Examining vaccine coverage among immigrant populations in Alberta, Canada and factors associated with vaccination

by

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Abstract

Study 1: Human papillomavirus vaccine coverage among immigrant children in Alberta: a population-based cohort study

Background: Previous studies have shown that parents of immigrant children have more negative perceptions about human papillomavirus (HPV) vaccine than parents of non-immigrant children. However, there is a lack of studies measuring HPV vaccine coverage amongst school-aged immigrant children in Canada. Therefore, the objective of this study was to assess HPV vaccine coverage and factors associated with uptake among foreign-born immigrant children relative to the non-immigrant population in Alberta, Canada.

Methods: In this cohort study, we analyzed population-based linked administrative health data to measure HPV vaccine coverage for 346,749 school-aged children in Alberta, Canada, of which 31,656 were immigrants. Coverage was examined at 12 years old for the years 2014 to 2018; vaccine series completion was considered receipt of 3 doses during this period. We used multivariable logistic regression to examine the association of vaccine coverage with migration status, adjusting for socio-demographic variables. Difference in coverage between age 12 and 17 was also analyzed in females from the years 2008 to 2013.

Findings: Since the start of the program in 2008 until 2018, HPV vaccination coverage (receipt of 3 doses) among immigrant children was significantly higher (52.58%) in comparison to non-immigrant children (47.41%). When excluding the first two years of program implementation for each sex, combined HPV vaccination coverage was 58.14% (95% CI 57.64, 58.63) among immigrants and 54.95% (95% CI 54.78, 55.11) among non-immigrants. Immigrants from Asia and Africa had the highest coverage (57.09 – 64.14%), while immigrants from North America,

Oceania, and South America had the lowest coverage (38.30 – 44.96%). A multivariable logistic regression model analyzing data from 2014 to 2018 found vaccine coverage was relatively similar across income quintiles; however, immigrants living in rural residences had lower vaccine coverage in comparison to non-immigrants (39. 76% vs 45.05%). When comparing vaccine coverage at age 12 to age 17 in only females (from 2008 to 2013), the total increase was insignificant between immigrant (30.93%) and non-immigrants (31.96%).

Conclusion: Overall, immigrant children had higher HPV vaccination coverage in comparison to non-immigrants, which is encouraging given some previous literature has suggested the opposite. This implies that efforts to increase vaccination rates among immigrant children may be having a positive impact. Among immigrants, routine immunization promotion strategies should be targeted to those living in rural residences and from North America, Oceania, and South America, in order to improve HPV vaccination coverage in this group even further.

Study 2: COVID-19 vaccine coverage among immigrants and refugees in Alberta: A population-based cross-sectional study

Background Studies have shown that immigrants often have lower vaccination rates than the Canadian-born population. We sought to assess COVID-19 vaccine coverage and factors associated with uptake among foreign-born immigrants relative to the non-immigrant population in Alberta, Canada.

Method: In this cross-sectional study, we analyzed population-based linked administrative health data from Alberta to examine vaccine coverage for 3,931,698 Albertans, of which 731,217 were immigrants. We calculated COVID-19 vaccination coverage as the proportion of eligible Albertans with a record of receiving at least one dose of a COVID-19 vaccine as of November

29, 2021. We used multivariable logistic regression to examine the association of vaccine coverage with migration status (immigrants: four categories based on time since migration and non-immigrants) adjusting for socio-demographic variables.

Results Overall, COVID-19 vaccination coverage was 78.2% (95% CI: 78.1%-78.3%) among immigrants and 76.0% (95% CI: 75.9%-76.0%) among non-immigrants. Coverage among immigrants differed by continent of origin, with North America, Oceania, and Europe having the lowest coverage. Although vaccine coverage was relatively uniform across neighborhood income quintiles for immigrants, immigrants living in rural areas had lower vaccine coverage compared to non-immigrants living in rural areas. Multivariable logistic regression analysis showed a significant interaction between age category and migration status. While immigrants below 50 years of age generally had significantly higher vaccine coverage compared to non-immigrants, there was some variation based on time since migration. Immigrants above 50 years of age showed significantly lower coverage compared to non-immigrants of the same age.

Conclusions In conclusion, high COVID-19 vaccination coverage among immigrant populations is an encouraging outcome. However, continued efforts are needed to target public health interventions towards older immigrants, immigrants living in rural areas, and immigrants from specific continental backgrounds in order to improve COVID-19 vaccination coverage.

Preface

The first part of this research project, HPV vaccination coverage, received research ethics approval from the University of Alberta Ethics Board, “HPV vaccination coverage in immigrant populations in Alberta”, No.00122164, August 24, 2022. The second part, COVID-19 vaccination coverage, received research ethics approval from the University of Alberta Ethics Board, “COVID-19 vaccine coverage in Alverta,” No.00114786, December 2, 2021.

Some of the research conducted for this thesis forms part of a national research collaboration, led by Professor S.E. MacDonald at the University of Alberta. Chapter 2 is my original work, alongside the literature review in chapter 1 and the conclusions in Chapter 4. S.E. MacDonald, D. Voaklander, and S. Meherali were supervisory authors for the manuscript in chapter 2 and contributed to manuscript edits; Y.R. Paudel provided advice on analysis. No part of Chapter 2 in this thesis has been previously published.

Chapter 3 of this thesis has been published as S.E. MacDonald, Y.R. Paudel, and C. Du, “COVID-19 vaccine coverage among immigrants and refugees in Alberta: A population-based cross-sectional study.” I was a member of the study team, with input at all stages plus primary responsible for data interpretation and writing, including original draft, review and editing. S.E. MacDonald was the supervisory author and was involved in conceptualization, methodology, investigation, and writing (review and editing). Y.R. Paudel was involved in conceptualization, methodology, investigation, formal analysis and writing (original draft, review, editing).

Dedication

I would like to dedicate this thesis work to my family. Your unconditional love, unwavering support, and constant encouragement have been the cornerstone of my academic journey. You have stood by me through the ups and downs, and your faith in me has been the driving force behind my success.

To my mom and dad, who immigrated to Canada over 20 years ago, your guidance and sacrifices have made me the person I am today. Thank you for instilling in me the values of hard work, perseverance, and dedication.

To my siblings, thank you for always being my rock and cheering me on every step of the way. Your love and support have been my greatest motivation.

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I would also like to acknowledge my co-supervisors, Dr. Salima Meherali and Dr. Don Voaklander, for their valuable feedback and constructive criticism, which have helped me refine my research and improve my writing.

I would also like to thank Yuba Raj Paudel for his assistance and mentorship throughout my thesis journey. His mentorship, advice, support and time have been invaluable to me.

I want to extend my thanks to the rest of the Aimm team who have provided a supportive and collaborative environment throughout my graduate studies.

Thank you to the examining committee for taking the time to review my thesis and for their insightful comments and suggestions.

Last but not least, I would like to thank my family and friends for their unconditional love and support. Your belief in me has been the driving force behind my academic achievements, and I am forever grateful for your unwavering encouragement.

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List of Abbreviations

AHCIP	Alberta Health Care Insurance Plan
CSDH	Commission on Social Determinants of Health
COVID-19	Coronavirus disease 2019
CI	confidence interval
HPV	human papillomavirus
Imm/ARI	Immunization and Adverse Reaction to Immunization
NACI	National Advisory Committee on Immunization
STIs	sexually transmitted infections
ULI	unique lifetime identifier
VPD	vaccine-preventable disease

Chapter One: Background

Introduction

In Canada, the proportion of immigrants in the population is increasing over time (1). Policies and events, including in healthcare, have disproportionately impacted immigrant groups. Existing literature has largely shown that immigrant populations historically have had lower rates of vaccination in comparison to non-immigrant groups in Canada and globally (2,3). However, there are inconsistent data and lack of research regarding vaccination coverage in certain vaccines among immigrants and subpopulations such as adolescents. It is thought that due to factors such as nativity to the healthcare system and disproportionate effect of the pandemic, vaccination coverage of human papillomavirus (HPV) and Coronavirus disease 19 (COVID-19) might differ between immigrant and non-immigrant groups.

This project aimed to expand on the understanding of different patterns and trends in vaccination coverage amongst immigrant populations through evaluation of vaccination coverage and examining determinants associated with vaccine uptake to drive evidence-based interventions and policies. This thesis was compromised of two studies conducted in the Alberta setting: one focused on HPV coverage specifically amongst immigrant adolescents and another focused on vaccination coverage and factors related to uptake of COVID-19 vaccine.

In this introductory chapter, the background and context will be provided, which includes information on the study setting of Alberta, vaccines and vaccination programs, HPV disease and vaccine, COVID-19 disease and vaccine, and immigrants, including the HPV and COVID-19 context. This will be followed by the research project objectives, aims and rationale.

Contextual Background

Study Setting

Alberta is a western Canadian province, with a population of 4.5 million residents (4). Approximately 99% of residents are registered under the publicly funded Alberta Health Care Insurance Plan (AHCIP), which provides services such as physician care, diagnostic and laboratory services, hospital care, and public health services.

Vaccination

Vaccination is a safe and cost-effective form of protection from multiple vaccine-preventable diseases, eventually becoming one of the top ten great public health achievements in the 20th century (5). As such, infectious diseases are no longer the leading cause of deaths in Canada, contributing to less than 5% of all deaths (6). Routine immunization has been crucial for protection from diseases at the individual level and the prevention of disease outbreaks at the community level (7). However, the negative impacts of vaccine-preventable diseases (VPDs) still exist and are consequential. For example, severe outcomes such as encephalitis, amputations and death may occur; the economic and societal costs are substantially high, with an estimated 729 lost health adjusted-life years annually and $8.3 billion attributed to infectious diseases (3,8).

Vaccine policies

In Canada, Health Canada is the federal body responsible for vaccine regulation and licensing (9). The National Advisory Committee on Immunization (NACI) is responsible for vaccination recommendations and guidelines. However, it is the provinces and territories that are responsible

for the distribution and administration of vaccines through individual public health programs, which differ across jurisdictions.

Routine immunization programs

Routine immunization programs are typically provided by provincial government-funding, where vaccines are administered following a recommended schedule to eligible individuals. Vaccines under the routine immunization program are provided free of charge by public health nurses, physicians, and other healthcare providers. Only three provinces - Ontario, New Brunswick, and Manitoba - have vaccination legislation in place that require up-to-date immunizations for school entry.

In Alberta, the routine immunization schedule is divided into several programs, starting from infancy to school-based and into adulthood (10). Typical vaccines include diphtheria, tetanus, pertussis, polio, *Haemophilius influenza* type b, hepatitis b, measles, mumps, rubella, varicella, HPV, meningococcal, and pneumococcal. Influenza vaccine is also recommended annually. Alberta does not have any vaccination legislation in place for required up-to-date immunizations.

Terminology

Terminology associated with vaccines and vaccination have been inconsistent in literature (11). For the purposes of this project, 'vaccination coverage' refers to 'the proportion of a defined population that receives the specified number of doses of a particular vaccine' where the numerator is the number of individuals who received the requisite doses, and the denominator is the number of individuals who are eligible to receive the specific vaccine; therefore, vaccination coverage refers to a percentage. 'Vaccine uptake' refers to the numerator of vaccination coverage, i.e., the number of eligible individuals who received dose(s) of the vaccine and utilized

it as an absolute number. ‘Catch-up vaccination rate’ refers to the change in vaccination coverage between two different time points. This is determined by the proportion of individuals who were previously unvaccinated or partially vaccinated and subsequently received a full series of vaccines during a specific time period.

Human papillomavirus (HPV)

Disease

Sexually transmitted infections (STIs) are a significant public health concern in Canada, with approximately 1.4 million cases reported annually (12). HPV is one of the most common STIs in Canada and worldwide (13). It is estimated to affect more than 70% of sexually active men and women at some point in their lives. Risk factors include number of sexual partners, drug use, immunosuppression, homosexual practices, and inconsistent condom use. Many of those infected are asymptomatic, but some may develop anogenital warts and cancer, including cervical, anal, and oropharyngeal cancers. There are over 200 related HPV viruses but 14 high-risk types including HPV 16, 18, 31, 35, 39, 45, 51, 52, 56, 59, 66, and 68; HPV16 and HPV18 are responsible for approximately 90% of anal cancers, 60% of penile cancers and 80% of oral cancers. There is currently no cure available for infections, but most symptoms are treatable. No data is yet available on costs associated with HPV treatment in Alberta, Canada; however, a study conducted in a neighbouring province, Manitoba, found a high economic burden of HPV, with approximately $145 million attributed to HPV infection treatment over the 15-year study period (14).

HPV vaccine

Three HPV vaccines are approved in Canada: Gardasil® quadrivalent vaccine provides protection against four HPV types (HPV6, 11, 16, 18) (14). Gardasil®9, a recombinant vaccine, provides protection against an additional five HPV types (HPV31, 33, 45, 52, 58). A third vaccine, Cervarix® is a bivalent vaccine protective against HPV16 and 18. HPV vaccination does not negatively interfere with uptake of other prevention methods such as screening; instead, a study conducted in Alberta showed HPV vaccination was associated with screening uptake (16).

Routine HPV immunization program

The HPV vaccine is one of the school-based vaccinations offered in Alberta since its introduction to the routine immunization program for females in 2008 (Figure 1) (17). Males became eligible for the program beginning in 2014. The first HPV vaccine used was Gardasil®. In 2016, the program switched to Gardasil®9. The HPV administration schedule at the beginning of the program was a 3-dose series that was administered to eligible students in grade 5. In 2018, the schedule was switched to the current schedule: a 2-dose series offered in grade 6, generally at 11 to 12 years up to and including 26 years of age.

The catch-up program in Alberta is a public health initiative that aims to ensure students who missed the HPV vaccine during the recommended schedule receive their missed dose(s) in a timely manner (17). This is conducted by public health nurses who visit schools to screen all students through grades 6 and 9 to identify those who missed the vaccine. The nurses then provide the students with the opportunity to catch up on the doses they missed.

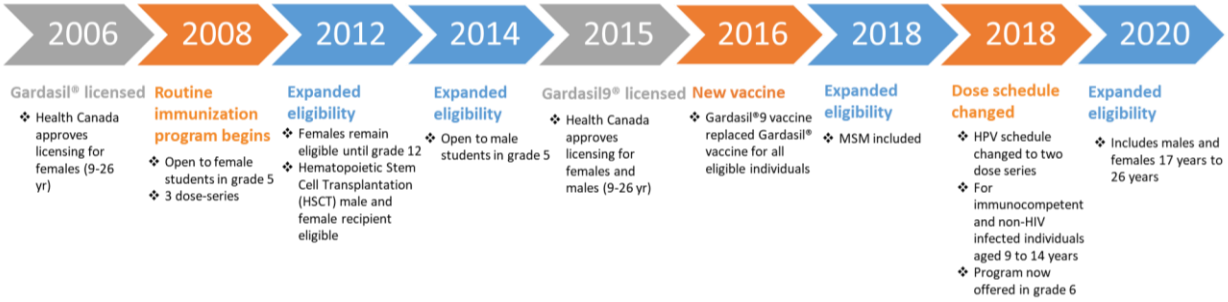

Figure 1. HPV Routine Immunization Program Timeline in Alberta, Canada

COVID-19

History of COVID-19

On December 31, 2019, health authorities from Wuhan, China reported to the World Health Organization (WHO) cases of pneumonia from an unknown source (18). On January 7, 2020, WHO identified the source as a novel disease and named it Coronavirus disease (COVID-19). The first case in Canada was reported on January 25, 2020; since then, over 4.5 million cases have been recorded, with approximately 50,000 deaths. Alberta declared a state of public health emergency on March 17, 2020.

Vaccine

Health Canada approved the Pfizer-BioNTech COVID-19 vaccine on December 9th, 2022, and the Moderna COVID-19 vaccine on December 23rd, 2022. Vaccine roll-out occurred in a phased manner, based on occupational risk and age (Figure 2) (19). While current COVID-19 vaccines do not prevent transmission and infection as efficiently compared to other vaccines, numerous studies have shown that they are extremely effective at preventing adverse outcomes such as hospitalizations and deaths (20).

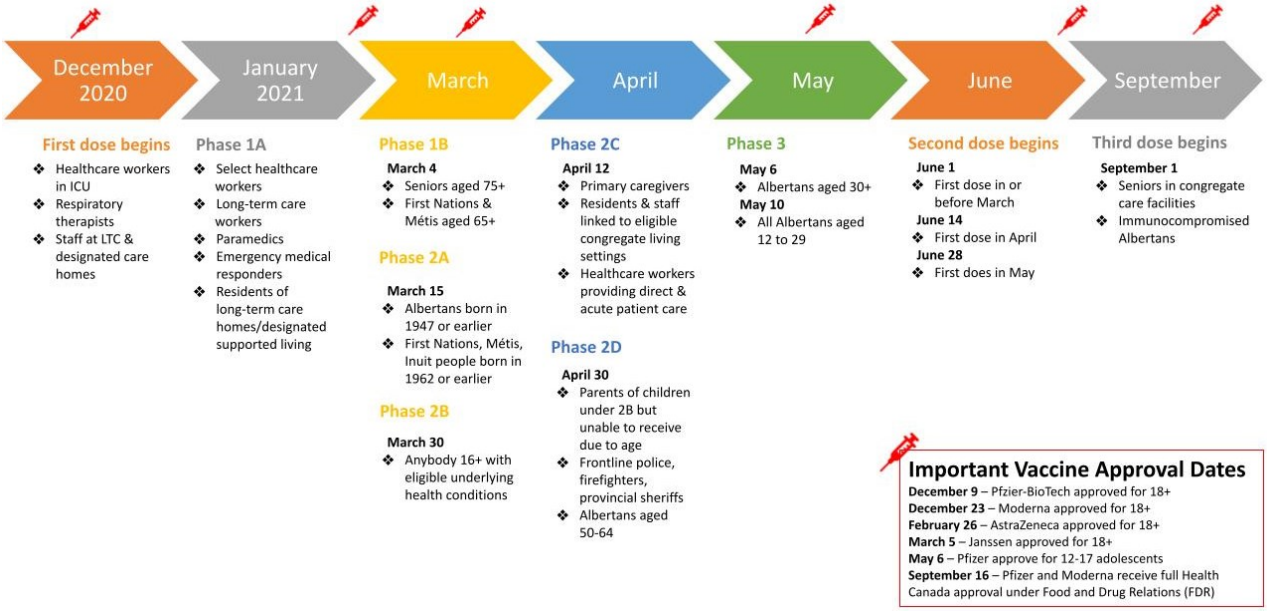

Figure 2. Timeline of COVID-19 Vaccine Rollout Program in Alberta

Immigrants

Description

Immigrants are defined as 'someone who moved from their host region of origin to live permanently in a foreign country" (21). At the time of the 2016 Census, foreign-born immigrants made up 21.9% of the Canadian population; the number had increased to 23.0% (~8.3 million) in 2021 (1). With factors such as aging population and decreased fertility rates, immigrants continue to be the main source of population growth: the projected growth estimates that immigrants could make up 29.1 to 34.0% of the Canadian population by 2041. As a result, the proportion of second-generation immigrants (defined as children of at least one foreign-born parent) has also increased from 26.7% in 2011 to 31.5% in 2021. Asian immigrants, including the Middle East, made up the majority of immigrants to Canada, with approximately 62.0%. On the other hand, the proportion of European immigrants continue to decline over time.

Healthcare system access

Before arriving in Canada, Immigration, Refugee and Citizenship Canada evaluates potential immigrants through Immigration Medical Examinations (IME), which includes a series of medical and laboratory testing (22). Immunization status review is not assessed until after arrival in Canada; assessment is dependent on the region of origin and may include any of the following: hepatitis B serologic testing, hepatitis C antibody, human immunodeficiency virus (HIV) serologic testing, tuberculin skin testing and more. Recommended vaccines include hepatitis A, hepatitis B, rubella-containing, varicella-containing, inactivated polio-containing (IPV), pertussis-containing, and recently, COVID-19. In Alberta, there are no mandatory vaccination policies and/or legislation for immigrants in place (23).

Immigrants who are granted permanent residency are then allowed to apply for provincial/territorial health insurance (24). Requirements and the application differ between each province and territory; full provincial health coverage equivalent to the resident population is provided immediately after arrival with the exception of British Columbia, Manitoba, and Quebec.

Incidence of vaccine-preventable diseases (VPDs)

Immigrants are an important group of interest when it comes to vaccination. Most coverage levels fall below national target goals (25). Sporadic outbreaks of VPDs still occur, including in immigrant groups. A scoping review found 89% of the literature reported a higher VPD burden among immigrants (3). Specific factors include lower immunization rates, low socio-economic status, and travel back to origin countries with high VDP incidence. Lower immunization rates amongst immigrant groups can be attributed to immigrants facing higher barriers such as knowledge gaps (i.e., general lack of knowledge about the disease and vaccine), poor access to

healthcare (i.e., language, transportation, accessibility), and cultural norms/beliefs. This will be expanded on later. As aforementioned, some immigrants arriving in Canada are categorized as refugees, who generally are forced to leave their host country due to danger or persecution. Therefore, they may not arrive with many resources. Living in low socio-economic environments leads to inadequate housing and food which increases the risk of infectious diseases. Travel to areas with high VDP incidence increases exposure to the disease (26).

While there are certain factors that can be attributed to lower vaccine uptake amongst immigrant populations, it should also be noted that immunization records provided by immigrants when arriving in Canada do not always accurately reflect their immunization status. This can occur when the host country does not provide immunization records and/or when the authenticity and reliability of the records are in question. In addition, the translation of vaccine records may be difficult. Vaccination legislations in Canada may differ from other international bodies (27). As such, certain vaccines approved in other countries may not be recognized in Canada.

HPV in relation to immigrants

Incidence of HPV

A study examined the crude rate of invasive cervical carcinoma (ICC) in female immigrants in Ontario, Canada (28). In the younger demographic groups (<50 years), immigrants had a lower rate compared to non-immigrants; however, this trend switches in the older demographic groups. The overall risk for ICC was lower among immigrants compared to non-immigrants. Crude rate also differed by country of origin; in general, immigrants from Europe and Central Asia had a higher rate for ICC. In addition, time since migration was a factor; immigrants who arrived more than 10 years ago were at a lower risk. However, rates of cervical cancer mortality among

foreign-born women were still higher (29). The discrepancy between lower prevalence of HPV infection but increased risk of negative HPV-related outcomes indicates that HPV vaccination rates among foreign-born women and men may be lower, which was confirmed by later findings in the study. Several studies have reinforced these results in adult foreign-born populations, attributed to factors such as limited language proficiency, poor access to healthcare, and structural and interpersonal racism (30).

Knowledge, attitudes, and perceptions about HPV

A study examining knowledge, attitudes, and perceptions of HPV vaccine among adult and caregiver newcomers was conducted in Ottawa, which also has a routine immunization program (31). The majority of respondents had not heard of HPV; awareness was associated with education level. Of those who had heard of HPV, most were aware of how it was transmitted. Of those who were aware of the vaccine, half knew it was available for both males and females and its effectiveness in preventing certain cancers and believed that the vaccine was only for those sexually active while almost one third had no intention of vaccination. Some had negative perceptions of the HPV vaccine, believing it would encourage unsafe sexual and promiscuous practices. However, willingness to vaccinate was not associated with the region of origin, language, biological sex, education level, or migration status. Of those who were not aware of the vaccine, most expressed the intention of vaccination for themselves and/or their children. Provider recommendation was one reason for uptake. This study reflected other studies showing perceptions towards HPV vaccine was influenced by cultural beliefs and intentions for vaccination were affected by provider recommendations and language-appropriate resources (32).

HPV vaccination coverage

In regard to HPV vaccination coverage among immigrant populations, study results have been inconsistent. A US study examining immigrant women aged 18 to 36 years old found lower odds of HPV vaccine initiation in foreign-born women, even after adjusting for sociodemographic variables and other health indicators (33). Most unvaccinated immigrant women came from high HPV endemic countries with poor access to preventative HPV care and therefore had less knowledge about preventative measures. Other factors included healthcare insurance access and time since migration. However, another US study found opposing results in adolescent immigrants; male immigrants had higher coverage compared to the US-born population, while females had comparable results, although these results were nonsignificant (34). Results were connected to the region of origin.

Analysis of HPV vaccination coverage in Denmark's routine immunization program found Danish-born girls had almost double the odds of receiving HPV immunization compared to refugee girls (35). Predictors of uptake included region of origin, time since migration and income.

COVID-19 in relation to immigrants

COVID-19 incidence

Several studies around the world, including Canada, have shown that COVID-19 has disproportionately affected immigrant groups in terms of incidence (36). Immigrants are at higher risk of getting COVID-19 (some studies have shown as high as double the risk) as they were overrepresented in essential occupations that had increased exposure to COVID-19; 36% of certain front-line workers (e.g., nurse aides, orderlies, patient service associates) identified as an

immigrant (36–38). Immigrants have a large proportion of communities with high racial and ethnic minorities who often have higher housing density and multigenerational households, leading to less chance of social distancing (38). Poor language proficiency and health literacy have contributed to lower adherence to public health guidelines. This has also translated to higher COVID-19 morbidity. In addition to these factors, difficulty in transportation, lower rates of testing, ongoing stigma and discrimination, and structural barriers to healthcare systems have resulted in almost double the risk of death from COVID-19 amongst immigrants compared to non-immigrants.

Impact of COVID-19 on immigrants

Immigrants were disproportionately affected by COVID-19 in the employment sector, incidence rate, and mortality rate. Most economic lockdowns in Canada occurred in March and April of 2020, with a significant number of recent immigrants losing their jobs as a result of recent immigrants being more likely to work in low-wage (22% vs. 12% and/or short-tenure jobs (31% vs. 15%) compared to Canadian-born workers (39). Approximately one out of four health care sector worker was an immigrant, which meant many immigrants were eligible in the first phase of vaccine rollout.

Conceptual Framework

Ecological models are designed to help understand determinants of health in order to organize and prioritize public health strategies/interventions to target these determinants. One such conceptual framework is the Commission on Social Determinants of Health (CSDH) framework (see Figure 3), which examines how social and economic factors influence health outcomes (40). This framework is based on the premise that structural and social determinants such as the

distribution of power, money and resources shape intermediary and social determinants of health, otherwise referred to as the conditions in which individuals are born, live, work, and age. This determines the impact on equity in health and well-being or health outcome.

In the context of vaccination, the CSDH framework explains how social factors, such as education, biological sex, healthcare access, culture, and economic factors, such as income can influence vaccination uptake among different population groups, including immigrants.

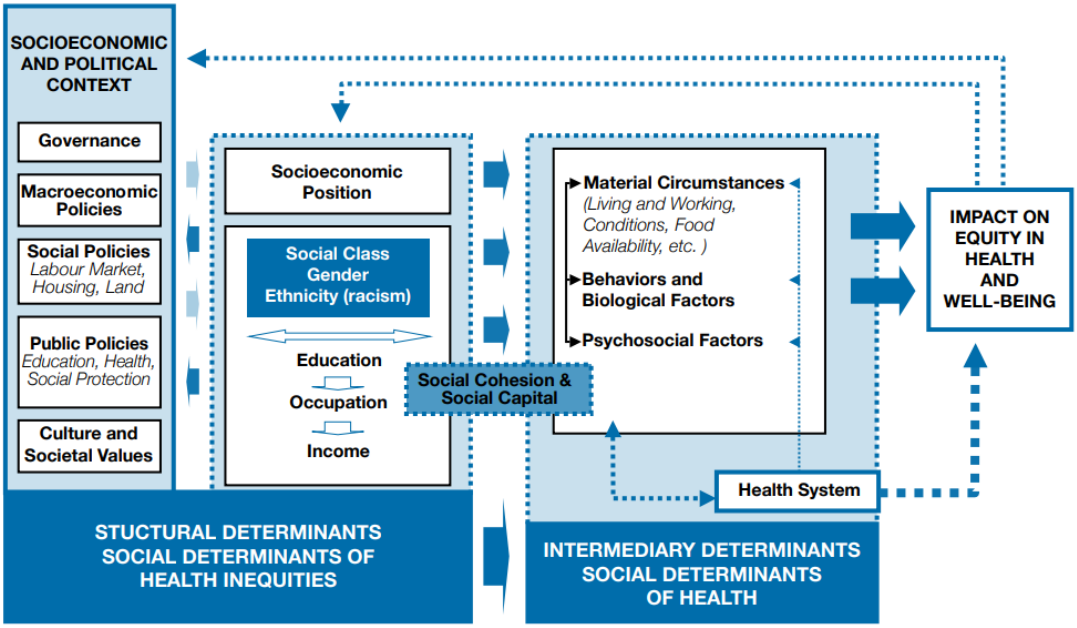

Figure 3. Commission on Social Determinants of Health (CSDH) Conceptual Framework. (Solar & Irwin 2010) (40)

Previous studies have examined how certain key social determinants of health identified in the CSDH framework impact vaccination uptake. For example, populations living in low-income settings tend to have less access to healthcare, including vaccinations, due to financial and time constraints (41). In general, studies have shown that females are more likely to access healthcare services compared to their male counterparts, in addition to being more likely to be familiar with vaccines and discussing vaccines with healthcare providers. Another SDOH is education; people with higher levels of knowledge have been shown to be more knowledgeable and understanding

of the importance and safety of vaccinations (42). Cultural and community aspects have also been shown to be a key SDOH; different cultural beliefs and customs influence perceptions and attitudes towards vaccination, which influences uptake (42). Finally, those living in rural and/or remote communities, have less availability to healthcare services, including vaccination clinics, due to transportation constraints (43).

This research project examined many of these social determinants of health, such as age, biological sex, income, and place of residence, and how they were associated with vaccination coverage (health outcome).

Research Aims

Immigrant populations often face numerous barriers to vaccination, including lack of access and language barriers. Existing literature has shown that the immigrant population historically has lower rates of vaccination in comparison to non-immigrant groups (2).

However, there is an evident lack of research examining vaccination coverage within immigrants in several settings. Current Canadian literature has not examined HPV vaccination coverage in the context of routine immunization programs for immigrant children. In addition, at the time of the study, the examination of vaccination coverage on COVID-19 was relatively new, and no research was conducted specifically on uptake within immigrant populations.

The lack of up-to-date analysis in the current context of today's healthcare system is problematic, especially with the rapidly growing immigrant population in Alberta. It is important to identify disparities so that policymakers and clinicians can understand what strategies would

effectively increase vaccination coverage. This information can aid in the planning of future vaccination strategies should similar challenges arise in the future.

Objective and Research Questions

The objective of this thesis was to examine vaccination coverage of immigrant populations and factors associated with the uptake of vaccines, specifically HPV and COVID-19 vaccination. The following research questions were explored:

1. In regard to HPV vaccination of school-aged children in Alberta:
    a) Does coverage for HPV vaccination differ between international immigrants and non-immigrant children?
    b) Does HPV catch-up at a later date differ between international immigrants and non-immigrant children?
2. Does coverage for COVID-19 vaccination differ between immigrants and non-immigrants?

Research question one was explored in the first study outlined in Chapter 2, while research question two was explored in the second study outlined in Chapter 3.

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Chapter 2: Human papillomavirus vaccine coverage among immigrant adolescents in Alberta: a population-based cohort study

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The work in this Chapter will be submitted to a peer-reviewed journal.

Introduction

In Canada, foreign-born immigrants are estimated to make up 21.9% of the total population; children with an immigrant background (foreign-born or born to at least one foreign-born parent) represent about 40% of the total children population (1). Immigrants often face numerous barriers to vaccination, including lack of access and language barriers (2). Existing literature has shown that the immigrant population historically has lower rates of vaccination in comparison to non-immigrant groups (3,4).

Particularly for human papillomavirus (HPV), several studies have examined knowledge, attitudes, and perceptions of the HPV vaccine in immigrant parents. Lack of HPV disease and vaccine knowledge, cultural and/or religious beliefs that HPV vaccine encourages sexual activity, and lack of provider recommendations were some major factors for immigrant parents who chose not to vaccinate their child(ren) (5,6). A US study examined HPV vaccine knowledge and initiation in adolescents of immigrant parents (7). Immigrant parents had significantly lower knowledge about the vaccine compared to US-born parents, despite high education levels and access to health care.

Studies regarding HPV vaccination coverage among immigrants have had inconsistent findings. A study conducted in Denmark, where a free-of-charge HPV routine immunization program is also available, found refugee girls had lower odds of receiving the HPV vaccine compared to Danish-born girls; predictors of uptake included the region of origin, time since migration, and income status (8). On the other hand, a US study found higher coverage in adolescent immigrants compared to the US-born population, due to differences in vaccinations practices by region of origin (9)

It is important to understand HPV vaccination coverage amongst immigrant adolescents and factors associated with uptake, to help drive evidence-based policies to increase vaccination. Accurate estimates of HPV vaccination coverage are crucial to understanding where gaps in vaccination lie and provide further support for routine immunization programs. Therefore, the objectives of this study were to examine the difference in HPV vaccine coverage between international immigrants and non-immigrant adolescents, factors associated with uptake, and whether HPV catch-up at a later date differs between the two groups.

Methods

Setting

This study took place in Alberta, a western Canadian province with a population of approximately 4.5 million people, 99% of whom are registered with the publicly funded Alberta Health Care Insurance Plan (AHCIP). The HPV vaccine is licensed for those aged 9 years and older (10). The routine HPV school-based immunization program was first introduced in 2008 for females, and in 2014 for males. The HPV vaccine was originally delivered as a 3-dose series in grade 5, before switching to a 2-dose series for grade 6 in 2018. This meant that there was no school-based program for the HPV vaccine in the 2018/2019 school year. The school program was further impacted from 2019 to 2021 due to the COVID-19 pandemic. In Alberta, the school-based catch-up program is provided in grade 9 for students who have not received a complete series by that time.

Cohort, Data Sources, and Coverage Assessment

This was a retrospective population-based cohort study utilizing data from 2008 to 2018, during which the HPV vaccine schedule consisted of three doses. Multi-year cohorts were created using linked administrative data held at the Alberta Ministry of Health. The AHCIP supplied a unique lifetime identifier (ULI) that allows linkage between various databases, and also identifies age, biological sex, and other sociodemographic characteristics of the students. The Immunization and Adverse Reaction to Immunization (Imm/AIR) database includes data on all publicly funded childhood vaccines administered in the province. The Immigrant registry was used to identify foreign-born immigrants and refugees who arrived in Alberta from outside Canada prior to 9 years of age; immigrants who arrived after 9 years of age were excluded as it was unknown if they received an eligible HPV vaccine prior to arrival in Alberta. Individuals who died or migrated out of Alberta during each respective cohort year, identified as First Nations (as data is not consistently submitted to the data registries), or lived in Lloydminster (as a neighbouring province delivers their vaccines) were excluded from the study. Minimal interval dose criteria between doses were applied to determine valid doses for inclusion in the analysis: vaccine doses were included if the time between dose 1 and dose 2 was 4 weeks or more and if the time between dose 2 and dose 3 was 12 weeks or more.

Outcome measure

HPV vaccine coverage was defined as the proportion of eligible adolescents who received three doses of the vaccine at the designated age. Each cohort year was defined from January 1st to December 31st.

Exposure variables

Biologic sex at birth was categorized into male and female. Neighbourhood income quintiles was categorized based on the 2016 Canadian census, with quintile 1 (Q1) indicating the poorest neighbourhood and Q5 indicating the richest. Place of residence was categorized into three categories based on the 2016 census: metro and moderate metro, urban and moderate urban, and rural and remote rural. Region of origin among the immigrant population was divided into several regional categories: North America (elsewhere from Canada), South America, Europe, Middle East, East Asia, Southeast Asia, South Asia, Africa, and Oceania.

Statistical analysis

We measured how vaccination coverage varied by immigrant status by calculating the proportion of eligible Alberta adolescents who received three doses of HPV vaccine and compared them using confidence intervals (CI). A sensitivity analysis was conducted on second-generation immigrants (defined as Alberta-born adolescents born to foreign immigrant mothers). The purpose was to examine whether second-generation immigrant adolescents had more similar HPV vaccination status to first-generation immigrants or non-immigrant adolescents. For this analysis, we recategorized immigrants and non-immigrants into 3 categories: first-generation (foreign-born) immigrants, second-generation immigrants, and non-immigrants. Due to database limitations, only two years of data (2017 and 2018) were available for this sensitivity analysis. We also stratified coverage based on immigrant status and compared vaccination coverage by biologic sex, place of residence, and income quintile. Those with missing data on key sociodemographic variables (biologic sex, postal code) were excluded from analysis.

We also measured vaccination coverage among first-generation immigrant adolescents by region of origin.

We used multivariable logistic regression (MLR) to adjust for possible confounders associated with the outcome (receipt of three doses of HPV vaccine). The MLR data analysis was conducted on Alberta adolescents aged 12 years from 2014 to 2018. Variables adjusted for in the multivariable model included: biological sex, place of residence, income quintile, and cohort year. Before running the multivariable model, we tested for multicollinearity among exposure variables and for plausible interactions.

We also analyzed the difference between immigrants and non-immigrants in terms of the catch-up in vaccination rates between age 12 and age 17 for the 2008 to 2013 cohorts. Vaccination coverage was measured at 12 years and later at 17 years; the difference was compared between immigrant and non-immigrant groups using two-sample proportion tests. Only females were included in this part of the analysis as males were not eligible during this time period. Another sensitivity analysis was conducted on the inclusion/exclusion of immigrants who arrived after 9 years of age. The purpose was to examine whether catch-up rates between ages 12 and 17 were different in the immigrant group when immigrants who arrived after 9 years old were included in the study cohorts compared to when they were excluded. It was hypothesized that the catch-up rate would be different due to the potential reclassification of the vaccination status of those specific subsets of immigrants when public health nurses catch-up with them in grade 9.
We performed statistical analysis using SAS 9.4 (SAS Institute Inc., Cary, NC) with statistical significance set at $P<0.05$. The University of Alberta Health Research Ethics Board granted ethical approval for this study (Pro00114786).

Results

After excluding participants with missing data on postal codes, sex, and time on migration (n=19), the final sample size from 2008 to 2018 was 346,749, of which 31,656 (9.13%) were first generation immigrants (Figure A1). The largest proportion of immigrants came from elsewhere in North America (17.33%) and Asian regions (8.17-18.34%) (Table A1).

HPV vaccine coverage

On average over the 10 years, HPV vaccine coverage was 52.58% (95% CI 52.03, 53.13) among immigrant adolescents and 47.41% (95% CI 47.24, 47.59) among non-immigrants (Figure 4). While overall coverage differed between the two groups, the difference in coverage appeared to change over time. Since the start of the routine immunization program for females in 2008, HPV vaccine coverage was relatively similar between immigrants and non-immigrants, with non-significant differences of less than 2% (Figure 4, Table A1). An increased discrepancy of HPV vaccine coverage between female immigrants and non-immigrants started to become more evident in the later years, with female immigrants displaying higher coverage.

The same pattern was present in the male group, with insignificant differences between male immigrants and non-immigrants in the earlier stages of the program before HPV vaccine coverage became higher in immigrants (Figure 4). There was a lag in vaccine coverage for the first two years after the program was introduced for each biological sex group (2008, 2009 for females and 2014, 2015 for males) before increasing to the 50-70% range. When excluding the first two years after program implementation for females (2008 & 2009), the average HPV vaccination coverage was 63.96% among immigrants (95% CI 63.24, 64.67) and 61.39% among

non-immigrants (95% CI 61.16, 61.61) (Table A2). When excluding the first two years after program implementation for males (2014 & 2015), the average HPV vaccination coverage was 66.20% (95% CI 65.17, 67.23%) among immigrants and 62.21% (95% CI 62.62, 62.95%) among non-immigrants (Table A2). When the two sexes were combined, the average HPV vaccination coverage was 58.14% (95% CI 57.64, 58.63) among immigrants and 54.95% (95% CI 54.78, 55.11) among non-immigrants.

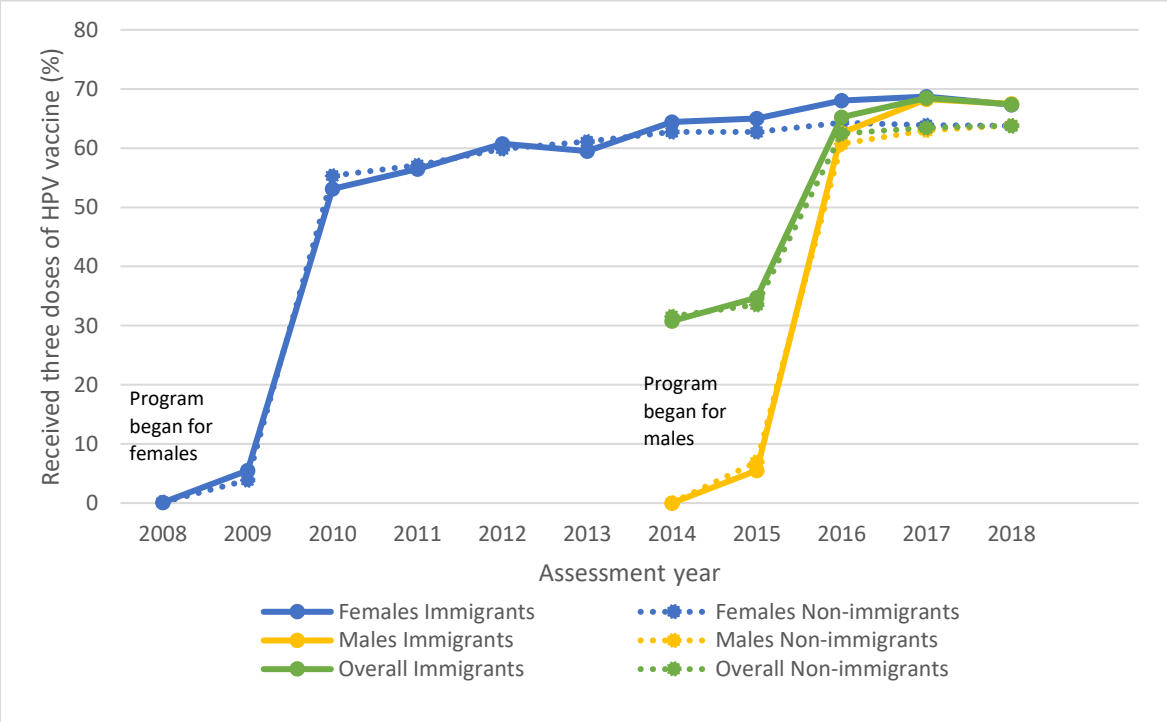

Figure 4. HPV vaccination coverage at age 12 by immigrant status and biological sex from 2008 to 2018

Vaccine coverage for immigrants differed by region of origin (Table 1); immigrants from Asian regions had the highest vaccine coverage (64.14% for Southeast, 60.94% for South and 57.09% for East) followed by African immigrants (56.05%). On the other hand, immigrants from elsewhere in North America (38.30%) and South America (43.95%) had the lowest vaccine coverage.

Table 1. Vaccination coverage of international immigrants to Alberta at age 12 between 2008 and 2018 categorized by region of origin (N=31,656)

Region	n	%
North America (outside Canada)	2103	38.30
South America	552	43.95
Europe	2295	48.66
Middle East	1252	51.23
East Asia	1477	57.09
Southeast Asia	3724	64.14
South Asia	2962	60.94
Africa	1524	56.05
Oceania	183	44.96
Unknown/missing	845	46.53

HPV vaccine coverage in relation to sociodemographic characteristics

Potential sociodemographic characteristics associated with HPV vaccination stratified by immigration status was analyzed from 2014 to 2018, when both males and females were included in the program. Males became eligible for the program starting in 2014. After excluding participants with missing data on postal codes, sex, and time on migration (n=19), the final sample size from 2014 to 2018 was 232,293, of which 24,045 (10.35%) were first generation immigrants (Figure A1).

The proportions of adolescents vaccinated with three doses of HPV vaccine varied by sociodemographic characteristics (Table 2). Vaccine coverage was significantly higher in immigrants regardless of biologic sex in comparison to non-immigrants. Additionally, vaccine coverage was higher in females than males. Coverage was also significantly higher in immigrants compared to non-immigrants living in metro and urban areas, but lower in immigrants living in rural areas. Overall, those living in metro areas had the highest vaccine coverage. Amongst immigrants, vaccine coverage was consistent across income quintiles (ranging from 54.34 – 56.71%) while coverage increased as income quintiles increased for non-

immigrants (48.92-53.39%). Overall, vaccine coverage was higher in immigrants regardless of income quintile in comparison to non-immigrants.

Table 2. Proportion of Alberta adolescents who received three doses of HPV vaccine between 2014 and 2018 by migration status and sociodemographic characteristics

Variables	Immigrants	Non-immigrants	P-value
	% (n)	% (n)	
Sex			
Female	66.90 (7,811)	63.51 (64,606)	<0.0001
Male	44.72 (5,531)	39.76 (42,357)	<0.0001
Place of residence			
Rural	45.05 (1,350)	46.65 (21,597)	0.087
Urban	49.93 (1,003)	45.76 (12,574)	0.0003
Metro	57.72 (10,989)	54.13 (72,792)	<0.0001
Income quintile			
Q1 (lowest)	54.34 (3,496)	48.92 (17,873)	<0.0001
Q2	56.37 (2,669)	49.80 (19,428)	<0.0001
Q3	56.71 (2,531)	51.54 (20,887)	<0.0001
Q4	55.73 (2,408)	52.41 (23,364)	<0.0001
Q5 (highest)	54.69 (2,238)	53.39 (25,411)	0.11

Multivariable logistic regression analysis showed that immigrant adolescents at age 12 had 1.10 the odds of receiving 3 doses of HPV vaccine compared to non-immigrant adolescents (95% CI 1.07, 1.14), after controlling for place of residence, income quintile, biological sex, and year (Table 3). Those living in rural and urban areas had lower odds of receiving 3 doses of HPV vaccine compared to those living in metro areas (aOR 0.68, 95% CI 0.66, 0.70, aOR 0.69, 95% CI 0.69, 0.72 respectively), after controlling for immigrant status, income quintile, biological sex, and year. By income quintile, those living in lower income quintiles compared to the richest had lower odds of being vaccinated by age 12, after controlling for immigrant status, place of residence, biological sex, and year.

Table 3. Bivariate and multivariable logistic regression (MLR) of fully vaccinated (receipt of 3 doses) against HPV, relative to unvaccinated/partially vaccinated from 2014 to 2018

Variables	Unadjusted OR	95% CI	Adjusted OR (aOR)[a]	95% CI
Immigrant status				
Immigrant	1.18	1.15, 1.21	1.10	1.07, 1.14
Non-immigrant	Ref		Ref	
Place				
Rural	0.71	0.69, 0.73	0.68	0.66, 0.70
Urban	0.73	0.71, 0.74	0.71	0.69, 0.72
Metro	Ref		Ref	
Income quintile				
Q1 (lowest)	0.86	0.84, 0.88	0.86	0.84, 0.89
Q2	0.89	0.87, 0.91	0.91	0.88, 0.93
Q3	0.94	0.92, 0.97	0.95	0.93, 0.98
Q4	0.97	0.95, 0.99	0.97	0.95, 1.00
Q5 (highest)	Ref		Ref	
Biologic sex				
Male	0.38	0.38, 0.38	0.34	0.33, 0.34
Female	Ref		Ref	
Year				
2014	0.25	0.24, 0.26	0.23	0.22, 0.23
2015	0.28	0.28, 0.29	0.26	0.25, 0.26
2016	0.94	0.92, 0.97	0.94	0.91, 0.97
2017	0.99	0.97, 1.02	0.99	0.97, 1.00
2018	Ref		Ref	

[a]Adjusted for other variables included in the MLR model

A sensitivity analysis was conducted on second-generation immigrants to see if their vaccination coverage was more similar to foreign-born immigrants or non-immigrants. This data was limited to two years of data due to data availability. For this analysis, non-immigrants were reclassified into Albertan-born to an immigrant mother (second-generation immigrants) or Albertan-born with non-immigrant mother (non-immigrants). The sensitivity analysis showed that HPV vaccine coverage of second-generation immigrants (69.87%) was more similar to that of first-generation immigrants (67.87%) and had the highest coverage of the three groups (Table 4). The non-immigrant group had the lowest coverage of the three groups (62.66%).

Table 4. Sensitivity analysis of recategorization of vaccination coverage of second-generation immigrants from 2017 to 2018

Immigrant classification	HPV vaccine coverage (%)	Immigrant classification	HPV vaccine coverage (%)
Immigrants	67.87	First-generation immigrant	67.87
Non-immigrants	63.47	Second-generation immigrant	69.87
		Non-immigrants	62.66

Catch-up rates in HPV vaccine coverage from age 12 to 17

Next, we examined how much catch-up in vaccine coverage occurred for female adolescents between the ages of 12 and 17 years for the 2008 to 2013 cohorts (Alberta offered a catch-up program for HPV vaccine to students in grade 9). We then compared the difference in catch-up rates between immigrants and non-immigrants. The reason for focusing only on females was that the HPV routine immunization program began in 2008 for only females, so we were only able to analyze catchup in the female group.

Total increase in HPV vaccine coverage from age 12 to age 17 varied across the years, with an overall non-significant difference between immigrants and non-immigrant females ($p=0.0631$) (Table 5, Figure 5). However, excluding the first two years of the program, there was a significant difference between complete HPV vaccine uptake for immigrant compared to non-immigrant female adolescents.

Table 5. HPV vaccine coverage at age 12 and age 17 by cohort year (only females)

	Coverage at 12 years old (%)		Coverage at 17 years old (after catch-up program) (%)		Increase from 12 to 17 years (%)		P-value[b]
Cohort[a]	**Immigrant**	**Non-immigrant**	**Immigrant**	**Non-immigrant**	**Immigrant**	**Non-immigrant**	
2008	0.10	0.14	63.79	63.13	63.69	62.99	0.66
2009	5.49	3.9	67.76	66.46	62.27	62.56	0.8502
2010	53.1	55.34	74.51	73.52	21.41	18.18	0.0065
2011	56.47	57.11	76.48	73.44	20.01	16.33	0.0005
2012	60.74	59.88	78.86	76.68	18.12	16.8	0.1913
2013	59.51	61.13	78.59	76.7	19.08	15.57	0.0002
Overall	43.40	39.72	74.33	71.67	30.93	31.96	0.0631

[a] The year female students were 12 years old

[b] Statistical significance comparing increase in HPV vaccine coverage (from 12 to 17 years) between immigrants and non-immigrants

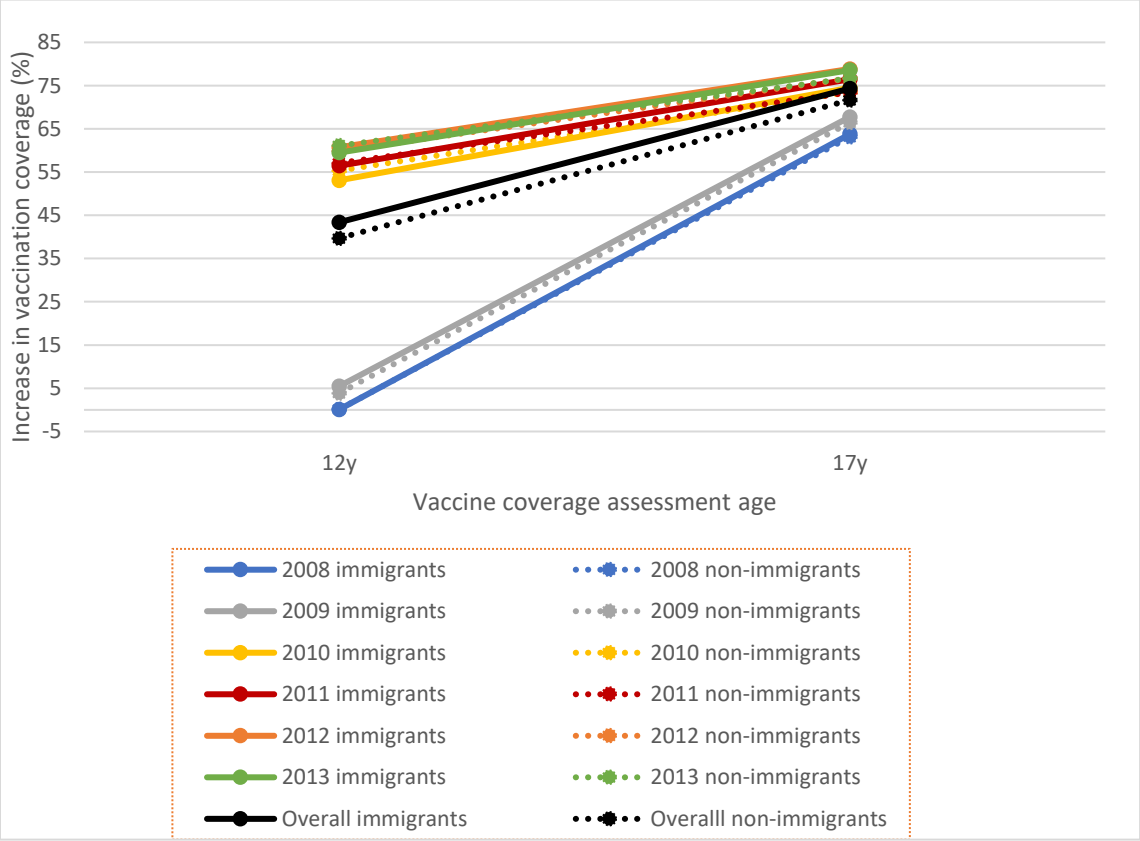

Figure 5. HPV vaccine coverage at age 12 and age 17 by cohort year (only females) from 2008 to 2013

A sensitivity analysis analyzed the difference in catch-up rate (between ages 12 and 17) of immigrants who arrived after 9 years old in Alberta were excluded and not excluded from the cohort (Table A4). Results found that the difference in catch-up rates was greater in the immigrant cohort that included immigrants who arrived after 9 years old compared to the excluded cohort. In other words, the difference in vaccination coverage at age 12 versus age 17 was greater for the immigrant cohort that included all immigrants regardless of arrival time compared to the cohort that excluded immigrant adolescents who arrived after 9 years old in Alberta.

Discussion

Summary of findings

This study examined the HPV vaccination coverage of immigrant adolescents in Alberta compared to non-immigrants. Overall, HPV vaccination coverage was higher in immigrant populations, regardless of biological sex and income quintile. Immigrants from Asian regions and Africa had the highest vaccination coverage while immigrants from elsewhere in North America and South America had the lowest. Difference in catch-up rates between female immigrants and non-immigrants were insignificant.

Interpretation

On average over 10 years (2008 to 2018), HPV vaccination coverage was 52.58% in immigrants and 47.41% in non-immigrants. In both groups, HPV vaccination coverage falls below the Canadian national target of 90% (11). Previous studies showed lower HPV vaccination coverage amongst immigrant populations compared to non-immigrants (12–14). However, a study in the United States examined HPV coverage prevalence in foreign-born and US-born adolescents

(aged 13 to 17 years old) from 2012 to 2014 (9). Their study found that male immigrants had higher coverage rates for all HPV vaccine doses, and female immigrants had higher coverage rates for two doses or less, compared to the U.S. born population.

In this study, HPV vaccination coverage was highest among Asian immigrants and lowest in North American immigrants from outside Canada. Region of origin was a possible reason suggested by a previous study for differences in vaccination by migration status. In the US study, parents from Caribbean countries had differing attitudes towards HPV vaccination (support ranged from 30-70%) (9). Many had limited knowledge and various misconceptions (transmission dependent on sexual position, HPV causes AIDs, experimentation/discrimination tool, taboo against premarital sex, not necessary for youth). Latinos had high initiation but poor completion rates. Results also indicated Asian communities had lower rates of screening but still had similar vaccination rates to white girls. Collectively, Asian immigrants in our study compromise approximately 40% of our immigrant population. A study on vaccination rates among different Asian ethnic immigrant groups found that certain subgroups had higher rates of vaccination for HPV, hepatitis B, and influenza vaccines (15). Specifically, the Chinese and Filipino subgroups had higher coverage compared to the non-Hispanic white group. In addition, immigrants from other Asian regions outside of China, the Philippines, and India had significantly higher coverage for the hepatitis B, influenza, and shingles vaccine compared to the non-Hispanic white group.

In our study, second-generation immigrants had the highest HPV vaccination coverage amongst the three groups (first-generation immigrants, second-generation immigrants, and non-immigrants). Few studies have examined specifically second-generation immigrants, and as far as we know, none were conducted in Canada (16,17). Factors associated with vaccine uptake for

first-generation immigrants and non-immigrants may all apply to second-generation immigrants, which could be attributed to the higher vaccination coverage. Acculturation has been shown to be a factor in HPV vaccine knowledge amongst foreign-born immigrants (18); longevity and familiarity with the native healthcare system are possible contributors to second-generation immigrants having the highest coverage. Further studies should be conducted to expand on these findings.

While immigrants had higher vaccination coverage when comparing other sociodemographic groups, rural-residing immigrants had lower coverage compared to rural non-immigrants. Several studies have examined rural residents, regardless of migration status, have lower coverage due to factors such as transportation issues, limited providers, and higher costs (19). Rural-residing immigrants may face further barriers such as language barriers and unfamiliarity on how to access rural healthcare resources. Rural and non-metro residents are an important group for interventions as studies have found that they are at greater risk of cervical cancer compared to metro residents (20).

Vaccination coverage has been consistently higher in females throughout the HPV routine immunization program. Several studies have shown that immigrant parents are less likely to immunize their male child(ren) compared to females due to misconceptions that HPV does not impact them (2,18,21). In general, males are an important group for targeted interventions as research has shown that HPV vaccine for males is cost effective and effective in preventing infection in not only males but females as well.

Studies have looked at the time since migration and age for immigrants as a factor for vaccine uptake, where immigrants who have resided longer are more likely to receive the vaccine after increased exposure to the healthcare system and provider recommendations (22,23). However,

our results have shown that the catch-up rate for immigrants is not significantly different than those of non-immigrants. In other words, when comparing to the change in vaccination rate at age 12 to age 17 between immigrants and non-immigrants, there was no significant difference. Similarity in catch-up rate between foreign-born born and Alberta-born adolescents could be attributed to common exposure to catch-up interventions such as follow-ups from public health nurses in schools and no mandatory vaccination policies for either group. However, a sensitivity analysis conducted showed a higher catch-up rate for the immigrant group when including those who arrived in Alberta after 9 years old. A feasible reason is that initial misclassification of vaccination status is corrected, i.e. immigrant adolescents who arrived after 9 years old were vaccinated for HPV in their home country but were classified as unvaccinated at age 12 in Alberta due to lack of sharing or loss of vaccine records (24).

Future directions

While the HPV routine immunization program is provided in schools, it should be noted that a catch-up program for males and females 17 years up to and including 26 years of age (10) is now available. Examining catch-up rate from adolescence to adulthood has been understudied and therefore is a potential avenue for future exploration. This study examined coverage in second-generation immigrants; as an “in between group” of immigrants and non-immigrants; future studies could examine if the result is present in other vaccines and if so, factors that are associated with the difference. Given the low vaccination rates among the non-immigrant group, our results imply targeted interventions such as community leader outreach, and provider recommendations may be beneficial (25).

Strengths/limitations

To the best of our knowledge, this is the only study in Canada that examined HPV vaccination coverage specifically within immigrant adolescents in comparison to non-immigrants. Utilization of population-based immunization, immigrant, and resident databases allowed for a large, robust, and complete data set.

Our study has a few limitations. Data was not included post-2018 due to the dose series change (3 doses to 2 doses) and the COVID-19 pandemic. The analysis of second-generation immigrants was limited to a sensitivity analysis as the data was only available for 2 years, which could result in potential misclassification and overestimation of coverage in non-immigrants. In addition, due to a lack of a variable identifying immigrant fathers, adolescents of immigrant fathers and Canadian-born mothers were classified as non-immigrants. In addition, it was not possible to distinguish between interprovincial migrants to Alberta and foreign-born immigrants; foreign-born immigrants who migrated from another province were potentially misclassified as non-immigrants, which might overestimate non-immigrant coverage levels. As this study used provincial data, these findings may not be generalizable to other jurisdictions due to different immigrant characteristics and vaccination programs. Finally, it is possible that HPV vaccines received outside of Alberta were not updated in the provincial immunization respiratory, which may underestimate vaccination coverage in both groups.

Conclusion

Overall, immigrant children had higher HPV and COVID-19 vaccination coverage in comparison to non-immigrants. This implies that efforts to increase vaccination rates among immigrant children may be having a positive impact. With the immigrant proportion predicted to

increase in Canada, it is important to understand that not all immigrant groups should be treated the same and appropriate, group-specific interventions should be used. Among immigrants, routine immunization promotion strategies should be targeted to those living in rural residences and from North America, Oceania, and South America in order to improve HPV vaccination coverage in this group even further. Future research may expand on vaccination coverage amongst second-generation immigrants and examining individual-level factors associated with vaccine uptake. In addition, analysis of post-pandemic effect on routine immunization may be informational.

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Appendix

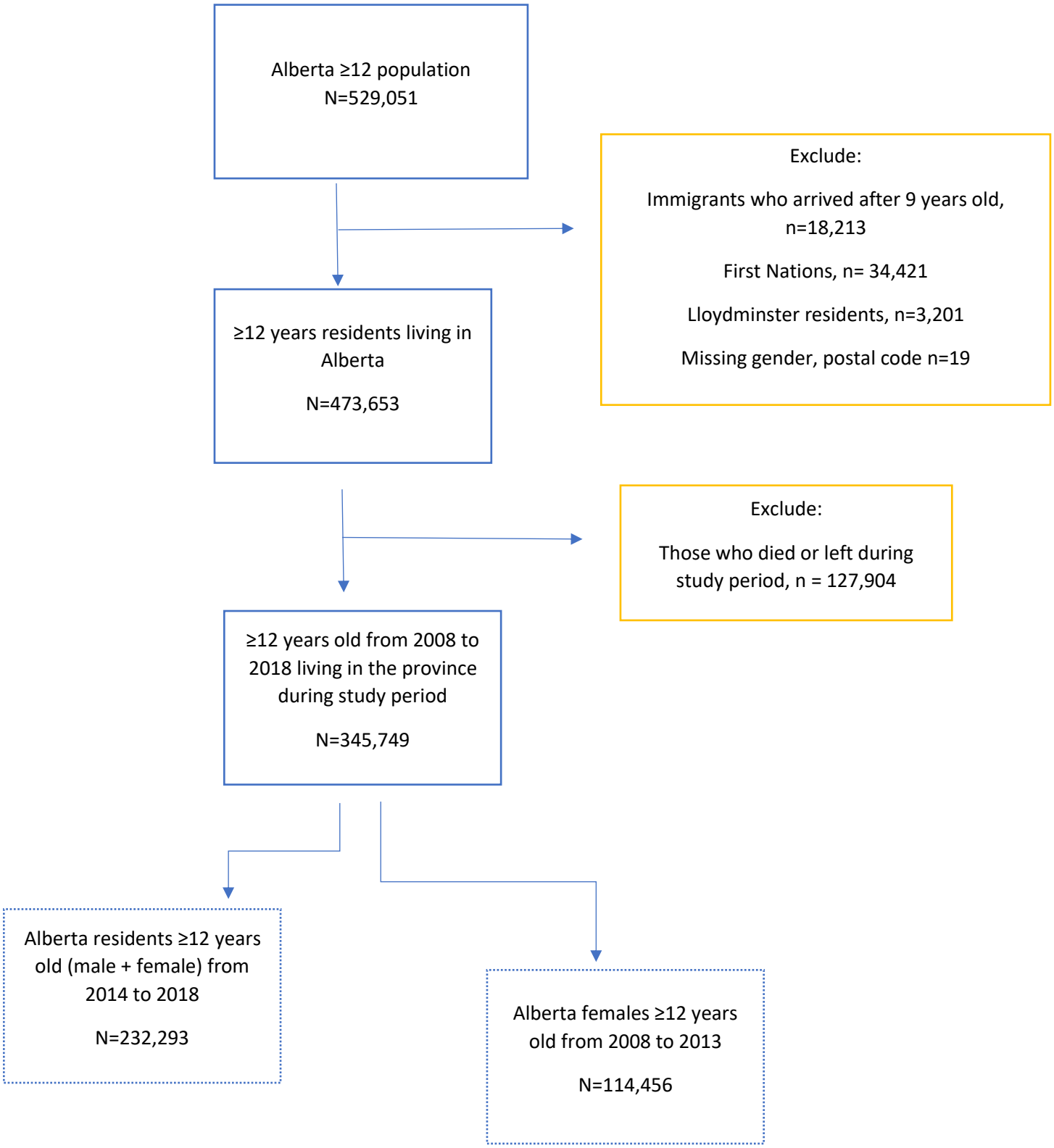

Figure A1. Flow diagram showing selection of participants.

Table A1. HPV vaccination coverage by immigrant status and biological sex from 2008 to 2018

	Female		Male		Male & female combined		P-value
	Immigrants	Non-immigrants	Immigrants	Non-immigrants	Immigrants	Non-immigrants	
2008	0.10	0.14	N/A	N/A	N/A	N/A	0.80[b]
2009	5.49	3.90	N/A	N/A	N/A	N/A	0.01[b]
2010	53.1	55.34	N/A	N/A	N/A	N/A	0.14[b]
2011	56.47	57.11	N/A	N/A	N/A	N/A	0.65[b]
2012	60.74	59.88	N/A	N/A	N/A	N/A	0.51[b]
2013	59.51	61.13	N/A	N/A	N/A	N/A	0.19[b]
2014	64.41	62.73	0.00	0.06	30.77	31.58	0.30[c]
2015	65.00	62.77	5.51	6.97	34.73	33.55	0.12[c]
2016	68.03	64.31	62.60	60.73	65.26	62.47	0.0001
2017	68.72	63.91	68.26	63.04	68.48	63.46	<0.0001[c]
2018	67.32	63.79	67.49	63.84	67.40	63.82	<0.0001[c]
Average[a]	57.62	51.32	44.72	39.76	52.58	47.41	<0.0001[c]

[a] Average refers to HPV vaccine coverage over the years

[b] P-value is comparing vaccination coverage between immigrants and non-immigrants for only females

[c] P-value is comparing vaccination coverage between immigrants and non-immigrants for males and females combined

Table A2. HPV vaccination coverage by immigrant status and biological sex comparing full program timeline and exclusion of first two years after program implementation for each sex

	Female (%)		Male (%)	
	Immigrants	Non-immigrants	Immigrants	Non-immigrants
Full program	57.62[a]	51.32[a]	44.72[b]	39.76[b]
Excluding first two years of program	63.96[c]	61.39[c]	[d]66.20[d]	[d]62.58[d]

[a] From 2008 to 2018

[b] From 2014 to 2018

[c] Years 2008 and 2009 were excluded from analysis

[d] Years 2014 and 2015 were excluded from analysis

Table A3. Region of origin of international immigrants to Alberta between 2008 and 2018 (N=31,656)

Region	n	%
North America (outside Canada)	5491	17.35
South America	1256	3.97
Europe	4716	14.90
Middle East	2444	7.72
East Asia	2587	8.17
Southeast Asia	5806	18.34
South Asia	4416	13.95
Africa	2717	8.58
Oceania	407	1.29
Unknown/missing	1816	5.74

Table A4. Sensitivity analysis showing difference in coverage rates at age 12 and age 17 between cohort with no immigrant exclusion applied and cohort with immigrant exclusion applied (removing immigrants who arrived after 9 years old)

	Coverage (%)		
	No exclusion	**Exclusion**	**Difference [a]**
2008	63.69	63.69	0
2009	63.69	62.27	1.42
2010	26.86	21.41	5.45
2011	27.00	20.01	6.99
2012	26.73	18.12	8.61
2013	26.55	19.18	7.37

[a] Difference – the difference in follow-up coverage rates between no exclusion and exclusion criteria applied (immigrants who arrived after 9 years old)

Chapter 3: COVID-19 vaccine coverage among immigrants and refugees in Alberta: A population-based cross-sectional study

The work presented in this chapter has been published in a peer-reviewed journal. The journal reference is provided below.

Journal Reference: Paudel YR, Du C, MacDonald SE. COVID-19 vaccine coverage among immigrants and refugees in Alberta: A population-based cross-sectional study. *J Glob Health*. 2022 Nov 7;12. doi: 10.7189/jogh.12.05053

Introduction

Control of the COVID-19 pandemic in Canada is dependent on most of the population receiving COVID-19 vaccination (1). More than one in five (21.9%) people in Canada are foreign-born immigrants (2). Exposure on the front lines, and working and living in densely populated areas, have contributed to higher COVID-19 infections among immigrants (3). Thus, it is critical to ensure high COVID-19 vaccination coverage in immigrant populations.

Studies have shown that immigrant populations in Canada tend to have lower vaccination rates for some routine vaccines and higher vaccine-preventable disease-related hospitalizations than the Canadian-born population (4,5). Specific barriers to vaccination for immigrants include cultural factors, knowledge barriers, inadequate health care access, and vaccine hesitancy; barriers specific to COVID-19 vaccination include language barriers and novelty of the vaccines (6,7).

In the province of Alberta, as in most of Canada, COVID-19 vaccines have been available free-of-charge, irrespective of immigration status. Roll-out has occurred in a phased manner, based on occupational risk and age (8). COVID-19 vaccines are provided by public health nurses, pharmacists, physicians, and other health care providers. COVID-19 vaccine coverage in Alberta varies by age and place of residence (9), but there is limited information on coverage in the immigrant population compared with the non-immigrant population.

Given the large size of the immigrant population and their potentially higher risk for COVID-19 infection, it is imperative to assess COVID-19 vaccination coverage for this population. It is also important to understand factors associated with vaccine uptake, so that appropriate and timely actions can be taken to improve coverage. Thus, the primary objectives of this study were to [1]

compare COVID-19 vaccine coverage between foreign-born immigrants and refugees in Alberta to Canadian-born residents, and [2] to measure the association of time since migration with uptake of at least one dose of a COVID-19 vaccine.

Methods

Setting

Alberta is a western Canadian province of 4.5 million residents, 99% of whom are registered with the publicly funded Alberta Health Care Insurance Plan (AHCIP). While the Canadian government oversees vaccine approval and procurement, provinces are responsible for the roll-out of vaccination programs (10,11). COVID-19 vaccination programs in Alberta began in December 2020 in a phased manner, with vaccine availability to the entire population aged 12 and above by mid-May 2021. Records for all COVID-19 vaccines administered in the province, regardless of provider, are submitted to the provincial immunization repository, known as Imm/ARI (with a few exceptions, noted below).

Study design, population, and data sources

This was a population-based cross-sectional study using administrative data held by the Alberta Ministry of Health and including all residents of Alberta aged 12 years and above. Albertans <12 years were excluded because they were not eligible to receive the COVID-19 vaccine during the study period. We used the AHCIP quarterly population registry for the last quarter of 2020 to identify residents of the province, irrespective of birthplace. We excluded First Nations residents of Alberta (since data was not consistently submitted to Imm/ARI), Lloydminster residents (since vaccines are delivered by the neighbouring province), and those who left the province or

died during the study period. Figure S1 provides further detail on exclusions. We used the provincial immigrant registry to identify foreign-born immigrants and refugees who migrated to Alberta from another country between 1983 and 2020. We considered interprovincial migrants as non-immigrants since it is impossible to differentiate between foreign-born immigrants and Canadian-born individuals moving to Alberta from another province. We used the Imm/ARI repository to determine COVID-19 vaccination status. We extracted data on November 29, 2021, then deterministically linked the databases using unique personal health numbers (see Figure S2 in the Online Supplementary Document).

Outcome measure

We defined 'COVID-19 vaccination coverage' as the proportion of eligible Alberta residents who received at least one dose of a COVID-19 vaccine and 'full COVID-19 vaccination coverage' as the proportion who received at least two doses.

Exposure variables

We created a migration status variable with five categories, including non-immigrants and four categories of immigrants based on year since migration: (1) in or after Jan 2019 (i.e., in the past 2 years), (2) Jan 2011 to Dec 2018 (i.e., in the past 3-10 years), (3) Jan 2000 to Dec 2010 (i.e., in the past 11-20 years), (4) Jan 1983 to Dec 1999 (i.e., more than 20 years ago).

We grouped participants into six age categories based on the categories used to prioritize COVID-19 vaccine eligibility in Alberta: 12-17 years, 18-29 years, 30-49 years, 50-64 years, 65-74 years, and 75 years and above. Biologic sex at birth was categorized into male and female. Neighborhood income quintiles (Q1 indicating the poorest neighborhood and Q5 indicating the richest) were based on the 2016 Canadian census. Place of residence was categorized into three

categories based on the 2016 census: metro and moderate metro, urban and moderate urban, and rural and remote rural. Place of origin among the immigrant population was divided into six continental categories: North America, South America, Europe, Asia, Africa, and Oceania.

Statistical analysis

We measured vaccination coverage among immigrants by continent of origin and age category. We also stratified coverage based on migration status (time since migration or non-immigrant) and compared vaccination coverage by age category, sex, place of residence, and income quintile. Those with missing data on key sociodemographic variables (age, gender, and postal code) were excluded from analysis.

We used multivariable logistic regression to adjust for possible confounders associated with the outcome (uptake of at least one dose of a COVID-19 vaccine). Variables adjusted for in the multivariable model included: age category, sex, place of residence, and income quintile. Before running the multivariable model, we tested for multicollinearity among exposure variables and for plausible interactions. Since a strong interaction was detected between the age category and migration status, interaction terms for migration status and age category were included in the final model.

We performed a sensitivity analysis using full vaccination coverage (i.e., two or more doses) as the outcome in the multivariable model. For this sensitivity analysis, we excluded those who received the first dose of a COVID-19 vaccine after October 15, 2021, to allow everyone in the cohort to have at least the minimum required interval (42 days) between two doses.
We performed statistical analysis using SAS 9.4 (SAS Institute Inc., Cary, NC) with statistical significance set at $P<0.05$. This research, involving data from human participants, conformed to

the principles embodied in the Declaration of Helsinki and was granted ethical approval by the University of Alberta Health Research Ethics Board (Ethics ID: Pro00114786).

Results

Cohort characteristics relative to migration status

After excluding participants with missing data on time since migration (n=13), postal codes (n=117), and sex (n=8) from age-eligible Albertans, the final sample size was 3,931,698, of which 731,217 (18.5%) were international immigrants to Alberta. Those above 50 years of age comprised nearly 30% of the immigrant population and 40% among non-immigrants. Females comprised 51.8% of immigrants and 49.2% of non-immigrants. Immigrants from Asia comprised nearly half of the immigrant population in this study (48.3%).

COVID-19 vaccine coverage

Overall, COVID-19 vaccine coverage was 78.2% (95% CI: 78.1%, 78.3%) among immigrants and 76.0%; 95% CI:75.9%, 76.0%) among non-immigrants Coverage among immigrants differed by continent of origin (Table 6). Asian immigrants had the highest overall vaccine coverage (83.3%) followed by African immigrants (79.3%). In contrast, immigrants from elsewhere in North America had the lowest overall coverage (62.9%). For the age categories between 12 and 74 years, immigrants from North America, Oceania, and Europe had the lowest coverage. For the oldest age group (75 years and older), immigrants from North America, Asia, and Europe had the lowest coverage. Coverage on sub-continental regions is available in Table B1).

Table 6. Vaccination coverage of international immigrants to Alberta categorized by continent of origin and age.

		Age categories					
	TOTAL	**12-17 years**	**18-29 years**	**30-49 years**	**50-64 years**	**65-74 years**	**75 years & above**
Continent	**% (n)**	**% (n)**	**% (n)**	**% (n)**	**% (n)**	**% (n)**	**% (n)**
North America	62.85% (48,758)	57.68% (3,624)	59.00% (8,861)	64.17% (22,610)	67.45% (9,723)	61.28% (2,739)	55.81% (1,201)
South America	75.67% (17,299)	73.65% (833)	73.14% (3,109)	76.27% (7,616)	78.16% (4,008)	79.14% (1,275)	60.74% (458)
Europe	67.74% (58,334)	66.99% (3,030)	68.06% (8,716)	66.81% (25,654)	70.59% (15,617)	66.79% (3,733)	59.26% (1,584)
Asia	83.32% (353,540)	86.65% (22,508)	85.72% (69,753)	85.21% (16,567)	84.09% (65,038)	74.17% (19,881)	58.30% (10,793)
Africa	79.34% (51,142)	71.39% (3,811)	78.77% (11,176)	80.90% (27,233)	81.47% (6,841)	76.56% (1,388)	65.32% (693)
Oceania	64.60% (7,700)	60.37% (297)	48.87% (1,213)	68.48% (4,226)	71.67% (1,361)	70.75% (433)	64.39% (170)
Unknown/ missing	80.16% (35,255)	69.26% (1,336)	66.84% (1,183)	59.08% (2,538)	84.37% (19,282)	85.63% (7,312)	78.47% (3,604)

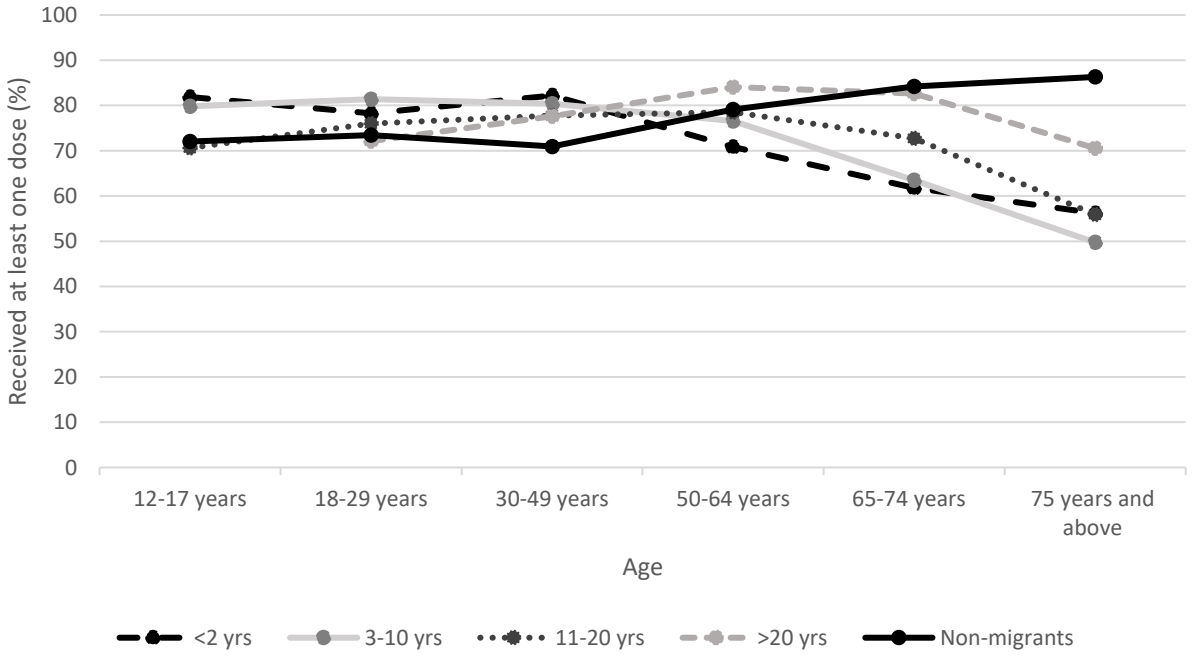

Figure 6. Vaccination coverage (≥1 dose) in different age categories by migration status

The proportions of individuals vaccinated with ≥1 dose was significantly different (*P*<0.001) by age and migration status (Table 7). Vaccination coverage for immigrants generally trended downwards after 50 years of age, irrespective of time since migration. Among immigrants under 50 years of age, those who migrated within the past 20 years tended to have higher vaccination coverage than those who migrated more than 20 years ago. However, among older immigrants (50 years of age and older), those who migrated within the past 20 years had lower coverage than those who migrated more than 20 years ago. In non-immigrants, vaccination coverage increased substantially in older age categories; 70.9%-73.5%% of those 12-49 years old were vaccinated, increasing thereafter, with 86.3% of those 75 years and above having received at least one dose.

Table 7. Vaccination coverage (≥1 dose) in different age categories by migration status

	Immigrant categories by time since migration (N=731,217)				**Non-immigrants (N=3,200,481)**	***P*-value**
	<2 years	**3-10 years**	**11-20 years**	**> 20 years**		
Variables	**% (n)**	**% (n)**	**% (n)**	**% (n)**	**% (n)**	
Age						
12-17 years	81.99% (3,546)	79.80% (23,422)	70.63% (8,471)	*N/A	72.07% (177,414)	<0.001
18-29 years	78.23% (16,359)	81.40% (53,102)	76.01% (30,423)	72.14% (4,127)	73.46% (384,093)	<0.001
30-49 years	82.20% (22,355)	80.37% (119,317)	77.74% (91,172)	77.62% (22,600)	70.94% (783,846)	<0.001
50-64 years	70.81% (3,008)	76.54% (22,500)	78.52% (46,292)	84.07% (50,070)	79.13% (564,189)	<0.001
65-74 years	61.76% (1,702)	63.50% (7,903)	72.75% (8,403)	82.66% (18,753)	84.19% (307,192)	<0.001
75 years & above	56.19% (558)	49.74% (3,421)	55.91% (4,189)	70.56% (10,335)	86.31% (214,558)	<0.001
Sex						
Female	78.63% (24,105)	79.27% (120,856)	77.23% (97,798)	81.52% (56,494)	77.75% (1,223,034)	<0.001
Male	78.67% (23,423)	78.11% (108,809)	75.54% (91,152)	79.11% (49,391)	74.24% (1,208,258)	<0.001
Place of residence						
Rural	64.24% (4,225)	71.08% (18,082)	59.50% (12,615)	66.97% (7,941)	68.14% (443,505)	<0.001

Urban	76.43% (3,738)	79.25% (19,180)	75.38% (13,576	75.44% (5,883)	71.19% (301,335)	<0.001
Metro and moderate Metro	80.81% (39,565)	79.46% (192,403)	78.22% (162,759)	82.14% (92,061)	79.31% (1,686,452)	<0.001
Income quintile						
Q1 (lowest)	80.15% (13,625)	79.35% (61,772)	74.88% (41,535)	79.97% (22,785)	71.43% (382,968)	<0.001
Q2	78.11% (11,078)	79.64% (50,469)	75.59% (37,562)	80.38% (23,281)	74.21% (467,438)	<0.001
Q3	78.23% (7,983)	78.62% (40,920)	76.52% (36,741)	80.26% (21,730)	76.38% (499,438)	<0.001
Q4	78.04% (7,854)	78.26% (39,871)	77.60% (37,558)	80.77% (20,500)	77.64% (535,676)	<0.001
Q5 (highest)	77.83% (6,988)	77.03% (36,633)	77.77% (35,554)	80.61% (17,589)	79.03% (545,772)	<0.001

*There was no one in this age category among immigrants who migrated more than 20 years ago.

There was also variability by other sociodemographic characteristics and migration status. Vaccination coverage among female immigrants was slightly higher than males (except for those who migrated in the last 2 years), with coverage difference increasing slightly with increasing time since migration (Table 7). This difference between females and males was more pronounced in non-immigrants (77.8% vs 74.2%). By place of residence, metro areas had the highest vaccination coverage compared to urban and rural areas, regardless of migration status. There was a wider gap in immigrants who lived in rural areas compared to immigrants who lived in urban areas (76.4% vs 64.2% among those migrating in the last 2 years). Among non-immigrants, the gap between urban and rural residents was 3% (68.1% vs 71.2%). In immigrants, coverage was consistent across the income quintiles, while in non-immigrants, coverage ranged from 71.4% in the poorest quintile to 79.0% in the richest quintile. Intervals between dose 1 and 2, and coverage results for zero, one, and two doses are presented in Table B2 and Table B3.

Interaction between age and migration status

There was a significant interaction between age category and migration status as it relates to vaccine coverage with ≥1 dose of vaccine (see Table 8 and Figure 6); Figure B3 shows comparable results for 2 dose coverage. Among immigrants, younger age groups that immigrated most recently (10 years or less) had higher coverage than those who immigrated more than 10 years ago. This trend changes after 50 years of age, when coverage in more recent immigrants starts to drop below those who immigrated more than 10 years ago. Among non-immigrants, vaccine coverage continues to increase with age, peaking in those 75 years and above (86.3%). Multivariable logistic regression analysis showed that immigrants generally had significantly higher vaccine uptake for those aged 12 to 49 years old compared to non-immigrants. However, among those aged 50 years and above, immigrants had significantly lower vaccine uptake compared to non-immigrants. Immigrants who migrated in the last 2 years had nearly twice the likelihood of getting vaccinated compared to non-immigrants (OR = 1.73, 95% CI: 1.61, 1.86) among those aged 12-17 years. Conversely, among those aged 75 years and above, immigrants who migrated in the last 2 years had an 83% lower chance of getting vaccinated compared to non-immigrants (OR = 0.17, 95% CI: 0.14, 0.19).

Table 8. Bivariate and multivariable association of vaccination with migration status

Migration status		**Unadjusted OR**	**95% CI**	**Adjusted OR***	**95% CI**
Migrated in last 2 years	12-17 years	1.76	1.63-1.91	1.73	1.61-1.86
Migrated in last 3-10		1.53	1.49-1.58	1.49	1.45-1.53
Migrated in last 11-20 years		0.93	0.90-0.97	0.90	0.87-0.93
Non-migrants		Ref		Ref	

Migrated in last 2 years	18-29 years	1.3	1.26-1.34	1.34	1.29-1.38
Migrated in last 3-10		1.58	1.55-1.63	1.51	1.48-1.54
Migrated in last 11-20 years		1.15	1.12-1.17	1.07	1.04-1.09
Migrated before 20 years		0.94	0.88-0.99	0.88	0.83-0.93
Non-migrants		Ref		Ref	
Migrated in last 2 years	30-49 years	1.89	1.83-1.95	1.83	1.77-1.89
Migrated in last 3-10		1.68	1.66-1.70	1.57	1.55-1.60
Migrated in last 11-20 years		1.43	1.41-1.45	1.34	1.32-1.36
Migrated before 20 years		1.42	1.38-1.46	1.34	1.31-1.38
Non-migrants		Ref		Ref	
Migrated in last 2 years	50-64 years	0.64	0.60-0.68	0.51	0.48-0.54
Migrated in last 3-10		0.86	0.84-0.88	0.73	0.71-0.75
Migrated in last 11-20 years		0.96	0.94-0.98	0.83	0.81-0.84
Migrated before 20 years		1.39	1.36-1.42	1.24	1.21-1.27
Non-migrants		Ref		Ref	
Migrated in last 2 years	65-74 years	0.3	0.28-0.33	0.23	0.21-0.25
Migrated in last 3-10		0.33	0.32-0.34	0.25	0.24-0.26
Migrated in last 11-20 years		0.5	0.48-0.52	0.42	0.40-0.43

Migrated before 20 years		0.9	0.86-0.93	0.77	0.74-0.80
Non-migrants		Ref		Ref	
Migrated in last 2 years	75 years and above	0.2	0.18-0.23	0.17	0.14-0.19
Migrated in last 3-10		0.16	0.15-0.17	0.12	0.11-0.13
Migrated in last 11-20 years		0.2	0.19-0.21	0.16	0.15-0.17
Migrated before 20 years		0.38	0.37-0.39	0.31	0.30-0.33
Non-migrants		Ref		Ref	

OR – odds ratio
*Adjusted for age category, sex, place of residence, and neighborhood income quintile.

Discussion

Summary of findings

This study reports on the status of COVID-19 vaccination coverage among immigrants in comparison to non-immigrants in Alberta. Overall, vaccine coverage among immigrant populations is slightly higher compared to non-immigrants and was significantly higher among immigrants under 50 years of age. Unlike the non-immigrant population, which had very high coverage in older adults, coverage decreased in older immigrants, regardless of time since migration.

Interpretation

Overall, COVID-19 vaccine coverage among Albertans was high in both immigrant and non-immigrant populations (78% in immigrants and 76% in non-immigrants), and comparable with

national coverage across Canada (79%) and Australia (80%) during a comparable period (the last week of Nov 2021) (12,13).

Although the coverage among immigrants was slightly higher than non-immigrants, the absolute difference in coverage was minimum (2.2%). Previous studies have shown lower uptake of routine vaccines among immigrant populations compared to non-immigrants (6,14–16). However, COVID-19 vaccination intention in a study from California, USA was higher among immigrant adults (75%) compared to non-immigrant adults (68%) (17). Similarly, a Canadian web survey of participants aged 18 years and older also found that immigrants had a higher intention to receive the COVID vaccine (75%) compared to Canadian-born residents (69%). The difference in intention was the highest in Alberta (86% in immigrants versus 61% in Canadian-born) (18). The same survey reported that nearly 80% of the immigrants were satisfied with the federal government's handling of the pandemic (19). Immigrants in Alberta generally have a high trust towards government and health authorities regarding vaccination decisions (20). Additionally, immigrants are more likely to be employed in essential occupations where there are higher chances of exposure to COVID-19 infection (21), which could have motivated immigrants to get vaccinated (22). Some employers instituted vaccine mandates for workers in essential occupations at the beginning of the pandemic. As well, the availability of vaccines free-of-charge through public health centers, pharmacies, and physician clinics irrespective of migration status might have reduced barriers. Although studies have not further explored COVID-19 vaccine hesitancy between immigrants and non-immigrants, differing concerns about safety, efficacy, and perception of mild disease may also explain the differences (23). Immigrants from Europe, Oceania, and North America had lower vaccine coverage for those aged 12 to 74 years, compared to immigrants from Asia. Older immigrants (75 years and above)

had lower vaccine coverage than middle-aged (30-49 years) immigrants for all continents of origin. Consistent with our findings of higher overall coverage in Asian immigrants, an earlier study from Norway found that immigrants from Asian countries (Vietnam, Sri Lanka, Thailand) had COVID-19 vaccine coverage similar to Norwegian-born individuals (>90%) (24). They also found that vaccine coverage among immigrants from other Asian countries (India, Philippines, Iran) and from Northern Europe (Denmark, UK, Sweden) was much higher than immigrants from Eastern Europe (Latvia, Bulgaria, Poland, Romania, and Lithuania, and proposed that vaccine hesitancy translated into lower vaccine uptake (24). Vaccine hesitancy in these countries is believed to be associated with a history of authoritarian governments (25,26).

Older immigrants (65 years and older) had significantly lower coverage compared to older non-immigrants and this difference was higher among recent immigrants. This finding is particularly relevant as older age groups were one of the first priority groups for COVID-19 vaccination in Alberta. A study from Ontario, Canada also showed that COVID-19 vaccine coverage was significantly lower among immigrants and refugees aged 70 years and over, compared to their Canadian-born counterparts (27). Lower uptake of pneumococcal vaccine among older immigrants was also reported in the US (16). Possible reasons for lower uptake among older immigrants may be related to cultural and language barriers, higher exposure to misinformation from informal sources and social media, distance to clinics/pharmacies, opening hours, and challenges with online booking systems (28). Additionally, residents in long term care (LTC) and designated supported living (DSL) facilities were the highest priority groups for COVID-19 vaccination in Canada (29). Lower admission rate among older immigrants in LTC and DSL facilities due to their ‘strong preference to grow old at home’ and LTC-related barriers might have resulted in lower coverage (30).

We found that vaccination coverage by migration status showed an interaction with age category. Vaccination coverage among immigrants who migrated in the last 10 years started to drop after 50 years of age. Among non-immigrants, vaccine coverage rose after 50 years of age. Interestingly, immigrants who migrated more than 20 years ago followed a pattern similar to non-immigrants, i.e., increasing coverage after 50 years of age, until the oldest age groups, when coverage started to decline. Since views and beliefs about vaccines are influenced by interpersonal relationships, as well as an individual's historical and social context (31), it is possible that migrating later in life means that early lifetime influences of older immigrants continue to affect their vaccination behaviour to present day. Among younger immigrants, however, higher educational status before migration, and smooth acclimatization and integration into Canadian society may have instilled positive views towards vaccines. It can thus be suggested that factors such as time since migration, age at migration, and acculturation window determine the occurrence of the healthy immigrant effect in terms of COVID-19 vaccination, and it does not hold for older immigrants.

Future directions

Understanding how COVID-19 vaccine uptake varies in Canada's immigrant population is important to design strategies for vaccine delivery and messaging (14). This is particularly true for older immigrants who had disturbingly low coverage levels, despite their high risk from COVID-19 infection. Our findings suggest that COVID-19 vaccination strategies need to be tailored to the needs of diverse immigrant populations. This could include translating educational materials about vaccines into the language they understand (18). Strategies may vary for immigrants from North America, Oceania, and Europe, who may not face language barriers, but nonetheless had lower coverage. Moreover, rural-residing immigrants might need additional

strategies to receive the COVID-19 vaccine. These might include co-designing tailored approaches according to local needs, leveraging the role of social media, reconsidering current models for vaccine distribution (32), and partnering with local community-based organizations (28), faith leaders, and underserved communities, including immigrant communities either directly or through local partners (33). Communication through text messages, mass media, or telephone, as well as offering vaccines on a walk-in basis can attract diverse and hard-to-reach populations (34).

Strengths and limitations

This is one of the few studies in Canada to investigate vaccine coverage across different age groups of immigrant populations in comparison to non-immigrant populations. We used population-based immunization, immigrant, and resident registries to derive our coverage estimates, ensuring a large and complete dataset for analysis.

Our study has some limitations. Our dataset likely included individuals who moved out of Alberta without reporting this to the provincial health insurance registry, which may have resulted in an underestimation of vaccine coverage in all groups. Thus, our denominator is larger than reported by Alberta Health (35), which applies aggregate weights to offset the population inflation, an approach that was not possible for our individual-level data. We did attempt to remove non-residents from our denominator through other approaches. For instance, we tried excluding individuals aged 50 years and over who had not used any of the health services in seven domains in 2020 and 2021 (ambulatory care, inpatient care, laboratory data, COVID-19 test data, long term care, pharmacy data, physician claims), assuming that if they did not use any of these health services then they were probably living out of the province. However, although

vaccine coverage by immigration status showed a similar pattern as was seen in the full sample, we lost a significant number of individuals who received COVID-19 vaccines in Alberta in the past year. Therefore, we decided to conduct analysis on the full sample. Unfortunately, we did not have access to data on other important variables that might be associated with vaccination such as ethnicity, religion, household size, and medical risk group.

In addition, since interprovincial migration was included in the non-immigrant population, there may have been some misclassification of international immigrants as non-immigrants, thereby overestimating the non-immigrant coverage levels. Furthermore, since children born to immigrants in Canada are included in the non-immigrant populations, it might have also overestimated the vaccine coverage among non-immigrants. The findings from this study may not be generalizable to other jurisdictions due to differences in immigration trends, and immigrant characteristics, among others. Finally, COVID-19 vaccines received outside of Alberta may not have been captured in Alberta's immunization repository.

Conclusions

Public health interventions should focus on older immigrants, immigrants living in rural areas, and immigrants from specific continental backgrounds to improve COVID-19 vaccination coverage. Future research should examine COVID-19 vaccination uptake in children of immigrants, specifically the newly eligible 5- to 11-year-old age group.

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Appendix

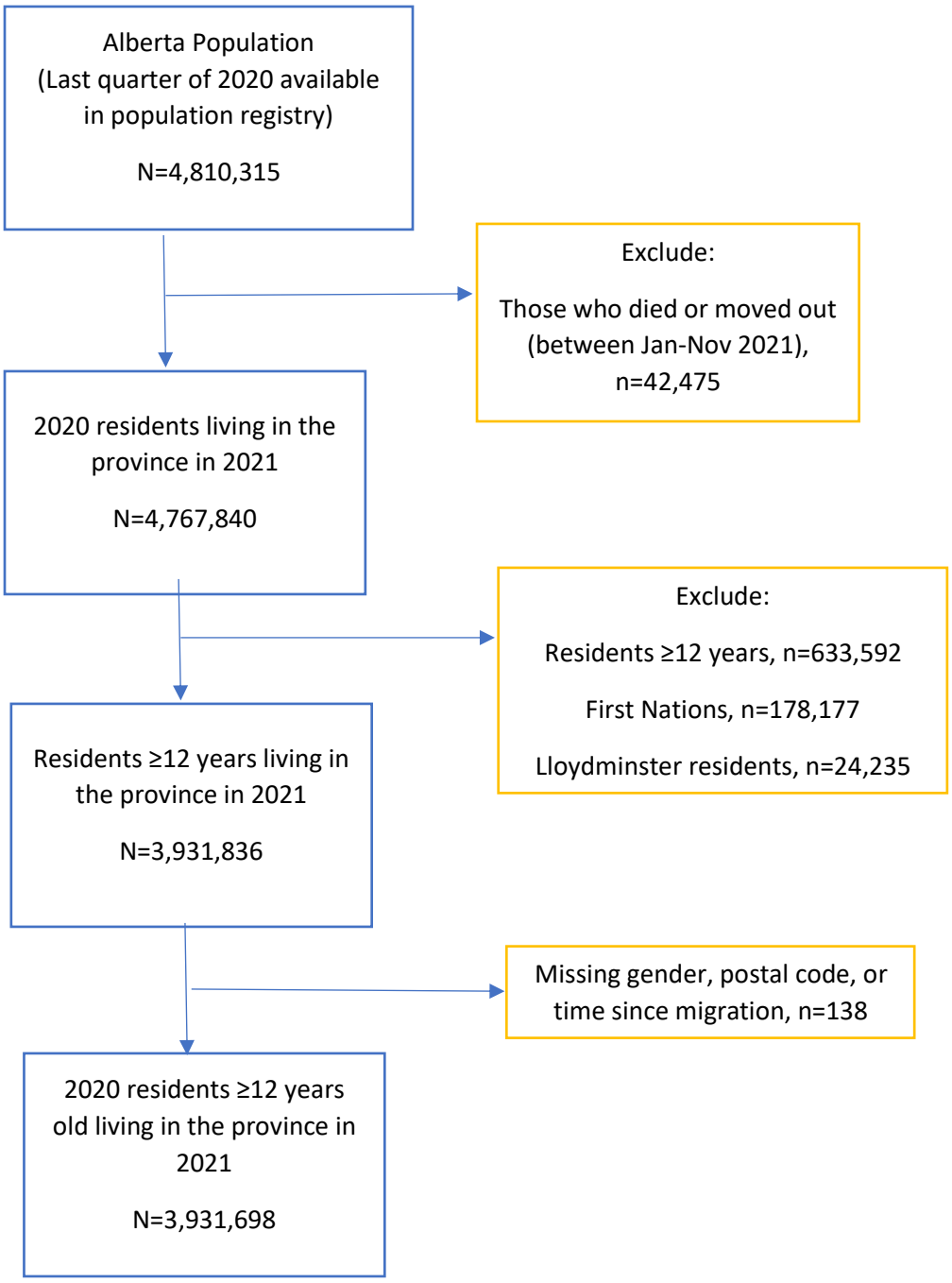

Figure B1. Flow diagram showing selection of participants.

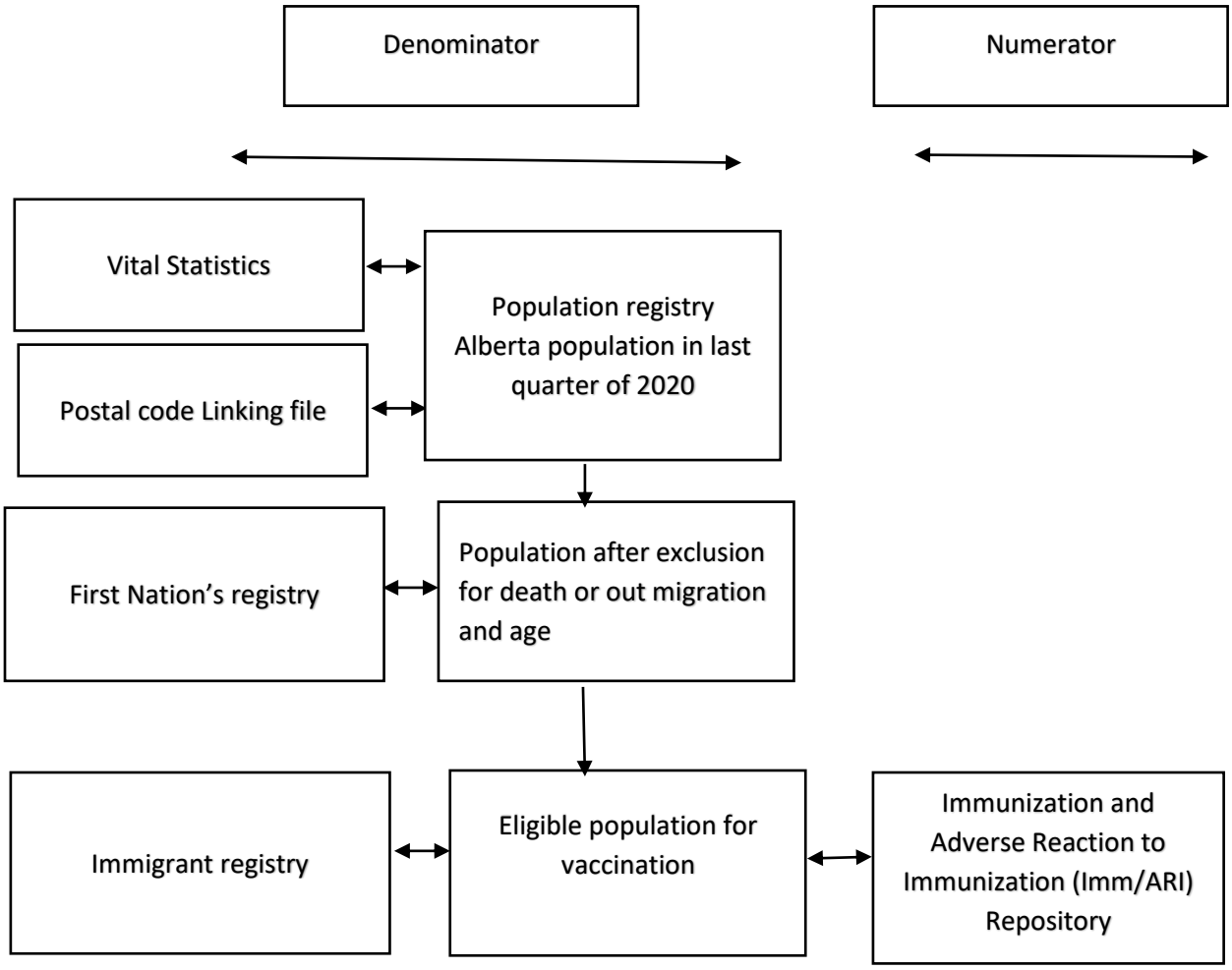

Figure B2. Linkage of different databases.

Table B1: Vaccination coverage of Albertan immigrants categorized by sub-continental region of origin.

Continent	**% (n)**
North America	63.19% (43,439)
Meso America	62.42% (34,137)
South America	75.67% (17,299)
Europe Unspecified	72.45% (4,191)
East Europe	60.69% (11,512)
West Europe	64.05% (9,417)
North Europe	71.50% (24,356)
South Europe	70.34% (8,858)
Central Asia	64.59% (5,370)
Middle East	75.67% (41,263)
Africa Unspecified	79.70% (2,308)
North Africa	75.41% (7,825)
East Africa	79.51% (20,122)
Central/South Africa	76.41% (6,775)
West Africa	82.94% (14,112)
Asia Unspecified	86.21% (11,857)
East Asia	85.47% (193,589)
South Asia	83.71% (101,461)
Oceania	64.60% (7,700)
Unknown/Missing	80.16% (35,255)

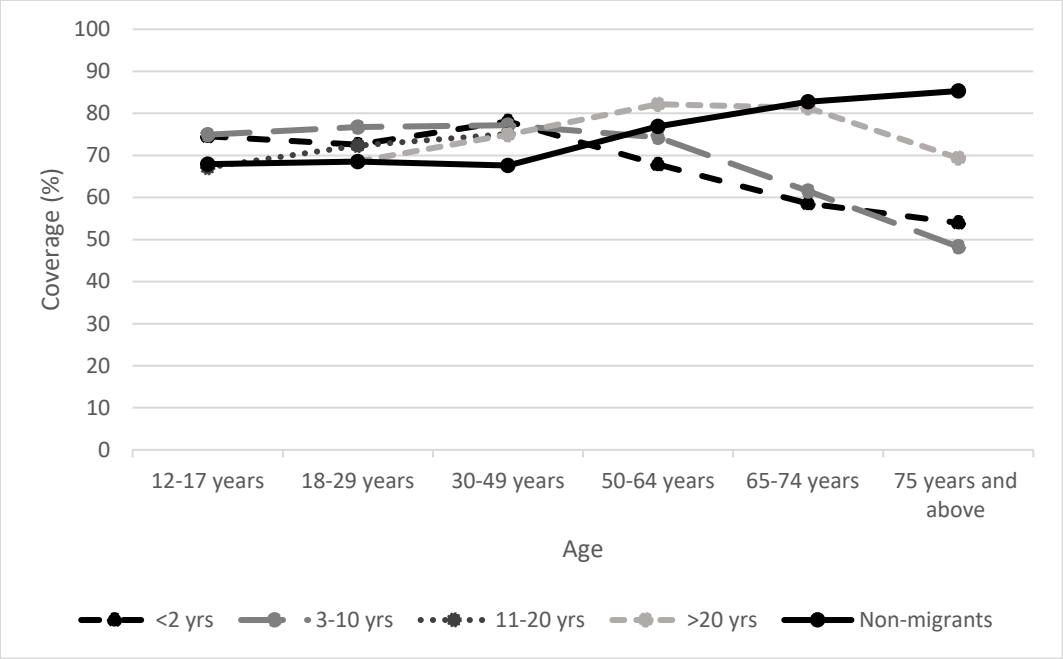

Figure B3. Vaccination coverage (2 doses) in different age categories by migration status.

Table B2. Time interval between two doses of COVID-19 vaccine (days)

Migration status	N	Mean (days)	Std Dev (days)	Median (days)
Immigrants (last 2 years)	44684	52	62	48
Immigrants (last 3-10 years)	219498	51	21	48
Immigrants (last 11-20 years)	182633	52	20	49
Immigrants (>20 years)	103301	55	21	53
Non-immigrants	2335331	54	28	51

Table B3: Proportion of Alberta residents who received no dose, one dose or two doses of a COVID-19 vaccine by migration status and sociodemographic characteristics.

Variables	Immigrants												Non-immigrants		
	Last 2 years			3-10 years			11-20 years			>20 years					
	No dose % (n)	One dose % (n)	Two doses % (n)	No dose % (n)	One dose % (n)	Two dose % (n)	No dose % (n)	One dose % (n)	Two doses % (n)	No dose % (n)	One dose % (n)	Two doses % (n)	No dose % (n)	One dose % (n)	Two dose % (n)
Age															
12-17 years	18.01 (779)	7.45 (322)	74.54 (3,224)	20.2 (5,930)	4.89 (1,434)	74.91 (21,988)	29.37 (3,523)	3.5 (420)	67.13 (8,051)	na	na	na	27.93 (68,763)	4.14 (10,202)	67.92 (167,212)
18-29 years	21.77 (4,553)	5.62 (1,175)	72.61 (15,184)	18.6 (12,136)	4.63 (3,021)	76.77 (50,081)	23.99 (9600)	3.69 (1,475)	72.33 (28,948)	27.86 (1,594)	3.55 (203)	68.59 (3,924)	26.54 (138,778)	4.88 (25,531)	68.58 (358,562)
30-49 years	17.8 (4,840)	4.1 (1,114)	78.11 (21,241)	19.63 (29,140)	3.18 (4,716)	77.19 (114,601)	22.26 (26,104)	2.63 (3,087)	75.11 (88,085)	22.38 (6,516)	2.72 (791)	74.9 (21,809)	29.06 (321,146)	3.33 (36,746)	67.61 (747,100)
50-64 years	29.19 (1,240)	2.92 (124)	67.89 (2,884)	23.46 (6,896)	2.23 (657)	74.31 (21,843)	21.48 (12,663)	1.78 (1,048)	76.74 (45,244)	15.93 (9,490)	1.88 (1,118)	82.19 (48,952)	20.87 (148,767)	2.25 (16,035)	76.88 (548,154)
65-74 years	38.24 (1,054)	3.16 (87)	58.6 (1,615)	36.5 (4,543)	1.93 (240)	61.57 (7,663)	27.25 (3,147)	1.84 (212)	70.92 (8,191)	17.34 (3,933)	1.33 (301)	81.34 (18,452)	15.81 (57,689)	1.37 (5,017)	82.81 (302,175)
75 years & above	43.81 (435)	2.22 (22)	53.98 (536)	50.26 (3,457)	1.44 (99)	48.3 (3,322)	44.09 (3,304)	1.0 (75)	54.9 (4,114)	29.44 (4,312)	1.17 (171)	69.39 (10,164)	13.69 (34,046)	0.98 (2,430)	85.33 (212,128)
Sex															
Female	21.37 (6,551)	4.62 (1,416)	74.01 (22,689)	20.73 (31,610)	3.37 (5,138)	75.9 (115,718)	22.77 (28,827)	2.38 (3,012)	74.86 (94,786)	18.48 (12,804)	1.83 (1,271)	79.69 (55,223)	22.25 (349,932)	2.58 (40,653)	75.17 (1,182,381)
Male	21.33 (6,350)	4..8 (1,428)	73.88 (21,995)	21.89 (30,492)	3.61 (5,029)	74.5 (103,780)	24.46 (29,514)	2.74 (3,305)	72.8 (87,847)	20.89 (13,041)	2.1 (1,313)	77.01 (48,078)	25.76 (419,257)	3.4 (55,308)	70.84 (1,152,950)
Place of residence															
Metro/ moderate Metro	19.19 (9,396)	4.66 (2,282)	76.15 (37,283)	20.54 (49,723)	3.47 (8,408)	75.99 (18,3997)	21.78 (45,321)	2.51 (5,225)	75.71 (157,535)	17.86 (20,014)	1.88 (2,102)	80.27 (89,959)	20.69 (439,843)	2.65 (56,242)	76.67 (163,0253)
Urban	23.57 (1,153)	4.93 (241)	71.5 (3,497)	20.75 (5,023)	3.98 (963)	75.27 (18,217)	24.62 (4,434)	2.87 (517)	72.51 (13,059)	24.57 (1,916)	2.32 (181)	73.11 (5,702)	28.81 (121,975)	3.6 (15,249)	67.58 (286,090)
Rural	35.76 (2,352)	4.88 (321)	59.36 (3,904)	28.92 (7,356)	3.13 (796)	67.95 (17,284)	40.5 (8,586)	2.71 (575)	56.79 (12,039)	33.02 (3,915)	2.54 (301)	64.44 (7,640)	31.86 (207,371)	3.76 (24,470)	64.38 (418,988)
Income Quintile															
Q1 (lowest)	19.85 (3,374)	6.09 (1,035)	74.06 (12,590)	20.65 (16,073)	4.57 (3,554)	74.78 (58,210)	25.12 (13,936)	3.14 (1,743)	71.73 (39,790)	20.03 (5,707)	2.27 (647)	77.7 (22,137)	28.58 (153,186)	3.87 (20,760)	67.55 (362,089)

Q2	21.88 (3,103)	4.36 (618)	73.76 (10,459)	20.34 (12,887)	3.48 (2,204)	76.19 (48,282)	24.4 (12,122)	2.6 (1,293)	72.99 (36,260)	19.62 (5,684)	1.94 (562)	78.44 (22,724)	25.8 (162,465)	3.19 (20,060)	71.02 (447,201)
Q3	21.78 (2,220)	4.27 (435)	73.96 (7,539)	21.39 (11,114)	3.16 (1,642)	75.45 (39,203)	23.52 (11,275)	2.33 (1,115)	74.15 (35,547)	19.77 (5,349)	1.88 (510)	78.35 (21,199)	23.62 (154,353)	2.87 (18,765)	73.51 (480,332)
Q4	21.98 (2,211)	4.01 (403)	74.02 (7,446)	21.76 (11,070)	2.99 (1,520)	75.26 (38,290)	22.41 (10,830)	2.37 (1,146)	75.21 (36,340)	19.23 (4,881)	1.8 (456)	78.97 (20,042)	22.37 (154,341)	2.73 (18,836)	74.89 (516,622)
Q5	22.15 (1,993)	3.92 (353)	73.92 (6,650)	22.96 (10,958)	2.61 (1,247)	74.42 (35,513)	22.18 (10,178)	2.22 (1,020)	75.6 (34,696)	19.35 (4,224)	1.87 (409)	78.78 (17,199)	20.95 (144,844)	2.54 (17,540)	76.52 (529,087)

Chapter 4: Conclusion

This concluding chapter summarizes key points and findings in relation to the research objectives and questions. Strengths and limitations of this research project will also be discussed, alongside potential future research opportunities and potential implications of the research for the broader field of study.

Overview of findings

The overall objective of this research project was to examine vaccination coverage of HPV and COVID-19 in immigrant populations in Alberta, Canada and determine factors associated with vaccine uptake.

The central questions for this research project were as follows:

1. Regarding HPV vaccination of school-aged children in Alberta:
    1. Does coverage for HPV vaccination differ between international immigrants and non-immigrant children?
    2. Does HPV catch-up at a later date differ between international immigrants and non-immigrant children?
2. Does coverage for COVID-19 vaccination differ between immigrants and non-immigrants?

Chapter 2 presented findings from a retrospective population-based cohort study, which used linked administrative data to determine vaccination coverage of HPV vaccine provided through the routine immunization program in Alberta and factors associated with uptake. The study

found higher coverage in immigrant children overall. Immigrants from North America, Oceania and Europe had the lowest coverage, while immigrants from Asia and Africa had the highest coverage. It was shown that second-generation immigrants had more similar vaccine coverage to that of foreign-born immigrants. Analysis examining total increase in vaccine coverage from age 12 to age 17 showed that there was no significant difference when comparing immigrant and non-immigrant females. The results from this study suggest that region of origin and place of residence (specifically rural areas) are important factors to consider when designing public health interventions targeting immigrants.

The retrospective cross-sectional study in Chapter 3 presented results on COVID-19 vaccination coverage in immigrants of all ages in Alberta. This study found overall higher COVID-19 vaccine coverage among immigrants compared to non-immigrants. Immigrants from North America, Oceania and Europe had the lowest coverage, while immigrants from Asia and Africa had the highest coverage. There was a significant interaction between age and time since migration; among immigrants, younger, recent immigrants had higher coverage compared to those who migrated more than 10 years. While income quintile did not appear to be associated with vaccine uptake amongst immigrants, rural immigrants had lower vaccine coverage compared to rural non-immigrants. Although overall high vaccine coverage in both groups was encouraging, it is important to recognize the importance of targeting public health interventions towards older immigrants living in rural areas given their higher risk for infection.

Both studies showed that overall vaccination coverage was highest in immigrant populations. This is contradictory to many previous studies that have examined vaccine coverage in immigrant populations in other settings. Previous literature examining perceptions and uptake towards either the HPV or COVID-19 vaccine have shown more negative attitudes amongst

immigrant populations compared to non-immigrants (1–4). Possible reasons for deviations in our results include different proportions of immigrants from different regions of origins from other studies; almost half of our study population was from Asian regions. Results from both studies showed that immigrants from Asia and Africa had the highest vaccination coverage. In general, Asian immigrants are a demographic group in which studies have shown to hold cultural values that place a strong emphasis on protecting the health and well-being of the community as a whole, which includes highlighting the importance of vaccination practices (5). In addition, these immigrants may have had higher vaccination coverage in their home countries and continued to prioritize vaccination once in Canada (6). In regard to COVID-19, immigrants from these regions may have faced mandatory vaccination policies for travel to their home countries, which may lead to higher uptake (7). However, it is important to note that Asian immigrants encompass a diverse group of individuals from different cultures. In addition, both studies showed that immigrants from elsewhere in North America had the lowest vaccine coverage, a large proportion being from the United States. This trend may be attributed to the individualistic mindset prevalent in the United States, as studies have shown that individuals from such backgrounds are less likely to engage in public health behaviour, including vaccination (8,9). However, the underlying reasons for lower vaccination coverage among this subgroup require further research and analysis. Additional future research could look at determining factors that differ between the immigrant groups in order to target gaps for vaccination coverage.

Immigrants living in rural areas had lower odds of being vaccinated compared to non-immigrants living in rural areas (although this result was not significant for HPV vaccination). Several studies have shown that residents of rural areas have poor access to healthcare services,

including transportation issues or lack of vaccine delivery options (10,11), in addition to lower perceived risk of the disease (12).

Conceptual Framework

The CSDH framework was used to explore how social and economic factors such as biological sex, place of residence, and income affect vaccination uptake in immigrant populations. The findings indicated that all factors had a significant impact on vaccination coverage in immigrants. However, there were some limitations of the application of the CSDH framework to this research project. The framework does not account for individual-level factors such as personal knowledge, attitudes, and perceptions toward vaccination. Although this data was not available due to the use of population-based administrative data, the framework could be enhanced by incorporating individual-level factors in future research. In addition, other factors included in the CSDH framework such as education level and employment status were not included in analysis. Further research that integrates individual-level factors with additional factors in the CSDH framework can provide a more comprehensive understanding of the multiple factors influencing vaccine uptake, which can be used to improve the design and promotion of vaccination programs for immigrant populations.

Strengths and limitations

Both studies conducted in this research project utilized population-based immunization, immigrant, and resident databases, which allowed for large and robust data sets. While the use of provincial databases might limit the generalizability of the results to other jurisdictions in Canada, as public health measures and immigrant policies differ across Canada, this approach allowed for a comprehensive and holistic look. Both studies presented novel information on

vaccination coverage specifically in immigrant populations in Canada. A sensitivity analysis conducted in Chapter 2 highlighted a potential path for immigrant research, expanding on the vaccination status of second-generation immigrants.

In the study presented in Chapter 2, changes and delays in the HPV vaccine program (due to changing schedules and COVID impact) made it not possible to use more recent data. However, the analysis of pre-COVID data can be utilized and be beneficial in comparing coverage between the two time points to examine whether the event had a significant impact, given that information was not previously presented before.

A further limitation was we did not have access to data on other potential factors associated with vaccination uptake due to limitations of the databases. This included individual-level (e.g., education, religion, ethnicity), and societal factors (e.g., healthcare access). Future expansion of these studies could utilize survey methodology to gather such data from immigrant participants directly. Lastly, reporting of immunization data to the Immm/ARI database is not inclusive of all First Nations data.

Future directions

While the HPV routine immunization program is provided in schools, it should be noted that a catch-up program for males and females 17 years up to and including 26 years of age (13) is now available. Examining catch-up rate from adolescence to adulthood has been understudied and therefore is a potential avenue for future exploration. The study presented in Chapter 2 briefly examined coverage in second-generation immigrants; as an “inbetween group” of immigrants and non-immigrants; future studies could examine if the same result is present in other vaccines and if so, factors that are associated with the difference.

In addition, it would be interesting to examine how the COVID-19 pandemic affected routine immunization coverage post-pandemic and how perceptions may have changed in immigrant populations. The post-pandemic period has resulted in a heightened awareness of infectious diseases and prevention methods, changes in public health behaviours, and emergence of other factors that may have affected vaccine coverage. Understanding whether and how these factors impacted vaccine coverage can help inform strategies to mitigate the effects of future pandemics on vaccination programs.

Canada's diverse population highlights the importance of comparing vaccination coverage rates across different jurisdictions, which can identify successes and gaps in vaccination promotions and uptake. This can provide valuable insight into factors that may be contributing to success or hindering progress, and identify best practices in vaccine promotion and uptake, ultimately contributing to the improvement of vaccination programs across the country.

To ensure that the results of this study are widely disseminated and translated in practice, it is important to share them with various stakeholders, such as policymakers, public health agencies, healthcare providers, and immigrant-serving organizations. This could be achieved through publications in peer-reviewed journals, presentations at conferences, and meetings with relevant stakeholders.

Implications for policy and practice

The findings from this research project have implications when designing vaccination policies and interventions targeting immigrant groups.

Immigrants are not a homogeneous group; they are a diverse collection of people with each their own beliefs, perceptions, and experiences of and towards vaccines. While vaccine knowledge

may be lacking in some immigrant groups, there is a strong desire to learn; therefore, cultural-appropriate teachings and language resources should be shared to help immigrants make informed decisions to promote vaccine uptake (14).

Contrary to previous literature, my research found that vaccination coverage was higher in immigrant populations, which is encouraging to witness. This suggests that current practices and strategies targeted towards immigrant populations are promising and effective and could be built upon in the future.

While it was interesting to note that vaccination coverage amongst immigrants was higher compared to non-immigrants overall, coverage levels did remain below national targets, even with the catch-up programs. Further opportunities for catch-up may be needed, in addition to the current catch-up practice. In Alberta, public health nurses are responsible for catch-up, primarily in school-based settings. Future policies may look at implementing additional practices such as adding physician offices, co-administration of vaccines, and social media/messaging reminders (15).

Some findings from the study had broader implications beyond the immigrant population. To encourage immunization among males, additional promotion strategies should be considered, such as encouraging healthcare providers to discuss HPV with their male patients, school visits from public health workers to provide sexual health education, and advertising campaigns promoting broader social benefits of HPV vaccine (16). Rural residents in general are a group that may require supplementary strategies.

Conclusion

In the two studies presented in Chapter 2 and 3, I found that vaccination coverage levels were higher in immigrant populations compared to non-immigrants in Alberta, and coverage was associated with income, place of residence and biologic sex. Differences in coverage also existed based on region of origin and may play a major role in uptake. In both cases, vaccination coverage levels did not meet national target goals. In particular, immigrants that are older, from elsewhere in North America and living in rural areas should be main considerations when designing vaccination promotion policies. Accounting for cultural differences based on region of origin can be a potential key to effective strategies. Future studies should consider community-level factors to determine which factors are associated with vaccination coverage and whether this same pattern is prevalent in other vaccines.

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