario	0.374 (0.361, 0.387)	Ref	Ref	Ref
Newfoundland	0.445 (0.418, 0.472)	1.495 (1.064, 2.102)	1.346 (0.948, 1.912)	1.433 (1.005, 2.043)
Prince Edward Island	0.345 (0.300, 0.389)	0.989 (0.573, 1.708)	0.933 (0.524, 1.660)	0.983 (0.552, 1.748)
Nova Scotia	0.286 (0.266, 0.306)	0.721 (0.521, 0.997)	0.712 (0.512, 0.991)	0.721 (0.516, 1.008)
New Brunswick	0.369 (0.326, 0.411)	0.791 (0.418, 1.495)	0.759 (0.397, 1.449)	0.713 (0.366, 1.388)
Quebec	0.555 (0.540, 0.570)	1.899 (1.506, 2.394)	1.788 (1.408, 2.271)	1.758 (1.377, 2.243)
Manitoba	0.421 (0.400, 0.442)	0.964 (0.712, 1.305)	0.981 (0.718, 1.340)	0.975 (0.712, 1.337)
Saskatchewan	0.400 (0.360, 0.440)	1.464 (0.830, 2.582)	1.367 (0.760, 2.460)	1.326 (0.741, 2.371)
Alberta	0.368 (0.349, 0.387)	1.041 (0.778, 1.394)	0.967 (0.716, 1.307)	0.932 (0.683, 1.272)
British Columbia	0.412 (0.398, 0.426)	1.167 (0.940, 1.449)	1.137 (0.912, 1.418)	1.172 (0.937, 1.467)
Sex				
Male	0.412 (0.402, 0.421)	Ref	Ref	Ref
Female	0.416 (0.407, 0.424)	1.000 (0.858, 1.166)	1.010 (0.861, 1.183)	1.014 (0.862, 1.193)
Urban or Rural				
Rural	0.467 (0.447, 0.487)	Ref	Ref	Ref
Urban	0.405 (0.399, 0.412)	0.709 (0.554, 0.907)	0.681 (0.530, 0.876)	0.686 (0.531, 0.885)
Household Income				
< 20000	0.481 (0.449, 0.513)	Ref	Ref	Ref
≥20000-<50000	0.417 (0.403, 0.431)	1.190 (0.846, 1.675)	1.167 (0.822, 1.657)	1.222 (0.853, 1.750)
≥50000-<100000	0.392 (0.381, 0.402)	0.784 (0.553, 1.110)	0.730 (0.510, 1.046)	0.791 (0.547, 1.146)
≥100000-<150000	0.427 (0.412, 0.442)	0.706 (0.481, 1.034)	0.666 (0.449, 0.988)	0.734 (0.488, 1.105)
≥150000	0.438 (0.422, 0.454)	0.651 (0.437, 0.968)	0.610 (0.404, 0.920)	0.672 (0.439, 1.029)
Education				
Less than secondary school graduation	0.399 (0.371, 0.428)	Ref	Ref	Ref
Secondary school graduation, no post-secondary education	0.439 (0.419, 0.459)	1.463 (1.002, 2.137)	1.537 (1.038, 2.274)	1.519 (1.022, 2.259)
Some post-secondary education	0.426 (0.402, 0.449)	1.263 (0.854, 1.868)	1.304 (0.871, 1.951)	1.247 (0.829, 1.876)

Post-secondary degree/diploma	0.411 (0.403, 0.418)	1.119 (0.811, 1.544)	1.173 (0.838, 1.641)	1.193 (0.847, 1.680)
Race				
White	0.410 (0.404, 0.417)	Ref	Ref	Ref
Non-White	0.498 (0.467, 0.529)	1.450 (1.066, 1.974)	1.440 (1.049, 1.976)	1.445 (1.053, 1.983)
Type of CMC				
Heart Disease	0.285 (0.268, 0.303)	0.915 (0.738, 1.134)	0.935 (0.750, 1.165)	1.034 (0.818, 1.307)
Lung Problems	0.314 (0.291, 0.337)	0.829 (0.631, 1.088)	0.844 (0.636, 1.120)	0.867 (0.646, 1.163)
Kidney Disease or Failure	0.333 (0.300, 0.367)	0.621 (0.424, 0.910)	0.637 (0.432, 0.940)	0.688 (0.466, 1.014)
Asthma	0.343 (0.327, 0.360)	0.704 (0.570, 0.871)	0.709 (0.572, 0.880)	0.813 (0.639, 1.035)
Diabetes	0.294 (0.275, 0.312)	0.727 (0.625, 0.846)	0.725 (0.621, 0.848)	0.900 (0.724, 1.118)
Cancer	0.305 (0.291, 0.319)	0.727 (0.596, 0.887)	0.719 (0.586, 0.881)	0.842 (0.668, 1.061)
Other CMC	0.336 (0.327, 0.345)	0.722 (0.617, 0.845)	0.724 (0.616, 0.850)	0.875 (0.687, 1.115)
Number in Household				
0	0.385 (0.372, 0.399)	Ref	Ref	Ref
1	0.385 (0.376, 0.393)	0.948 (0.777, 1.158)	0.941 (0.760, 1.165)	0.921 (0.741, 1.144)
≥ 2	0.505 (0.492, 0.519)	1.127 (0.886, 1.433)	1.134 (0.877, 1.467)	1.085 (0.835, 1.411)
Gender of Care Recipient				
Male	0.412 (0.401, 0.423)		Ref	Ref
Female	0.415 (0.408, 0.423)		0.919 (0.780, 1.082)	0.937 (0.793, 1.106)
Recipient Relation to Caregiver				
Spouse/Partner	0.320 (0.306, 0.333)		Ref	Ref
Father/Mother	0.502 (0.489, 0.515)		1.089 (0.771, 1.537)	1.047 (0.738, 1.486)
Child	0.417 (0.393, 0.441)		1.441 (0.995, 2.088)	1.363 (0.939, 1.978)
Sibling	0.385 (0.360, 0.410)		1.088 (0.692, 1.711)	1.064 (0.676, 1.674)
Non-Immediate Family (Grandfather, Grandmother, Grandson, or Granddaughter)	0.390 (0.317, 0.462)		0.531 (0.186, 1.511)	0.556 (0.190, 1.628)
Other Relative	0.464 (0.447, 0.481)		1.197 (0.829, 1.729)	1.192 (0.821, 1.732)
Friend or Neighbor	0.378 (0.366, 0.389)		1.177 (0.833, 1.662)	1.156 (0.816, 1.638)
Weekly Hours of Care Provided				
1-20	0.421 (0.414, 0.428)		Ref	Ref
21-40	0.389 (0.365, 0.413)		1.041 (0.771, 1.405)	1.045 (0.770, 1.418)
41+	0.386 (0.361, 0.410)		1.015 (0.743, 1.385)	1.057 (0.774, 1.442)
Number of Care Recipients				
1	0.408 (0.400, 0.417)		Ref	Ref
≥2	0.422 (0.412, 0.431)		1.000 (0.856, 1.167)	0.995 (0.849, 1.165)
Location of Care Recipients				

Living in Your Household	0.361 (0.348, 0.373)		Ref	Ref
Living in Another Household	0.434 (0.426, 0.442)		0.964 (0.717, 1.296)	0.994 (0.736, 1.343)
Living in a Health Care Institution	0.411 (0.391, 0.431)		1.174 (0.811, 1.700)	1.181 (0.812, 1.717)
Now Deceased	0.424 (0.396, 0.451)		0.947 (0.618, 1.451)	0.953 (0.619, 1.465)
Number of CMC				
0	0.514 (0.503, 0.524)			Ref
1	0.408 (0.397, 0.418)			0.858 (0.636, 1.158)
≥ 2	0.288 (0.277, 0.299)			0.671 (0.426, 1.056)
Type of Healthcare Utilization				
Family Doctor Contact	0.390 (0.384, 0.397)			0.381 (0.264, 0.548)
Specialist Contact	0.362 (0.354, 0.370)			0.706 (0.597, 0.834)
Self-Rated Health				
Excellent	0.449 (0.434, 0.464)			Ref
Very Good	0.419 (0.41, 0.429)			1.154 (0.858, 1.551)
Good	0.408 (0.396, 0.419)			1.174 (0.870, 1.583)
Fair	0.358 (0.338, 0.379)			1.151 (0.809, 1.638)
Poor	0.323 (0.278, 0.368)			1.507 (0.900, 2.523)
Exercise				
None or Seldom	0.407 (0.400, 0.414)			Ref
Sometimes or Often	0.436 (0.423, 0.449)			1.021 (0.836, 1.247)
Smoking				
Not at All	0.404 (0.397, 0.410)			Ref
Occasionally	0.520 (0.469, 0.572)			1.283 (0.675, 2.438)
Daily	0.555 (0.529, 0.582)			1.360 (0.991, 1.866)
Alcohol				
Never	0.410 (0.392, 0.428)			Ref
Occasionally	0.424 (0.406, 0.441)			1.006 (0.769, 1.315)
Regular	0.413 (0.406, 0.420)			1.007 (0.804, 1.260)

[a]Grey cells indicate variables that were not included in the model represented by that column.

Table 4. Proportion Unvaccinated and Factors Associated with Non-Vaccination Against Seasonal Influenza Among Care Recipients Aged 65 Years and Older (N=5,559)

	Proportion Unvaccinated (95% CI)	Model 1[a] (N=1,197)	Model 2[a] (N=664)	Model 3[a] (N=658)
Total	0.248 (0.237, 0.260)			
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Age				
65-74	0.306 (0.287, 0.325)	Ref	Ref	Ref
75-84	0.207 (0.191, 0.224)	0.581 (0.427, 0.792)	0.684 (0.454, 1.029)	0.673 (0.437, 1.036)
85-94	0.205 (0.177, 0.233)	0.563 (0.329, 0.965)	0.472 (0.242, 0.918)	0.446 (0.221, 0.900)
Province of Residence				
Ontario	0.195 (0.172, 0.218)	Ref	Ref	Ref
Newfoundland	0.321 (0.264, 0.377)	3.572 (1.805, 7.071)	4.228 (1.444, 12.373)	5.793 (1.844, 18.199)
Prince Edward Island	0.185 (0.117, 0.254)	0.833 (0.245, 2.827)	0.727 (0.207, 2.556)	0.623 (0.160, 2.423)
Nova Scotia	0.155 (0.122, 0.188)	0.615 (0.296, 1.277)	1.009 (0.392, 2.601)	0.976 (0.365, 2.606)
New Brunswick	0.271 (0.198, 0.345)	0.943 (0.348, 2.557)	0.912 (0.306, 2.718)	0.931 (0.307, 2.820)
Quebec	0.335 (0.306, 0.363)	1.326 (0.854, 2.059)	1.504 (0.836, 2.707)	1.431 (0.773, 2.651)
Manitoba	0.264 (0.225, 0.303)	0.921 (0.473, 1.793)	1.399 (0.594, 3.295)	1.693 (0.709, 4.040)
Saskatchewan	0.281 (0.206, 0.357)	2.065 (0.589, 7.241)	2.290 (0.655, 8.001)	2.270 (0.702, 7.339)
Alberta	0.201 (0.169, 0.232)	0.984 (0.543, 1.784)	1.157 (0.503, 2.661)	1.181 (0.505, 2.762)
British Columbia	0.265 (0.239, 0.291)	1.239 (0.806, 1.907)	1.112 (0.588, 2.103)	1.071 (0.559, 2.054)
Sex				
Male	0.235 (0.218, 0.253)	Ref	Ref	Ref
Female	0.257 (0.243, 0.272)	1.311 (0.967, 1.778)	1.390 (0.910, 2.123)	1.319 (0.842, 2.066)
Urban or Rural				
Rural	0.288 (0.248, 0.328)	Ref	Ref	Ref
Urban	0.242 (0.230, 0.254)	0.719 (0.438, 1.179)	0.745 (0.431, 1.289)	0.706 (0.395, 1.263)
Household Income				
< 20000	0.370 (0.327, 0.412)	Ref	Ref	Ref
≥20000-<50000	0.286 (0.266, 0.306)	1.087 (0.696, 1.698)	0.934 (0.535, 1.632)	1.068 (0.577, 1.977)
≥50000-<100000	0.211 (0.192, 0.230)	0.610 (0.372, 0.999)	0.649 (0.346, 1.216)	0.675 (0.332, 1.370)
≥100000-<150000	0.165 (0.133, 0.197)	0.633 (0.322, 1.246)	0.668 (0.269, 1.660)	0.792 (0.283, 2.215)
≥150000	0.171 (0.126, 0.215)	0.485 (0.203, 1.160)	0.501 (0.142, 1.764)	0.593 (0.164, 2.138)
Education				
Less than secondary school graduation	0.291 (0.253, 0.329)	Ref	Ref	Ref
Secondary school graduation, no post-secondary education	0.259 (0.226, 0.293)	0.945 (0.521, 1.712)	0.673 (0.322, 1.406)	0.704 (0.323, 1.533)
Some post-secondary education	0.272 (0.233, 0.312)	0.854 (0.446, 1.637)	0.636 (0.284, 1.423)	0.619 (0.267, 1.433)
Post-secondary degree/diploma	0.237 (0.223, 0.250)	0.708 (0.435, 1.152)	0.603 (0.333, 1.094)	0.618 (0.336, 1.139)

Race				
White	0.245 (0.233, 0.256)	Ref	Ref	Ref
Non-White	0.362 (0.291, 0.432)	2.963 (1.654, 5.309)	1.780 (0.707, 4.485)	1.720 (0.658, 4.497)
Type of CMC				
Heart Disease	0.225 (0.203, 0.247)	0.834 (0.599, 1.161)	1.003 (0.627, 1.604)	1.116 (0.694, 1.796)
Lung Problems	0.199 (0.170, 0.227)	0.659 (0.432, 1.003)	0.627 (0.359, 1.095)	0.569 (0.312, 1.038)
Kidney Disease or Failure	0.214 (0.173, 0.255)	0.554 (0.328, 0.935)	0.618 (0.326, 1.173)	0.630 (0.326, 1.215)
Asthma	0.229 (0.200, 0.258)	1.159 (0.782, 1.717)	1.560 (0.896, 2.717)	1.615 (0.913, 2.856)
Diabetes	0.215 (0.189, 0.241)	0.851 (0.624, 1.160)	1.258 (0.742, 2.133)	1.324 (0.765, 2.289)
Cancer	0.216 (0.197, 0.236)	0.790 (0.577, 1.081)	0.987 (0.631, 1.543)	1.037 (0.655, 1.641)
Other CMC	0.236 (0.222, 0.250)	0.634 (0.451, 0.892)	1.056 (0.583, 1.915)	1.064 (0.592, 1.912)
Number of CMC				
0	0.293 (0.265, 0.321)		Ref	Ref
1	0.273 (0.252, 0.295)		1.016 (0.334, 3.094)	0.959 (0.299, 3.072)
≥ 2	0.219 (0.204, 0.234)		0.404 (0.114, 1.428)	0.307 (0.083, 1.131)
Care or Assistance Received				
Professional	0.229 (0.213, 0.245)		1.053 (0.661, 1.676)	1.118 (0.699, 1.791)
Non-Professional	0.254 (0.241, 0.267)		1.196 (0.683, 2.092)	1.245 (0.700, 2.212)
Type of Healthcare Utilization				
Family Doctor Contact	0.242 (0.231, 0.254)		0.163 (0.030, 0.892)	0.155 (0.027, 0.903)
Specialist Contact	0.232 (0.220, 0.244)		0.996 (0.574, 1.728)	0.904 (0.511, 1.600)
Hospitalization History	0.252 (0.231, 0.272)		0.869 (0.558, 1.355)	0.930 (0.593, 1.458)
Self-Rated Health				
Excellent	0.279 (0.238, 0.319)			Ref
Very Good	0.254 (0.232, 0.275)			2.111 (0.494, 9.015)
Good	0.240 (0.221, 0.259)			3.603 (0.866, 14.997)
Fair	0.253 (0.228, 0.279)			3.060 (0.697, 13.438)
Poor	0.213 (0.171, 0.255)			1.757 (0.292, 10.565)
Number in Household				
0	0.268 (0.250, 0.286)			Ref
1	0.230 (0.214, 0.246)			0.934 (0.569, 1.535)
≥ 2	0.258 (0.219, 0.298)			1.035 (0.490, 2.184)
Self-Rated Healthy Aging				
Excellent	0.291 (0.256, 0.327)			Ref
Very Good	0.237 (0.218, 0.256)			0.565 (0.275, 1.162)
Good	0.239 (0.220, 0.258)			0.342 (0.161, 0.726)
Fair	0.263 (0.232, 0.294)			0.696 (0.294, 1.645)
Poor	0.241 (0.182, 0.301)			0.299 (0.050, 1.797)
Exercise				

None or Seldom	0.245 (0.233, 0.257)			Ref
Sometimes or Often	0.274 (0.241, 0.307)			0.801 (0.389, 1.649)
Smoking				
Not at All	0.243 (0.231, 0.255)			Ref
Occasionally	0.333 (0.191, 0.476)			0.594 (0.066, 5.377)
Daily	0.345 (0.287, 0.402)			1.734 (0.832, 3.613)
Alcohol				
Never	0.271 (0.245, 0.297)			Ref
Occasionally	0.281 (0.253, 0.308)			1.166 (0.665, 2.044)
Regular	0.232 (0.218, 0.246)			0.968 (0.580, 1.616)

[a]Grey cells indicate variables that were not included in the model represented by that column.

Supplementary Table 1: Variable Categorization

CLSA Question and Label	CLSA Participant Response → Variable Characterization for Models
Have you had… Flu shot in the last 12 months PHB_FLUV_COF1[a] PHB_FLUV_TRF1[a]	1 = Yes 2 = No 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Participant age at FU1 (in years) AGE_NMBR_COF1 AGE_NMBR_TRF1	45-54, 55-64, 65-74, 75-84, 85-94
Province of residence WGHTS_PROV_COF1 WGHTS_PROV_TRF1	Newfoundland, Prince Edward Island[b], Nova Scotia, New Brunswick[b], Quebec, Ontario, Manitoba, Saskatchewan[b], Alberta, British Columbia
What was your sex at birth? SDC_BTHSEX_COF1 SDC_BTHSEX_TRF1	1 = Male → 0 2 = Female → 1 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
Urban/ rural classification SDC_URBAN_RURAL_COF1 SDC_URBAN_RURAL_TRF1	0 = Rural area → Rural 1 = Urban core → Urban 2 = Urban fringe → Urban 3 = Rural fringe in CMA/CAs → Rural 4 = Urban Areas out CMA/CAs → Urban 5 = Rural fringe out CMA/CAs → Rural 6 = Secondary urban core → Urban 9 = Link to DA → NA -88888 = Missing → NA
What is your best estimate of the total household income received by all household members, from all sources, before taxes and deductions, in the past 12 months? INC_TOT_COF1 INC_TOT_TRF1	1 = Less than $20,000 2 = $20,000 or more, but less than $50,000 3 = $50,000 or more, but less than $100,000 4 = $100,000 or more, but less than $150,000 5 = $150,000 or more 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern
Highest Level of Education - Respondent, 4 Levels ED_UDR04_COM ED_UDR04_TRM	1 = Less than secondary school graduation 2 = Secondary school graduation, no post-secondary education 3 = Some post-secondary education 4 = Post-secondary degree/diploma

	9 = At least one required question was not answered → NA
Cultural / Racial Background SDC_DCGT_COM SDC_DCGT_TRM	1 = White only → White 2 = Black only → Non-White 3 = Korean only → Non-White 4 = Filipino only → Non-White 5 = Japanese only → Non-White 6 = Chinese only → Non-White 7 = South Asian only → Non-White 8 = Southeast Asian only → Non-White 9 = Arab only → Non-White 10 = West Asian only → Non-White 11 = Latin American only → Non-White 12 = Other racial or cultural origin (only) → Non-White 13 = Multiple racial or cultural origins → Non-White 99 = Required question was not answered → NA
Type of CMC Has a doctor ever told you that you have heart disease (including congestive heart failure or CHF)? CCC_HEART_COF1 CCT_HEART_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Type of CMC Has a doctor told you that you have/had any of the following: emphysema, chronic bronchitis, chronic obstructive pulmonary disease (COPD), or chronic changes in lungs due to smoking? CCC_COPD_COF1 CCT_COPD_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Has a doctor ever told you that you have kidney disease or kidney failure? CCC_KIDN_COF1 CCT_KIDN_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Has a doctor ever told you that you have asthma? CCC_ASTHM_COF1 CCT_ASTHM_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA

	-88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Were you diagnosed with? Type I, Type II, Neither [Type of Diabetes] DIA_TYPE_COF1 CCT_DIABTYPE_TRF1	1 = Type I → 1 2 = Type II → 1 3 = Neither → 0 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Type of CMC … Has a doctor ever told you that you had cancer? CCC_CANC_COF1 CCT_CANC_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
Type of CMC Other CMC: **composite variable**[c] Has a doctor ever told you that you have had a heart attack or myocardial infarction?; Has a doctor ever told you that you have high blood pressure or hypertension?; Has a doctor ever told you that you have dementia or Alzheimer's disease?;. Has a doctor ever told you that you had Parkinsonism or Parkinson's Disease?; Has a doctor ever told you that you have experienced a Stroke or CVA (cerebrovascular accident)?; Has a doctor ever told you that you have experienced a ministroke or TIA (Transient Ischemic Attack)? CCC_AMI_COF1 and/or CCC_HBP_COF1 and/or CCC_ALZH_COF1 and/or CCC_PARK_COF1 and/or CCC_CVA_COF1 and/or CCC_TIA_COF1 and/or CCT_AMI_TRF1 and/or CCT_HBP_TRF1 and/or CCT_ALZH_TRF1 and/or PKD_PARK_TRF1 and/or CCT_CVA_TRF1 and/or CCT_TIA_TRF1	0 = No other CMC 1 = Other CMC
Number of CMC: **calculated variable**[d] Heart disease (Y = 1, N = 0) + lung problem (Y = 1, N = 0) + kidney disease (Y = 1, N = 0) + asthma (Y = 1, N = 0) + diabetes (Y = 1, N = 0) + cancer (Y = 1, N = 0) + other CMC (Y = 1, N = 0) = ∑Y = Total CMC	0 = 0 1 = 1 2-7 = ≥2
Received professional care in past 12 months: **composite variable**[c] During the past 12 months, did you receive short-term or long-term professional assistance at home, because of a health condition or limitation that affects your daily life, for any of the following activities?:	0 = 0 → No professional care received for any activity listed 1 = 1 → Professional care received for any activity listed

Received professional personal care; Received professional medical care; Received professional managing care; Received professional assistance with meal preparation or delivery; Received professional assistance with activities; Received professional assistance with transportation; Received professional physical therapy; Received professional training and adaptation assistance; Received other professional assistance CR1_PRO_PR_COF1 and/or CR1_PRO_MD_COF1 and/or CR1_PRO_MG_COF1 and/or CR1_PRO_MH_COF1 and/or CR1_PRO_WK_COF1 and/or CR1_PRO_TR_COF1 and/or CR1_PRO_PT_COF1 and/or CR1_PRO_TA_COF1 and/or CR1_PRO_OT_COF1 and/or CR1_PRO_PR_TRF1 and/or CR1_PRO_MD_TRF1 and/or CR1_PRO_MG_TRF1 and/or CR1_PRO_MH_TRF1 and/or CR1_PRO_WK_TRF1 and/or CR1_PRO_TR_TRF1 and/or CR1_PRO_PT_TRF1 and/or CR1_PRO_TA_TRF1 and/or CR1_PRO_OT_TRF1	
Received non-professional care in past 12 months: **composite variable**[c] Received non-professional personal care; Received non-professional medical care; Received non-professional managing care; Received non-professional assistance with activities; Received non-professional assistance with transportation; Received non-professional assistance with meal preparation; Received non-professional physical therapy; Received non-professional training and adaptation assistance; Received other non-professional assistance CR2_FAM_PR_COF1 and/or CR2_FAM_MD_COF1 and/or CR2_FAM_MG_COF1 and/or CR2_FAM_WK_COF1 and/or CR2_FAM_TR_COF1 and/or CR2_FAM_MH_COF1 and/or CR2_FAM_PT_COF1 and/or CR2_FAM_TA_COF1 and/or CR2_FAM_OT_COF1 and/or CR2_FAM_PR_TRF1 and/or CR2_FAM_MD_TRF1 and/or CR2_FAM_MG_TRF1 and/or CR2_FAM_WK_TRF1 and/or CR2_FAM_TR_TRF1 and/or CR2_FAM_MH_TRF1 and/or CR2_FAM_PT_TRF1 and/or CR2_FAM_TA_TRF1 and/or CR2_FAM_OT_TRF1	0 = 0 → No non-professional care received for any activity listed 1 = 1 → Non-professional care received for any activity listed
During the past 12 months, have you had contact with any of the following about your physical or mental health? Has had contact with: Family Doctor HCU_FAMPHY_COF1 HCU_FAMPHY_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA

	-88888 = Missing → NA -99999 = Skip Pattern → NA
Has had contact with: Medical specialist (such as a Cardiologist, Gynaecologist, Psychiatrist or Ophthalmologist) HCU_SPEC_COF1 HCU_SPEC_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
Were you a patient in a hospital overnight during the past 12 months? HCU_HLOVRNT_COF1 HCU_HLOVRNT_TRF1	1 = Yes 2 = No 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip Pattern → NA
In general, would you say your health is excellent, very good, good, fair, or poor? GEN_HLTH_COF1 GEN_HLTH_TRF1	1 = Excellent 2 = Very good 3 = Good 4 = Fair 5 = Poor 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
How many people, not including yourself, currently live in your household?: c**alculated variable**[d] SN_LIVH_NB_COF1 SN_LIVH_NB_TRF1	0 = 0 1 = 1 2-9 = ≥2 -88880 = Did not complete a DCS visit → NA -88888 = Missing → NA
In terms of your own healthy aging, would you say it is excellent, very good, good, fair, or poor? GEN_OWNAG_COF1 GEN_OWNAG_TRF1	1 = Excellent 2 = Very good 3 = Good 4 = Fair 5 = Poor 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
Over the past 7 days, how often did you engage in moderate sports or recreational activities such as ballroom dancing, hunting, skating, golf without a cart, softball or other similar activities?; Over the past 7 days, how often did you engage in strenuous sports or recreational activities such as jogging, swimming, snowshoeing, cycling, aerobics, skiing or other similar activities?: **composite variable**[c] PA2_MSPRT_COF1 and/or PA2_SSPRT_COF1 and/or PA2_MSPRT_TRF1 and/or PA2_SSPRT_TRF1	1 = Never → None or Seldom 2 = Seldom (1 to 2 days) → None or Seldom 3 = Sometimes (3 to 4 days) → Sometimes or Often 4 = Often (5 to 7 days) → Sometimes or Often 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA

At the present time, do you smoke cigarettes daily, occasionally or not at all? SMK_CURRCG_COF1 SMK_CURRCG_TRF1	1 = Daily (at least one cigarette every day for the past 30 days) 2 = Occasionally (at least one cigarette in the past 30 days, but not every day) 3 = Not at all (you did not smoke at all in the past 30 days) 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA
Type of Drinker (Past 12 Months) ALC_TTM_COF1 ALC_TTM_TRF1	1 = Regular drinker (at least once a month) 2 = Occasional drinker 3 = Did not drink in the last 12 months -77771 = Inconclusive due to at least one missing item → NA
Caregiver Status: **composite variable**[c] During the past 12 months, have you provided any of the following types of assistance to another person because of a health condition or limitation? Provided personal care; Provided medical care; Provided managing care; Provided assistance with meals or housework; Provided assistance with house maintenance or outdoor work; Provided assistance with transportation; Provided social/ emotional assistance; Provided mobility assistance; Provided monetary assistance or financial management; Provided other types of assistance CAG_HLT_PR_COF1 and/or CAG_HLT_MD_COF1 and/or CAG_HLT_MG_COF1 and/or CAG_HLT_MH_COF1 and/or CAG_HLT_WK_COF1 and/or CAG_HLT_TR_COF1 and/or CAG_HLT_CS_COF1 and/or CAG_HLT_MB_COF1 and/or CAG_HLT_MF_COF1 and/or CAG_HLT_OT_COF1 and/or CAG_HLT_PR_TRF1 and/or CAG_HLT_MD_TRF1 and/or CAG_HLT_MG_TRF1 and/or CAG_HLT_MH_TRF1 and/or CAG_HLT_WK_TRF1 and/or CAG_HLT_TR_TRF1 and/or CAG_HLT_CS_TRF1 and/or CAG_HLT_MB_TRF1 and/or CAG_HLT_MF_TRF1 and/or CAG_HLT_OT_TRF1	0 = No 1 = Yes -88888 = Missing → NA -99999 = Skip pattern → NA
Is the person to whom you provided the most assistance male or female? CAG_GNDR_COF1 CAG_GNDR_TRF1	1 = Male → 0 2 = Female → 1 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern → NA
What is the relationship between you and this person? Is s/he your… CAG_RELN2_COF1	1 = Husband/wife → Spouse 2 = Common-law partner → Spouse

CAG_RELN2_TRF1	3 = Father/mother 4 = Son/daughter 5 = Brother/sister 6 = Grandfather/grandmother → Non-immediate family 7 = Grandson/granddaughter → Non-immediate family 8 = Father-in-law/mother-in-law → Other relative 9 = Son-in-law/daughter-in-law → Other relative 10 = Brother-in-law/sister-in-law → Other relative 11 = Other relative → Other relative 12 = Friend → Friend or neighbor 13 = Neighbour → Friend or neighbor 98 = Don't know/No answer → NA 99 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern → NA
About how many hours per week, on average, did you spend assisting this person?: **calculated variable**[d] CAG_HRWK_NB_COF1 CAG_HRWK_NB_TRF1	0-20 = 0-20 21-40 = 21-40 41+ = 41+ 998 = Don't know/No answer→ NA 999 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern → NA
During the past 12 months, how many people in total have you provided any type of assistance to because of a health condition or limitation, including financial assistance?: **calculated variable**[d] CAG_PPL_NB_COF1 CAG_PPL_NB_TRF1	1 = 1 2-50 = ≥2 98 = Don't know/No answer→ NA 99 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern → NA
Dwelling location of person who participant provided most care giving assistance CAG_MOST_COF1 CAG_MOST_TRF1	1 = Living in your household 2 = Living in another household 3 = Living in a health care institution 4 = Now deceased 8 = Don't know/No answer → NA 9 = Refused → NA -88888 = Missing → NA -99999 = Skip pattern → NA

[a]COF1 indicates the Comprehensive cohort; TRF1 indicates the Tracking cohort
[b]There were no participants in the Comprehensive cohort in these provinces
[c]Respondents who responded "Y" or "1" to at least one of the multiple included variables were coded as "Y" or "sometimes or often" in the new composite variable
[d]Re-categorization of existing categories for single variable

Supplementary Table 2. Demographic Characteristics by Cohort: Caregivers Aged 45 Years and Older (N=23,500)

	Comprehensive Cohort (N=14,563)	Tracking Cohort (N=8,937)
	N(%)	N(%)
Outcome Variable		
Received influenza vaccination in last 12 months		
Yes	8547(58.7)	5224(58.5)
No	6016(41.3)	3713(41.5)
Sociodemographics		
Age		
45-54	2387(16.4)	1234(13.8)
55-64	5230(35.9)	3203(35.8)
65-74	4194(28.8)	2650(29.7)
75-84	2375(16.3)	1521(17.0)
85-94	377(2.6)	329(3.7)
Province of Residence		
Newfoundland	873(6.0)	401(4.5)
Prince Edward Island	N/A	444(5.0)
Nova Scotia	1354(9.3)	591(6.6)
New Brunswick	N/A	496(5.5)
Quebec	2661(18.3)	1518(17.0)
Ontario	3182(21.8)	2017(22.6)
Manitoba	1505(10.3)	625(7.0)
Saskatchewan	N/A	577(6.5)
Alberta	1536(10.5)	979(11.0)
British Columbia	3445(23.7)	1288(14.4)
Sex		
Male	6594(45.3)	3998(44.7)
Female	7969(54.7)	4928(55.1)
Urban or Rural		
Urban	13490(92.6)	6593(73.8)
Rural	840(5.8)	1545(17.3)
Household Income		
≥20000-<50000	563(3.9)	366(4.1)
≥50000-<100000	2762(19.0)	2217(24.8)
≥100000-<150000	5062(34.8)	3138(35.1)
≥150000	2781(19.1)	1451(16.2)
≥20000-<50000	2586(17.8)	1189(13.3)
Education		
Less than secondary school graduation	576(4.0)	538(6.0)
Secondary school graduation, no post-secondary education	1240(8.5)	1095(12.3)

Some post-secondary education	1077(7.4)	666(7.5)
Post-secondary degree/diploma	11650(80.0)	6609(74.0)
Race		
White	13806(94.8)	8665(97.0)
Non-White	744(5.1)	262(2.9)

Supplementary Table 3. Demographic Characteristics by Cohort: Care Recipients Aged 65 Years and Older (N=5,559)

	Comprehensive Cohort (N=3,315)	Tracking Cohort (N=2,244)
	N(%)	N(%)
Outcome Variable		
Received influenza vaccination in last 12 months		
Yes	2516(75.9)	1662(74.1)
No	799(24.1)	582(25.9)
Sociodemographics		
Age		
65-74	1456(43.9)	874(38.9)
75-84	1448(43.7)	977(43.5)
85-94	411(12.4)	393(17.5)
Province of Residence		
Newfoundland	176(5.3)	86(3.8)
Prince Edward Island	N/A	124(5.5)
Nova Scotia	309(9.3)	156(7.0)
New Brunswick	N/A	140(6.2)
Quebec	652(19.7)	382(17.0)
Ontario	670(20.2)	494(22.0)
Manitoba	332(10.0)	168(7.5)
Saskatchewan	N/A	135(6.0)
Alberta	374(11.3)	248(11.1)
British Columbia	801(24.2)	311(13.9)
Sex		
Male	1340(40.4)	904(40.3)
Female	1974(59.5)	1336(59.5)
Urban or Rural		
Urban	3129(94.4)	1689(75.3)
Rural	133(4.0)	364(16.2)
Household Income		
≥20000-<50000	268(8.1)	219(9.8)
≥50000-<100000	1061(32.0)	844(37.6)
≥100000-<150000	1104(33.3)	646(28.8)
≥150000	343(10.3)	171(7.6)
≥20000-<50000	181(5.5)	94(4.2)
Education		
Less than secondary school graduation	298(9.0)	252(11.2)
Secondary school graduation, no post-secondary education	339(10.2)	313(13.9)
Some post-secondary education	285(8.6)	196(8.7)

Post-secondary degree/diploma	2387(72.0)	1467(65.4)
Race		
White	3187(96.1)	2192(97.7)
Non-White	127(3.8)	50(2.2)

Chapter 5: Discussion

In this thesis, I evaluated the prevalence of not having received an influenza vaccine in the prior 12 months and factors associated with non-vaccination among adults aged ≥65 and adults aged 45-64 with at least 1 CMC, two groups at high risk of severe outcomes, and caregivers aged ≥45 and care recipients aged ≥65, two groups that could both directly and indirectly benefit from vaccination using data from the CLSA FUP1 (2015-2018). The comprehensive set of variables collected by the CLSA study allowed for the exploration of many domains relevant to influenza vaccination, including sociodemographics, health services utilization, health behaviors, and social characteristics, across a large study sample (N=44,372). This study also allowed the examination of influenza vaccination in both groups that are at high risk of severe outcomes, which are often the main targets of influenza vaccination programs, and groups that are not specifically evaluated in the context of influenza vaccination programs, such as care recipients. The prevalence of non-vaccination was 29.5% (95% CI: 28.9%, 30.1%) for participants aged 65 years and older, 49.9% (95% CI: 49.0%, 50.9%) for participants aged 45-64 with CMC, 41.4% (95% CI: 40.8%, 42.0%) for caregivers, and 24.8% (95% CI: 23.7%, 26.0%) for care recipients. Influenza vaccination was strongly associated with healthcare utilization in both lower-vaccination groups (those aged 45-64 years with CMC and caregivers aged 65 years and older). Discussion of the results is already present in manuscript 1 (Chapter 3) and manuscript 2 (Chapter 4), and so this chapter will primarily focus on connecting these findings to the broader context of vaccination in Canada.

It is important to evaluate the prevalence of influenza non-vaccination and the factors associated with non-vaccination due to the individual and community impact that vaccination can have. A modeling study of influenza transmission and vaccination in the United States found that even low-efficacy influenza vaccines can significantly reduce the number of hospitalizations and deaths (Sah et al., 2018). Preventing severe outcomes from influenza infection like hospitalization is particularly important in the current context of the SARS-CoV-2 pandemic, where healthcare systems are already facing a heavy burden (Sen-Crowe et al., 2021).

There are many potential mechanistic explanations that may underlie the results observed in our analysis. One result of particular interest was the magnitude of the association between influenza

non-vaccination and hospitalization history in those aged 45-64 with CMC in the fully adjusted model. While hospitalization is generally considered to be associated with poor health and an increased awareness of disease prevention, it is also possible that influenza vaccination is preventing hospitalization in these individuals, thus creating this unexpected association (Chen et al., 2007). Reasons for hospitalization were not provided in this dataset, so it is unclear what the proportion of ILI-related hospitalizations is compared to the total number. Additionally, for both those at high risk of severe outcomes and those at risk of influenza transmission, cultural/racial background, age, province of residence, contact with a family doctor, and urban/rural classification were strongly associated with influenza vaccination in the fully adjusted models. A systematic review and meta-analysis of influenza vaccine uptake in older adults in the United States found that the factors associated with lower influenza vaccination uptake among ethnic minorities is associated with a complex interplay of covariates, including associations between ethnicity and health-influencing factors such as health status and income (Okoli et al., 2019). Age is one of the strongest determinants of influenza vaccination (Yeung et al., 2016). This may be because older adults typically have a higher number of physician visits (Isenor et al., 2018), which could mean more exposure to influenza vaccination recommendations from a trusted healthcare provider. The association between provider contact and influenza vaccination recommendations has been widely demonstrated (Okoli et al., 2020). The National Influenza Immunization Coverage Survey for the 2015/2016 influenza season in Canada found that for those aged 18-64 with CMC, "Recommended by health care professional" was in the top 3 most frequent reasons for vaccination (Public Health Agency of Canada, 2021a), while the 2019/2020 survey found that 69% of respondents strongly or somewhat agreed that the opinion of their family doctor, general practitioner or nurse practitioner is an important part of influenza vaccine decision-making (Public Health Agency of Canada, 2020). These results show the importance of maintaining trust in the healthcare system and provider recommendations. The influence of provider contact may also be related to the higher odds of influenza vaccination in those in urban areas compared to rural areas. A study of the impact of immunization polices on influenza vaccination coverage in Nova Scotia from 2006-2016 found that physicians provided more influenza vaccinations in urban areas, while pharmacists and public health providers provided more vaccinations in rural areas (Isenor et al., 2018).

The association between influenza non-vaccination and province of residence was found to be highly variable across and within the groups of interest of this study. This is not surprising, as each province offers its own version of an influenza vaccination campaign. For one, universal vaccination was not recommended in Quebec, New Brunswick, or British Columbia, although these provinces did target those at high risk in their campaigns (Andrew and McNeil, 2021). Available influenza vaccines also vary by province (Andrew and McNeil, 2021), which may impact perceived efficacy for residents of those provinces. Provider contact is also variable between provinces: one study of 2003 CCHS data found that residents of Quebec had reduced odds of reporting a regular medical doctor, while the odds of reporting a regular doctor for residents of Nova Scotia had a more than twofold increase (Sibley and Weiner, 2011). Interestingly, in our study, residents of Quebec generally had low vaccination prevalence and notably higher odds of non-vaccination, while residents of Nova Scotia generally had higher vaccination prevalence.

Another model-related aspect of note from this study is that, for all 4 groups of interest, the point estimates of the included covariates across the 3 models remained relatively consistent. The lack of change in point estimates may indicate that some of the additional covariates in the least parsimonious models (Models 2 and 3 in all analyses) were not acting as confounders between the Model 1 variables and influenza non-vaccination. Because model fit was not assessed in this study, it is unclear if the variables added in Models 2 and 3 improved the overall fit despite the lack of change in point estimates. For all analyzed groups except caregivers aged 45 years and older, the width of the 95% CIs for variables included in all 3 models generally increased (often notably) from Model 1 to Model 3, likely from reduced precision due to the added variables. For caregivers aged 45 years and older, the 95% CI width remained relatively constant across all models, which may indicate correlation between the variables from Model 1 and Models 2 and 3 or simply higher precision due to the large sample size of this group across all 3 models.

These results can be used by public health officials to evaluate and improve influenza vaccination campaigns. An advanced understanding of the factors that influence influenza vaccination in these previously targeted groups allows for more effective planning of influenza vaccination programs to optimize vaccination coverage. Methods of vaccination promotion that

are not reliant on the healthcare system for recommendations could be used to reach those without provider contact and therefore likely less exposure to vaccination recommendations. Additionally, vaccination prevalence in new target populations, such as the group of caregivers of those with limitations analyzed in this study, needs to be periodically measured and influenza vaccination educational content targeted accordingly; the lower vaccination in this previously unexplored group may indicate that there are other potential drivers of influenza transmission that are not being sufficiently educated by existing vaccination campaigns.

Knowledge of who is not getting vaccinated is an important first step to improving influenza vaccination programs. However, additional work is needed to expand upon these results. This study did not look at the impact of vaccination across individual influenza seasons, which may show how annual influenza strains also impact vaccination. Although not addressed in this study, vaccine hesitancy is also an important determinant of influenza vaccination. Additionally, while this study was designed to provide knowledge that can be used for targeted public health vaccination programs based on the categories associated with non-vaccination in groups that can highly benefit from influenza vaccination, future work could build upon these logistic regression models to predict the proportions of vaccination within an individual adjusted for the relevant vaccination-associated factors. This could help tailor vaccination messaging for public health campaigns on a more specific level.

Chapter 6: Conclusion

In this thesis, I conducted a secondary analysis of cross-sectional data from the CLSA FUP1 collected between 2015-2018 to evaluate influenza vaccination coverage and associated factors in those at high risk of severe outcomes (i.e., adults aged 65 years and older and adults aged 45-64 years with at least 1 CMC) and those at risk of influenza transmission (i.e., caregivers aged 45 years and older and care recipients aged 65 years and older). The many domains related to influenza vaccination that are represented in the CLSA dataset allow for a comprehensive assessment of non-vaccination-associated factors in a large sample. This study was also one of the first to analyze influenza vaccination in caregiver and care recipient populations for both professional and unprofessional caregiving individuals. The prevalence of non-vaccination was particularly high in 2 groups of interest: 49.9% (95% CI: 49.0%, 50.9%) of participants aged 45-64 with CMC and 41.4% (95% CI: 40.8%, 42.0%) of caregivers had not received an influenza vaccination in the past 12 months. For both of these groups, no contact with a family doctor was strongly associated with non-vaccination in the fully adjusted model, and the magnitude and direction of association with influenza non-vaccination was highly variable across each province. These findings could be used to optimize influenza vaccination campaigns, identify provinces in need of additional vaccination support, and increase the prevalence of vaccination in those at high risk of severe outcomes or influenza transmission.

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