HPV VACCINATION UPTAKE: IDENTIFYING GAPS, BARRIERS AND DISPARITIES IN CANADIAN POPULATION

A Thesis Submitted to the College of Graduate and Postdoctoral Studies

In Partial Fulfilment of the Requirements

For the Degree of Doctor of Philosophy

In the School of Public Health

University of Saskatchewan Saskatoon

Canada

By Olatunji Sunday Obidiya

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Director, Vaccinology & Immunotherapeutics Program
School of Public Health
104 Clinic Place University of Saskatchewan
Saskatoon, Saskatchewan,
S7N 2Z4 Canada
OR
Dean
College of Graduate and Postdoctoral Studies
University of Saskatchewan
116 Thorvaldson Building, 110 Science Place
Saskatoon, Saskatchewan,
S7N 5C9 Canada

ABSTRACT

Human papillomavirus (HPV) causes the most common viral infection of the reproductive tract worldwide. It is implicated in cervical, anal, oropharyngeal cancers and genital warts in males and females. Infections with HPV are common, it is estimated that 550,000 Canadians are infected yearly. Without prevention measures, it is projected that 75% of the population will contract HPV infection at one point in their lifetime.

The World Health Organization recognizes vaccination as a strategic approach in the prevention of HPV-related diseases. In Canada, the HPV vaccine was approved in 2006. In spite of proven benefits, HPV vaccine uptake is suspected to be low and variable across Canada. To maximize obtainable benefits from HPV vaccination, it is crucial to understand the dynamics and interplay of factors underpinning HPV vaccine uptake in Canada.

Using systematic literature review, meta-analysis and analysis of reliable secondary data; this thesis examined rates of HPV vaccine uptake, identified determinants of uptake and HPV vaccination gaps among different subpopulations in Canada.

From the pooled result of meta-analysis; the proportion of HPV vaccination uptake was 47.0% (male) and 57.0% (female). Using the American College Health Assessment-National College Health Assessment (ACHA-NCHA), proportion of HPV vaccine uptake was 56.1% (female) and 22.2% (male). Furthermore, using the Childhood National Immunization Coverage Survey (CNICS) 2015; proportion of HPV vaccine uptake is 73.7% in girls. In terms of HPV vaccination trend; proportion of HPV vaccine uptake is 41.1%, 68.6% and 73.7% for CNICS 2011, 2013 and 2015 respectively. The observed HPV vaccine uptake proportions across Canadian subpopulations were well below the >80% target set by the Government of Canada. Significant determinants of HPV vaccine uptake were: age, birthplace of child, province of residence, race/ethnicity, history of vaccination, history of sexually transmitted infections and marital status. There were significant gaps in the HPV vaccine uptake among different subpopulations namely: male, men-sleeping-with-men (MSM), older age individuals, international and Aboriginal students (p-value <0.05).

To improve on current HPV vaccination uptake in Canada, health education programs and intentional HPV catch-up vaccination programs are required. This is crucial especially for subpopulations with evidence of gaps in HPV vaccine uptake

ACKNOWLEDGEMENTS

I am forever indebted to Almighty God for taking me to this pinnacle in my academic pursuit.

I am also eternally grateful to the following people:

My supervisors Dr. George Mutwiri (who took me across the finishing line) and Dr. Yelena Bird (who started this journey with me). They gave me the guidance and necessary encouragement to finish despite daunting challenges.

My Advisory Committee members (past and present); Drs. Suresh Tikoo (Chairman), Carol Henry, Cindy Feng, John Moraros, Philip Griebel; for their expertise and unparalleled support.

My colleagues (Mr. Razi Mahmood and Dr. Chijioke Nwankwo); Ms. Vicky Duncan (Librarian, Health Sciences Library U of S) who all contributed immensely to the systematic review and meta-analysis part of this thesis.

Dr. Ruben Mercado, Senior Analyst, Saskatchewan RDC-Statistics Canada who was of tremendous assistance in the analysis of the CNICS datasets.

My parents (late Chief Gabriel Olasunkanmi Obidiya and Madam Emilia Serewola Obidiya) who undoubtedly laid the foundation of honesty, integrity and dedication to duty in my infantile mind.

My indefatigable and loving wife (Engr. Oladunni Temidayo Obidiya); adorable children (Joshua Olaoluwa Obidiya, Peace Iyanuoluwa Obidiya and Esther Eniola Obidiya) for their invaluable support especially when things sometimes seemed falling apart amidst competing commitments.

The Government of Saskatchewan, for the financial support through the Saskatchewan Innovation and Opportunity Scholarship.

Last but not the least, all those I cannot mention because of space constraint, who assisted me on the way and without whose input completing this thesis would have been a phantasm.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACHA-NCHA - American College Health Assessment-National College Health Assessment

ACS - Advisory Committee Statement

ECDC - European Centre for Disease Prevention and Control

DNA - Deoxyribonucleic acid

CEGEP - Collège d'enseignement Général et Professionnel

CCSACCS - Canadian Cancer Society's Advisory Committee on Cancer Statistics

CC – Cervical cancer

CDC - Center for Disease Prevention and Control

CIC - Canadian Immunization Committee

CIG - Canadian Immunization Guide

CMA - Canadian Medical Association

CNICS - Childhood National Immunization Coverage Survey

CPAC - Canadian Partnership Against Cancer

CPhA - Canadian Pharmacists Association

CSPR - Cancer System Performance Report

FMWC - Federation of Medical Women of Canada

GACVS - Global Advisory Committee on Vaccine Safety

GAVI - Global Alliance for Vaccines and Immunization

GC - Government of Canada

GSK - GlaxoSmithKline

HBM – Health Belief Model

HC – Health Canada

HCP - Health Care Practitioner

HIV - Human immunodeficiency virus

HPV - Human Papillomavirus

IME - Immigration Medical Examinations

NACI – National Advisory Committee on Immunization

NCCID - National Collaborating Centre for Infectious Diseases

NCHA - National College Health Assessment

MMR – Measles, Mumps and Rubella

NMSCs – Non-melanoma skin cancers

OECD - Organization for Economic Co-operation and Development countries

PAMP - Precaution Adoption Model Process

PEI - Prince Edward Island

PMK - Person most knowledgeable

PIN - Perineal intraepithelial neoplasias

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSC - Paediatric Society of Canada

RDC – Research Data Center

ROC - Receiver operating curve

SC - Statistics Canada

SPSS – Statistical Package for the Social Sciences

STI – Sexually transmitted infection

TRI - Translational Research Institute

UNICEF - United Nations Children's Fund

USA – United States of America

VIF - Variant inflation factor

WHO - World Health Organization

WTP - Willingness to Participate

CHAPTER 1: LITERATURE REVIEW

1.1 Human Papillomavirus (HPV)

Human papillomavirus (HPV) is a double-stranded circular deoxyribonucleic acid (DNA) virus belonging to the Papillomaviridae taxonomic family (Brianti *et al.*, 2017). Harald zur Hausen postulated in the 1970s against common belief, that HPV is important in the etiology of genital warts and cervical cancer (Davis, 2015; Nour, 2009). He hypothesized that oncogenic HPV caused cervical cancer and further posited that HPV-DNA are present in non-productive format in cervical cancer tumors and can be detected by careful targeted probes for viral DNA in these tumors (The-Nobel-Prize., 2008). For his effort in HPV research, he was awarded the Nobel Prize in Physiology or Medicine for 2008 (Davis, 2015; Nour, 2009; The-Nobel-Prize., 2008). HPV is an extensive viral group comprising over 100 types and subtypes; of which at least 40 can infect the human genital track and 14 are cancer causing (Bernard *et al.*, 2010; Steben *et al.*, 2019). Human papillomavirus types comprise of five genera namely: alpha-, beta-, gamma-, mu- and nu-), depending on structural variations in DNA morphology (Bernard et al., 2010; Doorbar et al., 2015). The alpha and beta HPV types are of utmost etiological interest in infection causation. Alpha HPVs affect mucosal epithelium; the "high-risk" types are associated with various forms of cancers, while the "low risk" types infect cutaneous epithelia cells allegedly implicated in non-melanoma skin cancers (NMSCs) (Aldabagh *et al.*, 2013; Bernard *et al.*, 2010; Cardoso *et al.*, 2011; Van Doorslaer *et al.*, 2012; White *et al.*, 2014).

1.1.1 Human Papillomavirus Infection

Human papillomavirus (HPV) is reportedly the commonest viral infection of the reproductive tract (World-Health-Organization., 2019b). There is a causal link of HPV with cervical cancer (females) and genital warts of both gender (World-Health-Organization., 2019b). Furthermore, HPV is linked with proportions of cancers of the anus, vulva, vagina, penis and oropharynx (World-Health-Organization., 2019a). Infection by HPV is usually through sexual contact with noticeable onset in majority of people shortly after sexual encounter, although penetrative sex is not an absolute necessity for infection to occur (World-Health-Organization., 2019b). In essence, this means infection transmission is still possible via skin-to-skin genital contact (World-Health-Organization., 2019b).

1.1.2 Epidemiology of HPV Infection and Cervical Cancer

About 5% of all cancers globally, nearly all cervical cancers and a large portion of anogenital cancers are attributable to HPV (Bosch *et al.*, 2013; De Martel *et al.*, 2012; de Sanjose *et al.*, 2018). Report from the World Health Organization (WHO) indicates that a diagnosis of at least one cervical cancer is made every minute, thus making it an existential threat to women's health (World-Health-Organization., 2019c). Cervical cancer is the second most common cancer in women living in less developed parts of the world (Ferlay *et al.*, 2018; World-Health-Organization., 2019b) The causal nexus between HPV infections and cervical cancer was postulated by Harold zur Hausen who contrary to widely held opinion of that time linked both HPV and cervical cancer (Davis, 2015; Nour, 2009). *High risk* (HPV types 16 and 18) are involved in about 90% of cervical cancer and 75% of pre-cancerous lesions. In the less developed regions of the world, there were reportedly about 570, 000 new cases of cervical cancer in 2018 alone; which represented about 80% of all global incidence (Ferlay *et al.*, 2018; Ljubojevic *et al.*, 2014). Ninety percent of women who die from cervical cancer are from resource constrained countries (World-Health-Organization., 2019c).

Notwithstanding the aforementioned statistics, the threat of HPV-related cervical cancer is not restricted to resource constrained countries. Globally, cervical cancer is number four among all cancers and represented about 7.5% of all female cancer deaths in 2018 (World-Health-Organization., 2019b). It is noteworthy however that many individuals infected with HPV are asymptomatic and many HPV infections do not result into cancer.

1.1.3 HPV and Non-Cervical Health Problems

The existing classification of HPV depends on correlations in genomic sequences which tallies with clinical categorization applicable to HPV infections: mainly anogenital or mucosal, non-genital or cutaneous and epidermodysplasia verruciformis (Ljubojevic *et al.*, 2014; Shenefelt *et al.*, 2018). Aside from its role in the etiology of cervical cancer, (HPV) is reported to be involved in about 90% of anal cancers (9 in 10 are caused by HPV types 16 and 18) (Ljubojevic *et al.*, 2014). Penile cancer, a rare form of cancer occurring mostly in uncircumcised men is caused mainly by HPV type 16. (Daling *et al.*, 1992; Ljubojevic *et al.*, 2014; Shenefelt *et al.*, 2018). Condylomata acuminata, commonly known as genital wart is caused by HPV types 6, 11, 30, 42, 43, 44, 45, 51, 52, and 54 (Ljubojevic *et al.*, 2014). Non-genital cutaneous lesions, often called common wart or verruca vulgaris are caused by HPV types 1, 2, 4, 27, and 57 (Ljubojevic

et al., 2014; World-Health-Organization., 2019b). Plantar warts occur mainly on the foot and are caused by HPV types 57, 60, 63, 65, and 66) (Ljubojevic *et al.*, 2014; World-Health-Organization., 2019b). Furthermore, HPV types 6 and 11 are implicated in skin tags. Epidermodysplasia is a rare genetic disorder attributable to impaired immunity to HPV (types 5 and 8) infection (Ljubojevic *et al.*, 2014; Sterling, 2005).

Some non-genital mucous lesions caused by HPV are: recurrent laryngeal papillomatosis (types 6, 11), squamous cell lung cancer (types 6, 11, 16, 18), laryngeal cancer (types 16, 18), oral warts (types 2, 4), conjunctival papillomas, oral condyloma and florid oral papillomatosis (types 6, 11) (Ljubojevic *et al.*, 2014).

1.1.4 Global Public Health Strategies for Combating HPV Infection

The World Health Organization (WHO) advocates a comprehensive, multifaceted approach in combating HPV infection prevention and control of undesirable health consequences (World-Health-Organization., 2019b). According to the WHO, measures of control should include community education, social mobilization, vaccination, screening, treatment and palliative care. Measures geared towards prevention and treatment of the sequel of HPV infection can be categorized into primary, secondary and tertiary approaches (World-Health-Organization., 2019b).

Primary preventive measures involve HPV vaccination, health information, male circumcision and sex education. In this regards emphasis is on delayed sexual intimacy, outright abstinence if possible, or safe sex if already sexually active. Preventive efforts and educational campaigns are often geared towards adolescents, parents, guardians and other decision makers (World-Health-Organization., 2019b). Secondary prevention involves majorly screening alone or more appropriately screening and offering of point-of-care treatment of HPV infection especially the "high-risk" types (World-Health-Organization., 2019b). Tertiary measures involve treatment of the sequel of HPV infection (such as cervical cancer) and may involve surgery, radiotherapy, chemotherapy or/and palliative care (World-Health-Organization., 2019b).

1.1.4.1 Vaccination a Global Public Health Strategy in Combating HPV

The development of vaccines and immunization have proven over time to be cost-effective public health strategies at promoting health, preventing diseases and safeguarding the health of the general populace (World-Health-Organization., 2013). The significance of vaccines was

underscored by Dr. Tedros Adhanom Ghebreyesus (Director General of the World Health Organization), who emphasized that vaccination is of utmost importance and one of the critical tools in keeping infections at bay and keeping our world safer (United-Nations-Children's-Fund., 2019). Moreso, the Centre for Disease Control and Prevention (CDC) recognizes immunization as one of the top 10 public health interventions with proven positive result (Center-for-Disease-Prevention-and-Control., 2011).

Human papillomavirus (HPV) vaccines are not therapeutic and also do not protect against infection with every HPV type. In view of this, there are strategic global alliances aimed at combating HPV infection and its aftermath. The core of such strategies [(by agencies such as the World Health Organization (WHO), United Nations Children's Fund (UNICEF) and the Global Alliance for Vaccines and Immunization (GAVI)] consist of vaccination, screening and treatment (United-Nations-Children's-Fund., 2019). GAVI's support is directed at the world's poorest countries and eligibility is based on national income (Global-Alliance-for-Vaccines-and-Immunization., 2020). A country is eligible if its average Gross National Income (GNI) per capital is less than or equal to US$ 1,580 over the past three years. As of 2019, fifty-eight (58) countries were eligible to apply for GAVI's new vaccine support program (Global-Alliance-for-Vaccines-and-Immunization., 2020).

1.1.5 *Human Papillomavirus Vaccines*

Human Papillomavirus (HPV) vaccines protect against infection by certain disease-causing HPV's. Historically, the development of HPV vaccine is attributed primarily to Ian Hector Frazer, a Scottish-Australian scientist at the Translational Research Institute, and then, other researchers working at institutions in Australia and the United States (Frazer, 2014; McNeil, 2006). They researched into finding mechanisms of inducing both neutralizing antibody (important in preventing HPV infection) as well as cell-mediated immunity (important in treating existing HPV infection and mitigating against precancerous consequences of HPV infection). Additionally, they showed that a prominent capsid protein of HPV can self-aggregate into virus-like particles (VLPs) which is an integral step in the pathway to the manufacture of HPV vaccine (Frazer, 2014; McNeil, 2006).

Austria became the first country to introduce the HPV vaccine into its national vaccination program (Tabrizi *et al.*, 2012). Afterwards; Australia, the United States, Canada and countries across Europe introduced the HPV vaccine (Government-of-Australia., 2020). Expectedly, there

were oppositions to the introduction of this vaccine on religious, moral, ethical and safety grounds among others. Besides, the vaccine is relatively expensive and mostly requires government financial support for an effective public vaccination program. Alliances and collaboration with manufacturers and agencies such as WHO, UNICEF and GAVI have ensured introduction of HPV vaccination programs in most parts of the world especially developing and resource-constrained countries.

1.1.5.1 Types of HPV Vaccines

Currently, there are three HPV vaccine types with prophylactic action against HPV infections and prevention of associated disease conditions (World-Health-Organization., 2017). The quadrivalent Gardasil (for HPV types 6, 11, 16, 18) was introduced in 2006, bivalent Cervarix (for HPV types 16 and 18) was introduced in 2007 and the nonavalent Gardasil (for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58) was introduced in 2014.

1.1.5.2 Evidence in Support of HPV Vaccines

In the development of analytical framework for immunization programs, efficacy and safety are paramount vaccine characteristics that must be considered (Erickson *et al.*, 2005). The safety, tolerability and efficacy of HPV vaccines in humans have been severally demonstrated and documented (Handler *et al.*, 2015; Pomfret *et al.*, 2011; Zhu *et al.*, 2017). Notwithstanding abundant data, safety concerns on HPV vaccines are common and pose significant impediment in the implementation of HPV vaccination programs globally (De Vincenzo *et al.*, 2014; Handler *et al.*, 2015; Pomfret *et al.*, 2011; Zhu *et al.*, 2017). After a thorough review of all existing evidences by the WHO's Global Advisory Committee on Vaccine Safety (GACVS), it was concluded that commercially available HPV vaccines are safe (World-Health-Organization., 2017). Besides, countries where HPV vaccines have been introduced have protocols demonstrating safety and efficacy (De Vincenzo *et al.*, 2014; Huh *et al.*, 2017; La Torre *et al.*, 2010; Mah *et al.*, 2011). Usually, observable side effects on HPV vaccine administration are easily resolvable pain and redness at the point of injection (De Vincenzo *et al.*, 2014). Those opposed to HPV vaccines on the basis of safety usually cite reported incidence of prolonged pain similar to complex regional pain syndrome in Japan (De Vincenzo *et al.*, 2014). However, there is no obvious scientific causal link of this reported syndrome with HPV vaccination (De Vincenzo *et al.*, 2014).

1.1.6 Introduction of HPV Vaccines in Canada

Health Canada initially endorsed two HPV vaccines Cervarix (HPV type 16,18) and Gardasil-4 (HPV type 6,11,16,18) in 2006 for use in both females and males aged 9 to 26 years old. In February 2015, Health Canada also approved Gardasil-9. In addition to HPV types covered by Gardasil-4, Gardasil-9 also covers types 31, 33, 45, 52, and 58 that are responsible for roughly 20% cases of cervical cancer (Government-of-Canada., 2016a). As of 2010, all provinces and territories had implemented organized school-based HPV immunization programs for girls (Canadian-Partnership-Against-Cancer., 2018b). As at 2018, all Canadian jurisdictions except the Territories Nunavut have publicly funded HPV programs for boys (Government-of-Canada., 2020b).

1.1.7 HPV Vaccine Awareness in Canada

In 2017, Canada dedicated a week to create awareness and engagement in educational activities targeted towards promoting HPV immunization as a crucial first step in fighting HPV infection and associated cancers (Federation-of-Medical-Women-of-Canada., 2017). This HPV Prevention Week was anchored by the Federation of Medical Women of Canada (FMWC) and aimed at getting across the right information on HPV infection and HPV vaccines to Canadians (Federation-of-Medical-Women-of-Canada., 2017). In creating awareness about HPV and HPV vaccination programing, emphasis should be placed on communities and populations that are underserved (such as Indigenous Aboriginal population and men who sleep with other men [MSM]).

In addition, it was reported that racial and ethnic minorities are underrepresented in vaccine trials in North America, and willingness to participate (WTP) and retention in participation vaccine trials differ in Caucasian and non-Caucasian populations (Dhalla *et al.*, 2014). Thus, existing programs on women's health need to be re-evaluated and improvements made in program planning and implementation.

1.1.8 HPV Vaccination Schedules in Canada

Health Canada and the National Advisory Committee on Immunization **(**NACI) endorses a 2 or 3 dose HPV vaccination schedule. For a 3-dose schedule; 0.5ml of Cervarix should be given at months 0, 1, and 6 while 0.5ml of Gardasil-4 or Gardasil-9 should be given at months 0, 2, and 6. For an exclusively 2-dose schedule, the second dose of vaccine should be administered at least

24 weeks after the first dose (Government-of-Canada., 2017b). The summary of dose and schedule of HPV vaccination as recommended by NACI is shown below in Table 1.1

Table 1.1: NACI Recommendations for the HPV Immunization Schedule		
Recommended Groups	Recommended Schedule	Recommended HPV Vaccine(s)
• Healthy (immunocompetent, non-HIV infected) females 9-14 years of age (and healthy females ≥15 years of age in whom the first dose was administered between 9-14 years of age)	• 2- or 3-dose schedule	• Cervarix, Gardasil-4 or • Gardasil-9
• Healthy (immunocompetent, non-HIV infected) females ≥15 years of age	• 3-dose schedule	• Cervarix, Gardasil-4 or • Gardasil-9
• Healthy (immunocompetent, non-HIV infected) males 9-14 years of age (and healthy males ≥15 years of age in whom the first dose was administered between 9-14 years of age)	• 2- or 3-dose schedule	• Gardasil-4 or • Gardasil-9
• Healthy (immunocompetent, non-HIV infected) Males ≥15 years of age	• 3-dose schedule	• Gardasil-4 or • Gardasil-9
• Immunocompromised individuals and immunocompetent HIV-infected individuals	• 3-dose schedule	• Cervarix, Gardasil-4 or Gardasil-9 (females); • Gardasil-4 (males)

Source: (Government-of-Canada., 2017b)
https://www.canada.ca/en/public-health/services/publications/healthy-living/updated-recommendations-human-papillomavirus-immunization-schedule-immunocompromised-populations.html

1.1.9 Female HPV Vaccination Program in Canada

Health Canada ratified two HPV vaccines Cervarix (HPV type 16,18) and Gardasil-4 (HPV type 6,11,16,18) in 2006 for use in both females and males aged 9 to 26 years old (Government-of-Canada., 2017b). Although Health Canada approval for HPV vaccine was gender neutral, initial publically funded HPV vaccination program was restricted to school-based girls. As of 2010, all jurisdictions in Canada have in place publically funded HPV vaccination programs for females (Canadian-Partnership-Against-Cancer., 2018a). This gender biased public funding of HPV vaccine program although not supported by literature, nevertheless continued until 2014 when the province of Prince Edward Island (PEI) pioneered a public funded HPV vaccination program for boys in Canada. Compared with female HPV vaccination, a synopsis of contemporary empirical evidence supporting male HPV vaccination will be provided later.

1.1.10 Introduction of Male HPV Vaccination in Canada

When the Human Papillomavirus (HPV) vaccine was introduced globally, it was predominantly promoted as a vaccine against cervical cancer targeting mainly females. A good example of such promotion is from the pharmaceutical giant; Merck's with its "*One Less*" public health campaign focusing solely on prevention of cervical cancer (Grantham *et al.*, 2011). This feminized market approach affected public perception of HPV infection and HPV vaccine as "*women matter"*, creating significant barriers for its recognition, acceptance and use among boys and males in general.

A meta-analysis involving studies from USA, Australia, Sweden, Canada, Germany, the Netherlands, New Zealand, Philippines, Singapore and South Korea; revealed that public health campaigns promoting positive HPV vaccine attitudes and creating awareness about HPV risk in men may support HPV vaccine acceptability for men. It was further suggested that interventions to promote healthcare provider recommendation of HPV vaccination for boys and mitigating obstacles due to cost and logistical barriers may increase HPV acceptability and uptake in men (Newman *et al.*, 2013). Furthermore, a Pan-European study examining parental attitudes to HPV vaccination of boys reported that parents want their sons protected from HPV infection and disease. It was also reported that gender equality in HPV vaccination programming was important to parents (Mortensen *et al.*, 2015).

In Canada, obstacles to parents accepting the HPV vaccine for boys include lack of recommendation of the vaccine by doctors and other health care professionals and paucity of information about HPV infection in males. Other barriers reported in literature include; cost, lack of awareness on the need for HPV vaccination in boys and a general apathy towards vaccination in general (Dahlström *et al.*, 2010; G. S. Ogilvie *et al.*, 2008; Reiter *et al.*, 2011; Shapiro *et al.*, 2017). In addition, unfavorable disposition from many Catholic school boards towards HPV vaccination because of fear of sexual promiscuity and unsubstantiated negative media coverage served as an added barrier towards HPV vaccination in boys (McCarthy, 2015). It is also possible that some critical media reporting on HPV vaccination at the initial introduction of HPV vaccine to females served as impediment to introducing HPV vaccination programs in males. Examples of such sensational and biased reporting included *[“Our girls are not guinea pigs”, (from Macleans’); “A wonder drug's dark side” (from Toronto Star's) and “Urgent call for a moratorium on HPV vaccination in Quebec” (from Le Devoir's)]* (Gulli, 2007; McCarthy, 2015; Rail *et al.*, 2015).

There are direct and indirect cost implications to extension of public funding for male HPV vaccination. According to the analytical frame work for immunization programs in Canada, cost-effectiveness analyses are undoubtedly needed to justify public funding of male HPV vaccination program (Brisson *et al.*, 2007; Dasbach *et al.*, 2006; Erickson *et al.*, 2005; Kim *et al.*, 2008). Despite gender bias in the initial roll-out of HPV vaccination programs, there is overwhelming evidence supporting the effectiveness and the appropriateness of including males in HPV vaccination (Crosignani *et al.*, 2013; Olsen *et al.*, 2015; Shapiro *et al.*, 2016). HPV has been implicated as a cause of cervical cancer, genital, oropharyngeal (OPC) anal and penile cancers (Gillison *et al.*, 2008; Kensler *et al.*, 2016; Parkin *et al.*, 2006; Prue *et al.*, 2016). Evidence garnered from systematic literature reviews reveal that extra benefits derived from including males in HPV vaccination is dependent on the level of uptake in females.

Those not keen on or out-rightly opposed to male HPV vaccination often cite the report that when population uptake of HPV vaccine in female is low, the impact of concurrently vaccinating males is huge and noticeable (Hanley *et al.*, 2015; Matsumoto *et al.*, 2017). They further surmise that as the HPV vaccine uptake in females increases to around 70%, the added impact of vaccinating males appears to wane (Crosignani *et al.*, 2013; Hanley *et al.*, 2015; Marty *et al.*, 2013; Matsumoto *et al.*, 2017; Prue *et al.*, 2016). In counteracting such biased one-sided

argument, it suffices to note that the HPV vaccination rate in females in most Canadian provinces is neither consistently near 70%; nor near that which will confer herd immunity. Even if the foregoing argument against including males in HPV vaccination were true, there are numerous reasons backed by empirical evidence to justify HPV vaccination in males. Notable among the reasons is that HPV infections are gender neutral, affecting both males and females. The Canadian health system is noted for its principle of equity and universality; this principle should also apply to male populations that need HPV vaccination (Erickson *et al.*, 2005). A female only vaccination policy will leave many men unprotected against HPV infection and its aftermath. This is particularly detrimental for the immunocompromised and men who sleep with other men (MSM); who also have documented higher burdens of HPV infection (Prue *et al.*, 2016; Shapiro *et al.*, 2016; Stanley, 2012).

Although, it was earlier reasoned that a female only HPV vaccination would protect males through herd immunity (Crosignani *et al.*, 2013; Leon, 2008; Paul, 2004; Shapiro *et al.*, 2016). It is obvious from experience that chances of herd immunity protection for males is unrealistic if HPV vaccine coverage is not greater than 80% in females. Even if Canada were to achieve greater than 80% coverage, Canadian males are still very vulnerable and would not be protected in international, non-Canadian spaces like Japan with as low as 49% HPV vaccine uptake (Shapiro *et al.*, 2016; Stanley, 2012).

Very strong advocacy in support of gender-neutral HPV vaccination also came from professional health associations. Professional groups such as the Canadian Medical Association (CMA), the Canadian Cancer Society (CCS), the Canadian Paediatric Society (CPS) and the Canadian Pharmacists Association (CPhA) among others have advocated for inclusion of Canadian male population. This agrees with recommendations from the National Advisory Committee on Immunization (NACI) and the Canadian Immunization Guide (CIG) (Canadian-Pharmacists-Association., 2015; Eggertson, 2012; Government-of-Canada., 2016b; Sagan, 2014).

Lastly, the analytical framework for immunization programs often entail some political considerations and lobbying; carrying political benefits or demerits (Erickson *et al.*, 2005). In particular, the voice of advocacy and success for inclusion of boys in the HPV vaccination programs came strongly from Gordon Gosse, a Member of the Legislative Assembly (MLA)

from Nova Scotia; who was diagnosed with throat cancer secondary to infection with the human papillomavirus (HPV) (Shapiro *et al.*, 2016). Unfortunately, Gosse died of oropharyngeal cancer on November 14, 2019.

1.1.10.1 Epidemiology of HPV Infection in Males

An in-depth knowledge and understanding of the prevalence of HPV infection in males is important in the prevention of HPV associated diseases (L. M. Smith *et al.*, 2011). In comparison to females, there are fewer population-based studies on HPV prevalence in men globally (J. S. Smith *et al.*, 2008; L. M. Smith *et al.*, 2011). There are also fewer studies examining HPV vaccine decision-making conducted exclusively among parents of boys (Liddon *et al.*, 2010; Perez *et al.*, 2016; Trim *et al.*, 2012). Smith et al., 2011 reported that the age- specific global prevalence of HPV infection varied widely in men according to geographic regions. They further reported that compared to women, HPV prevalence in men peaks at older ages; remaining constant thereafter or decreasing slightly with increasing age, suggesting that there is persistent HPV infection or a higher rate of reinfection (L. M. Smith *et al.*, 2011). In addition, they reported that HPV prevalence was highly variable (1%- 84%) in *low risk* men and (2% - 93%) in *high risk* men (L. M. Smith *et al.*, 2011). High risk males include MSM and "*street involved"* children. According to UNICEF *"street involved"* children are children who leave on the street or/and unoccupied buildings; usually vulnerable, facing many health inequalities and prone to various social vices (United-Nations-Children's-Fund., 2017).

Available data indicate that over 80% of anal, 50 % of penile and 13–56% of oropharyngeal cancers are HPV related (Forman *et al.*, 2012; Perez *et al.*, 2016). Like their female counterparts, males are equally at risk of HPV-related genital warts (GW), which can negatively impact quality of life (Forman *et al.*, 2012; Perez *et al.*, 2016).

As a result of overwhelming evidences that HPV vaccination should be gender neutral, Canada was one of the earliest countries to introduce HPV vaccination programs among boys (Government-of-Canada., 2016b).

In a Pan-Canadian survey using the Precaution Adoption Process Model (PAPM) to assess the HPV vaccination uptake in Canada and understanding Canadian parents position in the HPV vaccine decision-making process for their son; Perez and colleagues concluded that *"HPV vaccination uptake in Canadian boys was very low in the absence of a publicly funded HPV vaccination programs for boys* (Perez *et al.*, 2016).

1.1.10.2 Recommendation for HPV Vaccination in Males

There are 3 (three) types of HPV vaccine approved and recommended for use by Health Canada: HPV2 vaccine (Cervarix), HPV4 vaccine (Gardasil-4) and HPV9 vaccine (Gardasil-9). The decision on which vaccine type to use depends on the goal of immunization. If goal of vaccination is to prevent HPV types 16 or 18 associated health problems, then any of the three vaccines can be used bearing in mind the cost implications. If aim of vaccination and suspected spectrum of HPV infections includes HPV types 31, 33, 45, 52, and 58; then Gardasil-9 becomes the vaccine of choice. Furthermore, if genital wart protection is envisaged in addition to cancer prevention, then either Gardasil-4 or Gardasil-9 is a good choice (Government-of-Canada., 2016b). There is no data on use of HPV vaccine in boys less than 9 years, however vaccination may be considered if subject is at risk of HPV infection as in boys with history of sexual abuse or with previous history of HPV infection (Government-of-Canada., 2016b).

As stated earlier, MSM (and particularly HIV positive MSM) have comparatively higher burden of HPV infection with the *high risk* HPV types 16 and 18. Thus it is essential and beneficial to have them receive either the Gardasil-4 or Gardasil-9 early so as to confer maximum immunity possible (Government-of-Canada., 2016b). Like in females, as much as possible administration of HPV vaccine should be done before sexual activities begin or exposure to HPV. Notwithstanding, administration of HPV vaccine after onset of sexual activity is still beneficial because the vaccine recipient is very unlikely to have been infected with all disease implicated HPV types at a single time (Government-of-Canada., 2016b). In terms of HPV vaccine dose administration, a 2 or 3 dose schedule is recommended by Health Canada. Depending on the population group and immune competency of recipient(s); HPV vaccine should be administered as 2 separate 0.5 mL doses at months 0 and 6 (for Cervarix) or ([as 2 separate 0.5ml doses at months 0 and 6, or months 0 and 12 (for Gardasil-4 and Gardasil-9]). A summary of recommended dose schedule in males is presented below in Table 1.2.

Table 1.2: Recommended Immunization Schedule and HPV Vaccine in Males		
Category	**Immunization Schedule**	**Vaccine(s)**
• Healthy[1] boys (9 to less than 15 years of age)	• 2 or 3 dose schedules	• Gardasil-4[2]or Gardasil-9[3]
• Healthy1 boys and men (15 years of age and older)	• 3[4] dose schedules	• Gardasil-4 or Gardasil-9
• Immunocompromised individuals and immunocompetent HIV-infected individuals	• 3 dose schedules	• Gardasil-4 or Gardasil-9
1 = Immunocompetent, non-HIV infected 2 = Quadrivalent human papillomavirus vaccine 3 = 9-valent human papillomavirus vaccine 4 = A 2-dose schedule of HPV4 vaccine is sufficient for healthy boys and men 15 years of age and older in whom the first dose was administered between 9 and less than 15 years of age.		

Source: (Government-of-Canada., 2019)
https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-9-human-papillomavirus-vaccine.html

1.1.10.3 Projected Population Impact of HPV Vaccination in Males

Monitoring real-time or projected impacts of HPV vaccination programs on HPV infection and infection outcomes in males poses similar challenges encountered with females (e.g. long term cancer outcomes) (J. M. Brotherton *et al.*, 2016). In addition, and unlike in females; collection of relevant specimen used to monitor HPV prevalence are not done routinely for the purpose of diagnosis or/and screening in males (J. M. Brotherton *et al.*, 2016). This situation makes determination of pre-HPV vaccination (baseline) and projected post-HPV vaccination endpoints (such as reduction in HPV related cancers, anogenital warts and recurrent respiratory papillomatosis) very challenging.

It is commendable that Canada is one of the pioneer countries that introduced HPV vaccination program for boys into its immunization schedule. With evidence-based support for a universal gender-neutral HPV vaccination; concerted effort should continue in bringing HPV coverage in boys to be at par with that of girls. It is needful to extend publically funded HPV vaccination for boys in all jurisdictions of Canada, especially in Northern Territories of Canada and the Canadian Aboriginal populations living on Reserves. Furthermore, it could also be beneficial to consider a publically funded HPV vaccination programing for specific population of males such as men who sleep with men (MSM) who are at higher risk of infection from HPV.

A suggestion of selected HPV vaccination program endpoints in female, comparable adaptations for males and possible challenges (J. M. Brotherton *et al.*, 2016) is reproduced in Table 1.3 (Appendix B).

Chapter 2. RATIONALE, HYPOTHESES, OVERALL OBJECTIVE AND AIMS

2.1 Rationale and Hypothesis

2.1.1 Rationale

Similar to that of the global epidemiology, infection with HPV is common among Canadians and prevalence is reportedly variable among different subpopulations. Without prevention measures such as HPV vaccination, it is estimated that 75% of the Canadian population will contract HPV infection at one point in their lifetime. According to Health Canada and the National Advisory Committee on Immunization (NACI), immunocompromised individuals, those living in poor neighborhood or having lesser access to screening facilities are at greater risk of HPV infection and have a high probability of co-infection with HIV (Government-of-Canada., 2017b).

In Canada, studies have documented a higher rate of HPV infection among Aboriginal population and suggested interventions that could possibly mitigate many of the consequences of this disproportionate burden of infection (Bennett *et al.*, 2015; Demers *et al.*, 2011; Hamlin-Douglas *et al.*, 2008; Jiang *et al.*, 2013a; Severini *et al.*, 2013). These studies reported a 2 to 3-fold higher burden of HPV infection in the Aboriginal population compared to the Canadian general population (Bennett *et al.*, 2015; Demers *et al.*, 2011; Hamlin-Douglas *et al.*, 2008; Jiang *et al.*, 2013a; Severini *et al.*, 2013). Apart from the Aboriginal population, men who have sex with other men (MSM) are at greater risk to potentially carry the HPV virus that cause anal, throat and penile cancer (Blas *et al.*, 2015; Cranston *et al.*, 2015; Grennan, 2015).

Despite the high prevalence of HPV and incidence of cervical cancer in Aboriginal populations, there are reportedly low levels of awareness about HPV, cervical cancer and accessibility to preventive services in Aboriginal women (Cerigo *et al.*, 2011; Russell *et al.*, 2012). Moreover, it has been reported that HPV and vaccine awareness were both higher in Caucasian women when compared to non-Caucasian women (Sadry *et al.*, 2013). It was also concluded that improving HPV vaccination knowledge in susceptible populations has the potential to improve positive attitudes and vaccine uptake (Sadry *et al.*, 2013).

Research findings have confirmed that ethnicity, income, and education are key determinants in creating awareness, having access, and making use of available health care services. Thus, all effort should be geared towards bringing everyone on board and getting community buy-in to fully harness the potentials of HPV vaccines in reducing the incidence of

cervical cancer and HPV-related cancers in Canada (Russell *et al.*, 2012). This would have considerable health benefits due to a reduction in the incidence of cervical cancer related morbidity and mortality (Bryer, 2011). There would also be considerable savings in healthcare costs associated with cancer treatment (Bryer, 2011; Gonik, 2006).

2.1.2 Hypotheses

1) There are no disparities in HPV vaccination coverage among different subpopulations in Canada.
2) HPV vaccination programs and HPV vaccination coverage are intentionally targeted towards vulnerable population with documented higher burden of HPV infection in Canada.
3) HPV vaccination uptake among Canadians meet up with Canadian government agencies recommendation of 80% coverage of eligible population been fully vaccinated against HPV within 2 years (and 90% within 5 years) of the introduction of the HPV vaccination program.

This thesis explores the validity of aforementioned hypotheses and examines determinants of HPV vaccine uptake in the Canadian population.

2.2 Research Objectives

1) To determine the level of HPV vaccine uptake in Canada through a systematic review of the literature.
2) To determine whether disparities in HPV vaccine uptake exist among different subpopulations in Canada by using pre-existing, highly reliable and valid secondary data.

2.3 Research Questions

1) What are the rates of HPV vaccine uptake among different subpopulations in Canada?
2) What are the disparities in HPV vaccine uptake among post-secondary students in Canada?
3) What are the determinants (barriers, facilitators) of HPV vaccine uptake among children in Canada?

2.4 Methodology

2.4.1 Research Design

This research seeks to explore the HPV vaccination uptake rate in Canada, identify possible barriers as well as gaps in HPV vaccine use among Canadian population. It would also provide functional recommendations for public health interventions that could help address identified barriers and gaps.

2.4.1.1 Systematic Review and Meta-Analysis (Phase I)

Through a systematic review and meta-analysis, we endeavour to answer *Research Question 1:* This entails exploring the rates of HPV vaccine uptake among the general population and subpopulations in Canada.

2.4.1.2 Secondary Data Search and Analysis (Phase II)

Through searching and analysis of secondary data bases, we endeavour to answer *Research Questions 2 and 3*: This entails exploring the disparities in HPV vaccine uptake among post-secondary students and examining determinants of HPV vaccine uptake among children in Canada.

2.5 Outline of Thesis

This thesis is structured as follows:

Chapter 1

Consists of literature review and provides background knowledge about the theme of this thesis. This chapter serves as gateway into the body of knowledge and what is already known from literature.

Chapter 2

This chapter gives us the rationale behind this research and provides research questions this thesis endeavours to answers. The chapter summarizes the aims and objectives of the thesis and outlines the pathways to achieving these objectives in subsequent chapters.

Chapter 3

This chapter summarizes HPV vaccination uptake in Canada using a systematic review and meta-analysis, describing general trends and gaps in the literature. It also helped to ascertain and reinforce novel research questions for this thesis.

Chapter 4

This chapter focuses on HPV 'vaccination uptake among an important subpopulation of Canadians, students in a Canadian university. An understanding of HPV uptake in this population segment serves as a proxy indicator of HPV vaccine uptake among young adults in Canada.

Chapter 5

Building on conclusions from chapter 4 on HPV vaccine uptake in a Canadian university; and to make the result generalizable to a larger spectrum of young adults in Canada, chapter 5 explores HPV vaccination uptake among students across several universities in Canada.

Chapter 6

HPV vaccination program in Canada was initially publically funded, school-based and for females only. Chapter 6 explores HPV vaccination uptake among female children and adolescents in Canada.

Chapter 7

This concluding chapter summarizes key research findings from the thesis and outlines limitations. It also highlights important gaps in HPV vaccination programs and HPV vaccine uptake in Canada while suggesting areas where future researches should be directed.

CHAPTER 3 - HUMAN PAPILLOMAVIRUS VACCINATION UPTAKE IN CANADA: A SYSTEMATIC REVIEW AND META-ANALYSIS

Article reproduced with minor edits. Originally published as: Bird Y, Obidiya O, Mahmood R, Nwankwo C, Moraros J. Human papillomavirus vaccination uptake in Canada: A systematic review and meta-analysis. Int J Prev Med 2017; 8:71.

My contributions to this manuscript included conceiving and designing the review, reviewing articles for inclusion/exclusion, conducting analysis and interpretation of the data, and preparing the manuscript.

Mahmood R and Nwankwo C assisted in reviewing articles for inclusion/exclusion, conducting analysis and interpretation of the data, and preparing the manuscript.

Dr. Bird Y and Dr. Moraros J guided in conception and design of the study, the interpretation of findings, and helped critically revise and finalize the document.

3.1 Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the world and the primary cause of various cancers and precancerous lesions (Carter *et al.*, 2011; Dunne *et al.*, 2007; Garland, 2002; World-Health-Organization., 2019b). For instance, cervical cancer is the second most common cancer and mainly affects women in the developing world (Carter *et al.*, 2011). However, even in developed countries such as Canada, cervical cancer remains a serious public health concern (Government-of-Canada., 2019). In 2019, it was estimated that 1350 Canadian women were diagnosed with cervical cancer and 410 would eventually die from it (Government-of-Canada., 2019). These staggering statistics are unacceptably for Canada, especially when one considers that we are a high-income country and cervical cancer is a preventable disease (SCHEURER *et al.*, 2005).

HPV infections are quite common and affect the majority of sexually active men and women (SCHEURER *et al.*, 2005). Most HPV infections are asymptomatic and resolve spontaneously usually within 2 years (SCHEURER *et al.*, 2005). However, longer lasting HPV types 16 and 18 infections are known to cause 70% of cervical cancers and precancerous cervical lesions, while HPV types 6 and 11 are associated with approximately 90% of all genital warts (Carter *et al.*, 2011). Most individuals do not even know that they have been infected with HPV and therefore may inadvertently transmit the HPV infection to their sex partners. In Canada, it is estimated that 550,000 people are infected with HPV each year and that approximately 80% of females of reproductive age will be infected at some point in their lifetime (Cristopher P Crum *et al.*, 2003a).

Given the strong link between HPV infections (Types 16 and 18) and cervical cancer, several new interventions have been introduced to curtail the burden of the disease. Chief among these is the population-based use of HPV vaccines. In 2006, two HPV vaccines Cervarix (which covers HPV types 16 and 18) and Gardasil (which covers HPV types 6, 11, 16, and 18) were approved for use mainly among females but also for males aged 9–26 years in Canada (Christopher P Crum *et al.*, 2003b). Publicly funded HPV immunization programs for females are available in all Canadian provinces and territories. In addition, all ten provinces (Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec, and Saskatchewan) have publically funded HPV

vaccination programs for males as well. In Canadian northern territories, Yukon and Northwest Territories also provide the HPV vaccine free of charge for boys and girls (Government-of-Northwest-Territories., 2017; Government-of-Yukon., 2017). This leaves just the Territories of Nunavut yet to come on board with a publically funded HPV vaccination programs.

The HPV vaccine has been reported to be highly effective in preventing the targeted HPV types, as well as the diseases caused by them (Cristopher P Crum *et al.*, 2003a; Christopher P Crum *et al.*, 2003b). Across Canada, the HPV vaccine uptake is quite variable with initial vaccination rates (i.e. first dose) ranging from 47% in the Northwest Territories to 93.8% in Newfoundland and Labrador (Canadian-Partnership-Against-Cancer., 2016; Rogers, 2015). The rates are significantly lower when one considers the HPV vaccine completion rates (i.e. all three doses) with a number of provinces not even keeping records for these important statistics (Canadian-Partnership-Against-Cancer., 2016; Rogers, 2015). Moreover, even less is known about the factors that may influence HPV vaccine uptake in Canada. Public discussion regarding the new HPV vaccines is characterized by strong feelings and beliefs and significant financial interest, but more research is needed to help inform policy choices, public health interventions, and decision making.

To the best of our knowledge, there are no systematic reviews examining HPV vaccination uptake in Canada. Instead, previous studies have primarily focused on HPV vaccine knowledge, attitudes toward vaccination, acceptability, and intention to vaccinate (Cerigo *et al.*, 2012; Drolet *et al.*, 2013; Duval *et al.*, 2007; Gainforth *et al.*, 2012; Kessels *et al.*, 2012; Kiely *et al.*, 2011; Meghani *et al.*, 2010; Pruitt *et al.*, 2010). However, to optimize the use of the HPV vaccination programs in Canada, it is critically important to determine the levels of HPV vaccine uptake. To this end, we conducted a systematic review and meta-analysis of the existing literature to address these key issues.

3.2 Methods

An extensive and systematic review of the literature was conducted on the following databases: Medline, PubMed, Cochrane Library, EMBASE, Global Health, ProQuest Public Health, and JSTOR. Searches were conducted using various combinations of keywords and Medical Subject Heading (MeSH) terms including “papillomavirus infections,” “virus diseases,” “uterine cervical neoplasms,” “papillomavirus vaccines,” “immunization,” and “Canada.”

3.2.1 Inclusion and Exclusion Criteria

Articles were included if they were in the English language, with a publication date of 2006 and later, were publicly available, included human populations in Canada, involved an HPV vaccination intervention, and provided quantitative data regarding levels of HPV vaccination uptake. Articles involving case reports or case series studies were excluded.

3.2.2 Data Extraction and Quality Assessment

Three steps were involved in the data extraction process. First, duplicates were removed, and the remaining articles were screened by their titles and abstracts for relevance. Second, full-text articles were reviewed by two of the authors (OO and RM) to assess their conformity with the study inclusion criteria. Third, the selected articles underwent methodological quality review by using a modified Newcastle-Ottawa Scale (NOS) (Peterson *et al.*, 2011)). Using the modified NOS, each study was assessed and scored under two domains: selection (representativeness of the vaccinated group, ascertainment of vaccination status, demonstration that outcome of interest was absent at start of study) and outcome (assessment of outcome, adequacy of follow-up of vaccinated group). Any disagreement between the two authors (OO and RM) was further discussed to reach a resolution, and if required, a third author (CN) provided the tie-breaking vote. Reference management and duplication were handled using the reference manager, Mendeley. Data extracted from the studies included vaccination rates, study design, participants' size, participants' demographic information, program location, period of vaccination, as well as key conclusions of the study. Data were collected into a common folder and shared between the researchers on Google Drive. Spreadsheets were constructed based on screening outcomes and data extraction from the final articles.

3.2.3 Statistical Analysis

The meta-analysis was carried out using the MedCalc analytic software version 16.2.1 (MedCalc-easy-to-use-statistical-software., 2020). Weighted pooled vaccination rates were obtained with the aid of a random effects model using the Freeman-Tukey transformation (DerSimonian *et al.*, 1986; Freeman *et al.*, 1950). Statistical analysis for heterogeneity was performed using Higgins I-squared (I^2) (Higgins *et al.*, 2002; Higgins *et al.*, 2003). This allowed us to determine the proportion of observed variation in vaccination rates across studies that could be attributed to heterogeneity. A value of I^2 >75% was considered a statistical indicator of the

likely presence of heterogeneity (Higgins *et al.*, 2002; Higgins *et al.*, 2003). Suspected heterogeneity was further explored using a subgroup analysis. The factors to be explored in the subgroup analysis were determined *apriori* and they included age (>18 vs. 18 years or younger), sex (male vs. female), type of program (community-based vs. school-based) and funding (publicly funded vs. out of pocket). The vaccination rates were pooled for the respective subgroups using a random effects model, with the subsequent computation of rate ratios and corresponding 95% confidence intervals (CIs), using the MedCalc analytic software version 16.2.1. (MedCalc-easy-to-use-statistical-software., 2020). A funnel plot was used to assess the risk of publication bias for the included studies.

3.3 Results

3.3.1 Study Selection

In the primary search, we found 718 peer-reviewed articles that were related to our topic. Of those, 205 were removed as duplicates. Of the remaining 513 articles, 366 were excluded after the title and abstract screening. Of the 147 articles that were assessed through full-text screening, 12 articles containing 624,604 participants remained. These articles underwent methodological quality review and were included for analysis in our study. A flow diagram of included studies is shown below in Figure 3. 1.

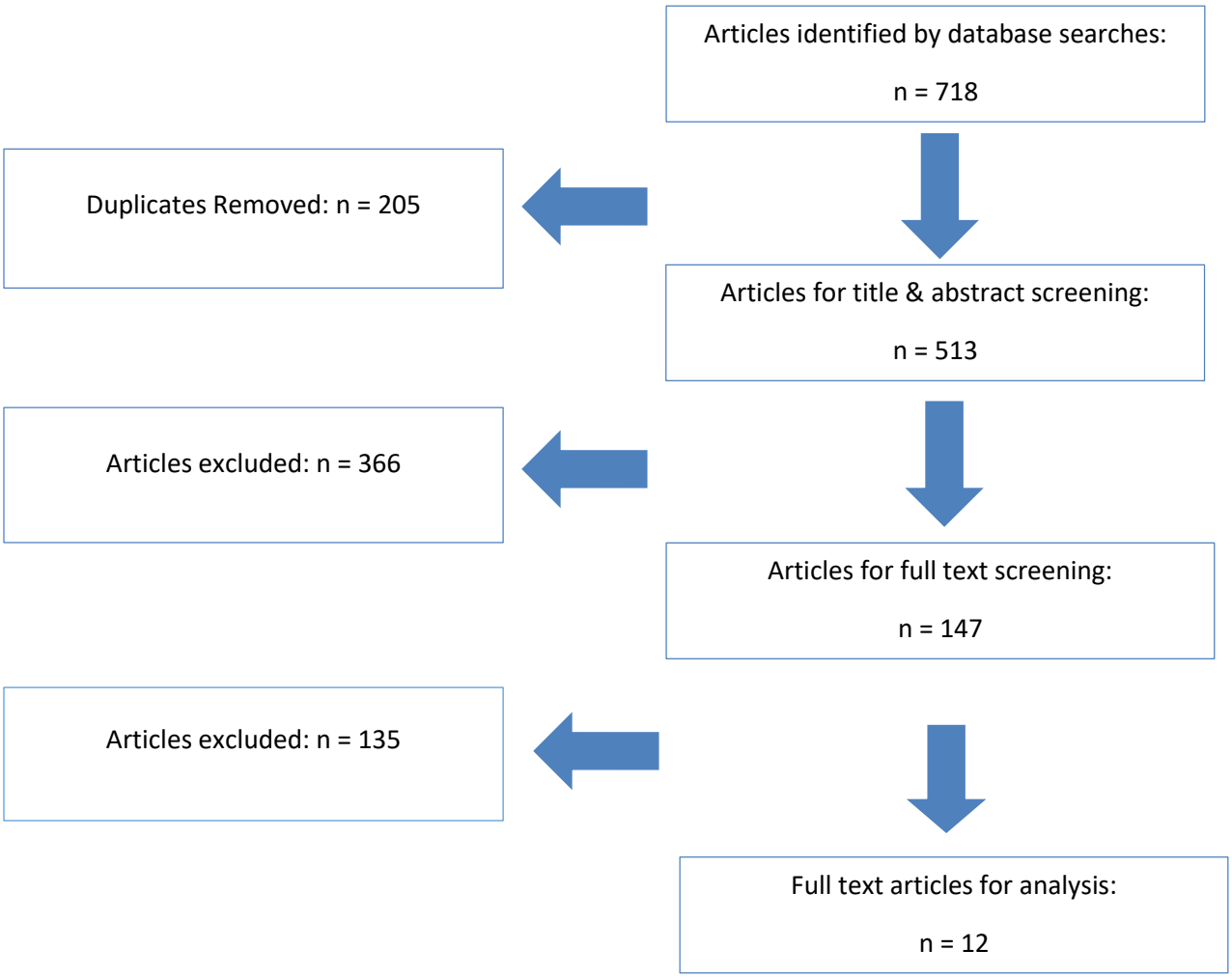

Figure 3.1: **PRISMA flow diagram of the included studies**

3.3.2 Study Characteristics

Of the 12 studies, (Ahken *et al.*, 2015; Burchell *et al.*, 2014; Krawczyk *et al.*, 2015; Lim *et al.*, 2014; Liu *et al.*, 2016; McClure *et al.*, 2015; Musto *et al.*, 2013; G. Ogilvie *et al.*, 2010; G. S. Ogilvie *et al.*, 2015; L. M. Smith *et al.*, 2011; Whelan *et al.*, 2014; S. E. Wilson *et al.*, 2013) eight were longitudinal and four were cross-sectional (Musto *et al.*, 2013; G. Ogilvie *et al.*, 2010; G. S. Ogilvie *et al.*, 2015; S. E. Wilson *et al.*, 2013). Sample size ranged from 105 to 223,051 participants (Ahken *et al.*, 2015; G. S. Ogilvie *et al.*, 2015). Two studies (Ahken *et al.*, 2015; Burchell *et al.*, 2014) involved participants over 18 years old, who had to pay out of pocket to receive their HPV vaccination, whereas participants in the other ten studies were younger than or equal to 18 years old and their HPV vaccination was publicly funded. Two studies involved male and female participants, (Liu *et al.*, 2016; McClure *et al.*, 2015) while the remaining ten studies only used female participants. One study (Burchell *et al.*, 2014; Krawczyk *et al.*, 2015; McClure *et al.*, 2015; G. Ogilvie *et al.*, 2010; G. S. Ogilvie *et al.*, 2015; S. E. Wilson *et al.*, 2013) and five were both community and school based. Overall, the risk of bias was found to be low across all studies. A summary table of the key characteristics of the included studies is shown in Table 3.1 (Appendix C).

3.3.3 Vaccine Uptake

Of the 12 studies, four were conducted in the province of Ontario, two in Quebec, two in Alberta, two in British Columbia, one in Prince Edward Island, and one in Nova Scotia. The reported vaccination uptake rates varied widely among the 12 studies, with the lowest reported rate at 12.40% (Burchell *et al.*, 2014) and the highest at 88.20% (Ahken *et al.*, 2015). The pooled vaccination uptake using a random effects model was 55.91% (95% CI 44.87–66.65), with the test for heterogeneity; $I^2 = 99.98$ ($P < 0.0001$). A summary of the pooled meta-analysis is shown below in Table 3.2.

TABLE 3.2: POOLED META-ANALYSIS			
Study	**Sample size**	**Proportion (%)**	**95% CI**
Akhen	105	12.40	6.77 to 20.26
Krawczyk	774	88.20	85.72 to 90.39
Lim	111798	81.50	81.27 to 81.73
Liu	169259	31.30	31.08 to 31.52
McClure **(Male)** **(Female)**	 725 715	 79.00 85.00	 75.85 to 81.91 82.17 to 87.54
Musto **(School)** **(Community)**	 26304 9288	 75.00 36.00	 74.47 to 75.52 35.02 to 36.99
Ogilvie	2025	65.10	62.98 to 67.19
Ogilvie	223051	61.70	61.50 to 61.90
Smith	2519	56.60	54.64 to 58.55
Whelan	3219	74.20	72.65 to 75.70
Wilson	74340	59.00	58.65 to 59.35
Burchell	482	12.00	9.24 to 15.24
Total (Random effects)	624604	55.91	44.87 to 66.65

3.3.4 Subgroup Analysis

A subgroup analysis was conducted stratifying by a number of variables (age, sex, type of program, and method of payment) determined *apriori*. The pooled estimate for each subgroup was obtained using a random effects model after which rate ratios (with 95% CIs and P values) were calculated using the MedCalc analytic software to assess differences in vaccination rate between the predetermined variables. The subgroup analysis by age found the HPV vaccination uptake for participants younger than or equal to 18 years old to be 66.95% (95% CI: 55.00–77.89). This rate was significantly higher than the one observed for participants older than 18 years, 13.58% (95% CI 10.93–16.46). Participants younger than or equal to 18 years were 4.92 times more likely to be vaccinated for HPV compared to those over the age of 18 years ($P < 0.0001$; 95% CI 4.15–5.82). Vaccination uptake for females was higher 57.23% (95% CI: 45.40–68.66) when compared to that of males 47.01% (95% CI: 0.82–97.75). Females were 1.22 times more likely to be vaccinated for HPV compared to males ($P < 0.0001$; 95% CI 1.14–1.30).

The subgroup analysis also showed that HPV vaccine uptake among school-based programs was significantly higher 69.62% (95% CI 57.27–80.68) than community-based programs 18.66% (95% CI 6.66–34.92). Participants in school-based programs were 3.73 times more likely to be vaccinated for HPV compared to those in community-based programs ($P < 0.0001$; 95% CI 3.58–3.89). Furthermore, there were notable differences in the levels of HPV vaccination uptake when the source of funding was considered. Vaccination uptake for publicly funded programs was significantly higher 66.95% (95% CI 55.00–77.89) when compared to 13.58% (95% CI 10.93–16.46) for programs where participants had to pay out of pocket.

Participants in publically funded programs were 4.92 times more likely to be vaccinated for HPV compared to those who had to pay out of pocket ($P < 0.0001$; 95% CI 4.15–5.82). A summary of the results for the subgroup analysis is shown below in Table 3.3.

Additionally, proportion of HPV vaccination uptake according to selected characteristics variables are shown in Figures 3.2, 3.3, 3.4, 3.5 and 3.6.

TABLE 3.3: SUB-GROUP ANALYSIS						
Sub-Groups		**Total population**	**HPV Vaccine Uptake %**	**HPV Vaccine Uptake Rate Ratio (Sub-group 2 vs 1)**	**95% CI LL**	**95% CI UL**
Age	Age[1]>18	587	13.58	4.92	4.15	5.82
	Age[2]≤18	624017	66.95			
Sex	Male[1]	725	47.01	1.22	1.14	1.30
	Female[2]	623879	57.23			
Program	Community Based[1]	9875	18.66	3.73	3.58	3.89
	School Based[2]	614729	69.62			
Out of Pocket	Yes[1]	859	13.58	4.92	4.15	5.82
	No[2]	623745	66.95			

1 - Sub-group 1 *95% CI LL – 95% Confidence Interval lower limit*

2 - Sub-group 2 *95% CI UL – 95% Confidence Interval upper*

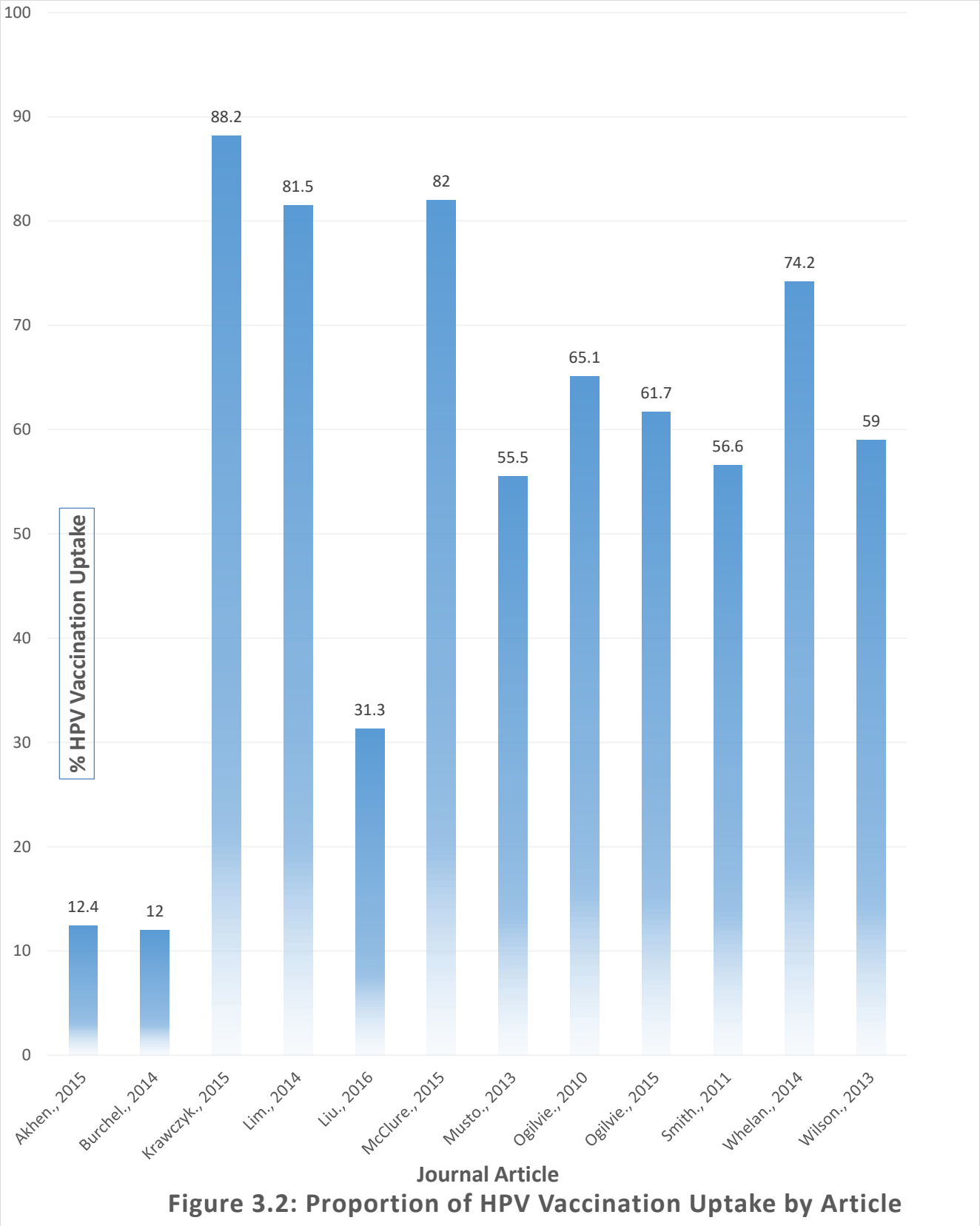

Figure 3.2: Proportion of HPV Vaccination Uptake by Article

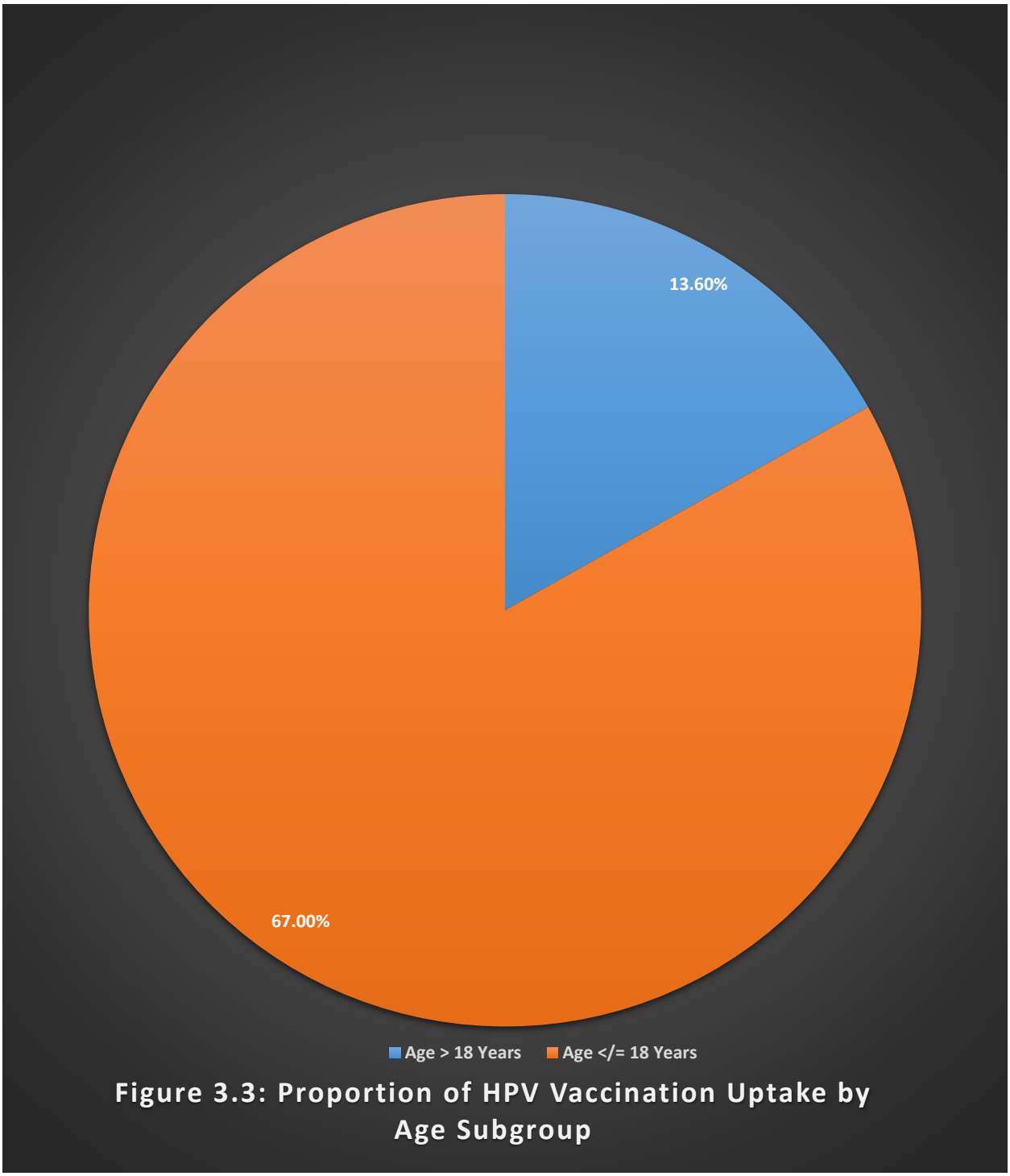

Figure 3.3: Proportion of HPV Vaccination Uptake by Age Subgroup

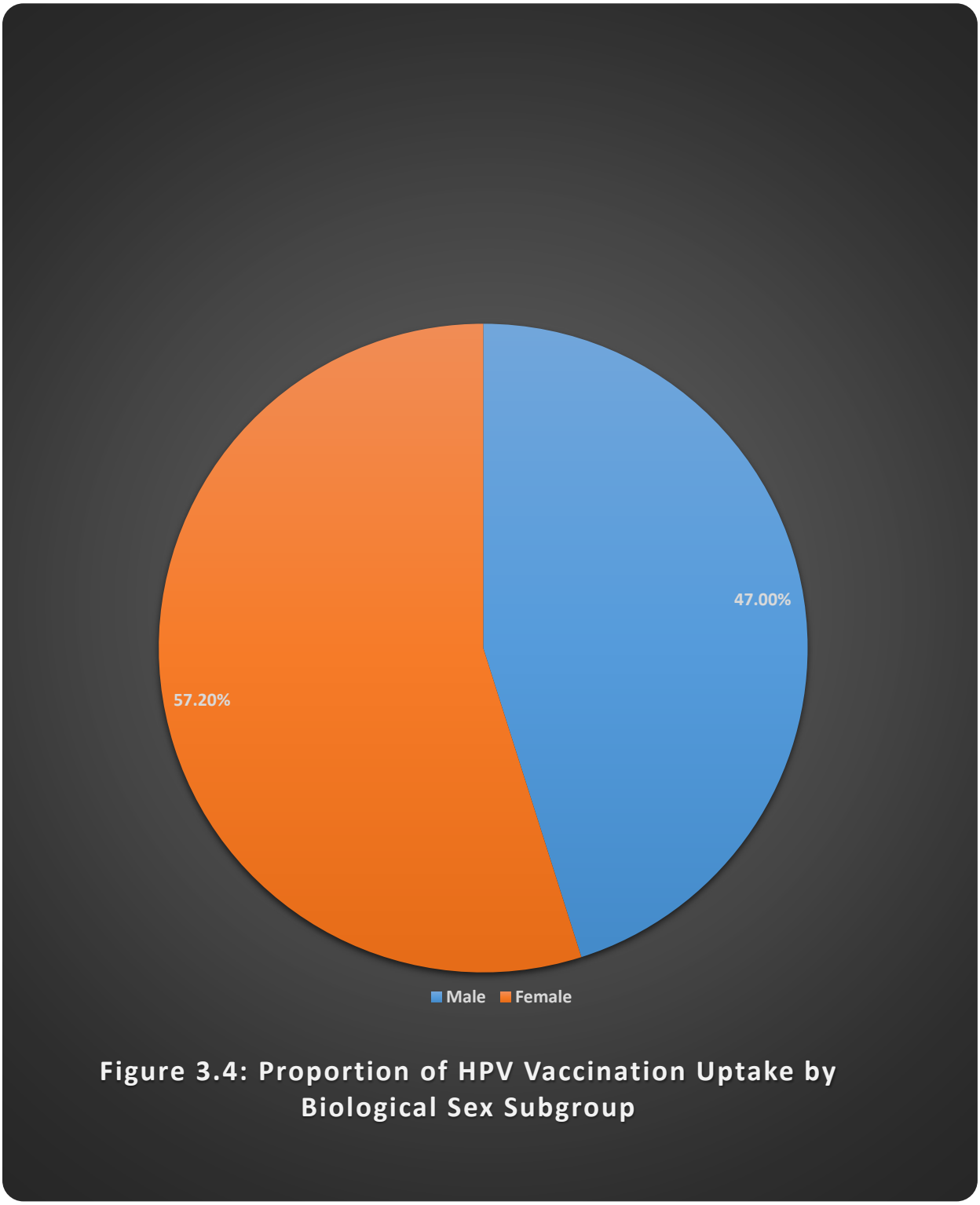

Figure 3.4: Proportion of HPV Vaccination Uptake by Biological Sex Subgroup

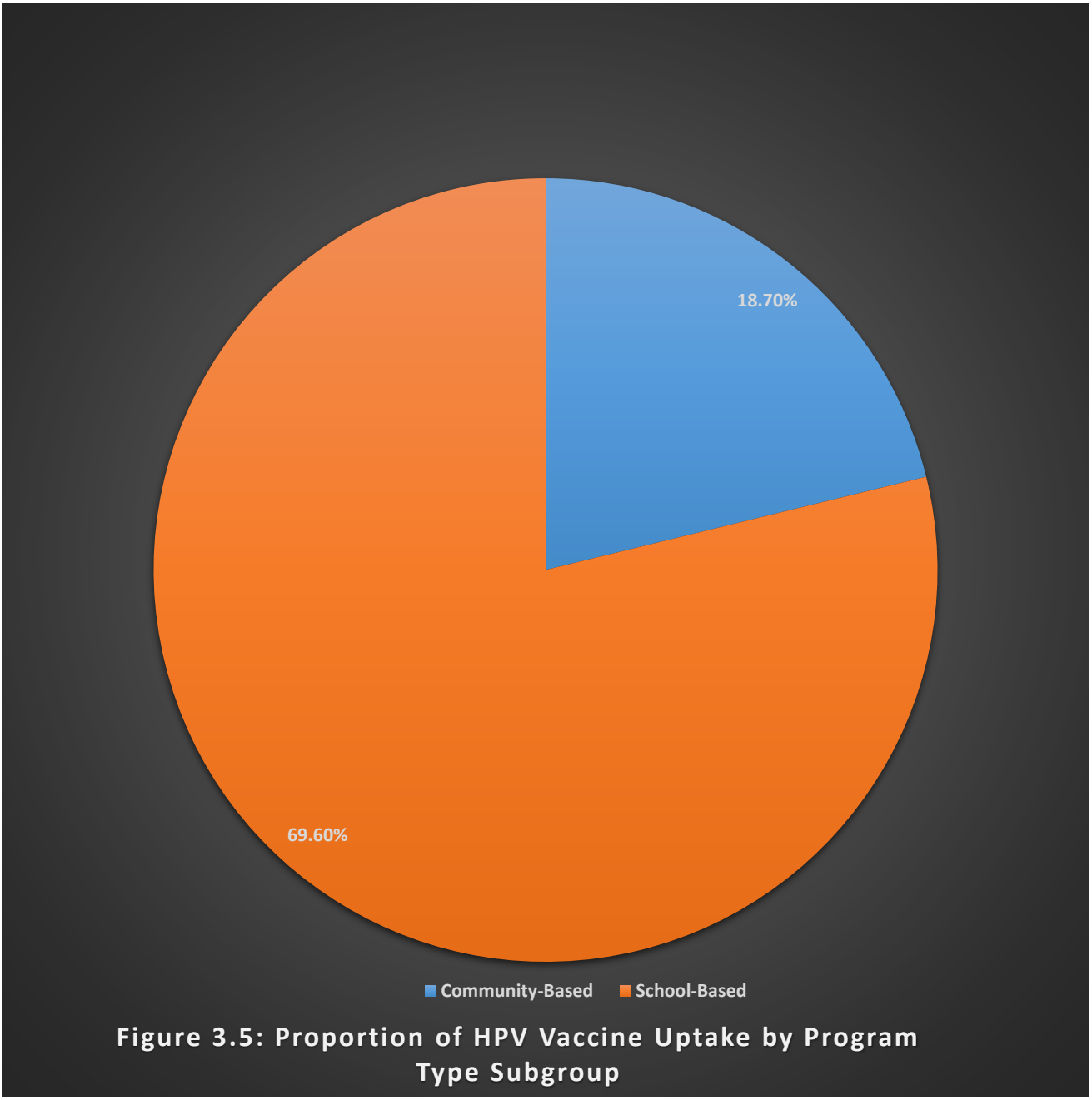

Figure 3.5: Proportion of HPV Vaccine Uptake by Program Type Subgroup

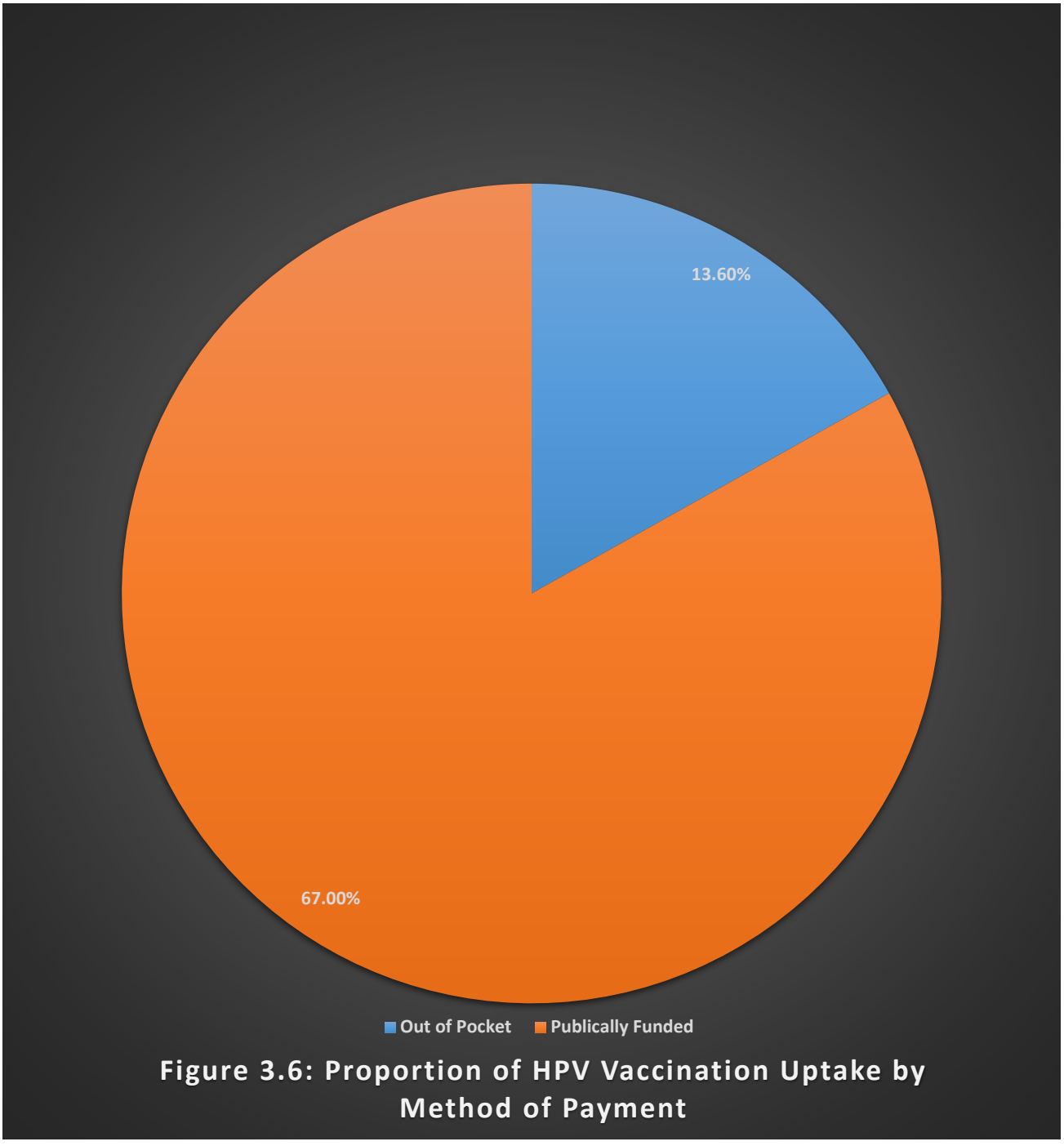

Figure 3.6: Proportion of HPV Vaccination Uptake by Method of Payment

3.4 Discussion

This systematic review was conducted to independently determine the HPV vaccine uptake in the Canadian population and to examine the various factors influencing vaccine uptake in different subpopulations that may require tailored interventions. Our pooled analysis showed the HPV vaccination uptake in Canada to be 55.91%, which is well below the >85% target set by the Canadian government (Canadian-Partnership-Against-Cancer., 2016).
It has been well documented that receiving the HPV vaccine at younger ages (10–14 years) is more advantageous as it offers earlier protection against infection and better immune response to the vaccine when compared to older women and men (Schwarz *et al.*, 2009).

Unsurprisingly, our study found that participants younger than or equal to 18 years old were 4.92 times more likely to be vaccinated for HPV compared to those over the age of 18. However, several clinical trials have shown that older girls and women, who are most at risk of infection (18–30 years), also have a strong immune response to the HPV vaccine, inducing high virus-neutralizing antibody titers (Einstein *et al.*, 2009; Muñoz *et al.*, 2009).

Consequently, implementation of programs that improve the levels of HPV vaccine uptake among older girls and women could prove very beneficial to Canadian women and help prevent a significant burden of the HPV-related diseases (including cervical cancer) on the nation.

Our findings showed that females were 1.22 times more likely to be vaccinated against HPV compared to males. In Canada, HPV vaccination for females was introduced in 2006 and for males in 2013. As of 2015, only three provinces (Alberta, Nova Scotia and Prince Edward Island) offered free vaccination to males (Shapiro *et al.*, 2016). This might help explain the observed gender disparity in our study. While the National Advisory Committee on Immunization (NACI) recommends HPV vaccination be extended to males aged 9–26, they also advise that the benefit of expanding HPV immunization to include males be compared to improving uptake amongst females to 85% in areas where uptake is < 85% (Eggertson, 2012). In addition, many sectors focusing on the direct association of HPV with cervical cancer and vaccination programs across the country are largely female oriented. These developments, alongside concerns regarding the financial cost, (Brisson *et al.*, 2007) have slowed progress toward achieving gender equity in HPV vaccination among Canadians. As an update, it is noteworthy however that as of 2020, publicly funded HPV vaccination program is available to

both boys and girls in almost all jurisdictions in Canada (Government-of-Canada., 2017b, 2019, 2020b).

Individuals participating in school-based programs were 3.73 times more likely to be vaccinated against HPV compared to community-based programs. This is similar to the findings in previous studies showing that school-based programs have higher rates of vaccination uptake in countries such as Spain, Scotland, Australia, and the USA (Hopkins *et al.*, 2013). It was reported that HPV vaccines delivered through schools in Australia and New Zealand had a high and relatively balanced uptake across socioeconomic groups, suggesting that school-based delivery can help reduce inequities in HPV vaccine delivery (Blakely *et al.*, 2014; J. Brotherton *et al.*, 2008). Moreover, school-based programs are known to provide an opportunity for children as well as their parents to be educated and make informed decisions about the importance of HPV vaccination (Blakely *et al.*, 2014; J. Brotherton *et al.*, 2008).

Participants in publicly funded programs were 4.92 times more likely to be vaccinated for HPV compared to those who had to pay out of pocket. This finding is not surprising as a systematic review conducted (Kessels *et al.*, 2012) among published articles in the USA found higher HPV vaccine uptake among individuals who had health insurance (private or public) as opposed to those who did not, suggesting that fee for service is negatively associated with vaccination uptake. Mathematical models of the clinical and economic impact of publically funded HPV vaccination programs have demonstrated significant clinical and cost benefits (Dasbach *et al.*, 2006; Kim *et al.*, 2008). However, these studies assumed high levels of vaccine uptake (>70%), and therefore, the clinical and economic impact of the HPV vaccine may have been overestimated (Elbasha *et al.*, 2007; Goldie *et al.*, 2004; Hughes *et al.*, 2002).

The HPV vaccine uptake rates in Canada appear to be much lower than in many other developed countries, which have reported coverage rates of > 70% (Hopkins & Wood., 2013). The reasons for this discrepancy are multifactorial. For instance, in 2013, the childhood National Immunization Coverage Survey (cNICS) found that approximately 75% of Canadian girls aged 12–14 years were immunized against HPV (Statistics Canada., 2015). By comparison in 2014, the adult NICS found Canadian females aged 18–26 and 27–45 years to have HPV vaccination uptakes of 44.7% and 8.3%, respectively (Statitistics-Canada., 2018). The dramatic fall in vaccination rates with increasing age among females may be attributed to the initial restriction of HPV vaccination programs to females in grades 4–8 (ages 10–14 years) in Canada. By 2012, the

NACI modified their HPV vaccination guidelines to include a larger age group (9–26 years) (Eggertson, 2012). However, despite these changes, our study results demonstrate that disparities in HPV vaccination uptake still persist by age group and setting as older cohorts, who are already out of school, are expected to pay out of pocket, potentially making the HPV vaccine unaffordable for them.

3.5 Limitations

Our study assessed the uptake of a relatively new vaccine, and as such, the amount of available data in the literature is scarce. Analysis of data showed significant heterogeneity that could be attributed to methodological and/or clinical variations in the characteristics of the included studies. There was little or no data available on the variation of vaccine uptake by ethnicity, especially with regards to the Aboriginal population in Canada. Furthermore, changing patterns of vaccine delivery, scheduling, and settings resulted in different uptake rates at different time periods. Finally, it is also possible that some of the findings may be due to factors unique to each study and could not be identified by means of a systematic review or meta-analysis.

3.6 Conclusions

Due to the relatively low number of studies and lack of long-term results, no firm conclusions can be drawn. To prevent infections and reduce the burden of HPV-related disease (including cervical cancer), communities should be made aware and encouraged to vaccinate their children. This study found that HPV vaccination rates were higher for females aged 18 years or younger, who were part of school based, publicly funded program. Better surveillance and additional research are needed in this area. The future success of the HPV immunization programs in Canada will depend on the concerted efforts and commitment of researchers, healthcare professionals, the public, and the provincial and federal government.

3.7 Recommendations

Based on the findings of our systematic review and meta-analysis, we recommend expanding the HPV vaccination programs to include young males and older females, subsidizing the costs for the vaccination and developing a national immunization surveillance program based on provincial databases to better determine the levels of HPV vaccination uptake within the Canadian population. Better surveillance will help identify at-risk subpopulations and yield epidemiological data that guide effective use of resources and inform tailoring of vaccination interventions.

Bridge to Manuscript 2

Having explored the HPV vaccination uptake in the general Canadian population through a systematic review and meta-analysis, we now look at HPV vaccination uptake in specific subpopulations starting with university/college students.

CHAPTER 4 (MANUSCRIPT 2): HPV VACCINATION STATUS AND DETERMINANTS OF UPTAKE AMONG STUDENTS IN A CANADIAN UNIVERSITY

Obidiya, O., Bird, Y., Mahmood, R., & Moraros, J. (2019). HPV Vaccination Status and Determinants of Uptake Among Students in a Canadian University *Unpublished manuscript, School of Public Health, University of Saskatchewan, Saskatoon, Canada.*

My contributions to this manuscript included conceiving and designing the study, doing background literature review on the topic, conducting analysis and interpretation of the data, and preparing the manuscript.

Mahmood R assisted in conducting analysis and interpretation of the data and preparing the manuscript.

Dr. Bird Y and Dr. Moraros J guided in conception and design of the study, the interpretation of findings, and helped critically revise and finalize the document.

Chapter 4: Manuscript 2

HPV VACCINATION STATUS AND DETERMINANTS OF UPTAKE AMONG STUDENTS IN A CANADIAN UNIVERSITY

4.1 Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in the world (Carter *et al.*, 2011; Clifford *et al.*, 2017; Crow, 2012; Tota *et al.*, 2011). It is implicated as a causal agent in several benign diseases (genital warts) and various cancers (cervical, oro-pharynx, vulva, vaginal, penile and anal) (Blas *et al.*, 2015; Clifford *et al.*, 2017; Cogliano *et al.*, 2005; Garland *et al.*, 2009; Miller *et al.*, 2015). The World Health Organization (WHO) reports that vaccination is one of the most effective public health strategy in reducing the burden of HPV infection and its serious health consequences (Audisio *et al.*, 2016; Matthijsse *et al.*, 2016; Patchay, 2017; Stein, 2011; Valentino *et al.*, 2016; World-Health-Organization., 2008).

Canada introduced a national HPV vaccine programming for girls in 2006 and for boys in 2014 with catch-up vaccination for adolescents and young adults, including university students (Government-of-Canada., 2017b, 2019). However, despite the wide implementation of HPV vaccination and catch-up programming, uptake among university students remains low in Canada (Piedimonte *et al.*, 2018). University students represent an important population that is at increased risk for HPV infection and can therefore, benefit from vaccination coverage.

Besides, Canada continues to be ranked first in terms of the proportion of college or university graduates to the general population among the most developed countries (Statitistics-Canada., 2017). As of 2016, approximately 54% of young adults (18 years old and above) were registered at one university or college in Canada (Statitistics-Canada., 2017). This population represents a heterogeneous mix with respect to lifestyle choices, health beliefs and behavioral patterns. Additionally, this group's demographic characteristics (age, sex, ethnicity, sexual orientation and relationship status), sexual behaviors (initiation of sexual intercourse, increased sexual activity, number of sexual partners and inconsistent condom use) and vaccination history (influenza, hepatitis B or MMR) have been linked with an increased burden of HPV infection (Couto *et al.*, 2014; E. M. Donadiki *et al.*, 2012; Lindley *et al.*, 2013; Piedimonte *et al.*, 2018; Rehn *et al.*, 2016; Thompson *et al.*, 2016a; Thompson *et al.*, 2016b; Winer *et al.*, 2008; Winger *et al.*, 2016).

Notwithstanding the known benefits of the HPV vaccine, a substantial proportion of university students are still hesitant to be vaccinated (Piedimonte *et al.*, 2018; Thompson *et al.*, 2016b). In Canada, HPV vaccination rates remain suboptimal among female (57%) and male (47%) young adults, which is well below the WHO recommended target level (80%) (Bird *et al.*, 2017; World-Health-Organization., 2017). Vaccine hesitancy among Canadian university students may be due to variety of factors including poor access to healthcare services, associated high costs, difficulty in adhering to the multi-dose regimen, and worries about safety and health concerns (Dubé *et al.*, 2016; Statitistics-Canada., 2018).

While previous researches have focused mainly on children and adolescents, few studies have evaluated the factors associated with HPV vaccination uptake among young adults. This information is critical for understanding the unique mechanisms at play among university students and can help contribute immensely to the success of health promotion interventions that increase HPV vaccination acceptance among this vulnerable population. The purpose of this study was to assess the HPV vaccination status and determinants of uptake among students in a Canadian university.

4.2 Methods

4.2.1 Study Sample

This study used the National College Health Assessment-II (NCHA-II) Survey (Spring 2016). It includes 990 student participants from a Canadian university. The NCHA is a self-reported survey that collects and collates information on students' health behaviours, attitudes, and perceptions. Participants consisted of male and female students, who were 18 years old and older. Only participants with a known HPV vaccination status (responded, "yes" or "no") were included in the study, while those who were unsure (responded, "not known") were removed.

4.2.2 Outcome Measure

A dichotomous variable ("yes," "no") signifying whether the student respondents had received shots or series of shots of the HPV vaccine was created. Participants were categorized accordingly.

4.2.3 Independent Variables

The variables of interest in this study were the following:

1) *Demographics:* Age (18-20, 21-24, 25-29, 30 years old or older); sex (females, males); race/ethnicity (Aboriginal, White, non-White); nationality (Canadian, international); sexual

orientation (straight/heterosexual, non-straight/non-heterosexual); and relationship status (not in a relationship, in a relationship but not living together, in a relationship living together).
2) *Sexual behaviours:* Number of sexual partners (none, one, two, three, four or more); use of protective barrier for oral, vaginal and anal sex (never did this sexual activity, have not during past 30 days, never, used protection); history of sexually transmitted infections (chlamydia, genital herpes, genital warts/HPV, gonorrhea and hepatitis B).
3) *Vaccination history:* Receipt of other vaccinations (influenza, hepatitis B or MMR).

4.2.4 Statistical Analysis

Descriptive analysis and cross-tabulation to estimate point prevalence of HPV vaccination with respect to selected variables (age, sex, race/ethnicity, nationality, sexual orientation, relationship status, number of sexual partners, use of protective barrier for sex, history of STIs and vaccination history) was conducted. Univariate analysis was conducted to assess the crude association between each independent variable and the outcome of interest (self-reported HPV vaccination). The level of significance $\alpha=0.25$ was used during univariate analysis (i.e., *P*-value >0.25 was not statistically significant). Assumptions of multivariable logistic regression were checked. Using the variant inflation factors (VIF) values**,** multi-collinearity was assessed for all the independent variables found to be statistically significant from the univariate analysis**.** A VIF>3 is taken as violation of the multi-collinearity assumptions (Hair *et al.,* 2019). Manual backwards selection strategy was used for our model construction. As variables were removed step-wisely from the model, confounding was assessed at each stage. A change of 20% or greater in the regression coefficient of a predictor ($\Delta\beta\geq20\%$) suggested that the variable is a confounder. If a variable was found to be a confounder, it remained in the model. Thereafter, possible two-way interactions involving biologically relevant predictors were assessed using a *P*-value of 0.05. To assess the characteristics of our final explanatory model, we did a receiver operating curve (ROC). characteristic analysis (probability cut-off of 0.5). Analysis was done using SPSS version 22.

4.3 Results

4.3.1 HPV Vaccine Uptake

Our study found that 37.90% of the student participants received the HPV vaccine. Further breakdown of HPV vaccine uptake according to relevant independent variable groupings is as highlighted below.

1) *Demographic characteristics:* Considering HPV vaccine uptake under demographic characteristics and according to age; 59.20% (18-20 years), 35.50% (21-24 years), 18.24% (25-29 years) and 16.13% (30 years or more) received the vaccine. According to sex, 44.14% (female) and 19.61% (male) received the vaccine. Vaccinated proportion according to race/ethnicity was 33.33% (Aboriginal), 34.57% (non-White) and 40.13% (White). Relative to nationality; 39.89% of those vaccinated were Canadian students while 16.84% were international students. Considering sexual orientation; 37.72% (straight/heterosexual) and 39.23% (non-straight/non-heterosexual) were vaccinated. Proportion vaccinated according to relationship status were as follows: 38.56% (not in a relationship), 42.94% (in a relationship but not living together), and 29.46% (in a relationship living together).

2) *Sexual behaviour:* When examining HPV vaccine uptake relating to sexual behaviours; vaccinated proportion according to number of sexual partners was 35.89% (no partner), 36.97% (one partner), 39.33% (two partners), 44.68% (three partners), 44.44% (four partners or more). Considering the use of protective barrier during oral sex; 35.53% (never did this sexual activity), 37.37% (have not during last 30 days), 39.52% (never), 36.84% (used protection) were vaccinated. Looking at the use of protective barrier during vaginal sex; 36.60% (never did this sexual activity), 32.54% (have not during last 30 days), 37.07% (never), 41.87% (used protection) were vaccinated. Under use of protective barrier during anal sex; 38.31% (never had sexual activity), 38.76% (had not during last 30 days), 38.27% (never), 34.88% (used protection) were vaccinated. Focusing on history of STIs; 37.30% (“no” STI) and 55.56% (“yes” STIs) were vaccinated.

3) *Vaccination history*: Under vaccination history, HPV vaccine uptake was as follow: For hepatitis B; 8.05% (“no,” hepatitis B vaccination) and 46.36% (“yes,” hepatitis B vaccination). For influenza; 29.86% (“no,” influenza vaccination) and 48.69% (“yes,” influenza vaccination). For MMR; 10.20% (“no,” MMR vaccination) and 42.62% (“yes,” MMR vaccine).

A summary of the proportion of vaccinated and unvaccinated participants according to variables under consideration are as shown below in Table 4.1.

Table 4.1: Characteristics of HPV Vaccination NCHA-II Web Spring 2016 of a Western Canadian University				
		Percentage		**Total**
HPV[2] vaccination status (n=990)	Yes	37.90		375
	No	62.10		615
Independent Variables		**Vaccinated (%)**	**Unvaccinated (%)**	**Total (n)**
Age (n = 989)	18 - 20 years old	59.20	40.80	326
	21 - 24 years old	35.50	64.50	369
	25 - 29 years old	18.24	81.76	170
	30 years or more	16.13	83.87	124
Sex (n = 989)	Female	44.14	55.86	734
	Male	19.61	80.39	255
Relationship status (n = 990)	Not in a relationship	38.56	61.44	402
	In a relationship but not living together	42.94	57.06	347
	In a relationship living together	29.46	70.54	241
Sexual orientation (n = 987)	Straight/ Heterosexual	37.72	62.28	806
	Non-Straight/Non-Heterosexual	39.23	60.77	181
Number of sexual partners in the last 12 months (n = 978)	None	35.89	64.11	248
	1	36.97	63.03	522
	2	39.33	60.67	89
	3	44.68	55.32	47

	4 or more	44.44	55.56	72
Nationality (n = 985)	Canadian	39.89	60.11	890
	International	16.84	83.16	95
Use of protective barrier during oral sex within the last 30 days (n = 984)	Never did this sexual activity	35.53	64.47	228
	Have not during last 30 days	37.37	62.63	198
	Never	39.52	60.48	501
	Used protection	36.84	63.16	57
Use of protective barrier during vaginal sex within the last 30 days (n = 984)	Never did this sexual activity	36.60	63.40	235
	Have not during last 30 days	32.54	67.46	169
	Never	37.07	62.93	205
	Used protection	41.87	58.13	375
Use of protective barrier during anal sex within the last 30 days (n = 978)	Never did this sexual activity	38.31	61.69	676
	Have not during last 30 days	38.76	61.24	178
	Never	38.27	61.73	81
	Used protection	34.88	65.12	43
History of STI[3] within past 12 months (n = 984)	Yes	5.56	44.44	957
	No	37.30	62.70	27
Race/Ethnicity (n = 990)	Aboriginal	33.33	66.67	84
	Non-White	34.57	65.45	156
	White	40.13	59.87	750
Vaccination history				

○ Hepatitis B (n = 888)	Yes	46.36	53.64	174
	No	8.05	91.95	714
○ Influenza (n = 975)	Yes	48.69	51.31	556
	No	29.86	70.14	419
○ MMR[4] (n = 926)	Yes	42.62	57.38	147
	No	10.20	89.80	779

[1]Outcome variable is HPV vaccination status with two levels ["Yes" and "No" (reference)]
[2]Human Papillomavirus
[3]Sexually Transmitted Infections (STIs) consist of chlamydia, genital herpes, genital warts/HPV, gonorrhea or hepatitis B
[4]Measles, Mumps and Rubella

4.3.2 Predictors of HPV Vaccine Uptake

4.3.2.1 Univariate Analysis

Univariate analysis was conducted with a level of significance of $\alpha=0.25$. Statistically significant associations at this level are as follows: age (*P*-value <0.0001), sex (*P*-value <0.0001), relationship status (*P*-value <0.0001), nationality (*P*-value <0.0001), use of protective barrier-vaginal (*P*-value <0.2080), history of STIs (*P*-value <0.0690), race/ethnicity (non-White) **(***P*-value <0.0530), vaccination history (*P*-value <0.0001). Odds ratios (ORs) for univariate analysis with respect to the reference category listed are presented below in Table 4.2.

Table 4.2: Univariate of NCHA-II Web Spring 2016 of a Western Canada University			
Independent Variables		**HPV[1] vaccination ("Yes" versus "No")**	**P value (α=0.25)**
		Odds (95% CI)	
Age **(Ref= "30 years old or older")**	18 - 20 years old	**7.64 (4.24 - 13.75)**	**<0.0001**
	21 - 24 years old	**3.07 (1.71 - 5.50)**	
	25 - 29 years old	1.04 (0.51 - 2.11)	
Sex **(Ref= "Male")**	Female	**2.88 (2.00 - 4.16)**	**<0.0001**
Relationship status **(Ref= "In a relationship living together")**	Not in a relationship	**1.81 (1.22 – 2.69)**	**<0.0001**
	In a relationship but not living together	**2.21 (1.48 – 3.29)**	
Sexual orientation **(Ref = "Non-Straight/Non-Heterosexual)**	Straight/ Heterosexual	0.92 (0.63 -1.33)	0.644
Number of sexual partners Within last 12 months **(Ref= 4 or more)**	None	0.61 (0.34 – 1.11)	0.322
	1	0.60 (0.34 - 1.05)	
	2	0.71 (0.35 – 1.45)	
	3	0.92 (0.41 – 2.09)	
Nationality **(Ref = "International")**	Canadian	**2.97 (1.63 – 5.41)**	**<0.0001**
Use of protective barrier during oral sex within the last 30 days **(Ref= "Used protection")**	Never did this sexual activity	1.12 (0.57 – 2.20)	0.861
	Have not during last 30 days	1.11 (0.56 – 2.21)	
	Never	1.24 (0.66 – 2.34)	
	Never did this sexual activity	0.84 (0.58 – 1.21)	**0.208**

Use of protective barrier during vaginal sex within the last 30 days **(Ref= "Used protection")**	Have not during last 30 days	**0.63 (0.41 – 0.98)**	
	Never	0.54 (0.54 – 1.18)	
Use of protective barrier during anal sex within the last 30 days **(Ref= "Used protection")**	Never did this sexual activity	1.32 (0.63 – 2.77)	0.800
	Have not during last 30 days	1.18 (0.53 – 2.61)	
	Never	1.14 (0.48 – 2.73)	
	I have not had vaginal intercourse in the last 12 months	0.73 (0.42 – 1.30)	
	No	0.72 (0.42 – 1.23)	
History of STIs within past 12 months **(Ref= "Yes")**	No	0.44 (0.18 – 1.06)	**0.069**
Race/Ethnicity			
	Aboriginal	0.69 (0.68 – 0.80)	0.360
Ref=White	Non-White	0.71 (0.50 – 1.00)	**0.053**
Vaccination History			
○ Hepatitis B	No	0.10 (0.05 – 0.19)	**<0.0001**
○ Influenza	No	0.50 (0.38 – 0.67)	**<0.0001**
○ MMR[2] **(Ref= "Yes")**	No	0.16 (0.09 – 0.29)	**<0.0001**

[1]Human Papillomavirus
[2] Measles, Mumps and Rubella
*** The outcome variable is HPV vaccination status with two levels ["Yes" and "No" (reference)]**

4.3.2.2 Multivariable Analysis

Variables identified as significant in the univariate analysis were firstly tested for multi-collinearity. A variance inflation factor **(**VIF) values of less than 3 was observed for all independent variables, indicating the independent variables are not highly correlated (Hair *et al.*, 2019). Likewise, tolerance values ranged from 0.63 to 0.98, providing further evidence of no violation of multi-collinearity assumption. The receiver operating characteristic (ROC) curve was used to assess the characteristics as of the final model. With a probability cut-off set at 0.5, the area under the ROC curve was 0.815 (95% CI 0.789-0.842).

Our final model depicted the association between self-reported HPV vaccination and the selected independent variables. The following variables: age, sex, other vaccinations (hepatitis B, influenza, MMR) and history of STI were significantly (p-value < 0.05) associated with the receipt of HPV vaccine.

Looking at age; individuals that were 18 – 20 years were 12.81 (95% CI 6.84 – 23.97) times more likely to receive the HPV vaccine compared to those that were 30 years and above (p-value <0.0001). Considering gender of participants, females were 2.94 (95% CI 1.94 – 4.47) times more likely to be vaccinated for HPV compared to males (p-value < 0. 0001). Looking at history of STI; individuals that had no history of STIs within the past 12 months were 30% (OR=0.70, 95% CI 0.16 - 0. 89) less likely to receive the HPV vaccine (p-value = 0. 022) compared to those reporting a history of a STIs within the past 12 months. Regarding vaccination history; individuals that were unvaccinated for hepatitis B were 17% (OR=0.83, 95% CI 0.64 – 0.91) less likely to receive the HPV vaccine (p-value < 0. 0001) compared to those that were vaccinated for hepatitis B. Likewise, individuals that were unvaccinated for influenza were 49% (OR=0.51, 95% CI 0.31 – 0.66) less likely to receive the HPV vaccine (p-value < 0. 0001) compared to those that were vaccinated for influenza. Also, individuals that were unvaccinated for MMR were 33% (OR=0.67, 95% CI 0.33 – 0.84) times less likely to receive the HPV vaccine (p-value = 0. 002) compared to those that were vaccinated for MMR. Relationship status, nationality, use of protective barrier and race/ethnicity were not found to be statistically significant.

A summary of the association of predictor variables with HPV vaccination after multivariable analysis is shown below in Table 4.3.

Table 4.3: Multivariable Analysis of NCHA-II Web Spring 2016 of a Western Canada University			
Independent Variables		**HPV[1] vaccination ("Yes" versus "No")** **Odds (95% CI)**	**P-value (α=0.05)**
Age **(Ref= "30 years old or older")**	18 - 20 years old	**12.81 (6.84 – 23.97)**	**<0.0001**
	21 - 24 years old	**3.25 (1.79 - 5.87)**	**<0.0001**
	25 - 29 years old	1.28 (0.63 - 2.63)	0.494
Sex **(Ref= "Male")**	Female	**2.94 (1.94 - 4.47)**	**<0.0001**
History of STI within past 12 months **(Ref= "Yes")**	No	**0.70 (0.16 – 0.89)**	**0.022**
Vaccination History			
○ Hepatitis B	No	**0.83 (0.64 – 0.91)**	**<0.0001**
○ Influenza	No	**0.51 (0.31 – 0.66)**	**<0.0001**
○ MMR[2] **(Ref= "Yes")**	No	**0.67 (0.33 – 0.84)**	**0.002**
[1]Human Papillomavirus **[2] Measles, Mumps and Rubella** ***The outcome variable is HPV vaccination status with two levels [Yes and No (reference)]**			

4.4 Discussion

This study was carried out in order to explore the HPV vaccination status and determinants of uptake among students in a Canadian university. This aligns with WHO and research recommendations that HPV vaccines should be incorporated as part of a coordinated and comprehensive strategy to prevent cervical cancer and other diseases caused by HPV in the general population (Lekoane *et al.*, 2017; World-Health-Organization., 2008). Findings from our study provide evidence of notable gaps in the HPV vaccine acceptance and program delivery in young adults, especially among university students. This study shows that uptake of the HPV vaccine is generally low among university students and particularly suboptimal in certain demographic subpopulations of students (male, older, and international).

Explicitly of note is the fact that 37.90% of participating students self-reported being vaccinated with the HPV vaccine. This rate is low compared with the recommended projected uptake of the HPV vaccine by the Canadian Immunization Committee (CIC) which states that 80% of eligible populace be fully vaccinated against HPV within 2 years (and 90% within 5 years) of the introduction of the HPV vaccination program (Government-of-Canada., 2017b, 2019). Likewise, we observed that the 37.90% HPV vaccine uptake in the university students' population is lower than the reported HPV vaccine uptake of 55.91% in the general Canadian populace in a systematic review and meta-analysis which used a pooled random effect model (Dubé *et al.*, 2016). This again underscores an obvious gap in HPV vaccine uptake and need for intervention to improve uptake among these university students (Dubé *et al.*, 2016).

In addition, there is notable disparity in HPV vaccination uptake between students identifying as Canadians (39.89%) and those identifying as international students (16.84%). According to Statistics Canada, immigration is presently responsible for about two-thirds of Canada's population growth and a sizeable portion of these immigrants are international students (Statitistics-Canada., 2018). At present, there are no HPV vaccination policies for new Canadian immigrants, making it difficult to track their vaccination status. The Immigration Medical Examinations (IME) does not include a review of immunization status (Government-of-Canada., 2019). Offering immunization services to international students at entry level for university studies could go a long way in addressing observed disparity in immunization coverage between

Canadian and international students. Besides, it is desirable that maximum effort be exerted to ensure optimal uptake of HPV vaccines for all Canadians who are under-immunized.

Furthermore, our findings indicate that individuals that were generally unvaccinated (with other vaccines) were less likely to be vaccinated with the HPV vaccine. Essentially, this might be due to vaccine hesitancy, a common trend for those not yet convinced about the benefit of vaccination as a preventive health measure. Vaccine hesitancy is an intricate and multifaceted phenomenon. Indeed, there is no single cause of vaccine hesitancy because an interplay various factors is involved (Dubé *et al.*, 2013; Larson *et al.*, 2014; Taddio, 2015). Significant pointers of vaccine hesitancy may include; concern about the safety, perception that vaccines are not beneficial, distrust of and conspiracy theories about role of the pharmaceutical industry in the making and marketing as well as implementation of vaccination programs (Dubé *et al.*, 2013; Larson *et al.*, 2014; Taddio, 2015). Historically; religious and perceived potential for promiscuous behaviour concerns regarding HPV vaccine makes it an easy target for vaccine hesitancy. Compared to older vaccines like MMR, Hepatitis B and influenza, HPV vaccine is relatively new. Thus, it is explainable that the observed HPV vaccine uptake from our study is even lesser than that of that of uptake for MMR, Hepatitis B and influenza.

Likewise, individuals differ in terms of knowledge, perception, attitude and willingness to accept vaccination as a wellness tool. According to the health belief model, individuals that are well informed and have a positive attitude are most likely to accept and utilize vaccination generally as strategy to promote health and prevent diseases (E. Donadiki *et al.*, 2014; Rosenstock *et al.*, 1988). Conversely, people that are averse to vaccines based on what constitute their health belief elements are most likely to have vaccine hesitancy (E. Donadiki *et al.*, 2014; Rosenstock *et al.*, 1988). Among university students, who are at increased risk of HPV infection, several studies have reported both poor knowledge and low perceived risks related to HPV infection and its health consequences. In addressing knowledge gaps and low-perceived risk, studies showed that implementation of HPV education via several media led to sustained increase within student health clinics (Piedimonte *et al.*, 2018; Thompson *et al.*, 2016b). It is noteworthy that such HPV education and vaccination campaign with significant success have previously been carried out in some universities in Canada and the United States (Piedimonte *et al.*, 2018; Thompson *et al.*, 2016b).

Our findings also indicate that younger age was a significant and positive predictor for HPV vaccine uptake. This is consistent with previous studies reported in the literature (Couto *et al.*, 2014; Fontenot *et al.*, 2014; Government-of-Canada., 2016b; Johnson *et al.*, 2017; Lindley *et al.*, 2013; Thompson *et al.*, 2016b; A. Wilson, 2015; Winger *et al.*, 2016). Vaccination uptake according to age ranges from 59.20% – 16.13% for age brackets 18-20 years and 30 years above respectively. The increased HPV vaccine uptake with younger age may be due to several reasons. The HPV vaccination is a comparatively new program that was introduced in Canada in 2006. Thus, the older the age cohort the less likelihood of being vaccinated compared to a younger age cohort. In addition, government policy and program delivery guidelines (school-based, public funded, 9-26 years) favors younger age cohorts to vaccinate as older individuals may have to pay out of pocket in community-based HPV vaccination programs. Since Health Canada has authorized use of specific HPV vaccines from ages 9-45 years, addressing observed disparity in vaccination uptake among these students should be a priority (Government-of-Canada., 2016b).

Findings from this study also shows that females were more likely to be vaccinated for HPV compared to males. Females had a higher vaccination uptake of 44.14% compared with their male counterparts with rate 19.61%. Previous studies reported a similar trend of gender disparity in HPV vaccination (Couto *et al.*, 2014; Fontenot *et al.*, 2014; Government-of-Canada., 2016b; Johnson *et al.*, 2017; Lindley *et al.*, 2013; Thompson *et al.*, 2016b; A. Wilson, 2015; Winger *et al.*, 2016). This could be partly attributed to the fact that publicly funded HPV programs were initially targeted for use by young females only (Government-of-Canada., 2016b). Although Prince Edward Island (PEI) started HPV vaccination for males in 2013 and other jurisdictions in Canada joining at later dates. However, there is still the need to focus on improving HPV vaccine uptake in the Territories of Northern Canada; where reported estimates of HPV coverage from Northwest Territories and Nunavut were more than 10% lower than the national coverage (Government-of-Canada., 2016d). Other plausible reasons for the observed disparities between male and female HPV vaccine uptake is the fact that females are known to access preventive healthcare more than their male counterparts. In addition, the erroneous but pervasive notion that HPV vaccine is just for females is not usually helpful for optimal uptake in

males (Hull *et al.*, 2009). This may further clarify observed higher vaccination uptake reported in females compared to males (Hull *et al.*, 2009).

Lastly, individuals that had no history of STIs were 30% less likely to receive the HPV vaccine compared with individuals reporting a history of STIs. This behavioral pattern is explained in part by the fact that a history of past infection increases peoples' knowledge on disease vulnerability and reinforces their need to pursue preventive measures such as vaccination (E. Donadiki *et al.*, 2014; Rosenstock *et al.*, 1988).

Based on the findings from this study, a pragmatic approach at increasing vaccination uptake could be educating and offering appropriate vaccination services to students with a history of STIs at the point of diagnosis or treatment.

4.5 Strength and Limitation of Study

To the best of our knowledge, this study is one of the first to examine HPV vaccination status and determinants of uptake among Canadian university students.
However, for our secondary data (National College Health Assessment-II Spring 2016); vaccination status was self-reported by the respondents so there could be under/over reporting biases. This study involved respondents from a single Canadian university, so results are not generalizable to all Canadian universities/colleges. It would be helpful to conduct future research on composite data on all participating Canadian institutions.
In order to conduct this study, respondents unsure of their vaccination status were excluded from the analysis. This could have led to those under/over reporting of those that were vaccinated.

4.6 Conclusions

The results of this study found significant gaps in the HPV vaccination uptake among various subpopulations of university students. To be most effective, future HPV vaccination programming need to account for these differences and focus on increasing awareness and student participation in health promotion initiatives. Such approach would optimize both short and long-term health benefits derivable from HPV vaccination.

Bridge to Manuscript 3

Having explored HPV vaccination uptake and determinants of HPV vaccine among students from a single Canadian university, it is needful to conduct similar research across more Canadian institutions so that results are generalizable to all Canadian universities/colleges.

CHAPTER 5 (MANUSCRIPT 3): HPV VACCINATION STATUS AND DETERMINANTS OF UPTAKE AMONG STUDENTS IN CANADIAN UNIVERSITIES

Obidiya O., Mutwiri G., Bird Y., Mahmood R., & Moraros J (2020). HPV Vaccination Status and Determinants of Uptake Among Students in Canadian Universities *Unpublished manuscript, School of Public Health, University of Saskatchewan, Saskatoon, Canada.*

My contributions to this manuscript included conceiving and designing the study, doing background literature review on the topic, conducting analysis and interpretation of the data, and preparing the manuscript.

Mahmood R assisted in conducting analysis and interpretation of the data and preparing the manuscript.

Dr. Bird Y and Dr. Moraros J guided in conception and design of the study, the interpretation of findings, and helped critically revise and finalize the document.

Dr. Mutwiri G guided in the interpretation of findings and helped in the review of the final document.

Chapter 5: Manuscript 3

HPV VACCINATION STATUS AND DETERMINANTS OF UPTAKE AMONG STUDENTS IN CANADIAN UNIVERSITIES

5.1 Introduction

Human papillomavirus (HPV) is the most common viral infection of the reproductive tract in the world (Carter *et al.*, 2011; Clifford *et al.*, 2017; Crow, 2012; Tota *et al.*, 2011; World-Health-Organization., 2019a). Sexually transmitted infections (STIs) are frequently spread through sexual contacts involving vaginal, anal and/or oral sex. Although most disease-causing HPV affect the cervix, it is equally implicated in cancers of the oro-pharynx, vulva, vaginal, penile and anal areas. HPV is equally involved in benign diseases such as genital warts and respiratory papillomatosis (Blas *et al.*, 2015; Cogliano *et al.*, 2005; Garland *et al.*, 2009; Miller *et al.*, 2015; World-Health-Organization., 2019a). Furthermore, co-infection with other sexually transmitted agents, like those that cause herpes simplex, chlamydia and gonorrhea are common (World-Health-Organization., 2019a).

The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) recognize vaccination as cardinal to reducing global HPV infection and associated cervical cancer and other HPV related diseases (Audisio *et al.*, 2016; Centers-for-Disease-Control-and-Prevention., 2019; Matthijsse *et al.*, 2016; Stein, 2011; World-Health-Organization., 2008, 2019a). In the fight against cervical cancer, the International Agency for Research on Cancer (IARC) aligned with the position of the World Health Organization (WHO) on human papillomavirus (HPV) vaccination; affirming that HPV vaccines are safe and efficacious (Ferlay *et al.*, 2018). In 2006, vaccines protective against four types of HPV were authorized in Canada for females 9 to 26 years.

In 2010, use of these HPV vaccines in males 9 to 26 years of age for prevention of genital warts were authorized (Government-of-Canada., 2012, 2016b).

Aside from Canada, many countries introduced the HPV vaccine program into their health systems. As of April 2019, about 100 countries and territories, representing 50% of the global total, have HPV vaccine in their national schedule (J. M. Brotherton *et al.*, 2015; Bruni *et al.*, 2016; Elam-Evans *et al.*, 2014; European-Centre-for-Disease-Prevention-and-Control., 2012; LaMontagne *et al.*, 2011; Markowitz *et al.*, 2012; Mawdsley *et al.*; Tabrizi *et al.*, 2012; United-

Nations-Children's-Fund., 2019). In Canada, school-based vaccination programs started with preteen-girls and was later expanded to boys across time depending on the provinces. Since then, there have been HPV catch-up vaccination programs in young adults, including university driven interventions (Government-of-Canada., 2017b, 2019).

Despite HPV vaccination catch-up efforts in Canada, it is alleged that HPV uptake among university students remains low (Piedimonte *et al.*, 2018). Besides, adolescents and young adults such as university students are at higher risk of acquiring sexually transmitted infections (STIs) (Patel *et al.*, 2012). Furthermore, it is well known that there are dynamic demographic characteristics and sexual behaviors among university students that make them quite vulnerable to HPV infection (E. M. Donadiki *et al.*, 2012; Lindley *et al.*, 2013; Stauffer, 2014; Thompson *et al.*, 2016a; Winer *et al.*, 2008; Winger *et al.*, 2016).

Notably, a substantial proportion of university students are still hesitant to be vaccinated (Piedimonte *et al.*, 2018; Thompson *et al.*, 2016b). Studies show that while most university students have basic knowledge of HPV, they had low perceptions of their susceptibility to HPV infection (Barnard *et al.*, 2017; Mehu-Parant *et al.*, 2010). Some authors have suggested that regular preventive medical checks built in as part of students' orientation programs may offer unique opportunity to recognize students who are eligible for HPV vaccines (Thompson *et al.*, 2016b). According to Barnard et al., who used the Precaution Adoption Model Process (PAMP); most unvaccinated students were still in the early stages of decision-making relative to HPV vaccination (Barnard *et al.*, 2017). Documented evidence across Canada show that HPV vaccine uptake is variable ranging from between 42% to 90%, depending on the jurisdiction (Piedimonte *et al.*, 2018). A systematic review and meta-analysis put HPV vaccination uptake in Canada among female at (57%) and male (47%) young adults which is well below the WHO recommended target level (80%) (Bird *et al.*, 2017; World-Health-Organization., 2017).

Although university environment may present new opportunities for exposure to STIs, especially HPV, studies of HPV vaccine acceptability conducted in this population reported that large number of respondents were uncertain concerning intent to take the HPV vaccine. In addition, some studies reported that many respondents decided not to take the HPV vaccine; depicting a high degree of vaccine hesitancy arising from cost, safety concerns and limited access to healthcare services (Allen *et al.*, 2009; Boehner *et al.*, 2003; Crosby *et al.*, 2007; Dubé *et al.*, 2016; Gerend *et al.*, 2008; Patel *et al.*, 2012; Shapiro *et al.*, 2018).

While previous research efforts focused mainly on HPV vaccination uptake in school-based adolescent (and also parental consent as decision makers on vaccination), few studies have assessed factors associated with HPV vaccination uptake among young adults. This knowledge is of utmost importance as these young adults are not only responsible for their personal vaccination decisions but would in future serve as proxy decisions makers for their own children.

A previous study with similar objectives as this present study examined the predictors of HPV uptake among young adults in a single Canadian university (Obidiya *et al.*, 2019). While the conclusion from that study is important, it cannot be generalized because of the small sample size. Furthermore, understanding of critical factors that can explain the behavior of Canadian university students related to HPV vaccine uptake would be helpful for planning and delivery of future HPV vaccine programs, especially in young adult populations in Canada. The purpose of this present study is to assess the HPV vaccination status and determinants of uptake among young adult population, represented by students in Canadian universities.

5.2 Methods

5.2.1 Study Sample

This study used the National College Health Assessment-II (ACHA-NCHA-II) Survey (Spring 2016). It included 35587 student participants from across Canadian universities. The ACHA-NCHA is a self-reported survey that collects information on students' health behaviours, attitudes, and perceptions. Participants consisted of male and female students, who were 18 years old and older. Only participants with a known HPV vaccination status (responded, "yes" or "no") were included in the study, while those who were unsure (responded, "not known") were removed.

5.2.2 Outcome measure

A dichotomous variable ("yes," "no") indicating whether the student respondents had received shots or series of shots of the HPV vaccine was created. Participants were categorized accordingly.

5.2.3 Independent variables

The variables of interest in this study were the following:

1) *Demographics:* Age (18-20, 21-24, 25-29, 30 years old or older); sex (females, males); race/ethnicity (Aboriginal, White, non-White); nationality (Canadian, international); gender

identity (woman, other identities, transwoman, transman, gender queer); and relationship status (not in a relationship, in a relationship but not living together, in a relationship living together), marital status (single, married/partnered, separated, divorced), year in school (1st year, 2nd year, 3rd year, 4th year, 5th year, graduate).

2) *Sexual behaviours:* Number of sexual partners (none, one, two, three, four or more); use of protective barrier for oral, vaginal and anal sex (never did this sexual activity, have not during past 30 days, never, used protection); use of a method of birth control to prevent pregnancy during last vaginal intercourse (N/A have not have vaginal intercourse, No have not had vaginal intercourse that could result in pregnancy, No did not want to prevent pregnancy, No did not use any birth control method).

3) *Engagement in Screening/Health Promotion and History STIs:* Dental examination and cleaning in the last 12 months (Yes, No); male performed a testicular self-examination in the last 30 days (Yes, No); females performed a breast self-examination in the last 30 days (Yes, No); females had a routine gynecological exam in the last 12 months (Yes, No); used sunscreen regularly with sun exposure (Yes, No); ever been tested for Human Immunodeficiency Virus (HIV) infection (Yes, No); within the last 12 months, have been diagnosed or treated for chlamydia, genital herpes, genital warts/HPV, Gonorrhea, Hepatitis B or C).

4) *History of Vaccinations:* Receipt of other vaccinations (influenza, hepatitis B, meningitis, chickenpox and Measles, Mumps and Rubella (MMR).

5.2.4 Statistical analysis

Descriptive analysis and cross-tabulation to estimate point prevalence of HPV vaccination with respect to selected demographic, sexual behavior, screening/health promotion as well as history of STIs and vaccinations was conducted. Univariate analysis was done to assess the crude association between each of the independent variables and the outcome of interest (self-reported HPV vaccination). The level of significance α=0.25 was used during univariate analysis (i.e., *P*-value >0.25 was not statistically significant). Assumptions of multivariable logistic regression were checked. Using the variant inflation factors (VIF) values**,** multi-collinearity was assessed for all the independent variables found to be statistically significant from the univariate analysis. A VIF>3 is taken as violation of the multi-collinearity assumptions (Hair *et al.*, 2019). Manual backwards selection strategy was used for our model construction. As variables were removed step-wisely from the model, confounding was assessed at each stage. A change of 20%

or greater in the regression coefficient of a predictor ($\Delta\beta \geq 20\%$) suggested that the variable is a confounder. If a variable was found to be a confounder, it remained in the model. Thereafter, possible two-way interactions involving biologically relevant predictors were assessed using a *P*-value of 0.05. To assess the characteristics of our final explanatory model, we did a receiver operating characteristic (ROC) curve analysis (probability cut-off of 0.5). Analysis was done using SPSS version 22.

5.3 Results

5.3.1 HPV Vaccine Uptake

Our study found that 47.2% of the student participants received the HPV vaccine. Further breakdown of HPV vaccine uptake according to relevant independent variable groupings is as highlighted below.

1) *Demographic characteristics:* Considering HPV vaccine uptake under demographic characteristics and according to age; 64.5% (18-20 years), 45.5% (21-24 years), 26.2% (25-29 years) and 14.8% (30 years or more) received the vaccine. According to sex; 56.1% (female) and 22.2% (male) received the vaccine. Vaccinated proportion according to race/ethnicity was 39.3% (Aboriginal), 49.9% (non-White) and 46.3% (White). Relative to nationality; 49.5% of those vaccinated were Canadian students while 24.6% were international students. According to gender identity; 56.2% (woman), 22.0% (man), 20.0% (transwoman), 44.0% (transman), 49.7% (genderqueer), and 56.6% (another identity) were vaccinated. Proportion vaccinated according to relationship status were as follows: 48.6% (not in a relationship), 52.9% (in a relationship but not living together), and 32.8% (in a relationship living together) According to marital status 50.6% (single), 28.2% (married/partnered), 14.2% (separated) and 19.6% (divorced) were vaccinated. According to year in school 56.7% (1st year), 54.0% (2nd year), 50.9% (3rd year), 45.9% (4th year), 35.9% (5th year, graduate) and 27.7% (graduate or professional) were vaccinated.

2) *Sexual behaviour:* When examining HPV vaccine uptake relating to sexual behaviours; vaccinated proportion according to number of sexual partners was 44.1% (no partner), 45.5% (one partner), 55.1% (two partners), 55.0% (three partners), 52.5% (four partners or more). Considering the use of protective barrier during oral sex; 46.6% (never did this sexual activity), 44.3% (have not during last 30 days), 50.0% (never), 47.4 (rarely), 49.7% (sometimes), 48.5% (most of the time), 45.3% (always) were vaccinated. Looking at the use of protective barrier

during vaginal sex; 45.6% (never did this sexual activity), 44.2% (have not during last 30 days), 44.3% (never), 52.5 (rarely), 50.8% (sometimes), 52.0% (most of the time), 50.4 (always) were vaccinated. Under use of protective barrier during anal sex; 48.3% (never did this sexual activity), 44.2% (have not during last 30 days), 45.4 (never), 50.0% (rarely), 47.0% (sometimes), 47.3% (most of the time), 42.8% (always) were vaccinated. Looking at use of a method of birth control to prevent pregnancy during last vaginal intercourse; 50.3% (Yes), 47.2% (N/A have not have vaginal intercourse), 39.4% (No, have not had vaginal intercourse that could result in pregnancy, 24.9% (No, did not want to prevent pregnancy), 41.5% (No, did not use any birth control method) were vaccinated.

3) *Engagement in Screening/Health Promotion and History STIs:* Proportion vaccinated with HPV vaccine in this variable category are as follows: Dental examination and cleaning in the last 12 months 51.6% (Yes), 33.9% (No); males performed a testicular self-examination in the last 30 days 27.9% (Yes), 19.7% (No); females performed a breast self-examination in the last 30 days 57.1% (Yes), 55.5% (No); females had a routine gynecological exam in the last 12 months 51.7% (Yes), 58.1% (No); used sunscreen regularly with sun exposure 52.1% (Yes), 40.9% (No); ever been tested for Human Immunodeficiency Virus (HIV) infection 48.7% (Yes), 45.6% (No); within the last 12 months, have been diagnosed or treated for – chlamydia 54.9% (Yes), 47.1% (No); genital herpes 50.8% (Yes), 47.2% (No); genital warts/HPV 42.5% (Yes), 47.2% (No); gonorrhea 44.0% (Yes), 47.2% (No); hepatitis B or C 44.1% (Yes), 47.2% (No); HIV 48.7% (Yes), 45.6% (No).

4) History of *Vaccination*: Under vaccination history, HPV vaccine uptake was as follow: hepatitis B 56. 8% (Yes), 6.8% (No); influenza 56.6% (Yes), 41.8% (No); MMR 54.1% (Yes), 17.7% (No); Meningitis 59.9% (Yes), 16.4% (No); chickenpox 59.3% (Yes), 33.1% (No).

A summary of the proportion of vaccinated and unvaccinated participants according to variables under consideration are as shown in Table 5.1 (Appendix D).

5.3.2 Predictors of HPV Vaccine Uptake

5.3.2.1 Univariate analysis

Univariate analysis was conducted with a level of significance of $\alpha=0.25$. Statistically significant associations at this level are as follows: age (*P*-value <0.0001), sex (*P*-value <0.0001), relationship status (*P*-value <0.0001), marital status (*P*-value <0.0001), gender identity (*P*-value <0.0001), nationality (*P*-value <0.0001), year in school (*P*-value <0.0001), number of

sexual partners (*P*-value <0.0001), Engagement in oral, vaginal and anal sex within the last 30 days (*P*-value <0.0001), use of protective barrier- oral, vaginal and anal sex (*P*-value <0.0001), race/ethnicity -Aboriginal, non-White *P*-value (<0.0001), vaccination history- hepatitis B, influenza, MMR, meningitis, chickenpox (*P*-value <0.0001). Odds ratios (ORs) for univariate analysis with respect to the reference category listed are presented in Table 5.2 (Appendix D).

5.3.2.2 Multivariable Analysis

Variables identified as significant in the univariate analysis were initially verified for multi-collinearity. A variance inflation factor (VIF) < 3 was observed as cut-off point for all independent variables, indicating the independent variables are not highly correlated (Hair *et al.*, 2019). Likewise, tolerance values ranged from 0.35 to 0.99, providing further evidence of no violation of multi-collinearity assumption. The receiver operating characteristic (ROC) curve was used to assess the characteristics as of the final model. With a probability cut-off set at 0.5, the area under the ROC curve was 0.836 (95% CI 0.831-0.840). Our final model depicted the association between self-reported HPV vaccination and the selected independent variables.

5.3.2.3 Determinants of HPV vaccine uptake

The following variables: age, sex, marital status, gender identity, year in school, number of sexual partners, use of protective barrier during anal intercourse, use of birth control to prevent pregnancy during last vaginal intercourse, race/ethnicity, and history of other vaccinations (hepatitis B, influenza, meningitis, chickenpox) were significantly (p-value < 0.05) associated with the receipt of HPV vaccine.

Looking at age; individuals that were [18 – 20 years were 10.13 (95% CI 8.58 – 11.97); 21 -24 years were 4.16 (95% CI 3.56 – 4.86); 25 – 29 years were 1.83 (95% CI 1.56 – 2.15)] times more likely to receive the HPV vaccine compared to those that were 30 years and above (p-value <0.0001). Considering biological sex of participants, females were 1.89 (95% CI 1.22 – 2.94) times more likely to be vaccinated for HPV compared to males (p-value = 0. 004). Looking at race/ethnicity; Aboriginals were 31% (OR = 0.69; 95% CI 0.58 – 0.80) less likely to be vaccinated compared to Whites (p-value <0.0001). According to gender identity; participants identifying as women were 2.15 (95% CI 1.39 – 3.35) more likely to be vaccinated for HPV compared to those identifying as men (p-value = 0.001). According to marital status; participants that were separated were 59% (OR = 0.41; 95% CI 0.20 – 0.85) less likely to be vaccinated with

HPV vaccine compared to those that were divorced (p-value = 0.016). Regarding number of years in school; participants that were [1st year students were 1.34 times (95% CI 1.77 – 1.53; p-value <0.0001); 2nd year students were 1.17 times (95% CI 1.03 -1.34; p - value = 016); 3rd year student were 1.16 times (95% CI 1.03 – 1.31; p–value = 019); 4th year student were 1.30 times (95% CI 1.14 – 1.46; p-value <0.0001) more likely to be vaccinated with the HPV vaccine compared to graduate/professional students. Concerning number of sexual partners: participants that have no sexual partner were 20% (OR = 0.80, 95% CI 0.68 – 0.93; p-value = 003) while participants that have just one sexual partner were 14% (OR = 0.86, 95% CI 0.76 – 0.96; p-value = 009) less likely to be vaccinated with HPV compared with participants that have four or more sexual partners. Regarding the use of protective barrier during anal sex within the last 30 days, participants that used protective barriers most of the time were 1.50 (95% CI 1.02 – 2.22) times more likely to be vaccinated against HPV compared to participants that always used protective barrier (p-value = 0.042). Concerning use of a method of birth control to prevent pregnancy during last vaginal intercourse, individuals that did use a method of birth control to prevent pregnancy were 1.18 (95% CI 1.04 – 1.34) times more like to be vaccinated with HPV compared to individuals that did not use any birth control method (p-value = 0.012). Regarding history of vaccination; individuals that did not receive the hepatitis B vaccine were 87% (OR = 0.13, 95% CI 0.11 – 0.15) less likely to be vaccinated with HPV compared to individuals that received the hepatitis B vaccine (p-value < 0. 0001). Individuals that did not receive the influenza vaccine were 40% (OR = 0.60, 95% CI 0.56 – 0.64) less likely to be vaccinated with HPV compared to individuals that received the influenza vaccine (p-value < 0. 0001). Individuals that did not receive the meningitis vaccine were 67% (OR = 0.33, 95% CI 0.31 – 0.37) less likely to be vaccinated with HPV compared to individuals that received the meningitis vaccine (p-value < 0. 0001). Likewise, individuals that did not receive the chickenpox vaccine were 33% (OR = 0.67, 95% CI 0.62 – 0.72) less likely to be vaccinated with HPV compared to individuals that received the chickenpox (p-value < 0. 0001).

The following variables were not significant of HPV vaccine uptake predictors at all levels (p-value of 0.05). Relationship status, nationality, engagement in oral, vaginal and anal sex, use of protective barrier for oral, vaginal and anal sex, history of STIs and history of vaccination against MMR.

A summary of the association of predictor variables with HPV vaccination after multivariable analysis is shown below in Table 5.3.

Additionally, proportion of HPV vaccination uptake in Canadian universities according to students' nationality and according to students' race/ethnicity is show in Figure 5.1 and Figure 5.2 respectively.

Table 5.3: Multivariable Analysis of NCHA-II Web Spring 2016 of Canadian Universities

Independent Variables		**HPV[1] vaccination ("Yes" versus "No")** **Odds (95% CI)**	**P-value (α=0.05)**
Age **(Ref= "30 years old or older")**	18 - 20 years old	**10.13 (8.58- 11.97)**	**<0.0001**
	21 - 24 years old	**4.16 (3.56 – 4.86)**	**<0.0001**
	25 - 29 years old	**1.83 (1.56 - 2.15)**	**<0.0001**
Sex **(Ref= "Male")**	Female	**1.89 (1.22 -2.93)**	**0.004**
Marital status	Single	0.94 (0.62 – 1.41)	0.762
	Married/Partnered	0.78 (0.52 – 1.18)	0.242
Ref= ("Divorced")	Separated	**0.41 (0.20 – 0.85)**	**0.016**
Gender Identity	Woman	**2.15 (1.39 – 3.35)**	0.001
	Another Identity	1.22 (0.75 – 1.98)	0.421
	Trans Woman	0.20 (0.02 – 1.71)	0.140
	Trans Man	2.59 (0.73 – 9.16)	0.140
Ref = ("Man")	Gender queer	1.66 (0.93 – 2.97)	0.89
Year in school	1st year undergraduate	**1.34 (1.18 – 1.53)**	**<0.0001**
	2nd year undergraduate	**1.17 (1.03 – 1.34)**	**0.016**
	3rd year undergraduate	**1.16 (1.03 – 1.31)**	**0.019**
	4th year undergraduate	**1.29 (1.14 – 1.46)**	**<0.0001**

Ref = (“Graduate or professional”)	5th year or more undergraduate	0.89 (0.76 – 1.03)	0.121
Number of sexual partners Within last 12 months (Ref= 4 or more	None	**0.80 (0.68 – 0.93)**	**0.003**
	1	**0.86 (0.76 – 0.96)**	**0.009**
	2	1.04 (0.90 – 1.21)	0.589
	3	0.96 (0.81 – 1.15)	0.667
Use of protective barrier during vaginal intercourse within the last 30 days (Ref= “Always used protection”)	N/A, never did this sexual activity	1.11 (0.91 – 1.36)	0.287
	Have not done this sexual activity during the last 30 days	1.08 (0.88 – 1.33)	0.451
	Never	1.17 (0.94 – 1.46)	0.171
	Rarely	1.42 (0.95 – 2.12)	0.090
	Sometimes	**1.77 (1.16 - 2.68)**	**0.008**
	Most of the time	**1.50 (1.01 – 2.22)**	**0.042**
Use of a method of birth control to prevent pregnancy during last vaginal intercourse	Yes	**1.18 (1.04 – 1.34)**	**0.012**
	N/A, have not have vaginal intercourse	0.95 (0.81 – 1.12)	0.560
	No, have not had vaginal intercourse that could result in pregnancy	0.99 (0.81 – 1.22)	0.932

(Ref= "No, did not use any birth control method")	No, did not want to prevent pregnancy	0.98 (0.75 – 1.29)	0.901
Race/Ethnicity Ref= "White"	Aboriginal	**0.69 (0.58 – 0.82)**	**<0.0001**
	Others (nonAbo/nonWhite)	**1.00 (0.93 – 1.07)**	0.990
Vaccination History			
○ Hepatitis B	No	**0.13 (0.11 – 0.15)**	**<0.0001**
○ Influenza	No	**0.60 (0.58 – 0.64)**	**<0.0001**
○ MMR[2]	No	**0.33 (0.31 – 0.37)**	**<0.0001**
○ Meningitis **(Ref= "Yes")**	No	**0.67 (0.62 – 0.72)**	**<0.0001**
[1]Human Papillomavirus **[2] Measles, Mumps and Rubella** *** The outcome variable is HPV vaccination status with two levels ["Yes" and "No" (reference)]**			

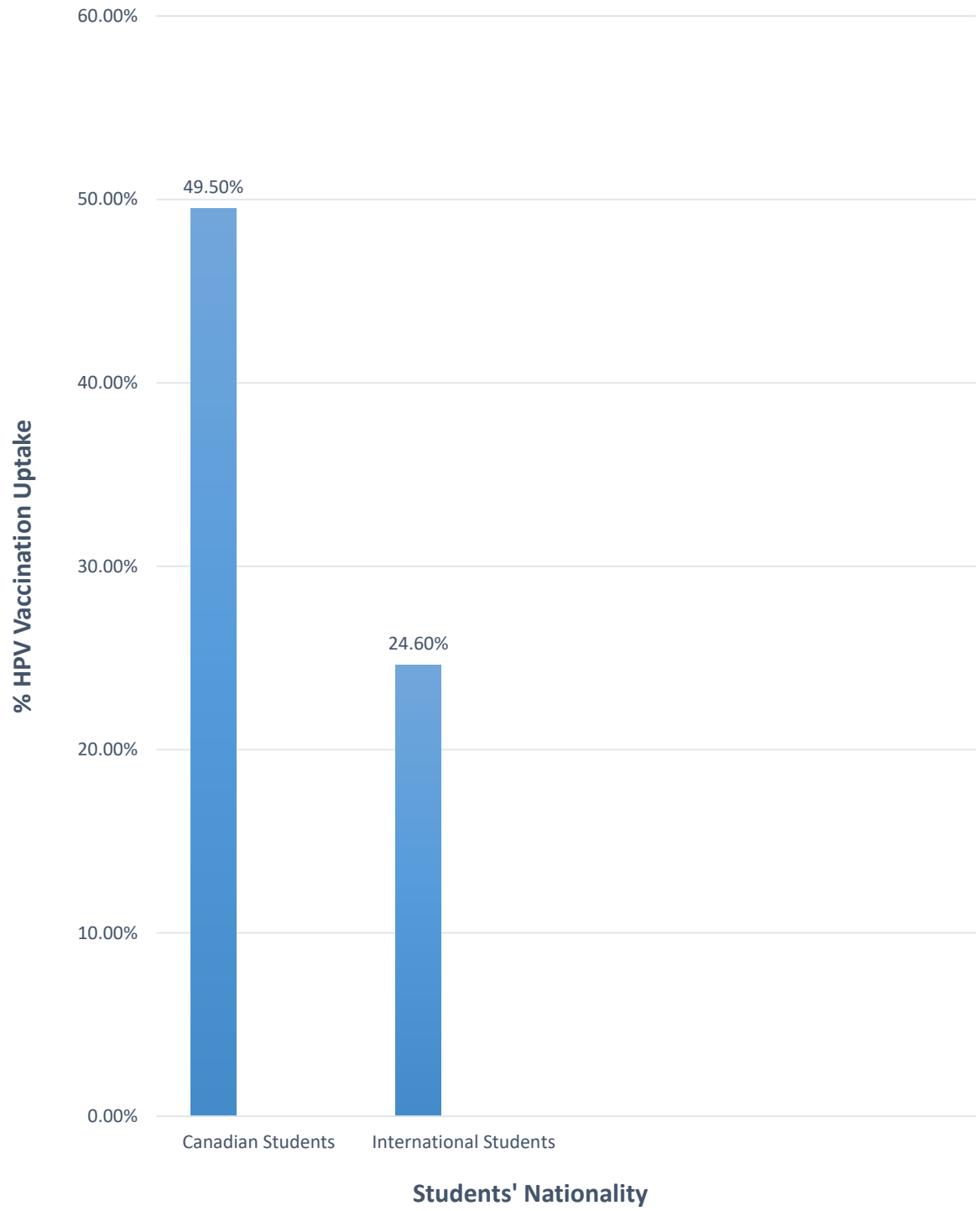

Figure 5.1: Proportion of HPV Vaccination Uptake in Canadian Universities According to Students' Nationality (ACHA-NACHA) - II Web Spring 2016)

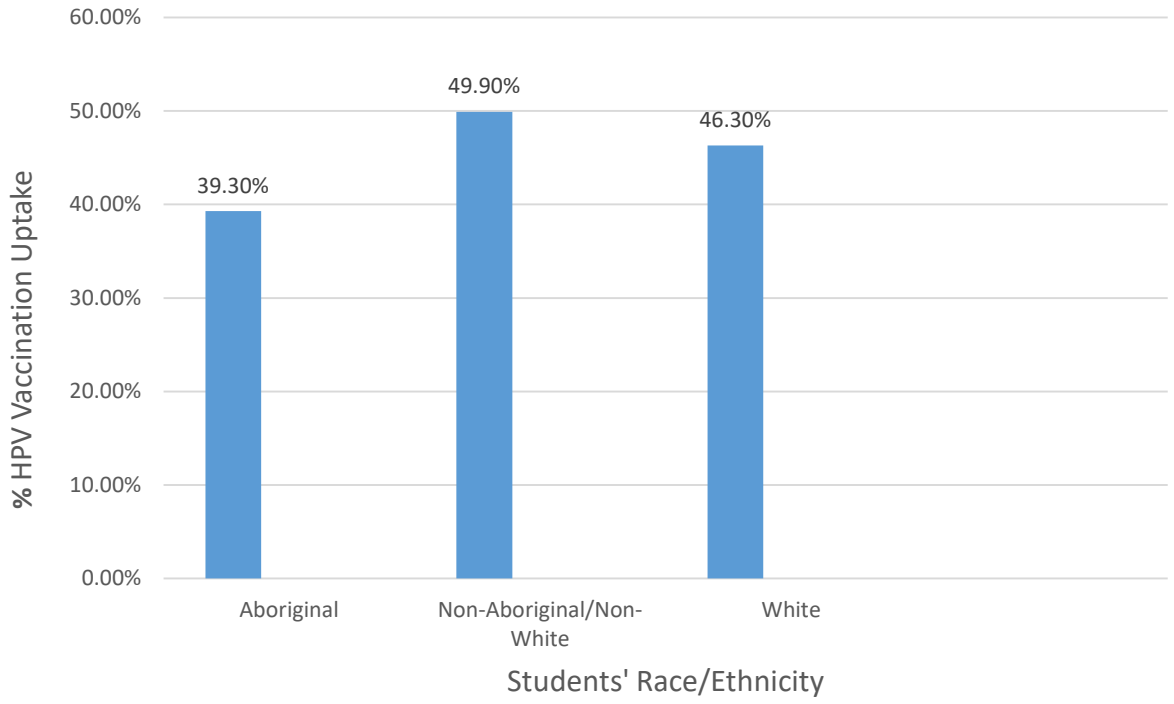

Figure 5.2: Proportion of HPV Vaccination Uptake in Canadian Universities According to Students' Race/Ethnicity (ACHA-NCHA) II Web Spring 2016)

5.4 Discussion

This study explores HPV vaccination status and determinants of uptake in young adults, represented by students in Canadian universities. This is essential in promoting the Public Health Agency of Canada (PHAC) goal of reducing vaccine-preventable HPV-related morbidity and mortality in the Canadian population and equally aligns with WHO recommendation that HPV vaccination should be integrated as part of a broad approach to prevent cervical cancer and other related diseases in the society (World-Health-Organization., 2016).

Findings from this study show that there is suboptimal acceptance and uptake of the HPV vaccine among Canadian university students. Specifically, there is disproportionate uptake among some demographic subpopulation of university students namely: those that are older, male, married and have single sexual partner. Our study also identified use of protective barrier during anal intercourse, use of birth control to prevent pregnancy during most recent vaginal intercourse as well as race/ethnicity and history of receipt of other vaccinations to be significant predictors of HPV vaccine uptake in Canadian universities students.

According to this study, overall self-reported HPV vaccine uptake among Canadian university students stands at 47.2%. This uptake figure is approximately half the recommended HPV vaccine uptake of 80% by the Canadian Immunization Committee (CIC). The CIC expectation is that 80% of eligible populace would be fully vaccinated against HPV within 2 years (and 90% within 5 years) of the introduction of the HPV vaccination program (CIC & PHAC., 2007) (Government-of-Canada., 2019). Thus, there is an obvious need to improve HPV vaccine coverage among students in Canadian universities to be at per with that of the Canadian general populace and a further need to actualize the recommended 80% uptake in the Canadian population for effective herd immunity (Drolet *et al.*, 2013; Government-of-Canada., 2017b, 2019; Tabrizi *et al.*, 2014).

Similarly, age was found to be a significantly positive predictor of HPV vaccine uptake. The younger age categories had incrementally higher uptake of HPV vaccine when compared to students that were 30 years old and above. This is consistent with previous studies that documented younger age as a positive predictor of HPV vaccine uptake (Bird *et al.*, 2017; Crosby *et al.*, 2007; Elam-Evans *et al.*, 2014; Government-of-Canada., 2016b; Patel *et al.*, 2012; Tabrizi *et al.*, 2012; World-Health-Organization., 2017). A plausible explanation is that at the inception of school-based government funded HPV vaccine programs, the cohort of pioneer

grade 5 to grade 6 adolescents are presently the cohort of younger aged university students that having the observed higher HPV vaccine uptakes. Concerted efforts should be made to target the older university students with observed suboptimal uptake in future catch up vaccination programs. This is desirable since it is documented that there is a peak age for HPV infection in the early twenties which leads to a peak prevalence of diseases around age thirty. It is equally paramount and should be a priority to expand coverage to older ages since Health Canada recommended the HPV vaccine from age 9 – 45 years (Government-of-Canada., 2019).

Regarding number of years in school; undergraduate students are generally more likely to vaccinate when compared to graduate or professional students. This is not surprising since lower year students generally tend to be younger compared to higher year students and younger age is a positive predictor of HPV vaccine uptake.

Although, nationality was not a significant predictor of HPV uptake amongst university students, there is nevertheless a notable disparity in HPV vaccination uptake between students identifying as Canadians (49.5%) and those identifying as international students (24.6%). Reasons from this disparity could range from cost to convenience in terms of logistic of relocation and adjusting to a completely different environment for immigrant students. Thus, there should be focus on international students to improve HPV vaccine uptake.

In terms of biological sex and gender identity, our study found that females and those identifying as women are slightly more likely to obtain the HPV vaccine compared to males. Again, this agrees with what has been reported in literature (Barnard *et al.*, 2017). It is uniquely notable however, that this study observed that females were just 1.89 (95% CI 1.22 – 2.94) times more likely to receive the HPV vaccine compared to males. This observed number is smaller than what has been previously reported in past studies (Couto *et al.*, 2014; Fontenot *et al.*, 2014; Johnson *et al.*, 2017; Lindley *et al.*, 2013; Thompson *et al.*, 2016b; A. Wilson, 2015; Winger *et al.*, 2016). Thus, it is possible that the HPV vaccine uptake gap between females and males is beginning to narrow and the narrative of HPV vaccine as just for females is starting to wane. To further narrow this gap, it is important to create more awareness for HPV vaccine as a vaccine for both male and females. This is important as some studies have reported that majority of male college students were unaware that HPV vaccine was available and are scarcely offered the vaccine by physicians and other health care providers (Barnard *et al.*, 2017).

Concerning marital status, our study revealed that those who were married but separated were 59% less likely to be vaccinated with HPV vaccine compared to those that were divorced. This finding agrees with previous studies reported prevalence of HPV infection of being twice as likely in women who were never married and three times as likely in widowed/divorced/separated or cohabiting women compared to married women (Dunne *et al.*, 2007; Patel *et al.*, 2012; Weiss *et al.*, 2011; A. Wilson, 2015). Previous studies also suggested that although older or married women are less inclined to get vaccinated, they may be more willing to do so following strong physician recommendation (Dunne *et al.*, 2007; Patel *et al.*, 2012; Weiss *et al.*, 2011; A. Wilson, 2015). This means that viewing marital status as a continuum, (with being married and living together at one end and divorced at the other end); being married could be a negative predictor of HPV vaccine uptake. A plausible explanation for this is that those that were married perceive a lesser risk and lesser vulnerability to HPV infection compared to those not married. This perception might be deceptive as it has been reported that married people have a prevalence of HPV infection as high as 17.3% (Weiss *et al.*, 2011; A. Wilson, 2015). To improve HPV vaccine uptake among older women whether married or unmarried, evidence supports that physician recommendation for vaccination play a positive role (Piedimonte *et al.*, 2018; Weiss *et al.*, 2011; A. Wilson, 2015).

Concerning number of sexual partners, previous studies have documented increased risk of HPV infection with increasing number of sexual partners (Mehu-Parant *et al.*, 2010; Winer *et al.*, 2008). The occurrence of genital HPV associated with acquisition of a new sexual partner is high; with the risk of infection even higher if a partner has been known for a short period and if a partner has concurrent multiple sex partners (Mehu-Parant *et al.*, 2010; Winer *et al.*, 2008).

Furthermore, this study found that individuals who have none or one sexual partner were less likely to be vaccinated with HPV compared with participants that have four or more sexual partners. An explanation for this observation is the concept of risk perception and lesser vulnerability to infection by those with none or fewer number of sexual partners. This behavioral pattern is explained in part by the fact that perceived disease vulnerability may serve as cue to seek for protective measures from infection such as vaccination (Rosenstock *et al.*, 1988; Weiss *et al.*, 2011). On the other hand, a feeling of invincibility towards infection is deceptive as it could create a false sense of security or lesser vulnerability which deter effort to partake in health promotion programs like vaccination.

Regarding the use of protective barrier during anal sex within the last 30 days, participants that used protective barriers most of the time were 1.5 times more likely to be vaccinated against HPV compared to participants that always used protective barrier. This means individuals that always use protective barrier are less likely to vaccinate because they perceive lesser exposure and lesser risk of infection from HPV infection. According to the Center for Disease Control and Prevention (CDC) and other researches; correct and consistent condom use may reduce the risk for HPV infection and HPV-associated diseases (Nielson *et al.*, 2010; Pierce Campbell *et al.*, 2013)**.** However, this protection is not absolute and any feeling of invincibility towards HPV infection because of use of protective barrier is not helpful, especially in men who sleep with men with documented evidence of greater burden of HPV infection (Centers-for-Disease-Control-and-Prevention., 2013, 2016; King *et al.*, 2015; Quinn *et al.*, 2012)**.**

Concerning use of a method of birth control to prevent pregnancy during last vaginal intercourse, individuals that did use a method of birth control to prevent pregnancy were 1.18 times more like to be vaccinated with HPV vaccine compared to those not using any birth control method. This agrees with previous a study suggesting that that the protective behavior of dual method contraceptive use at first and most recent sexual intercourse could serve as predictor of another complementary health behavior such as HPV vaccination (Vanderpool *et al.*, 2014). It is also well documented that long-term use of birth control pills (> 5 years) is associated with increased risk of cervical cancer (Ghanem *et al.*, 2011; Marks *et al.*, 2011). Thus, there is a possible synergistic effect of hormonal contraceptive use and HPV infection causing cervical cancer (Klitsch, 2002). As demonstrated in this study it is a positive observation that those using birth contraceptives are slightly more likely to vaccinated with the HPV vaccine. This is because from the perspective of HPV infection prevention, it is erroneous for individuals to think that use of contraceptives is a guarantee against contacting of HPV infections.

Regarding race/ethnicity our study found a significantly lower HPV vaccine uptake in students identifying as Aboriginal compared to those that identified as White. Aboriginal students were 31% less likely to be HPV vaccinated compared to Whites. In another vein, the HPV vaccine uptake for students that identified as non-Whites (and non-Aboriginal) was not statistically significant. A 31% lesser vaccine uptake in Aboriginal university students is a proxy indicator of probable suboptimal HPV vaccine uptake in the larger Aboriginal population in Canada. This is against the backdrop of documented higher burden of infection with HPV but

lower awareness in Canadian Aboriginal population (Brassard *et al.*, 2012; Cerigo *et al.*, 2011; Healey *et al.*, 2001; Jiang *et al.*, 2013b; Klitsch, 2002; YOUNG *et al.*, 1997). Consequently, it is of paramount importance to urgently address the observed disparity in HPV vaccine uptake in students of Aboriginal descent and probably in the Aboriginal population at large.

Lastly, findings from our study show that individuals that did not receive other vaccines namely: hepatitis B, influenza, meningitis, chickenpox were less likely to be vaccinated with the HPV vaccine. Thus, it is likely these individuals were generally vaccine hesitant across a large spectrum of vaccines. HPV vaccine is a relatively new vaccine that is still unfortunately speculated (without evidence) to certain behaviors like promiscuity, so hesitancy is a real problem in its uptake. Furthermore, it has been suggested that policies supporting co-administration of HPV and meningococcal vaccines could be helpful in normalizing HPV vaccine acceptance as well as increasing demand for HPV vaccine in the general population (Erickson *et al.*, 2005; Perkins *et al.*, 2012).

5.5 Strength and Limitation of Study

To the best of our knowledge, this study is one of the first to examine HPV vaccination status and determinants of uptake among Canadian university students. Composite secondary data base consisting of several universities across and very large population of Canadian university students makes findings from our study generalizable to Canadian university students and to some extent young adults in Canada.

Nevertheless, for our secondary data (American College Health Assessment- National College Health Assessment-II Spring 2016); vaccination status was self-reported by the respondents so there could be under/over reporting biases. Similarly, in our analysis, respondents unsure of their vaccination status were excluded from the study. Thus, there is the likelihood of under/over reporting of those that were vaccinated.

5.6 Conclusions

The results of this study identified important factors that are predictors of HPV vaccination uptake among young adults represented by university students. Likewise, significant disparity in HPV vaccination uptakes in certain demographic subpopulation of university students were shown by this study. Concerted and consistent efforts at both policy and implementation stages should be taken to reinforce identified positive factors driving of HPV vaccine uptake and

address identified gaps in HPV vaccination among young adults in Canada. To reach the recommended 80% - 90% HPV vaccination coverage level advocated by the Canadian Immunization Committee (CIC), further research on innovative and youth friendly programs that improve HPV vaccination uptake especially in colleges and universities, and in young adults is imperative.

CHAPTER 6 (MANUSCRIPT 4) - HPV VACCINATION IN CANADA: DETERMINANTS OF UPTAKE, TREND AND AWARENESS IN FEMALE ADOLESCENTS

Obidiya O., Mutwiri G., Bird Y., Mahmood R., & Moraros J (2020). HPV Vaccination in Canada: Determinants of Uptake, Trend and Awareness in Female Adolescents. *Unpublished manuscript, School of Public Health, University of Saskatchewan, Saskatoon, Canada.*

My contributions to this manuscript included conceiving and designing the study, doing background literature review on the topic, conducting analysis and interpretation of the data, and preparing the manuscript.

Mahmood R assisted in conducting analysis and interpretation of the data and preparing the manuscript.

Dr. Bird Y and Dr. Moraros J guided in conception and design of the study, the interpretation of findings, and helped critically revise and finalize the document.

Dr. Mutwiri G guided in the interpretation of findings and helped in the review of the final document.

Chapter 6: Manuscript 4

HPV VACCINATION IN CANADA: DETERMINANTS OF UPTAKE, TREND AND AWARENESS IN FEMALE ADOLESCENTS

6.1 Introduction

HPV vaccination is recognized globally as an effective strategy to combat HPV infection and its various health consequences (Center-for-Disease-Prevention-and-Control., 2011; World-Health-Organization., 2013). In women, HPV types 16 and 18 cause 70% of cervical cancers and precancerous cervical lesions; types 6 and 11 are associated with about 90% of genital warts (World-Health-Organization., 2019b). It is estimated that nearly 80% of reproductive-age females will be infected with HPV at some point in their lifetime. Overall, HPV infection affects about 550,000 Canadians annually at various stages of life (Christopher P Crum *et al.*, 2003b). In Canada and other countries that pioneered HPV vaccination programs, HPV vaccination was primarily targeted towards adolescent females in school-based, publicly funded programs. This was not surprising because from inception, the marketing of HPV vaccine was heavily gender biased; with Gardasil and Cervarix fundamentally promoted as vaccines against cancer of the cervix in women by both media and manufacturers (Grantham *et al.*, 2011; Mawdsley *et al.*).

The Canadian Immunization Committee (CIC) recommends that 80% and 90% of eligible recipients receive the required doses of HPV vaccine within 2 and 5 y of program introduction, respectively (Government-of-Canada., 2017b). The optimal coverage for herd immunity against HPV remains uncertain, but a systematic review and meta-analysis suggests that there could be herd effects in high-income countries when female HPV vaccination coverage rises to at least 50% (Gilbert *et al.*, 2016). Across Canada, HPV vaccine uptake is variable and mostly below public health goals in many provinces and territories. (Canadian-Partnership-Against-Cancer., 2016; Gilbert *et al.*, 2016).

Studies from the United States and Australia show disparity in initiation of HPV vaccination among those who receive the vaccine along racial-ethnic lines and recommend that HPV vaccination programs should aim at narrowing disparities in vaccine uptake among ethnic and racial groups (Henry *et al.*, 2015; Kessels *et al.*, 2012). The potential impact of the HPV vaccination in reducing cervical cancer and associated health issues is dependent on a high vaccination uptake among high-risk subpopulations (Drolet *et al.*, 2013).

In Canada, there are reported racial and ethnic inequalities in the burden of HPV infection (Demers *et al.*, 2011; Jiang *et al.*, 2013a; Severini *et al.*, 2013). Compared to the United States, Canada fares better with regards to HPV vaccine uptake, nonetheless it is lagging behind in performance compared to countries like Australia, New Zealand and the United Kingdom (Government-of-United-States-of-America., 2013; Saraiya *et al.*, 2013). Moreover, unlike most developed nations, Canada does not have a national HPV vaccine registry.

6.2 Research Objectives

The objectives of this study were to determine HPV vaccine uptake in Canada, examine the determinants of HPV vaccine uptake and explore possibility of ethnic disparity in vaccination uptake among Canadian female children population. This study would also perform a comparative analysis of HPV vaccination trend in Canada in the past decade using data from three Childhood National Immunization Coverage Survey (CNICS) 2011, 2013 and 2015.

Specifically, the study will address the following research questions.

1. What is the HPV vaccine uptake in girls in different jurisdictions across Canada and what is the trend in HPV vaccine uptake in Canada in the past decade?
2. Is there disparity in HPV vaccine uptake based on ethnic or racial background of girls in Canada?
3. What are the major determinants of HPV vaccine uptake, non-vaccination and vaccine refusal among girls in Canada?

6.3 Methods

6.3.1 Study Sample

Our study used the Childhood National Immunization Coverage Survey (CNICS) 2011, CNICS 2013 and CNICS 2015. Starting form 2011, CNICS is a population survey carried out by Statistics Canada on a two-year basis. This survey endeavors to evaluate routine vaccinations coverage for all recommended children vaccines by ages 2 (two), 7 (seven), 14 (fourteen) or 17 (seventeen) (Government of Canada 5., 2020). Because this study is specifically interested in HPV vaccination uptake, our study sample comprises of children aged 10 to 17 years. For our analysis there were 1056326 participants (CNICS 2011), 740943 participants (CNICS 2013) and 531780 participants (CNICS 2015) of children from ages 10 (ten) to 17 (seventeen). Study

population comprise of girls since only HPV vaccination for females were included in the three CNICS cycles under consideration. Furthermore, only participants that gave "yes" or "no" responses were included in the study. Every other response (e.g. unsure, unknown) were excluded.

6.3.2 Outcome variable

A dichotomous variable ("yes," or "no") indicating whether participants had received a shot or series of shots of the HPV vaccine was determined for all three cycles of CNICS.

6.3.3 Independent variables

Variables identified from rigorous literature review that meet the objectives of this study were located from CNICS 2011, CNICS 2013 and CNICS 2015 Master Files. Independent variables of interest so located and included in this study are listed below:

1) *CNICS 2011.* Under this survey cycle, variables considered include age of child, age of person most knowledgeable (PMK), highest education PMK, birthplace of child, birthplace of PMK, province, access to health care practitioner (HCP) and HCP discussion of immunization. Other variables were sufficient information on immunization, concern about side effect of vaccines, belief that vaccines cause diseases, importance of other vaccines (varicella, influenza, pneumococcal disease) and total household income.

2) *CNICS 2013:* Regarding this survey cycle, variables considered include age of child, age of person most knowledgeable (PMK), highest education PMK, birthplace of child, birthplace of PMK, province, access to health care practitioner (HCP) and HCP discussion of immunization. Other variables are sufficient information on immunization, reason not sufficient information, childhood vaccines safety, childhood vaccines effectiveness, childhood vaccines importance for child's health, understanding of how vaccines work, belief that alternative practices eliminate need for vaccine, concern about side effect of vaccines, belief vaccines cause diseases, importance of other vaccines (varicella, diphtheria, rubella, hepatitis B, influenza, measles, mumps, pneumococcal disease, polio, meningitis, tetanus, pertussis) and total household income.

3) *CNICS 2015.* According to this survey cycle, variables considered include age of child, age of person most knowledgeable (PMK), relationship of the PMK to the child, highest education PMK, birthplace of child, birthplace of PMK, province, access to health care practitioner (HCP) and HCP discussion of immunization. Other variables are sufficient information on immunization, concern about side effect of vaccines, belief vaccines cause diseases, importance

of other vaccines (varicella, influenza, mumps, pneumococcal disease pertussis) and total household income.

6.3.4 Statistical analysis

Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 24. Study interest was to collect data on the immunization coverage for human papilloma virus (HPV) for the total populations for girls at ages 10 -17 in the provinces and territories for CNICS cycles of 2011, 2013 and 2015. Multivariable logistic regression was used to examine factors associated with vaccination, non-vaccination and vaccine refusal, after adjusting for potential confounders. Survey sampling weights were applied so that data analysis was representative of the Canadian population of children age 10-17.

Data analysis consisted of two steps. The first step comprised of descriptive statistics; frequencies and cross-tabulations which were used to estimate prevalence and examine characteristics associated with HPV vaccination, non-vaccination and vaccine refusal. The second step involved building of logistic regression models for each of the independent variables influencing HPV vaccination.

Univariate analysis was done to assess the crude association between each of the independent variables and the outcome of interest (self-reported HPV vaccination). The level of significance $\alpha=0.25$ was used during univariate analysis (i.e., *P*-value >0.25 was not statistically significant). Assumptions of multivariable logistic regression were checked. Using the variant inflation factors (VIF) values, multi-collinearity was assessed for all the independent variables found to be statistically significant from the univariate analysis**.** A VIF>3 is taken as violation of the multi-collinearity assumptions (Hair *et al.*, 2019). Manual backwards selection strategy was used for our model construction. As variables were removed step-wisely from the model, confounding was assessed at each stage. A change of 20% or greater in the regression coefficient of a predictor ($\Delta\beta\geq20\%$) suggested that the variable is a confounder. If a variable was found to be a confounder, it remained in the model. Thereafter, possible two-way interactions involving biologically relevant predictors were assessed. A significance level of $p<0.05$ was applied in all cases.

6.4 Results

6.4.1 HPV Vaccine Uptake

Our study found that for CNICS 2011 cycle; out of 1056326 participants, 434454 participants (41.1%) received the HPV vaccine. For CNICS 2013 cycle; out of 740943 participants, 508642 participants were vaccinated (68.6%). Furthermore, for CNICS 2015; out of 531780 participants, 391988 (73.7%) received the HPV vaccine.

Further breakdown of HPV vaccine uptake according to relevant independent variable groupings and CNICS cycle is as highlighted below.

1) *CNICS 2011:* Considering HPV vaccine uptake according to age of child; 44.2% (10 to 14 years), 21.0% (15 to 17 years) were vaccinated. According to age of person most knowledgeable (PMK); 46.8% (15 to 30 years), 39.2% (40 to 54 years) and 41.0% (55 years and older) received HPV vaccine. Looking at highest education PMK; 25.6% (less than high school diploma or its equivalent), 43.4% (high school diploma or a high school equivalency certificate), 29.1% (trade certificate or diploma), 35.8% (college/CEGEP/other non-university certificate or diploma), 57.9% (university certificate or diploma below the bachelor's level), 46.4% (bachelor's degree), 42.3% (university certificate, diploma, degree above bachelor level) received the HPV vaccine. Regarding birthplace of child HPV vaccine uptake is 35.9% (born outside Canada) and 41.8% born in Canada. According to birthplace of PMK; 31.5% (born outside Canada) and 45.3% (born in Canada) received the HPV vaccine. Looking at province; 49.0% (other), 59.7% (Quebec) and 23.8% (Ontario) got the HPV vaccine. Under access to health care practitioner (HCP); 42.1% (yes) and 44.7% (no) were vaccinated with HPV vaccine. According to HCP discussion of immunization; 35.7% (yes) and 44.4% (no) got the HPV vaccine. Considering having sufficient information on immunization; 43.3% (yes) and 29.8% (no) got HPV vaccination). Regarding concern about side effect of vaccines; 38.7% (strongly agree), 39.4% (somewhat agree), 55.2% (somewhat disagree and 39.6% (strongly disagree) received the HPV vaccine. Looking at belief vaccines causing diseases 44.5% (strongly agree), 35.6% (somewhat agree), 50.1% (somewhat disagree and 38.4% (strongly disagree). Regarding the category of importance of other vaccines; [(varicella 48.7% (very important) 37.9% (important) 46.7% (somewhat important) 24.0% (not important at all); influenza 54.8%(very important), 42.1% (important) 43.5%, (somewhat important), 29.5% (not important at all); pneumococcal disease 43.5% (very important), 43.5% (important) 42.0%, (somewhat important), 18.7% (not important at all)] received HPV the

vaccine. Finally, regarding total household income; 42.3% ($0 to $46000), 39.3% ($46001 to $92000), 44.7% ($92001 to $143000), 31.1% ($143001 to $202900) and 56.3% ($202901 to $1500000) got the HPV vaccine.

A summary of the proportion of vaccinated and unvaccinated participants according to variables under consideration are as shown in Table 6.1 (Appendix E).

2) *CNICS 2013:* Considering age of child 69.2% (10 to 14 years), 67.3% (15 to 17 years) were vaccinated. According to age of person most knowledgeable (PMK); 68.8% (15 to 30 years), 68.4% (40 to 54 years) and 72.6% (55 years and older) received HPV vaccine. Regarding highest education PMK; 66.8% (less than high school diploma or its equivalent), 68.9% (high school diploma or a high school equivalency certificate), 71.4% (trade certificate or diploma), 68.9% (college/CEGEP/other non-university certificate or diploma), 74.6% (university certificate or diploma below the bachelor's level), 66.6% (bachelor's degree), 70.8% (university certificate, diploma, degree above bachelor level) received the HPV vaccine. Looking at birthplace of child; 62.8% (born outside Canada) and 69.6% born in Canada. Considering birthplace of PMK; 61.5% (born outside Canada) and 71.9% born in Canada. Looking at province; 87.0% (Newfoundland and Labrador), 80.6% (Prince Edward Island), 78.7% (Nova Scotia), 79.9% (New Brunswick), 81.4% (Quebec), 61.4% (Ontario), 57.8% (Manitoba), 67.1% (Saskatchewan), 70.0% (Alberta), 67.1% (British Columbia), 61.8% (Yukon), 58.3% (Northwest Territories) and 47.6% (Nunavut) received the HPV vaccine. Considering province in grouped format; 69.3% (other), 81.4% (Quebec) and 61.4% (Ontario) were vaccinated. In terms of access to health care practitioner (HCP); 72.2% (yes) and 67.0% (no) received the HPV vaccine. Looking at HCP discussion of immunization; 66.3% (yes) and 71.5% (n0) were vaccinated. Regarding having sufficient information on immunization; 69.3% (yes) and 67.2% (no) got HPV vaccine. Looking at reason not sufficient information; 65.0% (did not know where to get information), 53.1% (appointments were rushed), 74.0% (felt uncomfortable asking questions), 71.4% (did not take the time to review the information) 48.3% (did not understand the information provided), 86.9% (language difficulty), 64.2% (other), 89.8% (don’t know), 56.6% (not stated), and 71.4% (did not receive any/enough information from provider). According to childhood vaccines safety 72.0% (strongly agree), 68.0% (somewhat agree), 50.1% (somewhat disagree) and 45.6% (strongly disagree) reportedly got the HPV vaccine. Using the yardstick of childhood vaccines effectiveness; 71.4% (strongly agree), 67.3% (somewhat agree), 41.6% (somewhat disagree) and

50.1% (strongly disagree) reportedly received the HPV vaccine. In terms childhood vaccines importance for child's health; 72.0% (strongly agree), 64.5% (somewhat agree), 47.0% (somewhat disagree) and 35.4% (strongly disagree) were reportedly vaccinated. Looking at understanding of how vaccines work; 68.6% (strongly agree), 71.3% (somewhat agree), 64.9% (somewhat disagree) and 64.4% (strongly disagree) reportedly received the HPV vaccine. Lastly for this survey cycle and looking at belief that alternative practices eliminate need for vaccine; 56.0% (strongly agree), 59.2% (somewhat agree), 69.3% (somewhat disagree) and 73.1% (strongly disagree) were reportedly vaccinated.

Regarding the category of importance of other vaccines; [(varicella 73.1% (very important) 71.7% (important) 68.0% (somewhat important) 55.9% (not important at all); (diphtheria 72.3% (very important), 67.5% (important) 52.8% (somewhat important) 47.8% (not important at all); (rubella 72.5% (very important) 67.0% (important) 53.4% (somewhat important) 46.4% (not important at all); (hepatitis B 73.0% (very important) 66.6% (important) 48.9% (somewhat important) 38.1% (not important at all); influenza 73.8%(very important), 73.3% (important) 73.9%, (somewhat important), 58.1% (not important at all); measles 72.9% (very important), 67.6% (important) 61.0%, (somewhat important), 46.3% (not important at all); mumps 72.5% (very important), 67.5% (important) 64.5%, (somewhat important), 48.3% (not important at all) received HPV the vaccine; measles 72.9% (very important), 67.6% (important) 61.0%, (somewhat important), 46.3% (not important at all); pneumococcal disease 73.8% (very important), 71.0% (important) 62.6%, (somewhat important), 54.1% (not important at all)] received HPV the vaccine; polio 72.3% (very important), 66.6% (important) 49.6%, (somewhat important), 42.9% (not important at all); meningitis 73.2% (very important), 65.5% (important) 49.0%, (somewhat important), 31.7% (not important at all), tetanus 72.2% (very important), 66.4% (important) 62.3%, (somewhat important), 50.9% (not important at all), pertussis 73.7% (very important), 67.0% (important) 60.2%, (somewhat important), 47.5% (not important at all) received HPV vaccine. Finally, regarding total household income; 67.7% ($0 to $46000), 67.7% ($46001 to $92000), 70.4% ($92001 to $143000), 71.1% ($143001 to $202900) and 68.5% ($202901 to $1500000) got the HPV vaccine.

A summary of the proportion of vaccinated and unvaccinated participants according to variables under consideration are as shown in Table 6.2 (Appendix E).

3.CNICS 2015. According to this survey cycle, looking at age of child; 74.6% (10 to 14 years), 71.9% (15 to 17 years) were vaccinated, age of person most knowledgeable (PMK); 69.2% (15 to 39 years), 75.4% (40 to 54 years), 68.5% (55 years and older) were vaccinated. Regarding relationship of the PMK to the child; 57.8% (related as birth parent) and 57.8% (related but not as birth parent. Looking at highest education PMK; 68.5% (less than high school diploma or its equivalent), 74.7% (high school diploma or a high school equivalency certificate), 67.6% (trade certificate or diploma), 77.7% (college/CEGEP/other non-university certificate or diploma), 76.6% (university certificate or diploma below the bachelor's level), 71.7% (bachelor's degree), 71.8% (university certificate, diploma, degree above bachelor level) received the HPV vaccine. According to birthplace of child; 75.1% (born outside Canada), 67.2% (born in Canada) received the vaccine. Looking at birthplace of PMK; 67.2% (born outside Canada) and 70.2% (born in Canada) were vaccinated. Considering province; 73.8% (other), 85.2% (Quebec) and 67.9% got the HPV vaccine Looking at access to health care practitioner (HCP); 75.7% (yes) and 70.5% got the HPV vaccine. Focusing on HCP discussion of immunization; 77.3% (yes) and 75.6% (no) were vaccinated. Regarding sufficient information on immunization; 75.5% (yes) and 68.1% (no) received the HPV vaccine. Considering concern about side effect of vaccines; 67.0% (strongly agree), 73.5% (somewhat agree), 80.2% (somewhat disagree), and 81.7% (strongly disagree). Regarding belief vaccines cause diseases; 72.6% (strongly agree), 69.1% (somewhat agree), 79.6% (somewhat disagree) and 75.1% (strongly disagree). Regarding opinion that alternative practices eliminate need for vaccine; 65.3% (strongly agree), 63.9% (somewhat agree), 74.5% (somewhat disagree) and 77.1% (strongly disagree).

Regarding the category of importance of other vaccines; [(varicella 80.7% (very important) 75.1% (important) 74.1% (somewhat important) 50.2% (not important at all); influenza 76.8% (very important), 82.0% (important) 83.0%, (somewhat important), 56.6% (not important at all); mumps 77.3% (very important), 75.1% (important) 56.6%, (somewhat important), 38.3% (not important at all) received HPV the vaccine; pneumococcal disease 80.3% (very important), 72.2% (important) 73.5%, (somewhat important), 38.2% (not important at all) received HPV the vaccine; polio 72.3% (very important), 66.6% (important) 49.6%, (somewhat important), 42.9% (not important at all); pertussis 75.4% (very important), 75.0% (important) 78.9%, (somewhat important), 37.9% (not important at all) received HPV vaccine.

A summary of the proportion of vaccinated and unvaccinated participants according to variables under consideration are as shown in Table 6.3 (Appendix E).

6.4.2 Predictors of HPV Vaccine Uptake

6.4.2.1 Univariate analysis

Univariate analysis was conducted with a level of significance of α=0.25. Statistically significant associations at this level are as follows: age (*P*-value <0.0001), sex (*P*-value <0.0001), relationship status (*P*-value <0.0001), marital status (*P*-value <0.0001), gender identity (*P*-value <0.0001), nationality (*P*-value <0.0001), year in school (*P*-value <0.0001), number of sexual partners (*P*-value <0.0001), Engagement in oral, vaginal and anal sex within the last 30 days (*P*-value <0.0001), use of protective barrier- oral, vaginal and anal sex (*P*-value <0.0001), race/ethnicity -Aboriginal, non-White *P*-value (<0.0001), vaccination history- hepatitis B, influenza, MMR, meningitis, chickenpox (*P*-value <0.0001).

6.4.2.2 Multivariable Analysis

Variables identified as significant in the univariate analysis were initially verified for multi-collinearity. A variance inflation factor (VIF) < 3 was observed as cut-off point for all independent variables, indicating the independent variables are not highly correlated (Hair *et al.*, 2019). Our final model depicted the association between self-reported HPV vaccination and the selected independent variables.

6.4.2.3 Determinants of HPV vaccine uptake

CNICS 2011: The following variables: age of child, province and importance of other vaccines (varicella) were significantly (p-value < 0.05) associated with the receipt of HPV vaccine. Looking at age; individuals that were [10 – 14 years were 2.65 (95% CI 1.58 – 4.45) times more likely to receive the HPV vaccine compared to those that were 15-17 years (p-value <0.0001). Considering province of the participants, those in "other" provinces were 2.62 (95% CI 1.55 – 4.44; p-value <0.0001); Quebec were 5.11 (95% CI 2.90 - 9.01; p-value <0.0001) times more likely to be vaccinated for HPV compared to participants from Ontario. Looking at importance of other vaccines (varicella); those that belief that vaccines were very important were 2.68 (95% CI 1.36 – 5.28; p-value 0.004) times more likely to be vaccinated for HPV compared to participants that belief that vaccines are not important at all.

A summary of the association of predictor variables with HPV vaccination after multivariable analysis is shown below in Table 6.4.

Table 6.4: Multivariable Analysis of HPV[1] Vaccination CNICS[2] 2011			
Independent Variables		HPV[1] vaccination ("Yes" versus "No") Odds (95% CI)	P-value (α=0.05)
Age of Child (Ref= "15 to 17 years older")	10 - 14 years	2.65 (1.58 – 4.45)	<0.0001
Birthplace of PMK (Ref= "Born in Canada")	Born outside Canada	0.61 (0.36 – 1.02)	0.060
Province Ref= ("Ontario")	Other	2.62 (1.55 – 4.44)	<0.0001
	Quebec	5.11 (2.90 – 9.01)	<0.0001
Importance of other vaccines (Varicella) Ref = ("Not important at all")	Very important	2.68 (1.36 – 5.28)	0.004
	Important	1.22 (0.57 – 2.58)	0.610
	Somewhat important	1.72 (0.81 – 3.63)	0.158

[1]Human Papillomavirus
[2]Childhood National Immunization Coverage Survey
[3]Health Care Provider
[4]Parent/Guardian of Child
*** The outcome variable is HPV vaccination status with two levels ["Yes" and "No" (reference)]**

CNICS 2013. The following variables: age of child, birthplace of PMK, province (separately), childhood vaccines are important for child's health, concerned about the side effects of vaccines, importance of other vaccines (varicella), importance of other vaccines (meningitis) and total household income were significantly (p-value < 0.05) associated with the receipt of HPV vaccine.

Looking at age; individuals that were [10 – 14 years were 1.65 (95% CI 1.49 – 1.82) times more likely to receive the HPV vaccine compared to those that were 15-17 years (p-value <0.0001). For birthplace of PMK; those born outside Canada are 31% (OR 0.69; 95% CI 0.60 – 0.79) less likely to receive the HPV vaccine compared to those born in Canada. Considering province of participants (separately); individuals in [(Newfoundland and Labrador were 6.41 (95% CI 4.52 - 9.10; p-value <0.0001); Prince Edward Island were 4.54 (95% CI 3.19 – 6.47; p-value <0.0001; Nova Scotia were 4.27 (95% CI 3.07 – 6.00; p-value <0.0001; New Brunswick were 4.91 (95% CI 3.49 – 6.90; p-value <0.0001; Quebec were 7.61 (95% CI 5.43 – 10.66; p-value <0.0001; Ontario were 2.14 (95% CI 1.55 – 2.96, p-value <0.0001; Manitoba were 1.55 (95% CI 1.12 – 2.15, p-value 0.008; Saskatchewan were 2.03 (95% CI 1.47 – 2.82, p-value <0.0001; Alberta were 2.88 (95% CI 2.08 - 4.00 p-value <0.0001; British Columbia were 2.97 (95% CI 2.13 – 4.16 p-value <0.0001; Yukon were 2.13 (95% CI 1.47 – 3.10 p-value <0.0001; Northwest Territories were (95% CI 1.59 – 1.11 – 2.27 p-value 0.012)] more likely to receive the HPV vaccine compared to individuals in Nunavut.

Regarding HPV vaccine uptake according to the belief childhood vaccines are important for child's health; individuals that "strongly agree" were 2.71 times (95% CI 1.49 – 4.92; p-value <0.0001) more likely to be vaccinated than those that "strongly disagree".

Looking at understanding how vaccines work; individuals that "somewhat agree" were 1.79 (95% CI 1.06 – 3.02; p-value = 0.028;) more likely to be vaccinated than those that "strongly disagree". Looking at "concerned about the side effects of vaccines" individuals that "strongly agree" were 43% less likely [(OR 0.57: 95% CI 0.48 – 0.67; p-value <0.0001;) "somewhat agree" were 27% less likely (OR 0.73: 95% CI 0.62 – 0.87; p-value <0.0001;) to be vaccinated than those that "strongly disagree".

Looking at importance of other vaccines (varicella); those that belief that vaccines were [("very important" were 1.45 (95% CI 1.22 – 1.72; p-value <0.0001; "important" were 1.59 (95% CI 1.32 – 1.92; p-value <0.0001; "somewhat important" were 1.34 (95% CI 1.12 – 1.60; p-value =

0.002)] times more likely to be vaccinated for HPV compared to participants that belief that vaccines are not important at all.

Considering importance of other vaccines (meningitis); those that belief that vaccines were [("very important" were 2.85 (95% CI 1.76 – 4.61; p-value <0.0001; "important" were 2.29 (95% CI 1.41 – 3.71; p-value = 0.001; "somewhat important" were 1.74 (95% CI 1.05 – 2.87; p-value = 0.031)] times more likely to be vaccinated for HPV compared to participants that belief that vaccines are not important at all.

Finally, looking at total household income; participants from households earning "$0 to $46000" 25% (OR 0.75 95% CI 0.57 – 0.97; p-value 0.027) less likely to be vaccinated compared to participants from households earning ("$202901 to $1500000").

A summary of the association of predictor variables with HPV vaccination after multivariable analysis is shown below in Table 6.5.

Table 6.5: Multivariable Analysis of HPV[1] Vaccination CNICS[2] 2013			
Independent Variables		HPV[1] vaccination ("Yes" versus "No") Odds (95% CI)	P-value (α=0.05)
Age of Child (Ref= "15 to 17 years older")	10 - 14 years	1.65 (1.49 – 1.82)	<0.0001
Birthplace of PMK (Ref= "Born in Canada")	Born outside Canada	0.69 (0.60 – 0.79)	<0.0001
Province Ref= ("Nunavut")	Newfoundland and Labrador	6.41 (4.52 - 9.10)	<0.0001
	Prince Edward Island	4.54 (3.19 – 6.47)	<0.0001
	Nova Scotia	4.27 (3.07 – 6.00)	<0.0001
	New Brunswick	4.91 (3.49 – 6.90)	<0.0001
	Quebec	7.61 (5.43 – 10.66)	<0.0001
	Ontario	2.14 (1.55 – 2.96)	<0.0001
	Manitoba	1.55 (1.12 – 2.15)	0.008
	Saskatchewan	2.03 (1.47 – 2.82)	<0.0001
	Alberta	2.88 (2.08 - 4.00)	<0.0001
	British Columbia	2.97 (2.13 – 4.16)	<0.0001
	Yukon	2.13 (1.47 – 3.10)	<0.0001

	Northwest Territories	1.59 – 1.11 – 2.27)	0.012
Childhood vaccines are important for child's health Ref= ("Strongly disagree")	Strongly agree	2.71 (1.49 – 4.92)	0.001
	Somewhat agree	1.72 (0.95 – 3.13)	0.073
	Somewhat disagree	1.20 (0.62 – 2.32)	0.583
Understand how vaccines work Ref = (Strongly disagree)	Strongly agree	1.57 (0.94 – 2.64)	0.086
	Somewhat agree	1.79 (1.06 – 3.02)	0.028
	Somewhat disagree	1.71 (0.94 – 3.10)	0.080
Concerned about the side effects of vaccines Ref= ("Strongly disagree")	Strongly agree	0.57 (0.48 – 0.67)	<0.0001
	Somewhat agree	0.73 (0.62 – 0.87)	<0.0001
	Somewhat disagree	0.99 (0.81 – 1.20)	0.880
Importance of other vaccines (Varicella) Ref = ("Not important at all")	Very important	1.45 (1.22 – 1.72)	<0.0001
	Important	1.59 (1.32 – 1.92)	<0.0001
	Somewhat important	1.34 (1.12 – 1.60)	0.002
Importance of other vaccines (Meningitis) Ref = ("Not important at all")	Very important	2.85 (1.76 – 4.61)	<0.0001
	Important	2.29 (1.41 – 3.71)	0.001
	Somewhat important	1.74 (1.05 – 2.87)	0.031
Total Household Income	$0 to $46000	0.75 (0.57 – 0.97)	0.027
	$46001 to $92000	0.81 (0.63 -1.05)	0.111

Ref = ("$202901 to $1500000")	$92001 to $143000	0.87 (0.67 – 1.13)	0.283
	$143001 to $202900	1.06 (0.81 – 1.40)	0.667
[1]Human Papillomavirus **[2]Childhood National Immunization Coverage Survey** **[3]Health Care Provider** **[4]Parent/Guardian of Child** *** The outcome variable is HPV vaccination status with two levels ["Yes" and "No" (reference)]**			

CNICS 2015: The following variables: province, concerned about the side effects of vaccines and importance of other vaccines (varicella, influenza, pneumococcal disease) income were significantly (p-value < 0.05) associated with the receipt of HPV vaccine.

Considering province of the participants, those in Quebec were 2.70 (95% CI 1.27 – 4.80; p-value = 0.007) times more likely to be vaccinated for HPV compared to participants from Ontario.

Looking at individuals "concerned about the side effects of vaccines" individuals that "strongly agree" were 61% less likely (OR 0.39: 95% CI 0.18 – 0.83; p-value <0.015) to be vaccinated than those that "strongly disagree".

Considering importance of other vaccines varicella; those that belief that vaccines were ("very important" were 3.19 (95% CI 1.51 – 6.75; p-value <0.002) times more likely to be vaccinated for HPV compared to participants that belief that vaccines are not important at all.

Considering importance of other vaccines influenza; those that belief that vaccines were ("important" were 2.99 (95% CI 1.56 – 5.72; p-value <0.0001; "important" were 2.29 (95% CI 1.41 – 3.71; p-value = 0.001; "somewhat important" were 1.74 (95% CI 1.05 – 2.87; p-value = 0.031)] times more likely to be vaccinated for HPV compared to participants that belief that vaccines are not important at all.

A summary of the association of predictor variables with HPV vaccination after multivariable analysis is shown below in Table 6.6.

Additionally, Figure 6.1 depicts proportion of HPV vaccination uptake in Canadian female children according to province/territory looking at CNICS 2013 cycle.

Table 6.6: Multivariable Analysis of HPV[1] Vaccination CNICS[2] 2015			
Independent Variables		HPV[1] vaccination ("Yes" versus "No") Odds (95% CI)	P-value (α=0.05)
Province Ref= ("Ontario")	Other	0.72 (0.46 – 1.14)	0.158
	Quebec	2.47 (1.27 – 4.80)	0.007
Concerned about the side effects of vaccines Ref= ("Strongly disagree")	Strongly agree	0.39 (0.18 – 0.83)	0.015
	Somewhat agree	0.60 (0.29 – 1.23)	0.164
	Somewhat disagree	0.99 (0.44 – 2.23)	0.974
Importance of other vaccines (Varicella) Ref = ("Not important at all")	Very important	3.19 (1.51 – 6.75)	0.002
	Important	1.77 (0.85 – 3.66)	0.125
	Somewhat important	1.71 (0.81 – 3.62)	0.159
Importance of other vaccines (Influenza) Ref = ("Not important at all")	Very important	1.69 (0.79 – 3.63)	0.179
	Important	2.99 (1.56 – 5.72)	0.001
	Somewhat important	2.81 (1.63 – 4.85)	<0.0001
Importance of other vaccines (Pneumococcal disease)	Very important	3.55 (1.34 – 9.45)	0.011
	Important	1.67 (0.63 – 4.44)	0.303
	Somewhat important	2.76 (1.03 – 7.42)	0.045

Ref = (“Not important at all”)			
[1]Human Papillomavirus **[2]Childhood National Immunization Coverage Survey** **[3]Health Care Provider** **[4]Parent/Guardian of Child** *** The outcome variable is HPV vaccination status with two levels [“Yes” and “No" (reference)]**			

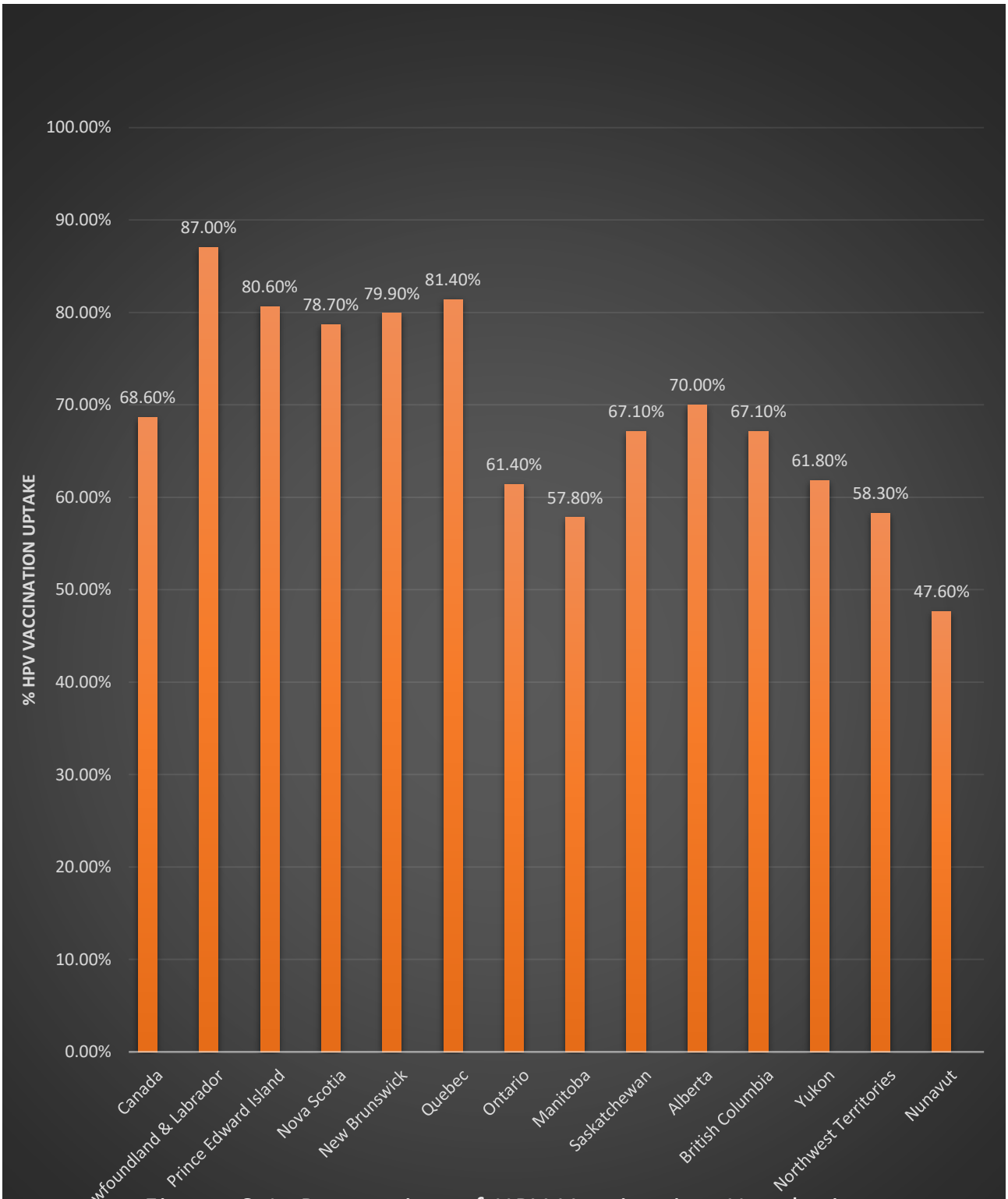

Figure 6.1: Proportion of HPV Vaccination Uptake in Canadian Female Children According to Province/Territory

(CNICS 2013)

6.5 Discussion

This study examines HPV vaccine uptake as well as determinant of uptake among Canadian female children. In-depth understanding of this concept is crucial in defining the impact of HPV vaccination programs not only in female populace but in the Canadian population. Furthermore, if the HPV vaccination uptake and underlying determinants are well conceptualized; it could serve as an empirical template for future program designs and rollout especially now that Canada, like many other countries has moved towards evidenced based universal HPV vaccination.

The HPV vaccination uptake in Canadian female children (10 - 17 years) was 41.1%, 68.6% and 73.7% for CNICS cycles 2011, 2013, 2015 respectively. According to these CNCIS survey cycles trend, there is a progressive increase in HPV vaccine uptake spanning the period 2011 to 2015. However, an HPV vaccine uptake of 73.7% for 2015 still falls short of the Canadian Immunization Committee (CIC) recommendation stating that 80% of eligible populace be completely vaccinated against HPV within 2 years (and 90% within 5 years) of the introduction of the HPV vaccination program (Government-of-Canada., 2017b). Notably, the HPV vaccine programming was introduced into Canada in 2007 following approval of the HPV vaccines by Health Canada in 2006.

Looking at the 2011 CNICS cycle, determinants of HPV vaccine uptake in Canadian female children were found to be age, province and importance of other vaccines (specifically, varicella). Thus, those that were 10 to 14 years were 2.65 times more likely to have received the HPV vaccine compared to those that were in the age bracket of 15 to 17 years. This observation is consistent with previous researches that have reported younger age as a positive predictor of HPV vaccine uptake (Bird *et al.*, 2017; Crosby *et al.*, 2007; Elam-Evans *et al.*, 2014; Government-of-Canada., 2016b; Patel *et al.*, 2012; Tabrizi *et al.*, 2012; World-Health-Organization., 2017). This is explainable from the fact that initial publicly funded HPV vaccine programs were school based, starting with female children from mostly grade 5 or grade 6. Thus, it is expected that the younger cohort of girls would have higher HPV vaccine uptakes compared to the older cohorts.

Considering province of the participants, those in "other" provinces combined [(comprising, Newfoundland and Labrador, Prince Edward Island, New Brunswick, Manitoba, Saskatchewan, Alberta, British Columbia, Yukon, Northwest Territories, Nunavut) were 2.62 times; Quebec

participants were 5.11 times)] were more likely to receive the HPV vaccine compared to participants from Ontario. Although jurisdictions across Canada have some similarities in vaccination programs and scheduling, there is no singular, federally enforced HPV vaccination programing adapted by provinces or territories across Canada. Thus, an empirically informed explanation of observed differences in HPV vaccine uptake from coast to coast across Canada may be challenging. Notwithstanding this limitation, it is suggested that province(s) with suboptimal HPV vaccine uptake understudy HPV vaccination programs from those with higher HPV vaccine uptakes to get better vaccination outcomes.

Looking at importance of other vaccines (varicella); this study found that participants believing that vaccines were very important were 2.68 times more likely to be vaccinated for HPV compared to participants that belief that vaccines are not important at all. Thus, incorporating HPV vaccination campaign programs alongside with that of other vaccination program that are already well accepted and established could be helpful in improving HPV vaccination uptake in the population.

In CNICS 2013; we found that age of child, birthplace of PMK, province (separately), childhood vaccines are important for child's health, concerns about the side effects of vaccines, importance of other vaccines (varicella, meningitis) and total household income were the significant determinants of HPV vaccination uptake. Thus, individuals that were 10 – 14 years were 1.65 times more likely to receive the HPV vaccine compared to those that were 15-17 years. The same explanation of younger age as a positive predictor of HPV uptake in CNICS 2011 cycle also applied to the CNICS 2013 cycle.

For birthplace of PMK, this study found that those born outside Canada were 31% less likely to receive the HPV vaccine compared to those born in Canada. Again, this is consistent with previous reports and is partly due to the fact that Canada was one of the early countries that initiated publically funded HPV vaccination into its national vaccination program. Therefore, uptake is expected to be comparatively higher for participants born in Canada compared to those born outside Canada. Further research is needed to explore HPV vaccination status of immigrants and determinants of HPV vaccine uptake in this subpopulation of Canadians.

Based on known and postulated determinants of HPV vaccine uptake among immigrants to Canada, closing observed gaps in HPV vaccine uptake among Canadian immigrants is needed and should be a priority for public health planners. Thus, incorporating HPV vaccination

program alongside with that of other vaccination program that are already well accepted and established could be helpful in improving HPV vaccination uptake in the population.

Considering province of participants; when compared with Nunavut, all other provinces/territories had higher HPV vaccination uptake. It is also observed that compared to provinces, territories had a lower HPV vaccination uptake. There should be a conscious effort to bridge this observed HPV vaccination gap among female children in the territories with high proportion of Aboriginal people who coincidentally also have higher burden of HPV infection (Bennett *et al.*, 2015; Demers *et al.*, 2011; Hamlin-Douglas *et al.*, 2008; Jiang *et al.*, 2013a; Severini *et al.*, 2013).

Regarding HPV vaccine uptake according to the belief that "childhood vaccines are important for child's health" This study found that individuals that "*strongly agree*" were 2.71 times more likely to be vaccinated than those that "*strongly disagree*". A higher HPV vaccine uptake from those recognizing the importance of childhood vaccines is explainable since such people are usually positively disposed to receiving vaccination as a tangible public health approach in the prevention of childhood diseases.

Looking at "understanding how vaccines work"; our study found that individuals that "*somewhat agree*" were 1.79 more likely to be vaccinated than those that "*strongly disagree*". This may signify knowledge gap and underscores the need for more educational program to enlighten and impart knowledge on the role of HPV vaccines in the prevention of HPV infection and HPV-related diseases.

Considering "concerned about the side effects of vaccines" individuals that "*strongly agree*" were 43% less likely; "*somewhat agree*" were 27% less likely to be vaccinated than those that "strongly disagree". Again, this could be associated with a knowledge gap and need for more educational promotion of HPV vaccination campaigns.

Looking at "importance of other vaccines" (varicella and meningitis) this study found that participants belonging to a spectrum of "*very important*" to "*somewhat important*" categories were at different levels (ranging from 1.45 to 2.85) more likely to have received the HPV vaccine compared to participants with the belief that vaccines are *"not important at all*". This invariably means those individuals having regards towards the importance of other vaccines are equally favorably disposed to receiving the HPV vaccine. A feeling of vulnerability or

susceptibility to other diseases (e.g. varicella and meningitis) could serve as cue for action according to the Health Belief Model (HMB) (Rosenstock *et al.*, 1988).

Finally, looking at income; which is represented by "total household income"; participants from households earning "$0 to $46000" were 25% less likely to be vaccinated compared to participants from households earning "$202901 to $1500000". Considering that HPV vaccination for female children in Canada is mostly school-based and publicly funded; it is difficult to ascribe this observed lower HPV vaccine uptake in household at the lowest rung of income to direct vaccine cost alone. This observed disparity in uptake might be linked to indirect cost (e.g. transportation cost, consideration for missed income for attending parent/guardian).

For the CNICS 2015 cycle, determinants of HPV vaccine uptake were found to be: province, concerned about the side effects of vaccines and importance of other vaccines (varicella, influenza, pneumococcal disease) and total household income. Reasons given under CNICS 2011 and CNICS 2013 to explain the observed effects of the determinants of HPV vaccine uptake equally applies to relevant determinants of HPV vaccine uptake for the CNICS 2015 cycle.

A comparison of statistically significant variables under the different cycles of CNICS (i.e. 2011, 2013 and 2015) shows some similarities and differences. Thus, age of child was found to be significant for CNICS cycles 2011 and 2013 but not for 2015. However, for CNICS 2013 cycle, the effect of younger age was less prominent compared to that of CNICS 2011 cycle (1.65 times and 2.68 times for 2013 and 2011 respectively). Also, province of residence was significant with similar patterns across all three CNICS cycles. This is the only variable that is significant across all three CNICS cycles. Furthermore, "concerns about side effects of childhood" as well as "total household income" were significant for CNICS cycles 2013 and 2015 but not for 2011.

It is difficult to ascribe observed similarities and differences in statistically significant variables across the three CNICS cycles to any specific factor or trend because CNICS cycle are always updated to minimize intrinsic variations within and across cycles as much as possible. Thus, further research is needed to fully explain the observation of similarities and differences in variables that are statistically significant across different CNICS cycles.

6.6 Strength and Limitation of Study

This study exploring HPV vaccination status and determinants used secondary data from CNICS 2011, CNICS 2013 and CNICS 2015 data collected by Statistics Canada depending on reliable and rigorously standardized data collection method. Furthermore, participants for this study comprised of very large population of female children from every province and territory in Canada. Thus, the results of this study are representative of the general Canadian female children population. However, because vaccination status is self-reported, there is the possibility of over/under reporting. Apart from being self-reported, CNICS data are collected over the phone and subject to nonresponse bias as well as inability to collect data from hard-to-reach individuals (e.g. those without telephone services). Furthermore, CNICS data may not include Aboriginal female children living on Reserves because the CNICS survey cycle does not usually include data on the Aboriginal people living on Reserves. Thus, data on a very important segment of Canadian children is not represented.

6.7 Conclusions

This study successfully determined the HPV vaccination status and determinants of HPV vaccine uptake among female children in Canada. With regards to HPV vaccination uptake trend, there was a progressive increase in uptake from 2011 through 2015 (CNICS 2011; 41.1%, CNICS 2013; 68.6%, CNICS 2015; 73.7%). Despite the progressive increase in HPV vaccination, uptake was still suboptimal and fell short of the recommended 80% - 90% HPV vaccination coverage level advocated by the Canadian Immunization Committee (CIC). There was also notable disparity in HPV vaccination uptake among female children in certain jurisdictions of Canada. Concerted effort should be made at program planning and implementation phases to improve HPV vaccination uptake in the jurisdiction with identified low uptake.

Chapter 7: GENERAL DISCUSSION AND CONCLUSIONS

7.1 Overall Findings and Relevance to Research and Policy

In this thesis, we explored HPV vaccination status as well as determinants of HPV vaccine uptake among different subpopulations and jurisdictions across Canada. Specifically, we set out to answer the following research questions: (1) What are the rates of HPV vaccination uptake among different subpopulations in Canada? (2) What are the disparities and gaps in HPV vaccination uptake among different subpopulations in Canada? (3) What are the determinants of HPV vaccine uptake among different subpopulations and especially among children in Canada?

Getting valid answers to aforementioned research questions would enable decision makers and those implementing policies to have strategic roadmap as well as feedback on the impact of HPV vaccination programs across Canada. Identifying determinants of HPV vaccine uptake and gaps in HPV vaccination programs offer a roadmap to improving existing program delivery based on sound empirical evidence.

7.1.1 More than One Decade of HPV Vaccination in Canada

After more than a decade of HPV vaccination campaigns in Canada, there is a need to evaluate vaccination strategies and monitor progress relative to goals and objectives set out by various global and national organizations such as WHO, GAVI, UNICEF, Health Canada, CIC and NACI (Global-Alliance-for-Vaccines-and-Immunization., 2020; Government-of-Canada., 2017b).

For instance in Canada, the National Immunization Strategy objectives for 2016-2021 is to achieve 90% vaccination coverage of HPV vaccine by 17 years of age. This is in alignment with Canada's allegiance to the World Health Organization (WHO) disease prevention and elimination target as well as the Global Vaccine Action Plan objective on HPV vaccine uptake (Government-of-Canada., 2020a).

In answer to research question (1): **Chapters 3, 4, 5 and 6** of this thesis give us insight into rates of HPV vaccine uptake among different subpopulations in Canada. From the pooled meta-analysis of **Chapter 3**; the HPV vaccination uptake in the Canadian general population was 55.9%. This is well below the at least greater than 80% uptake target set by Health Canada. **Chapters 4 and 5** gives us the HPV vaccine uptake for another subpopulation in Canada; university students

(a proxy indication of uptake in young adults). **Chapter 4** (student participants from one Canadian university) determined HPV vaccine uptake to be 37.9% while **Chapter 5** (student participants from universities Canada-wide and thus generalizable) to be 47.2%. **Chapter 6** result gives us the vaccination uptake among Canadian female adolescent children to be 41.1%, 68.6% and 73.7% for the CNICS cycles 2011, 2013 and 2015 respectively.

7.1.2 Identified Gaps and Determinants of HPV Uptake in Canada

The sub-group analysis of different categories of the general Canadian population in **Chapter 3** identified gap in HPV vaccine uptake in men when compared to women. It is hoped that with the introduction of public funding for HPV vaccine in boys in Canada, this observed gap will be addressed over time.

In Chapter 4 and 5, findings from our study provide evidence of notable gaps in the HPV vaccine acceptance and program delivery in young adults, especially among university students. This study shows that uptake of the HPV vaccine is generally low among university students and particularly suboptimal in certain demographic subpopulations of students namely: those that are male, of older age, and international students. Health education programs and intentional vaccination program design that incorporates HPV vaccination (and other vaccines) into university healthcare system especially for fresh students and during orientation programs could go a long way at closing observed vaccination gaps and improving HPV vaccine uptakes among young adults.

In Chapter 6, children of individuals that were concerned about the side effects of vaccines were between 27% to 43% less likely to be vaccinated than children of individuals not concerned about side effects of vaccines. Again, this may be associated with a knowledge gap and need for vigorous educational campaigns targeted towards parents and other decision makers, promoting HPV vaccination as strategic public health intervention. This is very important considering that parents are the major decision makers on whether their children take the HPV vaccine or not. According to **Chapters 3, 4, 5 and 6**; among Canadian subpopulations; younger age was identified as a positive significant determinant of HPV vaccine uptake. Thus, from the perspective of program planning and implementation, it is crucial to initiate HPV vaccination as early as possible (possibly before sexual exposure) and organize adequate catch-up vaccination programs for individuals that missed out at younger ages.

Other significant determinants of HPV according to results from this thesis are: history of receiving other vaccines (and importance attached to other vaccines; history of sexually transmitted infections (STIs) and marital status. In addition, we found birthplace of a child; race/ethnicity and province of residence of residence to be significant determinants of HPV vaccine uptake.

7.1.3 HPV Vaccination Trend in Canada

Similar to other vaccination programs in Canada, there is no Pan-Canadian HPV vaccination registry that gives a vaccination snapshot or better still, trend of HPV vaccination uptake. However, information garnered from secondary datasets such as several CNICS cycles serve as proxy indicator of gap(s) as well as progress made in HPV vaccination campaigns across Canada.

For instance, the HPV vaccine uptake is 41.1%, 68.6% and 73.7% among Canadian female adolescent children for the CNICS 2011, 2013 and 2015 cycles respectively. This shows an upward trend of HPV vaccine uptake from 2011 to 2013 through 2015. It should be noted however that the highest HPV vaccine uptake which is 73.7% for 2015; is still suboptimal when compared to expected uptake of at least greater than 80% after 5years of vaccine introduction.

A summary of HPV vaccination uptake trend according different variables relevant to HPV vaccine uptake for Canadian female children (CNICS 2011 – CNICS 2015) is shown below in Table 7.1.

Additionally, a graphic depiction of this HPV vaccination uptake trend is shown in Figure 7.1.

Table 7.1: HPV Vaccination Status: Trends in Canadian Female Children CNICS 2011 - 2015

Variables & Categories ↓		**2011** (n=1056326) **HPV Vaccine Uptake (%)**	**2013** **(n=**232301) **HPV Vaccine Uptake (%)**	**2015 HPV Vaccine Uptake (%)**
Age of Child	10 to 14 years	44.2	69.2	74.6
	15 - 17 years	21.7	67.3	71.9
AGE_PMK	15 to 39 years (Younger)15 to 38 years	46.8	31.2	69.2
	40 to 54 years (Middle)39 to 48 years	39.2	31.6	75.4
	55 years and older	41.0	27.4	68.5
Highest Education PMK[4]	Less than high school diploma or its equivalent	25.6	33.2	68.5
	High school diploma or a high school equivalency certificate	43.4	31.1	74.7
	Trade certificate or diploma	29.1	28.6	67.6
	College/CEGEP/other non-university certificate or diploma	35.8	31.1	77.7
	University certificate or diploma below the bachelor's level	57.9	25.4	76.6

	Bachelor's degree (e.g. B.A., B.Sc., LL.B.)	46.4	33.4	71.7
	University certificate, diploma, degree above the BA level	42.3	29.2	71.8
Birthplace of Child	Born outside Canada	35.9	62.8	75.1
	Born in Canada	41.8	69.6	67.2
Birthplace of PMK	Born outside Canada	31.5	69.6	70.2
	Born in Canada	45.3	61.5	75.8
Province	Other	49.0	69.3	73.8
	Quebec	59.7	81.4	85.2
	Ontario	23.8	61.4	67.9
Accessed HCP[3]	Yes	42.1	70.2	75.7
	No	44.7	67.0	70.5
HCP discussed Immunization	Yes	35.7	66.3	77.3
	No	44.4	71.5	75.6
Have Sufficient Information on Immunization	Yes	43.3	69.3	75.5
	No	29.8	67.2	68.1
Concerned about side effect of vaccines	Strongly agree	38.7	62.1	67.0
	Somewhat agree	39.4	70.6	73.5
	Somewhat disagree	55.2	75.4	80.2
	Strongly disagree	39.6	78.1	81.7
Vaccine Cause Diseases	Strongly agree	44.5	59.5	72.6
	Somewhat agree	35.6	67.4	69.1
	Somewhat disagree	50.1	69.8	79.6
	Strongly disagree	38.4	76.2	75.1

Importance of other vaccines (Varicella)	Very important	48.7	73.1	80.7
	Important	37.9	71.7	75.1
	Somewhat important	46.7	68.0	74.1
	Not important at all	24.0	55.9	50.2
Importance of other vaccines (Influenza)	Very important	54.8	73.8	76.8
	Important	42.1	73.3	82.0
	Somewhat important	43.5	73.9	83.0
	Not important at all	29.5	58.1	56.6
Importance of other vaccines (Pneumococcal disease)	Very important	56.5	73.8	80.3
	Important	56.5	71.0	72.2
	Somewhat important	58.0	62.6	73.5
	Not important at all	81.3	54.1	38.2

[1]Human Papillomavirus
[2]Childhood National Immunization Coverage Survey
[3]Health Care Provider
[4]Parent/Guardian of Child

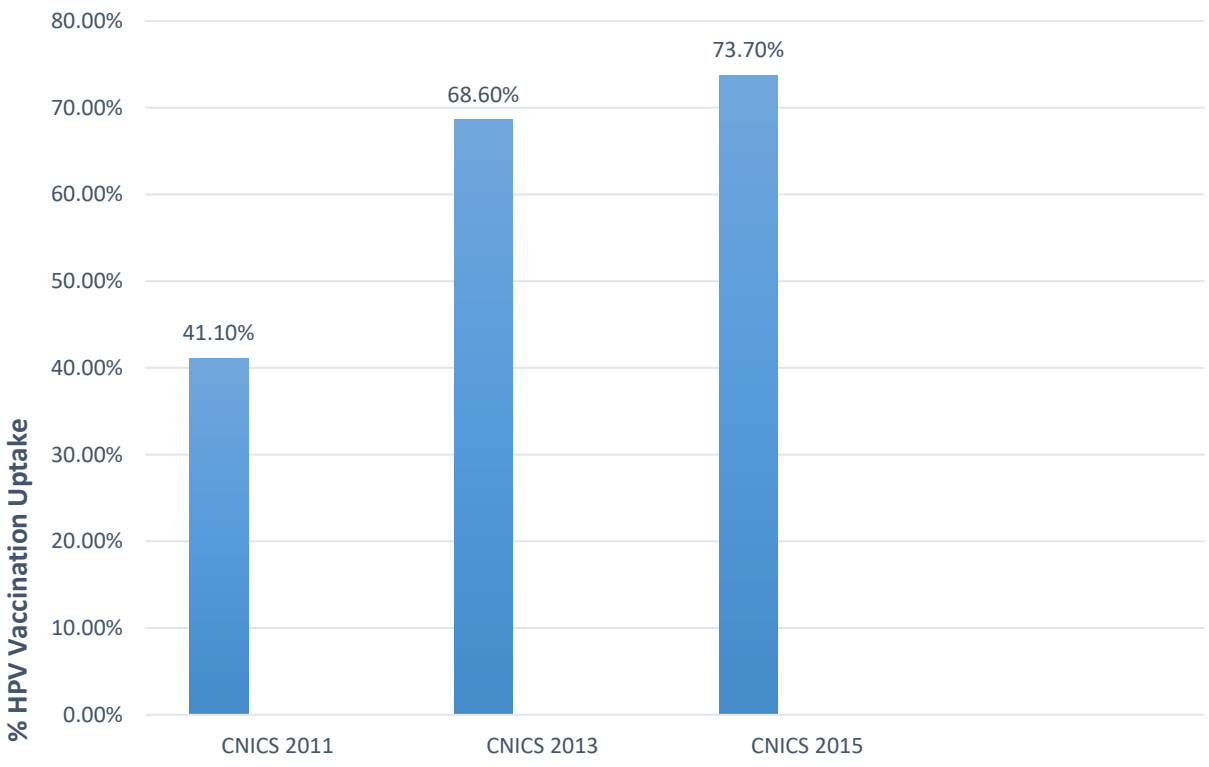

Figure 7.1: Trend of HPV Vaccination Uptake in Canadian Female Children (CNICS 2011 - 2015)

7.1.4 Thesis Limitations

As highlighted under various chapters of this thesis, HPV vaccination uptake for different subpopulations in Canada were largely self-reported therefore there is the possibility of under or/and over reporting bias.

Furthermore, this thesis does not include HPV vaccination data for Indigenous Canadian population living in Reserves as the secondary data used for this research did not include residents in these Reserves.

Finally, there was no Pan-Canadian vaccination program or vaccine registry for HPV vaccination program (or of any vaccination program in Canada). Thus, a direct comparison of HPV vaccination across provincial (or territorial) jurisdictions in Canada is problematic.

7.1.5 Future Work

Results and conclusions from this research project give valuable insights into gaps in HPV vaccination programs, predictors of HPV vaccine uptake and recommendations for better program planning and implementation to improve HPV vaccination uptake in Canada. However, arising from limitations highlighted in the course of carrying out this research and similar studies (e.g. limited or/and no access to HPV vaccination data), further research is needed on HPV vaccination in certain subpopulations in Canada.

Specifically, more research on HPV vaccination that focus on sub-populations such as immigrants and Aboriginal Peoples of Canada is needed.

Also considering that HPV vaccination programs is now publically funded for both boys and girls in most jurisdictions of Canada; future research endeavours should focus on the effect of government funding on attitude towards male HPV vaccination, intention to vaccinate, HPV vaccine uptake and impact on HPV-related diseases in the Canadian population.

Appendix A

Ethics Exemption

MEMORANDUM

From:
Dr. Vivian Ramsden
Acting Chair, Behavioural Research Ethics Board

Date: February 15, 2019

Re: Exemption of Saskatchewan Research Data Centre data from REB review

The exclusive use of data held in the Saskatchewan Research Data Centre (SKY-RDC), including both Public Use Microdata Files (PUMF) and Master Files, meets the requirements for Exemption as per Article 2.2 of the Tri-Council Policy Statement (TCPS): Ethical Conduct for Research Involving Humans, December 2014, which states "Research that relies exclusively on publicly available information does not require REB review when: a. the information is legally accessible to the public and appropriately protected by law."

For the purposes of this Policy, publicly available information is any existing stored documentary material, records or publications, which may or may not include identifiable information. Some types of information are legally accessible to the public in a certain form and for a certain purpose, as specified by law or regulations: registries of deaths, court judgments, or public archives and publicly available statistics (e.g., Statistics Canada public use files), for example. In Canada, all publicly available archives (national, provincial or municipal) have policies governing access to their records. An archival record or database that is subject to restrictions, such as those under access to information and privacy legislation or contractual restrictions imposed by the donor of the records, may also be considered publicly available for the purposes of this Policy.

Research that relies exclusively on information that is publicly available, or made accessible through legislation or regulation, does not require REB review. Exemption from REB review for research involving information that is legally accessible to the public is based on the presence of a legally designated custodian/steward who protects its privacy and proprietary interests (e.g., an access to information and privacy coordinator or a guardian of Canadian census data).

The data housed in the SKY-RDC meets all of these criteria. The SKY-RDC site is a secure data portal with carded-door entry. It is my understanding that in order to access Master File data, researchers are required to write a proposal which is reviewed by a Statistics Canada Subject Matter Expert, facilitated by SSHRC. After project approval, researchers must undergo a security clearance procedure prior to moving forward with the project to be undertaken.

Dr. Vivian R Ramsden, Acting Chair
Behavioural Research Ethics Board
University of Saskatchewan

Appendix B

Additional Files from Chapter 1

Table 1.3: Outcomes for HPV monitoring: existing female strategies, possible male strategies and challenges

Projected HPV vaccination Outcome	**Existing female methods**	**Plausible Male options**	**Possible Challenges (M=males, F=females)** *
Genital HPV infection (vaccine targeted types and non-targeted types)	a) HPV typing of liquid based samples obtained from cervical screening b) HPV typing of self-collected vaginal samples c) HPV typing of urine samples from i) residual specimens from Chlamydia screening progams ii) purpose collected specimens d) HPV typing from oral specimen (e.g. rinse)	a) HPV typing of samples collected from external genitalia (glans, shaft, scrotum), self-collected or clinician collected b) HPV typing of anal swabs c) HPV typing from oral specimen (e.g. rinse) d) HPV typing of urine samples from i) residual specimens from Chlamydia screening progams ii) purpose collected specimens	1)Representativeness of study population (F+M, a,b,c,d) 2) Ensuring consistency of HPV typing methods over time so that results are comparable (F+M, a,b,c,d) 3) Availability of vaccination status and sexual history data from participants (F+M, a,b,c,d) 4) Distinguishing deposition from infection (F+M,a,b,c,d)

			5) Standard collection method not established (M, a, b) 6) Urine has low sensitivity in males to detect the presence of genital HPV infection (M,d)
Genital intraepithelial neoplasia	a) Trend analysis of CIN2+ in cervical screening registry data i) existing registers ii) purpose-built registers b) Trend analysis of vaginal/vulval intraepithelial neoplasia in Nordic registers c) Vaccine effectiveness estimation against CIN from registry-based data linkage studies in vaccinated populations	a) Monitor rates of AIN diagnoses in populations using hospitalisation data, health insurance databases or population based health data (Nordic countries only) Because PIN is very rare and not screened for, monitoring rates (even where possible) is unlikely to provide useful monitoring data b) Use data collected from trials of AIN screening in MSM in pre vs post vaccine	1) Ecological nature of register data/time trends in populations of abnormalities. Can be impacted by trends in diagnosis, participation, sexual activity etc (F a,b,c +M a) 2) Incomplete/inaccurate data linkage (F,c) 3) Lack of population-based testing for AIN/PIN means no register data or stable diagnostic rates in most countries (M, a) 4) Monitoring rates of AIN due to HPV16/18 in MSM over time requires research studies being undertaken of screening at

	d) HPV typing of CIN specimens to determine proportion due to vaccine preventable types over time	periods to monitor AIN attributable to vaccine types over time	appropriate time points as HPV typing and screening is not routine clnical practice (M,b)
Genital warts	a) Trend analysis of genital warts/anogenital warts diagnoses in sentinel clinics b) Trend analysis of anogenital warts diagnosed in general practice c) Trend analysis of diagnoses and treatment in insurance populations d) Trend analysis of national hospitalisation data e) Trend analysis of national health registry data (Nordic) f) Vaccine effectiveness estimation against	Female surveillance methods also applicable to males	1) Ecological nature of time trends of genital warts in populations. Can be impacted by trends in treatment modalities, access to health care services, sexual activity etc (F+M, a,b,c,d,e,f) 2) Representativeness of study population (F+M,a,b,c,d) 3) Need to obtain information about sexual orientation in order to monitor in MSM populations (M,a,b,c,d,e,f)

	genital warts from registry-based data linkage studies in vaccinated populations (Nordic)		
Recurrent respiratory papillomatosis	a) Monitoring hospitalisations over time b) Register based RRP surveillance (Canada) c) Rare childhood diseases surveillance through ENT surgeons and paediatricians d) Monitoring of HPV types in RRP lesions	Female surveillance methods (monitoring of incident cases of RRP) also applicable to males	1) Rare disease (F+M,a,b,c,d) 2) Ecological nature of time trends (F+M,a,b,c,d) 3) Usually no RRP surveillance/register established prior to vaccination programs to provide baseline data (F+M,b,c) 4) HPV typing of RRP lesions not routine in many countries (F+M,d)
Cancer	a) Use of cancer registries and cause of death registers to monitor rates of cervical, vagnial, vulval, anal and HPV-associated head and neck cancers over time.	Female surveillance methods (analysis of cancer incidence data over time) also applicable to males. Add monitoring of penile cancers.	1) Data quality. In many countries' cancer registries are incomplete, of poor quality or do not exist. (F+M,a) 2) Long time frame between HPV vaccination and impact on cancers. (M>F,a) 3) Consider systems to record vaccination status against cancers

			- e.g. for verifying and recording vaccination status on cancer registers. (F+M,a) 4) HPV typing of cancers is not routine- consider development of methods to record on registers. (F+M,a) 5) May be changes over time in which cancers are classified as HPV-related so care is needed in applying consistent inclusion critreria. Site-specific coding for head and neck cancers is incomplete in some registers. (F+M,a)
Cancer mortality	a) Use of cancer registries and cause of death registers to monitor rates of cervical, vagnial, vulval, anal and HPV-associated head and neck cancers over time	Female surveillance methods (analysis of cause of death data over time) also applicable to males. Add monitoring of mortaliy from penile cancers.	1) Data quality. In many countries cause of death registries are incomplete, of poor quality or do not exist. (F+M,a) 2) Long time frame between HPV vaccination and death from cancers. (M>F,a)
[*]Letters in brackets refer to the subsections in the adjacent male and female surveillance columns.			

Source: (J. M. Brotherton *et al.*, 2016). *Brotherton, J. M., Giuliano, A. R., Markowitz, L. E., Dunne, E. F., & Ogilvie, G. S. (2016). Monitoring the impact of HPV vaccine in males—considerations and challenges. Papillomavirus Research, 2, 106-111.*

Appendix C

Additional Files from Chapter 3

Medline Search Strategy:

1. HPV.mp. or exp Papillomaviridae/
2. "HPV Infection".mp.
3. viral vaccines/ or papillomavirus vaccines/ or human papillomavirus recombinant vaccine quadrivalent, types 6, 11, 16, 18/
4. gardasil.mp. or exp Human Papillomavirus Recombinant Vaccine Quadrivalent, Types 6, 11, 16, 18/
5. Human papillomavirus 16/ or Cancer Vaccines/ or Papillomavirus Vaccines/ or Papillomaviridae/ or Human Papillomavirus Recombinant Vaccine Quadrivalent, Types 6, 11, 16, 18/
6. Immunization/ec, ed, pc, sn, td [Economics, Education, Prevention & Control, Statistics & Numerical Data, Trends]
7. uptake.mp.
8. coverage.mp.
9. rate.mp.
10. exp Ethnic Groups/ or exp Healthcare Disparities/ or disparity.mp. or exp Health Status Disparities/
11. 1 or 2
12. 3 or 4 or 5 or 6
13. 7 or 8 or 9 or 10
14. exp Canada/
15. exp Nunavut/
16. exp Yukon Territory/
17. exp Northwest Territories/
18. exp Saskatchewan/
19. exp Manitoba/
20. exp Quebec/
21. exp Alberta/

22. exp British Columbia/
23. exp Prince Edward Island/
24. exp Nova Scotia/
25. exp New Brunswick/
26. exp Ontario/
27. exp "Newfoundland and Labrador"/
28. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. 11 and 12 and 13 and 28

JSTOR Search Strategy:

((((canada) AND ("human papillomavirus" or HPV)) AND (Coverage or uptake)) AND (vaccin*))

TABLE 3.1: SUMMARY OF THE KEY CHARACTERISTICS OF ELIGIBLE ARTICLES FROM THE LITERATURE SEARCH					
Author/ Purpose of the Study	**Study Design**	**Sample Size & Characteristics**	**Study Setting & Location**	**Vaccination Uptake (%)**	**Key Findings**
Akhen, 2015 To determine: • Rates of awareness of HPV infection. • The HPV vaccination rates. Acceptability of HPV vaccination catch-up program.	Cross - Sectional	105 females. Age range: 13-25 years old.	Community-based. Ottawa, Ontario	12.4	• Higher-risk young women have high levels of HPV infection/vaccine awareness. • Lack of knowledge with regard to HPV infection consequences.
Burchell, 2014 To study: • Prevalence of HPV in new sexual partnerships among young adults. Explore impact of condom use & woman's HPV vaccination status.	Longitudinal	482 females. Mean age: 21 (18-26) years old.	School-based. Montreal, Quebec.	12.0	• 88% of women unvaccinated. • 67% dyads harbored HPV. • Condom use limited spread of HPV.
Krawczyk, 2015 To identify: • Key differences between parents who vaccinate their daughters against HPV	Longitudinal	774 females. Mean age: 9.5 years old.	School-based. Quebec.	88.2	• HPV vaccination decision-making among parents is a multifactorial process. • Health Belief Model (HBM) adds

and those who refuse the HPV vaccine for their daughters.					value to the study of decision-making. • Parents who perceived their daughter to be susceptible to HPV were more likely to have vaccinated their daughter.
Lim, 2014 To evaluate: • HPV vaccine completion rates (adherence). On-time dosing (compliance)	Longitudinal	111,798 females Mean age: 13 years old.	School & community based. Ontario.	81.5	• Publicly funded, school-based HPV immunization overcome financial and accessibility barriers. • Removing financial and accessibility barriers may not be sufficient for ensuring high HPV vaccine coverage.
To determine: • HPV vaccine uptake in Alberta from 2008 to August 31, 2014. The cumulative proportion of the female population, who	Longitudinal	169,259 males & females. Mean age: 17.5 years old. Age range: 15 - 26 years old.	School & community based. Alberta.	31.3	• HPV vaccine uptake increased among the targeted population in Alberta. Females aged 9–14 years old had the highest

were vaccinated by the end of the 2013/14 school year.					HPV vaccine uptake. • Females aged 10–11 years old had the highest uptake rates for the three doses of the publicly funded vaccine.
McClure, 2015 To determine: • HPV vaccination uptake in boys after the first year of a provincially implemented school-based program. If there were any changes in the girls' recent HPV vaccine uptake relative to previous years.	Longitudinal	1,440 males & females. Mean Age: 11.5 years old (Grade 6 estimate)	School-based. Prince Edward Island.	79.0 male 85.0 female	• Greater proportion of girls (85%) received all three doses of the HPV vaccine compared to boys (79%). • Students in the English Language School Board were twice as likely to receive all 3 HPV vaccine doses (OR=2.14, 95% CI: 1.25-3.66) compared to the students in the French Language School Board doses.

Musto, 2013 To determine: • Difference in HPV vaccine uptake between the two service delivery models, "in-school" and "community". • If socioeconomic status (SES) was a contributing factor.	Cross - Sectional	35,592 females. (School=26304; Community= 9288). Grade 5 (ages 9–11) and grade 9 (ages 13–15)	School & community based. Calgary, Alberta.	75.0 school 36.0 community	• Service delivery models make a difference in HPV vaccination uptake and create inequities in disease prevention based on socioeconomic status
Ogilvie, 2010 To determine: Parental factors associated with acceptance of the HPV vaccine.	Cross - Sectional	2,025 females. Mean age: 11 years old.	School-based. British Columbia.	65.1	• Factors associated with increased likelihood of HPV vaccination: ➢ Positive parental attitude towards vaccination. ➢ Parental belief that HPV vaccination had limited impact on sexual practices. ➢ Completed childhood vaccination.

To evaluate: • Impact of the HPV vaccine program on cervical intraepithelial neoplasia trends in young women aged 15–22 years old before and after its implementation.	Longitudinal	223,051 females. Mean age: 11 years old.	School-based. British Columbia.	61.7	• Significant reduction in CIN21 lesions in young women aged 15–17 years old in British Columbia after the introduction of the HPV vaccine. • Uptake below 70%.
Smith, 2011 To determine: • HPV vaccine use. • Factors associated with the HPV vaccination of young girls.	Longitudinal	2,519 females. Mean age: 13 years old.	School & community-based. Ontario.	56.6	• Girls in the lowest income quintile were the least likely to complete the three-dose HPV vaccine regimen. • Program delivery modified to improve HPV vaccine completion in vulnerable populations.
Whelan, 2014 To explore:	Longitudinal	3219, females Mean age: 13 years old.	School & community based.	74.2	• HPV vaccine initiation was significantly

• Activities and strategies utilized in PHNs' practice in fostering youth, parental and school engagement in the HPV Immunization Program.			Halifax, Nova Scotia		associated with Public Health Nurses providing: ➢ Reminder calls for consent form returns and missed school clinic appointments. ➢ HPV education to schoolteachers. ➢ Thank-you notes to school teachers. • Completion of the HPV series was associated with vaccine consents being returned to the teacher and a Public Health Nurse being assigned to a school.
Wilson, 2013 • The provincial HPV vaccine uptake. • The source of denominator data	Cross - Sectional	74340, females. Mean age: 13 years old (Grade 8)	School-based. Ontario.	59.0	• HPV vaccine coverage has improved since the program was initiated in 2007.

used to estimate the vaccine program's target population. The feedback received on the local methods used for HPV vaccine coverage assessment**.**					• However, only 59% of grade eight girls in Ontario completed the HPV vaccine series in the program's third year. • All Health Units should be encouraged to include girls attending independent schools, home schools, and non-participating schools in their denominators. Excluding such schools falsely raises coverage estimates.

Appendix D

Additional Files from Chapter 5

Table 5.1: Characteristics of HPV Vaccination ACHA-NCHA II Web Spring 2016 Canada-wide

		Percentage		**Total**
HPV[2] vaccination status (n=35587)	Yes	47.2		16794
	No	52.8		18793
Independent Variables		**Vaccinated (%)**	**Unvaccinated (%)**	**Total (n)**
Age (n = 35367)	18 - 20 years old	64.5	35.5	13860
	21 - 24 years old	45.5	54.5	13322
	25 - 29 years old	26.2	73.8	4545
	30 years or more	14.8	85.2	3640
	Total	47.3	52.7	35367
Sex (n = 35482)	Female	56.1	43.9	26183
	Male	22.2	77.8	9299
	Total	47.2	52.8	35482
Relationship status	Not in a relationship	48.6	51.4	16774

(n = 35490)	In a relationship but not living together	52.9	47.1	12305
	In a relationship living together	32.8	67.2	6411
Marital status (n = 35443)	Single	50.6	49.4	29257
	Married/Partnered	28.2	71.8	4626
	Separated	14.2	85.8	190
	Divorced	19.6	80.4	281
	Other	50.2	49.8	1089
Gender Identity (n = 35495)	Woman	56.2	43.8	25837
	Man	22.0	78.0	9142
	Trans woman	20.0	80.0	25
	Trans man	44.0	56.0	25
	Genderqueer	49.7	50.3	169
	Another identity	56.6	43.4	297
Year in school	1st year undergraduate	56.7	43.3	7819
	2nd year undergraduate	54.0	46.0	7168
	3rd year undergraduate	50.9	49.1	6571
	4th year undergraduate	45.9	54.1	5286

(n = 35399)	5th year or more undergraduate	35.9	64.1	2367
	Graduate or professional	27.7	72.3	5165
	Not seeking a degree	36.6	63.4	374
	Other	32.2	67.8	649
Number of sexual partners in the last 12 months (n = 35587)	None	44.1	55.9	10552
	1	45.5	54.5	16266
	2	55.1	44.9	3081
	3	55.0	45.0	1866
	4 or more	52.5	47.5	3822
Type of sexual partner (s) (n =25653)	Women	44.5	55.5	7481
	Men	48.7	51.3	17508
	Trans women	34.4	65.6	96
	Trans men	35.6	64.4	118
	Genderqueer	42.3	57.7	291
	Other identity	52.8	47.2	159
Nationality (n = 35461)	Canadian	49.5	50.5	32223
	International	24.6	75.4	3238
Engagement in oral sex within the last 30 day	No, have never done this sexual activity	44.4	55.7	9855
	No, have done this sexual activity in the	44.7	55.3	8413

(n=35267)	past but not in the last 30 days			
	Yes	50.3	49.7	16999
Engagement in vaginal intercourse within the last 30 days	No, have never done this sexual activity	45.4	54.6	10476
	No, have done this sexual activity in the past but not in the last 30 days	44.8	55.2	6335
(n=35263)	Yes	49.1	50.9	18452
Engagement in anal intercourse within the last 30 days	No, have never done this sexual activity	48.1	51.9	25422
	No, have done this sexual activity in the past but not in the last 30 days	44.7	55.3	7635
(n=35115)	Yes	46.6	53.4	2058
Use of protective barrier during oral sex within the last 30 days	N/A, never did this sexual activity	44.6	55.4	9991
	Have not done this sexual activity during the last 30 days	44.3	55.7	6440
(n = 35270)	Never	50.0	50.0	16841
	Rarely	47.4	52.6	833

	Sometimes	49.7	50.3	330
	Most of the time	48.5	51.5	233
	Always	45.3	54.7	602
Use of protective barrier during vaginal intercourse within the last 30 day (n = 35264)	N/A, never did this sexual activity	45.6	54.4	10363
	Have not done this sexual activity during the last 30 days	44.2	55.8	5563
	Never	44.3	55.7	6332
	Rarely	52.5	47.5	2065
	Sometimes	50.8	49.2	2163
	Most of the time	52.0	48.0	3132
	Always	50.4	49.6	5646
Use of protective barrier during anal sex within the last 30 days (n = 35101)	N/A, never did this sexual activity	48.3	51.7	24719
	Have not done this sexual activity during the last 30 days	44.2	55.8	5700
	Never	45.4	54.6	2793
	Rarely	50.0	50.0	296
	Sometimes	47.0	53.0	279
	Most of the time	47.3	52.7	332

	Always	42.8	57.2	982
Use of a method of birth control to prevent pregnancy during last vaginal intercourse (n = 34605)	Yes	50.3	49.7	20216
	N/A, have not have vaginal intercourse	47.2	52.8	9415
	No, have not had vaginal intercourse that could result in pregnancy	39.4	60.6	1488
	No, did not want to prevent pregnancy	24.9	75.1	718
	No, did not use any birth control method	41.5	58.5	2768
Had a dental exam and cleaning in the last 12 months? (n = 35118)	Yes	51.6	48.4	26193
	No	33.9	66.1	8925
(Males) Performed a testicular self-exam in the last 30 days (n = 9157)	Yes	27.9	72.1	2651
	No	19.7	80.3	6506
(Females) Performed a breast self-exam in the last 30 days?	Yes	57.1	42.9	7836
	No	55.5	44.5	18082

(n = 25918)				
(Females) Had a routine gynecological exam in the last 12 months (n = 26021)	Yes	51.7	48.3	8371
	No	58.1	41.9	17650
Used sunscreen regularly with sun exposure (n = 35009)	Yes	52.1	47.9	19853
	No	40.9	59.1	15156
Ever been tested for Human Immunodeficiency Virus (HIV) infection (n = 35416)	Yes	48.7	51.3	8808
	No	45.6	54.4	25180
Received vaccination shot(s) – Hepatitis B (n = 32436)	Yes	56.8	43.2	26689
	No	6.8	93.2	5747
Received vaccination shot(s) – Influenza in the last 12 months	Yes	56.6	43.4	11664
	No	41.8	58.2	22996

(n = 34660)				
Received vaccination shot(s) – MMR[4] (n = 31526)	Yes	54.1	45.9	25030
	No	17.7	82.3	6496
Received vaccination shot(s) – Meningitis (n = 28422)	Yes	59.9	40.1	20050
	No	16.4	83.6	8372
Received vaccination shot(s) – Chickenpox (n = 30683)	Yes	59.3	40.7	15948
	No	33.1	66.9	14735
Within the last 12 months, have been diagnosed or treated for Chlamydia (n = 35500)	Yes	54.9	45.1	546
	No	47.1	52.9	34954
Within the last 12 months, have been diagnosed or treated for Genital herpes (n = 35345)	Yes	50.8	49.2	250
	No	47.2	52.8	35095
Within the last 12 months, have been diagnosed or treated for	Yes	42.5	57.5	322
	No	47.2	52.8	35183

Genital warts/Human Papillomavirus (HPV) (n = 35505)				
Within the last 12 months, have been diagnosed or treated for Gonorrhea (n = 35464)	Yes	44.0	56.0	125
	No	47.2	52.8	35339
Within the last 12 months, have been diagnosed or treated for Hepatitis B or C (n = 35464)	Yes	44.1	55.9	93
	No	47.2	52.8	35323
Within the last 12 months, have been diagnosed or treated for UT (n = 35380)	Yes	60.4	39.6	4339
	May	45.4	54.6	31041
Ever been tested for Human Immunodeficiency Virus (HIV) infection (n = 35416)	Yes	48.7	51.3	8808
	No	45.6	54.4	25180

Race/Ethnicity (n = 35587)	Aboriginal	39.3	60.7	1560
	Non-White	49.9	50.1	11724
	White	46.3	53.7	22303

[1]Outcome variable is HPV vaccination status with two levels ["Yes" and "No" (reference)]
[2]Human Papillomavirus
[3]Sexually Transmitted Infections (STIs) consist of chlamydia, genital herpes, genital warts/HPV, gonorrhea or hepatitis B
[4]Measles, Mumps and Rubella

Table 5.2: Univariate Analysis of ACHA-NCHA-II Web Spring 2016 of Canadian Universities

Independent Variables		**HPV[1] vaccination ("Yes" versus "No")**	**P value (α=0.25)**
		Odds (95% CI)	
Age (Ref= "30 years old or older")	18 - 20 years old	10.46 (9.49 - 11.54)	<0.0001
	21 - 24 years old	4.81 (4.37 – 5.31)	
	25 - 29 years old	2.04 (1.83 - 2.28)	
Sex (Ref= "Male")	Female	4.49 (4.26 – 4.75)	<0.0001
Relationship status (Ref= "In a relationship living together")	Not in a relationship	1.93 (1.82 – 2.05)	<0.0001
	In a relationship but not living together	2.30 (2.16 – 2.45)	
Marital status Ref= ("Divorced")	Single	4.20 (3.13 – 5.65)	<0.0001
	Married/Partnered	1.61 (1.19 – 2.18)	
	Separated	0.68 (0.41 – 1.13)	
Gender Identity Ref = ("Man")	Woman	4.54 (4.30 - 4.80)	<0.0001
	Another Identity	2.72 (2.15 - 3.44)	
	Trans Woman	0.89 (0.33 – 2.36)	
	Trans Man	2.78 (1.26 – 6.14)	
	Gender queer	3.50 (2.58 – 4.75)	
Year in school Ref = ("Graduate or professional")	1st year undergraduate	3.43 (3.18 – 3.70)	<0.0001
	2nd year undergraduate	3.07 (2.84 – 3.31)	
	3rd year undergraduate	2.71 (2.51 – 2.93)	
	4th year undergraduate	2.22 (2.04 – 2.40)	
	5th year or more undergraduate	1.47 (1.32 – 1.63)	

Number of sexual partners Within last 12 months (Ref= 4 or more)	None	0.72 (0.66 – 0.77)	<0.0001
	1	0.76 (0.71 – 0.81)	
	2	1.11 (1.01 – 1.22)	
	3	1.11 (0.99 – 1.24)	
Nationality (Ref = "International")	Canadian	3.00 (2.76 – 3.25)	<0.0001
Engagement in oral sex within the last 30 days Reference=Yes	No, have never done this sexual activity	0.78 (0.75 – 0.82)	<0.0001
	No, have done this sexual activity in the past but not in the last 30 days	0.80 (0.76 – 0.84)	
Engagement in vaginal intercourse within the last 30 days Reference=Yes	No, have never done this sexual activity	0.86 (0.82 – 0.91)	<0.0001
	No, have done this sexual activity in the past but not in the last 30 days	0.84 (0.79 – 0.89)	
Engagement in anal intercourse within the last 30 days Reference=Yes	No, have never done this sexual activity	1.06 (0.97 – 1.16)	<0.0001
	No, have done this sexual activity in the past but not in the last 30 days	0.93 (0.84 – 1.02)	
Use of protective barrier during oral sex within the last 30 days (Ref= "Always used protection")	N/A, never did this sexual activity	0.97 (0.82 – 1.15)	<0.0001
	Have not done this sexual activity during the last 30 days	0.96 (0.81 – 1.13)	
	Never	1.20 (1.02 – 1.42)	
	Rarely	1.09 (0.88 – 1.34)	

	Sometimes	1.19 (0.91 – 1.56)	
	Most of the time	1.34 (0.84 – 1.54)	
Use of protective barrier during vaginal intercourse within the last 30 days (Ref= "Always used protection")	N/A, never did this sexual activity	0.83 (0.77 – 0.88)	<0.0001
	Have not done this sexual activity during the last 30 days	0.78 (0.72 – 0.84)	
	Never	0.78 (0.73 – 0.84)	
	Rarely	1.09 (0.98 – 1.20)	
	Sometimes	1.02 (0.92 – 1.12)	
	Most of the time	1.07 (0.98 – 1.16)	
Use of protective barrier during anal sex within the last 30 days (Ref= "Always used protection")	N/A, never did this sexual activity	1.25 (1.10 – 1.43)	<0.0001
	Have not done this sexual activity during the last 30 days	1.06 (0.93 – 1.22)	
	Never	1.11 (0.96 – 1.29)	
	Rarely	1.34 (1.03 – 1.74)	
	Sometimes	1.18 (0.91 – 1.55)	
	Most of the time	1.20 (0.94 – 1.54)	
Use of a method of birth control to prevent pregnancy during last vaginal intercourse (Ref= "No, did not use any birth control method")	Yes	1.42 (1.32 – 1.55)	<0.0001
	N/A, have not have vaginal intercourse	1.26 (1.16 – 1.37)	
	No, have not had vaginal intercourse that could result in pregnancy	0.92 (0.81 – 1.04)	
	No, did not want to prevent pregnancy	0.47 (0.39 – 0.56)	

Had a dental exam and cleaning in the last 12 months Ref = (“Yes”)	No	0.48 (0.46-0.51)	<0.0001
(Males) Performed a testicular self-exam in the last 30 day Ref = (“Yes”)	No	0.63 (0.57-0.72)	<0.0001
(Females) Performed a breast self-exam in the last 30 day Ref = (“Yes”)	No	0.94 (0.89-0.99)	<0.0001
(Females) Had a routine gynecological exam in the last 12 months Ref = (“Yes”)	No	1.30 (1.23-1.37)	<0.0001
Used sunscreen regularly with sun exposure Ref = (“Yes”)	No	0.64 (0.61-0.67)	<0.0001
Ever been tested for Human	No	0.89 (0.93)	<0.0001

Immunodeficiency Virus (HIV) infection Ref = (“Yes”)			
Received vaccination shot(s) – Hepatitis B Ref = (“Yes”)	No	0.06 (0.05 – 0.06)	<0.0001
Received vaccination shot(s) – Influenza Ref = (“Yes”)	No	0.55 (0.53 – 0.58)	<0.0001
Received vaccination shot(s) – MMR Ref = (“Yes”)	No	0.18 (0.17 - 0.19)	<0.0001
Received vaccination shot(s) – Meningitis Ref = (“Yes”)	No	0.13 (0.12 – 0.14)	<0.0001
Received vaccination shot(s) – Chicken pox Ref = (“Yes”)	No	0.34 (0.32 – 0.36)	<0.0001
Race/Ethnicity Ref= “White”	Aboriginal	0.75 (0.68 – 0.83)	0.465
	Others (nonAbo/nonWhite)	1.15 (1.10 – 1.21)	

[1]Human Papillomavirus
[2] Measles, Mumps and Rubella
*** The outcome variable is HPV vaccination status with two levels [“Yes” and “No" (reference)]**

Appendix E

Additional Files from Chapter 6

Table 6.1: Descriptive Characteristics for HPV[1] Vaccination CNICS[2] 2011					
Overall HPV[1] Vaccination Status →	**Vaccinated n (percentage)**	**Unvaccinated n (percentage)**		**Total N (percentage)**	
	434454 (41.1%)	621872 (58.9%)		1056326 (100%)	
Variables Categories ↓		**HPV Coverage (Under Variable Categories) ↓**			
		Yes n (%)	**No n (%)**	**Total (%)**	**Missing/ Comment**
Age of Child AGEGROUP Pearson Chi-square <0.0001 N=1056326	10 to 14 years	402800 44.2	507928 55.8	910728 100	
	15 - 17 years	31654 21.7	113944 78.3	145598 100	
AGE_PMK Pearson Chi-square <0.0001 N=1056326	15 to 39 years (Younger)15 to 38 years	121404 46.8	138152 53.2	259556 100	
	40 to 54 years (Middle)39 to 48 years	302970 39.2	469217 60.8	772187 100	
	55 years and older	10080	14503	24583	

		41.0	59.0	100	
Highest Education PMK[4] Pearson Chi-square <0.0001 EHGI_Q01 N=1041461 Missing = 14865	Less than high school diploma or its equivalent	16573 25.6	48195 74.4	64768 100	Missing= 14865 "Don't know " "Refusal" "Not stated"
	High school diploma or a high school equivalency certificate	110004 43.4	143546 56.6	253550 100	
	Trade certificate or diploma	10709 29.1	26048 70.9	36757 100	
	College/CEGEP/other non-university certificate or diploma	113386 35.8	203526 64.2	316912 100	
	University certificate or diploma below the bachelor's level	31115 57.9	22639 42.1	53754 100	
	Bachelor's degree (e.g. B.A., B.Sc., LL.B.)	102468 46.4	118601 53.6	221069 100	
	University certificate, diploma, degree above the BA level	40041 42.3	54610 57.7	94651 100	
Birthplace of Child IMC_D01 Pearson Chi-square <0.0001	Born outside Canada	44667 35.9	799112 64.1	124579 100	
	Born in Canada	389788 41.8	541959 58.2	931747 100	

N=1056326					
Birthplace of PMK IMP_D01 Pearson Chi-square <0.0001 N= 1056326	Born outside Canada	101419 31.5	220531 68.5	321950 100	
	Born in Canada	333036 45.3	401340 54.7	734376 100	
Province PROV_Grouped Pearson Chi-square <0.0001 N=1056326	Other	191092 49.0	198547 51.0	389639 100	
	Quebec	140934 59.7	95011 40.3	235945 100	
	Ontario	102429 23.8	328313 76.2	430742 100	
Accessed HCP[3] MOI_01 Pearson Chi-square <0.0001 N=975144 Missing = 81182	Yes	297741 42.1	409208 57.9	706949 100	Missing = 81182 “Don’t know “ “Not stated”
	No	119808 44.7	148387 55.3	268195 100	
HCP discussed Immunization MOI_02	Yes	56423 35.7	101792 64.3	158215 100	Missing = 360173 “Don’t know “ “Not stated”
	No	238831	299107	537938	

Pearson Chi-square <0.0001 N=696153 Missing = 360173		44.4	55.6	100	
Have Sufficient Information on Immunization KN5_39 Pearson Chi-square <0.0001 N=1042893 Missing = 13433	Yes	366671 43.3	480424 56.7	847095 100	Missing = 13433 "Don't know " "Not stated"
	No	58276 29.8	137522 70.2	195798 100	
Concerned about side effect of vaccines KN2_14 Pearson Chi-square <0.0001 N=1037995 Missing = 18331	Strongly agree	149971 38.7	237617 61.3	387588 100	Missing =18331 "Refusal" "Not stated"
	Somewhat agree	155595 39.4	239149 60.6	394744 100	
	Somewhat disagree	84570 55.2	68741 44.8	153311 100	
	Strongly disagree	430645 39.6	607350 60.4	102352 100	
	Strongly agree	59382	74125	133507	

Vaccine Cause Diseases KN2_15 Pearson Chi-square <0.0001 N=959673 Missing = 96653		44.5	55.5	100	Missing = 96653 "Refusal" "Not stated"
	Somewhat agree	97995 35.6	177280 64.4	275275 100	
	Somewhat disagree	137646 50.1	137274 49.9	274920 100	
	Strongly disagree	106042 38.4	169929 61.6	275971 100	
Importance of other vaccines (Varicella) KN3_17 Pearson Chi-square <0.0001 N=1033086 Missing = 23240	Very important	194839 48.7	205400 51.3	400239 100	Missing = 23240 "Don't know " "Not stated
	Important	89956 37.9	147348 62.1	237304 100	
	Somewhat important	96857 46.7	110476 53.3	207333 100	
	Not important at all	45220 24.0	142990 76.0	188210 100	
Importance of other vaccines (Influenza) KN3_21 Pearson Chi-square <0.0001 N=1039142	Very important	97039 54.8	80039 45.2	177078 100	Missing = 17184 "Don't know " "Not stated"
	Important	85534 42.1	117573 57.9	203107 100	
	Somewhat important	166750 43.5	216219 56.5	382969 100	

Missing = 17184	Not important at all	81321 29.5	194667 70.5	275988 100	
Importance of other vaccines (Pneumococcal disease) KN3_24 Pearson Chi-square <0.0001 N=1024970 Missing = 31356	Very important	197770 43.5	256408 56.5	454178	Missing = 31356 "Don't know " "Not stated"
	Important	139312 43.5	180847 56.5	320161	
	Somewhat important	75333 42.0	104208 58.0	179541	
	Not important at all	13282 18.7	57808 81.3	71090	
Total Household Income THI_01 Pearson Chi-square <0.0001 N=1056326	$0 to $46000	118487 42.3	16163 57.7	280119	
	$46001 to $92000	171901 39.3	265631 60.7	437532	
	$92001 to $143000	92471 44.7	114347 55.3	206818	
	$143001 to $202900	27943 31.1	61939 68.9	89882	
	$202901 to $1500000	23652 56.3	18323 43.7	41975	

[1]Human Papillomavirus
[2]Childhood National Immunization Coverage Survey
[3]Health Care Provider
[4]Parent/Guardian of Child

Table 6.2: Descriptive Characteristics for HPV[1] Vaccination CNICS[2] 2013

Overall HPV[1] Vaccination Status→	**Vaccinated n (percentage)**	**Unvaccinated n (percentage)**	**Total N (%)**
	508642 (68.6%)	232301 (31.4%)	740943 (100%)

Variable Categories ↓		**HPV Coverage (Under Variable Categories) ↓**			
		Yes n (%)	**No n (%)**	**Total (%)**	**Missing/Comment**
Age of Child AGE_Grouped	12 to 14 years	373560 69.2	166645 30.8	540205 100	
	17 years	135082 67.3	65656 32.7	200738 100	
Pearson Chi-square < 0.0001					
N=740943					
AGE_PMK	15 to 39-year-old (Younger)	126953 68.8	57537 31.2	184490 100	
Pearson Chi-square < 0.0001	40 to 54-year-old (Middle)	363239 68.4	167813 31.6	531052 100	
N=740943	55 years and older (Older)	18450 72.6	6951 27.4	25401 100	

Highest Education PMK[4] EHGI_Q01 Pearson Chi-square < 0.0001 N=724587 Missing = 16356	Less than high school diploma or its equivalent	26645 66.8	13262 33.2	39907 100	Missing = 16356 "Don't know" "Refusal" "Not stated"
	High school diploma or a high school equivalency certificate	121567 68.9	54813 31.1	176380 100	
	Trade certificate or diploma	22275 71.4	8914 28.6	31189 100	
	College/CEGEP/other non-university certificate or diploma	161603 68.9	73052 31.1	234655 100	
	University certificate or diploma below the bachelor's level	25901 74.6	8822 25.4	34723 100	
	Bachelor's degree (e.g. B.A., B.Sc., LL.B.)	104547 66.6	52392 33.4	156939 100	

	University certificate, diploma, degree above the BA level	35976 70.8	14818 29.2	50794 100	
Birthplace of Child IMCD01 Pearson Chi-square < 0.0001 N=740943	Born outside Canada	63263 62.8	37466 37.2	100729 100	
	Born in Canada	445379 69.6	194835 30.4	640214 100	
Birthplace of PMK IMPD01 Pearson Chi-square < 0.0001 N= 729675 Missing = 11268	Born outside Canada	129382 61.5	81070 38.5	210452 100	Missing = 11268 "Not stated"
	Born in Canada	373160 71.9	146063 28.1	519223 100	
Province PROV	Newfoundland and Labrador	9269 87.0	1385 13.0	10654 100	

Pearson Chi-square < 0.0001 N=740943	Prince Edward Island	2813 80.6	675 19.4	3488 100	
	Nova Scotia	15161 78.7	4098 21.3	19259 100	
	New Brunswick	12272 79.9	3088 20.1	15360 100	
	Quebec	128311 81.4	3088 18.6	157683 100	
	Ontario	185512 61.4	116806 38.6	302318 100	
	Manitoba	16506 57.8	12034 42.2	28540 100	
	Saskatchewan	15970 67.1	7843 32.9	23813 100	
	Alberta	60434 70.0	25859 30.0	86293 100	
	British Columbia	60612 67.1	29685 32.9	90297 100	
	Yukon	500 61.8	309 38.2	809 100	
	Northwest Territories	687	491	1178	

		58.3	41.7	100	
	Nunavut	595 47.6	656 52.4	1251 100	
Province PROV Pearson Chi-square < 0.0001 N=740943	Other	194819 69.34	86123 30.66	280942 100	
	Quebec	128311 81.4	29372 18.6	157683 100	
	Ontario	185512 61.4	116806 38.6	302318 100	
Accessed HCP[3] MOI_01 Pearson Chi-square < 0.0001 N=728266 Missing = 12677	Yes	373981 70.2	158794 29.8	532775 100	Missing = 12677 “Don’t know” “Refusal” “Not stated”
	No	130950 67.0	64541 33.0	195491 100	
HCP discussed Immunization MOI_02	Yes	81039 66.3	41104 33.7	122143 100	Missing = 212557
	No	290391	115852	406243	“Don’t know”

Pearson Chi-square < 0.0001 N=528386 Missing = 212557		71.5	28.5	100	"Refusal" "Not stated"
Have Sufficient Information on Immunization KN5_39 Pearson Chi-square < 0.0001 N=727391 Missing = 13552	Yes	397882 69.3	176107 30.7	573989 100	Missing = 13552 "Don't know" "Refusal" "Not stated"
	No	103089 67.2	50313 32.8	153402 100	
Main reason not sufficient information	Did not know where to get information	5119 65.0	2752 35.0	7871 100	Missing = 573989 "Valid skip"
	Appointments were rushed	2000	1769	3769	

KN5_40 Pearson Chi-square < 0.0001 N=166954 Missing = 573989		53.1	46.9	100	
	Felt uncomfortable asking questions	2950 74.0	1037 26.0	3987 100	
	Did not take the time to review the information	14505 71.4	5815 28.6	20320 100	
	Did not understand the information provided	3435 48.3	3670 51.7	7105 100	
	Language difficulty	3372 86.9	510 13.1	3882 100	
	Other	41064 64.2	22918 35.8	63982 100	
	Don’t know	1542 89.8	175 10.2	1717 100	
	Not stated	7671 56.6	5881 43.4	13552 100	
	Did not receive any/enough	29103 71.4	11666 28.6	40769 100	

	information from provider				
Childhood vaccines are safe KN2_10 Pearson Chi-square < 0.0001 N=723743 Missing = 17200	Strongly agree	311859 72.0	121044 28.0	432903 100	Missing = 17200 "Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat agree	173918 68.0	81694 32.0	255612 100	
	Somewhat disagree	13426 50.1	13355 49.9	26781 100	
	Strongly disagree	3856 45.6	4591 54.4	8447 100	
Childhood vaccines are effective KN2_11 Pearson Chi-square < 0.0001 N=722347 Missing = 18596	Strongly agree	348862 71.4	140023 28.6	488885 100	Missing = 18596 "Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat agree	143612 67.3	69633 32.7	213245 100	
	Somewhat disagree	6324 41.6	8877 58.4	15201 100	
	Strongly disagree	2512 50.1	2504 49.9	5016 100	
	Strongly agree	384662	149572	534234	Missing = 14808

Childhood vaccines important for child's health KN2_12 Pearson Chi-square < 0.0001 N=726135 Missing = 14808		72.0	28.0	100	
	Somewhat agree	108303 64.5	59510 35.5	167813 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat disagree	8383 47.0	9461 53.0	17844 100	
	Strongly disagree	2213 35.4	4031 64.6	6244 100	
Understand how vaccines work KN2_13 Pearson Chi-square < 0.0001 N=726263 Missing = 14680	Strongly agree	323877 68.6	148336 31.4	472213 100	Missing = 14680
	Somewhat agree	161595 71.3	65030 28.7	226625 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat disagree	4354 64.9	7251 35.1	20664 100	
	Strongly disagree	4354 64.4	2407 35.6	6761 100	
	Strongly agree	153686 62.1	93768 37.9	247454 100	Missing = 18660

Concerned about side effect of vaccines KN2_14 Pearson Chi-square < 0.0001 N=722283 Missing = 18660	Somewhat agree	190191 70.6	79204 29.4	269395 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat disagree	81438 75.4	26549 24.6	107987 100	
	Strongly disagree	76129 78.1	213118 21.9	97447 100	
Vaccine Cause Diseases KN2_15 Pearson Chi-square < 0.0001 N=673602 Missing = 67341	Strongly agree	52741 59.5	35954 40.5	88695 100	Missing = 67341 "Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat agree	128311 67.4	61998 32.6	190309 100	
	Somewhat disagree	139808 69.8	60398 30.2	200206 100	
	Strongly disagree	148071 76.2	46321 23.8	194392 100	
Alternative practices	Strongly agree	19341 56.0	15172 44.0	34513 100	Missing = 77379

eliminate need for vaccine KN2_16 Pearson Chi-square < 0.0001 N=663564 Missing = 77379	Somewhat agree	52243 59.2	35999 40.8	88242 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat disagree	127320 69.3	56463 30.7	183783 100	
	Strongly disagree	260893 73.1	96133 26.9	357026 100	
Importance of other vaccines (Varicella) KN3_17 Pearson Chi-square < 0.0001 N=722109 Missing = 18834	Very important	233357 73.1	85683 26.9	319040 100	Missing = 18834 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	116537 71.7	46050 28.3	162587 100	
	Somewhat important	94963 68.0	44689 32.0	139652 100	
	Not important at all	56393 55.9	44437 44.1	100830 100	
	Very important	351089	134807	485896	Missing = 22296

Importance of other vaccines (Diphtheria) KN3_18 Pearson Chi-square < 0.0001 N=718647 Missing = 22296		72.3	27.7	100	
	Important	121539 67.5	58461 32.5	180000 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat important	21618 52.8	19363 47.3	40981 100	
	Not important at all	5629 47.8	6141 52.2	11770 100	
Importance of other vaccines (Rubella) KN3_19 Pearson Chi-square < 0.0001 N=721872 Missing = 19071	Very important	347087 72.5	131526 27.5	478613 100	Missing = 19071
	Important	122861 67.0	60473 33.0	183334 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat important	25487 53.4	22212 46.6	47699 100	
	Not important at all	5671 46.4	6555 53.6	12226 100	
	Very important	365970	135108	501078	Missing = 19804

Importance of other vaccines (Hepatitis B) KN3_20 Pearson Chi-square < 0.0001 N=721139 Missing = 19804		73.0	27.0	100	
	Important	108121 66.6	54250 33.4	162371 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat important	22753 48.9	23783 51.1	46536 100	
	Not important at all	4254 38.1	6900 61.9	11154 100	
Importance of other vaccines (Influenza) KN3_21 Pearson Chi-square < 0.0001 N=721166 Missing = 19777	Very important	96954 73.8	34451 26.2	131405 100	Missing = 19777
	Important	94844 73.3	34542 26.7	129386 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat important	191127 73.9	67408 26.1	258535 100	
	Not important at all	117212 58.1	84628 41.9	201840 100	
Importance of other vaccines (Measles)	Very important	308699 72.9	114531 27.1	423230 100	Missing = 18293
	Important	140459	67354	207813	"Valid skip"

KN3_22 Pearson Chi-square < 0.0001 N=722650 Missing = 18293		67.6	32.4	100	"Don't know" "Refusal" "Not stated"
	Somewhat important	42851 61.0	27371 39.0	70222 100	
	Not important at all	9907 46.3	11478 53.7	21385 100	
Importance of other vaccines (Mumps) KN3_23 Pearson Chi-square < 0.0001 N=721171 Missing = 19772	Very important	72.53	27.47	410239 100	Missing = 19772 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	67.45	32.55	209870 100	
	Somewhat important	64.54	35.46	78712 100	
	Not important at all	48.30	52.70	22350 100	
Importance of other vaccines (Pneumococcal disease) KN3_24	Very important	245827 73.8	87478 26.2	333305 100	Missing = 28855 "Valid skip" "Don't know" "Refusal"
	Important	137079 71.0	55949 29.0	193028 100	
	Somewhat important	81839	48841	130680	

Pearson Chi-square < 0.0001 N=712088 Missing = 28855		62.6	37.4	100	"Not stated"
	Not important at all	29804 54.1	25271 45.9	55075 100	
Importance of other vaccines (Polio) KN3_25 Pearson Chi-square < 0.0001 N=719916 Missing = 21027	Very important	363881 72.3	139068 27.7	502949 100	Missing = 21027 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	114991 66.6	57690 33.4	172681 100	
	Somewhat important	15878 49.6	16133 50.4	32011 100	
	Not important at all	5262 42.9	7013 57.1	12275 100	
Importance of other vaccines (Meningitis)	Very important	369321 73.2	135310 26.8	504631 100	Missing = 19326
	Important	109144	57551	166695	"Valid skip"

KN3_26 Pearson Chi-square < 0.0001 N= 721617 Missing = 19326		65.5	34.5	100	"Don't know" "Refusal" "Not stated"
	Somewhat important	18514 49.0	19250 51.0	37764 100	
	Not important at all	3969 31.7	8558 68.3	12527 100	
Importance of other vaccines (Tetanus) KN3_27 Pearson Chi-square < 0.0001 N=719985 Missing = 20958	Very important	330046 72.2	127030 27.8	457076 100	Missing = 20958 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	129317 66.4	65565 33.6	194882 100	
	Somewhat important	34114 62.2	20698 37.8	54812 100	
	Not important at all	6733 50.9	6482 49.1	13215 100	
	Very important	297605 73.7	106325 26.3	403930 100	Missing = 223

Importance of other vaccines (Pertussis) KN3_28					"Valid skip" "Don't know" "Refusal" "Not stated"
Pearson Chi-square < 0.0001 N=721482	Important	141721 67.0	69880 33.0	211601 100	
	Somewhat important	50418 60.2	33284 39.8	83702 100	
	Not important at all	10762 47.5	11905 52.5	22667 100	
Total Household Income THI_01 Pearson Chi-square < 0.0001 N = 740943	$0 to $46000	144220 67.7	68665 32.3	212885 100	
	$46001 to $92000	174309 67.7	83306 32.3	257615 100	
	$92001 to $143000	108005 70.4	45460 29.6	153465 100	
	$143001 to $202900	61608 71.1	25079 28.9	86687 100	
	$202901 to $1500000	20465 68.5	9408 31.5	29873 100	

[1]Human Papillomavirus
[2]Childhood National Immunization Coverage Survey
[3]Health Care Provider
[4]Parent/Guardian of Child

Table 6.3: Descriptive Characteristics for HPV[1] Vaccination CNICS[2] 2015

Overall HPV[1] Vaccination Status →	**Vaccinated n (percentage)**	**Unvaccinated n (percentage)**		**Total N (percentage)**	
	391988 (73.7%)	139792 (26.3%)		531780 (100%)	
Variables Categories ↓		**HPV Coverage (Under Variable Categories) ↓**			
		Yes n (%)	**No n (%)**	**Total %**	**Missing/ Comment**
Age of Child AGEGROUP Pearson Chi-square < 0.0001 N=531780	13 to 14 years	265145 74.6	90225 25.4	355370 100	
	17 years	126843 71.9	49567 28.1	176410 100	
AGE_PMK Pearson Chi-square < 0.0001 N=531780	15 to 39 years (Younger)	75475 69.2	33555 30.8	109030 100	
	40 to 54 years (Middle)	296083 75.4	96849 24.6	392932 100	
	55 years and older	20430 68.5	9388 31.5	29818 100	
Relationship of the PMK to the child	Related as birth parent	384692 74.1	134809 25.9	519501 100	

PMK_09 Pearson Chi-square < 0.0001 N= 531780	Related but not as birth parent	7094 57.8	5185 42.2	12279 100	
Highest Education PMK[4] EHGI_Q01 Pearson Chi-square < 0.0001 N=518124 Missing = 13656	Less than high school diploma or its equivalent	15811 68.5	7281 31.5	23092 100	Missing =13656 "Don't know" "Refusal" "Not stated"
	High school diploma or a high school equivalency certificate	101418 74.7	34325 25.3	135743 100	
	Trade certificate or diploma	14189 67.6	6798 32.4	20987 100	
	College/CEGEP/other non-university certificate or diploma	110092 77.7	31523 22.3	141615 100	
	University certificate or diploma below the bachelor's level	21774 76.6	6650 23.4	28424 100	
	Bachelor's degree (e.g. B.A., B.Sc., LL.B.)	82644 71.7	32605 28.3	115249	

	University certificate, diploma, degree above the BA level	38079 71.8	14935 28.2	53014 100	
Birthplace of Child IMCD01 N=523579 Missing = 8201	Born outside Canada	341020 75.1	112907 24.9	453927 100	Missing = 8201 "Not stated"
	Born in Canada	46832 67.2	22820 32.8	453927 100	
Birthplace of PMK IMPD01 Pearson Chi-square < 0.0001 N= 523579 Missing = 8201	Born outside Canada	111360 70.2	47368 29.8	158728 100	Missing = 8201 "Not stated"
	Born in Canada	276491 75.8	88360 24.2	364851 100	
Province PROV Pearson Chi-square < 0.0001 N=531780	Other	154828 73.8	54869 26.2	209697 100	
	Quebec	90584 85.2	15713 14.8	106297 100	
	Ontario	146576 67.9	69210 32.1	215786 100	

Accessed HCP[3] MOI_01 Pearson Chi-square < 0.0001 N=523376 Missing = 8404	Yes	297303 75.7	95248 24.3	392551 100	Missing = 8404 "Valid skip" "Don't know" "Not stated"
	No	92170 70.5	38655 29.5	13082 100	
HCP discussed Immunization MOI_02 Pearson Chi-square < 0.0001 N=384794 Missing = 146986	Yes	76899 77.3	22572 22.7	99471 100	Missing = 146986 "Valid skip" "Don't know" "Not stated"
	No	215833 75.6	69490 24.4	285323 100	
Have Sufficient Information on Immunization KN5_39 Pearson Chi-square < 0.0001 N=520325 Missing = 11455	Yes	308860 75.5	100240 24.5	409100 100	Missing = 11455 "Don't know" "Not stated"
	No	75738 68.1	35487 31.9	111225 100	
	Strongly agree	97011	47721	144732	Missing

Concerned about side effect of vaccines KN2_14 Pearson Chi-square < 0.0001 N=516294 Missing = 15486		67.0	33.0	100	= 15486 "Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat agree	148572 73.5	53444 26.5	202016 100	
	Somewhat disagree	81984 80.2	20282 19.8	102266 100	
	Strongly disagree	54936 81.7	12344 18.3	67280 100	
Vaccine Cause Diseases KN2_15 Pearson Chi-square < 0.0001 N=481036 Missing = 50744	Strongly agree	40220 72.6	15146 27.4	55366 100	Missing = 50744 "Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat agree	87205 69.1	39086 30.9	126291 100	
	Somewhat disagree	118312 79.6	30245 20.4	148557 100	
	Strongly disagree	113219 75.1	37603 24.9	150822 100	
Alternative practices eliminate need for vaccine KN2_16 Pearson Chi-square < 0.0001	Strongly agree	15819 65.3	8420 34.7	24239 100	Missing = 64500 "Valid skip" "Don't know" "Refusal"
	Somewhat agree	32755 63.9	18471 36.1	51226 100	
	Somewhat disagree	81095 74.5	27730 25.5	108825 100	

N=467280 Missing = 64500	Strongly disagree	218094 77.1	64896 22.9	282990 100	"Not stated"
Importance of other vaccines (Varicella) KN3_17 Pearson Chi-square < 0.0001 N=519581 Missing = 12199	Very important	177019 80.7	42460 19.3	219479 100	Missing = 12199 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	109925 75.1	36448 24.9	146373 100	
	Somewhat important	66277 74.1	23146 25.9	89423 100	
	Not important at all	32312 50.2	31994 49.8	64306 100	
Importance of other vaccines (Influenza) KN3_21 Pearson Chi-square < 0.0001 N=520446 Missing = 11334	Very important	58146 76.8	17613 23.2	75759 100	Missing = 11334 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	89921 82.0	19781 18.0	109702 100	
	Somewhat important	153947 83.0	31634 17.0	185581 100	
	Not important at all	84561 56.6	64843 43.4	149404 100	
Importance of other vaccines (Mumps)	Very important	242412 77.3	71258 22.7	313670 100	Missing = 7723

KN3_23 Pearson Chi-square < 0.0001 N=524057 Missing = 7723	Important	121210 75.1	40206 24.9	161416 100	"Valid skip" "Don't know" "Refusal" "Not stated"
	Somewhat important	18829 56.6	14451 43.4	33280 100	
	Not important at all	6016 38.3	9675 61.7	15691 100	
Importance of other vaccines (Pneumococcal disease) KN3_24 Pearson Chi-square < 0.0001 N=505159 Missing = 26621	Very important	201300 80.3	49468 19.7	250768 100	Missing = 26621 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	105115 72.2	40443 27.8	145558 100	
	Somewhat important	59497 73.5	21419 26.5	80916 100	
	Not important at all	10669 38.2	17248 61.8	27917 100	
Importance of other vaccines (Pertussis) KN3_28 Pearson Chi-square < 0.0001 N=516029 Missing = 15751	Very important	224327 75.4	73343 24.6	297670 100	Missing = 15751 "Valid skip" "Don't know" "Refusal" "Not stated"
	Important	121062 75.0	40308 25.0	161370 100	
	Somewhat important	32209 78.9	8606 21.1	40815 100	

	Not important at all	6123 37.9	10051 62.1	16174 100	

[1]Human Papillomavirus
[2]Childhood National Immunization Coverage Survey
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