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The epidemiology of influenza vaccination among young children in the Calgary Health Region

by

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Abstract

Background: Influenza is a viral respiratory illness and can be prevented by a vaccine. This study aimed to describe the epidemiology of influenza vaccinations among children 6 months to <9 years of age in the former Calgary Health Region(CHR).

Methods: This study used data from the CHR's immunization system comprising >140,000 influenza vaccine doses administered to children(2004-2008). Income data were obtained from the census. Census and insurance registry data provided population counts. Data analysis included proportions and linear regression analysis to describe events and rates by person, place and time.

Results: Influenza vaccination rates ranged from 7 to 14%. Variation in coverage was observed for different levels of age, area of residence and median household income(MHI). The association between MHI and getting vaccinated is not clinically significant.

Conclusions: Influenza vaccination coverage rates among children in the CHR are low. Several factors influence coverage estimates, including age and area of residence.

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List of Abbreviations

Abbreviation	Definition
AHCIP	Alberta Health Care Insurance Plan
AHW	Alberta Health and Wellness
CHR	Calgary Health Region
CI	Confidence Interval
IIS	Immunization Information System
ImmARI	Immunization and Adverse Reaction to Immunization
MADGIC	Maps, Academic Data, Geographic Information Centre
MHI	Median Household Income
NACI	National Advisory Committee on Immunization
OR	Odds Ratio
PHANTIM	Primary Health Activity Network & Timely Information Management
RSV	Respiratory Syncytial Virus
SES	Socioeconomic Status
U.S.	United States
VE	Vaccine Effectiveness

CHAPTER ONE: INTRODUCTION

Influenza is a contagious febrile respiratory illness caused by a virus and spread through respiratory secretions of infected individuals(1). Approximately 10 to 25% of Canadians are infected with influenza annually, resulting in 2,000 to 8,000 deaths every year(2). Although the greatest numbers of influenza-related deaths are consistently among older persons(3), influenza infection patterns among young healthy children are similar to those among the elderly(4). Children are also known to play an important role in introducing and spreading respiratory illness into households and communities(5, 6). Researchers are thus calling for vaccination strategies to include more widespread vaccination of children against influenza(7).

The most effective way to protect oneself from influenza is by getting vaccinated(3). A child under nine years of age requires at least two doses of vaccine to be considered adequately vaccinated for the season(3, 8). Prior to 2009, Alberta residents had to pay for influenza vaccines if they were not considered at high risk of influenza-related complications or capable of transmitting influenza to those at high risk.

Study purpose and objectives

Vaccinating young children is an effective way to reduce influenza-related illness in a community, but vaccination events and coverage estimates (considering one versus two doses) among young children in the Calgary Health Region, Alberta, have not been well-described or estimated previously. Further, in order to improve vaccination rates in young children in the Calgary Health Region, one needs to identify populations that require targeting and determine if an out-of-pocket fee for each influenza vaccine could be a barrier to vaccination for children in the Calgary Health Region.

The objectives of this research include:

1. To describe influenza vaccination events (by provider, facility in which the vaccine was given, and number of doses), reasons for vaccination and reasons for refusal for vaccination among children younger than nine years of age in the Calgary Health Region for each influenza season from 2004-05 to 2007-08 inclusive;

2. To estimate influenza vaccination coverage by attributes of person (age, sex), time (year of vaccination) and place

("rural" or "urban", social district, census tract) among children younger than nine years of age in the Calgary Health Region for each influenza season from 2004-05 to 2007-08 inclusive; and

3. To explore for an association between median household income and influenza vaccination among children younger than nine years of age in the Calgary Health Region for the 2005-06 influenza season.

CHAPTER TWO: BACKGROUND

Introduction

This section reviews the current state of knowledge on the epidemiology of influenza, the burden of disease among children and the role of children in the transmission of disease in a community. The influenza vaccine and the current national and provincial vaccination recommendations are discussed in the context of the service delivery systems in place during the study period. Several methodological issues in measuring vaccination coverage are identified and the effect of socioeconomic status on vaccination coverage is also considered.

Health service delivery in Alberta

At the start of this study, health services were delivered to residents in Alberta by nine Regional Health Authorities with specific geographic boundaries. One such health region was the Calgary Health Region, which is the focus of this thesis. On April 1, 2009, the Regional Health Authorities were replaced by a single body, Alberta Health Services, which is responsible for delivering health services to the entire province. The former Regional Health Authorities no longer exist as corporate entities and were replaced by five zones, one of which is the Calgary

Zone (Appendix A1). The boundaries of the former Calgary Health Region and the current Calgary Zone are the same. References to the "Calgary Health Region" in this report therefore refer to the boundaries of the current Calgary Zone(9).

Influenza

Clinical features and epidemiology of influenza

Influenza is a contagious febrile respiratory illness caused by a virus and spread through respiratory secretions of infected individuals(1). It affects all age groups but most deaths occur in the very young (less than two years of age) and the very old (65 years of age or older)(10). It is characterized by the acute onset of headache, muscle pain, runny nose, sore throat, fever, extreme tiredness, and cough. As these are non-specific symptoms, it is not possible to distinguish influenza from other respiratory viral infections without laboratory confirmation. The incubation period spans one to four days, and a person may remain infectious from before the onset of symptoms until the fifth day of illness(1).

The usual clinical course is one of complete recovery. Nonetheless, some people are at higher risk of influenza-related complications, such as pneumonia, which can lead to death. These groups include:

- people 65 years of age and older;
- children six months to less than two years of age;
- pregnant women;
- residents of nursing homes and other chronic care facilities; and
- anyone with underlying medical conditions such as cardiac or pulmonary disorders, metabolic and renal diseases, diabetes, anemia, or a suppressed immune system(3).

For these reasons, influenza vaccination recommendations are often targeted to protect those who are at high risk of influenza-related complications or who are more likely to require hospitalization.

Virology of influenza

Three types of influenza virus (A, B and C) have been identified according to the virus' genetic makeup and surface(1). While Influenza C is known to cause mild illness in humans, it is not known to cause epidemics or pandemics and is not included in immunization programs(11). For these reasons, Influenza C will not be discussed

further. The Influenza A and B viruses are known to cause annual epidemics of disease, and influenza A will infrequently cause global epidemics known as pandemics(12).

Influenza A is classified into subtypes according to its surface proteins, hemagglutinin (e.g., H1, H2, H3, H5, H7, H9) and neuraminidase (e.g., N1, N2, N3, N7, N8). Only some influenza A subtypes (H1N1, H1N2, H3N2) are generally circulating among human populations. However many other subtypes are found in other animal species, such as H5N1 in poultry, H7N7 in horses and H3N8 in dogs(11). Currently, the most commonly circulating subtypes in humans are H1N1 and H3N2(3). Since the mid-1980s, Influenza B has been classified into two lineages, Yamagata and Victoria, based on the B/Yamagata/16/88-like and B/Victoria/2/87-like viruses. Each subtype and lineage contributes variably to annual epidemics(3).

Influenza viruses undergo frequent antigenic change, meaning the virus can evade host immunity and persist in a population(10, 12). The virus may undergo minor genetic variation, or *antigenic drift*. These drift variants are assumed to cause epidemics of influenza every year(1). Major genetic variation, or *antigenic shift,* is a sudden change to the

virus' genetic makeup due to genetic reassortment of animal or human influenza strains, creating completely new surface antigens(1). These shift variants are completely foreign to host populations and can cause large-scale worldwide epidemics, known as pandemics(10). Such a shift occurred in 2009 when a new H1N1 strain emerged in North America with human, swine and avian components(13). The virus spread worldwide and by June 2009 the World Health Organization declared a pandemic(14). The 2009 pandemic influenza virus strain will not be discussed further as this paper is focused on vaccination against seasonal influenza for the period 2004-2008.

Burden of disease among children

Although the greatest numbers of influenza-related deaths are consistently among older persons(3), influenza infection patterns among young healthy children are similar to those among the elderly(4) and among adults at risk of influenza-related complications(15). One observational study in the United States (U.S.) used data from a medical insurance database to determine the effect of influenza on rates of hospitalization for acute cardiopulmonary conditions, outpatient visits, and courses of antibiotics for healthy children less than 15 years of age. The authors achieved this by comparing the "influenza season" rates

with the "peri-influenza season" (no influenza activity) rates during the winter months. The study found increased rates of hospitalization during the influenza season among all age groups, with the highest rates of hospitalization and excess outpatient visits among the youngest age group (less than two years of age). In addition, children less than one year of age were hospitalized at rates close to those of adults at high risk of influenza-related complications(15).

This study, however, raised important considerations when attempting to quantify influenza-related morbidity. For example, the contribution of other respiratory viruses, such as respiratory syncytial virus (RSV), to the overall morbidity of children during the winter was unknown(15).

An Australian study addressed this issue by comparing influenza-related hospitalization rates during a period of high influenza activity and low RSV activity (influenza-predominant periods) to the rates during a period of low influenza activity and low RSV activity (baseline periods). This takes into account that RSV is a major contributor to respiratory illness among children during the influenza season, which is an especially important consideration for studies without virological evidence for the presence of influenza. The findings from this study

showed that hospitalization rates were the highest in the younger age groups (zero to four years of age, and five to nine years of age)(16). One concern about this study is that it does not explicitly state the source of its denominator data for calculating the rates, or how they classified "population at risk." Nonetheless, the relative differences among age groups are important.

Other studies measured burden of disease using hospital and laboratory data, such as in Hong Kong(17) and the United States(18). Both studies found that children younger than five years of age contributed the most to influenza-related hospital admissions.

In Canada, influenza combined with pneumonia is the seventh leading cause of death in children less than 15 years of age(19). In the Calgary Health Region, several school-based influenza outbreaks were reported in 2005-06, 2006-07, 2007-08 and 2008-09. In 2006-07, the seasonal epidemic primarily affected young children, especially those in elementary schools. That year, 65% of outbreaks occurred in schools. In 2008-09, most outbreaks occurred in care centres (56%) followed by schools (24%)(20, 21).

Clearly, several methods can be used to measure the burden of influenza in a population, but studies from around the world continue to demonstrate the large contribution of young children to influenza-related morbidity(22-27). Therefore children, not necessarily limited to those younger than two years of age, should be an important target population in disease prevention efforts.

Children and community transmission

Not only are children affected by influenza themselves, several studies over the past 40 years have demonstrated that schoolchildren play an important role in introducing and spreading respiratory illness into households and communities(5, 6).

One prospective study in the United States examined influenza-associated illness among schoolchildren (kindergarten through grade eight) by obtaining school absentee records and sending surveys to the parents of children who were absent from school. The survey inquired about symptoms, medications, and illness among other household members. If a survey was not returned, the information was collected by telephone. The study found that for every ten children who missed school due to influenza illness, eight household members subsequently

became ill(28). This supports the earlier findings that influenza infections occur in family clusters(29, 30). Furthermore, disease transmission among family members is considered by some researchers to be an important link to other community groups such as schools and neighbourhoods(31).

Vaccination studies among schoolchildren, while also demonstrating vaccine effectiveness, show that schoolchildren have a major role in the spread of disease. A study conducted in the United States in 1968 found a reduction in illness rates in the entire community after vaccinating 86% of schoolchildren compared to the neighbouring unvaccinated community(32). Similarly, in the early 1960s, Japan implemented a program for vaccinating most schoolchildren that was followed by a reduction in excess mortality rates among the elderly. These rates increased again after the vaccination program was discontinued(33). Finally, a single-blind randomized controlled trial was conducted in California that involved vaccinating daycare children with either influenza vaccine or a placebo vaccine. The authors found that the unvaccinated household contacts of vaccinated children reported significantly fewer occurrences of febrile respiratory illness compared to the household contacts of children who received the placebo vaccine. An

80% reduction in respiratory illness among the school-aged household contacts of vaccinated children was also observed(34).

Several mathematical models and simulations of disease transmission support these findings. Halloran and Longini suggested that when a pandemic occurs, vaccinating schoolchildren may be the most efficient approach to minimize community transmission. Their simulations determined that vaccinating 20% of schoolchildren compared to vaccinating 90% of seniors would more effectively reduce overall mortality in seniors(5). Another simulation showed that vaccinating 80% of schoolchildren in the United States would result in a 95% reduction in the number of influenza cases among children and an 86% reduction in adults(35). Other models suggest that if 70% of U.S. schoolchildren were vaccinated then even those at high risk of influenza-related complications would be protected from influenza(36).

These studies, however, are not without their limitations. A 2006 systematic review of the evidence of the indirect benefits of vaccinating schoolchildren indicated that indirect benefits, such as community protection from illness by vaccinating schoolchildren against influenza, are difficult to quantify and that most of the research in this area is

limited in design or execution. Further research is needed to generate conclusive data with clear quantitative estimates for the possible level of protection gained from vaccinating schoolchildren(37).

Among the best evidence to date is a recent cluster randomized trial among Hutterite colonies in rural Alberta, Saskatchewan and Manitoba which assessed whether or not vaccinating children for influenza could prevent illness in unimmunized community members. In this study, 947 children aged three to 15 years old were randomly assigned to receive a vaccine for either influenza or hepatitis A. Influenza was then confirmed virologically among the vaccinated children as well as 2,326 community members who did not receive a study vaccine. The researchers found that immunizing children against influenza had a significant protective effect against influenza among unimmunized residents in the community(38).

These and other studies indicate that optimal vaccine allocation requires prioritizing children in vaccination programs. Researchers are therefore calling for vaccination strategies to include more widespread vaccination of children against influenza(7).

Influenza vaccination

Influenza vaccine

A vaccine is a biological substance that resembles a pathogen and that, when administered to the body, causes an immunologic response that produces antibodies(1). This allows for a quicker response if exposed again to the pathogen, possibly preventing infection or creating a milder illness if infected.

Due to the mutability of the virus' surface proteins, influenza vaccines are manufactured annually. Recommendations for the composition of the vaccine for each influenza season in each hemisphere are made by an international influenza surveillance network organized by the World Health Organization(39). This network detects antigenic variations in the virus in animal and human populations, and then indicates the most likely strains that will be responsible for human disease the following season. The vaccine manufacturing process takes about six months from production to delivery(39). Vaccines contain inactivated influenza virus or live attenuated influenza virus specific to the recommended strains(1).

In Canada, a trivalent inactivated influenza vaccine is manufactured, containing three components offering protection to three individual strains. These include protection for two influenza A strains, one H1N1 and one H3N2 subtype, and one influenza B strain from either the Yamagata or Victoria lineage(3, 39).

Vaccine effectiveness (VE) is highly dependent on how well-matched the vaccine is to the circulating virus during influenza season. A good match has been shown to prevent influenza infection in upwards of 70% of the healthy population(1, 3), although vaccine effectiveness varies for each component of the vaccine. Using a sentinel surveillance system in Canada to detect influenza in the community and estimate vaccine effectiveness during the 2006-07 season, one study estimated VE for each of the three components of the trivalent influenza vaccine. The highest VE estimate was found for the H1 component which was well-matched to the circulating H1 strain (VE=92%, 95% Confidence Interval (CI): 40, 99). In contrast, the B component was substantially mismatched to the strain circulating in the community and resulted in reduced protection (VE=19%, 95%CI: -112, 69%)(40). A well-matched vaccine can prevent significant illness and societal costs related to influenza illness(3).

Current national and provincial influenza vaccination policies

In Canada, the federal government is responsible for setting national policy for health care through the Canada Health Act and for financing health care services through fiscal transfers to the 10 provinces and three territories in Canada. The distribution of funds and delivery of health services, including immunizations, remain at the discretion of each provincial or territorial government(41). In addition, the federal government is responsible for providing direct health care services to some groups, including First Nations and Inuit people, veterans, refugee claimants, inmates of federal penitentiaries, and members of Canadian Forces and the Royal Canadian Mounted Police(42). Inuit people and First Nations living on reserve in Canada receive health services from federally funded health systems in their communities but may also receive some health services from their provincial or territorial health systems(43). In Alberta, the federal government provides public health services in remote areas and in non-isolated First Nation communities through the Medical Services Branch of Health Canada(44).

The National Advisory Committee on Immunization (NACI) provides recommendations for vaccine use in Canada. The 2009 NACI guidelines encourage all healthy Canadians aged two to 64 years without

contraindication to receive the influenza vaccine(3). NACI also identifies priority groups and recommends that all provincial immunization strategies should target citizens at high risk of influenza-related complications.

Ontario was the first province in Canada to offer a universal publicly funded influenza vaccination program, meaning all Ontario residents are eligible for a publicly funded vaccine regardless of age or health status. Other provinces may offer publicly funded influenza vaccines (provided free of charge) only to the priority groups identified by NACI. This includes people who are at high risk of influenza-related complications, are capable of transmitting influenza to individuals at high risk of complications, and who provide essential community services(3).

For children in Alberta prior to the 2008-09 vaccination season, only those: 1) six months to less than two years of age; 2) with chronic health conditions; and 3) living in a household with someone at high risk (including other young children) were eligible for publicly funded influenza vaccines. Parents of ineligible children had to pay for annual influenza vaccines. Age-eligibility in Alberta expanded in 2008 to include all children six months to less than five years of age, and expanded

again in 2009 to a universal program that offered publicly funded influenza vaccine to all Alberta residents six months of age and older(45).

Vaccination coverage among children

NACI advised Canadian vaccination programs to aim to vaccinate at least 90% of the eligible population(46), but measuring vaccination coverage can be difficult. The main challenges are defining "vaccinated" and identifying appropriate sources for numerator and denominator data. Influenza vaccination is a special consideration because it is delivered annually, and some children require two doses. One must also consistently use the same criteria and methods in order to make comparisons over time. Periodic measurement of vaccination coverage is important in order for health services to determine if they are reaching goals.

Definition of "vaccinated"

The 2009 NACI statement on the seasonal influenza vaccine recommends that previously unvaccinated children aged six months to less than nine years of age receive two doses of influenza vaccine administered at least 28 days apart. Children who received a dose in the

past are recommended to receive just one dose per season thereafter. NACI also mentions that if there is a major antigenic change in a vaccine component between two seasons, then children under two years of age may require two doses regardless of their immunization history. However, NACI indicates that further evidence is needed before this is incorporated into its recommendations.

The Alberta interpretation of these recommendations is outlined in the 2007 Alberta Immunization Manual, in which a child under nine years of age is considered "adequately vaccinated for the season" only if that child has received two doses of the season's antigens, administered at least 28 days apart and after the age of six months(8). If the vaccine antigens are the same as the previous influenza season, children who have received one dose in the previous season require only one dose for the current season.

Although there have been variable recommendations on how to regard previous influenza vaccination in children under nine years of age, the 2009 NACI recommendation will be used to assess adequacy of vaccination for all years in this study. Definitions for vaccination are shown in Table 1.

Table 1. Definitions to determine vaccination status

Adequately vaccinated	Partially vaccinated	Unvaccinated
If a child received two doses in one influenza season after the age of six months and at least 28 days apart, that child is considered adequately vaccinated for the season – or – If a child already received one or more doses of vaccine during a previous season, that child requires only one more dose delivered after the age of six months to be adequately vaccinated for the current season.	If a child has only one record of influenza vaccination in any year, that child is considered partially vaccinated for the year in which they were vaccinated.	If a child has no influenza vaccination events recorded and is older than six months, that child is considered unvaccinated.

When estimating vaccination coverage, it is essential to consider whether or not a child is adequately vaccinated according to this definition since studies have found that many children do not receive the required second dose for optimal protection against influenza infection. Verani and colleagues conducted a retrospective review for five influenza seasons (n=7,063) using registry data for children six to 23 months of age in the United States and found that every year, nearly half of the children who received one dose of vaccine failed to receive the required second dose(47). The authors recognized that they likely underestimated vaccinations due to under-reporting in the registry and possible scattering of medical records across different databases and service providers. Other studies from the United States also demonstrated that a large proportion of children do not receive the required second dose for protection against influenza infection (48-50).

The second dose is important for optimal protection against influenza. Using two different study designs to estimate vaccine effectiveness, both Ritzwoller and Shuler found that adequate vaccination (two doses) provided protection against influenza illness while partial vaccination (one dose) provided no significant reduction in illness among children less than two years of age(51, 52). In 2006 another U.S. study used

billing and immunization registry data to evaluate vaccine effectiveness in healthy children six to 21 months of age. The authors found that one dose of influenza vaccine was not effective in preventing primary care visits for influenza-related illnesses among previously unvaccinated children(53).

Despite these clear differences in protection, several studies report vaccination coverage by defining "vaccinated" as having "one or more" doses of vaccine(54, 55). For example, several studies used data from the Spanish National Health Survey 2003 in which parents were asked to answer yes or no to the question "Did your child have a flu shot in the last campaign?"(56-58). Collecting only the number of doses without any attention to a dose schedule is considered by some to be collecting "crude vaccinations" which would invariably produce an overestimate for coverage since it does not reflect the level of protection in the community(59). In response to this, other studies report separate vaccination coverage estimates for children who are partially or adequately vaccinated(47, 48, 60-63). One study estimated both "complete" (two doses) and "partial" (one dose) vaccination rates in Ontario children six months to 11 years of age by conducting a telephone survey among a sample of 3,029 households selected by

random digit dialling. The author attempted to compare the coverage estimate for Ontario children to the estimates attained from other provinces but, in order to compare the data, only combined rates (complete plus partial vaccination rates) could be used since the number of dose administrations could not be extracted for all provinces(63). The author also noted that the estimates from the different provinces used different denominator definitions(63). This further emphasizes the need for consistent definitions and data collection methodology in deriving vaccination coverage estimates. Standardizing data to make it possible to compare estimates from different sources can result in competition among immunization programs, which can also provide positive motivation to improve vaccination rates.

Timeliness of the doses must also be considered, in terms of both the influenza season and the time spanning the two dose administrations. The first dose could be as early as the first day of the influenza season (usually October 1) and the second dose must be at least 28 days afterwards, according to the NACI recommendations and Alberta Immunization Manual(3, 8). However, it is possible for a child to receive the second dose of vaccine less than 28 days after the first dose, in which case the child would not be adequately vaccinated. Further, if the

second dose is received at the end of the influenza vaccination season (usually April 30) that child would not be considered adequately vaccinated for the influenza season. For example, one study that estimated influenza vaccination coverage among children less than 14 years of age in Italy considered children to be vaccinated if they received at least one dose of vaccine between September 1 and November 30. This study does not consider children who received their first or second dose after November 30, which would largely underestimate final coverage estimates. However, the fact that it considers a child vaccinated after just one dose instead of two doses would overestimate the coverage rate(54).

Due to the clear differences in protection against influenza infection, it is important to properly classify children as vaccinated or not vaccinated by considering the number of doses delivered in a specified time period. Researchers also need to be consistent in their definitions in order to compare study results.

Numerator data source

Both numerator and denominator data are needed to estimate coverage. The numerator is a count of persons vaccinated. The denominator is a

count of persons eligible for vaccination or the population. Vaccination data can be obtained from several sources including medical records, immunization cards, surveys, vaccination registries, immunization information systems and insurance/billing systems. The quality of these data, however, can vary and needs careful consideration.

In a study examining the validity of reported vaccination coverage estimates across 45 countries, one researcher states that the two main sources of data used for estimating vaccination coverage worldwide are health service delivery records (e.g., medical records and immunization cards) and household-based surveys(59).

Medical records and immunization cards

Medical records and immunization cards contain dates of dose administrations which are useful in determining vaccination status. However, these data sources could underestimate coverage since some vaccinations may be undocumented, or the immunization card could be misplaced or lost at the time of data collection for a study. For example, vaccinations provided by a private provider or non-governmental organization may not be documented in the medical records, and would therefore cause an underestimate of coverage(59). Capturing private

data can be difficult when using public health medical records, and studies have shown this can heavily influence vaccination coverage estimates(64). For example, Arizona public provider sites administered 61% of influenza doses compared to 39% administered by private sites. In contrast, Michigan public provider sites administered 26% of doses and private sites administered 74% of influenza doses(64). These examples demonstrate the need for considering both public and private vaccine administrations or combining documented data with parental recall of immunizations to capture undocumented vaccines and vaccines administered by both sectors.

Surveys

Household surveys that rely primarily on parental recall and immunization cards are often used to collect vaccination data. The accuracy of parental recall of vaccination events is not clear in the literature. Some studies report that agreement between parental recall and provider records is high for single dose vaccines, but parents often underestimate coverage for multiple doses of vaccines(65, 66). Other studies found that maternal recall can result in overestimates of vaccination coverage(66, 67). One study investigated the validity of maternal recall among 1,171 mothers in Costa Rica by comparing

maternal recall with data from vaccination cards(66). The authors found a negative correlation between recall error and number of doses, implying that mothers tend to overestimate the number of vaccinations for under-vaccinated children, and underestimate the number of vaccinations for over-vaccinated children(66). This is a concerning finding since children who are most at risk for acquiring a vaccine preventable disease are perhaps less likely to be vaccinated since their mothers may overestimate the number of doses received. Several others report that parental recall is inadequate for determining a child's vaccination status and can be a source of recall bias(68-71). In contrast, some researchers maintain that using maternal recall for a child's vaccination status, despite its limitations, substantially improves coverage estimates(72).

The National Immunization Survey is the primary method for assessing vaccination coverage in the United States and collects data from both parental recall and provider records(73). It annually collects 400 to 500 completed household interviews in all 50 states and 28 additional large urban areas using random digit dialling. These data are later verified by provider immunization records(73). The National Immunization Survey is considered the gold standard for assessing vaccination coverage

among children in the United States. However, it cannot provide estimates in a timely manner (during or directly after the influenza season) or anything below the county level(48). Other studies opt to use only medical records(62) or only parent responses without record verification(74).

Some surveys can include school surveys and birth certificate follow-back surveys(73). School surveys use school immunization records to determine vaccination coverage, but school records may vary in completeness and quality since some schools require health care providers to update immunization cards while others permit parents to complete the cards. This can produce an inaccurate immunization history(73). The vaccination status of home-schooled children is not measured and the direction of this effect on a coverage estimate is not clear. Birth certificate follow-back surveys require considerable effort as they involve tracking children and collecting their immunization history after selecting them based on their date of birth. This method does not include children who moved into the area after birth(73).

Registries, immunization information systems and insurance/billing databases

Immunization Information Systems (IIS) contain computerized records of vaccine administrations that may have been collected from health care providers or billing systems. Some researchers believe these systems can be used for timely monitoring of coverage while also tracking multiple doses(61). It is also possible for these systems to capture both public and private data(61). In contrast to data collected by the National Immunization Survey, immunization information system data allow for county-level vaccination estimates soon after the influenza season(48). A limitation is that providers might not routinely report the administration of influenza vaccine doses, which would cause an underestimate in the vaccination coverage(48).

Insurance registries or billing databases are other sources of numerator data for vaccination coverage. In some areas, registries are known to capture more than 90% of vaccine administrations since providers are mandated to report to the registry(75), however in other areas participation in registries and completeness of immunization histories may vary(73). A limitation of using an insurance registry or billing data is that a child could migrate in or out of the registry catchment area

during the observation period or could change insurance providers, which could cause incomplete records and inaccurate population counts(75). Salmon and colleagues advocate for the use of immunization registries since they can be used to generate real-time coverage estimates for vaccination coverage estimates among children. However, enrolment in registries must be very high to report valid data (nearly all or a representative sample of children in the catchment area must have their complete immunization history included)(73).

In 2002, Alberta implemented a provincial immunization and adverse event registry known as ImmARI (Immunization and Adverse Reaction to Immunization). The purpose of the registry is to have one repository for immunizations and adverse events in Alberta. Through this registry, the province also hopes to reduce the number of unnecessary administrations of vaccine while maintaining complete immunization records for all Alberta residents. The ImmARI registry data does not have data on all years in the study period for this research and is still collecting data from 2006 and later.

Denominator data source

Denominator data can be challenging to acquire and the appropriateness of the source may vary depending on the objectives of the research. One study acknowledged the challenge of matching numerator and denominator data, and emphasized that even if the denominators are not exact matches for numerators, comparisons of vaccine coverage from year to year could still offer information on trends in vaccine coverage(76).

For this research, an ideal data source offers accurate and complete population counts for children less than nine years of age in the Calgary Health Region while permitting exploration of rural and urban residences. Exploration of rural and urban variance is of interest because the changes to the CHR boundaries in 2003 added rural areas into the region. The U.S. Department of Agriculture produced a 1973 report on health service problems in rural areas of the U.S. and it explicitly stated that rural and urban people have unequal access to health services(77). In Canada, it is known that rural populations are less healthy, more likely to be of lower socioeconomic status as well as to have to travel farther to health services than urban populations(78, 79). This emphasizes the importance of measuring health service

utilization among these two distinct areas. The definition of "rural" or "urban" varies in the literature. Statistics Canada defines an urban area as an area with a population of at least 1,000 persons and a population density of at least 400 persons per square kilometre. All other parts of Canada are considered rural (112). Other studies consider urban areas to be metropolitan cities with more than 100,000 residents (109). This study uses a definition for urban and rural that is consistent with that used by CHR management for administrative purposes. This will be discussed further in the methods section.

Four potential denominator data sources were identified for generating vaccination coverage. They are: the CHR electronic patient record database known as MediPatient™ and PHANTIM™; the Alberta Health Care Insurance Plan (AHCIP) registry; the Census of Canada; and the City of Calgary census.

MediPatient™ is the electronic patient record system that collects administrative data for surveillance purposes in the Calgary Health Region. PHANTIM™ is a specialized MediPatient™ application that collects public health information for the city of Calgary, the city of Airdrie and the town of Cochrane (the boundaries of the Calgary Health

Region pre-2003). Other areas are also included in the general MediPatient™ system after expanding the Calgary Health Region in 2003 to include: Canmore, Banff, Didsbury, Strathmore, Vulcan, Nanton, Okotoks, and Black Diamond (the boundaries of the CHR post-2003) (Appendix A2). Together, MediPatient™ and PHANTIM™ record immunization information for all individuals accessing public health services in the CHR. All children who were born in a hospital, have registered at a school or accessed any public health service in the CHR are entered into the MediPatient™/PHANTIM™ database. Therefore, this database has a relatively complete listing of all the children in the CHR, regardless of vaccination status. MediPatient™ and PHANTIM™ should have files on children who have received all, some, or none of their childhood vaccinations, in both "rural" and "urban" areas of the CHR.

Individual vaccination records include the dates and dosage of each vaccination event for all antigens. Influenza vaccinations began to be recorded in 2004 for children less than nine years old.

It is possible for a child in the CHR to receive an influenza vaccine in three ways: from a public health nurse, from a physician, or in a private

facility. Table 2 illustrates how this information is recorded or not recorded into MediPatient™/PHANTIM™.

Table 2. MediPatient/PHANTIM™ vaccination surveillance, by administrator and type of vaccine

Administrator of vaccine	Publicly or privately funded vaccine	Captured in MediPatient™ / PHANTIM™ (Yes/No)	Information tracking details
	Public	Yes	Whether or not a vaccine is publicly funded or paid for, patient information may be immediately uploaded into the MediPatient™ /PHANTIM™ database using an onsite computer. A vaccination form is also filled out by hand by the nurse and mailed to the CHR for entry into MediPatient™ /PHANTIM™ (Appendix A3).
	Private	Yes	

Table 2. MediPatient/PHANTIM™ vaccination surveillance, by administrator and type of vaccine (continued)

Physician	Public	Yes	The physician is required to submit a vaccination form to the Calgary Health Region (the same form as that used by Public Health Nurses) if a publicly funded vaccine was administered to a child less than nine years old.
	Private	Yes	If a parent paid for a vaccine for a child under nine years of age, the physician is requested to send the appropriate documentation to the CHR. However, this is not actively monitored by the CHR and sometimes physicians may not fill out the paperwork to include the vaccination data in MediPatient™/PHANTIM™.

Table 2. MediPatient/PHANTIM™ vaccination surveillance, by administrator and type of vaccine (continued)

Private vendor	Public	No	Private vendors do not sell publicly funded vaccines.
	Private	No	If a child receives a vaccine through a private facility, such as a pharmacy, no paperwork is required by the CHR. Thus the child's vaccination status will not be updated in MediPatient™/PHANTIM™.
Out-of-City/ Province	Other	No	Not captured in MediPatient™/PHANTIM™.

However, whenever a child accesses a public health service for a regular clinic visit, the public health nurse will often ask at the time of the visit if the parents would like to have the child vaccinated for influenza. In this case, if the child has already been vaccinated, MediPatient™/PHANTIM™ can be updated by entering historical data.

The MediPatient™/PHANTIM™ population is expected to include most children in the CHR but may not account for children immigrating out of the region, therefore population counts are expected to be overestimated. Postal codes are used to assign each child to a geographic area.

A second denominator source for vaccination coverage estimates in Alberta is the Alberta Health Care Insurance Plan (AHCIP) registry. In Alberta, all permanent residents are required to opt out or register themselves and their dependents to the AHCIP. This database captures approximately 99% of Alberta residents excluding members of the Armed Forces, Royal Canadian Mounted Police, people in federal penitentiaries and those from other provinces during their first three months in Alberta. The advantage of using this registry for denominator data is that all registrants' dates of birth are recorded

and there are quality assurance measures in place to account for the migration of people into or out of the province. There will inevitably be some Alberta residents who remain unregistered or who opt out from the insurance plan and therefore would not be represented in the population count. The number of uninsured Albertans is estimated to be less than 0.5% of the Alberta population(80). The registrant's postal code is used for geographic placement in the province(80).

The Census of Canada is a third source for population counts. It is conducted once every five years (the most recent year was 2006) and includes every Canadian citizen including native-born and naturalized Canadians, immigrants and non-permanent residents and their dependents. To participate, most Canadians complete a census form and submit it by mail. Online submissions are also accepted as of 2006(81). The physical address of Canadians is used for geographic placement in the country, which is more accurate than using a postal code as done for MediPatient™/PHANTIM™ and the AHCIP registry. Population projections need to be used for denominators corresponding to the years in between census years. This may not be a good measure of the population in a rapidly changing area like the Calgary Health Region.

The final denominator source to be discussed is the City of Calgary census. The civic census is an annual count of dwellings and residents in the City of Calgary conducted through door-to-door physical collection of data. Individual age data for children is not collected and the counts do not include people living in rural areas of the CHR.

All four data sources have the potential to represent children eligible for vaccine in the CHR. The appropriateness of using any one of these data sources is considered in the methods section.

Role of socioeconomic status on vaccination coverage

Socioeconomic status (SES) is a multidimensional construct that is often measured in epidemiological studies using indicators such as: education, income, occupation, employment status, social class, and living conditions, among others(82, 83). Canada's publicly funded health care system should in theory provide all citizens with equitable access to health services, independent of SES. However, SES continues to influence the use of publicly funded health services in Canada(84, 85), including the decision to receive immunization.

Several recent studies demonstrated that low SES is associated with lower vaccination rates. A cross-sectional study examining SES (measured by social class standing) and the uptake of preventive medical services among 3,652 British women found that women from lower social positions were found to be less likely to have recent influenza vaccinations(86). Another cross-sectional study examining parental beliefs and varicella vaccination coverage among Taiwanese children found that 94% of caregivers would have immunized their children against varicella if the vaccine was free or subsidized. In that same study, it was found that caregivers living in the city, parents with a relatively high level of education and income, and families with fewer children were significantly more willing to have their children immunized(87). Finally, among children less than two years of age in Calgary, 41% of children who were eligible for a publicly funded vaccine were vaccinated compared to 16% of ineligible children(88). Since ineligible children were required to pay for an influenza vaccine in Alberta at this time, this suggests that out-of-pocket costs for immunizations could be a barrier to obtaining immunizations.

As mentioned earlier, SES can be and is measured using different indicators, which can in turn affect the analysis of health-related

inequalities(82, 83, 89). Careful consideration must therefore be put into defining SES and interpreting study findings. Nonetheless, the evidence suggests that social status and financial barriers can influence rates of vaccination for influenza and other preventable diseases, and therefore should be considered when estimating vaccination coverage or modifying vaccination strategies.

Summary

The literature indicates that young children are at increased risk of influenza-related morbidity and play an important role in transmitting the disease in a community. For these reasons, children should be a priority group in vaccination strategies. Estimating vaccination coverage can be challenging as many factors can influence an estimate. It is best to use a consistent and nationally approved definition for "vaccinated" in order to reflect the level of protection from influenza in a community, a combination of sources for numerator data, and denominator data that is representative of the population and can permit exploration of trends in child age and place of residence. Socioeconomic status should also be considered in vaccination studies, especially in provinces that don't have a universal publicly funded vaccination policy.

This research aims to examine influenza vaccination events and estimate vaccination coverage by attributes of person, place and time among children six months to less than nine years of age in the CHR over four influenza seasons. Consistent definitions are used to allow for comparisons over time. It also aims to explore for an association between income and getting vaccinated. The findings from this study will inform regional vaccination policies and strategies in the CHR. The findings may also identify strengths and limitations in the current CHR surveillance system and electronic medical record database.

CHAPTER THREE: METHODS

Introduction

This chapter addresses the study design, study population and study period. The source of data and method of collecting data are described. Exclusion criteria are outlined, as are the procedures for cleaning data, imputing missing data and analyzing data to meet the objectives. All analyses were carried out using STATA Intercooled 10.0 statistical software(90).

Study design

This study used a retrospective observational design in which administrative data are used to describe influenza vaccination events and to estimate vaccination coverage among children in the CHR over four influenza seasons.

For the purpose of this research, an "influenza season" runs from October 1 of the calendar year to September 30 of the subsequent calendar year. The study's "influenza vaccination season" runs from October 1 to April 30 every year, which is the period in which influenza is assumed to be circulating in the northern hemisphere(45).

Vaccination data for all children six months of age to less than nine years of age were retrieved from the CHR's immunization information system MediPatient™/PHANTIM™ for the 2004-05, 2005-06, 2006-07, and 2007-08 influenza seasons. The data were extracted as separate files for each season by CHR employees who assigned a unique identifier to each child and removed all identifying information before releasing the data to the researcher. The unique identifiers allowed deterministic linkage of data files across influenza seasons.

Study population (Inclusion criteria)

The study population comprised children who were eligible for influenza vaccination between October 1, 2004 and September 30, 2008 inclusive. Accordingly, data for children who were six months to less than nine years of age for each influenza season between October 1, 2004 and September 30, 2008 inclusive were extracted from the CHR MediPatient™/PHANTIM™ immunization information system. This resulted in four data files representing four cohorts of children in the MediPatient™/PHANTIM™ information system.

As shown in Table 3, Cohort 1 included all children who were born between October 2, 1995 and March 30, 2005 for whom a record

existed in the MediPatient™/PHANTIM™ system. This resulted in a data file of all children who were six months to less than nine years of age for the influenza season that started on October 1, 2004 and ended on September 30, 2005. Cohorts 2-4 comprised children born October 2, 1996-March 30, 2006; October 2, 1997-March 30, 2007; and October 2, 1998-March 30, 2008, respectively.

Table 3. Influenza season and cohort definitions

Influenza Season	Dates of Influenza Season	Range of dates of birth for children ≥6 months and <9 years of age
#1: 2004-05	October 1, 2004 – September 30, 2005	October 2, 1995 – March 30, 2005
#2: 2005-06	October 1, 2005 – September 30, 2006	October 2, 1996 – March 30, 2006
#3: 2006-07	October 1, 2006 – September 30, 2007	October 2, 1997 – March 30, 2007
#4: 2007-08	October 1, 2007 – September 30, 2008	October 2, 1998 – March 30, 2008

Study period

The CHR began to consistently record influenza vaccination information for children under the age of nine years in 2004. This study used all the available data for complete seasons at the time of data extraction, which included the 2004-05, 2005-06, 2006-07 and 2007-08 influenza seasons.

Data source

MediPatient™ is the electronic patient record system used by the CHR to collect administrative data for surveillance purposes. The Primary Health Activity Network & Timely Information Management system (PHANTIM™) is a specialized MediPatient™ application into which public health data are entered specifically for the pre-2003 boundaries of the Calgary Health Region. The pre-2003 boundaries comprise the city of Calgary, the city of Airdrie and the town of Cochrane. The CHR expanded in 2003 to include other areas such as Canmore, Banff, Didsbury, Strathmore, Vulcan, Nanton, Okotoks, and Black Diamond. These areas are included in the general MediPatient™ system. A map of the CHR as of December 2003 is in the Appendix (Appendix A2).

Together, MediPatient™ and PHANTIM™ record immunization information for all individuals accessing public health services in the CHR.

Children are registered into the MediPatient™/PHANTIM™ database when they are born in a hospital, register at a school or when they access any public health service in the CHR.

Influenza vaccination event data for children are recorded into the MediPatient™/PHANTIM™ database in two ways (Table 2 in Background Section):

1. If an influenza vaccine is administered by a public health nurse, the nurse uploads the patient information into the MediPatient™/PHANTIM™ database using an on-site computer (if accessible) and a vaccination form is also filled out by hand and mailed to the CHR for entry into MediPatient™/PHANTIM™ (Appendix A3).
2. If the vaccine is administered by a physician, the physician must submit the same vaccination form to the CHR as that used by public health nurses if a child younger than nine years of age is vaccinated.

Data for privately funded vaccinations, such as when a parent takes a child to a pharmacy or an influenza vaccination clinic organized by his or her place of work, and data for vaccinations that occurred outside of the CHR are not captured by MediPatient™/PHANTIM™ unless provided by the parent as "historical data."

When a vaccination form is received at the CHR, a CHR employee searches the MediPatient™/PHANTIM™ database for the child's Alberta Public Health Number to retrieve that child's record. If a record of the child is found and the current address matches that from previous records, a new vaccination event is recorded for that client. Otherwise the child's address is first updated or that child is registered into MediPatient™/PHANTIM™ as a new client, and the vaccination event is recorded. The process of data entry is further outlined in the Appendix (Appendix A5) including a verification process conducted by a second CHR employee. Individual vaccination records include the date and dosage of each vaccination event for all antigens.

MediPatient™ and PHANTIM™ thus have files on children who received all, some, or none of their childhood vaccinations, in both "rural" and "urban" areas of the CHR. The city of Calgary is considered the "urban"

area of the CHR, while all other communities including Cochrane and Airdrie are considered "rural" areas of the CHR. These definitions are consistent with those used by CHR management.

Data cleaning

Data cleaning involved range checks, consistency checks and imputing missing data.

The data were extracted as separate files for each season by CHR employees. Range checks on dates of birth and vaccinations determined if the correct cohorts were extracted for each of the four seasons as outlined in Table 3 above. If an incorrect range was generated, the researcher made a request to the CHR data analyst to modify his extraction methodology so that the next round of data would have the correct date ranges. Six rounds of data extraction took place between June 18 and November 10, 2009, at which point the researcher was provided with all the data variables required and no range errors.

Additional consistency checks led to further cleaning of the data. The number of social districts, census tracts and dissemination areas were

expected to be similar across all four seasons. Provider and facility information were expected to match in some cases, such as a physician is expected to administer a vaccine in a physician's office not a mass venue site. Inconsistencies were rare, individually investigated, and, if required, recoded as missing data. Some reasons for vaccination were obvious errors, such as the child was "a health care worker" or "a pregnant woman" in which case the reason was recoded as "missing."

Missing data were imputed as much as possible. If the provider of the vaccine was documented but not the facility, it was possible to impute these data in some cases. For example, if a vaccine was administered by a physician but the facility in which the vaccine was administered was "missing", then the missing facility data field was replaced with "physician's office". Data were also imputed for records with a missing reason for vaccination. It is expected that the reason for vaccination among children younger than two years of age was on the basis of age, even though there were no clear instructions for reason coding during the study period (Kirkwood,M. 2010 Feb 11).

Data file organization

Cohort data files contained a child's unique identifier, sex, date of birth, date of death (if applicable) and area of residence. Geographic areas such as dissemination area, census tract, social district and urban or rural residence were assigned by CHR employees based on the child's postal code current at the time of data extraction in January 2009. Every entry in the cohort files represented a unique child.

Influenza vaccination data for each season were merged with cohort data to produce four vaccinated cohorts of children (Appendix A6). Influenza vaccination data files contained the date, provider, facility and reason for vaccine administration, and whether or not the data are historical. A single child could have several records of influenza vaccination in a single year, which would result in multiple vaccination events for the same unique identifier.

In addition, reasons for children not being vaccinated ("non-vaccinations") when there was an opportunity to vaccinate for influenza or any pertussis-containing vaccine were also extracted by CHR employees and provided to the researcher as a separate data file. Data linkage was possible through unique identifiers.

Non-vaccinations for pertussis were used to compare with non-vaccinations for influenza because historically, pertussis vaccines were frequently refused due to parent concerns about adverse events. Furthermore, children are recommended to have four doses of pertussis by the age of 18 months and therefore have several opportunities to be vaccinated for it(91). A child who did not receive vaccines for both pertussis and influenza may indicate a family with a belief that immunizations are unsafe or ineffective.

Exclusion criteria

Objective 1: Describing vaccination events

The federal government is directly responsible for providing health services to First Nations and Inuit people living on reserve in Canada(42). Most children living on a reserve in the CHR receive vaccinations through the federal government and not through health services offered by the CHR. Data on children living on reserve were excluded from all analyses because it was known that these data would be incomplete. A variable "living in region on reserve" is used in the MediPatient™ system to identify these children, however the CHR does not use a systematic method for identifying children who live on reserve. Nurses from rural areas in the CHR determine if a child lives

on reserve through investigation and becoming familiar with members of the community.

In addition, duplicate vaccination entries were identified by date of administration and excluded.

Objective 2: Estimating vaccination coverage

Some children died during an influenza season. Since the chance to receive a second dose of vaccine was not possible for some children, children who died were removed from the analyses. Vaccinations that occurred after April 30 of each year are considered outside of the study's defined influenza vaccination season and were therefore removed from the estimations of vaccination coverage. As a result, children who received their first or only dose of influenza vaccine after April 30 were excluded. Finally, children who were nine years of age or older or who were known to be living on reserve were removed from all analyses.

Objective 3: Exploring for an association between income and getting vaccinated

The same exclusion criteria for Objective 2 apply to Objective 3.

Data analysis

Objective 1: Describing vaccination events

A vaccination event refers to a vaccine administration that is recorded in the MediPatient™/PHANTIM™ system. Vaccination events for each child were organized into four influenza seasons: 2004-05, 2005-06, 2006-07 and 2007-08.

For each influenza season, the proportion of children who received one, two or more doses of vaccine were calculated in three separate analyses. The numerator for each analysis was the count of children who received one, two or three doses of vaccine. The denominator for each analysis was the total number of vaccinated children recorded in the database for each season.

Vaccine providers, facilities and reasons were categorized to generate proportions. The proportion of vaccines administered by a public health nurse or physician were calculated using counts of recorded vaccination events administered by each type of professional as numerators and the total number of recorded vaccination events in the database for each season as the denominator. Records for children with missing provider data were not included in the denominator.

Similarly, the proportion of vaccination events that occurred at a community health centre, a physician's office, an influenza or mass vaccination clinic, and those that occurred elsewhere (private facility, or another health region or province) were calculated. "Community health centres," also referred to as "public health offices," are permanent sites in the CHR where people can access health information and primary health care, including but not limited to vaccinations. "Influenza clinics" are held at these community health centres but nurses are stationed there solely for administering influenza vaccine at designated times during the influenza vaccination season. "Mass venues" are high-volume public sites where nurses are stationed to administer influenza vaccines to CHR residents at designated times during the influenza vaccination season. Mass venues may include churches, malls and grocery stores. In these analyses, the numerators were total counts of vaccination events at each facility and denominators were the total number of vaccination events recorded in the database for each season. Records for children with missing facility data were not included in the denominator.

Reasons for vaccination were explored by calculating proportions of children who were vaccinated on the basis of age, chronic health

condition, being a member of a household that includes at least one person who is at high risk of influenza-related complications or requesting to pay for a vaccine. Children who are less than two years of age, those who have a chronic health condition or those who are living with people at high risk of influenza-related complications are eligible for a publicly funded vaccine. Parents whose children do not qualify for a publicly funded vaccine are required to pay for the vaccine. For these analyses, the numerators were counts of each reason and the denominator was the total number of vaccination events recorded in the database for each season. Records for children with missing reason data were not included in the denominator.

Reasons for children not being vaccinated ("non-vaccinations") when there was an opportunity to vaccinate for influenza or any pertussis-containing vaccine were also explored and proportions were calculated for each reason. The data were first organized by influenza season. Reasons entered into the data file were categorized by theme including parent refusal, vaccine unavailability, deferral, and child illness. Reasons for pertussis non-vaccinations included parent refusal, vaccine unavailability, deferral, child illness, consent not obtained, patient no show, absence from school and insufficient vaccination history. For

these analyses, numerators were counts of each reason for each type of vaccine, and the denominator was the total number of non-vaccination events for each type of vaccine that were recorded in the database for each season.

Additionally, the researcher explored the number of children whose parents "refused" both pertussis and influenza vaccines, compared to children whose parents "refused" just the influenza vaccine. Children whose parents "refused" both pertussis and influenza vaccination may indicate a family who is opposed to vaccinations generally. For these analyses, numerators were the number of children who were not vaccinated for both pertussis and influenza due to parent refusal. Denominators were the number of children with non-vaccinations for influenza each year.

Objective 2: Estimating vaccination coverage

Age-sex specific counts of adequately and partially vaccinated children from the MediPatient™/PHANTIM™ database were used for numerators. Denominators were counts of all children of the corresponding age group who were eligible for an influenza vaccine. As there is no single ideal source of denominator data, four different

sources were considered for obtaining the denominator counts including the MediPatient™/PHANTIM™ database (2004-2008), the Alberta Healthcare Insurance Plan (AHCIP) Registry (2004-2008), the Census of Canada (2006), and the City of Calgary census (2004-2008).

The civic census for the City of Calgary does not have individual age data for children and does not include counts from the rural areas of the CHR. Population counts for children younger than nine years of age in the CHR were therefore not possible to obtain. For these reasons, the civic census is considered an inappropriate denominator source for this research.

The MediPatient™/PHANTIM™ source is expected to have the highest population counts since the CHR does not have a systematic way of removing people from the database if patients move out of the health region. This is expected to cause overestimates of the population in all age groups. In contrast, the AHCIP registry requires all Alberta residents to register for health insurance and has frequent internal audits that remove people from the registry if they are no longer living in the province.

A recent AHW report compared population counts from the AHCIP registry to those of the federal census and found higher counts in the AHCIP registry for women and young children. The authors hypothesized that the absence of young children and their mothers in the health insurance database is unlikely but perhaps there is less motivation for these groups to self-enumerate in the census(80). Another disadvantage associated with the use of census data is that census population projections would be required for population counts in inter-censal years, which may be difficult to interpret in areas of high migration such as Alberta(80).

In view of the above, the AHCIP registry was deemed the most appropriate denominator source for age-, sex-, and geography-specific influenza vaccination coverage in the Calgary Health Region for all four seasons in this study. Alberta Health and Wellness provided the AHCIP data to the researcher. The youngest age category in the AHCIP data was zero to less than one year of age. The population count for this age group was divided in half to represent the population of children aged six months to less than one year of age.

Estimates of adequate influenza vaccination coverage were generated by rural or urban area of residence, for each of 19 social districts and each of the 193 census tracts in the CHR. Social districts are geographic areas made by the Calgary Data Consortium comprising members from the City of Calgary, the Calgary Board of Education, United Way of Calgary, and the CHR. The construction of social districts required that boundaries did not cross neighbourhood, natural or census tract boundaries. Social district populations are contiguous, cover the entire CHR and are made to represent no less than 40,000 people. Census tracts are relatively small areas with a population of 2,500 to 8,000 people. They are only located in the urban part of the CHR(92).

Confidence intervals were calculated for each coverage estimate at a 95% confidence level, setting alpha levels at 5%. A clinically significant difference refers to a 5% difference in coverage according to CHR management. Small declines that steadily occur every year also require attention (MacDonald, J. 2010 Apr 29). A statistically significant difference is identified if confidence intervals do not overlap.

Objective 3: Exploring for an association between income and getting vaccinated

The 2006 MHI census data were obtained from the MADGIC service area at the University of Calgary. This provided the researcher with a median household income for every dissemination area in the CHR.

Vaccination coverage was calculated for each dissemination area and plotted against median household income for each dissemination area. Linear regression determined if a predictive linear relationship exists between level of income and proportion vaccinated within each dissemination area.

Before running the regression, the assumptions for linear regression were considered. This included verifying that:

1. INDEPENDENCE: The observations are independent (accomplished by verifying that there is no more than one observation for each dissemination area);
2. LINEARITY: There is a linear relationship between x and y (accomplished by plotting residuals of the dependent variable against the independent variable);

3. NORMAL DISTRIBUTION: The residuals are normally distributed and have a mean of zero (accomplished by examining a histogram and the summary statistics for the residuals); and
4. HOMOSKEDASTICITY: The residuals have the same variability (constant variance) for all the fitted values of y (accomplished by conducting a Breusch-Pagan/Cook-Weisberg test for heteroskedasticity).

If any of the above assumptions are violated, the researcher considered transforming or stratifying the data and doing separate analyses for these modified data sets.

Linear regression analysis was conducted after verifying that all four assumptions were satisfied. A p-value is the probability that an observation occurred by random error(94, 95). If the output from the regression analysis returned a p-value that is less than 0.05, then one would conclude that there is an association between MHI and getting vaccinated and therefore the null hypothesis that no association exists is not an acceptable explanation for these data. In this case one would reject the null hypothesis. Alternatively, if the p-value generated from the linear regression is higher than 0.05, the null hypothesis cannot be

rejected as there is no evidence of an association between income and getting vaccinated (95). The R-squared (R^2) value will also help to determine the model's goodness of fit. A high value for R^2 indicates that the variation in the dependent variable is well explained by the model. Similarly, a low value indicates that the variation is not well explained by the model and therefore the proposed model is not suitable for this association.

Ethics and privacy

This study was approved by the Conjoint Health Research Ethics Board of the University of Calgary, on January 19, 2009 (Appendix A4). Ethical approval was extended until January 19, 2011.

Privacy risks related to the use of personal health information were mitigated as much as possible. Authorized Calgary Health Region employees compiled records for each child using personal health care numbers and then assigned a unique study ID to each child. They then stripped all identifying data fields from the data file before releasing it to the researchers. Unauthorized access to identifying information was mitigated by the use of computer-passwords and private work stations for the Calgary Health Region employees within

Calgary Health Region facilities. These employees are data custodians who are authorized to see personal health information. These practices of accessing, collecting, using and disclosing health information are regulated by the Health Information Act in Alberta. As a result, no identifying information was released to the researcher.

CHAPTER FOUR: RESULTS

Introduction

Study results are presented in this chapter and organized by objective. The final sample size for each objective is explained using the exclusion criteria for the study. Vaccination events and reasons for children not being vaccinated when there was an opportunity to vaccinate for influenza or any pertussis-containing vaccine are described.

For each influenza vaccination season, coverage estimates are determined for children considered adequately and partially vaccinated. The proportions of children adequately vaccinated are also determined for children of: urban and rural area of residence and for all social districts and census tracts in the CHR. Finally, the association between MHI and influenza vaccination in 2005-06 is explored.

Description of Population

As shown in Table 4, the majority of children in each of the four cohorts were male (52%), approximately three years of age (median range: 2-3 years) and lived in an urban area of the CHR (range: 82-88%). The number of doses administered each season is described in the next section.

Table 4. Age, sex and area of residence of children in the MediPatient/PHANTIM immunization information system, 2004-08

	2004-05 N=15,760	**2005-06** N=29,175	**2006-07** N=28,436	**2007-08** N=28,722
Age (Years)				
Mean (SD*)	3.5 (2.5)	3.4 (2.5)	3.4 (2.5)	3.2 (2.4)
Median	2.9	2.7	2.6	2.3
Range	0.2, 9.5	0.2, 9.6	0.2, 9.4	0.04, 9.7
Sex				
Male	51.6%	51.4%	51.3%	51.4%
Female	48.4%	48.6%	48.7%	48.6%
Area of Residence				
Urban	81.6%	87.9%	86.3%	86.4%
Rural	18.4%	12.1%	13.7%	13.6%

***SD = Standard Deviation**

Objective 1: Describing vaccination events

Sample

As shown in Figures 1 to 4, duplicate entries ranged from 486 to 1,000 during the four influenza seasons. Very few records were dropped due to the child living on reserve.

Figure 1. Derivation of sample for Objective 1, 2004-05

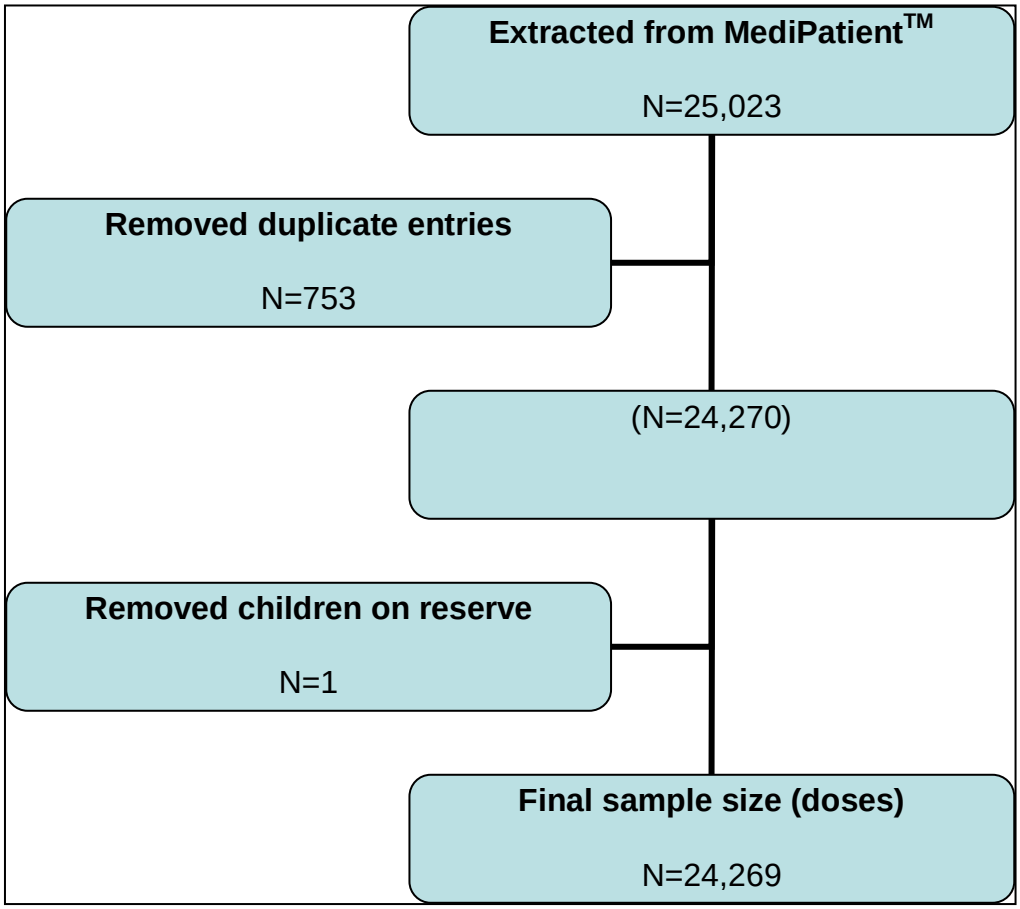


Figure 2. Derivation of sample for Objective 1, 2005-06

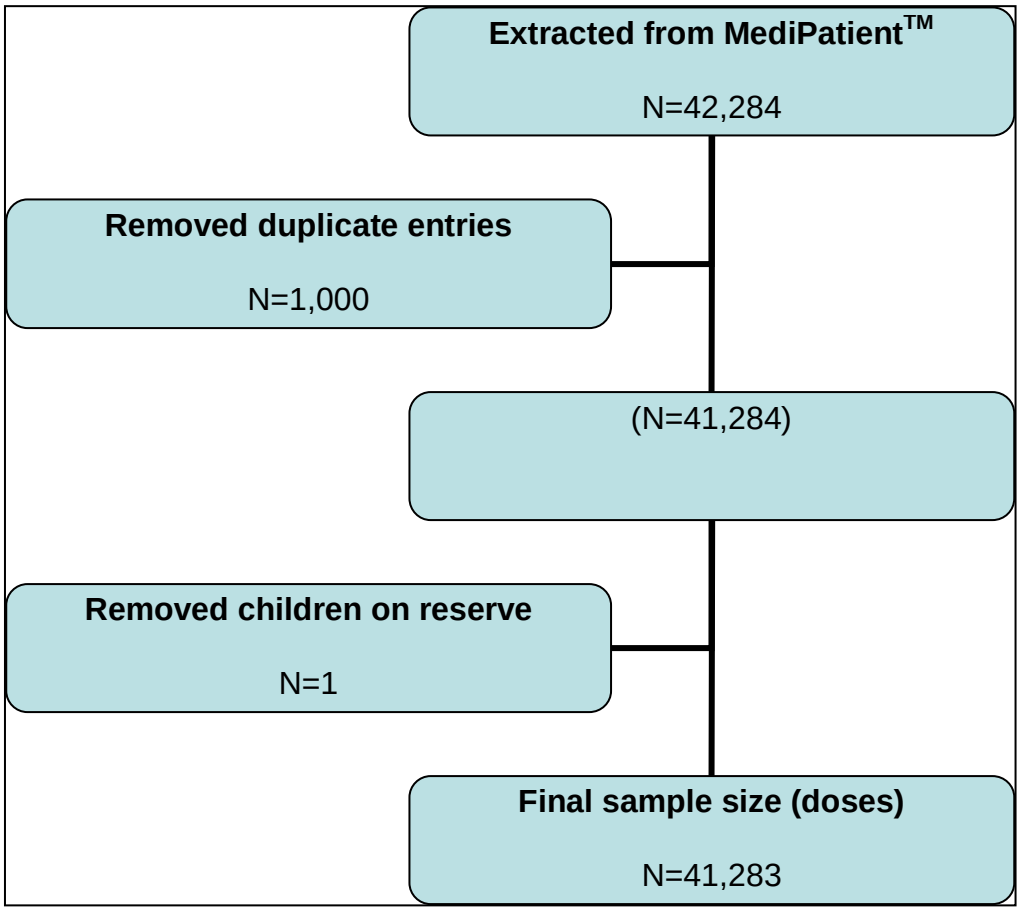


Figure 3. Derivation of sample for Objective 1, 2006-07

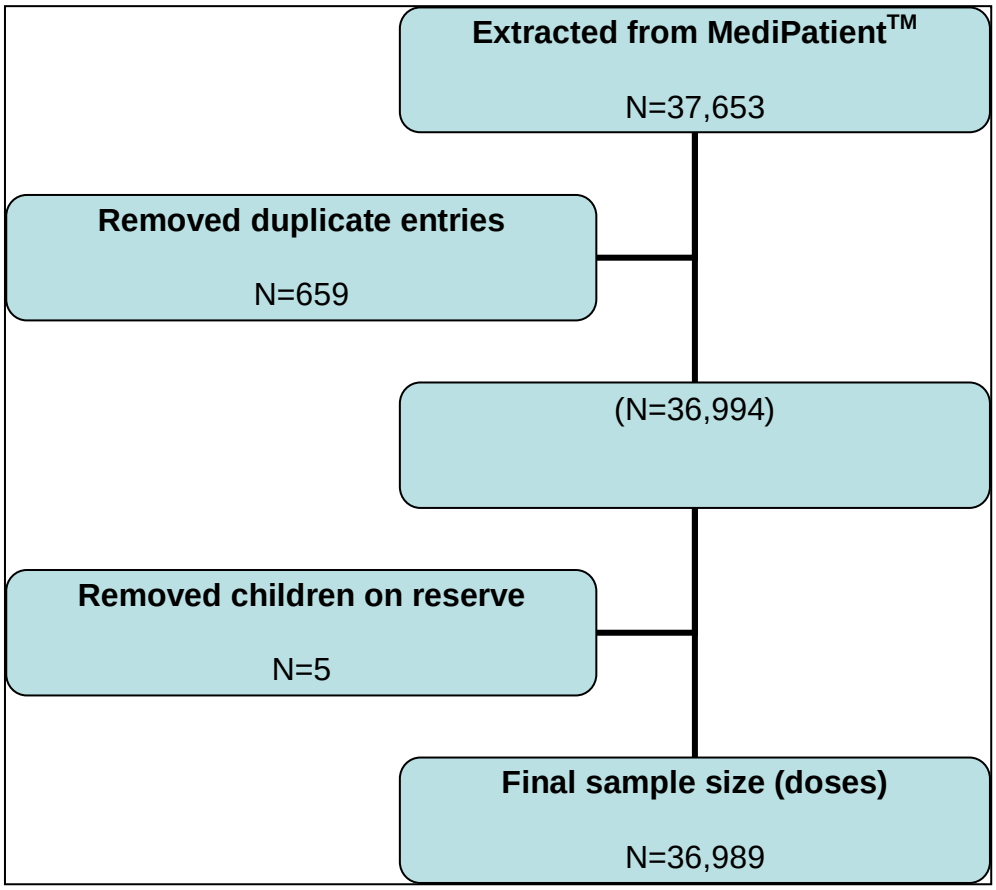
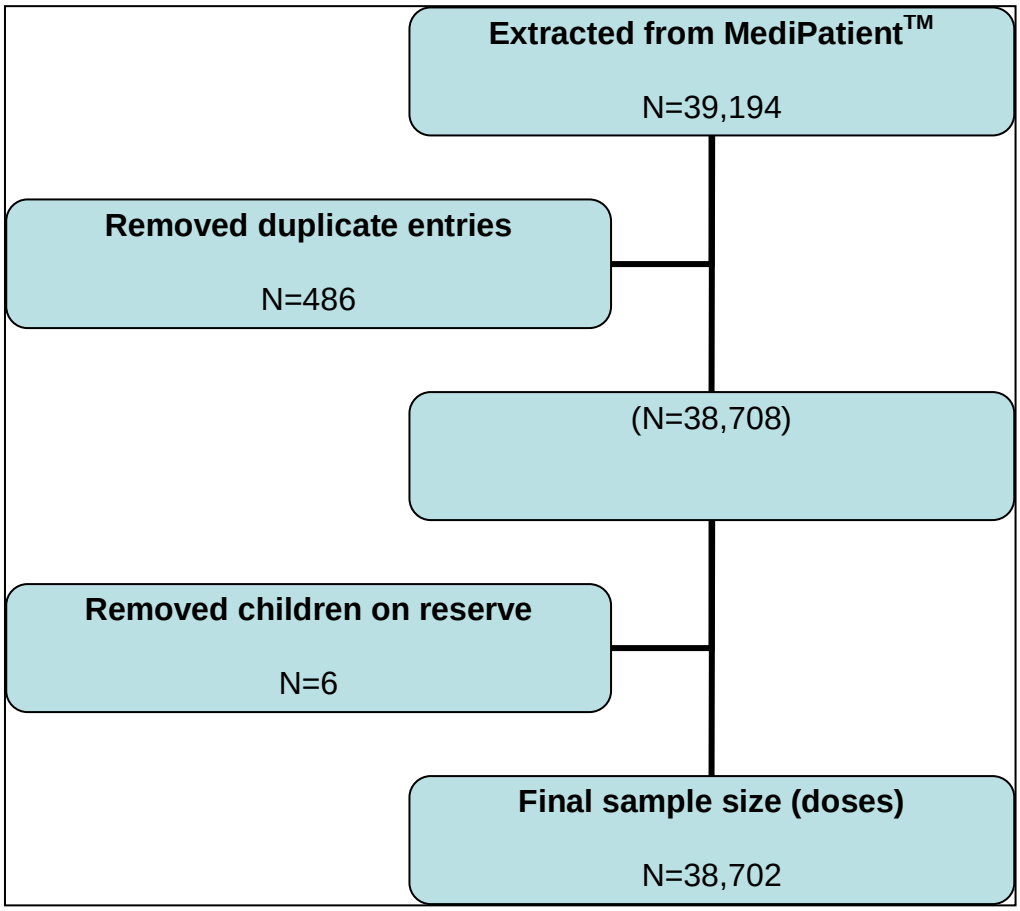


Figure 4. Derivation of sample for Objective 1, 2007-08



Number of doses of influenza vaccine

As shown in Table 5, the smallest number of vaccination events occurred in the first year of recording influenza data. The number of children vaccinated almost doubled between the 2004-05 and 2005-06 influenza seasons. The number of vaccinations declined in 2006-07 compared to the previous year, and increased slightly in 2007-08. More males than females were vaccinated in all years. In the first season, the majority of vaccinated children received two doses, but in the final three seasons the majority of vaccinated children received just one dose.

As shown in Figures 5 to 8, most influenza vaccine doses were administered between October 1 and April 1 of every year, and the large majority of doses were administered before January of each year. In 2006-07, the first doses of vaccine occurred in late October, approximately three weeks later than the other three seasons.

Table 5. Number of vaccination events and number of children in each vaccination season, 2004-08

		2004-05	2005-06	2006-07	2007-08
Number of Vaccination Events		24,269	41,283	36,989	38,702
Number of Children		**15,760**	**29,175**	**28,436**	**28,722**
		N (%)	N (%)	N (%)	N (%)
	Female	7,628 (48.4)	14,172 (48.6)	13,837 (48.7)	13,971 (48.6)
	Male	8,132 (51.2)	15,003 (51.4)	14,599 (51.3)	14,751 (51.4)
	1 dose	7,276 (46.2)	17,097 (58.6)	19,909 (70.0)	18,771 (65.4)
	2 doses	8,459 (53.7)	12,048 (41.3)	8,501 (29.9)	9,922 (34.5)
	3 doses	25 (0.2)	30 (0.1)	26 (0.1)	29 (0.1)

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Figure 5. Frequency of influenza vaccination events by month, 2004-05

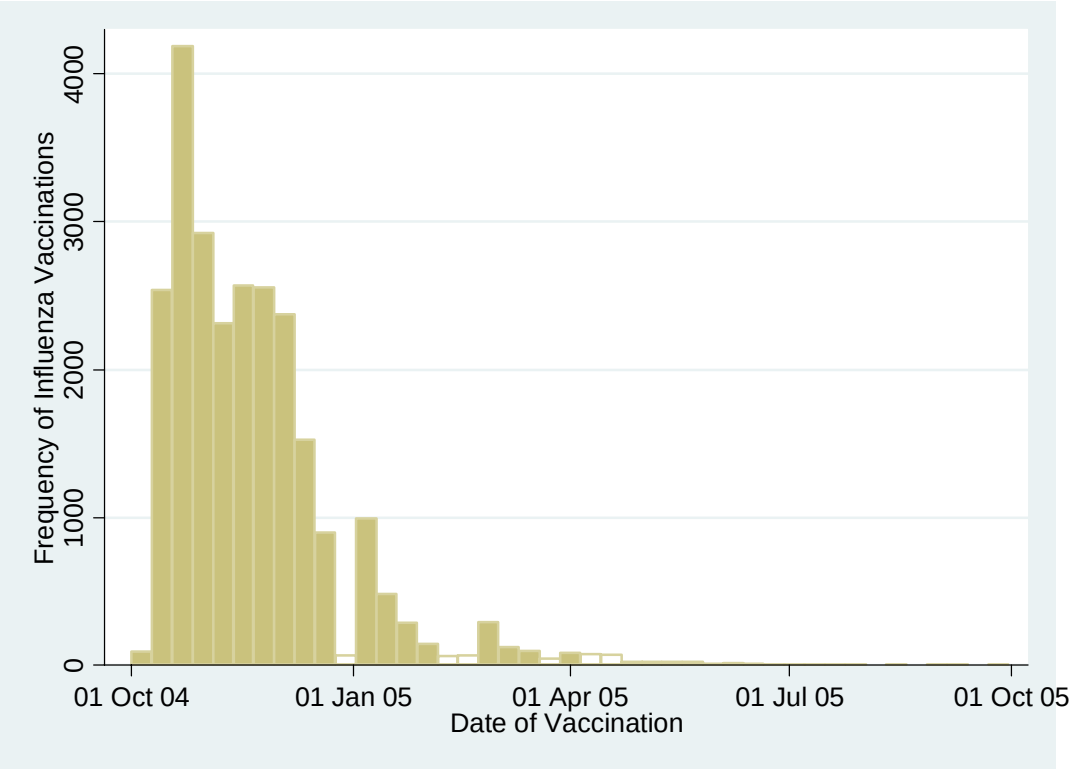


Figure 6. Frequency of influenza vaccination events by month, 2005-06

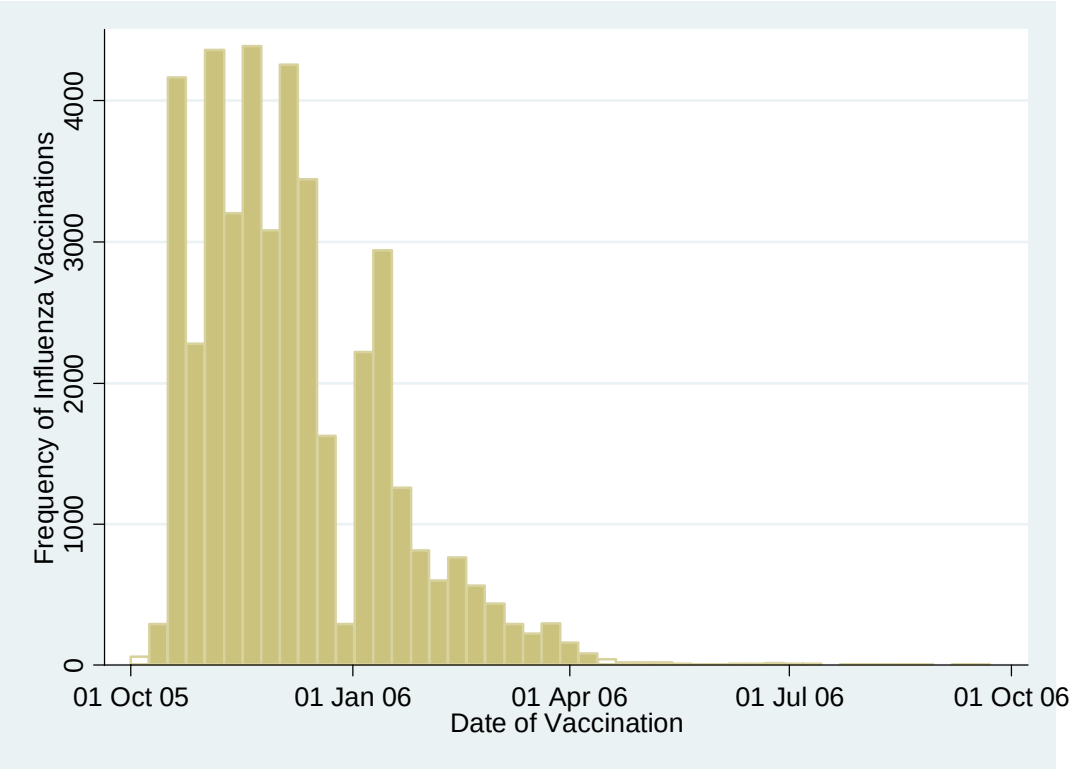


Figure 7. Frequency of influenza vaccination events by month, 2006-07

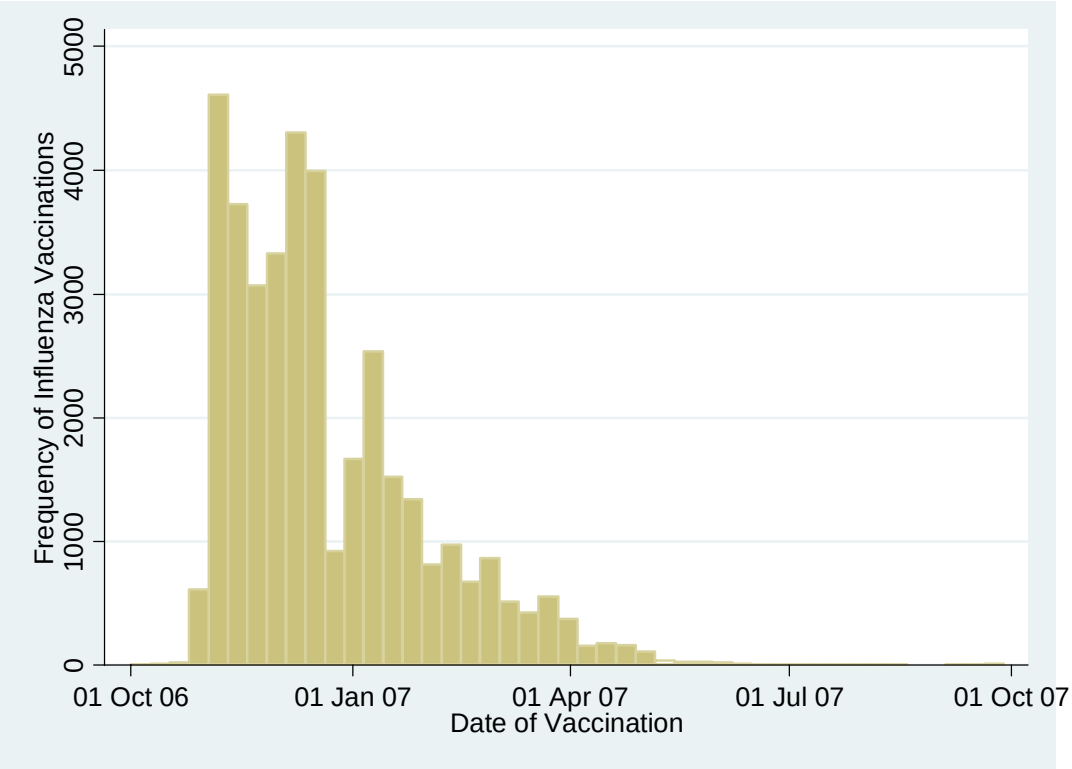
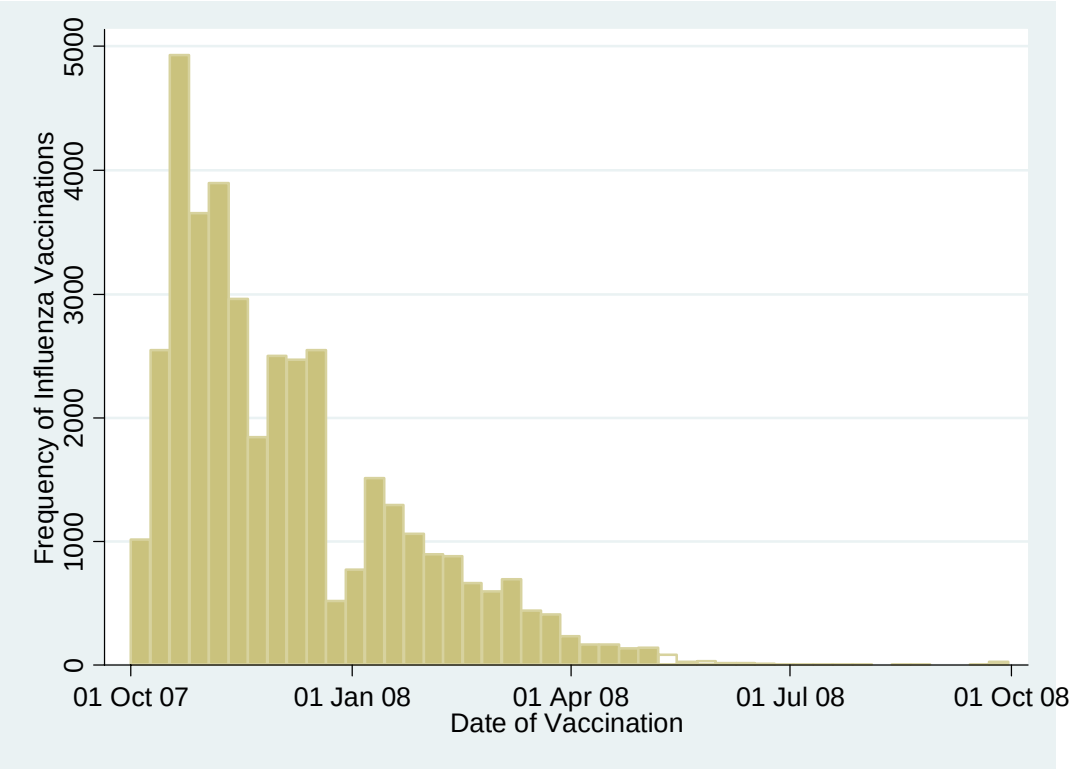


Figure 8. Frequency of influenza vaccination events by month, 2007-08



Vaccine provider

As shown in Table 6, public health nurses administered the majority of vaccinations across all seasons (99%). Very few vaccinations were administered by physicians (1%). "Other" providers administered less than 1% of vaccinations and included clinical educators, nursing students, and hospital staff.

Vaccine facility

For the first three influenza vaccination seasons, the majority of vaccinations occurred in an influenza clinic or mass venue, ranging from 78% in 2004-05 to 60% in 2006-07(Table 6). Over the four seasons examined, the proportion of vaccinations that occurred in the influenza clinics and mass venues declined and the proportion of vaccinations administered at community health centres increased. In 2007-08 just over half (58%) of vaccinations occurred in community health centres. A minority of vaccinations (1%) occurred in physician offices.

Vaccine reason

As shown in Table 6, approximately half of all vaccinations in each season were administered to a child on the basis of age, and these proportions increased with time (50 to 55%). Just over a third of

vaccinations (34 to 36%) were administered to children because they lived in the same household as another person at risk of influenza-related complications. A smaller proportion of vaccinations was delivered to children who had chronic health conditions (7 to 11%) or to children for whom parents purchased a vaccine (3 to 6%). Proportions for both these reasons declined with time.

Table 6. Frequencies of vaccine providers, facilities, and reasons for vaccination, by vaccination season, 2004-08

	2004-05	2005-06	2006-07	2007-08
Vaccine provider	**N=23,511[a]**	**N=40,613[b]**	**N=36,533[c]**	**N=38,265[d]**
Public Health Nurse	23,320 (99.2)	40,203 (99.0)	36,024 (98.6)	37,839 (98.9)
Physician	140 (0.6)	284 (0.7)	387 (1.1)	327 (0.9)
Other	62 (0.2)	126 (0.3)	122 (0.3)	99 (0.3)
Vaccination facility	**N=23,513[e]**	**N=40,615[f]**	**N=36,533[g]**	**N=38,258[h]**
Influenza Clinic / Mass Venue	18,386 (78.2)	28,510 (70.5)	21,744 (59.7)	15,016 (39.2)
Community Health Centre	4,698 (20.0)	11,554 (28.5)	13,978 (38.3)	22,352 (58.4)
Physician Office	142 (0.6)	284 (0.7)	390 (1.1)	329 (0.9)
Other	287 (1.2)	157 (0.4)	367 (1.0)	561 (1.5)

Table 6. Frequencies of vaccine providers, facilities, and reasons for vaccination, by vaccination season, 2004-08 (continued)

Reason for vaccination	N=23,841[i]	N=40,893[j]	N=36,738[k]	N=38,498[l]
6-23 months of age	11,811 (49.5)	20,803 (50.9)	19,694 (53.6)	21,038 (54.7)
Household contact of someone at high risk*	8,112 (34.0)	13,994 (34.2)	12,647 (34.4)	13,849 (36.0)
Chronic condition**	2,498 (10.5)	3,801 (9.3)	3,064 (8.3)	2,603 (6.8)
Vaccine was purchased	1,420 (6.0)	2,295 (5.6)	1,333 (3.6)	1,008 (2.6)

[a] 758 missing
[b] 670 missing
[c] 456 missing
[d] 437 missing
[e] 756 missing
[f] 668 missing
[g] 456 missing
[h] 444 missing
[I] 428 missing
[j] 390 missing
[k] 251 missing
[l] 204 missing

Table 6. Frequencies of vaccine providers, facilities, and reasons for vaccination, by vaccination season, 2004-08 (continued)

*People at high risk of complications from influenza infection include: children <24 months of age, people ≥ 65 years of age, people of any age who are residents of nursing homes/chronic care facilities, pregnant women, children <18 years of age with conditions treated for long periods with acetylsalicylic acid, and people of all ages with chronic conditions (outlined below) (3).

**Chronic conditions include: cardiac or pulmonary disorders (including bronchopulmonary dysplasia, cystic fibrosis and asthma), diabetes mellitus and other metabolic diseases, cancer, immunodeficiency, immunosuppression (due to underlying disease and/or therapy), renal disease, anemia or hemoglobinopathy, conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration, and children with conditions treated for long periods with acetylsalicylic acid (3).

Reasons for not getting vaccinated

Reasons for children not getting vaccinated with the influenza vaccine or any pertussis-containing vaccine were explored and divided into categories. A list of pertussis-containing vaccines used in this analysis is displayed in the Appendix (Appendix A7).

The most frequent reason for a child not getting vaccinated for influenza was parent refusal, representing 79% of non-vaccinations in 2004-05 and increasing to 96% in 2007-08 (Table 7). Vaccine unavailability accounted for 10% of reasons for non-vaccinations in 2004-05. However in the following three seasons the combination of vaccine unavailability, deferral, and child illness represented a minority of reasons (8% or less) for children not getting vaccinated for influenza.

There was more variability in the reasons given for a child not receiving a pertussis-containing vaccine (Table 7). In 2004-05, the most frequent reason for children not being vaccinated was vaccine unavailability (28%), however the frequency of this declined to close to 0% in subsequent years. The most frequent reasons for a child not receiving a pertussis-containing vaccine in the final three seasons were: school absenteeism (29 to 32%), parent refusal (24 to 27%) and missing

consent form (18 to 20%). Child illness, deferral, insufficient history and client no-show represented a minority of reasons for a child not being vaccinated with a pertussis-containing vaccine.

Of the children who did not receive an influenza vaccine due to parent refusal, zero (0%) also refused a pertussis vaccination in 2004-05; and five (0.1%) also refused a pertussis vaccination in each of the following three seasons.

Table 7. Reasons for not getting vaccinated at a vaccination opportunity, by season and antigen, 2004-08

	2004-05	2005-06	2006-07	2007-08
Reasons for not getting vaccinated for influenza	**N=922**	**N=5,336**	**N=6,930**	**N=9,064**
Parent refusal	731 (79.3)	4,910 (92.0)	6,522 (94.1)	8,692 (95.9)
Vaccine not available	93 (10.1)	127 (2.4)	97 (1.4)	28 (0.3)
Deferred	76 (8.2)	180 (3.4)	125 (1.8)	139 (1.5)
Child ill at time of clinic visit	4 (0.4)	76 (1.4)	91 (1.3)	114 (1.3)
Other	18 (2.0)	43 (0.8)	95 (1.4)	91 (1.0)

Table 7. Reasons for not getting vaccinated at a vaccination opportunity, by season and antigen, 2004-08 (continued)

Reasons for not getting vaccinated by any pertussis-containing vaccine	N=3,603	N=3,228	N=3,723	N=4,131
Vaccine not available	1,005 (27.9)	2 (0.1)	0 (0.0)	9 (0.2)
Absent from school	682 (18.9)	939 (29.1)	1,165 (31.3)	1,307 (31.6)
Parent refusal	611 (17.0)	852 (26.4)	888 (23.9)	1,121 (27.1)
Consent form not received	465 (12.9)	591 (18.3)	727 (19.5)	732 (17.7)
Child ill at time of clinic visit	288 (8.0)	247 (7.7)	272 (7.3)	269 (6.5)
Deferred	215 (6.0)	143 (4.4)	182 (4.9)	149 (3.6)
Insufficient history	166 (4.6)	285 (8.8)	327 (8.8)	337 (8.2)
Client no show	140 (3.9)	131 (4.0)	143 (3.8)	188 (4.6)
Other	31 (0.9)	38 (1.2)	19 (0.5)	19 (0.5)

Objective 2: Estimating vaccination coverage

Sample

For Objective 2, the number of children vaccinated was of importance to the sample rather than the number of vaccination events, which was used for Objective 1.

As shown in Figures 9 to 12, a relatively small number of children (approximately 0.5% each year) were excluded from all analyses in each influenza season. The majority of exclusions were made because the child was older than nine years of age or received the first or only dose of vaccine after April 30. A smaller number of children who lived on reserve or died after receiving only one dose of influenza vaccine were also removed.

The final number of children who received at least one dose of vaccine in any year ranged from 15,683 in 2004-05 to 29,041 in 2005-06.

Figure 9. Derivation of sample for Objective 2, 2004-05

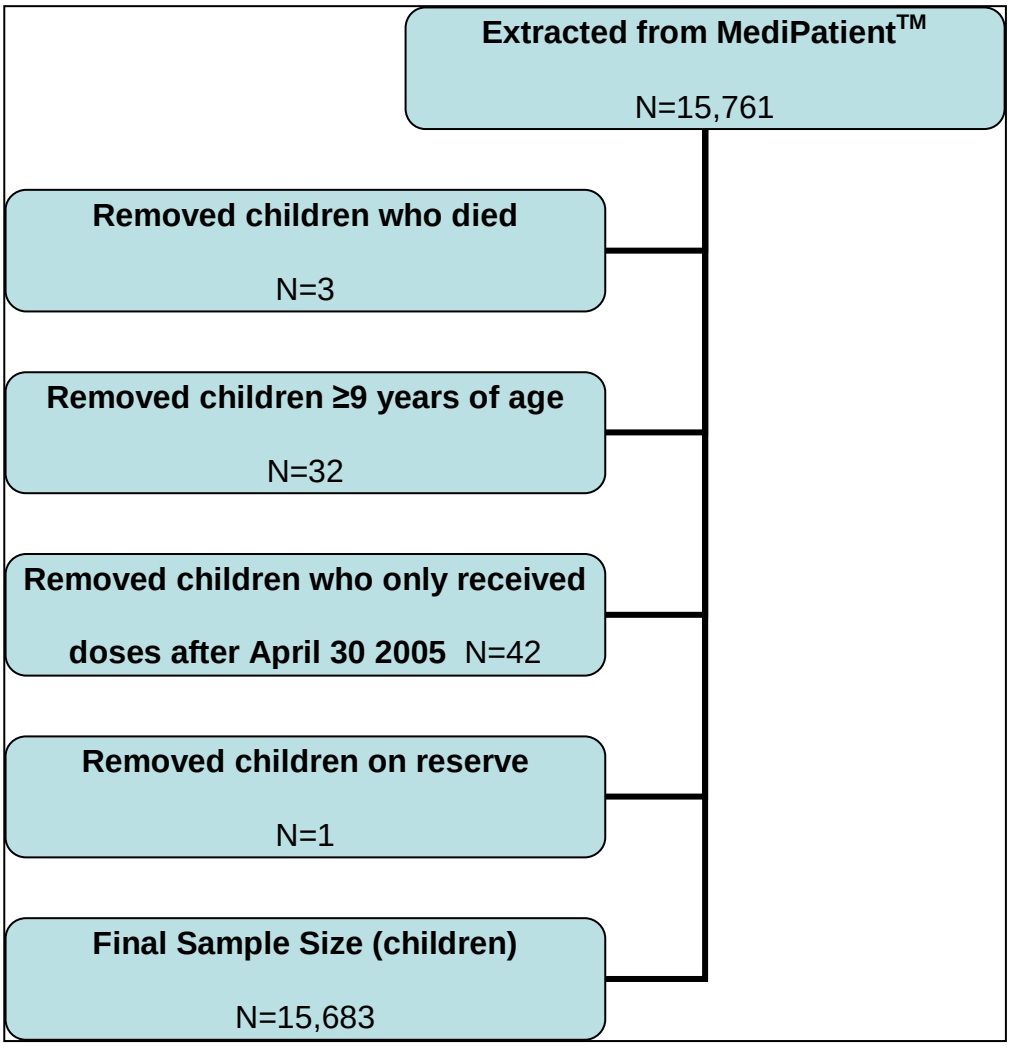


Figure 10. Derivation of sample for Objectives 2 and 3, 2005-06

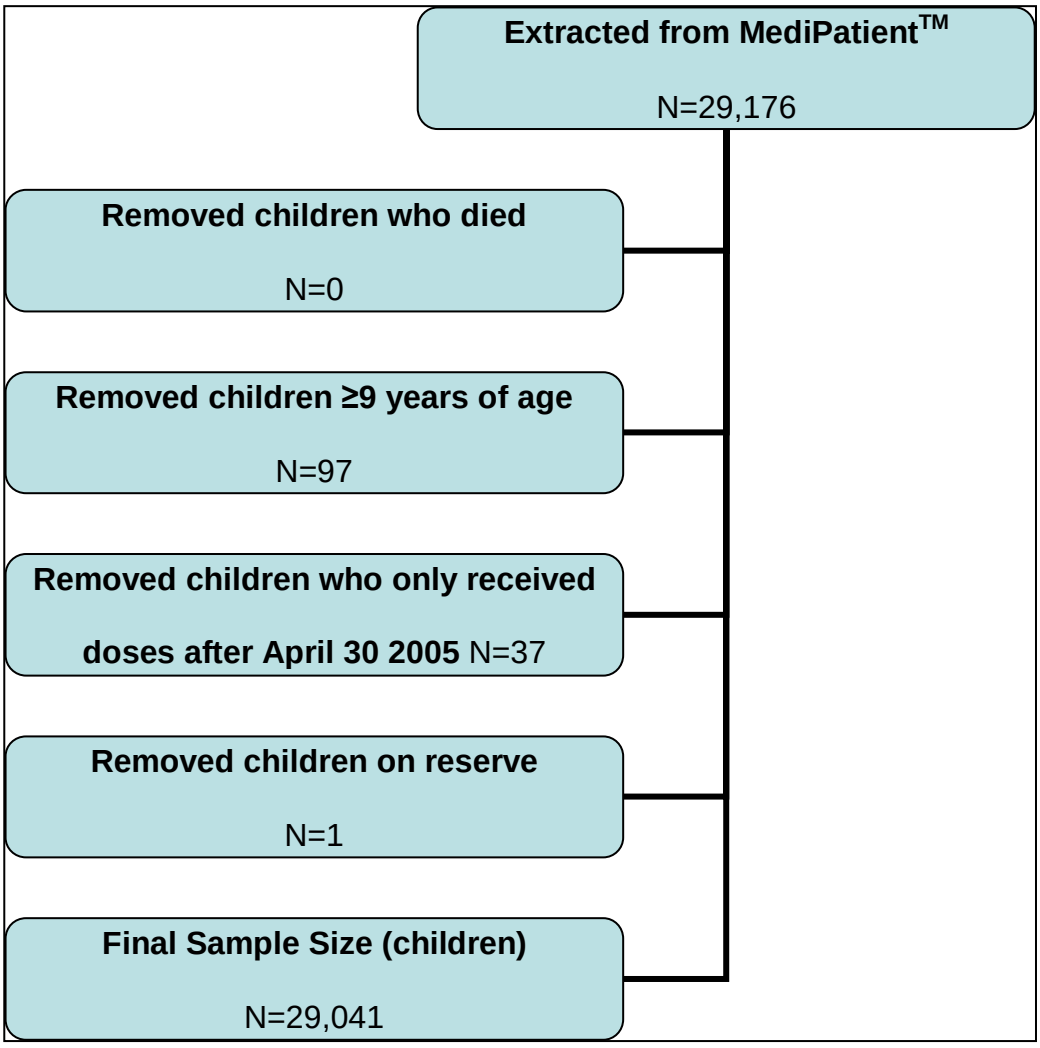


Figure 11. Derivation of sample for Objective 2, 2006-07

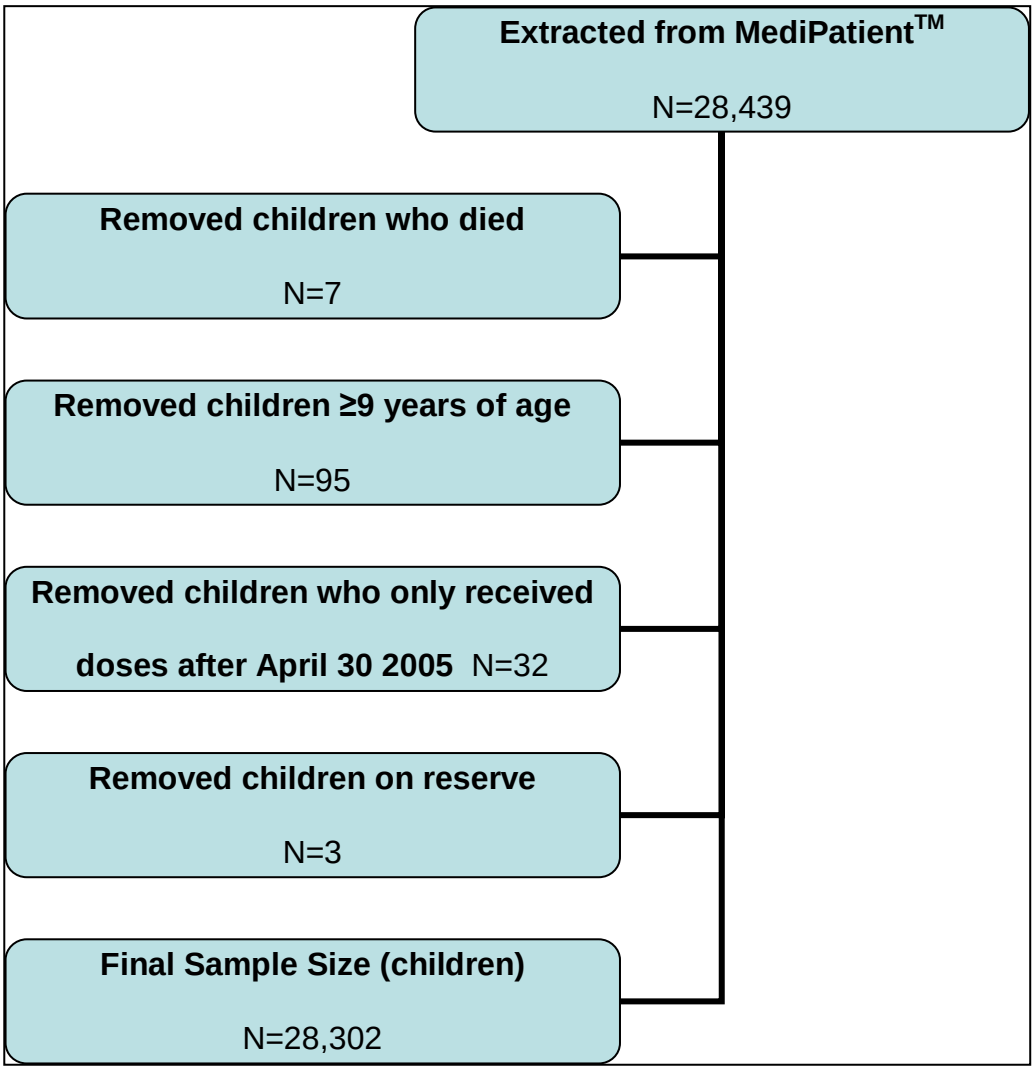
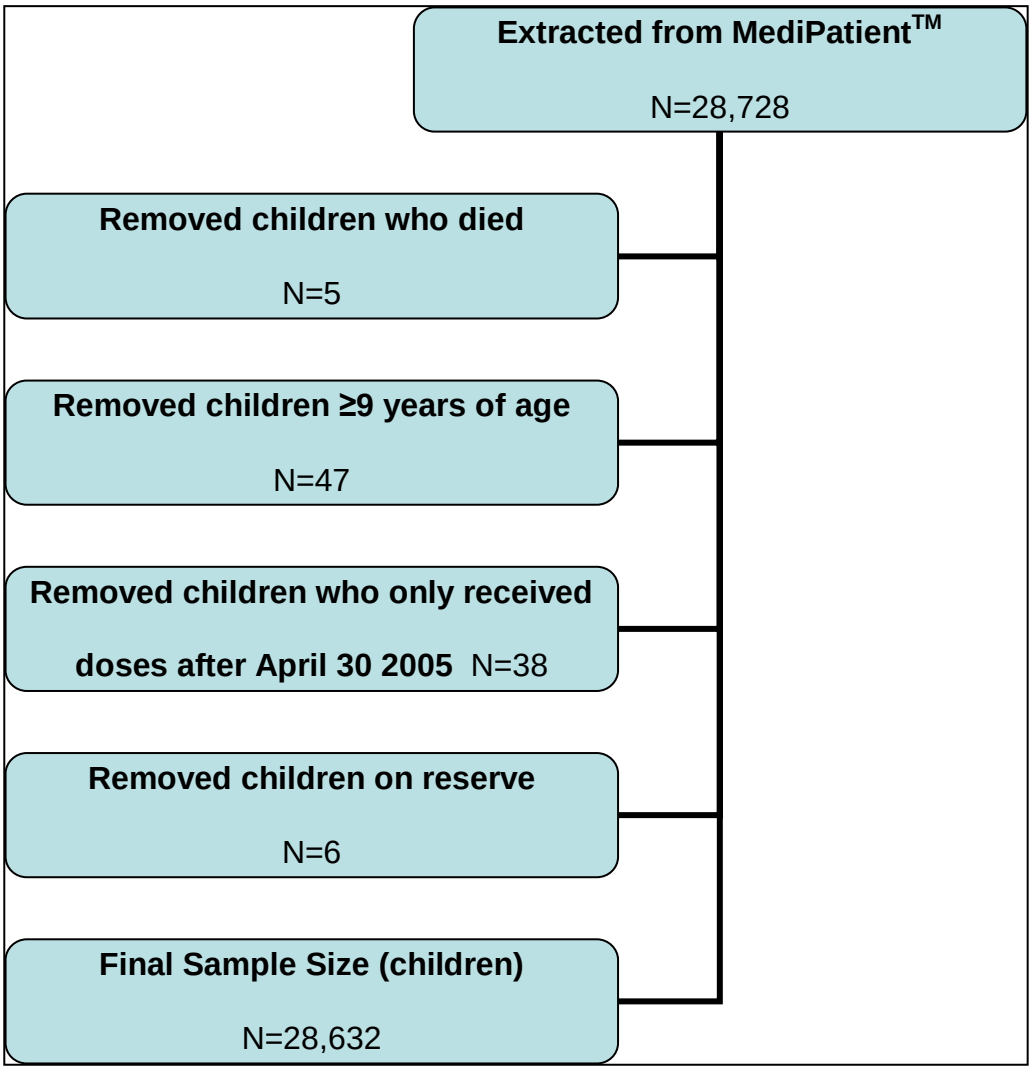


Figure 12. Derivation of sample for Objective 2, 2007-08



Number of children adequately and partially vaccinated

Table 8 presents the total number of children who received at least one dose of influenza vaccine in each influenza season. Every year the total number of children who received at least one dose of vaccine for influenza increased, with the largest increase occurring between the first and second influenza season. The number of adequately vaccinated children was similar to the number of partially vaccinated children in the first two seasons. In 2006-07 and 2007-08, the number of adequately vaccinated children was nearly double that of partially vaccinated children.

Table 8. Number of children adequately and partially vaccinated by influenza season, 2004-08

	Influenza Season			
	2004-05	**2005-06**	**2006-07**	**2007-08**
Total children	**N=15,683**	**N=29,041**	**N=28,302**	**N=28,632**
Adequately	8,284	14,297	18,536	19,085
Partially	7,399	14,744	9,766	9,547

Adequate and partial vaccination coverage estimates

The Alberta Health Care Insurance Plan (AHCIP) registry was used as the source of denominator data to determine adequate and partial vaccination coverage among children in the Calgary Health Region.

Adequate and partial vaccination coverage estimates for each season are presented in Table 9. Adequate vaccination coverage increased over the four years, ranging from 6 to 13% with the largest increase in coverage between Seasons 1 and 2. Partial vaccination coverage was 6% in 2004-05, more than doubled to 11% in Season 2, and declined to 7% in Seasons 3 and 4. Adequate vaccination and partial vaccination estimates are similar in the first two seasons, however in Seasons 3 and 4 the adequate vaccination rates are approximately double those of the partial vaccination rates.

Table 9. Adequate and partial vaccination coverage and corresponding 95% confidence intervals among children <9 years of age in the CHR, by influenza season, 2004-08*

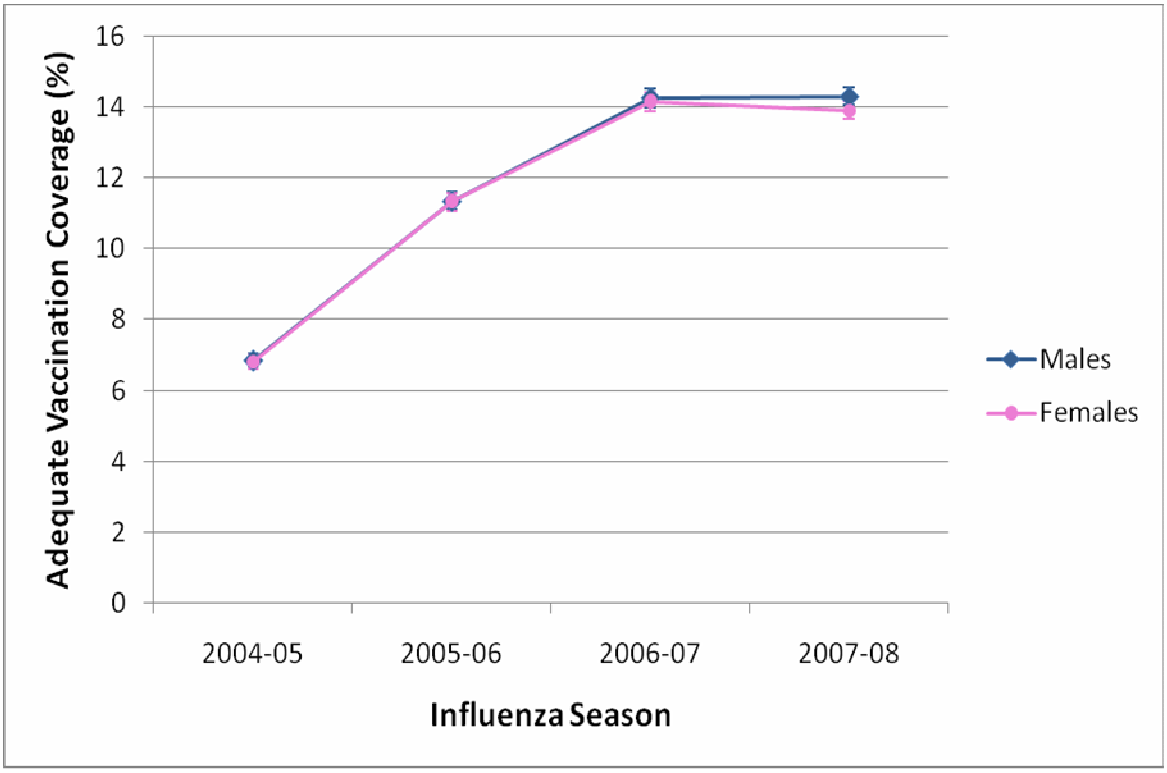
	Influenza Season			
	2004-05	**2005-06**	**2006-07**	**2007-08**
	% (95%CI)	**% (95%CI)**	**% (95%CI)**	**% (95%CI)**
Adequate Vaccination Coverage	6.4 (6.29-6.56)	10.7 (10.50-10.83)	13.3 (13.15-13.51)	13.2 (13.1-13.4)
Partial Vaccination Coverage	5.7 (5.61-5.87)	11.0 (10.83-11.17)	7.0 (6.89-7.16)	6.6 (6.49-6.75)
≥1 Doses Coverage	12.1 (12.0-12.3)	21.7 (21.5-21.9)	20.4 (20.1-20.6)	19.9 (19.7-20.1)

*Denominator source: AHCIP

Adequate and partial vaccination coverage estimates by sex

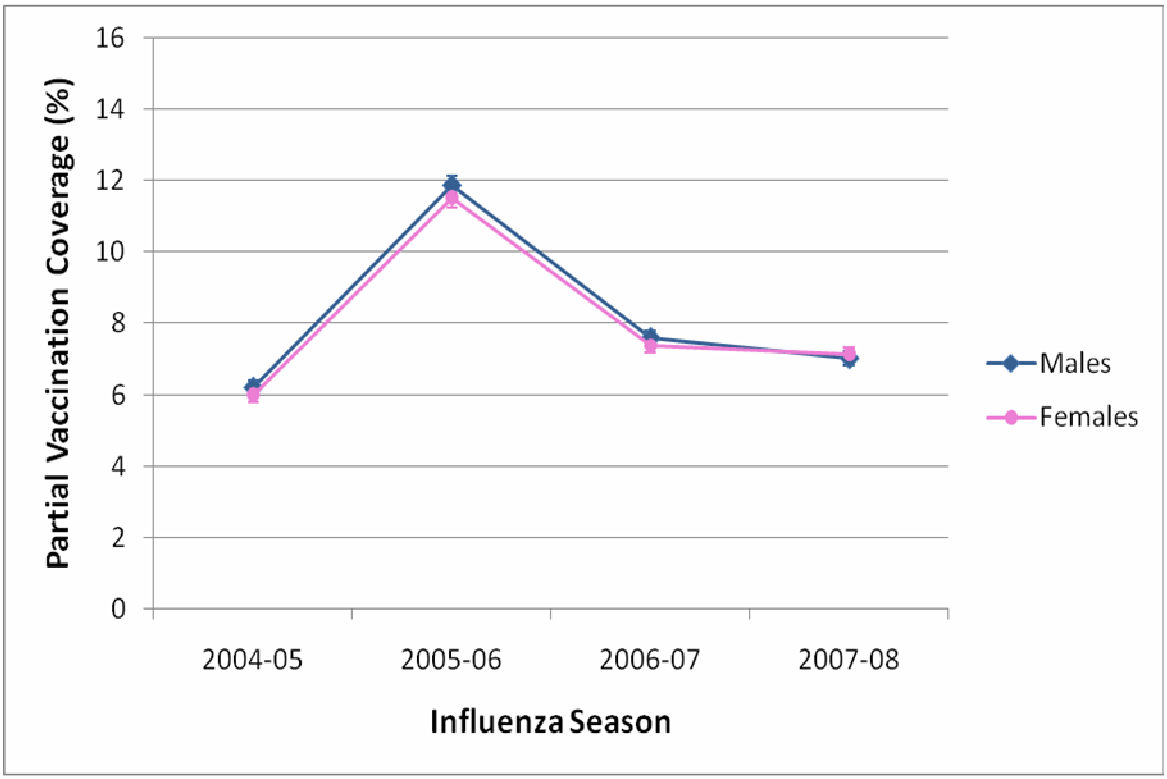
Sex-specific estimates for adequately and partially vaccinated children are presented in Figures 13 and 14 respectively. Confidence intervals for sex-specific estimates overlapped in all years.

Figure 13. Adequate vaccination coverage and corresponding 95% confidence intervals among children <9 years of age in the CHR, by sex and influenza season, 2004-08*



*Denominator source: AHCIP

Figure 14. Partial vaccination coverage and corresponding 95% confidence intervals among children <9 years of age in the CHR, by sex and influenza season, 2004-08*

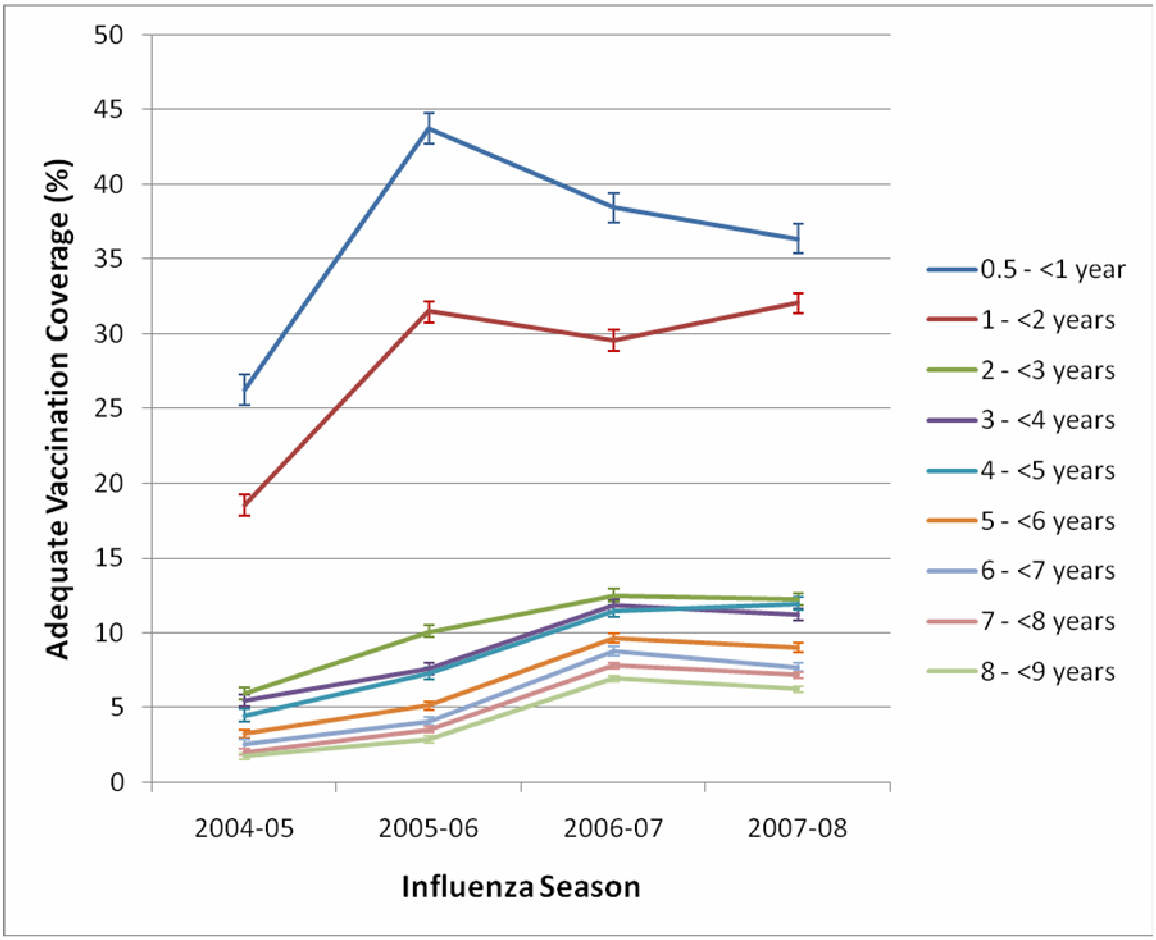


*Denominator source: AHCIP

Adequate and partial vaccination coverage estimates by age

Coverage estimates for adequately vaccinated children were generated for each year of age as shown in Figure 15. Generally, coverage rates for each level of age increased from 2004 to 2008. Children between the ages of six months and one year of age had the highest vaccination coverage rates in all years (range: 26 to 44%), while children one year of age to less than two years of age had the second highest rates in all years (range: 19 to 32%). There is a decline in coverage between Seasons 2 and 3 for children less than two years of age, while coverage for children of all other ages increased. Season-specific coverage rates generally decreased with increasing age.

Figure 15. Adequate vaccination coverage and corresponding 95% confidence intervals among children <9 years of age in the CHR, by age and influenza season, 2004-08*



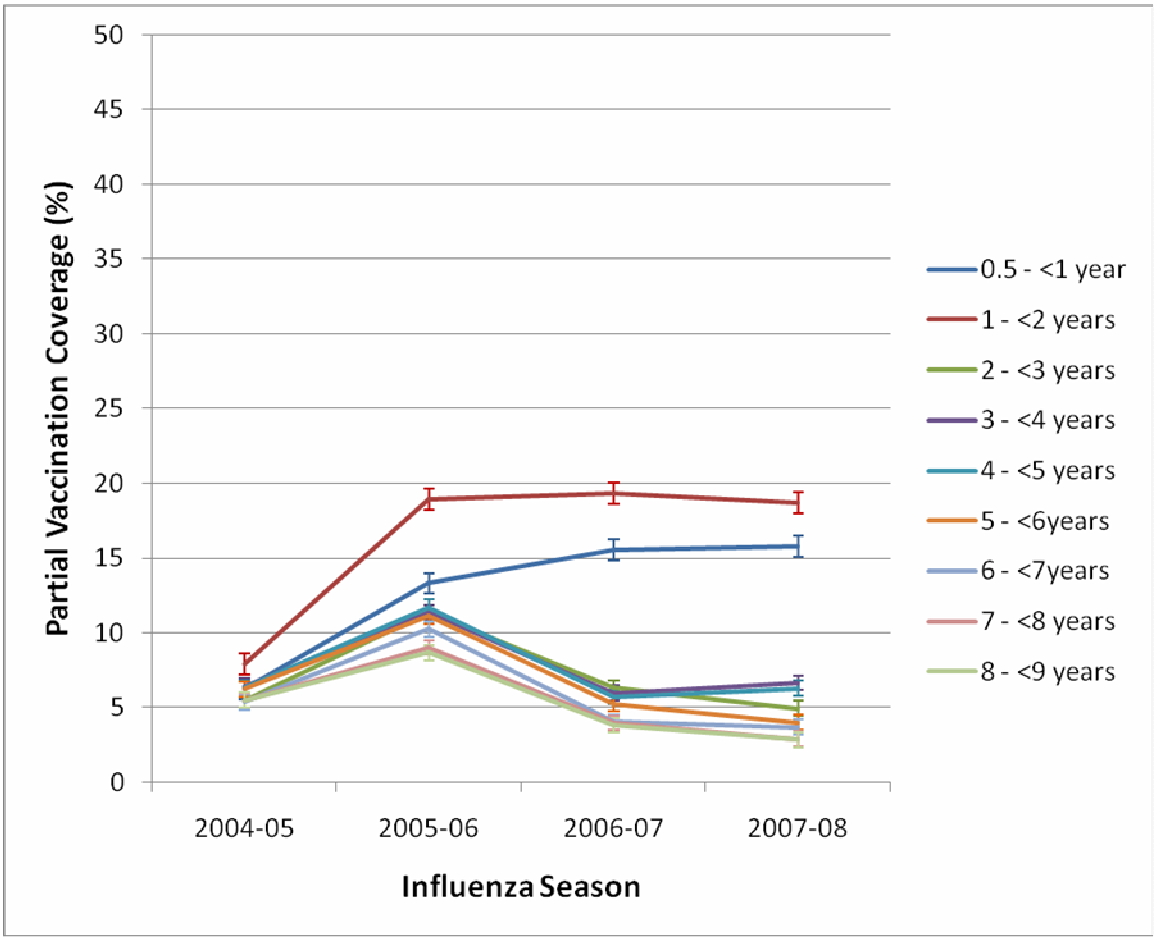
*Denominator source: AHCIP

Two types of curves are seen in Figure 16 which presents age-specific partial vaccination coverage rates over the four influenza seasons.

Partial vaccination coverage among the two youngest groups increased more than the other age groups between Seasons 1 and 2. Coverage among children six months to less than one year of age continued to increase into Season 3 and remained at that level for Season 4. In contrast, coverage among children one year to less than two years of age remained at the same level for Seasons 2, 3 and 4.

Partial coverage among all other age groups increased between Season 1 and Season 2, but then declined the following season. The largest proportion of partially vaccinated children occurs among children between the ages of one and two years, ranging from 8% in 2004-05 to 19% in subsequent seasons. The highest coverage estimates in all ages occur in 2005-06 or are similar in magnitude to the values in 2005-06. In contrast to the data in Figure 15, the data in Figure 16 show no obvious increasing or decreasing trend in coverage with increasing age.

Figure 16. Partial vaccination coverage and corresponding 95% confidence intervals among children <9 years of age in the CHR, by age and influenza season, 2004-08*



*Denominator source: AHCIP

Adequate vaccination coverage by area of residence and age

Coverage rates were estimated for children living in rural and urban areas of the CHR as defined in the Methods section. Coverage rates were also estimated for each of 19 social districts and 193 census tracts.

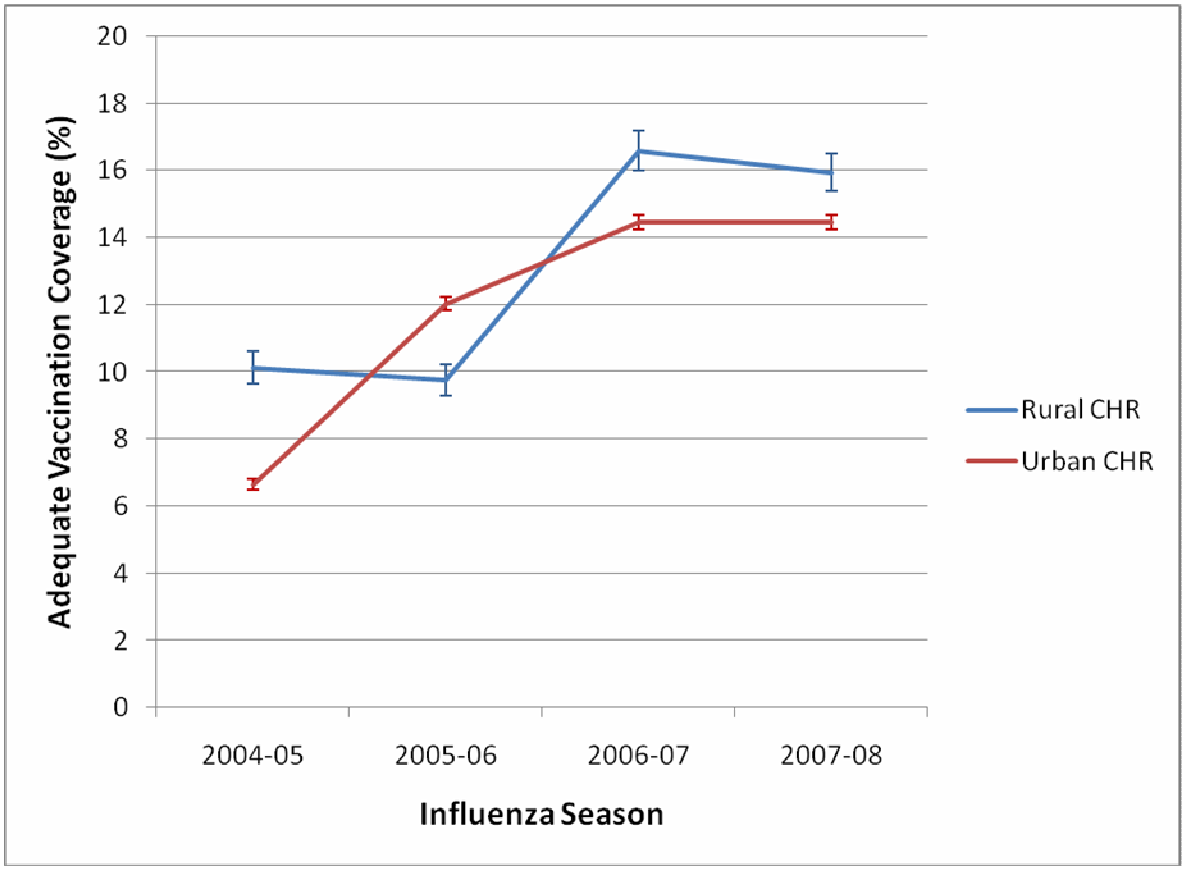
Urban and rural area of residence

Employees at Alberta Health and Wellness provided the researcher with ACHIP age-specific population counts for each dissemination area. These data were merged with the cohort database from MediPatient™/PHANTIM™ to determine if a dissemination area was considered by the CHR to be "rural" or "urban". These urban-rural population counts were slightly lower than overall AHCIP population counts due to missing data in the vaccinated cohort database.

Rural and urban coverage estimates are shown in Figure 17. In 2004-05, a larger proportion of children living in a rural area (10%) were adequately vaccinated compared to children living in an urban area (7%). In 2005-06, there was an increase in coverage among urban children to 12%, while coverage among rural children remained the same as in 2004-05 (10%). In 2006-07 and 2007-08, coverage among

rural children rose to 17% and 16% respectively, and among urban children it rose to 14% in both years. Confidence intervals for both groups are shown and never overlap.

Figure 17. Adequate vaccination coverage and corresponding 95% confidence intervals among children <9 years of age in the CHR, by urban and rural area of residence and influenza season, 2004-08*

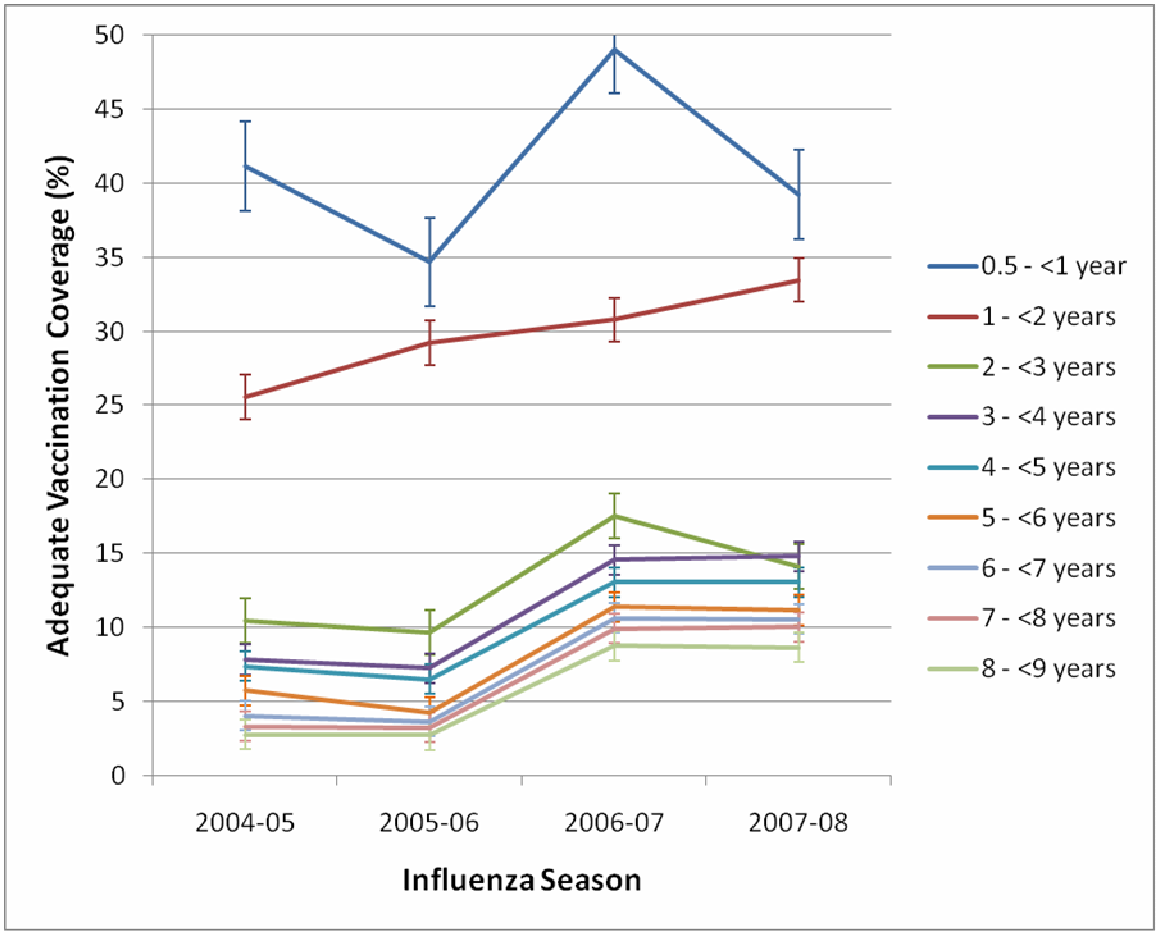


*Denominator source: AHCIP

Rural and urban coverage estimates by age in years are shown in Figures 18 and 19 respectively.

Among children living in a rural area, adequate vaccination coverage increased every year for all four seasons among children aged one year to less than two years (Figure 18). For all other children, coverage was similar or declined between 2004-05 and 2005-06, then increased for 2006-07. Adequate vaccination coverage for children aged six months to less than one year and for those aged two years to less than three years declined from 2006-07 to 2007-08 whereas for all older children, coverage rates were similar for 2006-07 compared to 2007-08.

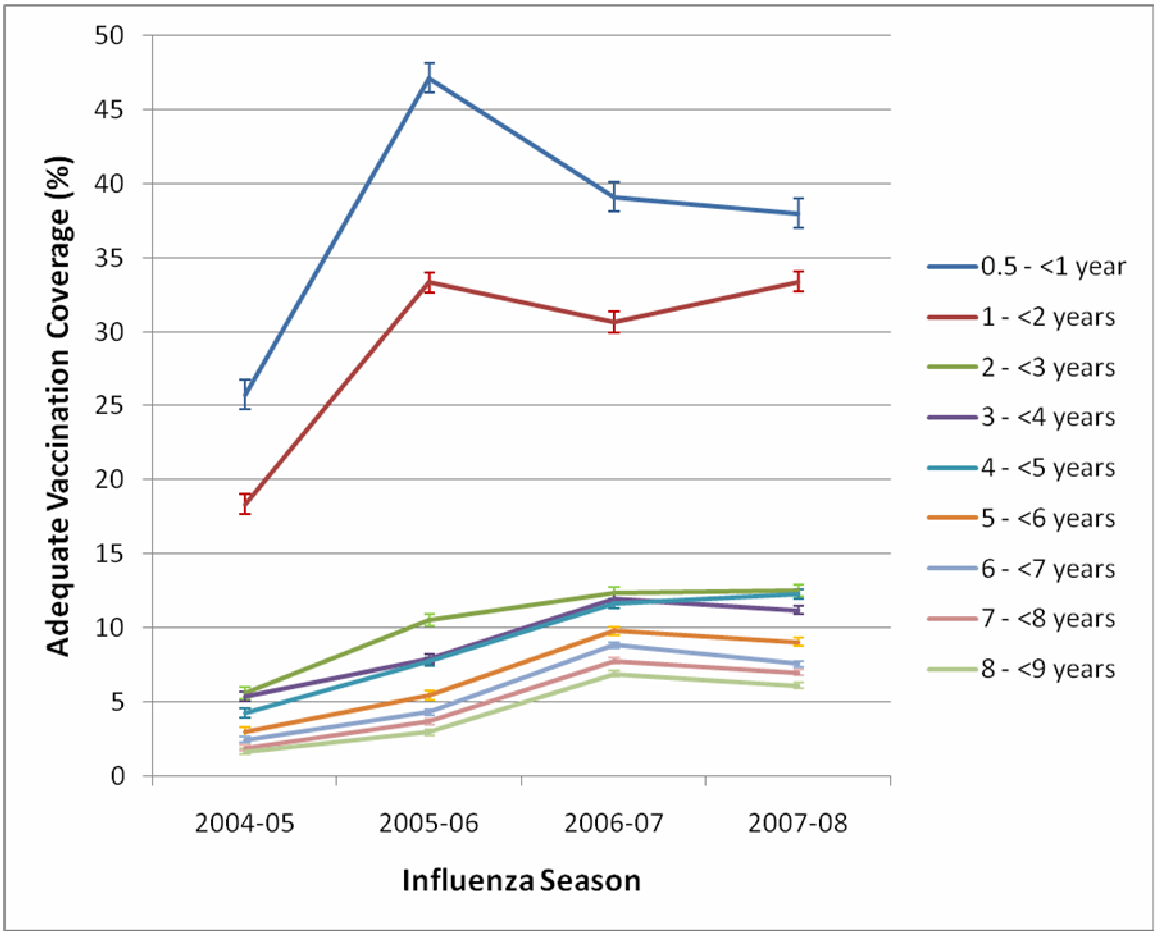
Figure 18. Adequate vaccination coverage and corresponding 95% confidence intervals among children <9 years of age from a rural area in the CHR, by age and influenza season, 2004-08*



*Denominator source: AHCIP

Among children living in an urban area, adequate vaccination coverage increased between Season 1 and 2 among all age groups (Figure 19). The largest increase in coverage over this period was among children under the age of two years, who also had the highest coverage rates in all seasons compared to children from other age groups. Coverage increased between 2005-06 and 2006-07 among children older than two years of age, and remained at these levels for 2007-08. In contrast, coverage decreased between 2005-06 and 2006-07 among children younger than two years of age. In 2007-08, coverage among children six months of age to less than one year slightly declined as coverage among children one to less than two years of age slightly increased.

Figure 19. Adequate vaccination coverage and corresponding 95% confidence intervals among children <9 years of age from an urban area in the CHR, by age and influenza season, 2004-08*



*Denominator source: AHCIP

To summarize, in both urban and rural areas of residence, children under the age of two years had the highest coverage rates for each year in this study. Among children aged two years or older, adequate vaccination coverage decreased with increasing age in all seasons for both rural and urban children.

Social districts

Coverage estimates by social district are useful within the CHR to describe rates in the region, identify areas of low coverage and to position vaccination programs for improvement in subsequent years.

As shown in Table 10, overall coverage for children aged six months to less than nine years ranged from 7% in 2004-05 to 14% in 2007-08. Confidence intervals never overlapped across the four years of study. The largest increase in coverage occurred between the first two influenza seasons. Social Districts #9, #10 and #16 are among the areas with the lowest adequate vaccination coverage rates every year.

Table 10. Adequate vaccination coverage among children <9 years of age in the CHR, by social district and influenza season, 2004-08*

	Adequate Vaccination Coverage			
	2004-05	**2005-06**	**2006-07**	**2007-08**
Social District	**%**	**%**	**%**	**%**
1	7.6	13.8	16.6	14.6
2	7.3	12.6	15.9	15.0
3	3.4	10.1	10.7	12.6
4	8.9	14.0	17.7	16.0
5	4.9	9.5	12.3	12.1
6	3.8	9.3	11.4	12.8
7	10.7	13.9	16.9	17.3
8	5.5	9.8	11.2	12.0
9	2.7	6.5	8.6	9.8
10	2.8	8.3	10.5	12.0
11	7.3	10.5	14.2	14.7
12	7.3	10.8	14.1	16.3
13	6.0	9.4	12.8	14.9
14	7.9	14.3	17.2	16.9

Table 10. Adequate vaccination coverage among children <9 years of age in the CHR, by social district and influenza season, 2004-08* (continued)

	Adequate Vaccination Coverage			
	2004-05	**2005-06**	**2006-07**	**2007-08**
Social District	**%**	**%**	**%**	**%**
15	7.5	13.0	15.9	15.3
16	5.4	5.5	11.0	9.6
17	11.0	7.4	16.0	16.7
18	9.4	10.7	14.8	14.2
19	7.4	8.0	11.8	10.0
Total	**6.7**	**11.0**	**14.0**	**14.0**
95% CI				
Lower	6.5	10.8	13.8	13.8
Upper	6.8	11.1	14.1	14.2

*Denominator source: AHCIP

Census tracts

Census tracts are small geographic areas that are located in urban centres that must have a core population of 50,000 or more(92). In contrast to social districts, census tracts are located in other urban parts of Canada. Therefore, vaccination rates for census tracts in the CHR can be compared to census tracts outside of the CHR. AHCIP population counts by dissemination area were used to build population counts by census tract.

The data for 2007-08 are shown in Appendix A8. Adequate vaccination coverage varied by census tract, ranging from 6% in Census 8250043 to 32% in Census Tract 8250070. All census tracts are in the urban area of the CHR.

Objective 3: Exploring for an association between income and getting vaccinated

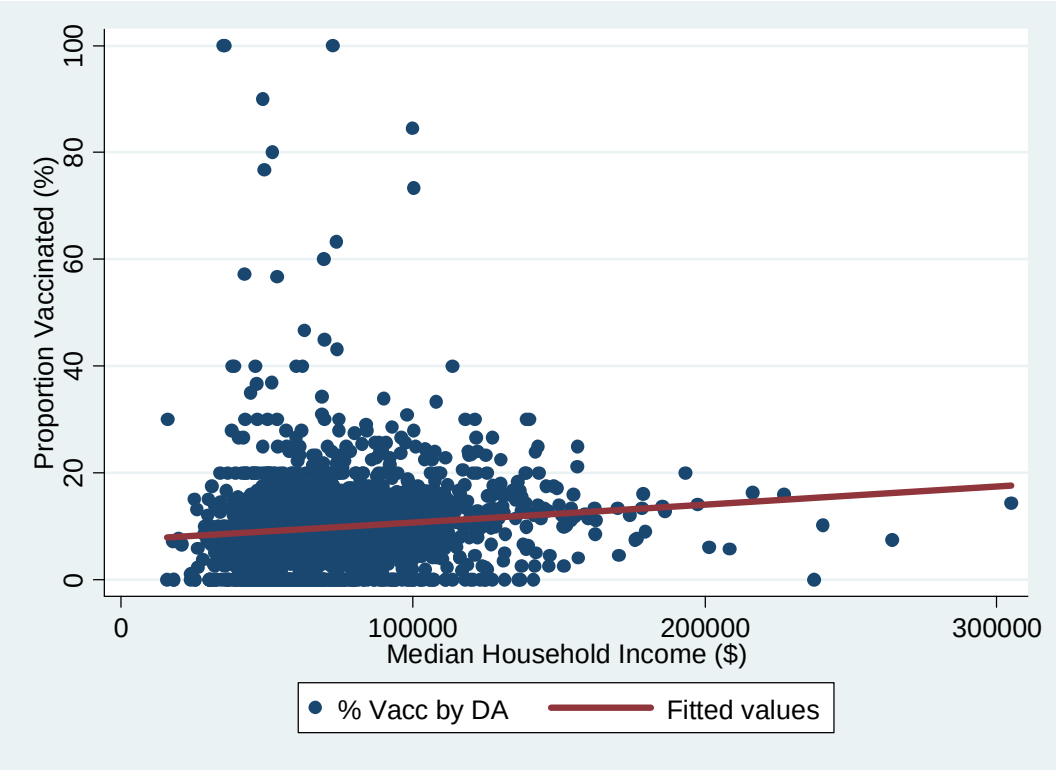
Sample

Figure 10 illustrates the derivation of the sample for Objective 3 (n=29,041).

Association between MHI and getting vaccinated

Vaccination coverage was calculated for each dissemination area in the CHR and plotted against MHI in a scatter plot. As shown in Figure 20, the large majority of data points are situated in the bottom-left corner of the scatter plot, indicating that most of the points are below 20% for vaccination coverage, and below $200,000 for MHI.

Figure 20. Scatter plot of Vaccination Coverage and Median Household Income for 1,759 Dissemination Areas in the Calgary Health Region, 2005-06.



Before running the linear regression analysis, the assumptions for linear regression were considered. The Breusch-Pagan/Cook-Weisberg test for heteroskedasticity showed a significant p-value ($p<0.004$) indicating that the null hypothesis of constant variance must be rejected. These data therefore do not satisfy the assumption of homoskedasticity for linear regression.

To meet the assumptions for the linear regression, the researcher considered log-transforming the data, but this resulted in another significant p-value for the Breusch-Pagan/Cook-Weisberg test for heteroskedasticity ($p<0.001$). The assumption of constant variance was therefore violated with this data transformation.

The researcher then stratified the data into "high" and "low" vaccination coverage groups. Dissemination areas with a vaccination coverage that is higher than the mean coverage plus two standard deviations (>28.1%) are considered to have "high" coverage. Dissemination areas with vaccination coverage estimates below or equal to 28.1% were considered of "low" coverage. The assumptions for linear regression were then considered for each group. The scatter plot showing MHI and vaccination coverage among dissemination

areas of "low" coverage are shown in Figure 21, and that among dissemination areas of "high" coverage are shown in Figure 22.

Figure 21. Scatter plot of Vaccination Coverage and Median Household Income for 1,717 Dissemination Areas of "Low" Vaccination Coverage in the Calgary Health Region, 2005-06.

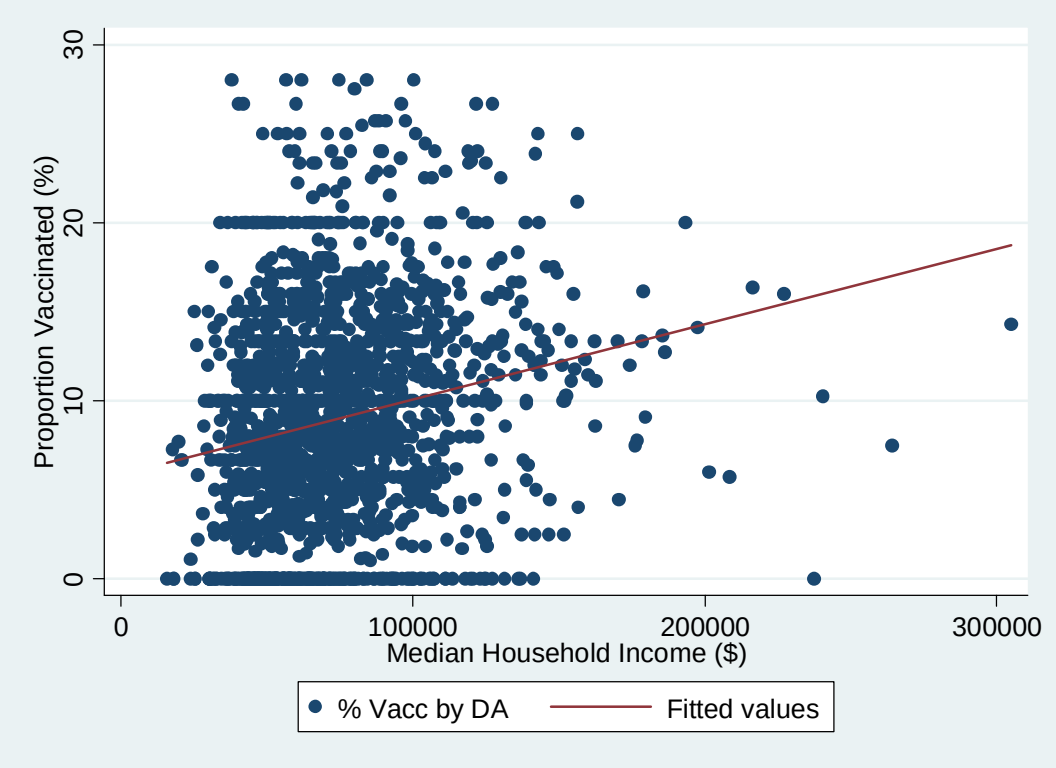
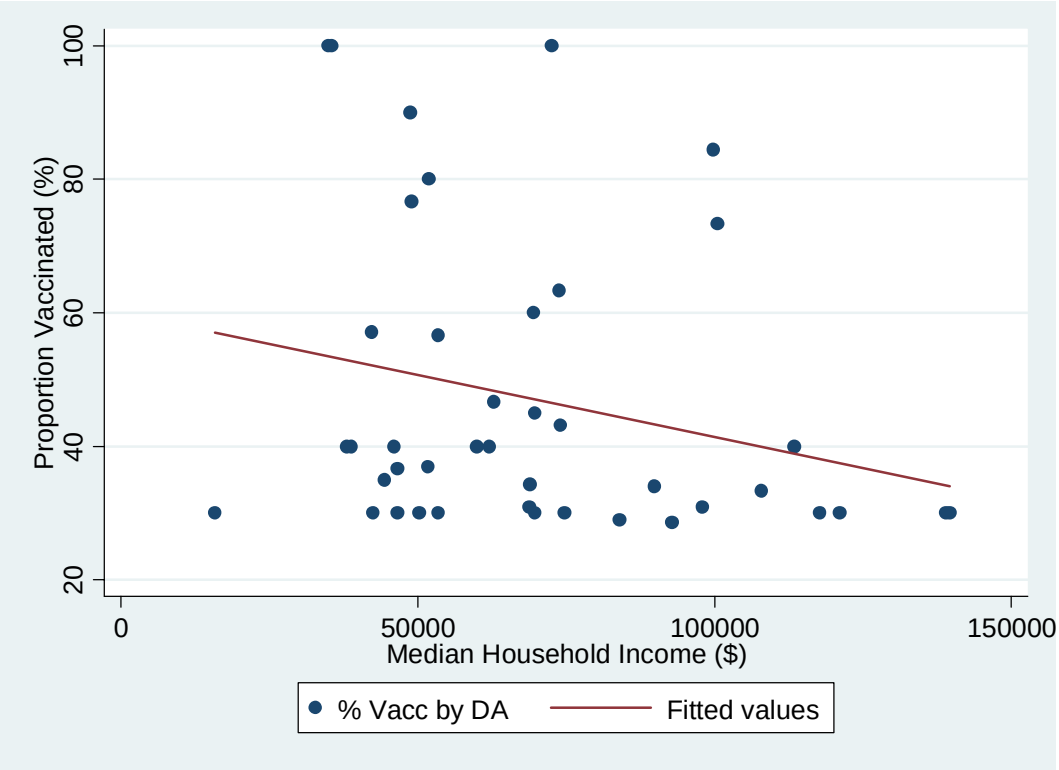


Figure 22. Scatter plot of Vaccination Coverage and Median Household Income for 42 Dissemination Areas of "High" Vaccination Coverage in the Calgary Health Region, 2005-06.



The four assumptions required for linear regression analysis were satisfied for the "low" coverage group. The output from the linear regression analysis for this group is outlined in Table 11.

Table 11. Results from linear regression analysis examining the relationship between median household income and vaccination coverage for dissemination areas with "low" vaccination coverage (≤28.1%) in the Calgary Health Region (n=1,717), 2005-06

	Coefficient	p-value	95% CI	R^2
MHI	0.00004	P<0.001	0.00003, 0.00005	0.042

The assumption of normality was violated for the "high" coverage group. These data were then log-transformed at which point all assumptions for linear regression analysis were satisfied. The output from the linear regression analysis for the "high" coverage group is outlined in Table 12.

Table 12. Results from linear regression analysis examining the relationship between median household income (log-transformed) and vaccination coverage (log-transformed) for dissemination areas with "high" vaccination coverage (>28.1%) in the Calgary Health Region (n=42), 2005-06

	Coefficient	p-value	95% CI	R^2
MHI	-0.0002	p=0.12	-0.0004, 0.00005	0.060

As shown in Table 11, the coefficient for the relationship between MHI and vaccination coverage among dissemination areas with "low" coverage ($\leq$28.1%) is very close to zero (0.00004). The p-value indicates that a positive linear relationship exists, however, due to the absolute value of the coefficient and confidence interval limits, the researcher concluded that the value is very close to zero and therefore no meaningful relationship exists between MHI and proportion vaccinated. This is further supported by the R^2 value (R^2=0.042) indicating that just 4.2% of the variation in vaccination coverage is explained by the MHI variable.

As shown in Table 12, among dissemination areas with a mean coverage of 28.1% or higher (those of "high" coverage), the p-value indicates that no relationship exists between log-transformed MHI and log-transformed vaccination coverage (p=0.12). This is further supported by the R^2 value (R^2=0.060) indicating that just 6.0% of the variation in vaccination coverage is explained by the MHI variable.

These data suggest that MHI does not predict vaccination coverage among dissemination areas of either high or low coverage, and therefore there is no meaningful association between MHI and vaccination coverage in this study.

CHAPTER FIVE: DISCUSSION

Introduction

Several factors influence the measurement of vaccination coverage, including the definition of "vaccinated" and the sources of numerator and denominator data. This research is unique in both its consistent use of definitions and its ability to directly compare data over four influenza seasons among children in the CHR. Previous research among children in the CHR examined data from a single season and was not population-based(88). The current study explores age-, sex- and geography-specific vaccination coverage rates among all children in the CHR from 2004-05 to 2007-08 and offers explanations and hypotheses for variability in rates over time. It also provides influenza vaccination rates for children two to less than nine years of age, an age group that plays an important role in the transmission of respiratory illness within households and communities(5, 6) and about whom reports are not produced by Alberta Health and Wellness.

Alberta adopted a provincial immunization registry and universal publicly funded influenza vaccination program after the start of data

collection for this study. The study results and their value are discussed in the context of these new tools and policies.

This section is thus divided into two parts: 1) interpretation of the study findings in the CHR context; and 2) implications of the study findings and future research.

Interpretation of the study findings in the CHR context

Objective 1: Describing vaccination events

During the study period, influenza vaccination recommendations for children in Canada varied by institution and by year. The context in which vaccines were administered may cause annual variation in the number of doses given to a child, the vaccine providers, the facilities where the vaccines were delivered and the reasons for administration.

Number of doses of influenza vaccine

The CHR recommended in all years of study that children six months of age to younger than nine years of age receive two doses of influenza vaccine with an interval of 28 days. In 2004-05, 2005-06 and 2006-07, the CHR indicated that the second dose of influenza vaccine is not needed if the child received one or more doses of vaccine during a

previous influenza season. In theory, every year fewer children required their primary series of two doses. This is reflected in the study data. In the first three seasons of the study, the proportion of children receiving two doses of vaccine decreased with time. In 2007-08, the CHR changed its recommendation: children required two doses in the 2007-08 year if they received one or no doses in the previous season and never before received two doses within a single season. Effectively, some children were required to restart their two-dose series even if they received influenza vaccinations in the past. Accordingly, in the 2007-08 study data, there was an increase in the proportion of children who received two doses and a decrease in the proportion of children who received just one dose. These data show that changing recommendations may partly explain the variation in the recorded number of doses children received from year to year. Further, the number of children who received three doses is relatively small, and those who did get three doses were those who received their two-dose influenza vaccine series in less than the recommended interval of 28 days. Some children who received three doses also received a first dose around the age of six months. One can infer that a third dose of influenza vaccine is given to some children when the

nurse is uncertain if the recommended dosage schedule was properly followed.

The data show a large increase in the number of doses recorded between Season 1 (24,269 doses) and Season 2 (41,283 doses). This is likely due to the addition of children six to 23 months of age to the list of eligible recipients for publicly funded influenza vaccine in the previous year. One must recognize that it takes time for nurses and parents to become familiar with the new program, which could explain the large increase in the year following the new eligibility requirement. This increase could also be explained by the fact that more vaccinations were recorded in Season 2 due to the gradual uptake of a new reporting requirement for influenza that started in 2004.

In 2006-07 vaccine delivery was delayed due to manufacturing challenges, and in 2007-08 the CHR reduced the number of mass venue sites and discontinued the use of the Calgary Co-op grocery stores. These changes to the program may have contributed to the decline in vaccination rates after the 2005-06 season(96).

Vaccine administrations occurred at similar times throughout the calendar year from 2004 to 2008. Figures 5 to 8 show a bimodal curve, with the highest frequencies occurring around October or November, which is at the beginning of the influenza season. There is an obvious delay in the administration of influenza vaccines in 2006-07, which is explained by the fact that influenza vaccines were not available until November due to production challenges(97). Clearly very few children were vaccinated in the summer months that lie outside of the influenza season.

Vaccine provider

Public health nurses administered nearly all vaccinations in all years of the study. This could be a true finding, or the study data could be missing records of vaccinations administered by other providers. It is expected, however, that most vaccinations for children were administered by public health nurses. This is corroborated by the fact that every year CHR physicians received a letter from the CHR Deputy Medical Officer of Health encouraging physicians to refer their young patients to public health clinics for influenza vaccinations. In 2004-05, the letters stated that "Public health will take responsibility for influenza vaccinations for children six to 23 months of age." In the

following three seasons, the letters explicitly stated that "Public health will take sole responsibility for administering vaccines to children from six months to nine years of age," and the specific vaccine recommended for this age group was not made available to physician offices. In all letters, physicians were also reminded that if they were to vaccinate a child younger than nine years of age, this information needed to be entered into the public health vaccination system by submitting the appropriate documentation. Notwithstanding these instructions, some physicians may have purchased the vaccine, administered it to patients younger than nine years of age, and neglected to submit the necessary paperwork to the CHR. These data would be missing from the database entirely and would underestimate coverage estimates. This also introduces the possibility of selection bias, which will be discussed in the limitations section.

Vaccine facility

The large majority of vaccinations occurred in a community health centre, an influenza clinic or a mass vaccination clinic. Influenza clinic and mass venue data were merged since they represent sites with the single purpose of vaccinating people for influenza.

Over the four-year period, the proportion of vaccinations that occurred at an influenza clinic or mass venue declined, while the proportion at community health centres increased. A possible reason for this is that a larger proportion of young children receive their influenza vaccinations at community health centres compared to mass venues, and that every year a larger proportion of young children received a vaccine compared to older children. The researcher investigated this further and found that the proportion of vaccinated children under the age of two years increased over the four seasons, ranging from 40% of all vaccinated children in 2004-05 to 47% in 2007-08. This could explain an increase in vaccinations occurring at community health centres. The decline in vaccinations in influenza clinics or mass venues between 2006-07 (60%) and 2007-08 (39%) may also be attributable to the downsizing of mass venue sites in 2007-08. In that year, fewer but bigger and more permanent sites were offered for influenza vaccinations.

Vaccine reason

When a child is given an influenza vaccine, a reason for the vaccination is entered into the vaccination database. Reasons for receiving a publicly funded vaccine among the study sample include:

the child is younger than two years of age; the child has a chronic condition; or the child is a household contact of someone at high risk of influenza-related complications. Parents can also pay for an influenza vaccine if a child does not fall into one of these three categories.

Several challenges exist for the reason coding for influenza vaccination. Some confusion can occur over whether or not a two-year-old child's second dose of vaccine should be publicly funded or paid for by the parent if their first dose of vaccine occurred while they were younger than two years of age. Chronic conditions include pulmonary disorders such as asthma and it can be difficult to assess their level of severity. Questions such as "Does the child have medication for asthma?" and "How frequently does the child have asthma attacks?" may help a nurse to qualify if the child has a chronic condition or not, and this subjectivity could vary by the nurse administering the vaccine. Another challenge is presented by children falling into multiple eligibility categories for a publicly funded vaccine. For example, a 12-month-old child may also live with a grandparent who is older than 65 years of age, thereby falling into two different eligibility categories on the basis of age and household contact. Since 2008, a hierarchy of coding now exists which dictates how to code the

reason for a vaccination if a patient falls into multiple reason categories. In the period of this study, however, there were no clear instructions for nurses on how to code patients that fell into multiple categories. This means children were not consistently classified by the reason for which they were vaccinated and it is not possible to quantify the extent of misclassification. Errors could also occur due to data entry errors, such as clicking on the wrong reason from a pull-down list on a computer data entry screen. For example, some vaccination entries indicated a child was given a vaccine because the child "worked in chicken culling" or "was a health care worker," which are obvious errors in the database. Further, once a file is electronically saved in MediPatient™/PHANTIM™, it cannot be edited. If an error was made, a new record must be generated and the old record must be flagged as an error entry. This tedious process may discourage nurses from fixing relatively small data entry mistakes.

The majority of vaccinations occurred because a child was younger than two years of age. According to key informants in the CHR, this is expected to be the most common reason for vaccination if a child fell into multiple categories including age. The increasing proportion of vaccinations due to household contacts may be attributable to an ever-expanding list of people at high risk of influenza-related complications.

For example, in 2007-08 NACI added all pregnant women regardless of trimester to the list of people at high risk of influenza-related complications. This may partly explain the increase in the proportion of children who received a publicly funded vaccine due to household contact in Season 4. Relatively few children were coded as getting an influenza vaccine based on having a chronic condition or having to purchase the vaccine.

Reasons for non-vaccinations

Reasons for not getting vaccinated for influenza or any pertussis-containing vaccine were explored. This information is collected when a child is at a community health centre for a reason that may or may not be for an immunization, and the nurse offers the child a vaccine according to the recommended vaccination schedule. Parents may refuse for several reasons, including inconvenience and philosophical opposition. A parent who "refused" a vaccine therefore does not necessarily indicate that the parent is opposed to the vaccine.

A much higher proportion of non-vaccinations for influenza are coded as "parent refusals" (range: 79 to 96%) compared to those for pertussis-containing vaccines (range: 17 to 27%). This is despite the

fact that there are more opportunities to refuse a pertussis-containing vaccine due to the routine immunization schedule that requires children to be vaccinated for pertussis at two, four, six and 18 months of age, and again between the ages of four and six years. These findings may be explained by the reason for the clinic visit. It is likely that most visits to a public health clinic are made for a reason other than influenza vaccination, such as to receive a different vaccine. It is possible that when a nurse notices that a child has not received his or her seasonal influenza vaccine and offers to administer it, the parent might refuse it for reasons such as: the child already received a vaccination for a different antigen that day; or the family would like to come back another time for the influenza vaccine. Unfortunately, information on the reason for clinic visit is not included in the study data and therefore cannot be explored.

It is also possible that non-vaccinations occurred because parents had concerns about adverse events related to the influenza vaccine, or perceived that their children are not at risk or that the vaccine is ineffective. This is consistent with the data from a Calgary-based study on parental beliefs and behaviours about influenza immunization, in which most non-vaccinations among young children occurred because

a parent thought the vaccine was unnecessary(88). As shown in other studies, parental concerns about vaccine safety influence vaccinations rates among children(98, 99). The researcher attempted to explain non-vaccinations by examining children who consistently refused both pertussis and influenza vaccinations, perhaps due to a negative family belief about vaccines. However, very few children in this study refused both vaccines.

Objectives 2 and 3: Estimating vaccination coverage and exploring for an association between income and getting vaccinated

Estimates of adequate vaccination coverage among all children younger than nine years of age ranged between 7 and 14% over the four seasons, with the largest annual rate occurring in 2005-06. The 2004-05 adequate vaccination coverage rate is underestimated and subsequently the partial rate is overestimated due to censorship of the previous year's vaccination data. Some children are effectively misclassified as partially vaccinated when in fact they are adequately vaccinated for the season. To try to quantify the extent of the misclassification, one could look at how many children in 2005-06 switched from partially vaccinated to adequately vaccinated after considering the previous year's vaccination history. The data showed

that in 2005-06, 14,297 of 29,041 children were considered adequately vaccinated for the season. Of those 14,297 adequately vaccinated children, 2,415 (17%) received one dose in 2004-05 and a second dose in 2005-06, compared to 11,882 (83%) who received two doses in 2005-06. One could infer that perhaps the same proportion of children would be reclassified from partially vaccinated to adequately vaccinated in 2004-05.

Coverage rates varied by age but not by sex. Children under the age of two years had the highest adequate influenza vaccination coverage rates among the study sample. This might be attributable to the routine immunization schedule that requires children to visit a public health clinic for immunizations at two, four, six, 12 and 18 months of age(91). After the age of 18 months, children are required to return just one more time for immunization, between four and six years of age, according to the routine immunization schedule. These younger age groups are therefore expected to have more frequent access to health services and, as a result, have more opportunities to be immunized against influenza compared to children from older age groups. Although the reason for these visits is not specifically for influenza immunization, the visits represent opportunities for the nurse

to offer an influenza vaccine to these children. To explore this hypothesis, the researcher further stratified the 2007-08 data and found that approximately 75% of vaccinations among children under two years of age occurred in a community health centre, compared to 25 to 45% of vaccinations among children of other ages. Accordingly, approximately 20% of vaccinations among children under two years of age occurred in a mass venue or influenza clinic, compared to 50 to 70% of vaccinations among children of other ages. This variation in the utilization of health services at a community health centre may explain the variation in vaccination coverage by age. Children younger than two years of age were also eligible for publicly funded vaccines during the study period, which might have motivated parents to vaccinate their children in these age groups. Public health nurses might also be more inclined to offer an influenza vaccine to children younger than two years of age since they are considered at high risk for influenza-related complications(3).

Adequate vaccination coverage rates in children two years of age and older appear to decrease consistently with increasing age in all years. This is expected due to the less frequent utilization of health services that comes with increasing age. Public health messaging also advises

parents to vaccinate their children, especially those under the age of two years, but there is less emphasis on vaccinating older children. Improving public health messaging to include recommendations for older children may help to improve vaccination rates in this group.

Urban or rural area of residence

Adequate influenza vaccination rates generally increased with time among children from both rural and urban areas. A more gradual increase was seen among children from urban areas, while a delayed but large increase was seen the following year among children from rural areas. Rates were similar among both groups in the final two years of study.

The change in the CHR boundaries in 2003 could partly explain these findings. In 2003, the CHR expanded to include more rural areas in the region (Appendix A2). The observation of a delayed increase in rural coverage compared to urban coverage may be related to a "catch-up period" as CHR employees learned to standardize and share resources across the different parts of the region. This included the understanding and amalgamation of data sources from two data systems: rural MediPatient™ and urban PHANTIM™. It appears that

coverage rates plateaued between 2006-07 and 2007-08, which could indicate the stabilization of the program after the boundary shift in 2003.

In this study, the city of Airdrie and town of Cochrane were considered rural areas of the CHR, however, over the period 2004-2008, their placement into a rural or urban category by CHR employees varied. Further analysis showed that vaccination coverage rates in Airdrie and Cochrane were higher than the coverage rates in all other areas in the CHR. Accordingly, classifying Airdrie and Cochrane as rural is expected to increase the coverage estimates for rural areas. By inconsistently classifying Airdrie and Cochrane as rural or urban over time, one would expect to see fluctuations in annual coverage rates by rural and urban area of residence. This means that the CHR should specifically consider the rates in Airdrie and Cochrane when exploring for explanations for variation in coverage by urban and rural areas. This again emphasizes the importance of using consistent definitions for the comparison of rates over time.

Social districts and census tracts

By calculating coverage rates for each social district and census tract, it was possible to identify geographic areas with the highest and lowest rates every year. Social Districts 9, 10 and 16 are among those presenting the lowest rates every year. According to the Social District Map (Appendix A9), Social Districts 9 and 10 are part of the urban CHR in the centre and mid-east of the city. Social District 16 is a rural part in the west of the CHR.

This is consistent with the findings for census tracts, since Census Tract 8250043 had the lowest vaccination coverage and is located in Social District 9. Differences in health service utilization by geographic area are discussed further in the Implications section.

Implications of the study findings

Coverage rates among children

This research is important because it provides data on an under-studied population and it also allows for the comparison of influenza vaccination rates over time. Currently Alberta Health and Wellness (AHW) does not publish influenza immunization coverage rates for

children (Svenson, J. 2010 May 7) and estimates over time may not be comparable since AHW's definition of "vaccinated" changed over the study period. In 2004-05, AHW required all the health regions to report the "number of children immunized with the **first dose only** for the entire season." In 2005-06 and 2006-07, this reporting requirement changed to the "number of children who have **complete** influenza immunization for the season." In 2007-08, it changed again to the "number of children who have received **any dose** of influenza immunization for the season." Clearly, these estimates aren't comparable since the numerator in 2004-05 will be relatively larger than those in 2005-06 and 2006-07. The numerator in 2007-08 is expected to be the largest in magnitude due to fewer qualifiers in the definition of "vaccinated." According to unpublished data from AHW, vaccination coverage rates for children under two years of age in Alberta ranged from 40 to 64% from 2004-05 to 2007-08 (Alberta Health and Wellness, 2010 May 2). As expected, the highest vaccination coverage rate among children less than two years of age in Alberta occurred during the 2007-08 season. Hence, rate variance by year may be attributable to changes in program delivery or demand, but may also be due to inconsistent measures for numerator data.

Despite definitional inconsistencies, the rates presented in this paper are comparable to rates reported elsewhere in Alberta and Canada(Alberta Health and Wellness, 2010 May 2)(63). Using unpublished data from AHW, Moran reported that in 2005-06 influenza vaccination rates among children six to 23 months of age ranged from 24 to 52% across six provinces in Canada(63). The highest rate occurred in Alberta (52%). These estimates are for children who received at least one dose of vaccine, not the recommended two doses(63). Using the data from this thesis, the rates in the CHR are similar: by adding the 2005-06 adequate and partial rates together, the coverage rate for children under two years of age was 53%.

The study findings indicate that, although coverage improved over time and may be among the highest in Canada, the large majority of children younger than nine years of age in the CHR are not adequately vaccinated for influenza every year. Most children under nine years of age do not even receive a single dose of influenza vaccine, especially those in the older age groups. These findings emphasize the need to improve vaccination programs in order to improve coverage among this important population.

Increased awareness and parent education about influenza illness and vaccine safety and effectiveness are needed. Parent refusals represented a large proportion of the reasons given for non-vaccinations for influenza in this study. In order to measure whether or not a parent intended to vaccinate or not vaccinate their child for influenza, it would be useful to differentiate between a parent refusal due to disagreement with the vaccine and parent refusal due to inconvenience or intention to return another time. Unfortunately, these analyses were not possible with the data provided. Other studies showed that parents who chose to not vaccinate their children claimed that vaccinations are unsafe or unnecessary(63, 88, 98, 99). Interestingly, one Canadian study showed that 25% of parents who did not vaccinate their children for varicella were simply "undecided" about the vaccine(101).

Another suggestion to improve vaccination rates among young children comes from a recent study that examined the impact of school-based influenza vaccination programs in Ontario. The authors found that school-based delivery is associated with significantly higher vaccination rates and modest reductions in physician visits among school-age children (four to 11 years of age). This is in the context of a universal

publicly funded influenza immunization program in Ontario, which is also offered in Alberta as of 2009. Implementing school-based influenza vaccine delivery programs in the CHR may help to increase rates among school-age children.

Finally, the new provincial immunization and adverse event registry known as ImmARI (Immunization and Adverse Reaction to Immunization) will allow for the production of regular vaccination coverage rates among young children in Alberta. It aims to maintain complete immunization records for all Alberta residents and to reduce the number of unnecessary vaccine administrations through the maintenance of accurate and complete vaccination histories. This means that any vaccines administered within Alberta but outside of the CHR would be routinely captured in the system. The use of standardized definitions and methods across the province will further strengthen the data. However, national definitions of "vaccinated" may still vary by year and thus careful consideration is required for interpreting estimates over time.

Coverage variation by age, geographic area and income

This study showed different vaccination rates among children in different areas of the CHR. These variations in coverage may be explained by a behavioural model that predicts health service utilization.

As outlined by Andersen, health facilities must first be available where people live and work. Second, "people must have the means and know-how" to access and use those services(102). This is presented in a model initially developed by Andersen in the 1960s demonstrating that health service utilization can be predicted by predisposing, enabling, and need factors(102). This framework is illustrated in the Appendix (Appendix A10).

Predisposing factors include demographic variables (e.g., age, sex), social structure variables (e.g., education, employment, ethnicity, culture) and health belief variables (e.g., attitudes, values, knowledge). Enabling factors include access to regular sources of care, health insurance coverage, and income. Need factors include both actual and perceived need for care or level of illness. Revised versions of the model included health system factors such as the availability

and organization of resources such as physicians and hospitals(102, 103).

Applying this framework to the current study, perhaps there is some attribute about the populations from areas of low coverage that make them less likely to be vaccinated, or similarly about the populations from areas of high coverage that make them more likely to be vaccinated. For example, the people from these areas may differ by predisposing factors such as level of education. Other studies have shown that social variables such as family size, parental education, and parental employment could also play a role in influencing vaccination rates(104, 105). Unfortunately, these data were not available in this study, so these avenues could not be explored further.

Eligibility for free vaccines is an enabling factor to vaccination. Likewise, low income could have been an impeding factor to vaccination in Alberta when an out-of-pocket expense was required to purchase the vaccine. It follows that families with lower incomes and whose children are not eligible for publicly funded vaccines may be less likely to be vaccinated.

This is supported in the literature. One Canadian study examined disparities in childhood immunizations and found that parents who were not up-to-date with the immunization schedule for their children were more likely to have lower family income(105). The study also found that childhood coverage rates were significantly lower in low-income neighbourhoods compared to high-income neighbourhoods(105).

However, providing free vaccines may not be sufficient for eliminating vaccination coverage disparities by income. This is supported by the school-based study in Ontario that concluded that providing free vaccines to healthy school children may not be sufficient to obtain high vaccination rates among this age group(106). Other factors must be at play, such as parents with low income having different beliefs about influenza vaccinations compared to parents with high income. Similarly, parents with low incomes who rely on public transportation may not have convenient access to influenza clinics or a job that allows them to take time off work for medical appointments. Although this study found that median household income was not meaningfully associated with vaccination coverage, other socioeconomic variables, such as parental educational attainment, should be considered as

potential predictors of vaccination coverage in future studies. This study may have failed to see an association because the income variable was ecological and not at the individual-level. For more accurate findings, future studies should collect individual-level income when testing for associations with income. It is also possible that this study failed to see an association due to confounding by age. Age meets the definition of a potential confounder in this association because the age of a child is associated with family income, since younger families may have lower incomes, and is an independent predictor of vaccination coverage since children $\leq$2 years of age are considered a priority group for influenza vaccination. Since vaccination coverage rates vary substantially between children $\leq$2 years of age and those >2 years of age, future studies should examine these age groups separately.

Interestingly, one study hypothesized that the absence of public funding implies an unnecessary or less important health service compared to publicly funded services(101). This could have affected parental beliefs about influenza immunization in Alberta prior to the 2009-10 season when influenza vaccines became universally available to all Alberta residents. Prior to 2009, parents may have inferred that

influenza vaccination is not an important health service because, if it was important, the government would provide free vaccines to the public.

Other enabling factors include access to regular sources of care. This introduces the concept of access to health services. Barriers to accessing health services may be physical (e.g., distance to a mass venue site), temporal (e.g., working hours of influenza clinics), socio-cultural (e.g., only English-speaking nurses) or financial (e.g., fees for vaccines or the need to hire a babysitter). All these factors may play a role in coverage variation by geographic area. It would be useful for the CHR to record the details of its program delivery every year and use this information to explain annual variations in coverage and inform future practice.

Effective in the fall of 2009, Alberta implemented a universal publicly funded influenza vaccination program, meaning all Alberta residents can receive free influenza vaccines regardless of age or health condition. Future studies should examine if vaccination rates improve among families or dissemination areas with low MHIs after the

implementation of the universal vaccination program. This research provides baseline data for these analyses.

In Ontario, the universal influenza immunization program led to increases in vaccination coverage in all age groups(107). However, few studies examined the effect of income on vaccination. One study conducted telephone surveys among adults living in the Toronto area and found no association between income and receipt of influenza vaccine after the implementation of the universal immunization program in 2000(108). More studies are needed to determine if a universal program increases vaccination rates specifically in lower income groups due to the removal of a financial barrier to vaccination.

According to the framework, rates may also vary due to need factors. It is possible that people from lower income neighbourhoods are more likely to have a chronic health condition(109). The perceived need for care could thus explain higher coverage rates among children from areas of low income. This was not observed in the current study, however, since MHI was not found to be a significant predictor of vaccination coverage. However, one must keep in mind that the income data in this study were ecological and this study did not

measure coverage specifically for children with chronic health conditions because these data were not available. Future research should consider the association between income and vaccination coverage among children who have and do not have chronic health conditions.

Finally, variation in coverage rates by area of residence may be attributable to health system factors, such as fewer community health centres in some social districts compared to others. Exploring vaccination rates by geographic area (made possible by this research) and overlaying maps of community health centres and mass venue sites may help to explain these results.

Future research

New research questions and ideas for improving the current research evolved throughout this study. The comparison of rates over time might be improved by using modeling techniques that smooth secular trends and can measure the effect of individual years on the data(110). This would help to see if general patterns were similar or different among groups of children, such as those living in rural versus urban areas, or those from areas of high versus low MHI. Better

income data is also needed to better assess its influence on influenza vaccination. Future studies should collect household size data so they can consider Low-Income Cut-Offs (LICOs) generated by Statistics Canada as a meaningful income level cut-off. Obtaining annual income data at the individual level would further strengthen the data and allow for inferences that the associations occur among individuals and not groups. Data on other SES indicators such as family size, parental education, and parental employment would also be useful for future studies.

Publicly funded influenza vaccines are not available in all provinces, so ongoing surveillance of vaccination rates with an income or other SES measure in Alberta is needed to inform future policies in Alberta and in other parts of Canada. These data would also be useful in the evaluation of the new universal influenza immunization program in Alberta.

Study strengths

This study is a very large population-based study that is a good representation of the population of children younger than nine years old in the CHR. The large sample size generated precise estimates, although one must keep in mind that while this may result in statistically significant differences among two groups, these differences may not be clinically important(95). This research is especially useful because it can directly compare surveillance data over four influenza seasons due to the consistent use of definitions and careful consideration for appropriate data sources. It also addresses a gap in the literature as it presents data on an important child age group (two to less than nine years of age) that is rarely studied because these children are not at high risk of complications according to NACI.

Study limitations

There are several limitations to this study. The use of administrative data for this research inherently limits the validity of the data since they were collected for another purpose. The purpose of data collection was, at minimum, to provide individual-level health records for users of public health services. This explains why an income variable is not included in the administrative data file and consequently the researcher needed to obtain income data from another source (2006

Census). The administrative data also allow for public health surveillance, which has a strong emphasis on the tracking of publicly funded vaccines. Vaccines that were purchased by a parent through a physician or private vendor would not be recorded in the MediPatient™/PHANTIM™ system. This can introduce the possibility of systematic error. Systematic error refers to the systematic deviation of results from the truth that would threaten the internal validity of the study(111). This includes selection bias, information bias and confounding.

Selection bias causes a distortion in the study findings as a result of the way in which subjects are selected or retained in a study(111). There is a potential for selection bias in this study since influenza vaccinations that were purchased by a parent and administered by a physician or other private vendor were not recorded in the MediPatient™/PHANTIM™ database. This would result in underestimated coverage rates and would cause an underestimation in the association between income and getting vaccinated. Although it is not possible to measure in this study, this form of bias is expected to have a minimal impact on the results since physicians were given clear instructions to refer all children to public health offices for influenza

vaccination. Future studies should estimate the number of private vaccinations administered to children each year in the CHR.

Further, although the MediPatient™/PHANTIM™ database accounts for most children in the CHR, it may not include those who recently moved to Alberta who have also not yet accessed a school or public health service. Recently moved children between the ages of 18 months and four years are more likely to be excluded from the MediPatient™/PHANTIM™ system compared to children of other ages since they do not require routine appointments with public health nurses and many are too young to enrol in school. The effect of this missing population on coverage rates is unknown since this could cause an over- or underestimation in vaccination coverage based on the vaccination status of those missing children. One could hypothesize that frequently moving children may be less likely to be vaccinated and, therefore, this would cause an overestimation in the rates found in this study.

Measurement bias is a form of systematic error that causes a distortion in the study findings due to inaccurate measurement of data or misclassification of subjects regarding their exposure or outcome

status(111). Categorizing children as unvaccinated, partially vaccinated and adequately vaccinated is expected to be quite accurate since actual age and dates of vaccination were used in conjunction with a single definition of vaccinated. Further, parental recall of historical immunizations is rarely added to MediPatient^{TM}/PHANTIM^{TM} without documentation. Recall bias is therefore of little concern in this study. However, these examples of misclassification could result in non-differential misclassification bias in Objective 3 (exploring for an association between MHI and getting vaccinated), since the probability of erroneous classification on vaccination status is the same for all levels of income. Non-differential misclassification would dilute the true effect between income and getting vaccinated, thereby forcing the observed odds ratio closer to the null value of one.

The use of postal codes to assign children into a rural or urban area, a social district and census tract was also a source of information error. While the child's current postal code was used, the study spanned four years during which a child may have lived at more than one address. Additionally, due to the censorship of data before 2004, some children were misclassified as partially vaccinated when they were adequately vaccinated for the season. Some children were also misclassified with

respect to the reason for vaccination, due to the lack of a reason code hierarchy during the study period.

This study showed that the CHR's verification process to ensure accurate data entry into MediPatient™/PHANTIM™ is not perfect, which can lead to information errors. Duplicate records of influenza vaccinations were identified. Most duplications included one real-time vaccination entry and one historical vaccination entry, in which case the historical record was deleted for these analyses. Other duplications comprised only historical data. This emphasizes the challenge of entering historical vaccination data as they may have many sources, including parental recall, immunization cards, and health records. Duplicate entries could also occur by entering the same data twice at the time of vaccination. For example, a nurse may believe that the vaccination record entered by computer was not saved and therefore re-entered the vaccination data. Nurse unfamiliarity with computers or software is a likely explanation for the relatively small number of duplications identified in the database. More software training or software refinement could help to minimize the number of duplications in MediPatient™/PHANTIM™.

Confounding is a systematic error that causes a mixing of the effects in the data between a predictor and outcome variable due to the presence of an extraneous factor. The extraneous factor must be associated with the exposure, be an independent risk factor for the outcome, and must not be on the causal pathway between exposure and outcome(111). If a confounder is present, the researcher adjusts the estimate accordingly to remove the confounder's effect from the results. In future studies, researchers should consider the effect of household clustering on the association between MHI and getting vaccinated. Household size is associated with level of MHI (exposure) and can also be an independent risk factor for getting vaccinated (outcome) and therefore needs to be considered as a potential confounder in this relationship. Household size, however, could not be examined in this research because there was no clear household identifier in the dataset provided. In future research it may be possible to use household phone numbers or addresses to identify children living in the same household. Careful use of these data is required since some children may have multiple phones per household or may have more than one address, as in the case with divorced parents. Further, the phone numbers or addresses would need to be scrambled or given randomly assigned codes to ensure privacy.

Another limitation is the use of ecological data that can lead researchers to the ecological fallacy. The ecological fallacy occurs when associations among groups of people are used to draw conclusions about associations among individuals. Median household income data are only available at an aggregate level (at the dissemination area level) and therefore no conclusions can be drawn at the individual level.

Conclusions

Children should be a priority for vaccination programs since it is widely accepted that children are key players in the transmission of influenza in communities. According to this study, the large majority of children younger than nine years of age in the CHR are not adequately vaccinated for influenza every year. Vaccination coverage among children was also found to vary by age and geographic area of residence. Although MHI was not found to be significantly associated with vaccination coverage in this study, the literature indicates that other measures of socioeconomic status may influence rates, and these factors should be further explored in future studies.

This research is unique and timely. It is unique because it allowed for the exploration of vaccination trends over four influenza seasons among an under-studied population in the CHR. Rates were described by age, sex and area of residence in order to better understand the demographics of the children in the CHR who were adequately vaccinated for influenza every year. Limitations to the CHR's vaccination system MediPatient™/PHANTIM™ were also identified and recommendations made to improve the data entry process. The research is timely because it provides critical baseline vaccination coverage data for the period before the start of the provincial universal

influenza immunization program and the provincial immunization registry. Future studies should refer to these results for comparison with post-implementation findings.

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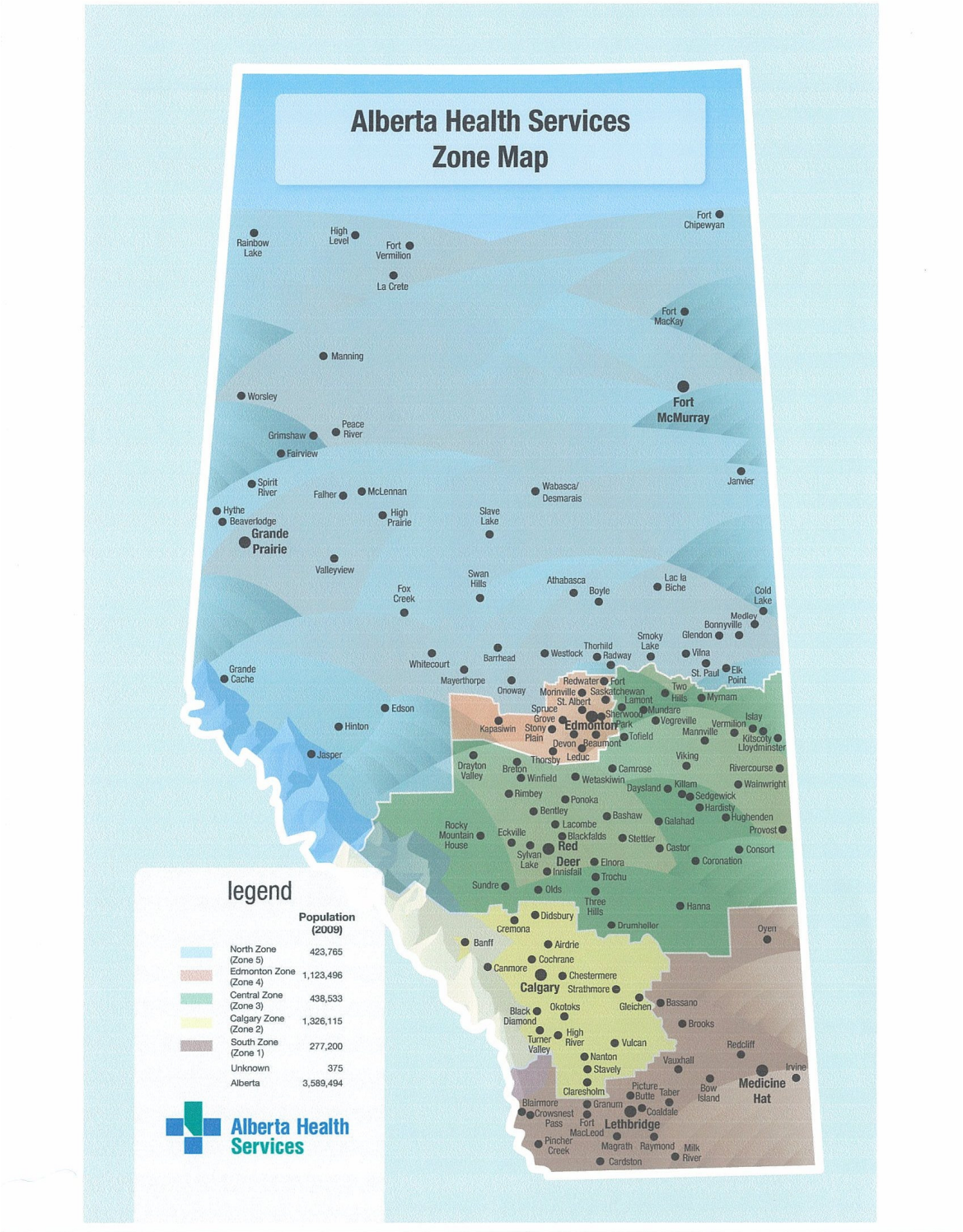
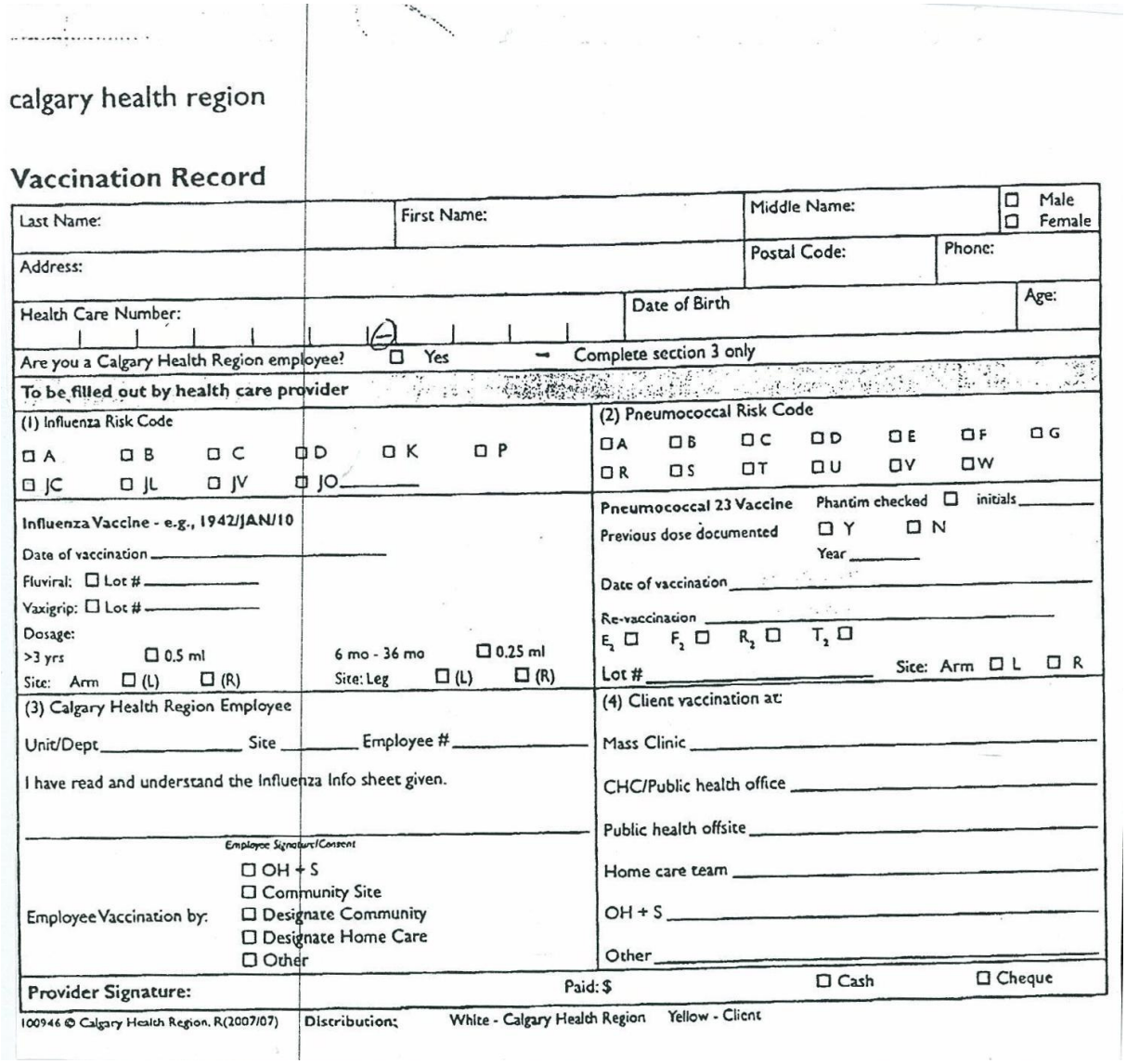
APPENDICES

A1. Alberta Health Services Zone Map



A2. Map of Calgary Health Region, 2003-2008

A3. Form for data entry into MediPatient™/PHANTIM™



calgary health region

Vaccination Record

Last Name:	First Name:	Middle Name:	☐ Male ☐ Female
Address:		Postal Code:	Phone:
Health Care Number:		Date of Birth	Age:

Are you a Calgary Health Region employee? ☐ Yes → Complete section 3 only

To be filled out by health care provider

(1) Influenza Risk Code

☐ A ☐ B ☐ C ☐ D ☐ K ☐ P

☐ JC ☐ JL ☐ JV ☐ JO_____

(2) Pneumococcal Risk Code

☐A ☐B ☐C ☐D ☐E ☐F ☐G

☐R ☐S ☐T ☐U ☐V ☐W

Influenza Vaccine - e.g., 1942/JAN/10

Date of vaccination _____

Fluviral: ☐ Lot # _____

Vaxigrip: ☐ Lot # _____

Dosage:

>3 yrs ☐ 0.5 ml 6 mo - 36 mo ☐ 0.25 ml

Site: Arm ☐ (L) ☐ (R) Site: Leg ☐ (L) ☐ (R)

Pneumococcal 23 Vaccine Phantim checked ☐ initials _____

Previous dose documented ☐ Y ☐ N

Year _____

Date of vaccination _____

Re-vaccination _____

E_1 ☐ F_2 ☐ R_2 ☐ T_2 ☐

Lot # _____ Site: Arm ☐ L ☐ R

(3) Calgary Health Region Employee

Unit/Dept _____ Site _____ Employee # _____

I have read and understand the Influenza Info sheet given.

_____

Employee Signature/Consent

Employee Vaccination by:

☐ OH + S
☐ Community Site
☐ Designate Community
☐ Designate Home Care
☐ Other

(4) Client vaccination at:

Mass Clinic _____

CHC/Public health office _____

Public health offsite _____

Home care team _____

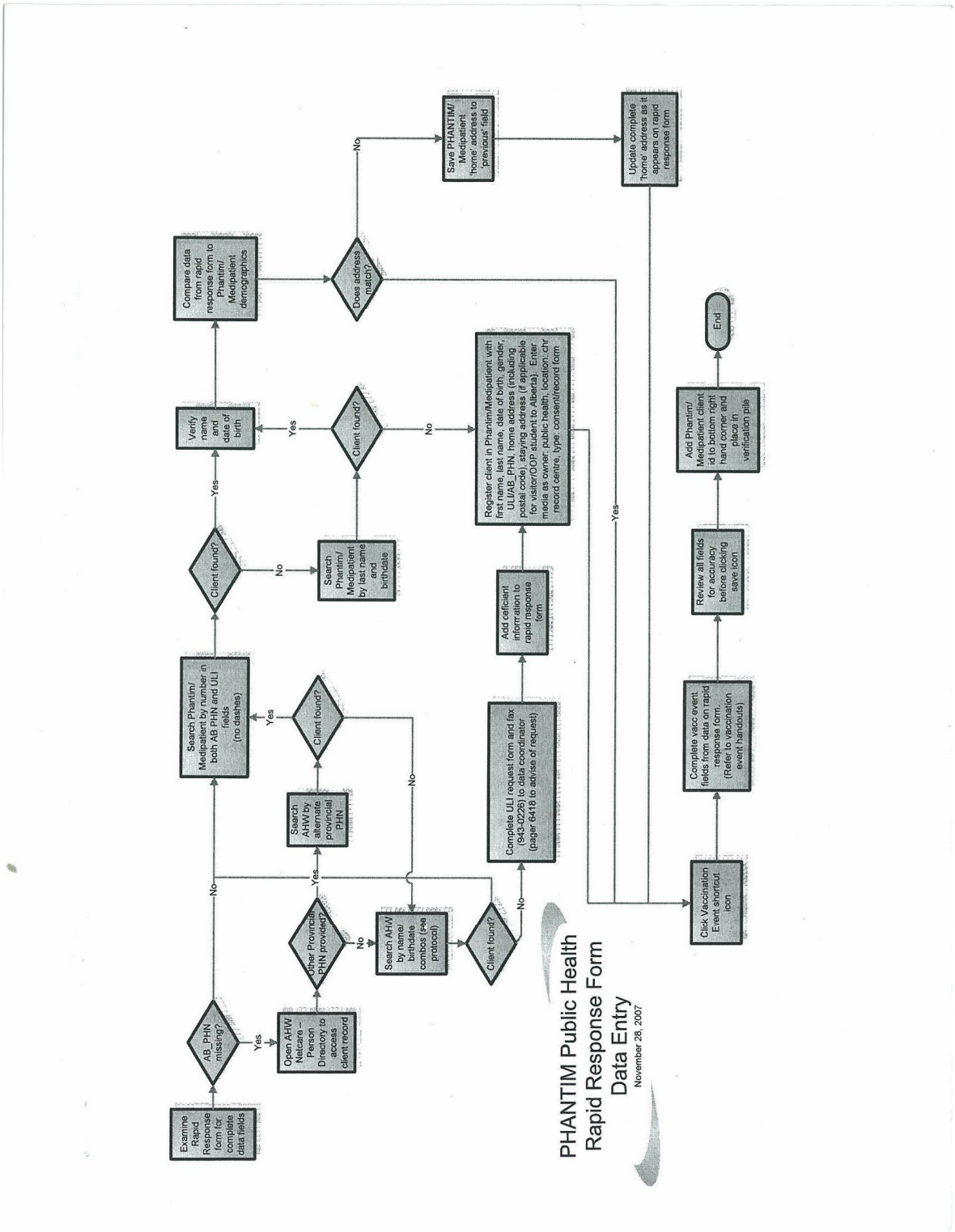
OH + S _____

Other _____

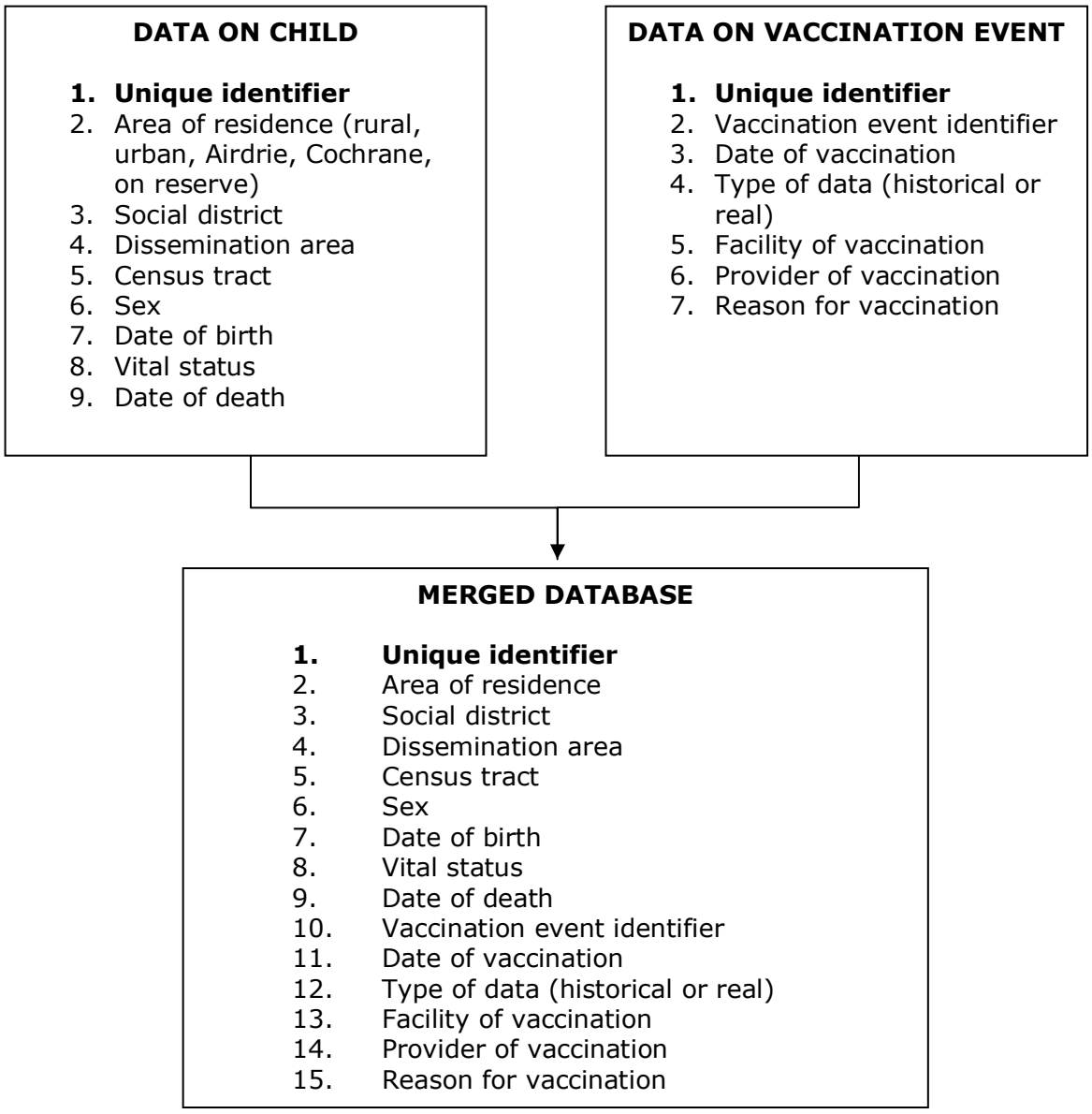
Provider Signature: Paid: $ ☐ Cash ☐ Cheque

100946 © Calgary Health Region. R(2007/07) Distribution: White - Calgary Health Region Yellow - Client

A5. PHANTIM^{TM} Public Health Data Entry and Verification Forms



A6. Diagram of study data file merging



A7. Pertussis-containing vaccines recorded in MediPatient™/PHANTIM™

Number	Vaccine	Name or Acronym
1	acellular Pertussis	aP
2	Diphtheria / whole cell Pertussis / Tetanus	DPT
3	Diphtheria / whole cell Pertussis / Tetanus / Inactivated Polio Vaccine	DPTP
4	Diphtheria / whole cell Pertussis / Tetanus / Inactivated Polio Vaccine / Haemophilus influenzae type B	DPTPHib
5	Diphtheria / Tetanus / acellular Pertussis	DTaP (Tripacel)
6	Diphtheria / Tetanus / acellular Pertussis	dT-ap (Adacel)
7	Diphtheria / Tetanus / acellular Pertussis / Inactivated Polio Vaccine	DTaP-IPV (Quadracel)
8	Diphtheria / Tetanus / acellular Pertussis (Pentacel) / Inactivated Polio Vaccine / Haemophilus influenzae B	DTaP-IPV-Hib
9	Diphtheria / Tetanus / acellular Pertussis / Inactivated Polio Vaccine / Haemophilus influenzae type B / Hepatitis B	DTaP-IPV-Hib-HB
10	Whole cell pertussis	P
11	Tetanus / Diphtheria / acellular Pertussis	TdaP

A8. Adequate vaccination coverage by census tract, 2007-08

CENSUS TRACT	ADEQUATE VACCINATION COVERAGE	RANK Highest coverage = 1 Lowest coverage = 193
8250001.01	**15.1**	66
8250001.02	**18.5**	13
8250001.03	**10.5**	166
8250001.04	**13.6**	104
8250001.05	**14.0**	93
8250001.06	**18.0**	21
8250001.07	**11.9**	140
8250001.08	**10.8**	157
8250001.09	**13.1**	115
8250001.10	**13.1**	114
8250001.11	**11.6**	146
8250001.13	**12.8**	122
8250001.14	**18.5**	15
8250001.17	**19.5**	7
8250001.21	**17.8**	23
8250001.22	**18.3**	17
8250001.23	**11.4**	150

8250001.24	**16.6**	37
8250001.25	**14.6**	80
8250001.26	**13.3**	110
8250001.27	**15.1**	67
8250001.28	**10.6**	162
8250001.29	**15.8**	49
8250002.02	**10.2**	170
8250002.04	**16.9**	35
8250002.05	**13.8**	99
8250002.06	**18.4**	16
8250002.07	**15.5**	56
8250002.08	**17.8**	22
8250002.09	**18.2**	18
8250002.10	**14.5**	82
8250002.11	**18.7**	10
8250002.12	**12.0**	139
8250002.13	**19.2**	8
8250003.00	**15.4**	57
8250004.00	**14.4**	85
8250005.00	**17.4**	27
8250006.00	**10.6**	165

8250007.01	**14.6**	79
8250007.02	**10.3**	168
8250007.03	**17.8**	24
8250007.04	**14.8**	71
8250008.00	**18.5**	12
8250009.00	**22.2**	3
8250010.00	**14.7**	77
8250011.00	**19.7**	6
8250012.00	**10.6**	163
8250013.00	**17.3**	31
8250014.00	**16.4**	41
8250015.00	**18.2**	19
8250016.00	**17.4**	26
8250017.01	**11.8**	141
8250017.03	**14.1**	91
8250017.04	**14.3**	89
8250017.05	**16.6**	36
8250017.06	**16.1**	45
8250018.00	**14.7**	75
8250019.00	**13.4**	107
8250020.00	**15.5**	52

8250021.00	**11.8**	142
8250022.00	**16.5**	40
8250023.00	**16.0**	47
8250024.00	**13.3**	108
8250025.00	**14.7**	76
8250026.00	**15.1**	65
8250027.00	**15.5**	54
8250028.00	**21.0**	4
8250029.00	**12.3**	133
8250030.00	**11.5**	149
8250031.00	**7.7**	190
8250032.00	**13.1**	113
8250033.01	**13.9**	96
8250033.02	**17.6**	25
8250034.00	**14.8**	74
8250035.01	**12.4**	130
8250035.02	**13.7**	101
8250036.01	**12.9**	119
8250036.02	**10.7**	160
8250037.00	**9.3**	181
8250038.02	**11.0**	155

8250038.03	**11.8**	143
8250038.04	**16.3**	42
8250038.05	**9.6**	180
8250038.06	**11.5**	148
8250038.07	**15.5**	55
8250038.08	**9.2**	182
8250038.10	**13.1**	116
8250038.11	**12.5**	128
8250038.12	**10.0**	174
8250038.13	**13.1**	117
8250038.14	**11.6**	147
8250038.15	**12.0**	138
8250038.17	**11.7**	144
8250038.18	**7.8**	188
8250038.20	**15.2**	63
8250038.21	**7.8**	189
8250038.22	**13.8**	97
8250038.23	**13.7**	103
8250038.24	**17.3**	28
8250038.25	**9.7**	178
8250038.26	**14.4**	86

8250038.27	**12.9**	120
8250038.28	**10.7**	159
8250038.29	**15.8**	50
8250038.30	**10.6**	164
8250039.00	**12.9**	121
8250040.00	**10.4**	167
8250041.00	**14.3**	88
8250042.00	**23.1**	2
8250043.00	**6.2**	193
8250044.00	**7.5**	191
8250045.00	**6.5**	192
8250046.01	**14.8**	72
8250046.02	**11.4**	151
8250047.00	**14.6**	78
8250048.00	**17.0**	34
8250049.01	**14.5**	83
8250049.02	**17.3**	29
8250049.03	**13.3**	109
8250050.01	**9.1**	184
8250050.02	**18.5**	14
8250051.00	**8.2**	187

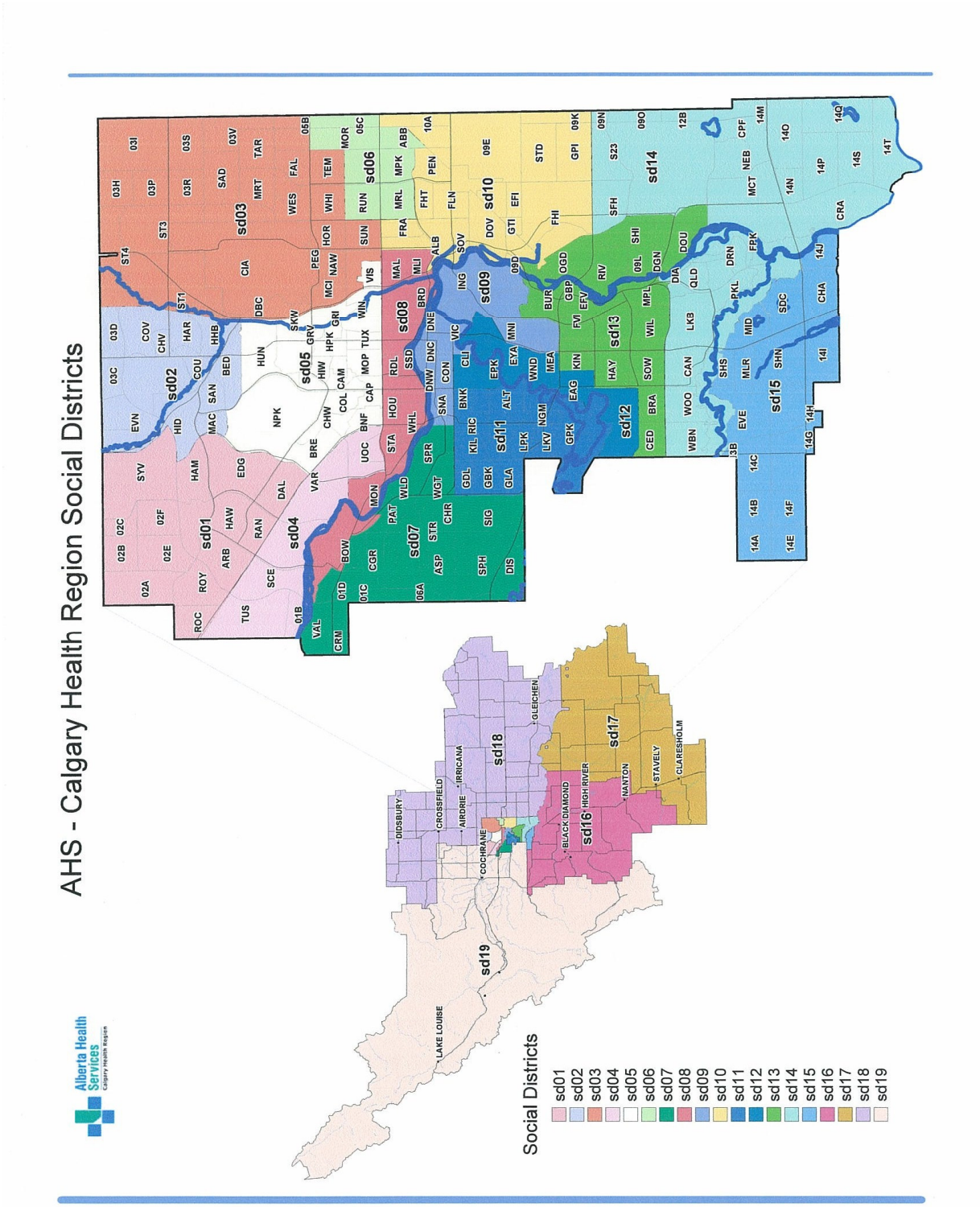
8250052.01	**18.6**	11
8250052.02	**14.5**	81
8250052.03	**15.8**	51
8250052.04	**15.5**	53
8250052.06	**14.0**	94
8250052.07	**12.2**	135
8250052.08	**16.3**	43
8250053.00	**8.8**	186
8250054.00	**17.2**	33
8250055.00	**10.1**	172
8250056.00	**17.3**	32
8250057.00	**13.6**	105
8250058.00	**13.2**	111
8250059.00	**14.0**	95
8250060.00	**11.0**	154
8250061.00	**9.8**	177
8250062.00	**9.1**	183
8250063.00	**14.1**	92
8250064.00	**13.4**	106
8250065.00	**9.8**	176
8250066.01	**20.5**	5

8250066.02	**14.5**	84
8250067.00	**12.7**	125
8250068.00	**16.6**	39
8250069.00	**16.1**	46
8250070.00	**32.1**	1
8250071.00	**10.9**	156
8250072.00	**8.9**	185
8250073.00	**10.2**	169
8250074.00	**15.0**	68
8250075.01	**12.6**	127
8250075.02	**10.2**	171
8250076.01	**9.9**	175
8250076.02	**13.2**	112
8250076.03	**12.3**	132
8250076.04	**12.7**	124
8250076.05	**10.7**	161
8250076.06	**10.8**	158
8250076.09	**12.1**	136
8250076.10	**16.6**	38
8250076.11	**15.2**	60
8250076.12	**12.7**	123

8250076.13	**15.9**	48
8250076.14	**14.8**	73
8250076.15	**11.3**	152
8250077.01	**10.1**	173
8250077.02	**11.6**	145
8250077.03	**15.2**	62
8250077.04	**11.2**	153
8250077.05	**12.6**	126
8250077.06	**14.9**	69
8250077.07	**13.7**	102
8250077.10	**15.1**	64
8250077.11	**12.4**	129
8250077.12	**14.3**	90
8250077.13	**13.8**	98
8250077.14	**12.3**	131
8250077.15	**19.0**	9
8250077.16	**18.1**	20
8250077.17	**14.8**	70
8250200.01	**12.0**	137
8250200.02	**9.7**	179
8250201.00	**15.2**	61

8250202.00	**13.0**	118
8250203.00	**17.3**	30
8250204.00	**14.4**	87
8250205.00	**13.8**	100
8250206.01	**16.2**	44
8250206.02	**15.3**	59
8250206.03	**15.4**	58
8250207.00	**12.2**	134

A9. Map of Social Districts in the Calgary Health Region



A10. Individual determinants of health service utilization (102)