

University of Alberta

**Determinants of immunization coverage by age 2 in a population cohort  
in the Capital Health Region (Edmonton)**

By

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## **Abstract**

The purpose of this study is to evaluate routine childhood immunization coverage rates within the Capital Health (CH) region of Alberta at 24 months of age and identify demographic, socioeconomic factors that are associated with immunization coverage. All children, born between 1 July and 31 December, 2002 and actively registered in the CH region centralized database, were included in the study. Immunization coverage rates were assessed as complete, partially complete or not immunized for each of the five routine childhood vaccines. Logistic regression was employed to compare statistical associations among level of coverage rates. Background variables included mother's age and marital status at the time of delivery; gender of the infants; gestational age; and socio-economic background. The findings of the study demonstrate that childhood immunization coverage rates vary widely in Capital Health region. Analysis from logistic regression suggests that children's socio-economic background had strong impact on immunization coverage rates.

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# Table of Content

1. Introduction . . . . .	1
2. Literature Review . . . . .	3
2.1 Methods . . . . .	3
Search Strategy . . . . .	3
Selection Criteria . . . . .	4
2.2 Results . . . . .	4
Parenta/family barriers . . . . .	5
Economic/socio-economic barriers . . . . .	7
Provider barriers . . . . .	8
System barriers . . . . .	9
2.3 Childhood immunization coverage status in Canada . . . . .	10
2.4 Summary . . . . .	10
3. Review on Logistic Regression . . . . .	12
3.1 Why logistic regression . . . . .	12
3.2 What is logistic regression . . . . .	14
<i>Odds and odds ratio.</i> . . . .	15
Logistic regression model. . . . .	15
Interpretation of the coefficients . . . . .	16
Hypothesis testing . . . . .	18
3.3 Multicollinearity . . . . .	19
3.4 Model selection . . . . .	20
4. Background and Data analysis . . . . .	22
4.1 Capital Health Region Childhood Immunization Programme . . . . .	22
4.2 Data sources . . . . .	24
4.3 Study population . . . . .	24
4.4 Dependent & independent variables . . . . .	25
Dependent variable . . . . .	25
Independent variables . . . . .	26
4.5 Hypothesis . . . . .	30
4.6 Data analysis . . . . .	31
5. Results . . . . .	33
5.1 Demographic and socioeconomic background . . . . .	33
5.2 Childhood immunization coverage rates . . . . .	34
5.3 Significant risk factors . . . . .	37
Univariate logistic regression . . . . .	37
Multivariate logistic regression . . . . .	38
5.4 Summary . . . . .	41
6. Discussion . . . . .	48
7. References . . . . .	53
8. Appendix . . . . .	59

# List of Tables

## TABLE 1

Descriptive Statistics of background variables . . . . . 43

## TABLE 2

Capital Health immunization coverage rates  
(at 2 years of age,  $n = 4,988$ ) . . . . . 44

## TABLE 3

Capital Health immunization coverage rates  
(at 2 years of age,  $n = 4,467$ ) . . . . . 44

## TABLE 4

Capital Health immunization coverage rates  
(at 2 years of age,  $n = 526$ ) . . . . . 45

## TABLE 5

p-values and t-test statistics for testing significance of the  
study childhood immunization complete rates depart from  
herd immunity (90%) . . . . . 45

## TABLE 6

*Odds Ratios* of statistically significant variables in the multivariate  
logistic regression models of five immunization programs :  
Complete vs. Not Vaccinated . . . . . 46

## TABLE 7

*Odds Ratios* of statistically significant variables in the multivariate  
logistic regression models of five immunization programs :  
Complete vs. Partially Complete. . . . . 46

## TABLE 8

*Odds Ratios* of statistically significant variables in the multivariate  
logistic regression models of five immunization programs :  
Partial Complete vs. Not Vaccinated . . . . . 47

## TABLE 9

*Odds Ratios* of statistically significant variables in the multivariate  
logistic regression models of five immunization programs :  
Complete vs. Not Complete (partially complete + not vaccinated) . . . . 47

## Abbreviate

ACC-CDC:	Alberta Advisory Committee on Communicable Disease Control
AH&W :	Alberta Health and Wellness
CHA:	Capital Health Authority
CHN:	Community Health Nurses
CHR :	Capital Health Region
DTaP-IPV :	Diphtheria tetanus, acellular pertussis, polio, <i>Haemophilus influenzae</i> type b
MMR :	Measles, mumps, rubella.
NACI :	National Advisory Committee on Immunization
NICS :	National Immunization Coverage Survey
OECD :	Organization for Economic Co-operation and Development
OLS :	Ordinary Least Squares
OR:	Odd Ratio
PHN:	Public Health Number
RHA:	Regional Health Authorities
UTD :	Up-today
WHO :	World Health Organization

# Chapter 1

## Introduction

Immunization has been considered as a cost-effective public intervention, which has had one of the greatest impacts on the world's health. Because of vaccination, the natural occurrence of smallpox has been eradicated globally since 1977 and paralytic poliomyelitis was reduced by 99% by 1988. In Canada, mortality from diphtheria has been eliminated since 1983 and polio free status has been certified officially since 1994 because of routine immunization programs (Health Canada, 1997). In the United Kingdom, Hib vaccination has prevented about 7,300 cases of Hib disease and 270 deaths in children under 4 years of age over the last 10 years (NHS Immunisation Information). Two million deaths among children under five have been prevented by immunization every year globally (WHO, 2005).

Coverage of routine immunization is one of the important indicators for monitoring progress toward protecting public from vaccine-preventable diseases and evaluating the capacity and performance of the immunization programs. Vaccine coverage need to attain at least 90% of the target population before an interruption of ongoing transmission of vaccine-preventable diseases among the public (herd immunity) has occurred (Lister et al. 1999). Achieving and maintaining high levels of immunization coverage is crucial in reducing epidemics of infectious diseases.

Canada has committed and contributed to improve children's health. Canadian children are protected from contracting debilitating, disabling, and fatal infectious diseases such as polio, tetanus, diphtheria, pertussis, measles, mumps, rubella, *Haemophilus Influenzae* type b and hepatitis B infection due to routine



childhood immunization programs.

In Canada, federal, provincial and territorial governments share immunization responsibilities. The federal government through Health Canada, is responsible for licensing new developed vaccines based on an extensive review of information about safety and effectiveness of the vaccine, recommending the optimal schedule of different vaccines, and ensuring equitable access to health care. Based on the local epidemiologic and financial consideration, the mandate of provincial and territorial ministries of health is to plan their own individual immunization programme, selectively purchase available licensed vaccines on the market, adjust recommended immunization schedule according to the National Advisory Committee on Immunization (NACI), and deliver the immunization to the public (Health Canada, 1997).

Following recommendations from the National Immunization Strategy, Alberta provides universal childhood immunizations for a variety of diseases. The Alberta goal for routine childhood immunization coverage is that 97% of children will receive four doses of DTaP-IPV-Hib and conjugate pneumococcal vaccine, three doses of meningococcal conjugate and 98% will receive one dose of MMR and varicella vaccine by the age of 24 months.

The objective of this project is to evaluate routine childhood immunization coverage rates within Capital Health Region (Edmonton) for babies who were born between July 1 and Dec 31, 2002, until age of 2 years, as well as to identify demographic and socio-economic background factors that have significant impact on those coverage rates.

## **Chapter 2**

### **Literature Review**

This literature review was undertaken to identify risk factors, strategies and policies impacting on childhood immunization levels, as well as to determine inclusion of background variables of this study suggested risk factors in the literature as benchmarks. In addition, national childhood immunization coverage rates were also searched for comparison references of this project.

The literature review included all published studies examining predictors of under-immunization. The literature review focus was framed and defined by specifications relating to geographic location, race, delivery setting and socioeconomic status. The scope included all 14 Canadian jurisdictions and selected developed countries (United States of America, United Kingdom, Australia, New Zealand et al) as well as selected international organization such as World Health Organization (WHO) and Organization for Economic Co-operation and Development (OECD).

#### **2.1 Methods**

##### ***Search Strategy***

A liberal approach was used to cast as wide a net as possible during the process of searching. The review materials included national, international peer-reviewed literature and “grey literature” identified by bibliographic sources of selected papers and data-based searches as well as manual web-based search. The search strategy used a database: PubMed (1994 – 2006). The source of manual web-based searches for “grey literature” included publications, policy documents, research

papers and other documentations, which have been posted on web sites of professional associations, government departments, and national and international health care organizations.

Major components of terms that were used for searching were identified based on the objective of this project. Canadian English-language articles were identified by searching abstracts containing at least one of keywords from each the following components: child, childhood, immunization, immunization program, coverage, status, determinants, and risk factor (Appendix Table A1).

### ***Selection Criteria***

Studies recognized by our search strategy were carefully evaluated based on relevance and quality of study. We included English-language studies that examined immunization coverage rates for infants up to 24 months of age and determined factors that resist improvement of coverage rates in a variety of study designs such as RCT, observational cohort study, case-control study, policy reports and systematic review. Eliminated studies included those evaluating vaccines other than in Alberta routine childhood immunization program (DTaP-IVP, Hib, pneumococcal conjugate, meningococcal conjugate, MMR and varicella); those had study population over 2 years of age; and those were not conducted in desired developed countries. Papers that did not report sufficient information about study approach and statistical analysis strategies and where primary outcome of the study was not immunization coverage were also excluded.

## **2.2 Results**

Over 450 potential relevant abstracts matched at least one of the desired

keywords components and were screened for retrieval. Approximately one tenth of abstracts were considered as relevant and pulled from literature for closer review. 16 articles were included in the final review.

Basically, barriers to immunization identified can be highlighted into four categories: parental/family barriers, economic/socio-economic barriers, provider barriers, and system barriers (Appendix Table A2).

### ***Parental/family barriers***

Of the 16 selected articles, 9 addressed parental barriers which reduced immunization coverage. These barriers included parental/family characteristics and negative parental attitude and beliefs towards immunization. The results are shown below.

#### ***Parental/family characteristics***

The most commonly reported parental or family characteristics associated with incomplete childhood immunization included marital status, maternal age, time interval between pregnancies, number of babies in the family, place of birth, education levels and birth weight.

Haynes and Stone (2004) showed that maternal factors significantly predicted incomplete immunization in children aged 12 to 24 months, including a 12 to 23-month interval between pregnancies, not being married, Aboriginal or Torres Strait Islander or born overseas, younger age, no private health insurance, home birth, and metropolitan place of birth. Low birth weight and singleton birth were also predictors of incomplete immunization in children aged 12 months, but low birth weight was not a significant predictor in children aged 24 months.

Hyatt and Allen (2005) examined the hypothesis that parental disability was inversely related to the timely receipt of early childhood immunization for dependent children. The study confirmed an inverse relationship between parental disability and the timely receipt of early childhood immunization for dependent children. Single parent household, more than 4 persons in the household, and black and other minority race were also negatively and significantly related to child immunization status. College-educated parent and residential stability were positively significantly related to child immunization status.

A cluster randomized control trial conducted by Hambidge and his colleagues (2004) highlighted the factors, like mothers born overseas, not speaking English at home, had an occupation as a student and was an illicit drug abuser, were negatively and significantly associated with childhood immunization.

Gust et al. (2004) also confirmed that young mothers, who had less than 12 years education, having multiple children and having a large family (more than 5 person), were less likely to get their child immunized.

#### ***Attitudes and beliefs towards immunization***

Attitudes, beliefs and concerns towards immunization had been shown as a substantial contributor to under-immunization.

An interview survey of 21 families (Hamilton, 2004) found parental concerns about safety and effectiveness of vaccines, risk of side-effects, multiple vaccines that might overwhelm or weaken childrens' immune systems, and increased numbers of adverse events all significantly influenced parental decision-making on immunizing their babies. Some participants also stated that there was no need to get their children

immunized because of low incident rates of diseases immunized against, protective effect of breast-feeding and use of complementary (alternative) medicine and healthy living to build up immunity.

Studies by Wilson (2000) and Yawn (2000) documented barriers to childhood immunization including parental misperceptions about communicable diseases and vaccines, medical problems of the child at the time of immunization due, concerns about safety of some vaccines, adverse reactions from past immunizations, busy daily work or task schedule, not knowing when the next shot was due, and transportation barriers.

Samad et al (2006) expressed factors like child being unwell or in hospital; parental concerns about vaccine safety; preference for homeopathy and parental concerns that they would feel personally responsible if immunization resulted in a serious adverse effect were related to under-immunization.

Lastly, religion has been claimed as another non-facilitator of childhood immunization (Kimmel, 1996 & Wilson, 2000).

### ***Economic/socio-economic barriers***

7 out of 16 articles touched on economic/socio-economic barrier issues. Economic/socio-economic barriers consist of two components: socio-economic characteristics of the family and cost of immunization services. Studies documented that the most powerful and persistent contributors to under-immunization coverage were low family incomes (poverty) or factors associated with poverty. The most common elements of socio-economic characteristics of the family include family income levels and health insurance coverage (Bate, 1998; Hyatt, 2005; Haynes, 2004;

Hambidges, 1999 & Kimmel, 1996). The cost of immunization services included the cost of the visit to an immunization provider, the fee for vaccine administration and the cost of the vaccine itself.

De Serres, Duval and Boulianne (2002) highlighted that cost apparently had a greater impact on parents than information on varicella complications. Hambidge (1999) also emphasized that cost was a significant barrier to adequate childhood vaccine coverage, especially for uninsured families and for families whose insurance did not cover childhood vaccines. Kimmel et al. (1996) stated that inadequate coverage of immunization services has increasingly fragmented the delivery of immunization. Salsberry and her colleagues (1994) found that cost of the vaccines and lack of insurance coverage were the most frequent cause of delay in immunization for all income classes. Wilson (2000) found lack of cost was, in fact, an incentive to get immunization.

### ***Provider barriers***

Provider characteristics, attitudes, and behaviors were demonstrated as another significant set of barriers to childhood immunization.

Keopke et al. (2001) suggested that pediatricians; number of pediatric patients seen in the past 30 working days; practices of physicians who were willing to give four or more injections simultaneously; practices of physicians who did not defer DTP under false contra-indications; and practices that held in-service training sessions were positively and significantly associated with immunization. Another lead regarding under-immunization was providers' misperception that all vaccines should not be administered simultaneously.

Guttmann et al. (2006) discovered that health care providers with a low volume of pediatric primary care were less than half as likely to provide Up-today (UTD) to their patients. Other factors associated with not being UTD included low continuity of care, and usual provider in practice for less than 5 years. Haynes (2004) also suggested that it is essential to conduct further education of parents and health professionals to ensure that low birth weight babies were fully immunized.

Hamilton (2004) documented that a large proportion of midwives and maternity care specialists ignored their obligation to provide immunization information to parents. As a result, over one third of the sample had decided not to immunize their babies before the birth of their children.

Doctor-patient relationships are also very important to under-immunization. Gust (2004) suggested that more highly educated parents were more likely to trust medical professionals and they tended to discuss their concerns about contraindications with doctors more often. A study also documented that parental satisfaction with the services also led to improvements in immunization (Wilson, 2000).

Davis (1999) stated that some health care providers had not conformed proper immunization schedules to premature or low birth weight babies. Gust (2004) showed that type of provider had significant influences on immunization.

### ***System barriers***

Health system played a critical role in the immunization delivery process. Inconvenience of clinic hours, dates of immunization clinics and locations of clinics were commonly reported as barriers leading to under-immunization (Hambidge,



1999). Other obstacles to receiving vaccines at the immunization at the child's site of primary care included long waiting times, dissatisfaction with the primary care physician and uncertainty as to when the vaccine was due (Hambidge, 1999 & Kimmel, 1996). Wilson (2000) proposed that there was a need for a reminder and tracking system. Also Rodewald (1999) showed that a reminder and tracking system could help improve immunization coverage.

### **2.3 Childhood immunization coverage status in Canada**

Every 2 years, National Immunization Coverage Surveys (NICS) are implemented to assess national coverage rates for routine childhood immunizations (Canadian National Report on Immunization, 2006). Appendices Table A3 displays routine childhood immunization coverage for children aged up to 2 years in 1997, 2002 and 2004.

According to the report, the coverage estimate for MMR was 94% in 2004 and coverage rates for four antigens of a quadrivalent (Quadracel<sup>TM</sup>) vaccine varied widely from lowest 64% (Hib) to 88% (Polio). Coverage estimates for new licensed vaccines, pneumococcal conjugate vaccine and meningococcal conjugate vaccine, were very low in 2004 (Canadian National Report on Immunization, 2006).

### **2.4 Summary**

A literature search was undertaken to help us to scope the study background variables. A large amount of literature was found; however, only 16 matched our selection criteria and have been selected. Barriers highlighted in these 16 articles can be categorized into 4 groups: parental barriers, economic/socio-economic barriers, provider barriers and system barriers.

The literature suggested that younger mothers, whose race other than Caucasian, first language was not English, marital status as not being married, were less likely to get their babies immunized. Low birth weight or premature babies were low in immunization due to both parental misconceptions and provider misconceptions. Low socio-economic status, low health insurance coverage and costs of immunization played critical obstacles. Parents with higher education were more likely not to immunize their babies because of preference of homeopathy and contraindications of immunization.

Studies also showed immunization coverage varied across different practice specialties. Pediatricians had higher immunization coverage than general practitioners or family doctors. Providers' attitudes, beliefs and behaviors also had influences on immunization. Inconvenient services had been recognized as significantly influencing risk factors to under-immunization.

## Chapter 3

### Review of logistic regression

The primary study outcome is status of timely receipt of early childhood immunization. The immunization status will be compared between two groups during each time period among three categories: being completely immunized, partially immunized and not immunized by coding any of these groups to be either 1 or 0. In addition, logistic regression was widely employed in the literature examining risk factors that had significant impacts on childhood immunization coverage when binary dependent variables are presented. Therefore, logistic regression analysis would be suitable in determining significant risk factors.

In this section, I will present a brief review of logistic regression.

#### 3.1 Why logistic regression

Before we review properties of logistic regression, it is worthwhile to know why logistic regression is the optimal technique to analyze dichotomous response variable. Using ordinary linear regression (OLR) analyzing a binary response variable may lead us to a problem (Allison, 1999). The following example is an illustration.

Suppose we are interested in examining effects of race and parental education level on adolescent drug abuse. Our dependent variable **Y, Abuse**, is coded 1 for drug abuse appeared and 0 for drug abuse not appeared. Potential predictors, **Xs**, are coded as: **White**, coded 1 if the adolescent was Caucasian; 0 if the adolescent was an other race than Caucasian. **Edu**: coded 1 if the highest parental education level was at least post secondary; 0 if the highest parental education level was lower than post

secondary. If we attempted to use a multiple linear regression, then the multiple linear regression could be defined as

$$Abuse = \alpha + \beta_1 * White + \beta_2 * Edu + \zeta$$

However, by submitting two values of  $Y$ , the necessary assumptions of OLR are invalid. First,  $Y$  is not a linear function of  $X$ .

The expected value of  $y_i$  can be obtained from

$$E(y_i) = 1 * Pr(y_i=1) + 0 * Pr(y_i=0) = Pr(y_i=1) = p_i \dots \dots (1)$$

as well as

$$E(y_i) = E(\alpha + \beta_1 * White + \beta_2 * Edu + \zeta) = \alpha + \beta_1 * White + \beta_2 * Edu \dots \dots (2)$$

Putting (1) and (2) together, we have

$$p_i = \alpha + \beta_1 * White + \beta_2 * Edu$$

This implies that the probability that  $y=1$  is a linear function of  $X$ , not all value of  $Y$  is a linear function of  $X$ . Furthermore, this relationship is also implausible, especially if  $x$  is a continuous variable because it would predict values of  $p_i$  to be outside of  $(0, 1)$  interval.

Second, the error terms,  $\zeta$ , cannot be approximately normally distributed.

This can be illustrated by a little preliminary algebra.

$$\text{If } y_i = 1, \text{ then } \zeta_i = 1 - \alpha - \beta_1 * White - \beta_2 * Edu;$$

&

$$\text{If } y_i = 0, \text{ then } \zeta_i = -\alpha - \beta_1 * White - \beta_2 * Edu.$$

It is impossible for  $\zeta_i$  to meet the normality assumption if it can take two values.

Third, the homogeneity (equal variance) assumption is also violated.

Since  $X$  is treated as fixed, the variance of  $\zeta_i$  is the same as the variance of  $y_i$ .

$$\text{Var}(\zeta_i) = p_i(1-p_i) = (\alpha + \beta_1 * \text{White} + \beta_2 * \text{Edu})(1 - \alpha - \beta_1 * \text{White} - \beta_2 * \text{Edu})$$

This suggests that variance of  $\zeta_i$  varies as different observations.

Violations of these necessary assumptions of OLR showed that analyzing dichotomous response variable with OLR would be problematic (Hosmer & Lemeshow, 1989). It would produce inefficient coefficient estimates and inconsistent standard error estimates of the true standard errors.

### 3.2 What is logistic regression?

Logistic regression is a form of regression, which extends ordinary multiple linear regression to data sets with a binary or categorical response and any type of independent variables (continuous and/or categorical) (Menard, 1995, Hosmer & Lemeshow, 1989). Similar to OLR, logistic regression requires a sufficiently large sample size and does parametric tests of one or more parameters (Hosmer & Lemeshow, 1989). However, logistic regression has many advantages over OLR. It is not restricted by most assumptions necessary for OLR (Seber, 1977). In addition, logistic regression provides a convenient forum for comparing categorical factors at their different stratum.

Logistic regression is a regression equation, which estimates probability that an individual will have a particular characteristic or will be in a particular event (Sprent, 1969). The estimate of the outcome variable by logistic regression is called *logit* of the proportion, which is obtained by taking nature logarithm of *odds*. Therefore, fundamental concept of logistic regression compresses of *odds* and *odds ratio* (Menard, 1995).

### ***Odds and odds ratio***

*Odds* of an event is defined as a ratio of the probability that an event occurs to the probability that it does not occur (Newman, 2001). Given  $\pi$  represents the probability that a particular event occurs, *odds* can be expressed mathematically as  $O = \pi / (1-\pi)$ . *Odds ratio (OR)* is a ratio of odds of an event occurring in one group to the *odds* of it occurring in another group. It is widely used to assess the association between two categorical variables (Newman, 2001). The value of *OR* lies between 0 and infinity with 1 as a neutral value for which the event is equally likely in both groups. If an *OR* is calculated to be greater than 1, we can conclude that the event is more likely to happen than not. Inversely, if an *OR* is less than 1, the event is less likely to happen than not. The more the *OR* departs from 1, the greater the association between the two groups (Shoukri, 1996)

One advantage of *OR* is that odds ratio is less sensitive to changes in the marginal frequencies than other measures of association (Menard, 1995 and Hosmer & Lemeshow, 1989). In other words, we can easily control the confounding factors when employing analysis method, such as logistic regression.

### ***Logistic regression model***

The logistic model for  $k$  explanatory variables and  $i^{\text{th}}$  individual can be defined as

$$G(x) = \log[\pi/(1-\pi)] = \alpha + \beta_1 X_{i1} + \beta_2 X_{i2} + \dots + \beta_k X_{ik}$$

The left-hand expression is usually referred as the *logit*, which are explained in a linear function of predictors,  $X_s$ . By taking the natural logarithm of *OR*, we remove the boundary of the estimates (i.e. estimates are not restricted within [0, 1] interval as

probability should lie). A positive *logit* suggests the independent variables have the effect of increasing the odds that the event may occur (Menard, 1995 and Hosmer & Lemeshow, 1989).

The coefficients of the logistic regression model,  $\beta$ , can be estimated by three readily available methods: ordinary least squares (OLS), weighted least squares (WLS), and maximum likelihood (Hosmer & Lemeshow, 1989). Using OLS method to estimate logistic model, we would simply take the *logit* transformation of  $\pi$  and regress on predictor variables. Similarly, applying WLS to estimate logistic regression, we could also take *logit* transformation of  $\pi$  and regress on weighted predictors. Moreover, the most commonly used method of estimating logistic regression model is *method of maximum likelihood*. Maximum likelihood estimators rely on iterative methods to obtain “converged” values that maximize the logarithm of the likelihood function, where the likelihood function is defined as the joint probability function of the random variables (Menard, 1995 and Hosmer & Lemeshow, 1989).

### ***Interpretation of the Coefficients***

The logistic regression model,  $G(x)$ , illustrates that *logit* holds a linear relationship with independent variables. Recall, for a linear regression model, coefficient,  $\beta_i$ , represents effect of independent variable,  $x_i$ , on the dependent variable (Seber, 1977). Similarly, in the logistic regression, a coefficient,  $\beta_i$ , implies the change in the *logit* for a change of one unit in the independent variable,  $x_i$ . The change in the *logit* can also be proven equal to *log-OR* (Hosmer & Lemeshow, 1989). Consequently, the coefficient,  $\beta_i$ , can be interpreted as *log-OR*. This can be shown as

the following algorithm.

Consider a situation where independent variable,  $x$ , is also a dichotomous. Then, the *odds* of the outcome being present among individuals with  $x=1$  is defined as  $\pi(1)/(1-\pi(1))$ . And the *odds* of the outcome being present among individuals with  $x=0$  is defined as  $\pi(0)/(1-\pi(0))$ . As a result, *OR* could be computed from

$$OR = \frac{\pi(1)/[1-\pi(1)]}{\pi(0)/[1-\pi(0)]}$$

The *log-OR* is

$$\ln(OR) = \ln\left[\frac{\pi(1)/[1-\pi(1)]}{\pi(0)/[1-\pi(0)]}\right] = G(1) - G(0) = \beta$$

which is equal to the change of the *logit*. Eventually, we have proved that the coefficient,  $\beta$ , is equal to *log-OR*.

To make interpretation of coefficient easier, we can convert a *logit* to an *OR* using exponential function, i.e.  $\exp(\beta)$ , since the probability, the *odds*, and the *logit* are three different ways of expressing exactly the same thing.

When independent variable,  $x$ , has more than two categories, the coefficient,  $\beta$ , can be interpreted as *log-OR* between current value of  $x$  and its reference group. Usually, reference group is set to be the highest/last value of  $x$ . Therefore, the converted *OR*,  $\exp(\beta)$ , indicates the presence of the event in certain group of  $x$  is  $\exp(\beta)$  as large as that in the reference group when other independent factors are held as constants. In multiple logistic regression, the coefficient,  $\beta$ , is also called *adjusted log odd ratio* when other independent factors are held as constants (Hosmer & Lemeshow, 1989)).

Recall, the closer the *OR* is to 1.0, the more equally likely two groups are



independent. An *OR* with a value greater than 1 implies the event is more likely to happen than not. Moreover, an *OR* with a value less than 1 means the event is less likely to happen than not. The more an *OR* departs from 1, the greater the association between the two groups.

### ***Hypothesis Testing***

Hypothesis testing involved in logistic regression can be testing significance of a single independent variable or testing significance of the overall model.

Likelihood ratio test, Wald test and Score test are three common techniques for testing significance of a single independent variable (Hosmer & Lemeshow, 1989). Of these, the likelihood ratio test is the most popular method and it is also called the goodness of fit test (Seber, 1977 and Hosmer & Lemeshow, 1989). The calculation of the likelihood ratio test is very standard for any good logistic regression; therefore, the likelihood ratio test is also flexible for examining the significance of the overall model. The underlying principle of the likelihood ratio test is to compare observed to predicted values by subtracting deviance of the model with the independent variable(s) from deviance of the model without the independent variable(s) based on log likelihood function and multiplying this difference by -2. The resultant statistic has approximately a chi-square distribution with degree of freedom of 1 for testing significance of a single independent variable (Seber, 1977).

The Wald test is obtained by comparing the estimate of the slope,  $\beta$ , and its estimated standard error (Hosmer & Lemeshow, 1989). The Wald test statistic follows a standard normal distribution. Moreover, the Score test is based on the distribution theory of the derivatives of the log likelihood (Hosmer & Lemeshow,

1989). In general, it is a multivariate test requiring matrix calculations. The resulting statistic is also following a standard normal distribution.

If any of above test statistics leads us to a small p-value, i.e. p-value is smaller than predefined significant level; rejection of the null hypothesis has to be made. This implies the significance either of an independent variable or of the overall model (Seber, 1977).

### **3.3 Multicollinearity**

*Multicollinearity* occurs when there are strong linear dependencies among the independent variables. When *multicollinearity* presents, estimates of coefficients would not be affected; however, it is hard to get good estimates of distinct effects for two highly correlated explanatory variables on a dependent variable. Variables that appear to have weak effects, individually, may actually have quite strong effects as a group. Standard errors may get inflated and become large (Huet, 1996). Therefore, it is essential to diagnose multicollinearity before fitting the logistic regression.

Examining the correlation matrix among explanatory variables is one of the helpful procedures to detect *multicollinearity* (Huet, 1996). However, it is not sufficient since it is possible that no pair of variables has a high correlation, but several variables together may be highly interdependent. *Tolerance* and *variance inflation factors* can be used as standard to diagnose *multicollinearity* in addition to examining only correlation matrix (Huet, 1996). The underlying rationale for using *tolerance* is that when there is high *multicollinearity* (i.e. high value of  $R^2$ ), the value of *tolerance* will be low since *tolerance* is obtained by subtracting  $R^2$  from 1. There is no strict cutoff point, but some authors suggest that there might exist a

*multicollinearity* if tolerance below 0.40 (Huet, 1996). *Variance inflation factors*, on the other hand, tells us how “inflated” the variance of the coefficient is, comparing the variance of the coefficient to what it would be if the variable were uncorrelated with any other variable in the model. The higher the degree of variance being inflated is shown, the stronger *multicollinearity* presents (Huet, 1996).

### **3.4 Model Selection**

There are many approaches for evaluating and selecting the “best” model. *Goodness of fit test* is a common procedure used in logistic regression for selecting the “best” model. The *goodness of fit test* is based on  $-2$  times the log likelihood ( $-2LL$ ) statistic, which represents deviance of observed values unexplained in the dependent variables (Linhart & Zucchini, 1986). “*Likelihood*” is a probability that the observed values of the dependent variable may be predicted from the observed values of the independents (Seber, 1977). The  $-2LL$  statistic is the likelihood ratio and has approximately a *chi-square* distribution. This test is testing the difference between two likelihood ratios (two  $-2LL$ ) to examine the significance of a model or significance of individual model parameters (Hosmer & Lemeshow, 1989). If the likelihood ratio statistics lead us to a small p-value, say less than 0.05, rejection of the model has to be made.

The forward stepwise logistic regression method and backward stepwise logistic regression method are two handy approaches to automatically determine which variables to add or drop from the model (Hosmer & Lemeshow, 1989). Forward selection starts with the constant-only model and adds variables one at a time in the order they are best by some criterion until some cutoff level is reached.

Backward selection, on the other hand, starts with all variables and deletes one at a time, in the order they are worst by some criterion. Usually, Rao's efficient score statistics is employed as entry criteria in forward stepwise selection, and any of the likelihood ratio test, the Wald statistic or the conditional statistic can be computed as removal criteria in backward stepwise selection (Hosmer & Lemeshow, 1989)

Stepwise methods, however, do not necessarily identify the "best model" at last. Other procedures are needed to emerge or examine from the results of stepwise selection method for choosing the "final model". We can choose the last step model, where adding or dropping any of variables would not improve the model significance. We also can choose the model with lowest Akaike Information Criterion (AIC) or lowest Bayesian Information Criterion (BIC) (Hosmer & Lemeshow, 1989).

Other procedures also can be employed by testing significance of individual logistic regression coefficients for each independent variable using Wald statistic test or Score statistic test. Unlike OLS,  $R^2$  cannot be compared directly for best model selection since the variance of a dichotomous dependent variable depends on the frequency distribution of that variable (Menard, 1995, Hosmer & Lemeshow, 1989).

## **Chapter 4**

### **Background and Data Analysis**

Following recommendations from the National Immunization Strategy (National Advisory Committee on Immunization, 1997), Alberta provides universal childhood immunizations for a variety of diseases (AH&W, 2002). In this section, we will briefly introduce how childhood immunization was delivered in Capital Health (CH) region and independent and dependent variables included in the study. Statistical analysis method will also be presented.

#### **4.1 Capital Health Region Childhood Immunization Programme**

Alberta childhood immunization is provided free of charge to all infants, preschoolers and school-aged children exclusively through the public health sector by public/community health nurses (CHNs) in Regional Health Authorities (RHA)s and First Nations Health Services (Honish, 2002). RHA provides vaccines on a cost-recovery basis before vaccines are added to the provincial immunization schedule. Approximately 200 CHNs working in the Capital Health Region deliver vaccines to infants, preschoolers and school-aged children. Each of them is expert in the knowledge of vaccines, adverse events and cold chain. The Provincial Health Officers, with advice from the ministry appointed Alberta Advisory Committee on Communicable Disease Control (AAC-CDC) recommend the schedule of routine childhood immunization, define strategies of improving levels of immunization and implement policies for publicly funded immunization programs (Honish, 2002).

The supply of vaccine is centralized at the provincial vaccine depot. The provincial depot ships vaccines to regional vaccine depots. There, vaccines are stored

and refrigerated. The refrigerator temperature is monitored daily to check whether the vaccine has been exposed to a combination of excessive temperature over time and whether it is likely to have been damaged. Centralized vaccine supply makes redistribution as need arises, as well as makes any changes to be simply managed.

Infants, preschoolers and school-aged children can obtain their vaccine from daytime, evening and weekend clinics and at home if necessary. Interpreters are available during the delivery of vaccine when non-English speaking parents are present. Parents are asked to report any adverse events by calling 24/7 health line referred back to Public Health. Vaccine errors, such as a vaccine given to the wrong person, or for the wrong dose, wrong vaccine, wrong time and wrong route, are required to be reported. Reminder letters are sent out to reach those who missed preschool boosters and parents of young children. The regional vaccine system also collaborates with physicians to reach at-risk population, such as hospitalized children. Public Health Nurses will obtain information on children, who have visited pediatric with anaphylactic allergy with eggs within one week.

In the Capital Health region, administrative immunization data are recorded and stored in a centralized database called *Caseworks*. For every child born in the region, individual records are created at birth and updated at each contact with the public health system, including vaccine administration. All parents are contacted by CHN on the day of newborn discharge and 95% are visited in 24 hours. Records of children known to have moved out of the region are inactivated and are therefore not included in coverage rate calculations. Records of children who move into the region are initiated at the time of first contact with the public health system and include

historical information, such as previous vaccination events.

The recommended schedule for children up to 2 years of age is shown in Appendix Table A4. Five recommended vaccines are providing protection for 11 different diseases. Scheduling depends on the age of the child when immunization was started and in case of chickenpox, whether the child has a history of the disease.

#### **4.2 Data sources**

This half-year cohort immunization data came from two sources: Capital Health Authority (CHA) and Alberta Health and Wellness (AHW). The CHA routinely collects childhood immunization information on all eligible children and records children's immunization visits within the region into its centralized database, *Caseworks*. Demographic and socio-economic information was provided by AHW. Missing demographic information was added by searching from the Alberta Central Stakeholder Registry database. Immunization records with the completed Public Health Number (PHN) were merged with the Alberta Stakeholder Registry-based mid-year population to obtain socio-economic information. The Health Surveillance Branch staff, AHW, performed the record cleaning process and scrambled the PHNs to create an anonymous identification for each individual before sending the new immunization data file for analysis.

#### **4.3 Study population**

The study population consisted of all children, newborns and new residents in the CH region of Alberta (2002 boundaries) with records in *Caseworks* and dates of birth between 1 July and 31 December, 2002 ( $n = 4,988$ ). The CHA collected 24 months' immunization data between 1 July, 2002 and 31 December, 2004, on all

study children for five recommended routine childhood immunizations. By 31 December, 2004, all children in the study had reached their age of 2.

The study has recorded University of Alberta medical Research Ethics Board approval.

#### **4.4 Dependent & independent variables**

Based on the results of the literature review and availability of the data, a total of 21 background (demographic and socio-economic) variables were extracted for cleaning and preliminary analysis. In addition, dates on each individual immunization shot that was given to a study subject were also extracted.

##### ***Dependent variable***

The dependent variable was immunization coverage rates, which was evaluated for each of the routine childhood vaccines (DTaP-IPV, Hib, meningococcal conjugate, pneumococcal conjugate, MMR, and varicella) separately. The DTaP-IPV and Hib components of Pentacel<sup>TM</sup> vaccines were evaluated separately, as this is the way in which they are entered into the database.

Coverage rates for each vaccine were assessed by determining the percentage complete, partially complete, not vaccinated and not completed according to primary and alternative AH&W recommendations for ages and intervals between doses (see Appendices Table A4). A child was considered *complete* for a vaccine if he/she received the correct number of doses with adequate spacing between doses. If a child had started a series of vaccines but did not complete the recommended number of doses or had inadequate spacing between doses, that child was considered *partially complete*. A child is considered *not vaccinated* if he/she had not received any doses



of the specific vaccine until his/her second birthday. Finally, a child is considered *not completed* if he/she is considered either *partially complete* or *not vaccinated*.

The numerator of percentage complete, partially complete, not vaccinated or not complete is total number of children who completed, partially complete, was not vaccinated or not complete respectively. The denominator is the total number of children,  $n = 4,988$ . Applicable only to varicella immunization status, the category “immune by disease” is assigned to those children who did not receive the vaccine but who are considered immune because of a recorded history of the disease. These children are not eligible for the vaccine under the AH&W guidelines. Therefore, the denominator for variacella vaccine is calculated by subtracting the number of children who had the disease from the total number of children in the study. Partial completion rates for MMR and varicella vaccines are not applicable since only one dose is required by 2 years of age. The algorithm is also presented in Brown-Ogrodnick (2006).

As each child is assessed as complete, partially complete or not vaccinated for his/her series of recommended vaccine, a numerical value of 0, 1 or 2 were assigned to categorize the study population as not vaccinated, partially complete and complete for each routine vaccine accordingly. Later, a number of binary variables were created to compare *complete* (value 1) and *not immunized* (value 0) groups, *complete* (value 1) and *partially complete* (value 0) groups, and *partially complete* (value 1) and *not immunized* (value 0) groups. These binary variables were used as dependent variables in logistic regression model.

### *Independent variables*

Of 21 background variables, 14 are from administrative data containing demographic characteristics of the study population and their mothers. These demographic characteristics were: gender of child; gestational age of child in weeks; age of mother at time of delivery in years; number of siblings of the baby; hospital delivery; permanent health center; mother's marital status at time of delivery (i.e. single, married, divorced, separated, widower or common law); a variable indicating whether a baby was delivered by a normal vaginal delivery (named Vaginal Deliveries); an indicator variable indicating if a caesarean section occurred (named Caesarean Section); indicator variable indicating whether forceps was used during childbirth (named Forceps); and four indicator variables indicating whether or not a baby was fed by breast milk only (named Breast Fed) or by formula only (named Formula Fed) or by both breast milk and formula (named Breast Fed and Formula Fed) or unknown feeding method (named Feeding Unknown).

Another seven background variables out of 21 included socio-economic information collected from the Alberta Stakeholder Registry based on the mid-year population. They were premium assistance level as Premium assistance level for the fiscal year; premium assistance category; Native Band names; active coverage indicator indicating whether or not the baby had health care coverage; in-migration indicator; out-migration indicator and welfare group of recipient identifier for this study.

A series of data cleaning procedures and a preliminary analysis were performed to condense the number of variables and create new independent variables.

For instance, we manually checked coding of each of four variables, Breast Fed, Formula Fed, Breast Fed and Formula Fed and Feeding Unknown, for the same child. We found most four indicator variables (3,742 out of 4,988) were mutually disjointed (i.e. if the code of variable, Breast Fed, was “Y” for a baby, then for the same baby the code for other 3 variables were “N”, where “Y” meant yes and “N” meant no). Additionally, among jointed cases, 1,234 of them were consistently reported in the variables, Breast Fed, Formula Fed and Breast Fed and Formula Fed (i.e. for the same baby, the code of these three variables were the same with a code of “N” in Feeding Unknown) and the rest of 12 joint cases had code of “N” in Breast Fed, Formula Fed and Breast Fed and Formula Fed but with code of “Y” in Feeding Unknown. As a result, a new variable, Feeding Method, was created with coding of 1 if the baby was fed by breast milk only or both breast milk and formula and a value of 0 if a baby was fed by formula only or feeding method was unknown. Similarly, another new variable, Deliver Method, was created by combining Vaginal Delivery, Caesarean Section and Forceps. Due to a fact that most instrumental vaginal deliveries were by forceps, we consider that a child was a vaginal delivery if coding of Forceps says “Y” for him/her.

Appendix Table A5 displays independent variables that were prepared for analysis. Newborn is classified at birth as premature if he/she was born before 37 weeks gestation (coding=1); as normal if one was born between 37 and 42 weeks gestation; or as late born if he/she was born after 42 weeks gestation (coding =1). Mother’s marital status was also separated into two dummy variables: Marital status as single and Marital status as common-law. The first variable, Marital status as

single, included status of being single, divorced, separated and widower (coding =1) compared with other marital status (coding = 0). Similarly, Marital status as common-law identified mothers' marital status of being in common-law relationship (coding =1) and being in other marital status (coding = 0). Later, location of hospital delivery and location of permanent health center were grouped by within Edmonton (coding = 1) or outside Edmonton (coding =0).

As suggested in the literature, the mothers, who used midwives to deliver their babies, had strong beliefs in Alternative Health Therapies. A new variable, Delivered by a midwife, was designed by assigning 1 to those babies who were delivered by a midwife and 0 to the babies who were born without using a midwife.

As notices, premium assistance category is a summary statistics of premium assistance level as premium assistance level for the fiscal year. They are highly correlated (coefficient correlation,  $r = 85.6\%$ ). Therefore, we dropped premium assistance level as PBF premium assistance level at fiscal year. We created two dummy variables: Welfare Subsidy and Premium Subsidy, examine the different effects of them on the childhood routine immunization coverage rates. Welfare Subsidy compared babies who were in a welfare subsidy program (coding = 1) with those who were not (coding = 0). Premium Subsidy variable separated babies into babies with premium subsidy program (coding = 1) and babies without premium subsidy program (coding = 0).

Among the collected socioeconomic factors, we chose not to use an out-migration indicator and in-migration indicator since frequencies of the two indicators were very low, 0.82% of being in-migration and 0.22% of being out-migration.

Besides this, 11 children did not have health care coverage, and 9 out of them moved out the region during the follow-up period. This implies that most of the children in the cohort covered by health care and the health care effect would be not significant; therefore, we decided to drop the variable when we did modeling.

The variable group “recipient identifier” for this study contained four types of Welfare subsidies: child welfare recipient, general welfare recipient, native welfare recipient and other welfare recipient (referring no-welfare recipients). As a result, three dummy variables were defined: Child Welfare Recipient, General Welfare Recipient, and Native Welfare Recipient. We consider no welfare recipient as the reference group.

Moreover, we kept mother’s age and number of siblings as continuous variables. We also consider that a mother who was between 30 years of age and 40 years of age and had two children at the time delivery as a marker of middle class categories. Therefore, we created an interaction variable called Mother aged 30 to 40 with one other child, representing those mothers who are between 30 and 40 of age and had one child in the family (code =1 and 0 otherwise). Some interaction terms among independent variables were also considered along with the analysis.

#### **4.5 Hypothesis**

The literature suggested that younger mothers, whose races are other than Caucasian, first language was not English, marital status as not being married, were less likely to get their babies immunized. Low birth weight or premature babies were low in immunization due to both parental misconceptions and provider misconceptions. Low socio-economic status, large family size, low health insurance

coverage and costs of immunization played as critical obstacles. Parents with high education were more likely not choose to immunize their babies because of preference of homeopathy and contraindications of immunization.

Accordingly, we hypothesize that babies who had more than one sibling, who were fed by breast milk only or with formula, whose gestational age were not between 38 to 40 weeks or who were delivered by a midwife, would have lower chance getting immunized than others. Marital status other than married and first nation status would also have negative effects on childhood immunization coverage. On the other hand, we assume as mother ages, the chance of a baby getting fully immunized would increase. Moreover, babies who were delivered within the Edmonton area and /or had a permanent health care center within Edmonton were suspected to have more convenient access to health care services; therefore, these babies would have higher probability to be fully immunized. Lastly, recipients of premium or welfare subsidy were assumed to have a negative impact on coverage rates.

#### **4.6 Data analysis**

We performed binominal logistic regression for each specific vaccine, regressing immunization coverage rates on background variables to predict impacts of independent variables on coverage rates. In this procedure, backward stepwise selection was employed. A series of student t-tests were used to examine disparity in our childhood complete immunization rates from 90%, which is required for reaching herd immunity.

A backward stepwise selection procedure was adopted at first in order to get a

sense of which background factors contribute significant impacts on childhood immunization coverage rates. Each independent variable then was added/dropped manually by checking its p-value and comparing  $-2$  log-likelihood score ( $-2LL$ ) between models we obtained.

The standard level of significance of 0.05 was employed to justify a statistically significant effect of each independent variable. The magnitude of evidence for rejecting a null hypothesis, which suggests an independent variable is significant, depends on how large the difference between p-value and the significant level. The more p-value exceeds 0.05, the stronger the evidence that the independent variable does not contribute significantly on the coverage levels at a significant level of 0.05. On the other hand, the more a p-value is smaller than 0.05, the stronger evidence appears.

*Goodness of fit test statistics* was calculated by taking difference between  $-2LL$  of two models to examine the significance of a model or significance of individual model parameters.  $-2LL$  scores are displayed in Model Summary table in SPSS. The underlying theory is that the larger value of *Goodness of fit test statistics* is, the stronger evidence that the model is significant.

All data analysis and modeling were performed in Statistical Package for the Social Sciences (SPSS) version 14.0. As a general rule, SPSS analysis commands omitted any cases with missing values when we perform data analysis and modeling.

## **Chapter 5**

### **Results**

Demographic information and socio-economic background factors of the half-year cohort were examined. This section highlights the major findings of the analysis including distribution of demographic and socio-economic background variables, immunization coverage rates for routine childhood immunization for babies age up to 24 months and significant risk factors that have an impact on immunization rates.

#### **5.1 Demographic and socioeconomic background**

Of the study cohort, 521 children did not have complete demographic information and 434 children did not have complete socio-economic background factors. The information was missing systematically in the database due to the fact that families of these babies moved out/in the region during the follow-up period. We excluded these missing values since the proportion of missing values is less than 10 percent, which would not have huge impact on the final result (Allison, 2001 and Afifi, 1966). Therefore, a final sample consisted of 4,467 children.

Demographic and socio-economic background information is presented in Table 1. Of the final sample population, 2,171 (48.6%) female babies and 2,296 (51.4%) male babies were born in this half-year cohort, only 3.8% of them hold a native status. Age of mothers at time of delivery ranged from 14 years of age to 45 years of age with an average age of 28.96 years. Most of the babies were the first-child (44.1%) or the second-child (35.1%) in the family. 818 (18.3%) babies were the second-child in the family with mothers' age ranging between 30 and 40 years old.

From the deliveries, 74.6 per cent were vaginal deliveries. Delivery by a



midwife occurred only in a small portion, about 0.8%. Most (86.3%) of the delivery took place within Edmonton area. 69% babies had a permanent Health Care Center located within Edmonton area. About 84.9% babies were fed by breast milk only or combination of breast milk and formula.

Socio-economic background factors indicate that majority of babies did not receive any premium subsidy or welfare subsidy. Among welfare recipients, 0.3% of all babies received Child Welfare; 3.7% received General Welfare; and 3.8% of all babies were Native Welfare recipients. Only 2 children were Child Welfare recipients and had one sibling already. There were 50 babies who received General Welfare benefits and were the second child in the family. And 54 babies were born in the families, which were eligible for Native Welfare benefits and were the second baby in the family.

## **5.2 Childhood immunization coverage rates**

The childhood immunization coverage rates were calculated before and after discarding the individuals with missing demographic information (Table 2- Table 4). P-values and t-test statistics resulted in Student t-test were also obtained for the final sample and the sub-sample, which contains all babies with missing information (Table 5).

The immunization coverage rates before discarding 521 babies varied widely. Even some vaccines (DTaP-IVP-Hib, pneumococcal conjugate, and meningococcal conjugate) could be given at the same visit, the coverage rates were different. Meningococcal conjugate vaccine had the highest complete rate (94.2%) and pneumococcal conjugate vaccine had the lowest complete rate (83.8%). MMR had

the second highest complete rate at 93.0% and the complete rates for the rest of three vaccines were around 86%. Over 11% of children started their vaccine series for DTaP-IVP, Hib and pneumococcal conjugate, but only 2.1% of children started their meningococcal conjugate vaccine series and did not complete it. The not vaccinated rates were also widely spread out. The lowest not vaccinated rate was 2.7% for DTaP-IVP. Varicella had highest not vaccinated rates, which was 10.9% (Table 2).

Similarly, the immunization coverage rates after discarding incomplete records also varied widely (Table 3). However, all complete rates were lower than those of original study population. MMR had highest complete rate (86.2%) and pneumococcal conjugate had lowest complete rate (67.0%). Meningococcal conjugate had the second highest complete rate (84.6%) and the complete rate of varicella was at the third place, which was 76.6%. DTaP-IVP and Hib had very close complete rates (71.8% and 70.8%). Partially complete rates increased dramatically compared to those of the original population. The lowest partially complete rate was meningococcal conjugate (3.8%). The other three partially complete rates were over 15%. Not vaccinated rates for discarded study sample were also larger than those of original population. The range of not vaccinated rates was from 7.5% (DTaP-IPV) to 20.7% (varicella). Varicella still had the highest not vaccinated rate. Table 4 presents the estimate of coverage rates for the incomplete records only.

Comparing the coverage rates between two subsets, the percentage complete for all five childhood routine vaccines among babies with missing information were lower than babies that had all demographic information. The complete rates decreased varying from highest in pneumococcal by 18.8% and lowest in MMR by

7.6%. Most of the percentage complete declined over or approximately 10.0% (DTaP-IPV 15.3%; Hib 16.7%; meningococcal 9.6% and varicella 11.4%).

Consequently, percentages partially complete of the discarded subset of the sample were overall higher than those for selected sub-sample (Table 3 & Table 4). Both rates partially complete of DTaP-IPV and Hib among discarded sub-sample are 9.9% higher than those among babies in the final sample. Similarly, percentages not vaccinated for excluded individuals are higher than for included babies.

One of the possible explanations about the inconsistency in coverage rates between missing data and final data could be that the missing demographic and socioeconomic background factors may hide some potential impact on coverage rates. Moreover, missing records or incomplete records on babies' immunization dates where we used to calculate the coverage rates might also lead to lower percentage complete and higher percentage partially complete due to the fact that these babies moved in or out of the Capital Health region. If this is the case, the difference of percentage complete between these two sub-samples could be getting smaller and smaller. Some of these babies might get immunized at some other regions/places. Unfortunately, it is not possible to obtain the exact reason why inconsistent coverage rates have been occurred.

P-values resulted from Student t-tests (Table 5) suggested that herd immunity has been reached among this half-year cohort. There is no evidence indicated the complete immunization rates differed from 90% significantly.

### **5.3 Significant risk factors**

#### ***Univariate logistic regression analysis***

A series of univariate logistic regressions were performed, regressing each background factor on childhood immunization coverage rates individually. The odd ratios (OR) are presented in Appendix Table A6 to Table A9.

When we compared compete vs. not vaccinated (Appendix Table A6), we found that mother's age only had positive effect on variacella vaccine and number of siblings had significantly negative effects on most of these five vaccines except pneumococcal conjugate vaccine. Baby girls were less likely to complete their meningococcal conjugate vaccine and MMR series than baby boys. Babies who were fed by breast milk or fed by combination of breast milk and formula were more likely to be immunized for all five routine vaccines; on the other hand, babies who were delivered by a midwife were less likely to be immunized for all five childhood immunization. Delivery that occurred within Edmonton area had significantly positive impact on completing childhood immunization series.

Appendix Table A7 suggested that as mother ages, the baby was more likely to complete their multi-dose immunization series. Babies who were fed by either breast milk only or a combination of breast milk and formula were also more likely to finish all their multi-dose immunization series than those who were fed by formula alone. Similarly, babies whose mother's age was between 30 to 40 years and who had one sibling already were more likely to complete their series. Table A7 also suggested that the more siblings a baby has, the smaller chance the baby has to complete her immunization series; and the babies who had gestational age longer than

42 weeks would be less likely to be fully immunized. Mother's marital status other than being married had negative effects on completing babies' immunization series. Babies who were enrolled in welfare program were less likely to be fully immunized.

Factors, (Appendix Table A8), including mother's marital status other than being married, babies were delivered in Edmonton hospital or having permanent health care center within Edmonton, and being welfare recipients, all facilitated to start the immunization series. On the other hand, babies who were delivered by a midwife were less likely to start their series.

Finally, when comparing complete vs. not complete (Appendix Table A9), variables, Mother's age, Breast feed only or with formula, Delivery by C-section and Mother aged 30 to 40 with one other child, shown to be significant facilitators of completing immunization series. In contrast, variables, Number of siblings, Single parent marital status, Common-law marital status, Delivery by a midwife and General welfare recipient, were negatively associated with completion of immunization series.

### ***Multivariate logistic regression analysis***

Multivariate logistic regressions were done to analyze all significant risk factors associated with childhood immunization coverage rates. Four comparisons were performed: *complete* (value1) vs. *not immunized* (value 0); *complete* (value1) vs. *partially complete* (value0), *partially complete* (value1) vs. *not immunized* (value0)] and *complete* (value 1) vs. *not completed* (value 0). The odd ratios (*OR*) of each significant risk factor is presented in Table 6 to Table 9.

For each of the five routine childhood immunizations, as the number of siblings increased, the chance of a baby getting immunized decreased. The *OR* for

this sibling effect varied from 0.708 (MMR) to 0.793 (DTaP-IPV and meningococcal conjugate). Type of delivery methods was also significantly associated with completing immunization series, especially when the family used a midwife as their maternity care provider. The presence of a midwife during the delivery had a significant negative association with immunization coverage rates. The *OR* for all five immunizations was less than 0.1, which implies more than a 90 percent chance that these families would not get their children fully immunized. Furthermore, a mother who was in a common-law relationship at the time of delivery was significantly and negatively associated with the MMR coverage rate (*OR*: 0.642)

On the other hand, as the mother aged, coverage rates for MMR and varicella increased (*OR*: 1.05 for MMR and 1.044 for varicella). Mothers aged 30 to 40 years old with one other child were more likely to have their babies immunized than other age group mothers with one other child (*OR* range: 1.601 to 2.248). Babies delivered in an Edmonton hospital were more likely to be fully immunized with Hib (*OR*: 1.882) and those delivered by C-section were more likely fully immunized with pneumococcal conjugate (*OR*: 1.972) and MMR (*OR*: 1.362). Finally, the First Nation was more likely to be fully immunized with variacella (*OR*: 1.794).

Similarly in comparison for complete versus not immunized, Table 7 suggested that the number of siblings had a significantly negative effect on completion of immunization series (*OR* range: 0.620 to 0.657). Marital status other than “married” had a significantly negative impact on completing childhood immunizations. Single mothers had a significant lower chance to finish DTaP-IVP vaccine (*OR*: 0.439), Hib vaccine (*OR*: 0.441), and pneumococcal conjugate vaccine

(*OR*: 0.481) for their children. Mothers in a common-law relationship had larger odds of not completing their babies in a four multi-dose immunization program (*OR* range: 0.384 to 0.450). Babies who had a longer gestational age were more likely to be partially immunized than babies with a normal gestational age (*OR*: 0.666 for DTaP-IVP and 0.674 for Hib). Recipients for the general welfare subsidy program had significantly lower possibilities to complete the four multi-dose vaccines.

Moreover, as mothers aged, the probability of getting the baby fully immunized also increased. Babies who were delivered by C-section also had a positive relationship with complete immunization coverage rates.

We also examined the association among factors, which significantly influenced the decision-making about starting childhood immunization series (Table 8). The factors, which negatively effect decisions to start a routine childhood immunization series, include Mother's Age (*OR* varied from 0.931 to 0.954) for DTaP-IVP, Pneumococcal Conjugate and Meningococcal Conjugate; Midwife delivery (*OR* varied from 0.105 to 0.166) for DTaP-IVP, Meningococcal Conjugate and Hib. On the other hand, being a single-parent (*OR* = 2.659 for Hib and *OR* = 2.775 for Pneumococcal Conjugate), being in a common-law relationship (*OR* increases from 2.279 for Meningococcal Conjugate to 2.581 for Hib) or being a general welfare recipient (*OR* = 9.033 for DTaP-IVP and *OR* = 16.046 for Meningococcal Conjugate, surprisingly) had a large odds of starting a routine immunization series. Moreover, a baby who was delivered in a hospital also located in the Edmonton area (*OR* varied 2.02 for Pneumococcal Conjugate vaccine to 4.26 for Meningococcal Conjugate) also help parents decide to start an immunization

series.

Overall, we compare complete vs. not complete, mother's marital status other than being married had negative effect on completing babies' immunization series; and as number of siblings increased, the chance of a baby got fully immunized decreased. The fact that a baby was delivered by a midwife is not a facilitator for completing immunization series. Babies who had gestation age greater than 42 weeks were less likely get fully immunized, so did recipients of general welfare. Babies who were delivered by C-section were more likely fully immunized. And as mother ages, more babies got fully immunized.

#### **5.4 Summary**

A final number of 4,467 children were included in the study. Estimates of the coverage rate for this cohort varied widely. Significant factors associated with immunization rates indicated that as the mother ages, the immunization rates increase; but as the number of siblings increase, the rates decrease. However, babies who had a mother aged between 30 and 40 years with one other child were more likely to get immunized. Conversely, a mother's marital status as common-law and single-parent was negatively associated with fully completing the vaccine series. Midwives attending delivery was significantly negatively associated with immunization coverage rate. Babies delivered by C-section or in Edmonton hospitals, showed a significant positive association with coverage rates. Being a recipient of welfare or a provincial health care premium subsidy was associated with incomplete immunization series significantly.

Both univariate and multiple logistic models provided consistent results of the



variables that were associated to the coverage rate. Within each model (e.g. complete vs. partially complete) variables that achieved statistically significant parameter estimates got *OR* estimates that were relatively close to each other.

**Table 1. Descriptive Statistics of background variables**

<b>Variables</b>	<b>N (%)</b>	<b>Variables</b>	<b>N (%)</b>
<b>Gender</b>		<b>Location of Hospital of Delivery</b>	
Female	2171 (48.6)	Within Edmonton	3855 (86.3)
Male	2296 (51.4)	Outside Edmonton	612 (13.7)
<b>Siblings</b>		<b>Location of Health Center</b>	
None	1969 (44.1)	Within Edmonton	3083 (69.0)
One	1566 (35.1)	Outside Edmonton	1384 (31.0)
More than one	932 (20.86)	<b>Subsidy recipient</b>	
<b>First-Nations</b>		Welfare Subsidy	648 (14.5)
Yes	168 (3.8)	Premium Subsidy	85 (1.9)
No	4086 (91.5)	None	3521 (82.77)
<b>Delivery Method</b>		<b>Welfare recipient</b>	
Vaginal delivery	3334 (74.6)	Child Welfare	15 (0.3)
C-section	1133 (25.4)	General Welfare	167 (3.7)
<b>Feeding method</b>		Native Welfare	168 (3.8)
Breast feed only or with formula		Others	3904 (91.77)
Formula fed only	3791 (84.9)	<b>Mother aged 30 to 40 with one other child already</b>	
Delivered by a midwife	676 (15.1)	Yes	818 (18.3)
Yes		No	3649 (81.7)
No	35 (0.8)	<b>General Welfare recipient with 1 sibling</b>	
<b>Mother's age</b>	4432 (99.2)	Yes	50 (1.1)
<20		No	4417 (98.9)
20-30	193 (4.32)	<b>Native Welfare recipient with 1 sibling</b>	
>30	2489 (55.71)	Yes	54 (1.2)
<b>Marital status</b>	1785 (39.96)	No	4413 (98.8)
Single parent			
Married	476 (10.7)		
Common-law	3335 (74.65)		
<b>Gestational age*</b>	656 (14.7)		
Premature			
Normal	387 (8.7)		
Late born	3605 (80.7)		
	475 (10.6)		

\* Premature: gestational age < 38 wks; normal: gestational age between 38 and 42 wks; and late born: gestational age > 42 wks.

**TABLE 2. Capital Health immunization coverage rates (at 2 years of age, n = 4,988)**

	<b>DTaP-IPV (or equivalent) n (%)</b>	<b>Hib n (%)</b>	<b>Meningococcal conjugate n (%)</b>	<b>Pneumococcal conjugate n (%)</b>	<b>MMR n (%)</b>	<b>Varicella n (%)</b>
<b>Complete</b>	4,265 (85.5%)	4,278 (85.8%)	4,701 (94.2%)	4,181 (83.8%)	4,641 (93.0%)	4,328 (86.8%)
<b>Partial</b>	590 (11.8%)	570 (11.4%)	107 (2.1%)	560 (11.2%)	N/A	N/A
<b>Not vaccinate d</b>	133 (2.7%)	140 (2.8%)	180 (3.6%)	247 (5.0%)	347 (7.0%)	546 (10.9%)
<b>Immune by disease</b>	N/A	N/A	N/A	N/A	N/A	114 (2.3%)

Table source: A Brown-Ogrodnick, A Hanrahan, J. Loewen, et al. Immunization coverage by age 2 for five recommended vaccines in the capital health region (Edmonton), Table 1. *Canada Communicable Disease Report*, 2006; 32(10): 117-121.

**TABLE 3. Capital Health immunization coverage rates (at 2 years of age, n = 4,467)**

	<b>DTaP-IPV (or equivalent) n (%)</b>	<b>Hib n (%)</b>	<b>Meningococcal conjugate n (%)</b>	<b>Pneumococcal conjugate n (%)</b>	<b>MMR n (%)</b>	<b>Varicella n (%)</b>
<b>Complete</b>	3,891 (87.1%)	3,909 (87.5%)	4,260 (94.2%)	3,832 (85.8%)	4192 (93.8%)	3,929 (88.0%)
<b>Partial</b>	482 (10.8%)	464 (10.4%)	87 (1.9%)	477 (10.7%)	N/A	N/A
<b>Not vaccinated</b>	94 (2.1%)	94 (2.1%)	120 (2.7%)	158 (3.5%)	275 (6.2%)	438 (9.8%)
<b>Immune by disease</b>	N/A	N/A	N/A	N/A	N/A	100 (2.2%)

**TABLE 4. Capital Health immunization coverage rates (at 2 years of age,  $n = 521$ )**

	DTaP-IPV (or equivalent) n (%)	Hib n (%)	Meningococcal conjugate n (%)	Pneumococcal conjugate n (%)	MMR n (%)	Varicella n (%)
<b>Complete</b>	374 (71.8%)	369 (70.8%)	441 (84.6%)	349 (67.0%)	449 (86.2%)	399 (76.6%)
<b>Partial</b>	108 (20.7%)	106 (20.3%)	20 (3.8%)	83 (15.9%)	N/A	N/A
<b>Not vaccinated</b>	39 (7.5%)	46 (8.8%)	60 (11.5%)	89 (17.1%)	72 (13.8%)	108 (20.7%)
<b>Immune by disease</b>	N/A	N/A	N/A	N/A	N/A	14 (2.7%)

**Table 5. P-value and t-test statistics for testing significance of the study childhood immunization complete rates depart herd immunity (90%)**

	DTaP-IPV (or equivalent) t-test (p-value)	Hib t-test (p-value)	Meningococcal conjugate t-test (p-value)	Pneumococcal conjugate t-test (p-value)	MMR t-test (p-value)	Varicella t-test (p-value)
<b>Final sample (N=4,467)</b>	-5.78 ( $7.9 \times 10^{-9}$ )	-5.05 ( $4.6 \times 10^8$ )	12.01 (0.00)	-8.04 (0.00)	10.53 (0.00)	-4.11 ( $4.0 \times 10^{-6}$ )
<b>Sub-missing sample (N=521)</b>	-9.22 (0.00)	-9.63 (0.00)	-3.41 ( $6.5 \times 10^{-4}$ )	-11.15 (0.00)	-2.51 (0.012)	-7.21 ( $6.19 \times 10^{-13}$ )

Table 6. ORs of statistically significant variables in the multivariate logistic regression model of five immunization programs: Complete vs. Not Vaccinated.

Variables	DTaP-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
<i>Mother's age</i>					1.050 (0.000)	1.044 (0.000)
<i>Common-law marital status</i>					0.642 (0.006)	
<i>Number of siblings</i>	0.793 (0.000)	0.777 (0.000)	0.782 (0.000)	0.762 (0.000)	0.708 (0.000)	0.709 (0.000)
<i>Mother aged 30 to 40 with one other child</i>	1.935 (0.049)				2.248 (0.002)	1.601 (0.009)
<i>Delivery by a midwife</i>	0.022 (0.000)	0.043 (0.000)	0.033 (0.000)	0.032 (0.000)	0.079 (0.000)	0.071 (0.012)
<i>Delivery by C-section</i>				1.972 (0.004)	1.362 (0.078)	
<i>Delivery in Edmonton Hospital</i>		1.882 (0.023)				
<i>First Nation</i>						1.794 (0.015)
<i>Edmonton Health center</i>				1.491 (0.021)		

All explanatory variables fitted in the logistic regression were independent

Table 7. ORs of statistically significant variables in the multivariate logistic regression model of five immunization programs: Complete vs. Partial complete.

Variables	DTaP-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
<i>Mother's age</i>	1.085 (0.000)	1.086 (0.000)	1.089 (0.000)	1.085 (0.000)	NA	NA
<i>Single parent marital status</i>	0.439 (0.000)	0.441 (0.000)		0.481 (0.000)	NA	NA
<i>Common-law marital status</i>	0.404 (0.000)	0.384 (0.000)	0.450 (0.001)	0.444 (0.000)	NA	NA
<i>Number of siblings</i>	0.634 (0.000)	0.620 (0.000)	0.657 (0.000)	0.626 (0.000)	NA	NA
<i>Delivery by a midwife</i>	0.288 (0.024)				NA	NA
<i>Delivery by C-section</i>	1.325 (0.039)		2.038 (0.042)		NA	NA
<i>Gestational age &gt; 42 wks</i>	0.666 (0.009)	0.674 (0.012)		0.662 (0.008)	NA	NA
<i>General welfare recipient</i>	0.605 (0.009)	0.606 (0.010)	0.369 (0.042)	0.620 (0.015)	NA	NA

All explanatory variables fitted in the logistic regression were independent

**Table 8. ORs of statistically significant variables in the multivariate logistic regression model of five immunization programs: Partial complete vs. Not Vaccinated.**

Variables	DTaP-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
<i>Mother's age</i>	0.936 (0.003)		0.931 (0.017)	0.954 (0.013)	NA	NA
<i>Single parent marital status</i>		2.659 (0.009)		2.775 (0.003)	NA	NA
<i>Common-law marital status</i>		2.581 (0.003)	2.279 (0.041)	2.564 (0.001)	NA	NA
<i>Delivery by a midwife</i>	0.166 (0.003)	0.105 (0.000)		0.106 (0.001)	NA	NA
<i>Delivery in Edmonton Hospital</i>	2.361 (0.013)	2.308 (0.009)	4.262 (0.002)	2.151 (0.005)	NA	NA
<i>General welfare recipient</i>	9.033 (0.033)		16.046 (0.010)		NA	NA

All explanatory variables fitted in the logistic regression were independent

**Table 9. ORs of statistically significant variables in the multivariate logistic regression model of five immunization programs: Complete vs. Not Complete (partially complete + not vaccinated).**

Variables	DTaP-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
<i>Mother's age</i>	1.077 (0.000)	1.079 (0.000)	1.060 (0.000)	1.065 (0.000)	1.050 (0.000)	1.044 (0.000)
<i>Single parent marital status</i>	0.473 (0.000)	0.477 (0.000)		0.531 (0.000)		
<i>Common-law marital status</i>	0.445 (0.000)	0.428 (0.000)	0.641 (0.013)	0.525 (0.000)	0.642 (0.006)	
<i>Number of siblings</i>	0.637 (0.000)	0.625 (0.000)	0.681 (0.000)	0.645 (0.000)	0.708 (0.000)	0.709 (0.000)
<i>Mother aged 30 to 40 with one other child</i>					2.248 (0.002)	1.601 (0.009)
<i>Delivery by a midwife</i>	0.091 (0.000)	0.109 (0.000)	0.058 (0.000)	0.093 (0.000)	0.079 (0.000)	0.071 (0.012)
<i>Delivery by C-section</i>	1.343 (0.020)		1.744 (0.008)	1.405 (0.004)	1.362 (0.078)	
<i>Gestational age &gt; 42wks</i>	0.685 (0.009)	0.706 (0.019)		0.721 (0.017)		
<i>General welfare recipient</i>	0.665 (0.033)	0.671 (0.039)				
<i>First Nation</i>						1.794 (0.015)

All explanatory variables fitted in the logistic regression were independent

## Chapter 6

### Discussion

Evaluating immunization coverage rates is important for assessing an immunization program and developing strategic plans. This study assessed childhood immunization coverage rates within Capital Health (CH) region for babies who were born between July 1 and Dec. 31, 2002, until the age of 2 years and identified demographic and socio-economic background factors that have a significant impact on those coverage rates.

Overall estimates of childhood immunization coverage within CH region for this half year cohort were encouraging. The CH region had a much higher routine childhood immunization coverage than national coverage in 2004 (Canadian National Report on Immunization, 2006). The CH regional immunization program has done a very good job on promoting childhood immunization by having convenient office hours/sites, providing language interpreters and a reminder system. This achievement also has been reached by CH collaborating with physicians to reach the at-risk population. However, our estimates remained well below the Alberta goal for routine childhood immunization coverage (Alberta Health and Wellness, 2002).

The immunization information of the study population was stored in public health database, *Caseworks*. *Caseworks* is a large database used for case management and it generates data for the calculation of statistics and epidemiological evaluation by Public Health in the CH region. In order to ensure data quality, extensive training involved in data entry and auditing activities were provided to clerical staff. *Caseworks* captures all activities and dates that each individual

interacted with public health sector each time. One advantage of using *Caseworks* is to eliminate recall and interview bias that any survey would encounter.

Coverage estimates calculated for babies who had complete socio-demographic background information was slightly different from the coverage rates published previously for the whole population (Brown-Ogrodnick et al. 2006). The percentage complete for all five routine immunizations are higher in this sub-population than those in the full population. On the other hand, both percentage partially complete and percentage not vaccinated across all five vaccines are lower in the sub-population than those in the full population. This implies that differences in percentages between sub-population and full population may be due to missing records or incomplete records on babies' immunization dates. Coverage rates obtained from the sub-population more precisely describe the true coverage rates in this half year cohort. Missing demographic and socio-economic background factors may also hide some potential impact on coverage rates. Moving in or out of the region could be a key factor for this difference; unfortunately, it is not possible to find out exact reasons why inconsistent coverage occurred.

There is a wide variation in coverage among the recommended vaccines. Complete coverage rates for MMR were higher than for DTaP-IPV-Hib. The number of doses required to complete a DTaP-IPV-Hib series was greater than that required for MMR series. As the number of required doses increases, the rate of complete immunizations decreases. There were 11.3% of babies who were partially covered for DTaP-IPV-Hib at two years, and some of those children who were *partially* covered at that age eventually completed their immunization series. Furthermore,



there is a discrepancy between the completion rate of Hib and the completion rate of DTaP-IPV doses. This is reflective of late onset of immunization schedules, which require fewer doses of Hib, making completion rates of Hib more frequent.

In addition, age of a child when immunization was started could be one possible confounding factor associated with lower not vaccinated rates. As starting age required for a recommended vaccine (Appendix Table A4) increases, the percentage not vaccinated is getting higher. MMR and variacella have higher not vaccinated rates than other recommended vaccines.

Logistic regression analysis was employed to analyze the data. Several demographic, care management and socioeconomic factors were illustrated to have significant association with different immunization coverage. The findings of the study were in line with risk factors that had been suggested in the literature. Low income families have been found to be significantly associated with low coverage rates in the USA (Samad, 2006 & Gust, 2006) and in Australia (Prislin, 1998). Gust et al (2006) and Haynes et al (2004) have found that marital status of the mother as common-law and single-parent was negatively associated with fully completing the immunization. Using a midwife in delivery were shown to have a negative effect in Hamilton's study (2004) conducted in New Zealand. However, some countries that use mainly midwives in delivery, like Finland and Sweden, have nearly 100% coverage rates (WHO 2006). Babies with few siblings had higher probability to get fully immunized than those who had more siblings in the family (Gust, 2006). Contrast to our findings, Gust et al. (2006) suggested that breast-feeding had a significant negative impact on coverage rates and Davis et al (1999) discovered

premature babies had low coverage rates.

There are four limitations of this study. First, although the *Caseworks* database captures the vast majority of children living in the CH region, there is the possibility that some children in this 6-month birth cohort were not included in the sample. In particular, children who have moved into the region and whose families have not made contact with the public health system would not be included. Second, the possibility of a cohort effect exists, although there is no reason to suspect that the cohort sampled in this study differs significantly from those of other children in the region. Third, publication bias may exist since we only selected published English-language articles. Lastly, other potential risk factors, such as mother's education and babies' immigration status, were not available in the data and thus were not included in this study.

Using our data, we could not determine the reason why immunization coverage varied among vaccines. Nevertheless, it appears that we cannot assume that immunization coverage rates for one vaccine will be the same as for another even when administered concurrently. Immunization schedules are becoming more complex when new vaccines are added. Our data suggest that there are differences in uptake and appropriate interventions are needed to reduce differences between vaccines and improve coverage in underserved population groups. In addition the study shows that socio-economic and demographic variables had consistently the same type of association with the immunization coverage rate in different vaccines if they reached a statistically significant level.

The study identified certain groups of children who were less likely to be completely immunized. This information could be used in the future planning of immunization services to target services and provide information to those groups most at risk.

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## Appendix

**Table A1. Search Strategy for Factors/Determinants of Childhood Immunization Coverage**

Database	#	Terms	Date
PubMed	1	factor OR factors	May 2, 2006
	2	determinant OR determinants	
	3	#1 OR #2 Limits: English, Humans	
	4	child OR children OR childhood	
	5	("Immunization/statistics and numerical data"[MeSH] OR "Immunization/trends"[MeSH] OR "Immunization/utilization"[MeSH]) Limits: English, Humans	
	6	("Immunization Programs/statistics and numerical data"[MeSH] OR "Immunization Programs/trends"[MeSH] OR "Immunization Programs/utilization"[MeSH]) Limits: English, Humans	
	7	#5 OR #6 Limits: English, Humans	
	8	cover OR coverage Limits: English, Humans	
	9	rate OR rates Limits: English, Humans	
	10	status Limits: English, Humans	
	11	#8 OR #9 OR #10 Limits: English, Humans	
	12	Search #3 AND # 4 AND #7 AND #11 Limits: English, Humans	

**Table A2. Risk factors were significant associated with childhood immunization coverage rates suggested in selected articles**

Author Year	Country Study Design	Objective	Setting and subjects	Risk factors	
				Positive association	Negative association
Gust 2004	USA Case-control	To examine impacts of parental attitudes, beliefs, and behaviors on childhood recommended vaccines.	A sample of households that participated in the National Immunization Survey were recontacted in 2001. Case subjects were underimmunized with respect to $\geq 2$ of 3 vaccines and control subjects were fully immunized.	<ol style="list-style-type: none"> <li>1. firstborn baby;</li> <li>2. mother's marital status as married;</li> <li>3. high income;</li> </ol>	<ol style="list-style-type: none"> <li>1. Low income;</li> <li>2. number of children in household <math>\geq 4</math>;</li> <li>3. number of vaccine providers <math>&gt; 2</math>;</li> <li>4. not wanting a new infant to receive all recommended vaccines (attitude)</li> <li>5. concern about safety of vaccine (belief) and administration of multiple vaccines (behavior).</li> </ol>
Wilson 2000	USA Survey	Assess parental perceptions regarding children's vaccination and describe parents' evaluation of immunization services.	12 mothers of children younger than age 3 years and underimmunized were interviewed using a semi-structured format.	<ol style="list-style-type: none"> <li>1. lack of cost</li> <li>2. convenient clinic hours, or locations.</li> </ol>	<ol style="list-style-type: none"> <li>1. misperception about infectious diseases and vaccines;</li> <li>2. adverse reactions;</li> <li>3. competing tasks;</li> <li>4. lack of transportation or inconvenient distance and reminder system;</li> <li>5. long office waits.</li> </ol>

Author Year	Country Study Design	Objective	Setting and subjects	Risk factors	
				Positive association	Negative association
Bates 1998	USA Prospective cohort study	Evaluate personal, financial, and structural barriers to vaccination in socioeconomically disadvantaged urban children	Mothers of 399 babies were interviewed in a large municipal teaching hospital.	1. high satisfaction with health care;	1. single parent household 2. no family support 3. no adequate prenatal care; 4. low income; 5. lack of insurance coverage.
Koepke 2001	USA Chart review	Examine impact of background characteristics and provider behaviors on immunization coverage.	In 1997, pediatric, family and general providers in Pennsylvania serving children aged <36 months completed immunization behavior surveys. These responses were linked to patient chart audits for immunization rates.	1. practice specialty as pediatricians; 2. high volume of pediatric practice; 3. physicians' willingness to give 4 or more injections simultaneously 4. not defer DTP	NR
Guttmann 2006	Canada Cohort study	Study the association between immunization coverage and pediatric provider and other health services characteristics.	A cohort of 101570 infants born in urban areas in Ontario, Canada, between July 1, 1997 and June 31, 1998 were examined.	1. frequent well-infant and primary care visit; 2. high volume of pediatric practice	1. lower continuity of care; 2. low income.
Hambidge 1999	USA Cross sectional survey	Determine the health care resources and perceived barriers to care of families attending free vaccine fairs.	A total of 553 consecutive parents or guardians of children receiving vaccine at the fairs were interviewed.	1. frequent well-child care visits;	1. long office waits; 2. inconvenient clinic hours and location; 3. cost of vaccines.

Author Year	Country Study Design	Objective	Setting and subjects	Risk factors	
				Positive association	Negative association
Salsberry 1994	USA Survey	Assess immunization status of 2-year-olds in middle/upper- and lower-income population.	The study group was drawn through a systematic random sample of a computerized frame of birth certificates for births to Franklin County residents from July 1, 1988 to June 30, 1989.	NR	<ol style="list-style-type: none"> <li>1. cost of immunization;</li> <li>2. lack of insurance coverage;</li> <li>3. long office waits;</li> <li>4. inconvenience hours;</li> <li>5. need for advance appointments;</li> <li>6. invalid contraindication to immunization.</li> </ol>
De Serres 2002	Canada survey	Examine impact of vaccine cost and information about complications of varicella on parental decision regarding varicella vaccine.	Parents of 330 infants aged 9 months were interviewed by telephone.	NR	<ol style="list-style-type: none"> <li>1. cost of immunization.</li> </ol>
Kimmel 1996	USA Policy report	Indicate barriers to childhood immunization in order to achieve national goal.	NA	1. lack of cost	<ol style="list-style-type: none"> <li>1. lack of knowledge of vaccine</li> <li>2. misconceptions about precautions and contraindications of vaccines;</li> <li>3. concern about side effects and administration of multiple vaccines;</li> <li>4. failure to track immunization;</li> </ol>

Author Year	Country Study Design	Objective	Setting and subjects	Risk factors	
				Positive association	Negative Association
Samad 2006	UK Cohort study	Examine uptake of primary immunization in infancy and the reasons given by mothers for either incompletely or not immunizing their infants.	A cohort of 18,819 infants born between September 2000 and January 2002 in the UK were included in the study.	NR	<ol style="list-style-type: none"> <li>1. illness of baby at the appointment was due;</li> <li>2. failure to track immunization;</li> <li>3. administrative difficulties;</li> <li>4. concerns about vaccine safety;</li> <li>5. preference for homeopathy.</li> </ol>
Hyatt 2005	USA Observational	Investigate the influence of parental disability on children's timely receipt of childhood immunization.	Observations on 11,997 babies between the ages 2 and 5 years were chosen.	<ol style="list-style-type: none"> <li>1. having health insurance;</li> <li>2. college educated parent(s);</li> <li>3. residential stability.</li> </ol>	<ol style="list-style-type: none"> <li>1. single parent household;</li> <li>2. large family size;</li> <li>3. low income;</li> <li>4. black and other minority race;</li> <li>5. high parental care limitation.</li> </ol>
Haynes 2004	Australia Cohort study	Determine the predictors of incomplete immunization in Victorian children.	Using probabilistic record linkage, all births records in Victoria in 1998 were linked with those of the Australia Childhood Immunization Register	<ol style="list-style-type: none"> <li>1. above average socio-economic status</li> <li>2. multiple birth;</li> <li>3. having private health care;</li> <li>4. delivered in urban hospital;</li> <li>5. using medicare.</li> </ol>	<ol style="list-style-type: none"> <li>1. more than 1 parity;</li> <li>2. 12 – 35 months pregnancy interval;</li> <li>3. Single mothers;</li> <li>4. mother's age &lt; 25 years;</li> <li>5. birthweight &lt; 2500 grams;</li> <li>6. home birth.</li> </ol>

Author Year	Country Study Design	Objective	Setting and subjects	Risk factors	
				Positive association	Negative association
Hambidge 2004	USA Clustered RCT	Measure the effect of a multimodal intervention on immunization rates in an inner-city population.	One-year cohort of 2843 infants born at a hospital in an integrated inner-city health care system were selected.	1. frequent prenatal visits	1. language barrier; 2. mother was a student; 3. mother was illicit drug abused.
Yawn 2000	USA Case-control	Determine the parent-reported barriers associated with underimmunization of infants.	A case-control study of a population-based sample of parents and guardians of children who were either fully immunized or underimmunized at 20 months of age.	NR	1. inconvenient office hours; 2. long office waits; 3. illness of baby at appointment was due; 4. fear of reaction; 5. failure to track immunization; 6. inconvenient transportation.
Davis 1999	USA Case-control	Describe immunization practices for premature and low-birth-weight infants and ascertain risk factors for poor immunization status.	A total of 11580 low-birth-weight and premature infants were enrolled from birth to age 2 months; 6832 of these were continuously enrolled from birth to age 24 months.	1. normal-birth-weight	1. birth weight <1500g 2. premature
Rodewald 1999	USA RCT	Compare and measure the effects and cost-effectiveness of two interventions designed to raise immunization rates.	9 primary care sites serving impoverished and middle-class children.	1. tracking system.	NR

Author Year	Country Study Design	Objective	Setting and subjects	Risk factors	
				Positive association	Negative association
Hamilton 2004	New Zealand cohort	Ascertain the reasons why some parents choose not to immunize their babies and where these parents obtained their immunization information.	Study population consisted of 76 parents declining immunization.	NR	<ol style="list-style-type: none"> <li>1. concern about vaccine safety;</li> <li>2. concern about administration of multiple vaccines;</li> <li>3. adverse events;</li> <li>4. misconception about protective effect of breast-feeding;</li> <li>5. belief in Rudolf Steiner philosophy;</li> <li>6. biased immunization information.</li> </ol>



**Table A3. Routine childhood immunization coverage aged up to 2 years, National Immunization Coverage Survey, 1997, 2002 and 2004 (in percent):**

Antigen	# of doses	1997†(%)	2002(%)	2004‡
<b>Diphtheria</b>	≥ 4	84	77	78
<b>Pertussis</b>	≥ 4	83	75	74
<b>Tetanus</b>	≥ 4	83	74	73
<b>Polio</b>	≥ 3§	85	88	89
<b>Hib</b>	≥ 4	72	64	70
<b>Measles</b>	≥ 1	95	95	94
<b>Mumps</b>	≥ 1	95	94	94
<b>Rubella</b>	≥ 1	95	94	94
<b>Varicella</b>	≥ 1	—	—	32
<b>Pneumococcal conjugate</b>	Up to date dependent on age at first dose	—	11	7
<b>Meningococcal conjugate C</b>	Up to date dependent on age at first dose	—	32	28

+Data from the 1997 immunization survey were based on different methodologies from those used in NICS 2002 and 2004, and may not be appropriate for comparison.

‡The margin of error for the 2004 NICS is estimated to be from 4.2% to 4.4%.

§According to the NACI schedule for routine childhood immunization, dose 3 of inactivated polio vaccine (IPV), given at 6 months, is given for convenience because of its combined administration in the form of Pentacel™. Since children at age 2 years require only 3 doses of IPV, the coverage estimate for this vaccine is calculated for 3 doses.

Source: Division of Immunization, Bureau of Infectious Diseases, Laboratory Center for Disease Control. Health Canada. *Canadian national report on immunization, 2006*. Can Communi Dis Rep 2006;32S3.

**Table A4. Schedule of childhood immunizations in Alberta**

<b>Vaccine</b>	<b>Primary series</b>	<b>Schedule alternations</b>
DTaP_IPV-Hib <sup>#</sup>	2 months 4 months 6 months 18 months	<ul style="list-style-type: none"> <li>• Can be started as early as 6 weeks.</li> <li>• Spacing can be shortened to 4 weeks.</li> <li>• Fourth dose can be given as early as 15 months provided there are <math>\geq 6</math> months between doses 3 and 4.</li> <li>• If DTaP-IPV and Hib are given separately, fourth dose of DTaP-IPV can be given as early as 12 months provided there are <math>\geq 6</math> months between doses 3 and 4.</li> </ul> <p><i>For Hib</i></p> <ul style="list-style-type: none"> <li>• If series starts at 7 to 11 months, two doses spaced 8 weeks apart with a third dose at 18 months (can be given as early as 15 months).</li> <li>• If series starts at 12 to 14 months, one dose with a second dose at 18 months (can be given as early as 15 months).</li> <li>• If series starts <math>\geq 15</math> months, one dose.</li> </ul>
Pneumococcal conjugate	2 months 4 months 6 months 18 months	<ul style="list-style-type: none"> <li>• Can be started as early as 6 weeks.</li> <li>• Spacing can be shortened to 4 weeks (except when series is started at 12 to 23 months).</li> <li>• If series starts at 7 to 11 months, two doses spaced 8 weeks apart with a third dose at 18 months.</li> <li>• If series starts at 12 to 23 months, two doses 8 weeks apart.</li> <li>• If series starts at <math>\geq 12</math> months, one dose.</li> <li>• Third and fourth dose can be given any time after 12 months provided there are at least 8 weeks between doses 3 and 4, and doses 2 and 3.</li> </ul>
Meningococcal conjugate	2 months 4 months 6 months 18 months	<ul style="list-style-type: none"> <li>• If series starts at 4 to <math>&lt; 12</math> months, two doses spaced 8 weeks apart.</li> <li>• If series starts at <math>\geq 12</math> months, one dose.</li> <li>• Spacing can be shortened to 4 weeks.</li> </ul>
MMR <sup>*</sup>	12 months	<ul style="list-style-type: none"> <li>• If dose administered prior to 1 year, consider invalid and give another dose after 12 months</li> </ul>
Varicella <sup>§</sup>	12 months	
<p><sup>#</sup> Diphtheria tetanus, acellular pertussis, polio, <i>Haemophilus influenzae</i> type b.  <sup>*</sup> Measles, mumps, rubella.  <sup>§</sup> if no history of disease or not previously immunized.</p>		

**Table A5: New Defined Demographic/Socioeconomic Independent Variables:**

<b>Independent Variable</b>	<b>Definition (Coding)</b>
Gender	Male = 1; Female = 0.
Breast fed only or with formula	Breast Fed or Breast Fed and Formula Fed = 1 Formula Fed = 0.
Delivery Method	Caesarean Section = 1; Vaginal delivery or Forceps = 0
Premature	Gestational age < 37 weeks = 1; Otherwise = 0.
Late born	Gestational age > 42; Otherwise = 0
Marital status as single	Single, divorced, separated or widower = 1; Otherwise = 0.
Marital status as common-law	Common-law = 1; Otherwise = 0.
Location of Hospital Deliver	Edmonton = 1; Otherwise = 0.
Location of Health Center	Edmonton = 1; Otherwise = 0.
Delivered by a midwife	Using midwife delivery = 1; Otherwise = 0.
First-Nation	Non-First Nation = 1; Otherwise = 0.
Welfare subsidy recipient	Welfare subsidy present = 1; Otherwise = 0.
Premium subsidy recipient	Premium subsidy present = 1; Otherwise = 0.
Child welfare recipient	Child welfare = 1; Otherwise = 0.
General welfare recipient	General welfare = 1; Otherwise = 0.
Mother aged 30 to 40 with one other child already	Yes = 1; No = 0.
Welfare recipients (Child, General, and Native) with 1 sibling	Yes = 1; No = 0.
Mother's Age & Siblings	Continuous variable

Table A6. ORs of statistically significant variables in the univariate logistic regression model of five immunization programs: Complete vs. Not Vaccinated.

	DTap-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
Mother's age	1.002 (0.926)	1.001 (0.947)	0.858 (0.409)	0.983 (0.262)	0.960 (0.741)	1.035 (0.000)
Number of siblings	0.734 (0.000)	0.734 (0.000)	0.999 (0.950)	0.720 (0.000)	1.049 (0.000)	0.733 (0.000)
Gender	0.855 (0.456)	0.856 (0.458)	0.746 (0.000)	0.905 (0.539)	0.723 (0.000)	1.083 (0.428)
Breast feed only or with formula	1.149 (0.627)	1.145 (0.635)	1.213 (0.429)	0.816 (0.413)	1.620 (0.002)	1.260 (0.080)
Delivery by C-section	1.911 (0.023)	1.887 (0.025)	1.982 (0.008)	2.260 (0.000)	1.651 (0.002)	1.344 (0.016)
Premature	1.682 (0.261)	1.679 (0.263)	1.040 (0.907)	1.565 (0.198)	0.991 (0.969)	1.105 (0.590)
Late Born	0.776 (0.420)	0.781 (0.431)	0.896 (0.705)	0.834 (0.467)	0.864 (0.448)	0.853 (0.307)
Single parent marital status	0.859 (0.654)	0.868 (0.676)	1.058 (0.856)	1.164 (0.607)	0.641 (0.011)	0.760 (0.070)
Common-law marital status	0.856 (0.597)	0.855 (0.595)	0.885 (0.630)	1.055 (0.828)	0.519 (0.000)	0.586 (0.000)
Delivery in Edmonton Hospital	3.280 (0.000)	3.283 (0.000)	2.898 (0.000)	2.628 (0.000)	1.215 (0.253)	1.288 (0.063)
Edmonton Health Center	1.265 (0.276)	1.275 (0.260)	1.434 (0.058)	1.511 (0.013)	0.779 (0.076)	0.845 (0.133)
Delivery by a midwife	0.019 (0.000)	0.022 (0.000)	0.029 (0.000)	0.025 (0.000)	0.074 (0.000)	0.071 (0.000)
First Nation	1.996 (0.179)	1.979 (0.185)	1.664 (0.228)	1.447 (0.289)	1.429 (0.176)	1.821 (0.009)
Welfare subsidy recipient	1.066 (0.846)	1.067 (0.843)	1.188 (0.551)	1.171 (0.539)	0.713 (0.037)	0.789 (0.080)
Premium subsidy recipient	1.605 (0.640)	1.575 (0.654)	1.092 (0.903)	0.892 (0.848)	1.034 (0.943)	1.224 (0.612)
Child welfare recipient	4*10 <sup>7</sup> (0.999)	4*10 <sup>7</sup> (0.999)	4*10 <sup>7</sup> (0.999)	6*10 <sup>7</sup> (0.999)	0.904 (0.922)	1.553 (0.671)
General welfare recipient	2.618 (0.341)	2.652 (0.334)	4.187 (0.155)	1.556 (0.454)	0.454 (0.001)	0.579 (0.015)
Mother aged 30 to 40 with one other child	1.844 (0.059)	1.839 (0.060)	1.748 (0.052)	1.225 (0.352)	2.696 (0.000)	1.879 (0.000)

Table A6. ORs of statistically significant variables in the univariate logistic regression model of five immunization programs: Complete vs. Partially Complete

	DTaP-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
Mother's age	1.092 (0.000)	1.090 (0.000)	1.096 (0.000)	1.086 (0.000)	NA	NA
Number of siblings	0.712 (0.000)	0.704 (0.000)	0.700 (0.000)	0.712 (0.000)	NA	NA
Gender	1.041 (0.675)	1.050 (0.616)	0.776 (0.246)	0.998 (0.981)	NA	NA
Breast feed only or with formula	1.768 (0.000)	1.764 (0.000)	1.820 (0.019)	1.726 (0.000)	NA	NA
Delivery by C-section	1.770 (0.000)	1.552 (0.000)	2.417 (0.007)	1.686 (0.000)	NA	NA
Premature	0.896 (0.506)	0.878 (0.437)	0.819 (0.576)	0.865 (0.377)	NA	NA
Late Born	0.716 (0.019)	0.741 (0.041)	0.912 (0.786)	0.735 (0.033)	NA	NA
Single parent marital status	0.367 (0.000)	0.376 (0.000)	0.522 (0.021)	0.388 (0.000)	NA	NA
Common-law marital status	0.385 (0.000)	0.373 (0.000)	0.333 (0.000)	0.417 (0.000)	NA	NA
Delivery in Edmonton Hospital	0.752 (0.066)	0.751 (0.070)	0.569 (0.155)	0.716 (0.036)	NA	NA
Edmonton Health Center	0.609 (0.000)	0.652 (0.000)	0.541 (0.024)	0.625 (0.000)	NA	NA
Delivery by a midwife	0.286 (0.011)	0.473 (0.182)	3*10 <sup>7</sup> (0.999)	0.538 (0.334)	NA	NA
First Nation	1.133 (0.500)	1.046 (0.808)	1.001 (0.998)	0.982 (0.916)	NA	NA
Welfare subsidy recipient	0.523 (0.000)	0.517 (0.000)	0.462 (0.002)	0.552 (0.000)	NA	NA
Premium subsidy recipient	0.751 (0.365)	0.654 (0.165)	1.689 (0.605)	0.605 (0.091)	NA	NA
Child welfare recipient	0.819 (0.793)	0.785 (0.751)	3*10 <sup>7</sup> (0.999)	0.819 (0.000)	NA	NA
General welfare recipient	0.270 (0.000)	0.274 (0.000)	0.211 (0.000)	0.291 (0.000)	NA	NA
Mother aged 30 to 40 with one other child	2.494 (0.000)	2.514 (0.000)	3.786 (0.004)	2.208 (0.000)	NA	NA

Table A6. ORs of statistically significant variables in the univariate logistic regression model of five immunization programs: Partially Complete vs. Not Vaccinated.

	DTap-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR OR (p)	Varicella OR (p)
Mother's age	0.930 (0.000)	0.930 (0.000)	0.919 (0.001)	0.916 (0.000)	N/A	N/A
Number of siblings	0.931 (0.372)	0.940 (0.447)	1.074 (0.431)	0.952 (0.470)	N/A	N/A
Gender	0.821 (0.385)	0.815 (0.367)	1.106 (0.724)	0.907 (0.596)	N/A	N/A
Breast feed only or with formula	0.650 (0.153)	0.649 (0.154)	0.667 (0.243)	0.473 (0.005)	N/A	N/A
Delivery by C-section	1.080 (0.803)	1.215 (0.523)	0.820 (0.630)	1.340 (0.258)	N/A	N/A
Premature	1.878 (0.194)	1.912 (0.182)	1.269 (0.621)	1.810 (0.115)	N/A	N/A
Late Born	1.084 (0.810)	1.054 (0.877)	0.983 (0.969)	1.134 (0.653)	N/A	N/A
Single parent marital status	2.340 (0.016)	2.308 (0.018)	2.028 (0.086)	2.996 (0.000)	N/A	N/A
Common-law marital status	2.223 (0.009)	2.296 (0.007)	2.658 (0.004)	2.531 (0.000)	N/A	N/A
Delivery in Edmonton Hospital	4.362 (0.000)	4.371 (0.000)	5.095 (0.000)	3.671 (0.000)	N/A	N/A
Edmonton Health Center	2.079 (0.002)	1.955 (0.005)	2.651 (0.003)	2.417 (0.000)	N/A	N/A
Delivery by a midwife	0.066 (0.000)	0.046 (0.000)	0.000 (0.998)	0.046 (0.000)	N/A	N/A
First Nation	1.762 (0.295)	1.893 (0.237)	1.662 (0.377)	1.474 (0.390)	N/A	N/A
Welfare subsidy recipient	2.036 (0.037)	2.063 (0.034)	2.574 (0.012)	2.122 (0.006)	N/A	N/A
Premium subsidy recipient	2.136 (0.469)	2.410 (0.400)	0.646 (0.723)	1.475 (0.546)	N/A	N/A
Child welfare recipient	2*10 <sup>7</sup> (0.999)	3*10 <sup>7</sup> (0.999)	N/A*	5*10 <sup>7</sup> (0.999)	N/A	N/A
General welfare recipient	9.712 (0.025)	9.672 (0.026)	19.871 (0.004)	5.349 (0.005)	N/A	N/A
Mother aged 30 to 40 with one other child	0.739 (0.399)	0.731 (0.385)	0.462 (0.153)	0.555 (0.026)	N/A	N/A

Table A6. ORs of statistically significant variables in the univariate logistic regression model of five immunization programs: Complete vs. Not Complete (partially complete + not vaccinated).

	DTaP-IPV (or equivalent) OR (p)	Hib OR (p)	Meningococcal I conjugate OR (p)	Pneumococcal conjugate OR (p)	MMR* OR (p)	Varicella* OR (p)
Mother's age	1.076 (0.000)	1.074 (0.000)	1.010 (0.002)	1.059 (0.000)	0.960 (0.741)	1.035 (0.000)
Number of siblings	0.705 (0.000)	0.699 (0.000)	0.699 (0.000)	0.701 (0.000)	1.049 (0.000)	0.733 (0.000)
Gender	1.008 (0.925)	1.015 (0.870)	0.822 (0.172)	0.974 (0.757)	0.723 (0.000)	1.083 (0.428)
Breast feed only or with formula	1.659 (0.000)	1.652 (0.000)	1.456 (0.035)	1.477 (0.000)	1.620 (0.002)	1.260 (0.080)
Delivery by C-section	1.792 (0.000)	1.602 (0.000)	2.147 (0.000)	1.804 (0.000)	1.651 (0.002)	1.344 (0.016)
Premature	0.973 (0.862)	0.959 (0.790)	0.936 (0.787)	0.978 (0.881)	0.991 (0.969)	1.105 (0.590)
Late Born	0.725 (0.016)	0.748 (0.032)	0.903 (0.646)	0.758 (0.032)	0.864 (0.448)	0.853 (0.307)
Single parent marital status	0.410 (0.000)	0.421 (0.000)	0.751 (0.172)	0.477 (0.000)	0.641 (0.011)	0.760 (0.070)
Common-law marital status	0.429 (0.000)	0.419 (0.000)	0.551 (0.000)	0.503 (0.000)	0.519 (0.000)	0.586 (0.000)
Delivery in Edmonton Hospital	1.070 (0.596)	1.080 (0.549)	1.755 (0.001)	1.112 (0.383)	1.215 (0.253)	1.288 (0.063)
Edmonton Health Center	0.698 (0.000)	0.741 (0.004)	0.997 (0.984)	0.803 (0.022)	0.779 (0.076)	0.845 (0.133)
Delivery by a midwife	0.095 (0.000)	0.117 (0.000)	0.053 (0.000)	0.095 (0.000)	0.074 (0.000)	0.071 (0.000)
First Nation	1.221 (0.256)	1.139 (0.455)	1.307 (0.359)	1.069 (0.680)	1.429 (0.176)	1.821 (0.009)
Welfare subsidy recipient	0.572 (0.000)	0.568 (0.000)	0.737 (0.105)	0.641 (0.000)	0.713 (0.037)	0.789 (0.080)
Premium subsidy recipient	0.817 (0.508)	0.720 (0.266)	1.291 (0.667)	0.655 (0.124)	1.034 (0.943)	1.224 (0.612)
Child welfare recipient	0.963 (0.961)	0.929 (0.923)	8*10 <sup>7</sup> (0.999)	1.076 (0.923)	0.904 (0.922)	1.553 (0.671)
General welfare recipient	0.316 (0.000)	0.323 (0.000)	0.495 (0.015)	0.367 (0.000)	0.454 (0.001)	0.579 (0.015)
Mother aged 30 to 40 with one other child	2.362 (0.000)	2.372 (0.000)	2.284 (0.001)	1.858 (0.000)	2.696 (0.000)	1.879 (0.000)