# EVALUATING SOCIETAL PREFERENCES FOR THE HUMAN PAPILLOMAVIRUS VACCINES USING A DISCRETE CHOICE EXPERIMENT

by

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## ABSTRACT

**Objectives:** The objectives of this thesis were to i) evaluate societal preferences for the Human Papillomavirus vaccines using a discrete choice experiment (DCE), ii) determine societal willingness to pay (WTP) for an additional protection for genital warts, iii) identify subgroups with different preferences and iv) determine the trade-offs between benefits and perceived risks.

**Methods:** Participants from across Canada were recruited for the study with a sample representative of the Canadian population. They completed a choice-based questionnaire which required them to choose between different combinations of attribute levels. The attributes were: (1) lifetime risk of cervical cancer (CC) and genital warts (GW); (2) frequency of Pap smear testing; (3) need for vaccine booster; (4) target group to vaccinate (girls only or girls and boys); (4) frequency of side effects and (5) cost of the vaccine. A mixed effect logistic model was used to analyze the data.

**Results**: The 1157 participants included in the analysis had a mean age of 44 years (SD=15), and 49% of them were females. About 79% had high school/trade school education, and 61% earned more than $55,000/year. About 46% of participants had children. Respondents had a strong relative preference to avoid a yearly Pap smear testing and the most preferred frequency was every 3 years. They preferred a vaccine that would give lifelong immunity, that is, there was a preference for not receiving the vaccine booster dose. Respondents were more likely to choose a vaccination and screening strategy that targeted both boys and girls rather than girls alone. On average, respondents had a WTP of 303 to administer the vaccine to both girls and boys and a mean WTP of $53 and $21 to avoid a 1% increase risk of cervical cancer and genital warts, respectively. To avoid a 1% risk of cervical cancer, respondents were willing to accept a 2.43% increase in the risk of genital warts

**Conclusions:** Society agrees with the introduction of the HPV vaccination program, but would prefer a vaccination strategy which targets both boys and girls and among the two HPV vaccines, Gardasil® was preferred because of its ability to prevent genital wart infection.

## TABLE OF CONTENTS

## LIST OF TABLES

## LIST OF FIGURES

## NOMENCLATURE

| | |
|---|---|
| HPV: | Human Papillomavirus |
| DCE: | Discrete Choice Experiment |
| CIN: | Cervical Intraepithelial Neoplasia |
| CDC: | Centre for Disease Control |
| BC: | British Columbia |
| HIV: | Human Immunodeficiency Virus |
| IARC: | International Agency for Research Cancer |
| OR: | Odds Ratio |
| Pap: | Papanicolou |
| CCSP: | Cervical Cancer Screening Program |
| VLP: | Virus-Like Particles |
| HBM: | Health Belief Model |
| CI: | Confidence Interval |
| PV: | Perceived Vulnerability |
| PS: | Perceived Severity |
| PBe | Perceived Benefit |
| PBa: | Perceived Barrier |
| CA: | Cues to Action |
| QALY: | Quality-Adjusted Life Years |
| WTP: | Willingness-To-Pay |
| RUT: | Random Utility Theory |
| IIA: | Independent Irrelevant Alternative |
| SD: | Standard Deviation |
| MXL: | Mixed Effect Logistic Model |
| LRT: | Likelihood Ratio Test |
| CLM: | Conditional Logistic Model |
| CC: | Cervical Cancer |
| GW: | Genital Warts |
| MeSH: | Medical Search Term |

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## CO-AUTHORSHIP STATEMENT

The work presented in this thesis was conducted and disseminated by the Master's candidate. The co-authors of the manuscript that comprise part of this thesis made contributions only as is commensurate with a thesis committee or as experts in a specific area as it pertains to the work. The co-authors provided direction and support. The co-authors reviewed the manuscript prior to submission for publication and offered critical evaluations; however, the candidate was responsible for the writing and the final content of the manuscript.

# CHAPTER 1

# INTRODUCTION

## 1.1 Epidemiology of Human Papillomavirus in Women

The Human Papilloma Virus (HPV) is a small non-enveloped double stranded DNA virus.[1] The virus is extremely diverse, consisting of over 100 different HPV subtypes, and infection with it is associated with cancer, genital warts and respiratory papillomas. There are two major phylogenetic branches differing in affinity for site of infection: the cutaneous (keratinized squamous epithelium), and the mucosal (non-keratinized squamous epithelium).[2] Of the 100 HPV subtypes, approximately 40 have an affinity for mucosal cells and infect the genital tract.[3] Mucosal-HPV is categorized as either high risk oncogenic (types 6, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58), or as low risk non- oncogenic (types 6, 11, 42, 43, 44).[4] Worldwide, the high risk HPV subtypes 16 and 18 are responsible for about 70% of all cervical cancers, high and low grade cervical abnormalities, and anogenital cancer, whilst subtypes 6 and 11 are responsible for low grade cervical abnormalities, recurrent respiratory papillomas and genital warts.[3]

The risk of acquiring HPV infection if sexually active is 75% in one's lifetime (i.e., 3 out 4 persons will acquire HPV).[3] Although HPV is a very common infection, most infected individuals clear the virus without ever developing clinically recognizable signs. Consequently, very few infected individuals progress to invasive cervical cancer.[5] As shown in Figure 1, an initial HPV infection can progress either to persistent infection or to intraepithelial neoplasia 1 (CIN1; abnormal cell growth). CIN 1 can result in persistent infection, which can progress to a more advanced CIN stage (2/3) and then to cervical cancer if not detected and treated early. It takes about 20 years for an initial HPV infection to develop into invasive cervical cancer.[6] HPV infection is the most commonly diagnosed sexually transmitted disease, and is highly prevalent in the younger population with a prevalence rate of approximately 30% in sexually active adolescent girls and young women.[7] In addition, a meta-analysis conducted by de Sanjose estimated a global prevalence of HPV infection among women with normal cytology as 10.41% (95% confidence interval, CI: 10.2–10.7%), with considerable variation by region.[8] The highest prevalence of oncogenic HPV types occurs within the age group 20-24 years, and the lowest within the age group 40-44 years.[9] The burden of infection with oncogenic HPV types is higher relative to other sexually transmitted infections.[10]

## 1.2 HPV Infection Prevention

The prevention strategies for HPV infection are categorized into primary, secondary and tertiary, as shown in figure 2. Primary prevention is aimed at reducing the risk of infection and the burden of disease, but cytological screening, a secondary prevention strategy, has played an important role in decreasing the incidence and mortality rates for cervical cancer. HPV vaccines, which serve, as a primary prevention strategy, aim at building immunity against the serotypes present in the vaccine before sexual debut.

Pap cytology screening is a widely used secondary prevention strategy for cervical cancer. Recently, recommendations for the use of HPV-DNA testing have been made.[26] The HPV-DNA test is more sensitive in identifying abnormal cancer cells, and its results are more easily reproducible than cytological screening.[26] Tertiary prevention strategy is administered after invasive cancer treatment. The strategy is either cancer-stage specific, or prognostically tailored. Although there has been much progress in the latter phase, tertiary prevention, a combination of vaccination and screening prevention strategies form the basis for further reduction in the incidence of, and mortality from, cervical cancer.[15] Other precautionary measures associated with prevention are abstinence, reducing the number of sexual partners, HPV education, using appropriate method(s) of contraception and sexually transmitted infection prevention measures.[9]

## 1.3 Epidemiology of Cervical Cancer in Women

Data from the United States Centre for Disease Control (CDC) shows that 99% of all cervical cancer cases are caused by the HPV.[11] Cervical cancer is the second most common cancer in women worldwide.[12] Every year, approximately 500,000 women are diagnosed with cervical cancer, and approximately 300,000 die from the disease globally.[12,13] According to the World Health Organization, approximately 80% of women affected with cervical cancer are from developing countries; 13% of these are from Africa, 15% from Latin America and 48% from Asia.[14] Generally, there is a correlation between incidence and mortality across all regions, but some areas, such as Africa, have a disproportionately higher mortality.[14] Incidence and mortality rates in North America are relatively low. In Canada, the estimated age-standardized incidence of cervical cancer is about 7.0 per 100,000, and the mortality rate is the lowest among

all developed regions (2.0 per 100,000).[15] However, cervical cancer is a leading cause of cancer in women between 20-44 years of age, and is the 12th most common cause of cancer in females in the country.[16] The Canadian provinces with the highest incidence rates of cervical cancer are Nova Scotia, Newfoundland and Prince Edward Island, and the lowest incidence rates are observed in Quebec and BC.[15] Cervical cancer is highly prevalent among North American Blacks and Aboriginals. Among the Canadian Inuit, cervical cancer accounts for nearly 15% of all cancers among women, and in registered Indians in Saskatchewan, it accounts for 29% of all cancers, a proportion which is six times higher than the nation age-standardized average.[15,17] Immigrants are also at high risk of getting cervical cancer because of the low rate of Pap smear testing, which might be due to language difficulties and lack of knowledge.[17]

### *1.3.1 Cervical Cancer Risk Factors*

HPV infection is the leading cause of cervical cancer. However, factors such as sexual behavior, smoking, use of oral contraceptives, parity, co-infection with Human Immunodeficiency Virus (HIV) and diet have been identified to potentiate the neoplastic potential of HPV.[19-22.] The association between oral contraceptives and cervical cancer was strongly demonstrated in a large pooled analysis of eight case-controlled studies of patients with histologically confirmed invasive cervical carcinoma by the International Agency for Research on Cancer (IARC).[18] Their findings showed an association between prolonged use of oral contraceptives of more than 5 years, and increased risk of cervical cancer (OR =2·82 (95% CI 1·46–5·42) for 5–9 years, and 4·03 (2·09–8·02) for use for 10 or more years).

Two large studies which looked at parity as a risk factor for cervical cancer found an association between the number of live births and risk of cervical cancer. Thus, the higher the number of full term live births, the higher the risk of being diagnosed with cervical cancer. This trend could be attributed to the cumulative trauma and immunosuppressive effect related to child birth, making the cervix more susceptible to HPV infection.[19, 20, 21] In addition, the IARC study also found that the odds ratio for cervical cancer in women with seven or more live births was higher compared to women with no children.[22] Nicotine metabolites have been found in cervical mucus of smokers and as such, have led to the assertion that smoking is a risk factor for cervical cancer. This assertion has been refuted on the basis of possible confounding by other variables:

since there is an existing strong relationship between smoking and sexual activities, it cannot be substantiated that smoking does indeed cause cervical cancer.[23, 24, 25]

### *1.3.2 Cervical Cancer Screening*

HPV infection is detected by HPV-DNA testing, and cervical cytology screening is used to identify the cellular changes that result in the cervix as a result of HPV infection. Existing evidence indicates the substantial contribution of cervical cytology screening in the reduction of invasive cervical cancer.[27] For example, a study by the IARC working group indicates a statistically significant decrease in the incidence and mortality rate of cervical cancer when cytological screening is employed.[28] In 2003, the BC cervical cancer screening program (CCSP) reported incidence and mortality rates for cervical cancer as 9.1/100,000 and 2.0/100,000, respectively. Since that time, there has been more than a 60% reduction in both the incidence and mortality rates following the introduction of screening programs in BC.[11, 29] The CCSP in Canada and other developed countries use the Papanicolou (Pap) test to determine pre-cancerous cervical lesions, followed by colposcopy and biopsy for women with abnormal pap smears.[30] Although these screening programs are effective, they are resource-intensive, which puts a strain on limited health care resources.

## 1.4 Human Papillomavirus Vaccines

Two vaccines have been developed for the prevention of HPV infection. In 2006, Gardasil®, a prophylactic HPV vaccine, prepared from virus-like particles through recombinant technology, was approved for use in Canada, the US and other countries. Gardasil®, manufactured by Merck & Co, is a quadrivalent vaccine which contains a mixture of four types of viral DNA-free, virus-like particles (VLP) derived from the L1 capsid protein for HPV types 6, 11, 16 and 18 for the prevention of cervical cancer and genital warts.[3,31] HPV L1 VLPs have a better delivery system than recombinant adenoviral [32.] The second vaccine, Cervarix®, manufactured by GlaxoSmithKline, is currently in its final stages of approval in Canada, but is currently being used in the United Kingdom and some other European countries. The vaccine is bivalent, and includes 2 types of VLPs assembled from recombinant HPV-16 and HPV-18 L1. The L1 protein is produced using baculovirus/insect cell expression system.[33] Both vaccines are

recommended for women aged 9-26 years and are administered intramuscularly as a three-dose regimen over a period 6 months.[34] Gardasil® is administered at months 0, 2 and 6, and Cervarix® at months 0, 1 and 6. Several studies have stated the need to vaccinate girls before sexual debut, since vaccination prior to this will ensure maximum efficiency against all HPV types covered by the vaccines.[35]

Randomized clinical trials evaluating these vaccines have used the prevention of precancerous lesions rather than cervical cancer as their primary efficacy endpoint, given the fact that cancer develops 20 years after acquiring an HPV infection.[36] In addition, the standard of care in the developed countries is to screen for precancerous lesions via the Pap smear screening programs and excise CIN grade 2, 3 lesions before development of cancer.[37] Clinical trials have shown approximately 100% efficacy (95% CI 86.4 -100.0) for Gardasil® against CIN 2,3. The quadrivalent vaccine was 100% effective ($p<0.001$ verses placebo) in two clinical trials: FUTURE I (97.5% CI 85-100%) and FUTURE II (97.6% CI 76-100%) in preventing cervical dysplasia related to HPV infection, and PARTICIA trial also showed a 90.4% efficacy (97.9% CI 53.4-99.3) for Cervarix® in the prevention of CIN 2 in women who have been unexposed to HPV infection.[34,38] In addition, Cervarix clinical trials have established protection against HPV types 45 and 31, which are the third and fourth most prevalent HPV cancer-causing types.[39] Both vaccines have demonstrated protection against precancerous lesions for up to 5.5 years, but there is currently no knowledge on the long term (i.e., greater than 10 or 20 years) length of immunity provided by the vaccines and cross-protection against other types of HPV strains. Gardasil® is a well tolerated vaccine; however, when compared with placebo, it was associated with increased injection-site related adverse events such as pain and erythema and a higher incidence of low-grade fevers. The most common systematic adverse event was headache.[40] Similar to the quadrivalent vaccine, Cervarix® is also well tolerated. During a clinical trial, both the study and control groups reported soreness at the injection site, and swelling and redness were also common. The injection site symptoms were reported by 94% of vaccine recipients. Other adverse events reported were flu-like symptoms, including fatigue, gastrointestinal tract upset, low-grade fever and headaches.[39]

The recent approval of Gardasil® in Canada, the US and other countries has sparked debates over the intended vaccination programs in elementary schools. Opponents are questioning the necessity of vaccination of young girls who are not sexually active, potential side effects and long term duration.[41] In spite of the opposition, the Canadian government announced

in 2006 that it would allocate $300 million over the next 3 years to help Provinces and Territories implement a school-based, publicly-funded HPV program.

## 1.5 Research Need and Justification

In B.C., Gardasil® is being used for the school-based HPV vaccination program, which started in the fall in 2008 with both grade 6 and grade 9 girls as recipients. It is anticipated that by next year, Cervarix® will be approved Health Canada. Thus, policy-makers need to make a decision on the use of the quadrivalent versus bivalent vaccine, given the former vaccine's ability to prevent genital warts, and to decide:

1. Whether to recommend both vaccines, but leave consumers to choose the vaccine they prefer.
2. Stay with the current recommended vaccine (Gardasil® ), or
3. Drop the current vaccine and use Cervarix® due to its potential lower acquisition cost.

For decision-makers to decide on which vaccination policy strategy to use, it is imperative that the public's opinion be incorporated in the decision making process. One possible way to evaluate public preferences for health related programs and treatments is to use choice-based conjoint analysis. There is currently no empirical evidence on public preferences for the different HPV vaccination strategy.

## 1.6 Thesis Hypothesis, Objectives and Organization

It is hypothesized that respondents will have positive relative preferences for the HPV vaccination and screening program. They will also have a stronger positive relative preference for a quadrivalent HPV vaccination and screening program relative to a bivalent vaccination and screening program because of the additional genital warts protection offered by the quadrivalent vaccine, and preferences will differ depending on respondents' sociodemographic status.

### *1.6.1 Primary Objectives*

The primary objective of the study is to quantitatively evaluate societal preferences for the different HPV vaccination strategies. This goal will be achieved by: (i) determining societal

preference for each specific attribute of the vaccination and screening strategy (e.g., cost, need for booster), and (ii) determining societal willingness to pay for additional protection for genital warts. This finding will be important, as we will be able to determine whether this value is in line with the cost difference between the two vaccines.

### *1.6.2 Secondary Objectives*

The secondary objectives are to: (i) determine the trade-offs between benefits and perceived risks, and (ii) identify subgroups with different preferences. For example, it may become apparent that parents with school-aged daughters have a strong preference to receive the vaccination program that also has cancer prevention properties, as well as genital wart coverage. The study will also assess whether different societal characteristics, such as age, and gender, will result in different preferences. Since the ultimate goal is to improve uptake, these findings will be important in determining which vaccine strategy to select. Results of this study will provide insight into the societal selection process of the two vaccines, as well as the relative preference for each of the attributes associated with the HPV vaccines.

This thesis will consist of five chapters. Chapter 1 will be a brief introduction of HPV, its epidemiology, cervical cancer and vaccines. The chapter will also include the study justification. The chapter 2 will be a literature on HPV vaccine acceptability. Chapter 3 will be an introduction of discrete choice experiments and it significance to this study. Chapter 4 will be the results and discussion and Chapter 5 will be summary, contribution and recommendation.

**Figure 1.1**: Disease progression for cervical cancer[6].

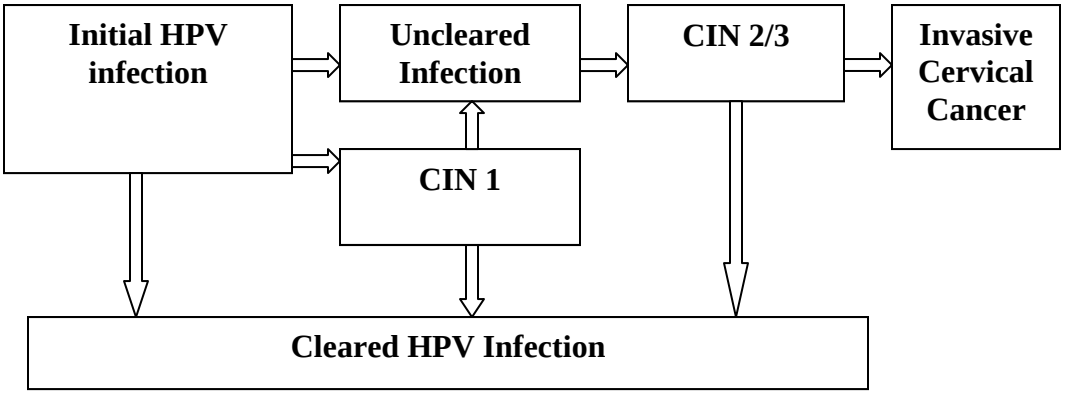
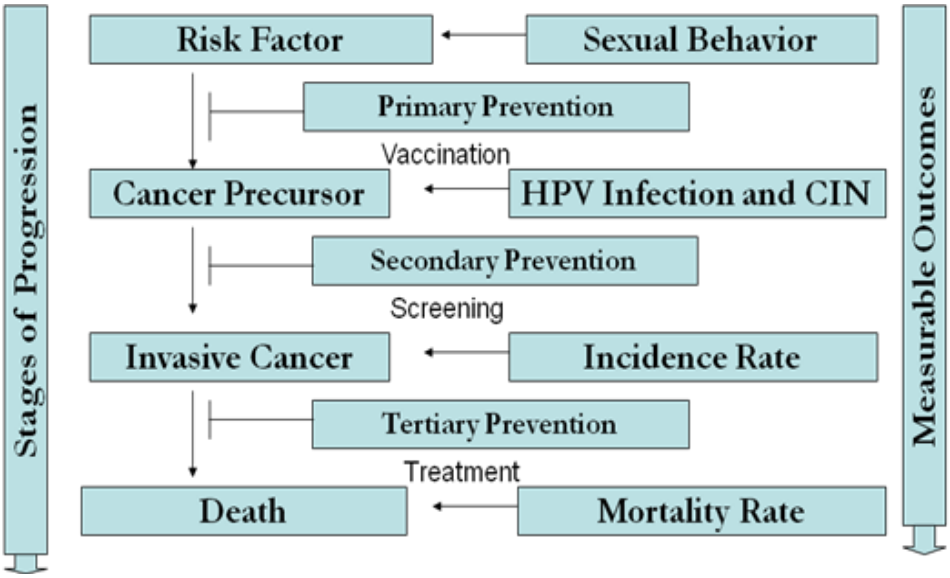



**Figure 1.2**: Different stages in HPV infection, and where prevention or intervention measures could be applied. (Adapted from Franco et al, 2006)[15]



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# CHAPTER 2

# PREDICTORS OF THE HUMAN PAPILLOMAVIRUS VACCINE ACCEPTABILITY A REVIEW*

## 2.1 Introduction

HPV is one of the most common sexually transmitted viruses, and is responsible for causing invasive cervical cancer or genital warts. The two vaccines currently available have been shown, through clinical trials, to be effective in the prevention of HPV infections.[1,2] In Canada, only one HPV vaccine, Gardasil® (Merck Frosst Ltd), has been approved for use, and the vaccination program is publicly funded and administered to school girls at months 0, 2 and 6. The target school grade for the publicly funded programs varies by province. In British Columbia, for instance, girls in grades 6 and 9 are the beneficiaries of the publicly funded program, whereas in Alberta, it is girls in grade 5. Variations in vaccination programs are observed not only within a country, but across different countries. For example, in Canada and the United States, Gardasil® is being used in the HPV vaccination program, but for the United Kingdom and other European countries, Cervarix® (GlaxoSmithKline Inc, United Kingdom) is the vaccine of choice for the publicly funded programs. Vaccines are an important component in controlling infectious diseases, but the success of any vaccination program depends on how well it is received by consumers and subsequent uptake.[3] The acceptance of the HPV vaccines could have an immense health benefit by decreasing cervical cancer morbidity and mortality, and also by reducing the psychosocial burden of both genital warts and abnormal Papanicolaou (Pap) test results.[4]

Studies have shown that high vaccine acceptability can lead to an increased vaccine uptake and studies that have assessed vaccine acceptability have often done so from a psychological perspective, using health belief models.[5,6,7] The health belief model (HBM) was constructed in 1950 by four clinical psychologists to predict and explain health behaviors. The model consists of five constructs which are perceived vulnerability, perceived barrier, perceived benefit, perceived severity and cues to action.[8] Perceived susceptibility captures an individual's opinion of the chances of getting a health condition such as being infected with HPV and perceived severity predicts an individual's opinion of how serious a condition is and what the after effects are. One's belief in the ability of a health intervention or program to reduce the risk

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of a health condition is captured by perceived benefits.[10] Any psychological cost or action that could potentially impede the success of an action is perceived as a barrier. Cues to action encompass all activities that activate readiness for a health action. The health belief model is based on the assumptions that (i) a health related action will be taken if a negative health condition can be avoided, and (ii) there is a positive expectation by taking recommended action and that the recommended action can be successfully executed.[10]

The model was first used to explain the lack of interest in preventive medicine, but was later extended to explain and predict people's health behaviors such as compliance with medical regimen, HIV risk behavior change, and dietary compliance, among many others. HBM has also been used to predict or explain people's acceptability for different health programs and interventions. For instance, when Bodenheimer et al applied the health belief model to determine the acceptance of hepatitis B vaccine among hospital workers in the United States, they found that safety and efficacy of vaccine had a major impact on the decision to accept or reject vaccine.[9] The prospect of a potential vaccine for Human papillomavirus led to an extensive research on HPV vaccine acceptability. Researchers were interested in the attitudes of parents, adolescents and society as a whole towards the vaccine, as this could potentially give an estimate of vaccine uptake.

The aim of this literature review is to use the health belief model as a conceptual framework to critically evaluate the findings of HPV vaccine acceptability studies, and to identify factors associated with willingness to accept the vaccine. The review will consider studies from countries that have approved the use of an HPV vaccine.

## 2.2 Methods

An electronic search was conducted using Medline, Embase, Cinahl and PsycINFO. The search period was from 1980 to March 2009, in order to capture studies conducted before and after the vaccine approval. The search strategy included the following medical search terms (MeSH): perceived severity, side effects perceived susceptibility, benefit, genital warts, uptake, knowledge, pap smear testing, attitude, human papillomavirus, and cervical cancer, pap smear, genital warts, vaccine booster, gender ( girls, boys and girls and boys), side effect, adverse effects, cost, prefer* accept* society and public. A study was included in the review if it evaluated HPV acceptability, factors that lead to high HPV vaccine uptake, knowledge of HPV,

and evaluated acceptability for parent, adolescents and healthcare providers. A grey literature search was also conducted using the following links to identify published and unpublished articles and abstracts: Papers First, Proceeding first, Google scholar and governmental agencies such as the Canadian Agency for Drug and Technologies in Health, National Institute for Health and Clinical Excellence (United Kingdom) and the United State Food and Drug Agency. All HPV vaccine preference studies published in the English language were included in the analysis.

## 2.3 Results

A total of 700 articles were retrieved from the literature search. Of these, 450 did not meet the inclusion criteria and 100 were duplicates. The abstracts for the remaining articles were reviewed for further selection. After a thorough review of the abstracts, 20 articles were selected for the review. The sample size of the selected studies ranged from 24 to 2002 participants (Table 1). Four of the articles were qualitative studies, 2 studies had university students as study population, and two studies had both adolescents and their parents as study participants. Most of the studies administered the study-designed questionnaire directly to the participants, and four studies used focused groups. Convenience sampling was the dominant sampling strategy, but four studies used random sampling methods and one study used snowball sampling

## 2.4 Review

Brewer et al[10] looked at studies of HPV-related beliefs and HPV vaccine acceptability, and organized their findings using health behavior theory and cervical risk factors. According to the authors, their review differed from previous systematic reviews because they used a theory to identify predictors of HPV vaccine acceptability and placed special emphasis on the population most affected by cervical cancer. The authors' reasons for using theories of health behavior were to enable them to assess a priori predictions about beliefs likely to increase adoption of the HPV vaccine and because of its proven relevance to vaccinations behaviors. They used the following health belief model constructs: perceived likelihood, which in the context of HPV vaccination is the belief that HPV infection and cervical cancer are likely to happen; perceived severity; the belief that HPV infections or cervical cancer would have serious negative consequences for health or well being; perceived effectiveness; the belief that the HPV vaccine will reduce the

likelihood or severity of the HPV infection or cervical cancer; perceived barriers to being vaccinated against the HPV, and cues to actions which are situational factors that prompt one to get vaccinated.

Brewer et al reviewed twenty-eight studies conducted in the United States from 1995 to January 2005. Only US studies were reviewed because of the many differences with the health care systems and potential cross-cultural differences in beliefs and motivations related to HPV vaccinations. The sample size used by the United States studies ranged from 20 individuals to 840. Most were small, cross-sectional studies of parents and adults, one used a quasi-experimental design and another used a controlled experimental design. A large number of them examined awareness, knowledge or attitude about the HPV infections. Brewer et al initially reviewed the public's levels of acceptability, then the potential predictors of acceptability. According to the authors, 50%-100% of parents were willing to vaccinate their adolescent children against HPV, although there were parents who were still undecided or who refused to vaccinate their children. They found that the majority of men and women in the studies reviewed had never heard of HPV. Across seven studies, 42% of respondents were aware of HPV, fifty-nine percent of respondents from eight studies knew the purpose of a Pap test, and 68% from six studies knew that HPV is a sexually transmitted disease. Only 55% of respondents from six studies had knowledge that HPV can cause genital warts. Between 21% and 46% of adolescents and young adults respondents perceived themselves as being at risk of getting infected with HPV, and in one of the reviewed studies, an association was found between perceived likelihood of getting cervical cancer and vaccine acceptability. Three of the twenty-eight studies found that higher perceived severity of HPV infections was not related to greater vaccine acceptability, but that severity was the second most influential factor in acceptability for sexually transmitted infection vaccines among parents. On perceived vaccine effectiveness, the authors reported greater HPV vaccination intentions for both parents of adolescents and adults in several of their reviewed articles. Parents rated vaccine effectiveness as the most important attribute of an acceptable sexually transmitted infection vaccine.

A perceived barrier identified by the authors is the concern among some parents that vaccinations could promote adolescent sexual activity. Four studies assessed the concern of vaccination promoting adolescent sexual behavior and found 6%-12% of parents in agreement. On the other hand, two studies found that parents had strong concerns that administering the HPV vaccines would implicitly condone youth sexual behavior. Cost was stated as the most

common barrier to receiving the HPV vaccine. Low perceived vaccine safety is another barrier to vaccination, and anticipated side effects from the HPV vaccine such as pain and discomfort were identified as reasons for low acceptability. HPV vaccine acceptability was higher among parents and young adults who believed that their physician would recommend the vaccine.
Other factors that were identified to influence vaccine acceptability were that parents reported that adolescents who are currently sexually active should receive the HPV vaccine, but those who are not sexually active should not. Also parents who were born-again or evangelical Christians as compared to other religions reported lower vaccine acceptability for daughters, and some studies reported that parents with history of genital warts of HPV infections were willing to vaccinate their adolescents.

Brewer et al[7] showed that the parents in the United States generally had a positive attitude towards the HPV vaccines and also showed that there is limited knowledge of HPV and HPV vaccines, and perceived severity was unrelated to vaccine acceptability as opposed to perceived effectiveness. However, the study's findings lack the ability to be generalized across countries and cultures. The subsequent session will evaluate the remaining selected studies using the health belief model and include studies from countries that have approved the use of an HPV vaccine.

### *2.4.1 Perceived Vulnerability*

Perceived vulnerability or susceptibility is a construct that reflects an individual's belief about the likelihood of a health threat's occurrence or the likelihood of developing a health problem[12]. This health belief construct captures the HPV vaccine attributes lifetime risk of cervical cancer and genital warts and evaluates an individual's perceived risk of getting genital warts or cervical cancer. The study by Woodhall et al[13]which looked at parental and adolescent knowledge and attitude towards HPV in Finland, found that parents were more likely to consider their child to be at higher risk (12%) of getting a sexually transmitted disease than the adolescents themselves (6%). Marlow et al[14] also found that mothers who thought their daughters were more susceptible to HPV infection were more likely to accept HPV vaccine. In Gerend et al[15] paper, respondents perceived themselves to be at high risk for HPV infection and higher risk perception was associated with being sexually active and having more than one sexual partner. However, a study on HPV acceptability of middle-aged women in Italy found that

women were less likely to accept HPV vaccination, even with history of abnormal Pap smear test or previous diagnosis of genital warts.[16] Overall, women who perceived themselves or their daughters as being at risk of HPV infection had higher vaccine acceptability than those who did not think they or their daughters were at risk of getting infected.[30] Women with more than one sexual partner perceived themselves as being at risk of HPV infection, and therefore were willing to accept vaccine for their daughters.[23]

### *2.4.2 Perceived Severity*

Perceived severity (or perceived seriousness) refers to the negative consequences an individual associates with an event or outcome.[12] Rosenthal et al[19] reported that 77% of their study participants indicated getting infected with HPV may lead to serious illness. Fazekas et al[17] study, which looked at the association between HPV vaccine acceptability and cervical cancer beliefs, HPV and HPV vaccine in a high risk cervical cancer population, found perceived severity of cervical cancer was related to intentions to vaccinate. In addition, parents with higher perceived severity of HPV infection have shown a positive attitude and high acceptance for the HPV vaccine.[14, 18] Conversely, parents who believe that their children experienced significant discomfort or danger when receiving immunization, had a negative attitude towards the vaccine. In addition, participants from Dempsey et al[27] study indicated that believing that HPV infection leads to serious consequence was not statistically associated with vaccine acceptability ($p=0.078$).

### *2.4.3 Perceived Barrier*

A perceived barrier is a person's estimation of a social, personal, environmental, and economic obstacle to a specified behavior.[12] This construct captures the effects of adverse reactions**,** cost and early sexual debut on vaccine acceptance. Studies have shown that fear of vaccine side effects is highly associated with non-acceptance of the HPV vaccines and that parents will decline to vaccinate their children because of the fear of unknown side effects.[18, 20, 21, 25, 30] Scarinci et al[25] found that an important determinant of vaccine acceptability in both Latina immigrants and African American women was side effect, and that those who rejected the vaccine were mostly concerned about the safety and side effects In Lenselink et al[22] study, some

parents actually stated they would prefer the vaccine to be used on other children for several years before they vaccinate their children.[22] Parental concern about vaccine side effects is justified; however, there are also misconceptions about side effects associated with the vaccine. For instance, Rosenthal et al[23] noted that some parents had stated misconceptions about vaccine side effects which included vaccine causing autism and allergic reactions.[23]

Another barrier associated with the acceptance of the HPV vaccine is the notion that vaccination implies condoning unhealthy behavior. In Waller et al[24] study, although women were excited about a cancer vaccine and were in favor of protecting their daughters from cervical cancer, abnormal Papanicolaou results and potentially from screening, they were very much concerned about increase in smoking and risky sexual behaviors. In addition, Woodhall et al [13] found that 42% of parents and 37% of adolescents believed that vaccines for sexually transmitted diseases increased the likelihood of early sexual debut, and 12% of mothers in Marlow et al study thought vaccination would make their daughters more likely to have sex. Scarinici et al[25] indicated that African American women were more concerned about a false sense of protection leading to unsafe sexual behavior.

Although the HPV vaccination program is publicly funded in countries such as Canada, those who do not qualify for the funded program have to pay for their daughters if the vaccine is not covered by their insurers. Fazekas et al[17] in their study reported that cost of vaccine had a negative effect on the acceptability and that most women (84%) were likely to vaccinate their adolescent daughters against HPV if the vaccine were free. Parents in a low income bracket are most likely to decline HPV vaccination for their children.[20, 26] Other perceived barriers associated with vaccine acceptability are religious beliefs, and effectiveness and safety of vaccine. Parents with strong religious backgrounds and those who were anxious about the effectiveness and safety of the vaccine were less likely to accept the HPV vaccine.[31, 32]

### *2.4.4 Perceived Benefit*

Perceived benefit is the belief that a positive outcome is associated with a behavior in response to a real or perceived threat.[12] Although the ultimate benefit to receiving HPV vaccine is reduced risk of HPV infection that could cause genital warts and invasive cervical cancer, vaccinating of both females and males is considered a benefit in increasing acceptability of the HPV vaccine.[20,27] In Olshen at al[18] study, most parents agreed that vaccine should be given to

both girls and boys even though it was of less benefit to boys. Middle-aged women in Italy considered vaccination of their sexual partner(s) to be very important, and inferred that such vaccination strategy will offer protection for their partner and will also indirectly help protect them from HPV infection. In Lascano et al[23] study, 84.2% of respondents had knowledge of the usefulness of the HPV vaccine, and this was a main factor that was associated with acceptability of the vaccine OR=5.05 (95% CI, 3.27-7.64). Believing in the benefit of HPV vaccine to society had a positive effect on vaccine acceptability.

### *2.4.5 Cues to Action*

Health practitioner influence plays an important role in HPV vaccine acceptance.[26, 28] In Ferris et al[29] study, participants were more inclined to receive HPV vaccine if it was recommended by a nurse. In addition, 72% of respondents in Marlow et al[14] study were likely to accept the HPV vaccine by talking to a health profession, and 75% were also more likely to accept the vaccine by talking to friends, 76% by reading HPV information in leaflets, 77% through the media and 78% by reading information on the internet. Giuseppe et al[16] acknowledged the importance of physician influence in educating and counseling and enhancing patient knowledge, but their study did not find a statistical significance between patient willingness to vaccinate and physician information. Ogilvie[6] et al study found that younger parents, parents who had a positive attitude towards vaccines (OR=9.9, 95% CI 4.7-21.1), those who were influenced by subjective norms such as those who considered a physician, public health nurse's, spiritual leader's or friend's recommendation to vaccinate as influential (OR=9.2, 95% CI 6.6-12.9), parents who thought someone they knew was likely to get cervical cancer (OR=1.5, 95%CI 1.1-2,1) and those who felt they had very little influence on their daughters' sexual behavior (OR=3.2, 95% CI2.2-4.6), were more likely to intend to vaccinate their daughters against HPV however, factors such as education, cultural background, sex, household composition, region of residence, religious affiliation and role of religious beliefs in their daily decisions were found not to be associated with intention to vaccinate their daughters against HPV. Another factor that influences parental intention to vaccinate their daughters against HPV is the age of the child. Parents with younger daughters are more hesitant to vaccinate them against HPV compared with parents with much older daughters. Kahn et al study[33] reported that 48% of their study participants with daughters intended to vaccinate a

daughter if she were 9 to 12 years old, 68% if she were 13 to 15 years of age, and 86% if she were 16 to 18 years of age, and that 48% of the mothers intended to receive the vaccine themselves if recommended. In addition, the authors found that factors such as gynecologic history, beliefs about cervical cancer prevention and beliefs about HPV vaccines were key determinants of mothers' intention to vaccinate their daughters against HPV.

## 2.5 Discussion

HPV vaccine acceptability is critical to the uptake of the vaccine and the reduction of HPV infections, invasive cervical cancer and genital warts. Vaccine acceptability could potentially inform public health decisions, and decrease morbidity and mortality of cervical cancer. Vaccine acceptability has gradually increased over time and most parents, especially mothers, are accepting of the HPV vaccine and plan on vaccinating their daughters.[19] The higher acceptance rate was attributed to self-perceived knowledge of HPV, knowledge of HPV as a risk factor of cervical cancer, self perceived risk of cervical cancer and history of Pap screening.[29, 30] However, Giuseppe et al[16] indicated that women's knowledge about HPV infection and cervical cancer was remarkably poor as only 23.3% had ever heard of HPV, and that a proportion of these women did not know that vaccination can prevent cervical cancer; but Lenselink et al[22] however, showed that acceptance of HPV vaccination was not influenced by knowledge or medical education. An extensive research on the effects of knowledge of HPV infection, cervical cancer and HPV vaccine needs to be done to clear any ambiguity surrounding this effect. In addition, more aggressive public health education needs be done and education needs to be directed towards those with the least knowledge, including men, young adults and the elderly.[20]

Women who thought they were at high risk of cervical cancer, either through history of abnormal Pap smear or previous HPV infections, and those who perceived their children would be vulnerable in the future were more accepting of the vaccine.[16] Two studies focused on the perceived vulnerability of genital wart and vaccine acceptability. Marshall et al[20] reported that the majority of participants were more likely to accept the HPV vaccination if it also prevented genital warts. In addition, if male participants were told explicitly that HPV infection causes genital warts and minor risk of penile carcinoma, they would have a higher acceptance for the

vaccine.[22] More research is needed in evaluating the effect of genital warts on vaccine acceptability.

Respondents who perceived their children as being at low risk of getting infected were parents who considered themselves as being very religious, who were in a monogamous relationship or who were sexually inactive. Parents who expressed safety as a concern believed too many vaccines can compromise the immune system of the child.[31]

Influence from family physician, partners, family and friends had a positive effect on HPV vaccine acceptability. Moreira et al [21] stated that advice from physicians contributed positively to vaccine acceptability. Similar findings were reported in a study that evaluated the acceptance of HPV immunization and hepatitis B vaccine.[4, 19] Physicians and other health practitioners could play a critical role is breaking down some of the barriers or negative stigma associated with the HPV vaccine, since they play a very influential role in their patients' decision making. This is evident in studies that evaluated physician and other health practitioners' influence in their decision to vaccinate their daughters. In Ogilvie et al study, physician's recommendation had the highest mean score for being influential in a participant's decision to vaccinate a daughter against HPV.

Socioeconomic status also plays an important role in vaccine acceptability. Marshall et al[20] reported that most socio-economically disadvantaged participants were more willing to accept the HPV vaccination. This group of people are more likely to take advantage of a publically funded health program due to the lack of financial commitment relative to those who are financially well off. Although well educated parents seem to be knowledgeable about HPV, educational background was not a factor that influenced intention to vaccinate their daughters against HPV in Ogilvie et al study. The age of both parent and child plays an important role in vaccine acceptability and intention to vaccinate. Younger parents are more likely to vaccinate their children against HPV than older parents, because they are probably more liberal-minded and so do not associate vaccination with condoning early sexual practices. As reported by Kahn et al[33], parents with children under 13 years of age are more hesitant about vaccinating their daughters against HPV than those with older children. This difference could be attributable to mothers being uncomfortable discussing sexually transmitted disease with their younger daughters, or fearing that they could be encouraging early sexually practices. [14, 33] To increase vaccine uptake, more parental education should be targeted on those with children less than 13 years as this is the recommended age for the HPV vaccination. Parents whose children had

received all recommended childhood vaccines were more inclined to accept the HPV vaccination. [22] Few studies addressed the effect of Pap smear testing on vaccine acceptability. Marlow et al study indicated that 70% of their respondents stated that they will be glad if vaccination meant the end of Pap smear testing. More research needs to be done to ascertain the extent of this effect.

Results from this systematic review, and that of Brewer and colleagues, showed that most parents and adolescents had a positive attitude towards the HPV vaccine. Respondents perceived themselves and their daughters as being at risk of HPV infections and accepted the HPV vaccine. However, parents who rejected HPV vaccine in both reviews had concerns about vaccine side effects and were of the opinion that vaccines for sexually transmitted infections encourage early sexual practices and give a false sense of protection. Healthcare decision-makers need to address both positive and negative factors that affect parental intention to vaccinate their daughters and acceptability of the HPV vaccines in countries that have not yet implemented the HPV vaccination programs, and for countries that have implemented the vaccination programs, addressing these issues could potentially help achieve a full vaccine uptake. Studies have extensively shown that parents have accepted the HPV vaccine and intend to vaccinate their daughters against HPV, but future research needs to focus on preferences for the HPV vaccines as there are major differences between the two vaccines, and also to determine the characteristics of the vaccines that are more important to society, which the subsequent chapters seek to address.

**Table 2.1**: Characteristics of the studies used in the literature review and the health belief model constructs they capture.

| Author | Year | Type of study | Population | Population size | Method | Sampling Strategy | HBM construct |
|---|---|---|---|---|---|---|---|
| Woodhall et al, | 2007 | Cross-sectional | 1990-born adolescent in 9th grade and their parents | 400 adolescent, 740 parents | Self administered study questionnaire (mailed) | Convenience sampling | PV, PBa |
| Marlow et al, | 2007 | Cross sectional | Mothers with at least one daughter aged (8-14 years) | 648 | Self administered study questionnaire | Convenience sampling | CA, PV, PS |
| Gerend et al, | 2008 | Cross-sectional | University students | 124 | Self administered study questionnaire | Convenience sampling | PV |
| Di Giuseppe et al, | 2008 | Cross-sectional | Female university students aged 14-24 years | 1341 | Self administered study questionnaire | Cluster sampling | PV, CA |
| Fazekas et al, | 2008 | Cross-sectional | Women from health service clinic | 149 | Self administered study questionnaire | Convenience sampling | PBa, PS |
| Olshen et al, | 2005 | Qualitative study | Parents with adolescent children | 25 | Focus group | Convenience sampling | PBa, PS |
| Rosenthal et al, | 2007 | Qualitative study | Women | 34 | Focus group | Convenience samplings | |
| Marshall et al, | 2007 | Cross-sectional | Household members | 2002 | Telephone survey | Random sampling | PBa, PBe |
| Moreira et al, | 2006 | Cross sectional | Women aged 16 to 23 | 204 | Interviewer facilitated | Convenience sampling | PBa |
| Lenselink et al, | 2007 | Cross-sectional | Parents with children aged 10-12 years | 356 | Self-administered study questionnaire | Convenience sampling | PBa |
| Waller et al, | 2004 | Qualitative study | Women with at least one daughter aged between 8-14 years | 24 | Focused group | Snowballing sampling | PBa |
| Scarinici et al, | 2007 | Qualitative study | African American and Latina immigrant women | 55 | Focused group | Convenience sampling | PBa |

| Author | Year | Type of study | Population | Population size | Method | Sampling Strategy | HBM construct |
|---|---|---|---|---|---|---|---|
| Ishibashi et al, | 2007 | Cross-sectional | Physicians(pediatrician) | 375 | Self administered study questionnaire (web-based) | Random sampling | PBa |
| Kahn et al, | 2007 | Cross-sectional | Physicians(pediatrician) | 31 | Interviewer facilitated | Purposeful sampling | CA |
| Ferris et al, | 2008 | Cross-sectional | Mid-adult women | 675 | Self administered study questionnaire | Convenience sampling | CA |
| Chan et al, | 2007 | Cross-sectional | Chinese women | 170 | Self administered study questionnaire | Convenience sampling | PBa, PV |
| Gellin et al, | 2000 | Cross-sectional | Parents | 1600 | Interviewer administered study questionnaire | Randomized study | PBa |
| Dempsey et al, | 2006 | Cross-sectional | Parent or caregivers of children from 8-12 years | 1600 | Self administered questionnaire | Randomized study | PBa, PBe |
| Lazcano-Ponce et al | 2001 | Cross-sectional | Women aged 15-49 | 880 | Interviewer administered study questionnaire | Randomized study | PV, PBe |
| Brabin et al | 2006 | Cross-sectional | Parents with children age 11-12 years | 317 | Self administered study questionnaire | Randomized study | PBa |
| Ogilvie et al | 2007 | Cross-sectional | Parents of children 8-18 years of age | 1370 | Interviewer administered study questionnaire | Random digit dialing | CA |
| Kahn et al | 2009 | Cross-sectional | Mothers who are nurses with daughters | 7202 | Self administered study questionnaire | Convenience sampling | CA |

PV: Perceived vulnerability; PS: Perceived severity; PBe: Perceived benefit; PBa: Perceived barrier; CA; Cues to action

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# CHAPTER 3

# DEVELOPMENT AND ANALYSIS OF DISCRETE CHOICE EXPERIMENT*

## 3.1 Introduction

Resource allocation between competing demands is a concern for economists in all sectors. In the health sector, there is an increasing need to find a balance between supply and resource demand. In the quest to achieve this equilibrium, healthcare decision makers are constantly seeking for health intervention programs that are more efficient, effective and require fewer resources. Health economists are able make such recommendations by using different economic evaluation methods to compare the costs and benefits of health care interventions[1]. The overall aim of an economic evaluation is to aid decision makers to make efficient and equitable healthcare decisions. The methods used in economic evaluation include cost-effectiveness analysis, cost benefit analysis and cost utility analysis.[2] Cost utility analysis is the most common economic evaluation method with the incremental cost per quality-adjusted life years (QALY) being the metric of outcome, as this allows for the assessment of both health and non health outcomes.[2,3] However, some economists have expressed concerns over the use of cost per QALY as an outcome measure, and they argue that the focus of economic evaluation should be on the analyses of patient preferences (asking what patients want) rather than enforcing some externally determined criteria such as cost/QALY.[3] This has led to the use of other valuation methods such as stated preference techniques in health economics.

The stated preference techniques consist of Willingness-To-Pay (WTP), conjoint analysis and qualitative analysis. These techniques involve valuing the costs and benefits of a health intervention or technology.[2] Although information obtained from the stated preference techniques are generated from hypothetical scenarios and not real market data, they are better able to predict choice behaviors. The different approaches used in measuring stated preferences include discrete choice experiments (choosing between two alternatives versus status quo), contingent rankings (ranking a series of alternatives), contingent ratings (score alternatives scenarios on a scale of 1-10) and paired comparisons (scoring pairs of scenarios on the same scale.[4] All four of these approaches employ choice modeling in evaluating preferences, and for

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the rest of this chapter the focus will be on the development and analyses of discrete choice experiments.

A discrete choice experiment (DCE) is an attribute based method used to model decision-making and establish consumer preferences for different goods and service.[5] DCEs were originally used in marketing, transport and environmental economics but have been widely adopted in health economics to evaluate healthcare programs.[6] The method assumes that a product can be categorized into a bundle of attributes and levels and consumers have a unique value (or utility) for each attribute level. Thus, each attribute level contributes to the aggregate value associated with a product and the overall utility for that product is achieved by summing up the different utilities associated with the attribute levels.[7] In a DCE, participants are presented with choices between hypothetical scenarios that vary in terms of their attribute levels. The objectives of a DCE are to: estimate the relative importance of the different attribute levels of a product, examine how consumers make trade-offs (marginal rate of substitution) between these attribute levels, determine the total benefit derived from that product and some cases, and determine the willingness to pay for the attribute levels.[8]

## 3.2 Theoretical Background

Discrete choice experiments are consistent with the Lancaster economic theory of demand, which suggests that consumers have preferences for, and derive utility from the attribute levels rather than the product as a whole.[9] DCEs are also in accordance with welfare and consumer theories.[10, 11, 12] The consumer theory has two components namely, choice and preference based approaches. The choice approach focuses on the choices consumers make, and the preference based approach suggests consumers have a preference relation over a set of possible choices which is based on the axiom of completeness (consumers can rank products in the order they prefer), transitivity (preferences are rational and consistent) and monotonicity (more is better).[13]

Discrete choice experiments are developed from the random utility theory (RUT). The RUT assumes that consumers are rational (will consider all available options before making a decision) and will always maximize their utility, which means when a consumer is presented with a choice, the best option which satisfies his or her wellbeing (utility) will be chosen.

The Utility (U) derived from a product is made up of two components, namely the deterministic and stochastic components. The stochastic component captures the uncertainty in the choice data which results from measurement error, variations in preferences, variation between consumers and effects of attributes and levels that were not included in the study. [14]

The utility function (U) for the, $i^{th}$ individual with choice $j$ is represented by:

$$U_{ij} = K_{ij} + w_{ij} \text{ , where } j = 1,..,J \quad (1)$$

and $K_{ij}$ represents the deterministic component and $w_{ij}$ is the stochastic component of the utility model. The deterministic component is a function of the attribute levels of the product in question and the respondents' specific characteristics. This is represented by the equation:

$$K_{ij} = X'_{ij}\beta + T'_{i}\delta \quad (2)$$

where $X'_{ij}$ and $T'_{i}$ represent all attribute levels and respondents' characteristics, respectively, and $\beta$ and $\delta$ represent the model coefficients. Under the utility maximizing assumption, respondents would only choose option 'b' if the utility derived from that option is greater than that derived from option 'a'. This is represented below as

$$U(k_{ib}, w) > U(k_{ia}, w) \quad (3)$$

and assuming a probability distribution for the error term 'w', the probability that utility is maximized by choosing option 'b' is given in the equation below:

$$P(Y_i = b) = P(U_{ib} > U_{ia}) \quad (4)$$
$$= P(U_{ib} + w_{ib} > U_{ia} + w_{ia})$$

where $Y_i$ is a random variable which represents a choice outcome. A linear utility function is assumed for the deterministic component and therefore a probit or logit regression model is used in its estimation. For the stochastic error term, a probability distribution is always assumed. For instance, if the error term is assumed to be independent and identically distributed, a conditional logistic model could be used to determine a choice probability as: [12, 13]

$$P(Y=b) = \frac{e^{\mu k_{ib}}}{\sum_{j=a}^{b} e^{\mu k_{i}b}}, \; a \neq b \quad (5)$$

## 3.3 Initiating a Discrete Choice Experiment

Performing a DCE requires a careful definition of an answerable research question that defines what the study aims at measuring. A well defined research question will determine the appropriate response format to use. The response format could be binary or multiple responses, labeled or unlabelled choice options, and with or without an opt-out or status quo option. The DCE questionnaire has to be simple for respondents to understand and have realistic attributes and levels. The following steps are involved in designing a discrete choice experiment.

### *3.3.1 Attribute and Level Selection*

Attribute and level selection are crucial in designing a DCE and are therefore considered the most important step in the design process. The selected attributes have to be significant in defining the product in question and should be influential in decision making. Attributes and levels are selected based on focus groups, extensive literature reviews, expert opinions, population based studies, surveys, key informant interviews and policy relevance. They can be either qualitative (e.g., target group to vaccinate) or quantitative (e.g., risk of genital warts). Using wider ranges between attribute levels is encouraged, as narrower ranges may inhibit participants from trading off between risks and benefits. In addition, a reasonable number of attributes are recommended to avoid respondents' fatigue; however, Lancaster et al[15] caution against excluding certain key attributes (also known as "omitted variable bias"). Inter-attribute correlation is avoided in a DCE because of its ability to affect the parameter estimates in a model. For instance, respondents often associate higher prices with higher quality goods and this perceived association may prevent respondents from treating these two attributes independently if they were both presented in a choice set[16]. Furthermore, attributes or levels that are correlated may affect the orthogonal design of the study and cause unrealistic or unreasonable attribute level combinations[17].

### *3.3.2 Choice Set Formation*

Although there is no set rule on the number of choice sets to include in a questionnaire as this decision is dictated by factors such as context of the study, and to a lesser extent, the target population, evidence suggests that respondents can conveniently answer between 9 and 16 choice questions and that anything above that may cause fatigue.[18] However, as the number of attribute and choice set increases, the complexity of the choice task increases as well. In a DCE, a choice set can be labeled or unlabeled. A labeled choice sets refer to options that have meaningful titles (e.g., Train and Bus) and the title conveys some information to the respondents. An unlabeled choice sets refer to options that have generic titles (e.g., Option A and Option B) which convey no information to the respondents. Choice sets can be presented in various forms such as visual or tabular, but most studies present the different options in a tabular form.

### *3.3.3 Experimental Design*

The aim of an experimental design is to generate choice sets that will provide enough statistical information for parameter estimation and preference determination.[19, 20]
The two experimental designs used in DCEs are full fractional and fractional factorial designs. A full factorial design consists of the full combination of all the attributes levels in a questionnaire, and a fractional factorial design consists of a subset of all the combination of attribute levels. The number of possible combinations of attribute levels is determined by the formula $L^A$ (where L is number of attribute levels and A is the number of attributes). For example, for 5 attributes, each with 3 levels, there are 243 ( $3^5$) possible combinations of attribute levels. A full factorial design allows for independent estimation of both main (attribute and level effect) and interactions (interaction between two or more attributes) effects, whereas a fractional factorial design is able to independently estimate all main effects and some interaction effects if they are defined *a prior i*.[16]
The majority of studies use a fractional factorial design because it is almost impossible for respondents to evaluate all the choice tasks in a factorial design. Evidence suggests that a full factorial design may be more feasible if a blocking technique is applied.[13] The technique allows

a full factorial design to be blocked into different versions and randomly administered to respondents.

The availability of statistical software has made the generation of a DCE design less onerous. Statistical programs such as Sawtooth, SAS NLOGIT, SPEED and SPSS are used to generate optimally efficient designs. Efficiency in a DCE refers to the precision with which effects are estimated. An optimal design is orthogonal (minimal correlation between attribute levels), level balanced (attribute levels occur at equal frequency), with minimal overlap (attributes do not appear at the same level within the presented scenario, thus the probability that an attribute level repeats itself in each choice set is as low as possible) and ensures an equal number of choice sets in each questionnaire version.

### *3.3.4 Questionnaire Design and Test of Validity*

A well designed DCE questionnaire is one which can be used to extract the maximum amount of information from respondent to generate efficient and precise parameter estimates. This could be ensured by adhering to the entire steps involved in designing a DCE (from attribute selection to experimental design). The complexity of a questionnaire is an important factor to consider in designing a DCE. Factors such as number of attributes, levels and choice sets can potentially contribute to the complexity of a questionnaire. To determine the effect of a complex task, Mozatta and Opaluch found that including more than 3 attributes in a choice set increased the complexity of the choice task and affected the quality of the response data.[21] Other studies have suggested that respondents use some lexicographic decision rule to simplify the decision process when faced with a complex choice task. However, this introduces systematic errors in the data and biases the study results.[13]

The stability of preferences decreases as choice task complexity increases but respondents' preferences are presumed to be stable in a random utility model. By comparing the responses made for the same choice set placed at the start and end of the experiment, one can test the stability of preferences. A consistent response can be an indication of stable preferences and an understanding of the choice task.[22] In addition, the random utility model also assumes that preferences are monotonic (more is better than less). To test the internal validity of this assumption, a dominant or better option (more benefits and fewer risks) is included in a choice set and often placed both at the beginning and the end of the experiment. The internal

consistency is evaluated based on the rationality of the choice respondents' make and they are expected to choose the dominant or better options in both choice sets. To also test the assumption of transitivity of preferences, three specific choice sets namely (1) option A versus option B, (2) option B versus option C and (3) option A versus option C, are included in the DCE. Transitivity assumes that respondents' preferences are rational and consistent and as such a respondent who chooses option A in the first choice set and option B is the second, is expected to choose option A in the third choice set.[25] The appropriate background information about the study and the instructions on how to answer the choice task is included in a DCE to facilitate respondents' understanding. Elicitation of respondents' specific health and demographic information is essential in determining differences in preferences that could potentially aid in informing policies.[23]

The inclusion of a neither, status-quo or opt-out option (non-demanders) is an important factor to consider in DCEs. Some studies suggest that the status-quo or opt-out option should be included because consumers are not forced to choose in real life scenarios, and that failure to include non-demanders when it is a viable option may lead to the overestimation of participants.[24] Alpizar et al suggest the inclusion of a status-quo or opt-out option if the purpose of the experiment is to determine welfare estimates as failure to do so will distort the welfare measure for non marginal changes.[25] The disadvantage of including an opt-out option is that, as in real life situations, it may prevent respondents from making difficult choices. The respondents must be aware of what a status-quo or an opt-out option represents in terms of the attributes and levels.

A labeled and unlabeled choice set has its advantages and disadvantages. The advantage of a labeled choice sets is that respondents can base their choices on a true policy context and for unlabeled choice sets respondents may provide better information regarding attribute trade-offs because they will be less likely to base their choice on the labels. The best approach to use depends on the objective of the study, but Blamey et al, suggests that if the objective is to estimate attribute values or marginal rates of substitution, then an unlabeled approach is recommended, and if the aim is to predict the amount of money respondents are willing to pay to obtain a given policy alternative, then a labeled approach is advised.[26]

Identification of dominant strategies in a DCE is essential to ensuring that respondents trade-off between the different attributes and levels. Trading-off occurs when respondents accept more of an attribute in compensation for less of another attribute. The lack of trading off occurs when

respondents make a choice based on a specific set(s) of attribute when these attribute(s) cannot be substituted. This scenario is referred to as lexicographic ordering.[27] It is usually difficult to determine if lexicographic ordering was used in self-administered DCE questionnaires. To avoid this, the DCE questionnaire is administered to a focus group and respondents are asked to give reasons as to why they focused on only one characteristic.

### *3.3.5 Piloting of Questionnaire*

The main aim of a pilot study is to test the contents and logistics of the survey process. The questionnaire is evaluated for its readability, respondents' ability to complete the entire questionnaire, the ability to complete the choice modeling components, the interviewer's understanding of the questionnaire and how it is administered.[16.] In addition, the length of time it takes to complete the questionnaire and the need for additional questions are also evaluated. Piloting a DCE questionnaire is essential to understanding the choice context, the experiment's appropriateness, attribute and levels, task complexity, likely response rate and timing.[13]

### *3.3.6 Sample Size and Data Collection*

There is no derived method for calculating sample size in DCEs. The minimum sample size depends on number of attributes, complexity of choice tasks, question format, need to undertake subgroup analysis and desired degree of precision.[28] According to Ryan et al, the overall sample size needs to be large enough to ensure an appropriate level of accuracy for the sub-groups.[8, 12] The rule of thumb is a minimum of 10 observations per independent variable in the model. Louviere et al have generated a formula to calculate the minimum sample size needed to measure choice probabilities with some level of accuracy. For any DCE, the sample size is often largely dependent on the budget of the study.[29]

A DCE can be mailed, or administered over the telephone or internet. It could also be self-administered or interviewer facilitated. However, the quality of the data can vary depending on the mode of administering. For example, it is assumed that data from an interviewer-facilitated mode of administering a DCE improves the quality of the data because of the ability of the interviewer to fully explain the choice task and also answer some questions.[17]

### 3.4 Statistical Analyses

Data analyses are an essential component in answering any research question. The attribute levels are first entered in the model as categorical covariates, however if a monotonic effect on the responses is observed, then the attributes are modeled as linear effects. The categorical variables are either dummy or effect coded. Categorical variables are coded so that they can be incorporated in a regression model to generate interpretable variable coefficients.[30] When effect coding is used zero equates the mean effect for each attribute rather than the combination of all omitted categories.[15] With effect coding, the omitted $K^{th}$ level on each effect coded variable is coded as -1, whereas the omitted $K^{th}$ level on each dummy coded variable is coded as 0. The appropriate random utility model is then specified for parameter estimation. The selection of a utility model is influenced by the experimental design and type of choice model (binary or multiple choice).[13] The two models which are commonly used in choice experiments are the conditional and mixed effect logistic model, and both models use maximum likelihood methods for parameter estimation.

The conditional logistic is the easiest and most widely used model in DCEs because its choice probabilities take a closed form and are readily interpretable. The three factors that contribute to the strengths and limitations of the conditional logistic model are taste variations, substitution patterns and repeated choice variations.[2] Taste in variation captures the systematic variations that are associated with respondents' observed characteristics (income, age and education). Independent irrelevant alternative (IIA) is the main property associated with substitution patterns. Substitution patterns affect the demand of a product when there is a change in demand and attributes. The IIA property assumes that the relative probability of choosing between any two alternatives is independent of all other alternatives. The IIA property allows for the consistent estimation of model parameters on a subset of alternative for each respondent. The conditional logistic model's IIA property is too strict to allow flexible substitution patterns and does not require that distributions be placed around parameter estimates.

Unlike the previous model, the mixed effect logit models account for heterogeneity in preferences, allow for random taste variations and relax the IIA assumption. Therefore these models are considered to be more flexible. In the mixed effect logistic model, variables can

either be fixed or random and a distribution is always assigned for the random variables. Aside from the mixed logit model, there are other models such as latent class and heteroscedatic error variance models, which also relax the IIA assumption.[32, 33, 34] The log likelihood estimate and pseudo R-squared are used to determine the goodness of fit for the random utility models.[13] In addition, mixed effect models account for the potential correlation in choices. For instance, for a respondent, color of car may be the most important attribute, and therefore the response to each choice set will not be independent of the other.

The parameter estimates from the regression outputs for both conditional and mixed effect logistic model have three components; the absolute magnitudes, and the signs and the significance of the estimate. In any of the models, a significant parameter estimate with the highest absolute magnitude is considered the most important attribute or level in the model. A positive parameter estimate suggests a preference (e.g., greater likelihood of benefit) for the attribute or level, whereas a negative estimate suggests dislike and respondents would prefer to have less of or at least avoid the level of that attribute. A negative coefficient suggests dislike and respondents would prefer to have less of or to avoid that attribute or level. The assumption of linear additivity for random utility models allows for the estimation of the alternative with the highest utility; since utilities can be combined across attribute levels as such, the overall utility is a function of the individual relative preferences for the various attributes. In addition, as shown in equation 5, the utility estimates can be used to determine the probability that an alternative will be selected over all other available alternative. The Z statistic test is carried out to determine if the mean and standard deviation estimates from the main effect model are statistically significant from zero. The Wald statistics is also calculated to test for statistically significant differences on the coefficients across subgroups.

The quantification of the relative preferences facilitates the calculation of the marginal rates of substitution of each combination of attributes The marginal rates of substitution and welfare estimates, such as the average willingness to pay are determined based on the ratios of the regression coefficients (e.g. $\beta_i/\beta_j$, where $\beta_i$ is the coefficient for attribute 'i' and $\beta_j$ is the coefficient for the monetary attribute, equals the willingness to pay for attribute 'i'). The methodology discussed in this chapter is what would be used to determine societal preferences for the HPV vaccines in Chapter 4.

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# CHAPTER 4
# USING DISCRETE CHOICE EXPERIMENT TO EVALUATE SOCIETAL PREFERENCES FOR THE HPV VACCINES[*]

## 4.1 Introduction

The Human Papillomavirus (HPV) is extremely diverse with more than 100 different types, most of which are benign. About 40 HPV types reside in mucosal cells and infect the genital tract.[1] Mucosal HPV types are characterized as either high- or low-risk. High-risk types 16 and 18 cause lesions that may develop into carcinomas, whereas types 6 and 11 are considered low-risk viruses and are responsible for causing low grade cervical abnormalities, recurrent respiratory papillomas and genital warts.[2] Types 16 and 18 account for about 70% of the high-risk types 45,31,33,52,56,35,59,56,51,39,68,73, and type 82 accounts for the other 30%. Types 40, 42, 43 and 44 are also classified as low-risk HPV types.[3] According to the Canadian Society of Obstetricians and Gynecologists, 75% of Canadians have at least one HPV infection in their lifetime, and at any one time 10% - 30% of the adult Canadian population are already infected with the virus. The highest rate of infection is found in those aged 20-25 years old.[4]

Cervical cancer is the leading cause of cancer in women between 20-44 years, and the 12$^{th}$ most common cause of cancer in Canadian females.[5] An estimated 1,500 Canadian women are diagnosed with cervical cancer each year, and about 400 die from the disease. From a global perspective, the World Health Organization reports that 80% of cervical cancer cases occur in developing countries: 13% from Africa, 15% from Latin America and 48% from Asia.[6] The lifetime risks of contracting cervical cancer and dying from it are 0.78% and 0.26% respectively.[1] Genital warts is a common sexually transmitted disease, with a 10% lifetime risk of contracting this condition.[7] HPV infection is detected by HPV-DNA testing, and cervical cytology screening is used to identify the cellular changes that occur in the cervix as a result of the infection. Cervical cytology screening has contributed substantially to the reduction of invasive cervical cancer in Canada, but across the country, different provinces and territories have distinct guidelines for cervical cancer screening.[8] For instance in British Columbia, sexually active women get screened every 24 months after 3 consecutive yearly negative Pap

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smear tests, whereas in Alberta, yearly screening is recommended for sexually active 18-69 women.[9]

Gardasil® and Cervarix® are the two vaccines that are currently been used for the prevention of HPV infection. Gardasil® prevents both cervical cancer and genital warts infection and is administered at months 0, 2 and 6, while Cervarix® prevents only cervical cancer and is administered at months 0, 1 and 6. Both vaccines have been shown to be safe and effective in the prevention of HPV infection.[10, 11] Despite these findings and the positive attitude towards the vaccines, parents remain concerned about their associated side effects, cost, and the notion that the vaccine would encourage early sexual practices.[12, 13] If these issues are not addressed, they could potentially affect the uptake of the vaccine and hinder the potential to reduce the incidence of genital warts, morbidity and mortality rates for cervical cancer. The type of vaccine, gender and age at which the vaccine is administered vary across countries. For instance, in Canada, Gardasil® is available through a publicly funded, school-based program for grades 6 and 9 girls only, while other countries have adopted programs using Cervarix and/or aimed at different target groups (for example, boys and girls). The variations in vaccination and screening strategies necessitate evaluating societal preferences for the different strategies; a better understanding of how society perceives and values the different aspects of the HPV vaccination and screening strategies is important for vaccine uptake. Moreover, incorporating these in decision-making may result in a health policy that better reflects the preferences of society.[14] Furthermore, knowing what is important to society could help in maintaining a sustainable healthcare system by balancing the increasing need for healthcare interventions and limited resources.

A discrete choice experiment (DCE) was conducted to: (i) evaluate preferences for the different vaccination and screening strategies; (ii) determine the relative importance of the attributes; (iii) determine the amount respondents are willing-to-pay for the additional protection of genital warts and determine subgroups within the sample populations that have different preferences.

## 4.2 Methods

### *4.2.1 Discrete Choice Experiment (Attribute and Level Selection)*

The DCE questionnaire (Appendix I) consisted of 7 important attributes, each with 3 or 4 levels. The attributes were selected based on the current vaccination and screening policy, literature reviews, and a CANADA-wide survey on parental intention to have their daughters receive the HPV vaccine.[15] Policy experts in infectious diseases and immunization also contributed to the selection of the attributes. The following attributes were selected for the study: lifetime risk of cervical cancer, lifetime risk of genital warts, need for vaccine booster, frequency of side effects, frequency of Pap smear testing, vaccine cost and target group to vaccinate. The attributes with their associated levels are shown in Table 1.

Sawtooth® CBC/SSI Web V.6.4.2 (Sawtooth Software, Inc. Sequim, WA, USA) was used to design a choice-based fractional factorial experiment, where each choice set had three options: (A and B) and neither. The respondents were told the neither option represented the baseline lifetime risk (in the absence of HPV vaccine) of cervical cancer and genital warts and the recommended yearly Pap smear testing. The questionnaires were optimally designed to ensure orthogonality (i.e., minimal correlation between attributes), minimal overlap (each attribute level in a survey appears only once in a choice task), and level balance (attribute levels occur at an equal frequency within a questionnaire). An example of a choice set is shown in Table 2. Ten versions of the questionnaire were generated, and each version had 10 choice sets plus 2 choice sets as a consistency check. The 2 consistency check choice sets had one choice that had clearly dominant (more benefits and fewer risks) attribute levels, and respondents were expected to choose the dominant choices as this suggested respondents understood the questionnaire content. An initial pilot study of 300 participants assessed DCE comprehension and the validity of the vaccination and screening attributes.

### *4.2.2 Recruitment and Study Sample*

Respondents who were 19 years or older, currently residing in Canada and fluent in speaking and writing English were recruited for the study. IPSOS Reid Vancouver, B.C., Canada, assisted in recruiting the respondents and ensured that the study sample was representative of the Canadian population. IPSOS REID (Vancouver branch) sent a letter of

initial contact (Appendix II) via email to each randomly selected individual who had previously stated their interest in participating in research. Individuals were selected from a balanced sample (balanced in terms of general population using socioeconomic demographics obtained from Statistics Canada), and were emailed an invitation with a unique universal resource locater that had a password-protected identification number embedded. This provided them access to the questionnaire. Respondents supplied informed consent and were asked to complete an online version of the DCE questionnaire which was hosted on the researchers' website. Apart from the DCE data, demographics, information on vaccine practices and personal or relatives' history of HPV-related diseases were also obtained from the respondents. The Behavioral Research Ethics Board of the University of British Columbia approved the study protocol (Appendix III).

### 4.3 Data Analysis

Descriptive analyses were performed to characterize the sample according to gender, age, income, education, marital status, having children, vaccination practices and personal or relatives' history of HPV-related diseases. The variables of cost, lifetime risk of cervical cancer, lifetime risk of genital warts and frequency of side effects were inputted as continuous variables, whereas the need for vaccine booster, target group to vaccinate and frequency of Pap smear testing were effect coded as categorical variables.

Two random utility models, conditional and mixed effect logistic models, were used for the analyses. Both models use the maximum likelihood method for parameter estimations.[16] In the conditional logistic model, all attribute levels were modeled as fixed parameters, but in the mixed effect model, the attribute levels for target group to vaccinate, need for vaccine booster and frequency of Pap smear testing were modeled as random parameters with normal distributions, and cost, lifetime risks of cervical cancer and genital warts and frequency of side effects were modeled as fixed parameters. The latter attributes were modeled as fixed parameter variables to enable the determination of their marginal rate of substitutions. The expected utility values for the three vaccinations and screening strategies were calculated to determine the most preferred HPV vaccination and screening strategy, and the predicted probability of choosing an HPV vaccination and screening strategy was calculated using a formula by Hall et al[17].

SAS (version 9.1, SAS Institute Inc, Cary NC) was used to run the conditional logistic model, and MATLAB code[18] was used to run the mixed effect logistic models. Statistical significance was defined at p-value < 0.05.

### *4.3.1 Marginal Rate of Substitution*

A main effect model was estimated, and the regression coefficients allowed for the determination of marginal rates of substitution. Under the marginal rate of substitution, two estimates were obtained: willingness-to-pay (the average amount a respondent is willing to pay to avoid or get an attribute level), and willingness-to-trade (the rate at which a respondent is willing to give up an attribute in exchange for another while maintaining the same level of satisfaction).[19] The equations below show how the two welfare estimates are calculated.

$$MRS = -[\beta_{(\text{attribute a})} / \beta_{(\text{attribute b})}] \qquad 4.a$$

$$WTP = -[\beta_{(\text{attribute 1})} / \beta_{(\text{cost})}] \qquad 4.b$$

$$WTT = -[\beta_{(\text{attribute 1})} / \beta_{(\text{attribute 2})}] \qquad 4.c$$

The willingness-to pay (WTP) calculation as shown in equation (4.b) has the cost variable as the denominator, whereas the willingness-to-trade (WTT) calculation includes another attribute as the denominator.[20]

### *4.3.2 Sub-Group Analyses*

We hypothesized that respondents' preferences for the HPV vaccination and screening strategies would differ by their sociodemographic status, such as income, gender, age, educational background and such other factors as having children, type of household, vaccination practices and personal or relatives' history of HPV-related disease. Segmentation analyses were carried out using the mixed effect logistic model to evaluate preferences across the various

subgroups. The Wald statistic test was used to test for differences in mean parameter estimates across the various subgroups.

## 4.4 Results

A total of 1275 respondents completed the questionnaire, but only 1157 (91%) chose at least one dominant option in both consistency check choice sets. Respondents who did not choose any dominant option in both consistency check choice sets were excluded from the analysis. Those who chose neither throughout the entire questionnaire were included in the analyses. The high percentage (91%) of respondents who answered at least one consistency check correctly is indicative that they understood the methods of the questionnaire. There were no significant differences in sociodemographic factors between those included and excluded from the analysis. With 1157 respondents and each having 30 choice options, a total of 34710 observations were used in both the conditional and mixed effect logistic analyses.

### *4.4.1 Sample Characteristics*

The baseline characteristics of the 1157 respondents who were included in the analysis are summarized in (Table 3). The average age of respondents was 44 years (SD=15), of whom five hundred and sixty nine (49%) were males. Seven hundred and three respondents (61%) reported an annual income of $55,000 or more. About half of the respondents (46%) reside in Ontario, and only one hundred and forty two (12%) of all respondents had either an undergraduate university education or graduate degree, but more than three quarters of the sample (79%) had acquired either some high school, high school, trade school, community college or some university education. Overall, the study population was fairly educated and middle-aged, with most individuals earning more than $55,000/year. Three hundred and sixty six of the study participants (68%) were from a two-parent household, which was defined as a family consisting of both parents and children, and eighty nine (17%) were from a single-parent household, defined as a parent who cares for one or more children without the assistance of the other parent. The rest were identified as being from a guardian, extended or blended household.

Five hundred and thirty two (46%) of the respondents indicated they had children. Of these, four hundred and fifty eight (86%) had had their children receive all childhood vaccines,

and only ten (2%) had had their children receive no childhood vaccine. The most predominant reason for not receiving all childhood vaccines was the child not being old enough, but three respondents were concerned about the safety of the vaccine. When asked if any of their children were sexually active, three hundred and seventy four (70%) said no, and one hundred and one (19%) indicated that their children were sexually active. Additionally, eight hundred and seventeen (70%) of all respondents indicated that they would vaccinate their child against HPV if they had one between the ages of 9-18 years.

One hundred and thirty nine (13%) respondents had either experienced, or a relative had experienced, an HPV-related illness such as abnormal Pap smear, genital warts or cervical cancer, and three hundred and twenty one (28%) knew someone suffering from a cancer disease.

## 4.5 Statistical Significance of Attributes

### *4.5.1 Conditional Logistic Model*

From the conditional logistic model, respondents had negative preferences for the attribute levels, *need for a vaccine booster every 5 years*, *yearly Pap smear testing*, *Pap smear testing every 5 years* and *vaccinating neither girls nor boys*. They had positive preferences for the attribute levels, *need for a vaccine booster every 10 years*, *never having a vaccine booster*, *Pap smear testing every 3 years*, *never having a Pap smear testing*, *vaccinating girls only*, *and vaccinating both girls and boys* (Table 4.4). The attribute level *vaccinating neither boys nor girls* had the lowest negative preference in terms of parameter estimate (-0.67), and also had the largest impact on respondents' utility. The four attributes, namely *risk of cervical cancer, risk of genital warts, cost of vaccine and frequency of side effects*, all had negative preferences. This means preference for an HPV vaccination and screening strategy decreases as the risk of cervical cancer, genital warts, cost of vaccine and frequency of side effects increases.

In addition, respondents were more averse to the *risk of cervical cancer* compared to the *risk of genital warts* but eliminating genital warts would have a higher impact on respondents' utility, as the baseline *risk for genital warts* is higher (10%) than that of cervical cancer (0.78%). With the exception of the attribute levels, *need for vaccine booster every 10 years* (p=0.29), *yearly Pap smear testing* (p=0.30) and *never having Pap smear testing* (p=0.60), all mean parameter estimates in the conditional logistic model were statistically significant. The results from the conditional logistic model suggest that respondents agree with the introduction of the

HPV vaccination program because they had the strongest negative preference for *vaccinating neither boys nor girls,* and they preferred administering the vaccine to both girls and boys, instead of giving it to girls only.

A WTP estimate is the value society places on an attribute or attributes level. On average, respondents valued avoiding *having a vaccine booster every 5 years* at $27. They also would have to be compensated with $318 to accept a "no vaccine" strategy (i.e., *vaccinating neither boys nor girls*) because of the strong aversion for the "no vaccine" strategy (Table 4.5). They also had an average WTP of $54, $20 and $11 to avoid a 1% increased risk of cervical cancer, 1% increased risk of genital warts and 1% increase frequency of side effects, respectively. As shown in Table 4.6, respondents were willing to accept a 2.70% increase in genital warts risk to avoid a percent increase in cervical cancer risk. This suggests that the study participants were more concerned about cervical cancer risk than they were about genital warts risk.

### *4.5.2 Mixed Effect Logistic Model*

A mixed effect logistic (MXL) model was used to re-analyze the data in order to account for heterogeneity among respondents' preferences. Respondents' preferences are considered heterogeneous if the standard deviation estimate for an attribute level is statistically significant. The results from the MXL model were generally consistent with the condition logistic model except for the attribute level *never having a Pap test* (Table 4.4). The attribute level with the largest impact on respondents' preferences was *vaccinating neither girls nor boys.* With the exception of the attribute levels *having a vaccine booster every 10 years* (p=0.85), *yearly Pap smear testing* (p=0.51), *Pap smear testing every 5 years* (p=0.36) and *never having Pap smear testing* (p=0.35), all the attribute levels, as well as the attributes risk of cervical cancer, risk of genital warts, frequency of side effects and vaccine cost, were statistically significant. Preferences decreased as the risk of cervical cancer, the risk of genital warts, frequency of side effects and cost of vaccine increased.

The study results suggest that there was heterogeneity in respondents' preferences because almost all variables in the model had a statistically significant standard deviation estimate, except for the attribute levels *need for vaccine booster every 5 years* (p=0.63) and *never having Pap smear testing* (0.90). The attribute level *never having Pap smear testing* did

not have an effect on respondents' preferences, because both mean and standard deviation estimates were statistically insignificant.

On average, respondents had a WTP of about $29 to avoid receiving a *vaccine booster every 5 years*. They also valued avoiding a 1% increase risk of cervical cancer and 1% increase genital warts at $53 and $22, to, respectively. Since *vaccinating neither girls nor boys* was the most important attribute level and an indicator that respondents agree with the introduction of the HPV vaccination program, on average, respondents would have to be compensated with $463 to not give the HPV vaccine, making them no worse off, but they had a mean WTP of $303 to *vaccinate both girls and boys* (Table 4.7). Regarding willingness to trade, on average, respondents were willing to accept a 2.43% increase in genital warts risk to avoid a 1% increase in the risk of cervical cancer, and they were also willing to accept a 1.89% increase in frequency of vaccine side effects to avoid a 1% increase in the risk of genital warts. Again, the mean willingness to trade estimates clearly shows that respondents were more concerned about the risk of cervical cancer than they were about the risk of genital warts and frequency of side effects (Table 4.8).

Unlike the conditional logistic model, the MXL model is able to predict the percentage of respondents who place either a positive or a negative value on all the attribute levels. As summarized in Table 4.9, about 22% of all respondents placed a negative value on *vaccinating both girls and boys*, which means that the majority (78%) of the respondents supported *vaccinating both boys and girls*. In addition, 95% of the respondents placed a negative value on *need for vaccine booster every 5 years*, which means that the majority of respondents did not like the idea of giving a vaccine *booster every 5 years.* These estimates further emphasize the preference for having the vaccine for both girls and boys, and the dislike of children receiving a vaccine booster every 5 years.

A Likelihood Ratio Test (LRT) was performed to statistically test the model that better fits the data.[21] The test uses the log likelihood values from the two models in its estimation, and it follows a chi-square distribution. The result from the LRT allows for the rejection of the conditional logistic model, and suggests the MXL model as the better fit for the data. As such, all subsequent sub-group analyses were conducted using the MXL model, and the results from each sub-group analyses were compared across the various attributes.

### *4.5.3 Sub-Group Analyses for Mixed Effect Model*

#### *4.5.3.1 Attribute 1: Need for Vaccine Booster*

Female respondents had a significant negative preference for *having a vaccine booster every 5 years*, and a significant positive preference for *never having a vaccine booster*. On the other hand, male respondents had insignificant mean parameter estimates for all three attribute levels, Male and female respondents showed no heterogeneity in preferences for *having a vaccine booster every 5 years* (Table 4.10). Individuals within the age group 36-55 years had significant negative and positive preferences for *having a vaccine booster every 5 years* and *never having a vaccine booster*, respectively, and respondents older than 65 years had a significant negative preference for *having a vaccine booster every 5 years* (Table 4.11). With regards to education (Table 4.12), respondents with high school to some university qualification and those with university undergraduate or graduate school qualifications had a significantly positive preference for *never having a vaccine booster,* but those with high school to some university education, had a significant negative preference for *having vaccine booster every 5 years*. Individuals with university undergraduate or graduate school education had significant standard deviation estimates across all three attribute levels.

Individuals who earned an annual income of less than $20,000 had a significant negative preference for *having a vaccine booster every 5 years* and those who earned an annual income of $55,000 or more had a significant negative preference for *having a vaccine booster every 5 years* and a significant positive preference for *never having a vaccine booster*. Respondents who earned an annual income of $20,000-$54,999 had insignificant mean parameter estimates for all three attribute levels (Tables 4.13). Respondents who earned an annual income of less than $20,000 also had insignificant standard deviation estimates for all three attribute levels. Respondents with and those without children had significantly negative preferences for *having a booster vaccine every 5 years* (Table 4.14), but both groups had insignificant standard deviation estimates for this attribute level. For respondents with children, *never having a vaccine booster* did not impact their preference as both the mean and standard deviation estimates were insignificant. On the other hand, *never having a vaccine booster* had significant mean and standard deviation estimates for those without children.

None of the three attribute levels had significant mean parameter estimates for single-parent respondents, but *having a vaccine booster every 5 years* was significant for two-parent household respondents. The standard deviation estimates for *having a vaccine booster every 5*

*years* and *never having a vaccine booster* were significant for single-parent respondents. For two-parent household respondents, the standard deviation estimate for *having a vaccine booster every 10 years* was significant (Table 4.15).

The mean parameter estimates for all three attribute levels were insignificant for those who knew their children were sexually active and for those who knew their children were not sexually active. Respondents who knew their children were sexually active showed heterogeneity in preferences for *having a vaccine booster every 5 years* and *never having a vaccine booster*, whereas those who knew their children were not sexually active showed heterogeneity in preferences for *having a vaccine booster every 10 years* and *never having a vaccine booster* (Table 4.16).

Respondents who would vaccinate their child against HPV if they had one between the ages of 9-18 years had a significantly negative preference *for having a vaccine booster every 5 years* Those who indicated that they would not vaccinate their children against HPV had a significantly negative preference for *having a vaccine booster every 10 years.* Respondents who will not vaccinate their children against HPV showed heterogeneity in preferences for all three attribute levels, and those who would vaccinate showed heterogeneity only in preferences for *having a vaccine booster every 10 years* and *never having a vaccine booster* (Table 4.17).

Respondents who had not, or whose relatives had not, experienced any HPV-related illness such as abnormal Pap smear, cervical cancer or genital warts showed heterogeneity in preferences across all three attribute levels, and had a significant negative preference for *having a vaccine booster every 5 years* and a significant positive preference for *never having a vaccine booster* (Table 4.18). Those who had, or whose relatives had, experienced an HPV-related illness had insignificant mean parameter estimates for all three attribute levels, and this group exhibited heterogeneity in preferences for *having a vaccine booster every 10 years* and *never having a vaccine booster*.

Individuals who knew someone suffering from cancer and those who had stated otherwise had insignificant standard deviation estimates for *having a vaccine booster every 5 years,* and the former group had insignificant mean parameter estimates for all three attribute levels (Table 4.19). Parents with only male children and those with only female children had insignificant mean parameter estimates for all three attribute levels, and both groups of parents had insignificant standard deviation estimates for *having a vaccine booster every 5 years* (Table 4.20).

#### *4.5.3.2 Attribute 2: Frequency of Pap Smear Testing*

Female respondents had positive preferences for all four attribute levels except for *never having a Pap smear test*, but the mean parameter estimates for all the attribute levels were insignificant. Male respondents had a significantly positive preference for *Pap smear testing every 3 years and* a significantly negative preference for *having Pap smear testing every 5 years*. Both groups exhibited heterogeneity in preferences for all four attribute levels (Table 4.10). The attribute, frequency of Pap smear testing, had insignificant mean parameter estimates across all age groups (Tables 4.11).

Individuals with less than high school education and those with university undergraduate or graduate school qualifications had insignificant mean parameter estimates for all four attribute levels, but the former group had a significant standard deviation estimate for *Pap smear testing every 3 years,* and the latter group had significant standard deviation estimates for all attribute levels except *Pap smear testing every 3 years.* Those with high school to some university education had a significantly positive preference for *Pap testing every 3 years* and showed heterogeneity in preferences for the attribute levels except *Pap testing every 5 years* (Table 4.12).

Respondents who earned an annual income of less than $20,000 had a significantly positive preference for *Pap smear testing every 5 years,* and insignificant standard deviation estimates for all four attribute levels except *yearly Pap smear testing*. Those who earned an annual income of $20,000-$54,999 and $55,000 or more had significant standard deviation estimates but insignificant mean parameter estimates at all attribute levels (Tables 4.13). Only *Pap smear testing every 3 yea*rs had a positive preference and significant mean and standard deviation parameter estimates for respondents who had children. Those who indicated otherwise had insignificant mean parameters estimates, but showed heterogeneity in preferences across all attribute levels (Table 4.14).

Mean parameter estimates for frequency of Pap smear testing were insignificant for both single- and two parent-households, but both *groups* showed heterogeneity in preferences *for yearly Pap smear testing* (Table 4.15). As shown in Table 4.16, *Pap smear testing every 3 years* had a significant positive preference for parents who knew their children were sexually active. Those who knew their children were not sexually active had a significantly preference for *Pap*

*smear testing every 5 years*. Both groups exhibited heterogeneity in preferences at all four attribute levels except *never having Pap smear testing*, which had an insignificant standard deviation estimate for those who knew their children were sexually active, and *Pap smear testing every 5 years* which also had an insignificant standard deviation estimate for those who knew their children were not sexually active.

Those who would, and those who would not vaccinate their children against HPV all had insignificant mean parameter estimates at all four attribute levels, but all standard deviation estimates were significant for those who would vaccinate their children against HPV (Table 4.17). Furthermore, respondents who had, or whose relatives had, experienced an HPV-related illness had insignificant parameter estimates across all four attribute levels, but those who had not experienced an HPV-related illness had a significant positive preference for *Pap smear testing every 3 years*, and also exhibited heterogeneity in preferences for all four attribute levels (Table 4.18).

As summarized in Table 4.19, respondents who knew someone suffering from cancer had insignificant mean parameter estimates for all the attribute levels, and *Pap smear testing every 5 years* had no impact on their preference because both mean and standard deviation estimates were insignificant. However, those who did not know someone suffering from cancer had a significantly positive relative preference for *Pap smear testing every 3 years*, and also showed heterogeneity in preference at all four attribute levels. Parents with only female children had insignificant mean parameter estimates for all four attribute levels, as did parents with male only children. Preferences for both groups of parents were not affected by *Pap smear testing every 5* years (Table 4.20).

#### *4.5.3.3 Attribute 3: Target Group to Vaccinate*

With the exception of those who indicated not to vaccinate their children and those whose annual income is less than $20,000, respondents across all the subgroups had significantly positive preferences for *vaccinating girls only* and *vaccinating both girls and boys*, and a significantly negative preference for *vaccinating neither girls nor boys*. Respondents who earn an annual income of less than $20,000 had an insignificant preference for vaccinating girls only. Those who would not vaccinate their children had a significantly negative preference for *vaccinating girls only*, and a significantly positive preference for *vaccinating neither girls nor*

*boys*. They also had an insignificant negative preference for *vaccinating both girls and boys* (Figure 4.1). The result from this subgroup serves as evidence of construct validity for the study, as those who would vaccinate their children against HPV had a significant negative preference for *vaccinating neither girls nor boys*, and those who stated otherwise had a significantly positive preference for the same attribute level. Across all subgroups, respondents exhibited heterogeneity in preferences for all four attribute levels (Tables 4.10-4.20).

#### *4.5.3.4 Attributes 4-7: Continuous Variables (Cost, Side Effects, Risk of Cervical Cancer and Genital Warts)*

Across all the subgroups, respondents had significant preferences for vaccine cost, frequency of side effects, risk of cervical cancer and risk of genital warts except for respondents who earned an annual income of less than $20,000, respondents ages 56-65, those who knew their children were sexually active, single parents and those who would not vaccinate their child against HPV, who had an insignificant negative preference for frequency of side effects. In general, the preference for an HPV vaccination and screening strategy decreases as the risk of cervical cancer, genital warts, cost and frequency of side effects increases across all groups (Tables 4.10 - 4.20).

The results from the Wald test revealed significant differences between males and females for the following three variables: cost, risk of cervical cancer and genital warts. Male respondents were more averse to the risk of cervical cancer and genital warts, whereas females were more concerned about the cost of the vaccine. Difference in preferences for risk of cervical cancer was observed across all age groups. Respondents aged 36-55 years and 56-65 years were more risk-averse to cervical cancer than those in the age groups 19-35 years and >65 years. In addition, respondents who knew their children were not sexually active were more risk-averse to cervical cancer and genital warts than those whose children were sexually active.

Those who had, or whose relative had, experienced HPV-related illness were more concerned about genital warts than those who had not, or whose relative had not, experienced any HPV-related illness.

From the main mixed effect logistic model, the expected utility for the no-vaccine option was -2.13, and about 11% of all respondents would choose this option (Table 4.21). In order to determine the expected utility for the optimal quadrivalent and bivalent vaccination and

screening strategies, the following assumptions were made for both strategies: Pap testing would be every 3 years, no vaccine booster, the vaccine would be administered to both girls and boys, a 6% frequency of side effect, no out-of- pocket cost and a 70% cervical cancer risk reduction. In addition, a 90% genital warts risk reduction was assumed for the quadrivalent vaccination strategy only. Based on the above assumptions, the optimal expected utility for the quadrivalent vaccination and screening strategy was 0.80, and about 69% of the respondents would choose this option. The optimal expected utility for the bivalent vaccination and screening strategy was 0.18, with about 54% of respondents choosing this option.

Although respondents have a higher preference for the quadrivalent vaccination, the breakpoint at which the bivalent and quadrivalent vaccination strategies have the same quality gain can be determined by varying the different levels of the attribute, target group to vaccinate in both strategies while keeping the other variables in the model constant. For instance, assuming the quadrivalent vaccine is given to both girls and boys and the bivalent vaccine is administered to girls only, then the bivalent vaccine recipients would have to be given $337 for both strategies to have the same quality gain. On the other hand, if the quadrivalent vaccine is given to girls only and the bivalent vaccine to both girls and boys, then bivalent vaccine recipients would need to receive $56 to achieve the same level of satisfaction as the quadrivalent recipients, and also the bivalent vaccine recipients would have to be compensated with $196 to achieve the same level of satisfaction as the quadrivalent vaccine recipients if the vaccines are given to both girls and boys.

In conclusion, both the conditional and mixed logistic models revealed respondents' preference for the HPV vaccination and screening program, but desire for the vaccine to be administered to both girls and boys instead of girls only, which is the current recommendation. In addition, the expected utility values from the three vaccination and screening strategies suggest that the majority of the study participants were in favor of the quadrivalent vaccination option. The results from the sub-group analyses suggest that respondents across the different groups were in favor of the introduction of the HPV vaccination program, but would prefer the quadrivalent vaccine over the bivalent vaccine. The majority of respondents were concerned about the frequency of side effect, and wanted a vaccine with lifelong protection (Table 4.22).

## 4.6 Discussion

The results from the study suggest that respondents want the HPV vaccines and are in favor of the vaccination program. Both the conditional and mixed effect logistic models showed that the target group to vaccinate was the attribute with the largest impact on societal preferences. Their preference was to vaccinate both girls and boys, rather than girls only. Moreover, respondents were most averse to the attribute level, 'vaccinating neither boys nor girls', which suggests a desire to have some sort of an HPV vaccine program. These findings are in line with other studies using a survey-based methodology, which have indicated that parents would like to have HPV vaccine administered to both boys and girls since immunizing boys against HPV will protect future partners and reduce disease transmission.[22-24] While their reason for wanting the vaccine for boys could be equity-related, most economic analyses which have evaluated the cost effectiveness of vaccinating both girls and boys have shown that it is more cost effective to vaccinate girls only than to vaccinate both boys and girls.[25-28]

The expected utility values from our model showed a higher relative preference for the quadrivalent vaccination than the bivalent vaccination. The high relative preference for the quadrivalent vaccination was a result of the vaccine's ability to reduce the risk of genital warts, a benefit the bivalent vaccine does not offer. Furthermore, the conditional and mixed effect logistic models revealed a higher risk aversion to a percent increase in cervical cancer than for genital warts. In other words, they were more concerned about protection against cervical cancer than genital warts, even though the baseline risk of genital warts is 10 times higher than the baseline risk of cervical cancer. It could be that respondents were less concerned about the risk of genital warts because it is not life as threatening as cervical cancer and also less than 1% of those infected with the disease develop clinically obvious warts.[29]

With respect to vaccine-related side effects, respondents were least averse to the frequency of getting vaccine side effects when compared with their risk of getting cervical cancer and genital warts. This observation was not expected, as earlier HPV acceptability studies showed that parents were concerned about the side effects associated with the vaccines.[30, 34] However, this could be because respondents consider cervical cancer and genital warts as more serious conditions when compared to vaccine side effects or respondents are convinced of the safety of the HPV vaccine. There is currently no recommendation on a vaccine booster. The clinical trial data show protection against HPV for at least 5.5 years, but there are ongoing

studies to determine the long term immunity of the HPV vaccines.[35-43] Our study showed a significantly positive preference for never receiving the vaccine booster dose, that is, respondents preferred a vaccine that would give lifelong immunity.

The willingness to pay (WTP) estimates suggest that on average the respondents will have to be compensated $463 in order to not vaccinate, which shows their strong preference for the vaccination program. In addition, respondents were willing to pay $303 to vaccinate both girls and boys. Respondents had a mean willingness to pay $53 and $22 to avoid a percent increase in the risk of cervical cancer and genital warts, respectively. This means they will pay these amounts to avoid a 1% increase in their baseline risk of cervical cancer and genital warts. While the respondents will pay more to avoid a 1% increase in cervical cancer risk, they will, however, be willing to pay about $219 to avoid the 10% baseline risk of getting genital warts. With regards to trading perceived risk, they were willing to accept approximately 2.43% increase in genital warts risk to avoid a 1% increase in cervical cancer risk. This finding further confirms the importance of cervical cancer prevention to our study participants.

The different subgroups that were evaluated were gender, education, income, type of household (single- and two-parent family), having children, child sexuality, child gender, and previous vaccination, genital warts and cancer history. Across all these subgroups, respondents were in favor of the introduction of the HPV vaccines, but had higher relative preference for the quadrivalent vaccination. Across gender, women were indifferent to having a Pap smear test whereas men felt that testing every 3 years was adequate protection for their spouses or partners. In general, men were more concerned about the risk of cervical cancer and genital warts than women. This finding is surprising, because one would expect women to be more concerned about their risk of cervical cancer than men. As such, further research is needed to confirm this finding. On the other hand, women were more concerned about the cost of the vaccine than men. Respondents aged 36 years and older were more risk-averse to cervical cancer than the 19-35 year old respondents. A significant difference in risk of genital warts was observed across the different educational groups, respondents with university undergraduate or graduate education being the most risk-averse to genital warts.

As expected, those who had indicated that they will not vaccinate their children against HPV had a high positive preference weight for ‘vaccinating neither boy nor girls’. This finding serves as face validity for this study, as the DCE questionnaire was able to predict an expected behavior for this group of respondents. Parents who knew their children were not sexually active

were more concerned about risk of cervical cancer and genital warts than those who had indicated otherwise. This could probably be attributed to the uncertainty about their children's ability to avoid sexually transmitted infections. The parents who knew their children were sexually active were less concerned because they have probably educated their children on sexually transmitted infections, and assume their children will take precautionary measures to avoid them. In addition, only respondents who were 65 years and older, those with an annual income of $20,000-$55,000, females, those with children, single parents, those who knew their children were sexually active and those who knew their children were not sexually active, and respondents who had, or whose relatives had, experienced HPV-related illness, preferred yearly Pap smear testing. Even though these respondents had a positive preference for yearly Pap smear testing, the attribute level was insignificant across all the groups.

## 4.7 Conclusions

Although there are possible limitations to this study (see Chapter 5), our results revealed that respondents wanted some sort of an HPV vaccination program, and they were willing to pay extra to receive the quadrivalent vaccine in order to benefit from the additional protection against genital warts. With that said, respondents were willing to accept an increased risk of genital warts and vaccine side effects to avoid an increased risk of cervical cancer. Finally, our study findings will provide policy makers with an insight into the attributes that are important to society, allowing them to select targeted messaging plans which will be aimed at increasing the vaccine uptake and to determine whether to administer the quadrivalent or bivalent vaccine for the public health program.

**Table 4.1**: Attributes and levels

| Attribute | Level |
|---|---|
| Need for vaccine booster | Every 5 years, Every 10 years, Never |
| Frequency of Pap smear testing | Yearly, Every 3 years, Every 5 years, Never |
| Target group to vaccinate | Girls only, Both girls and boys, Neither |
| Frequency of side effects | 0%, 2%, 6%, 10%, 14% |
| Lifetime risk of cervical cancer | 0%, 2%, 5%, 10% |
| Lifetime risk of genital warts | 0%, 2%, 5%, 10% |
| Cost | $0, $200, $400, $600 |

**Table 4.2**: Example of a choice set

| Attribute | Option A | Option B | Neither |
|---|---|---|---|
| **Lifetime CC risk** | 2 in 100 | 5 in 100 | |
| **Pap smear frequency** | Every 5 years | Every 3 years | |
| **Lifetime GW risk** | 2 in 100 | 5 in 100 | |
| **Need for booster** | Never | Every 10 years | |
| **Target group** | Both boys and girls | Both girls and boys | |
| **Frequency of side effects** | 6 in 100 | 10 in 100 | |
| **Vaccine cost** | Insurance | $400 | |
| **Which one would you prefer** | ☐ | ☐ | ☐ |

**Table 4.3**: Demographic information for all respondents who completed the survey

| Characteristics | N=1157 |
|---|---|
| Age mean(SD) | 44(15.0) |
| Females N (%) | 569(49) |
| **Education** N (%) | |
| Less than high school | 102(9) |
| High school/Trade school/Some University | 913(79) |
| University/Graduate school | 142(12) |
| **Income N (%)** | |
| <$20,000 | 91(8) |
| $20,000-$54,999 | 363(31) |
| ≥ $55,000 | 703(61) |
| **Province N (%)** | |
| Atlantic | 115(10) |
| British Columbia | 224(19) |
| Prairies | 218(19) |
| Ontario | 528(46) |
| Quebec | 72(6) |
| **Have Children** N (%) | |
| Yes | 532(46) |
| No | 625(54) |
| **Type of Household** N (%) | |
| Single Parent | 89(17) |
| Two Parent | 366(68) |
| Guardian | 3(1) |
| Extended | 15(3) |
| Blended | 57(11) |
| **Childhood Vaccines** N (%) | |
| All | 458(86) |
| Some | 64(13) |
| None | 10(2) |
| **Child Sexually Active** N (%) | |
| Yes | 101(19) |
| No | 374(70) |
| Don't know | 42(8) |
| PNTA | 15(3) |
| **Would you vaccinate child against HPV** N (%) | |
| Yes | 817(70) |
| No | 123(11) |
| Don't know | 217(19) |
| **Have you or your relative experienced HPV related illness** N (%) | |
| Yes | 139(13) |
| No | 948(80) |
| Don't Know | 56(5) |
| *PNTA | 14(2) |

| Characteristics | N=1157 |
|---|---|
| **Do you know any one with cancer N (%)** | |
| Yes | 321(28) |
| No | 836(72) |
| **Age of children N(%)** | |
| Under 6 only | 98(8) |
| 6-12 only | 91(8) |
| 13-17 only | 123(11) |
| Under 6 and 6-12 | 48(4) |
| Under 6 and 13-17 | 8(0.7) |
| 6-12 and 13-17 | 42(4) |
| All 3 | 5(0.4) |
| None under 18 | 742(64) |
| **Religious Affiliation N (%)** | |
| Evangelical Christian | 94(8) |
| Catholic Christian | 295(26) |
| Hindu | 5(0.43) |
| Jewish | 19(2) |
| Muslim | 6(0.52) |
| Protestant | 280(24) |
| Other | 88(8) |
| None | 88(8) |
| *PNTA | 282(24) |
| **Religion guides in daily decision N (%)** | |
| All of the time | 98(8) |
| Most of the time | 182(16) |
| A little of the time | 358(31) |
| None of the time | 519(45) |
| **Perceptions of vaccinating against HPV N (%)** | |
| Increase health care cost | 265(12) |
| Decrease genital warts | 678(30) |
| Increase number of sexual partners | 114(5) |
| Decrease cervical cancer | 877(38) |
| Increase side effects | 190(8) |
| Other[1] | 44(2) |
| None | 121(5) |

*PNTA: Prefer not to answer

[1] Majority of respondents who selected other stated decrease in health care costs.

**Table 4.4**: Parameter estimates for both Mixed Effect Logistic (MLM) and Conditional Logistic Models (CLM)

| | **CLM** | **MLM** | |
|---|---|---|---|
| **Parameter** | **Mean (StdErr)** | **Mean (StdErr)** | **SD (StdErr)** |
| **Need for vaccine booster** | | | |
| Every 5 years | -0.06* (0.019) | -0.09* (0.025) | 0.06 (0.120) |
| Every 10 years | 0.02 (0.019) | 0.01 (0.028) | 0.40* (0.034) |
| Never | 0.04* (0.018) | 0.09* (0.027) | 0.34* (0.129) |
| **Frequency of Pap testing** | | | |
| Yearly | -0.02 (0.023) | -0.02 (0.034) | 0.51* (0.043) |
| Every 3 years | 0.07* (0.023) | 0.09* (0.032) | 0.30* (0.061) |
| Every 5 Years | -0.06* (0.024) | -0.03 (0.032) | 0.22* (0.074) |
| Never | 0.01 (0.024) | -0.03 (0.038) | 0.01 (0.097) |
| **Target group to vaccinate** | | | |
| Girls only | 0.17* (0.020) | 0.51* (0.048) | 1.14* (0.051) |
| Both girls and boys | 0.50* (0.021) | 0.96* (0.050) | 1.24* (0.050) |
| Neither | -0.67* (0.033) | -1.47* (0.072) | 2.39* (0.066) |
| **Frequency of side effects‡** | -0.02* (0.003) | -0.04* (0.004) | |
| **Cost(per $100)** | -0.20* (0.00007) | -0.32* (0.010) | |
| **Lifetime risk of cervical cancer‡** | -0.11* (0.004) | -0.17* (0.006) | |
| **Lifetime risk of genital wart‡** | -0.04* (0.003) | -0.07* (0.005) | |
| ***Log Likelihood*** | ***-11674*** | ***-9014.5*** | |

‡: per 1% increase, *: Significant at 5% level, StdErr: Standard Error

**Table 4. 5**: Willingness-To-Pay (WTP) estimates for conditional logistic model

| **Parameter** | **WTP($)** |
|---|---|
| Need for vaccine booster every 5 years | -27 |
| Never having vaccine booster | 18 |
| Yearly Pap smear testing | -11 |
| Pap testing every 3 yrs | 34 |
| Target both girls and boys | 236 |
| Vaccinating neither girls nor boys | -318 |
| Frequency of side Effects (per 1% increase) | -11 |
| Lifetime risk of cervical cancer (per 1% increase) | -54 |
| Lifetime risk of genital warts (per 1% increase) | -20 |

WTP: Willingness To Pay
WTP= $-(\beta_{attribute1}/\beta_{cost})$

**Table 4.6**: Willingness to trade values for genital warts and side effect using estimates from the conditional logistic model

| Parameter | $WTT_1$ Genital Wart (%) | $WTT_2$ Side Effects (%) |
|---|---|---|
| Lifetime risk of cervical cancer | -2.70 | -4.75 |
| Lifetime risk of genital warts | | -1.77 |
| Frequency of side effects | -0.57 | |

WTT: Willingness To Trade

$WTT_1 = -(\beta_{attribute1}/\beta_{genital\ warts})$

$WTT_2 = -(\beta_{attribute1}/\beta_{side\ effects})$

**Table 4.7**: Willingness-To-Pay (WTP) estimates for mixed effect logistic model

| **Parameter** | **MWTP($)** |
|---|---|
| Need for vaccine booster every 5 years | -29 |
| Never having vaccine booster | 27 |
| Yearly Pap smear testing | -7 |
| Pap testing every 3 yrs | 27 |
| Target both girls and boys | 303 |
| Vaccinating neither girls nor boys | -463 |
| Frequency of side effects | -12 |
| Lifetime risk of cervical cancer | -53 |
| Lifetime risk of genital warts | -22 |

MWTP: Mean Willingness –To- Pay
MWTP= $-(\beta_{attribute1}/\beta_{cost})$

**Table 4.8**: Willingness to trade values for genital warts and side effects using estimates from the mixed effect logistic model

| Parameter | $MWTT_1$ Genital Warts (%) | $MWTT_2$ Side Effect (%) |
|---|---|---|
| Lifetime risk of cervical cancer | -2.43 | -4.60 |
| Lifetime risk of genital warts | | -1.89 |
| Frequency of side effects | -0.53 | |

MWTT: Willingness To Trade

$MWTT_1 = -(\beta_{attribute1}/\beta_{genital\ warts})$

$MWTT_2 = -(\beta_{attribute1}/\beta_{side\ effects})$

**Table 4.9**: Share of the study population who placed negative values on the attributes

| Parameter | Percentage of respondents placing negative values |
|---|---|
| **Need for vaccine booster** | |
| Every 5 years | 95 |
| Every 10 years | 49 |
| Never | 40 |
| **Frequency of Pap smear testing** | |
| Yearly | 52 |
| Every 3 years | 39 |
| Every 5 years | 55 |
| Never | 100 |
| **Target group to vaccinate** | |
| Girls only | 33 |
| Both girls and boys | 22 |
| Neither | 73 |

**Table 4.10**: Sub-group analyses for males and females

| | Females (N=569) | | | | Males (N=588) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.13* | 0.034 | 0.16 | 0.08 | -0.06 | 0.033 | 0.08 | 0.113 |
| Every 10 years | 0.03 | 0.039 | 0.40* | 0.05 | -0.01 | 0.039 | 0.40* | 0.049 |
| Never | 0.11* | 0.039 | 0.24* | 0.10 | 0.07 | 0.038 | 0.47* | 0.121 |
| **Frequency of Pap smear Testing** | | | | | | | | |
| Yearly | 0.02 | 0.050 | 0.59* | 0.06 | -0.06 | 0.046 | 0.42* | 0.067 |
| Every 3 years | 0.04 | 0.044 | 0.28* | 0.10 | 0.13* | 0.045 | 0.32* | 0.081 |
| Every 5 years | 0.05 | 0.045 | 0.25* | 0.10 | -0.11* | 0.045 | 0.23* | 0.110 |
| Never | -0.10 | 0.055 | 1.12* | 0.15 | 0.04 | 0.052 | 0.98* | 0.136 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.60* | 0.068 | 1.17* | 0.07 | 0.45* | 0.067 | 1.11* | 0.069 |
| Both girls and boys | 1.08* | 0.069 | 1.14* | 0.07 | 0.82* | 0.072 | 1.32* | 0.075 |
| Neither | -1.68* | 0.104 | 2.32* | 0.09 | -1.27* | 0.100 | 2.43* | 0.094 |
| **Frequency of side effects**‡ | -0.04* | 0.006 | | | -0.04* | 0.006 | | |
| **Lifetime risk of cervical cancer** ‡ | -0.18* | 0.008 | | | -0.16* | 0.008 | | |
| **Lifetime risk of genital warts**‡ | -0.07* | 0.007 | | | -0.07* | 0.007 | | |
| **Vaccine cost (per $100)** | -0.32* | 0.014 | | | -0.32* | 0.014 | | |

‡ 1% increase , * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 4.11:** Sub-group analyses for age groups 19-35years, 36-55 years, 56-65 years and >65years

| | 19-35 years (N=363) | | 36-55 years (N=532) | | 56-65 year (N=127) | | >65 years (N=135) | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean(SE)** | **Stdev(SE)** | **Mean(SE)** | **Stdev(SE)** | **Mean(SE)** | **Stdev(SE)** | **Mean(SE)** | **Stdev(SE)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.06(0.040) | 0.12(0.119) | -0.08*(0.036) | 0.07*(0.111) | -0.12(0.082) | 0.26(0.168) | -0.25*(0.073) | 0.14(0.233) |
| Every 10 years | -0.01(0.045) | 0.33*(0.063) | -0.02(0.043) | 0.41*(0.054) | 0.08(0.095) | 0.54*(0.112) | 0.14(0.080) | 0.37*(0.113) |
| Never | 0.07(0.044) | 0.22(0.145) | 0.10*(0.042) | 0.34*(0.123) | 0.04(0.095) | 0.80*(0.190) | 0.11(0.078) | 0.51*(0.233) |
| **Frequency of Pap smear Testing** | | | | | | | | |
| Yearly | -0.03(0.055) | 0.41*(0.073) | -0.01(0.053) | 0.55*(0.064) | -0.005(0.114) | 0.63*(0.139) | 0.01(0.105) | 0.63*(0.129) |
| Every 3 years | 0.07(0.051) | 0.19(0.124) | 0.07(0.049) | 0.35*(0.084) | 0.13(0.105) | 0.33(0.308) | 0.18(0.094) | 0.33(0.178) |
| Every 5 years | 0.004(0.052) | 0.14(0.138) | -0.05(0.048) | 0.17(0.138) | -0.08(0.116) | 0.57*(0.169) | -0.05(0.096) | 0.32*(0.156) |
| Never | -0.03(0.059) | 0.45*(0.204) | -0.01(0.059) | 0.73*(0.181 | -0.04(0.135) | 1.54*(0.319) | -0.14(0.118) | 0.02(0.250) |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.58*(0.071) | 0.92*(0.071) | 0.40*(0.080) | 1.34*(0.088) | 0.65*(0.146) | 1.06*(0.160) | 0.50*(0.138) | 1.24*(0.151) |
| Both girls and boys | 0.90*(0.079) | 1.10*(0.075) | 0.89*(0.076) | 1.23*(0.078) | 1.21*(0.191) | 1.66*(0.192) | 1.16*(0.153) | 1.27*(0.143) |
| Neither | -1.48*(0.115) | 2.02*(0.100) | -1.29*(0.111) | 2.56*(0.107) | -1.86*(0.257) | 2.71*(0.239) | -1.66*(0.222) | 2.51*(0.214) |
| **Frequency of side effects**‡ | -0.05*(0.007) | | -0.03*(0.006) | | -0.02(0.013) | | -0.05*(0.012) | |
| **Lifetime risk of cervical cancer**‡ | -0.26*(0.015) | | -0.36*(0.015) | | -0.37*(0.034) | | -0.32*(0.030) | |
| **Lifetime risk of genital warts**‡ | -0.17*(0.009) | | -0.18*(0.009) | | -0.17*(0.018) | | -0.15*(0.016) | |
| **Vaccine cost (per $100)** | -0.06*(0.008) | | -0.08*(0.008) | | -0.05*(0.017) | | -0.08*(0.015) | |

‡ 1% increase , * significant at 5% level , SE: Standard Error, Stdev: Standard deviation,

**Table 4.12**: Sub-group analyses for all levels of education

| | Less than high School (N=102) | | High school to some University(N=913) | | University or Graduate school (N=142) | |
|---|---|---|---|---|---|---|
| **Parameter** | **Mean(SE)** | **Stdev(SE)** | **Mean(SE)** | **Stdev(SE)** | **Mean(SE)** | **Stdev(SE)** |
| **Need for vaccine booster** | | | | | | |
| Every 5 years | -0.15(0.082) | 0.11(0.373) | -0.09*(0.027) | 0.08(0.103) | -0.07(0.072) | 0.31*(0.105) |
| Every 10 years | -0.02(0.09) | 0.34*(0.129) | 0.03(0.032) | 0.42*(0.04) | -0.12(0.078) | 0.34*(0.104) |
| Never | 0.17(0.088) | 0.45(0.364) | 0.06*(0.031) | 0.50*(0.104) | 0.19*(0.079) | 0.64*(0.144) |
| **Frequency of Pap smear Testing** | | | | | | |
| Yearly | -0.04(0.106) | 0.31 (0.176) | -0.002(0.039) | 0.57*(0.047) | -0.09(0.095) | 0.42*(0.133) |
| Every 3 years | 0.14(0.111) | 0.39*(0.166) | 0.07*(0.036) | 0.34*(0.065) | 0.15(0.086) | 0.13(0.225) |
| Every 5 years | -0.05(0.109) | 0.29(0.202) | -0.01(0.036) | 0.18(0.113) | -0.14(0.096) | 0.38*(0.153) |
| Never | -0.05(0.125) | 0.37(0.246) | -0.06(0.044) | 1.09*(0.131) | 0.09(0.105) | 0.67*(0.312) |
| **Target group to vaccinate** | | | | | | |
| Girls only | 0.43*(0.172) | 1.23*(0.18) | 0.51*(0.053) | 1.12*(0.055) | 0.51*(0.144) | 1.26*(0.159) |
| Both girls and boys | 0.95*(0.177) | 1.26*(0.181) | 0.98*(0.056) | 1.24*(0.056) | 0.90*(0.141) | 1.21*(0.146) |
| Neither | -1.38*(0.248) | 2.50*(0.229) | -1.49*(0.082) | 2.36*(0.074) | -1.41*(0.209) | 2.47*(0.195) |
| **Frequency of side effects**‡ | -0.04*(0.013) | | -0.04*(0.005) | | -0.03*(0.012) | |
| **Lifetime risk of cervical cancer**‡ | -0.29*(0.031) | | -0.34*(0.011) | | -0.22*(0.026) | |
| **Lifetime risk of genital warts**‡ | -0.13*(0.018) | | -0.17*(0.006) | | -0.20*(0.016) | |
| **Vaccine cost (per $100)** | -0.05*(0.017) | | -0.08*(0.006) | | -0.04*(0.014) | |

‡ 1% increase , * significant at 5% level, SE: Standard Error, Stdev: Standard deviation

**Table 4.13:** Sub-group analyses for all levels of annual income.

| | <$20,000 (N=91) | | $20,000-$54,999 (N=363) | | ≥$55,000 (N =703) | |
|---|---|---|---|---|---|---|
| **Parameter** | **Mean(SE)** | **Stdev(SE)** | **Mean(SE)** | **Stdev(SE)** | **Mean** | **Stdev(mean)** |
| **Need for vaccine booster** | | | | | | |
| Every 5 years | -0.20*(0.089) | 0.005(0.303) | -0.03(0.044) | 0.03(0.104) | -0.12*(0.031) | 0.21*(0.062) |
| Every 10 years | 0.11(0.092) | 0.20 (0.189) | -0.05(0.052) | 0.41*(0.064) | 0.02(0.035) | 0.41*(0.045) |
| Never | 0.09(0.091) | 0.20(0.351) | 0.08(0.050) | 0.44*(0.123) | 0.09*(0.035) | 0.62*(0.074) |
| **Frequency of Pap smear Testing** | | | | | | |
| Yearly | -0.13(0.138) | 0.65*(0.133) | 0.01(0.063) | 0.54*(0.079) | -0.02(0.043) | 0.50*(0.054) |
| Every 3 years | 0.09(0.113) | 0.02(0.380) | 0.11(0.059) | 0.33*(0.109) | 0.07(0.040) | 0.30*(0.077) |
| Every 5 years | 0.24*(0.115) | 0.09(0.366) | -0.06(0.060) | 0.26*(0.122) | -0.05(0.040) | 0.25*(0.088) |
| Never | -0.20(0.145) | 0.58(0.632) | -0.05(0.071) | 1.13*(0.174) | -0.01(0.048) | 1.05*(0.121) |
| **Target group to vaccinate** | | | | | | |
| Girls only | 0.22(0.180) | 1.17*(0.196) | 0.43*(0.095) | 1.29*(0.096) | 0.59*(0.057) | 1.07*(0.060) |
| Both girls and boys | 0.91*(0.230) | 1.65*(0.227) | 0.87*(0.094) | 1.31*(0.097) | 1.02*(0.061) | 1.14*(0.059) |
| Neither | -1.13*(0.303) | 2.82*(0.290) | -1.30*(0.136) | 2.59*(0.129) | -1.61*(0.091) | 2.21*(0.080) |
| **Frequency of side effects**‡ | -0.02(0.015) | | -0.03*(0.008) | | -0.04*(0.005) | |
| **Lifetime risk of cervical cancer**‡ | -0.31*(0.035) | | -0.36*(0.019) | | -0.30*(0.012) | |
| **Lifetime risk of genital warts**‡ | -0.15*(0.019) | | -0.16*(0.010) | | -0.18*(0.007) | |
| **Vaccine cost (per $100)** | -0.06*(0.019) | | -0.07*(0.009) | | -0.07*(0.006) | |

‡ 1% increase, * significant at 5% level , SE: Standard Error, Stdev: Standard deviation

**Table 4.14**: Sub-group analyses for those with and without children

| | Have Children (N=532) | | | | No Children (N=625) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.08* | 0.036 | 0.10 | 0.173 | -0.10* | 0.032 | 0.06 | 0.128 |
| Every 10 years | 0.00040 | 0.042 | 0.40* | 0.052 | 0.01 | 0.038 | 0.41* | 0.047 |
| Never | 0.08 | 0.040 | 0.31 | 0.189 | 0.10* | 0.036 | 0.36* | 0.141 |
| **Frequency of Pap smear Testing** | | | | | | | | |
| Yearly | 0.02 | 0.050 | 0.51* | 0.064 | -0.04 | 0.046 | 0.53* | 0.058 |
| Every 3 years | 0.10* | 0.047 | 0.32* | 0.091 | 0.07 | 0.043 | 0.32* | 0.076 |
| Every 5 years | -0.08 | 0.047 | 0.19 | 0.115 | 0.01 | 0.043 | 0.23* | 0.112 |
| Never | -0.04 | 0.056 | 0.64* | 0.164 | -0.04 | 0.052 | 0.44* | 0.158 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.53* | 0.070 | 1.11* | 0.075 | 0.48* | 0.065 | 1.16* | 0.067 |
| Both girls and boys | 0.87* | 0.078 | 1.35* | 0.080 | 1.00* | 0.065 | 1.16* | 0.062 |
| Neither | -1.40* | 0.108 | 2.46* | 0.101 | -1.49* | 0.097 | 2.32* | 0.089 |
| **Frequency of side effects**‡ | -0.03* | 0.006 | | | -0.04* | 0.006 | | |
| **Lifetime risk of cervical cancer**‡ | -0.31* | 0.014 | | | -0.33* | 0.013 | | |
| **Lifetime risk of genital warts**‡ | -0.17* | 0.008 | | | -0.17* | 0.007 | | |
| **Vaccine cost (per $100)** | -0.06* | 0.007 | | | -0.08* | 0.007 | | |

‡ 1% increase , * significant at 5% level , SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 4.15**: Sub-group analyses for single-and two-parent households

| | Single Parents (N=89) | | | | Two Parents (N=366) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.15 | 0.103 | 0.45* | 0.126 | -0.09* | 0.043 | 0.06 | 0.166 |
| Every 10 years | -0.05 | 0.097 | 0.27 | 0.166 | 0.06 | 0.050 | 0.41* | 0.062 |
| Never | 0.20 | 0.108 | 0.73* | 0.191 | 0.03 | 0.049 | 0.35 | 0.181 |
| **Frequency of Pap Smear testing** | | | | | | | | |
| Yearly | 0.10 | 0.128 | 0.52* | 0.165 | -0.02 | 0.062 | 0.55* | 0.080 |
| Every 3 years | 0.07 | 0.118 | 0.35 | 0.224 | 0.11 | 0.058 | 0.37* | 0.098 |
| Every 5 years | 0.003 | 0.119 | 0.35 | 0.210 | -0.08 | 0.057 | 0.20 | 0.136 |
| Never | -0.17 | 0.143 | 1.22* | 0.369 | -0.01 | 0.069 | 0.02 | 0.174 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.62* | 0.187 | 1.33* | 0.206 | 0.55* | 0.081 | 1.03* | 0.088 |
| Both girls and boys | 1.07* | 0.199 | 1.46* | 0.212 | 0.78* | 0.097 | 1.38* | 0.101 |
| Neither | -1.70* | 0.272 | 2.79* | 0.288 | -1.33* | 0.128 | 2.41* | 0.120 |
| **Frequency of side effects**‡ | -0.01 | 0.015 | | | -0.03* | 0.007 | | |
| **Lifetime risk of cervical cancer**‡ | -0.28* | 0.037 | | | -0.33* | 0.018 | | |
| **Lifetime risk of genital warts**‡ | -0.16* | 0.021 | | | -0.18* | 0.010 | | |
| **Vaccine cost (per $100)** | -0.05* | 0.018 | | | -0.07* | 0.009 | | |

‡ 1% increase , * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 4.16**: Sub-group analyses for those who knew their children were (not) sexually active

| | Child Sexually Active (N=101) | | | | Child not Sexually Active (N=374) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.11 | 0.088 | 0.42* | 0.120 | -0.08 | 0.044 | 0.10 | 0.114 |
| Every 10 years | 0.06 | 0.085 | 0.23 | 0.154 | -0.01 | 0.052 | 0.47* | 0.062 |
| Never | 0.03 | 0.093 | 0.35* | 0.165 | 0.08 | 0.051 | 0.57* | 0.128 |
| **Frequency of Pap smear testing** | | | | | | | | |
| Yearly | 0.08 | 0.105 | 0.36* | 0.161 | 0.05 | 0.062 | 0.53* | 0.086 |
| Every 3 years | 0.23* | 0.110 | 0.45* | 0.159 | 0.08 | 0.060 | 0.41* | 0.092 |
| Every 5 years | -0.12 | 0.108 | 0.34* | 0.162 | -0.12* | 0.057 | 0.08 | 0.347 |
| Never | -0.01 | 0.126 | 0.02 | 0.253 | 0.004 | 0.070 | 0.85* | 0.362 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.58* | 0.154 | 1.06* | 0.164 | 0.52* | 0.087 | 1.12* | 0.093 |
| Both girls and boys | 0.97* | 0.167 | 1.29* | 0.171 | 0.77* | 0.098 | 1.36* | 0.101 |
| Neither | -1.33* | 0.246 | 2.41* | 0.227 | -1.29* | 0.134 | 2.48* | 0.120 |
| **Frequency of side effects**‡ | -0.02 | 0.013 | | | -0.03* | 0.007 | | |
| **Lifetime risk of cervical cancer**‡ | -0.25* | 0.030 | | | -0.33* | 0.018 | | |
| **Lifetime risk of genital. warts**‡ | -0.11* | 0.017 | | | -0.19* | 0.011 | | |
| **Vaccine cost (per $100)** | -0.06* | 0.016 | | | -0.07* | 0.009 | | |

‡ 1% increase, * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 4.17**: Sub-group analyses for those who would (not) vaccinate their children against HPV

| | Will vaccinate against HPV (N=817) | | | | Will not vaccinate (N=123) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.11* | 0.026 | 0.11 | 0.069 | 0.06 | 0.154 | 0.48* | 0.172 |
| Every 10 years | 0.06 | 0.030 | 0.37* | 0.040 | -0.32* | 0.153 | 0.49* | 0.175 |
| Never | 0.05 | 0.030 | 0.48* | 0.076 | 0.26 | 0.162 | 0.96* | 0.267 |
| **Frequency of Pap smear testing** | | | | | | | | |
| Yearly | -0.06 | 0.037 | 0.46* | 0.047 | -0.09 | 0.205 | 0.87* | 0.182 |
| Every 3 years | 0.07 | 0.035 | 0.30* | 0.068 | 0.24 | 0.157 | 0.16 | 0.246 |
| Every 5 years | -0.02 | 0.036 | 0.26* | 0.073 | -0.21 | 0.163 | 0.02 | 0.298 |
| Never | 0.01 | 0.042 | 0.51* | 0.116 | 0.06 | 0.218 | 0.70 | 0.420 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.73* | 0.049 | 0.94* | 0.047 | -1.69* | 0.475 | 2.44* | 0.357 |
| Both girls and boys | 1.16* | 0.053 | 1.04* | 0.047 | -0.13* | 0.289 | 1.76* | 0.239 |
| Neither | -1.89* | 0.082 | 1.98* | 0.067 | 1.82* | 0.435 | 4.19* | 0.461 |
| **Frequency of side effects**‡ | -0.03* | 0.005 | | | -0.02 | 0.021 | | |
| **Lifetime risk of cervical cancer**‡ | -0.30* | 0.011 | | | -0.50* | 0.056 | | |
| **Lifetime risk of genital warts**‡ | -0.17* | 0.006 | | | -0.14* | 0.027 | | |
| **Vaccine cost (per $100)** | -0.07* | 0.006 | | | -0.03* | 0.027 | | |

‡ 1% increase, * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 4.18**: Sub-group analyses for those who or their relatives had (not) experienced any HPV related illness

| | Have Experienced HPV Disease (N=139) | | | | Have not Experienced HPV Disease (N=948) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.11 | 0.07 | 0.12 | 0.18 | -0.09* | 0.03 | 0.15* | 0.07 |
| Every 10 years | 0.11 | 0.08 | 0.47* | 0.10 | -0.02 | 0.03 | 0.38* | 0.04 |
| Never | -0.01 | 0.08 | 0.60* | 0.20 | 0.10* | 0.03 | 0.23* | 0.08 |
| **Frequency of Pap smear testing** | | | | | | | | |
| Yearly | 0.03 | 0.10 | 0.50* | 0.12 | -0.02 | 0.04 | 0.54* | 0.05 |
| Every 3 years | 0.04 | 0.09 | 0.03 | 0.29 | 0.08* | 0.04 | 0.31* | 0.07 |
| Every 5 years | -0.11 | 0.09 | 0.19 | 0.21 | -0.03 | 0.04 | 0.27* | 0.07 |
| Never | 0.04 | 0.10 | 0.66 | 0.37 | -0.04 | 0.04 | 0.57* | 0.12 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.66* | 0.13 | 1.06* | 0.13 | 0.52* | 0.05 | 1.16* | 0.06 |
| Both girls and boys | 1.18* | 0.14 | 1.12* | 0.12 | 0.94* | 0.06 | 1.22* | 0.05 |
| Neither | -1.84* | 0.21 | 2.18* | 0.18 | -1.46* | 0.08 | 2.38* | 0.07 |
| **Frequency of side effects**‡ | -0.04* | 0.01 | | | -0.04* | 0.00 | | |
| **Lifetime risk of cancer cancer**‡ | -0.35* | 0.03 | | | -0.31* | 0.01 | | |
| **Lifetime risk of genital warts**‡ | -0.21* | 0.02 | | | -0.16* | 0.01 | | |
| **Vaccine cost (per $100)** | -0.07* | 0.01 | | | -0.07* | 0.01 | | |

‡ 1% increase , * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation estimate

**Table 4 19**: Sub-group analyses for those who do (not) know someone suffering from cancer

| | Know cancer person (N=321) | | | | Don't know cancer person (N=836) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.06 | 0.044 | 0.06 | 0.128 | -0.10* | 0.028 | 0.11 | 0.084 |
| Every 10 years | 0.01 | 0.052 | 0.41* | 0.063* | 0.0002 | 0.033 | 0.40* | 0.042 |
| Never | 0.06 | 0.050 | 0.48* | 0.140* | 0.10* | 0.032 | 0.29* | 0.097 |
| **Frequency of Pap smear testing** | | | | | | | | |
| Yearly | -0.01 | 0.062 | 0.48* | 0.074* | -0.02 | 0.041 | 0.54* | 0.052 |
| Every 3 years | 0.07 | 0.059 | 0.28* | 0.112* | 0.09* | 0.038 | 0.29* | 0.078 |
| Every 5 years | -0.01 | 0.059 | 0.23 | 0.131 | -0.04 | 0.038 | 0.24* | 0.084 |
| Never | -0.05 | 0.069 | 1.00* | 0.176* | -0.04 | 0.045 | 0.49* | 0.137 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.56* | 0.080 | 0.97* | 0.082* | 0.49* | 0.058 | 1.22* | 0.061 |
| Both girls and boys | 1.04* | 0.087 | 1.12* | 0.084* | 0.91* | 0.061 | 1.27* | 0.060 |
| Neither | -1.60* | 0.125 | 2.10* | 0.111* | -1.40* | 0.088 | 2.49* | 0.082 |
| **Frequency of side effects**‡ | -0.04* | 0.008 | | | -0.03* | 0.005 | | |
| **Lifetime risk of cervical cancer**‡ | -0.33* | 0.018 | | | -0.31* | 0.012 | | |
| **Lifetime risk of genital warts**‡ | -0.17* | 0.010 | | | -0.17* | 0.007 | | |
| **Vaccine cost (per $100)** | -0.07* | 0.010 | | | -0.07* | 0.006 | | |

‡ 1% increase , * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 4.20**: Sub-group analyses for those with girls only and boys only children

| | Parents with girls only (N=163) | | | | Parents with boys only (N=149) | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** | **Mean** | **SE(Mean)** | **Stdev** | **SE(Stdev)** |
| **Need for vaccine booster** | | | | | | | | |
| Every 5 years | -0.12 | 0.068 | 0.02 | 0.117 | -0.05 | 0.069 | 0.22 | 0.1261 |
| Every 10 years | 0.04 | 0.079 | 0.41* | 0.103 | -0.08 | 0.073 | 0.31* | 0.1043 |
| Never | 0.08 | 0.077 | 0.43* | 0.164 | 0.13 | 0.073 | 0.53* | 0.152873 |
| **Frequency of Pap smear testing** | | | | | | | | |
| Yearly | 0.002 | 0.101 | 0.63* | 0.131 | -0.01 | 0.092 | 0.46* | 0.1199 |
| Every 3 years | 0.09 | 0.098 | 0.54* | 0.130 | 0.12 | 0.091 | 0.42* | 0.1435 |
| Every 5 years | 0.01 | 0.091 | 0.21 | 0.208 | -0.03 | 0.088 | 0.26 | 0.2016 |
| Never | -0.10 | 0.119 | 1.38* | 0.279 | -0.09 | 0.106 | 1.14* | 0.260133 |
| **Target group to vaccinate** | | | | | | | | |
| Girls only | 0.66* | 0.142 | 1.26* | 0.172 | 0.64* | 0.117 | 0.92* | 0.1193 |
| Both girls and boys | 1.04* | 0.168 | 1.54* | 0.192 | 0.84* | 0.149 | 1.46* | 0.1517 |
| Neither | -1.69* | 0.223 | 2.81* | 0.218 | -1.48* | 0.199 | 2.39* | 0.185845 |
| **Frequency of side effects**‡ | -0.06* | 0.012 | | | -0.003* | 0.011 | | |
| **Lifetime risk of cervical cancer**‡ | -0.37* | 0.030 | | | -0.30* | 0.026 | | |
| **Lifetime risk of genital warts**‡ | -0.20* | 0.017 | | | -0.16* | 0.015 | | |
| **Vaccine cost (per $100)** | -0.05* | 0.014 | | | -0.04* | 0.014 | | |

‡ 1% increase , * significant at 5% level, SE: Standard Error, Stdev: Standard deviation, SE(Mean): Standard error of mean, SE(Stdev): Standard error of standard deviation

**Table 21**: Expected utilities for possible HPV vaccination and screening strategies

| Attribute | No Vaccination | Quadrivalent Vaccination | Bivalent Vaccination |
|---|---|---|---|
| Vaccine booster (yearly) | Never | Never | Never |
| Pap smear testing (yearly) | 3 | 3 | 3 |
| Target group to vaccinate | Neither | Girls and Boys | Girls and Boys |
| Cost ($) | 0 | 0 | 0 |
| Cervical cancer risk (%) | 0.78 | 0.23 | 0.23 |
| Genital warts risk (%) | 10 | 1 | 10 |
| Side Effects (%) | 0 | 6 | 6 |
| Mean preference weight | -2.13 | 0.80 | 0.18 |
| Choice probability | 11% | 69% | 54% |

Assuming a 70% cervical cancer risk reduction, a 90% genital warts risk reduction for quadrivalent vaccination and 6% frequency of side effect

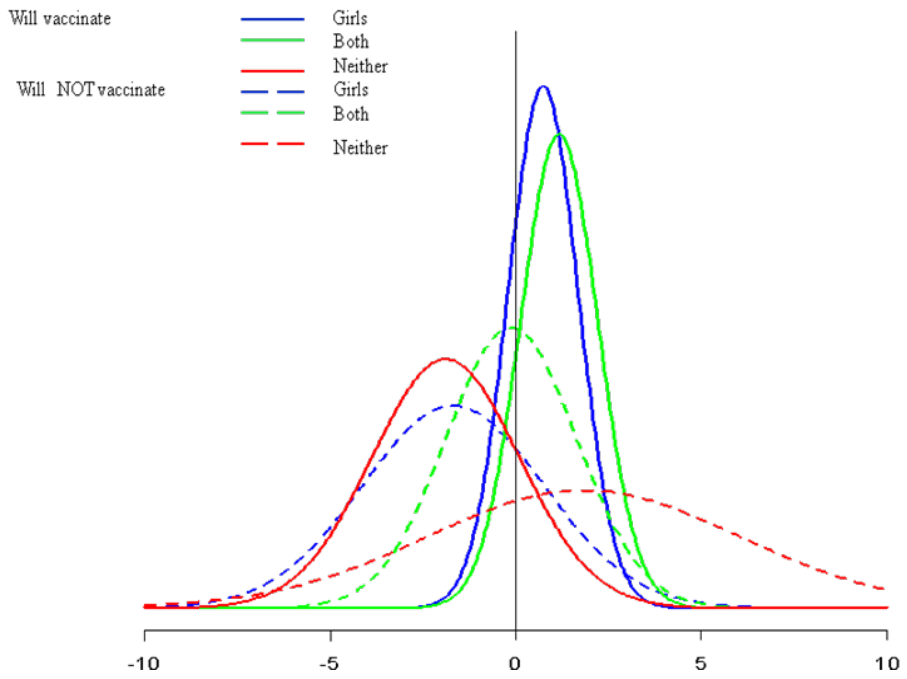
**Table 22**: An overview of all the sub-group analyses

| **Variables** | **Do they want Vaccination Program?** | | **Who do they want vaccine for?** | | **Which Vaccine?** | | **Care about Side Effect?** | | **Care about booster?** | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | Girls only | Girls/boys | Quadrivalent | Bivalent | Yes | No | Yes | No |
| Gender | | | | | | | | | | |
| Male | X | | | X | X | | X | | | X |
| Female | X | | | X | X | | X | | X(never) | |
| Age | | | | | | | | | | |
| 19-35 | X | | | X | X | | X | | | X |
| 36-55 | X | | | X | X | | X | | X(never) | |
| 56-65 | X | | | X | X | | | X | | X |
| >65 | X | | | X | X | | X | | | X |
| Education | | | | | | | | | | |
| < high school | X | | | X | X | | X | | | X |
| High school-some university | X | | | X | X | | X | | X(never) | |
| University or graduate school | X | | | X | X | | X | | X(never) | |

| **Variables** | **Do they want Vaccination Program?** | | **Who do they want vaccine for?** | | **Which Vaccine?** | | **Care about Side Effect?** | | **Care about booster?** | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | Girls only | Girls/boys | Quadrivalent | Bivalent | Yes | No | Yes | No |
| Income | | | | | | | | | | |
| ≤$20,000 | X | | | X | X | | | X | | X |
| $20000-$54,999 | X | | | X | X | | X | | | X |
| ≥$55,000 | X | | | X | X | | X | | X(never) | |
| Have Children | | | | | | | | | | |
| Yes | X | | | X | X | | X | | | X |
| No | X | | | X | X | | X | | X(never) | |
| Household | | | | | | | | | | |
| Single parent | X | | | X | X | | | X | | X |
| Two parent | X | | | X | X | | X | | | X |
| Parents with Girls only | X | | | X | X | | X | | | X |
| Boys only | X | | | X | X | | X | | | X |
| HPV experience | | | | | | | | | | |
| Yes | X | | | X | X | | X | | | X |
| No | X | | | X | X | | X | | X(never) | |

| **Variables** | **Do they want Vaccination Program?** | | **Who do they want vaccine for?** | | **Which Vaccine?** | | **Care about Side Effect?** | | **Care about booster?** | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | Girls only | Girls/boys | Quadrivalent | Bivalent | Yes | No | Yes | No |
| Child sexually active? | | | | | | | | | | |
| Yes | X | | | X | X | | | X | | X |
| No | X | | | X | X | | X | | | X |

**Figure 4.1**: Density plot showing the distribution of for target group to vaccinate for those who would (not) vaccinate their child against HPV



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# CHAPTER 5
# SUMMARY, CONTRIBUTION AND RECOMMENDATIONS

## 5.1 Summary of Key Research Findings

The objective of this study was to evaluate societal preferences for the HPV vaccination and screening programs using DCE. To the best of our knowledge, this is the only study that has evaluated preferences for the HPV vaccines from a societal perspective. As established in Chapter 1, the human papillomavirus is extremely diverse, consisting of over 100 different HPV subtypes, and infection with it is associated with cancer, genital warts and respiratory papillomas. There are two major phylogenetic branches differing in affinity for site of infection: the cutaneous (keratinized squamous epithelium), and the mucosal (non-keratinized squamous epithelium).[1] Of the 100 HPV subtypes, approximately 40 have an affinity for mucosal cells and infect the genital tract.[2] Mucosal-HPV is categorized as either high risk oncogenic (types 6, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58), or as low risk non-oncogenic (types 6, 11, 42, 43, 44).[3] Worldwide, the high risk HPV subtypes 16 and 18 are responsible for about 70% of all cervical cancers, high and low grade cervical abnormalities, and anogenital cancer, whilst subtypes 6 and 11 are responsible for low grade cervical abnormalities, recurrent respiratory papillomas and genital warts, and the risk of acquiring HPV infection if sexually active is 75% in one's lifetime (i.e., 3 out 4 persons will acquire HPV).[2] The highest prevalence of the HPV infection is among those aged 20-24 years, and the lowest prevalence among those 40-44 years.[4]

Every year, approximately 500,000 women are diagnosed with cervical cancer, and approximately 300,000 die from the disease globally.[5,6] In Canada, the estimated age-standardized incidence of cervical cancer is about 7.0 per 100,000, and the mortality rate is the lowest among all developed regions (2.0 per 100,000).[7] However, cervical cancer is a leading cause of cancer in women between 20-44 years of age, and is the 12$^{th}$ most common cause of cancer in females in the country.[8] The lifetime risks of contracting cervical cancer and dying from it are 0.78% and 0.26% respectively.[1] Genital warts is a common sexually transmitted disease, with a 10% lifetime risk of contracting this condition.[9] HPV infection is detected by HPV-DNA testing, and cervical cytology screening is used to identify the cellular changes in the cervix as a result of the HPV infection.[10]

The introduction of the HPV vaccines (Gardasil® and Cervarix®) is an advancement in preventative medicine. Gardasil ® prevents both cervical cancer and genital warts infection from HPV types 6,11,16 and 18 and is administered at months 0, 2 and 6, while Cervarix ® prevents only cervical cancer from HPV type 16 and 18 and is administered at months 0, 1 and 6. Both vaccines have been shown to be safe and effective in the prevention of HPV infection.[11, 12] Both vaccines are recommended for girls aged 9-26 years, and for the vaccine to be effective in preventing HPV infection it needs to be administered before sexual debut.[13, 14] The introduction of the HPV vaccine comes with its share of criticism. Skeptics of the vaccine argue that, it may encourage girls to indulge in early sexual practices, while others are concerned about the safety of the vaccine, although both vaccines have been shown through clinical trials to be safe and effective in the prevention of HPV infection.[13, 15-24]

In Chapter 2, a review was undertaken of the studies that had evaluated factors that affected HPV vaccine acceptability and effects on vaccine uptake. The health belief model was used as the framework for the literature review. This model was used because it is able to explain and predict health behavior. Results from the review, showed that parents were more accepting of the HPV vaccine if they considered themselves or their children as being at risk of cervical cancer or genital warts. Concerns about vaccine safety and the vaccine promoting promiscuity were also evident, but generally parents were in favor of the HPV vaccine. In addition, the review revealed the important role of the health care practitioner (e.g., family physicians) in determining a parent's decision to accept the HPV vaccine.

The objective of my study was to determine societal preferences for the HPV vaccination and screening strategies. I used the discrete choice experiment (DCE) design to conduct this study. The theoretical background of this methodology is laid out in Chapter 3. A DCE is an attribute based methodology used to elicit preferences. The method assumes that a product can be categorized into bundle of attributes and levels and consumers have a unique value (utility) for each attribute level. In a DCE, participants are presented with choices between hypothetical scenarios that vary in terms of their attribute levels. The objectives of a DCE are to: estimate the relative importance of the different attribute levels of a product, examine how consumers make trade-offs (marginal rate of substitution) between these attribute levels, determine the total benefit derived from that product and, in some cases, determine the willingness to pay for the attribute levels.[25]

Unlike other economic evaluation methodologies, the outcome measure for a DCE is consumer preferences (what consumers want) rather than some externally determined criteria such as cost/QALY.[26]

Chapter 4 discusses the design, recruitment and results of my study. The DCE questionnaire consisted of 7 important attributes, each with 3 or 4 levels. The attributes were selected based on the current vaccination and screening policy, literature reviews, and a CANADA-wide survey on parental intention to have their daughters receive the HPV vaccine. The following attributes were selected for the study: lifetime risk of cervical cancer, lifetime risk of genital warts, need for vaccine booster, frequency of side effects, frequency of Pap smear testing, vaccine cost and target group to vaccinate. One thousand one hundred and fifty seven respondents, who were 19 years or older, were recruited for the study. Two types of models were used, the conditional and the mixed effect logistic models. Both models showed similar results. The findings from this study revealed that respondents have different importance levels of the HPV vaccination and screening attributes. They preferred having the Pap smear test every 3 years instead of yearly testing. Regarding the need for vaccine booster, they had a significant positive relative preference for never having a vaccine booster, a significant negative preference for having a vaccine booster every 5 years, and were indifferent to having a vaccine booster every 10 years. In addition, they had a positive relative preference for vaccinating girls only as well as both girls and boys, but had a higher relative preference for vaccinating both girls and boys. The results also revealed that respondents are willing to pay to more to have the vaccine for both girls and boys. Furthermore, the results revealed that respondents preferences decreased as the risk for cervical cancer, risk for genital warts, cost of vaccine and frequency of vaccine-related side effects increased, but they were more averse to the risk of cervical cancer. Respondents were also willing to accept an increase in the risk of genital warts to avoid a 1% increase in the risk of cervical cancer, but were even more willing to accept a greater increase in the frequency of side effects to equally avoid a 1% increase risk of cervical cancer. This finding is somewhat surprising as the literature revealed that parents were highly concerned about the vaccine-related side effects.

Sub-group analyses showed that men were more risk averse to cervical cancer than women, another unexpected finding, but as expected, women were more concerned about the vaccine cost than men. Respondents who knew their children were not sexually active, interestingly were more averse to the risk of cervical cancer and genital warts than those who

knew otherwise. With the exception of those who would not vaccinate their children against HPV, all other respondents across the various sub-groups were in favor of a HPV but they preferred the quadrivalent vaccine as opposed to the bivalent vaccine. They also wanted the vaccine for both girls and boys and not girls only. They cared about the need for a vaccine booster, but would prefer never to have the booster. Although respondents wanted Pap smear testing every 3 years, the attribute did not impact preference across many subgroups.

## 5.2 Study Strengths and Limitations

The large sample size used serves as one of the strengths of this study. The advantage of having a large sample size and one which is representative of the Canadian population, is the ability to obtain a more robust and reliable parameter estimates. Another strength of this study is that respondents are able to make a more informed decision because of the amount of information they are provided with. For instance, instead of a family physician asking a parent to choose the HPV program he or she prefers, a DCE requires one to trade off between the negative and positive attributes of the program to determine their preference. Finally, if there were to be a change in the HPV vaccination program for instance, if a vaccine was unable to provide lifelong immunity against HPV and as such a booster vaccine was needed, the broad range of the attributes used in this study will still enable the determination of societal preferences for the new program or a totally different HPV vaccination program.

The major limitation of a DCE is the concern that participants may not truly understand the question, given the hypothetical nature of the choices and the need to make a decision while considering multiple criteria. However, this limitation is minimized by ensuring that the instructions on how to answer the DCE questionnaire are clear and concise, and measures are put in place to test the understanding of the study participants with regards to the DCE methodology (i.e, there is significant pilot testing in advance of releasing the questionnaire).

Another limitation is that DCE is the use of a “stated preference” technique as opposed to a “revealed preference” technique. Stated preference only requires respondents to make decisions based on how they think they would choose, whereas revealed preference studies actually observe the behavior of individuals to determine exactly what they would choose when given a choice. This limitation is not specific to this particular study, but rather is a limitation of the DCE technique. Although evaluating societal revealed preferences would be preferable, this is

much more difficult and not possible due to the high associated cost. As a result, a common assumption of stated preference techniques is that participants would actually choose the option that they state they would choose if presented with those options.

Although the study seeks to evaluate society preferences, one may argue that the study population is not representative of society as these are individuals who are more enlightened and have access to internet. It is virtually impossible to equally represent all demographic of people in society. For instance, running a recruiting advertisement in newspapers will only target those who read these papers and will leave out those who get their news online or from watching television. Even the use of random digit dialing will leave out the growing number of people who use Voice over Internet Protocol (VoIP) and, to some extent, mobile phone users. The study results may be biased if relative preferences differ for those who chose to participate and those who did not get the chance to participate in the study. This may result in a potential for differences in HPV vaccine preferences.

The fact that participants for the study were recruited from a panel of respondents who actively participate is surveys, makes the study results vulnerable to volunteer bias. Volunteer bias is an error that occurs as a result of low response rate because certain groups of people (usually healthier, younger and well educated) tend to have a high participation rate than others. This effect can likely compromise the interpretation and limit the generalization of the research finding.[27] In addition, the study result is vulnerable to systematic bias because study participants were rewarded for participation, though the rewards are used to increase response rates.[28] It can be argued that respondents who are in for the reward are certainly not interested in the study and will most likely avoid trading off between risks and benefits.

## 5.3 Knowledge Translation

To ensure an effective uptake and extensive circulation of the of the research finding to policy makers, healthcare professionals, general public and researchers, several dissemination strategies (e.g. presentation at conferences and seminars to policy makers) needs to be employed. On a local level, study findings could be incorporated in different clinical weekly or monthly bulletins. Study findings can be included in HPV vaccination program performance updates which could be distributed to family physicians using the BC Centre for Disease Control (BCCDC)'s monthly contribution to the BC Medical Journal. The relative preferences for the

different characteristics of the HPV vaccination and screening program observed in this analysis could be incorporated into future knowledge translation products tailored to healthcare professionals and the public. Whenever possible, the main conclusions drawn in this study will also be built into current and future vaccination initiatives, and highlighted during press releases.

Study findings can be dispersed to the public by holding community events to inform respondents about the benefits of the vaccine and highlighting the positive findings of the study. In the same way, more targeted messaging could be carried out to address concerns (based on the study findings) about the HPV vaccines. Policy makers will be informed through direct briefings with researcher and/or collaborators on societal preferences for the HPV vaccines, or through a report submitted to the BC Ministry of Health. All reports produced will be shared with the health authorities across the country. Finally, results from this study will be presented to researchers and policy makers in the form of a podium presentation on September 30th 2009 at the BCCDC research week. Additionally study findings will be published in the reputable journal of sexually transmitted infections.

## 5.4 Contributions and Impact

This is the first study to use DCE to evaluate preferences for Cervarix and Gardasil from the public's perspective. The only other study that has used a stated preference technique (conjoint analysis) to evaluate preferences for the HPV vaccine, did so from a mother-daughter perspective.[29] Brown et al used four key attributes in their study which were price, duration, effectiveness against cervical cancer and effectiveness against genital warts but failed to capture vaccine side effects. This is surprising as earlier studies on HPV vaccine acceptability had shown that vaccine side effects was a major deterrent in vaccinating children against HPV.[30-34] Like our study, they also evaluated willingness-to-pay for the HPV vaccine but did not evaluate the willingness of respondents to trade-off between perceived risk and benefits of the vaccines. The holistic nature of our study provides a broader perspective on how the public perceives the vaccines, how they perceive the effects of cervical cancer and genital and which aspects of the vaccines are important to them.

The stated preference approach used in our study successfully captures societal preferences for the HPV vaccine that will effectively reduce their risk of HPV infections. The result reveals that society is in favor of the HPV vaccination program and is willing to pay to

have their children vaccinated against these infections. In addition, they are also willing to trade frequency of vaccine side effects to avoid lifetime risk of cervical cancer and genital warts. It reveals that risk preferences also differ across different sociodemographic groups. For instance, older individuals are more risk averse to cervical cancer than younger respondents and individuals with more than high school education are more concerned about the risk of genital warts than those with less than high school education. These findings will provide useful information for policymakers with respect to HPV decision making. With the bivalent vaccine currently in its final stages of approval in Canada, decision makers will have actual consumer preference data to effectively recommend the appropriate vaccine for usage. Although the current vaccines are recommended for girls only, our study has shown a strong preference for administering the vaccine to boys therefore, policymakers would need to evaluate and address the issue of male vaccination even though economic analyses have shown it not to be cost-effective. The results will provide policy makers with insight into the attributes that are important to consumers, thereby allowing them to select targeted messaging plans which will be aimed at increasing the vaccine uptake.

## 5.5 Policy Recommendation

Our studying revealed a positive preference for a vaccination strategy which is provided by the government and comes at a zero out of pocket cost for society. However, the quadrivalent vaccination strategy was preferred to the bivalent vaccination strategy but since it comes at a higher cost, decision-makers will need to decide if the extra preference obtained from the quadrivalent vaccination is worth the additional cost. Furthermore, society revealed a preference for vaccinating both girls and boys but also had a positive preference for administering the vaccine to girls only. Although a vaccination strategy for both girls and boys will be the best option it is more expensive than vaccinating girls only. Therefore decision-makers will also need to trade off the extra cost with the added preference.

## 5.6 Conclusions

Through DCE, this study has been able to establish societal preferences for the HPV vaccines, and it has been determined that the public generally has a positive relative preference

for the HPV vaccination and screening programs and, indeed, than their preference for the quadrivalent vaccine is stronger than the bivalent vaccine. The study addresses the gap in the literature concerning the public's preference for the HPV vaccines and the aspects of the vaccine they consider important. It also has been established that preferences among the different levels of the vaccination and screening attributes differ, depending on one's socioeconomic status.

In conclusion, this thesis makes some important contributions to the current literature on application of discrete choice experiment in health. The study has demonstrated DCEs can predict relative preferences for a health technology and potentially predict the uptake of the HPV vaccines. Furthermore, it has shown that sociodemographic information and previous vaccine practices can be used to identify subgroups in the population that respond differently to the various attributes and levels. This permits programs to be targeted more specifically.

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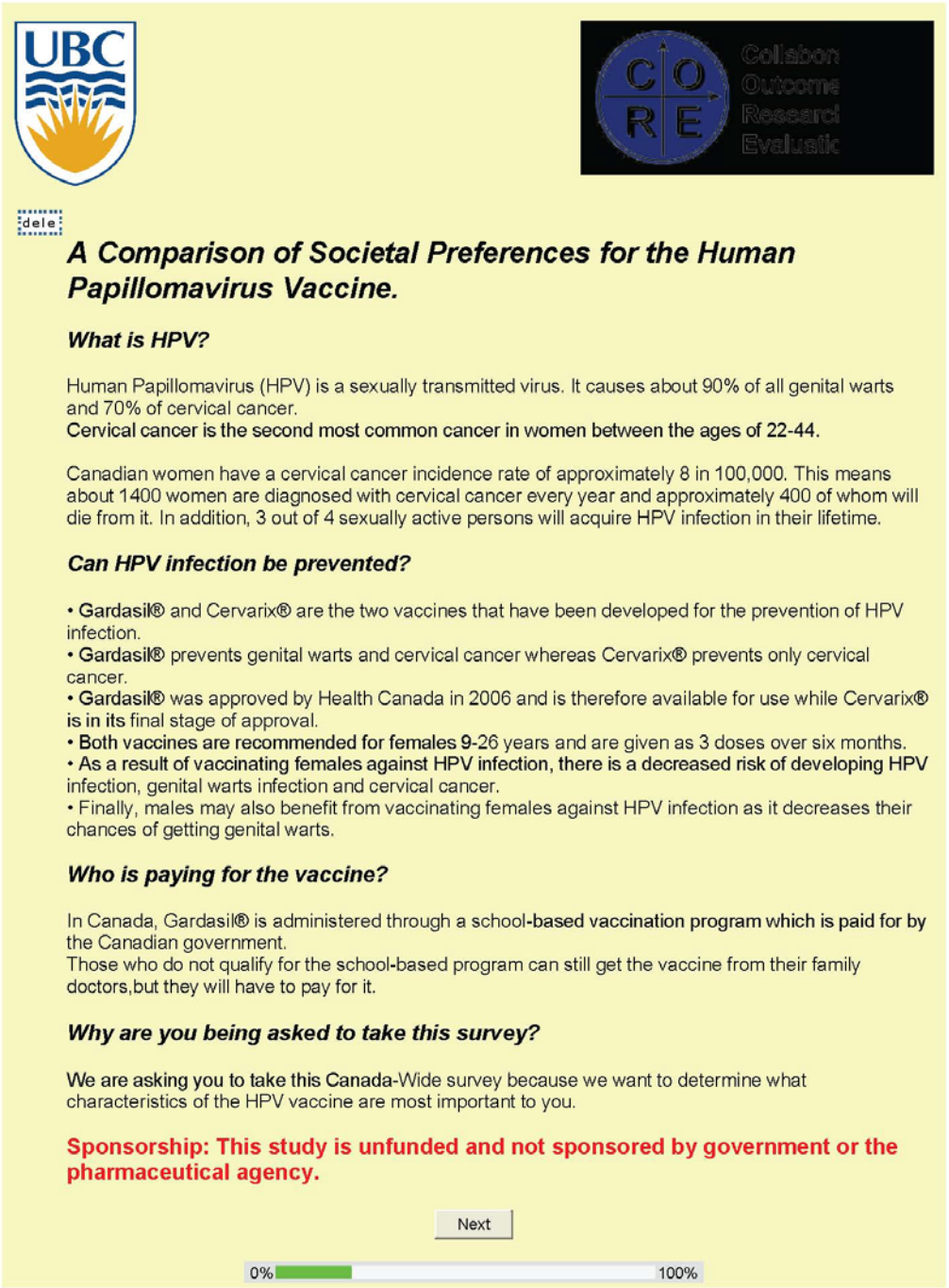
**APPENDIX I**
**THE DISCRETE CHOICE EXPERIMENT QUESTIONNAIRE**



dele

## *A Comparison of Societal Preferences for the Human Papillomavirus Vaccine.*

### *What is HPV?*

Human Papillomavirus (HPV) is a sexually transmitted virus. It causes about 90% of all genital warts and 70% of cervical cancer.
**Cervical cancer is the second most common cancer in women between the ages of 22-44.**

Canadian women have a cervical cancer incidence rate of approximately 8 in 100,000. This means about 1400 women are diagnosed with cervical cancer every year and approximately 400 of whom will die from it. In addition, 3 out of 4 sexually active persons will acquire HPV infection in their lifetime.

### *Can HPV infection be prevented?*

- **Gardasil®** and Cervarix® are the two vaccines that have been developed for the prevention of HPV infection.
- **Gardasil®** prevents genital warts and cervical cancer whereas Cervarix® prevents only cervical cancer.
- **Gardasil®** was approved by Health Canada in 2006 and is therefore available for use while Cervarix® **is in its** final stage of approval.
- **Both vaccines are recommended for females 9-**26 years and are given as 3 doses over six months.
- **As a result of vaccinating females against HPV infection, there is a decreased risk of developing HPV** infection, genital warts infection and cervical cancer.
- Finally, males may also benefit from vaccinating females against HPV infection as it decreases their chances of getting genital warts.

### *Who is paying for the vaccine?*

In Canada, Gardasil® is administered through a school**-based vaccination program which is paid for by** the Canadian government.
Those who do not qualify for the school-based program can still get the vaccine from their family doctors,but they will have to pay for it.

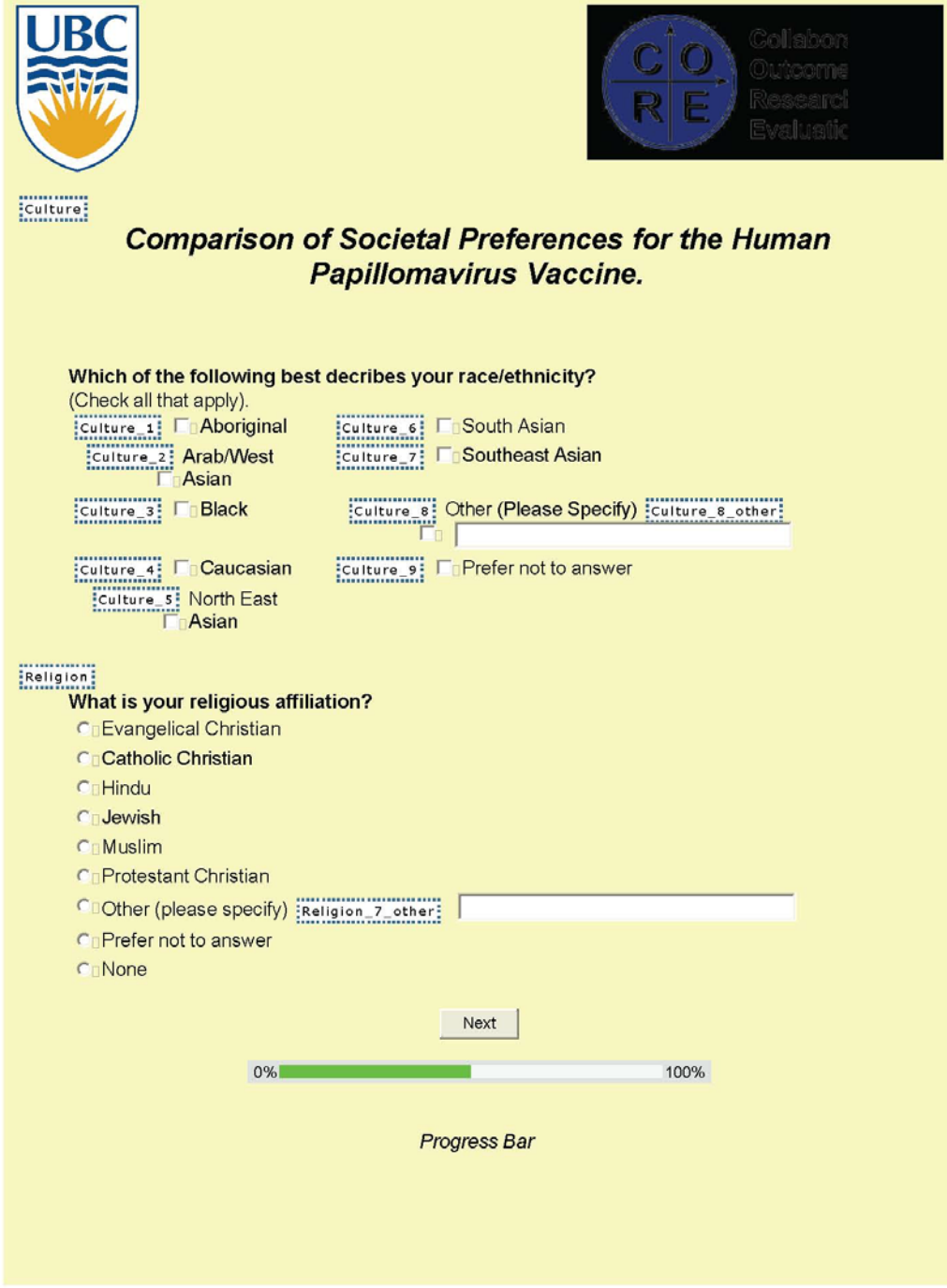
### *Why are you being asked to take this survey?*

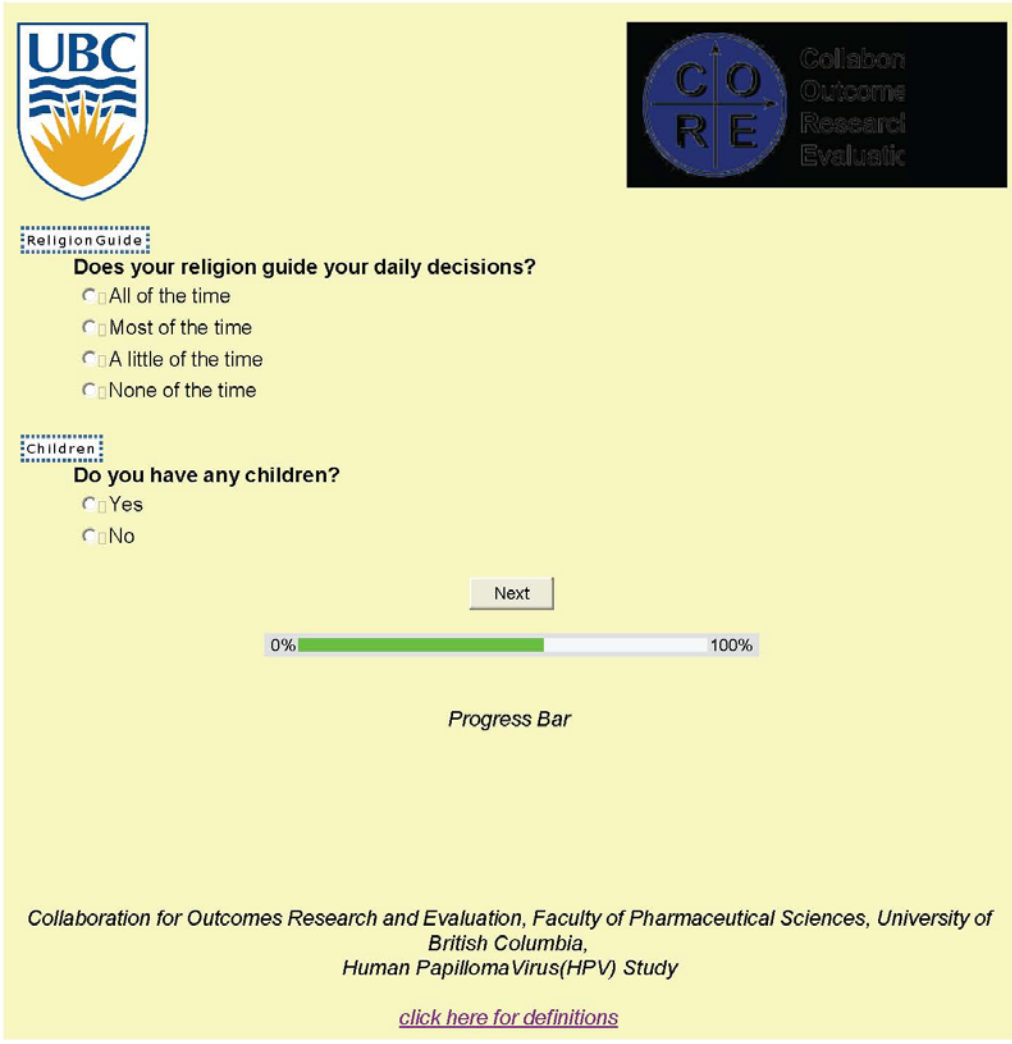
**We are asking you to take this Canada-**Wide survey because we want to determine what characteristics of the HPV vaccine are most important to you.

**Sponsorship: This study is unfunded and not sponsored by government or the pharmaceutical agency.**

Next

0% 100%


Culture
Comparison of Societal Preferences for the Human Papillomavirus Vaccine.
Which of the following best decribes your race/ethnicity?
(Check all that apply).
Culture_1 Aboriginal
Culture_2 Arab/West Asian
Culture_3 Black
Culture_4 Caucasian
Culture_5 North East Asian
Culture_6 South Asian
Culture_7 Southeast Asian
Culture_8 Other (Please Specify) Culture_8_other
Culture_9 Prefer not to answer
Religion
What is your religious affiliation?
Evangelical Christian
Catholic Christian
Hindu
Jewish
Muslim
Protestant Christian
Other (please specify) Religion_7_other
Prefer not to answer
None
Next
0%
100%
Progress Bar


ReligionGuide
Does your religion guide your daily decisions?
All of the time
Most of the time
A little of the time
None of the time
Children
Do you have any children?
Yes
No
Next
0%
100%
Progress Bar
Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia,
Human PapillomaVirus(HPV) Study
click here for definitions


FF2

## *Comparison of Societal Preferences for the Human Papillomavirus Vaccine.*

**Please answer the following for each child.**

*(For children one year and older, enter just the number of years old and click "years". If the child is less than one year old, then ente the number of months, and click "months")*

| | Child 1 | Child 2 | Child 3 | Child 4 | Child 5 | Child 6 | Child 7 | Child 8 | Child 9 |
|---|---|---|---|---|---|---|---|---|---|
| What are the child (ren)s age (s)? | ○ years ○ months | ○ years ○ months | ○ years ○ months | ○ years ○ months | ○ years ○ months | ○ years ○ months | ○ years ○ months | ○ years ○ months | ○ years ○ months |
| What is the sex of this child? | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male | ○ Female ○ Male |

Household

**Which of the following best describes your household?**

- ○ **Single Parent**: *(A parent who cares for one or more children without the assistance of the other parent)*
- ○ **Two Parent**: *(A family consisting of both parents and children)*
- ○ **Guardian**: *(A non-parent who is legally responsible for the care of another person, e.g. minor)*
- ○ **Extended**: *(A family in which relatives in addition to parents and children live in single household)*
- ○ **Blended**: *(A step-family in which one or both parents have children from previous relationships)*

Childvaccine

**Have your children received their childhood vaccines?**

- ○ All
- ○ Some
- ○ None

Next

vaccinate

## *Comparison of Societal Preferences for the Human Papillomavirus Vaccine.*

**Please state why your children have only received SOME or NONE of their childhood vaccines.**

Childsexuality

**We do acknowledge the difficulty of this question and we want you to answer it to the best of your ability. HPV is a sexually transmitted infection and some studies have shown that parents who are aware of their child being sexually active are more interested in the HPV vaccine. Therefore, we would like to know if your child's sexual activity influences your HPV vaccine decision-making.**

Please answer the question below.

**Are any of your children sexually active?**

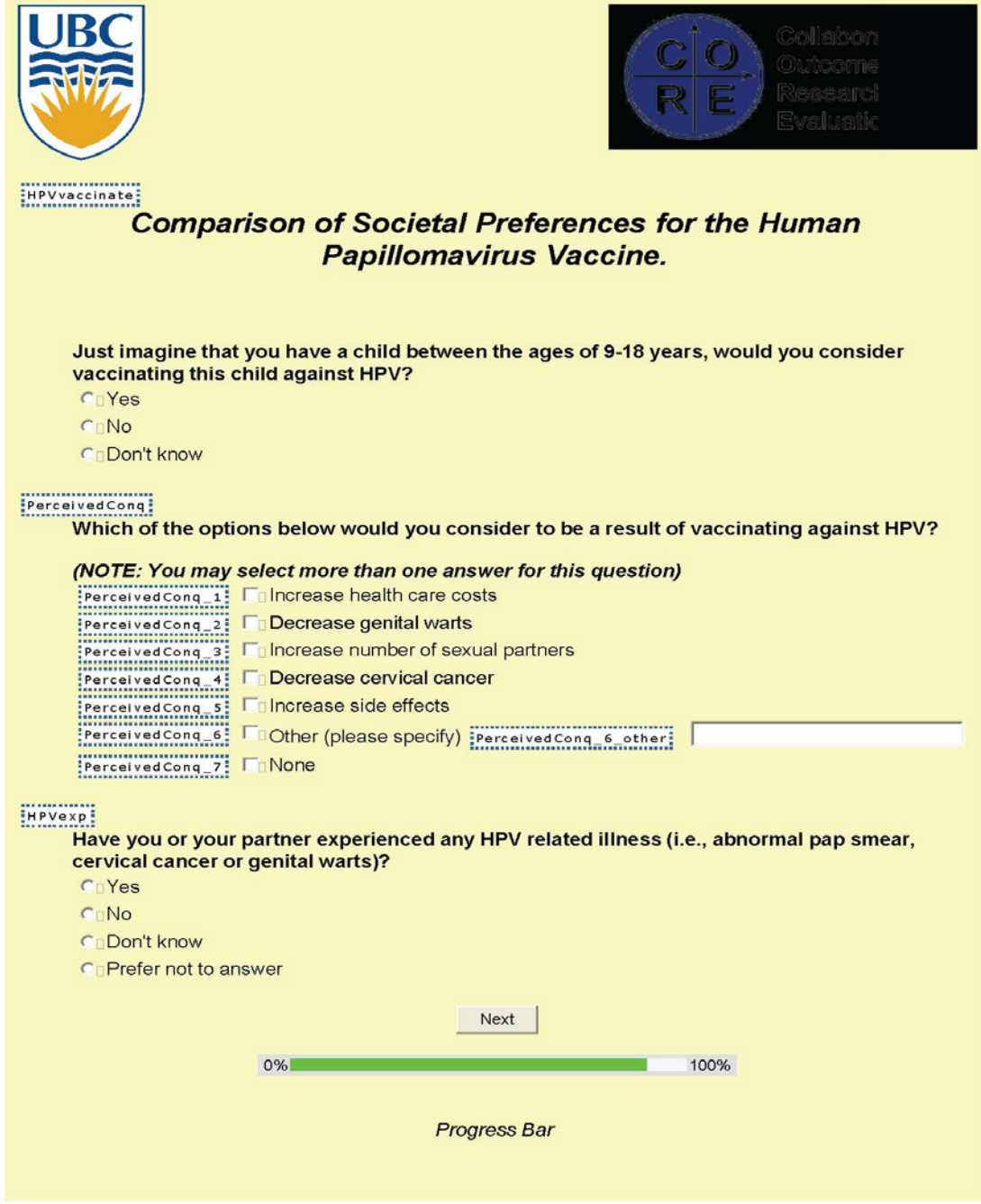
- Yes
- No
- Don't know
- Prefer not to answer

Next

0% 100%

*Progress Bar*

*Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia,*
*Human PapillomaVirus(HPV) Study*


HPVvaccinate
Comparison of Societal Preferences for the Human Papillomavirus Vaccine.
Just imagine that you have a child between the ages of 9-18 years, would you consider vaccinating this child against HPV?
Yes
No
Don't know
PerceivedConq
Which of the options below would you consider to be a result of vaccinating against HPV?
(NOTE: You may select more than one answer for this question)
PerceivedConq_1
Increase health care costs
PerceivedConq_2
Decrease genital warts
PerceivedConq_3
Increase number of sexual partners
PerceivedConq_4
Decrease cervical cancer
PerceivedConq_5
Increase side effects
PerceivedConq_6
Other (please specify)
PerceivedConq_6_other
PerceivedConq_7
None
HPVexp
Have you or your partner experienced any HPV related illness (i.e., abnormal pap smear, cervical cancer or genital warts)?
Yes
No
Don't know
Prefer not to answer
Next
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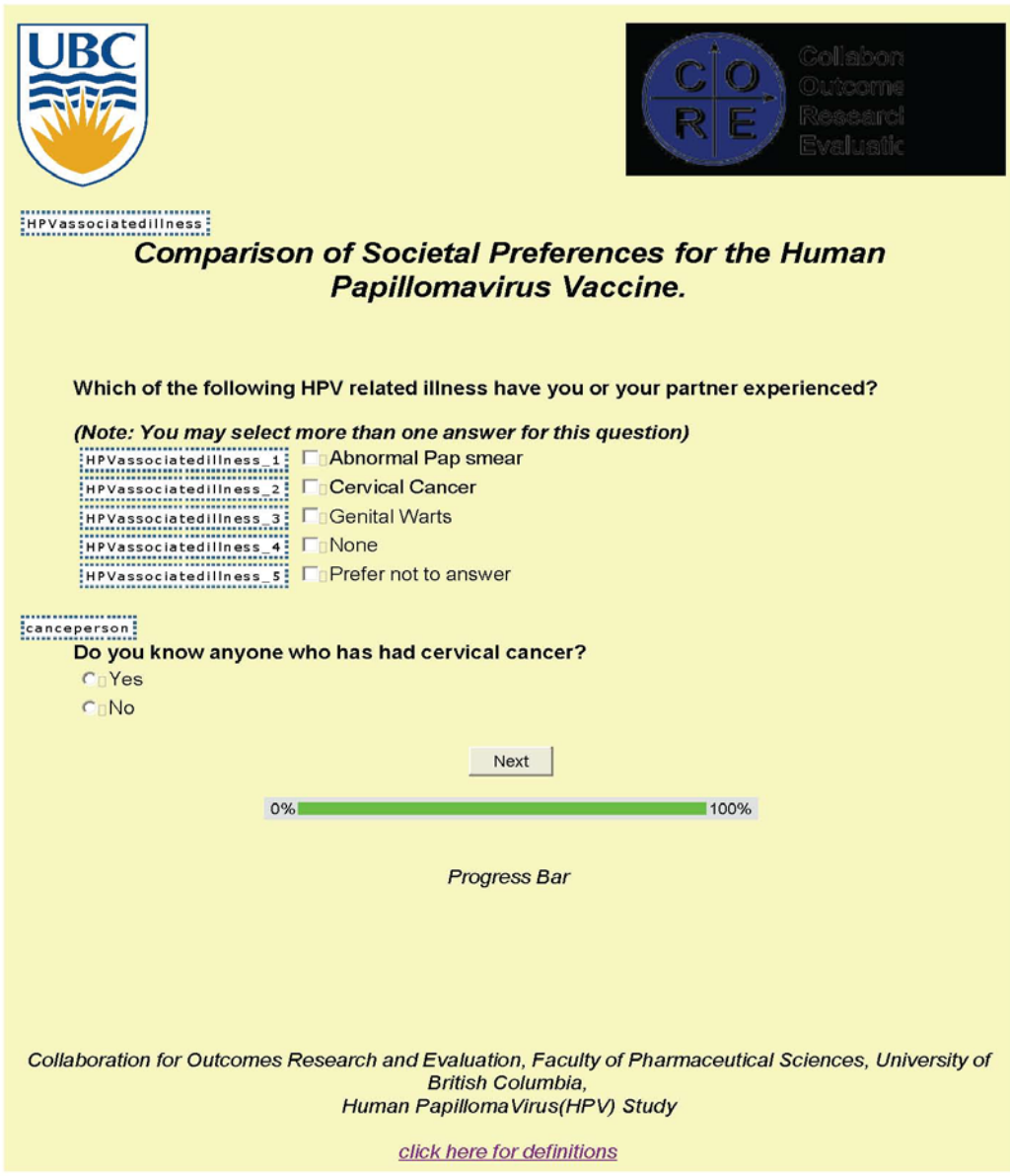
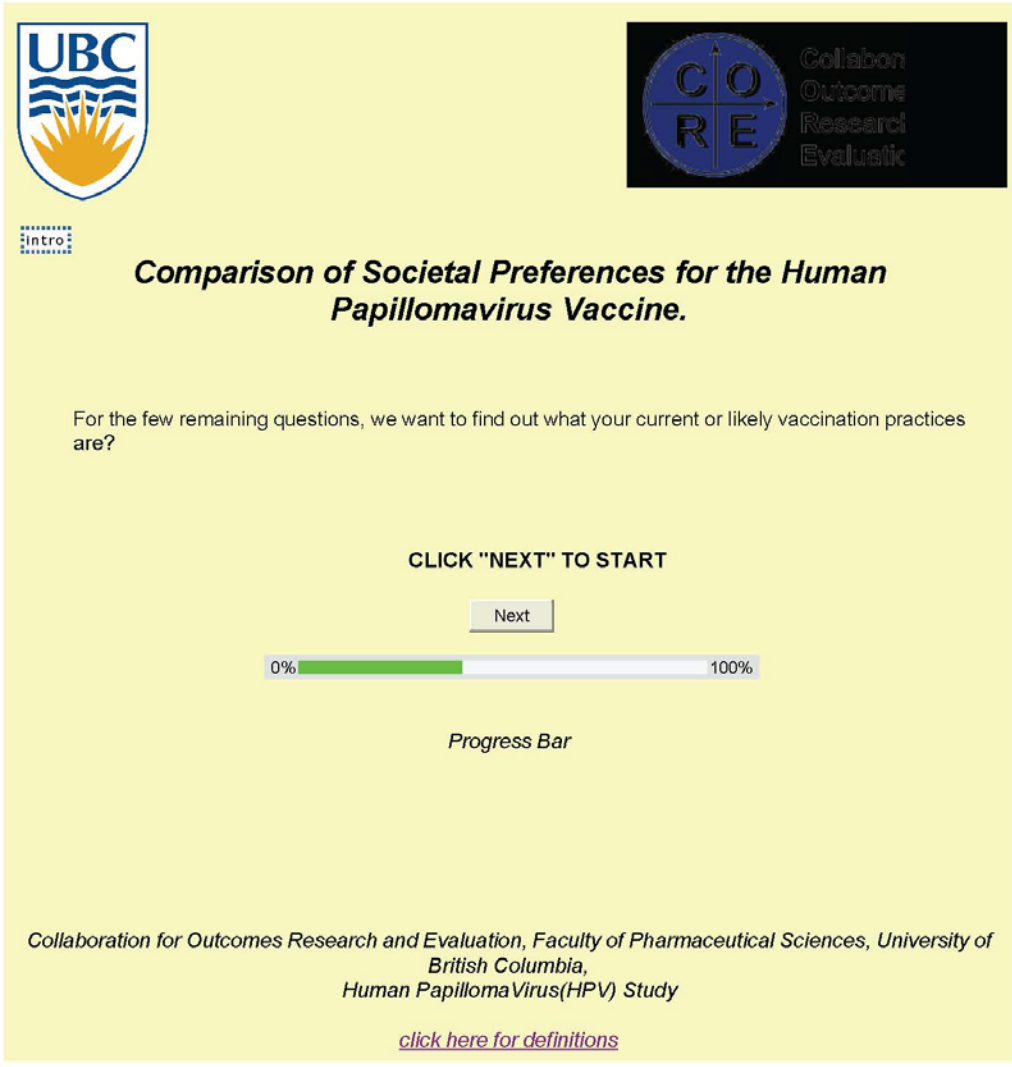
100%
Progress Bar


HPVassociatedillness
Comparison of Societal Preferences for the Human Papillomavirus Vaccine.
Which of the following HPV related illness have you or your partner experienced?
(Note: You may select more than one answer for this question)
HPVassociatedillness_1
Abnormal Pap smear
HPVassociatedillness_2
Cervical Cancer
HPVassociatedillness_3
Genital Warts
HPVassociatedillness_4
None
HPVassociatedillness_5
Prefer not to answer
canceperson
Do you know anyone who has had cervical cancer?
Yes
No
Next
0%
100%
Progress Bar
Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia,
Human PapillomaVirus(HPV) Study
click here for definitions


Intro
Comparison of Societal Preferences for the Human Papillomavirus Vaccine.
For the few remaining questions, we want to find out what your current or likely vaccination practices are?
CLICK "NEXT" TO START
Next
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Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia,
Human PapillomaVirus(HPV) Study
click here for definitions


## *Comparison of Societal Preferences for the Human Papillomavirus Vaccine.*

## DEFINITIONS

**In the following section, you will be given 12 choice questions. For each question, you will be asked to choose option A, option B or neither based on the following vaccine characteristics**:

1. Lifetime cervical cancer risk
2. Pap smear frequency
3. Lifetime genital warts risk
4. Need for vaccine booster
5. Frequency of serious side effects
6. Target group
7. Vaccine cost

Within each characteristic, there are two or more levels.

### Below are brief descriptions of all 7 vaccine characteristics and levels.

1. **Lifetime cervical cancer risk**

   This feature refers to the number of women who will develop cervical cancer in their **lifetime.**

   Cervical cancer occurs when abnormal cells on the cervix grow out of control. The cervix is the lower part of the uterus (womb) that opens into the vagina. Cervical cancer can often be cured when it is found early. It is usually found at a very early stage through a Pap smear test.The current risk of cervical cancer is about 1% in one's lifetime.**Note: If you are a man, please answer the questions based on your preference for a woman you know (it could be your mother, sister, partner or female relative).**

   **The levels below represent the number of women who will develop cervical cancer their lifetime:**

   I) **0 in 100**
   II) **2 in 100**
   III) 5 in 100
   IV) **10 in 100**

2. **Pap smear frequency**

This feature refers to the frequency for Pap Smear Testing.

A Pap smear is a medical procedure for women which allows for the detection of abnormal or cancerous cells in the cervix (the end of the uterus that extends into the vagina). The procedure involves taking a sample of cells from a woman's cervix and examining them for any abnormality. A Pap smear is a simple, quick, and relatively painless test. Existing evidence indicates a substantial reduction in cervical cancer due to frequent pap smear tests. **Note: If you are a man, please answer the questions based on your preference for a woman you know (it could be your mother, sister, partner or female relative).**

**The levels below represent the frequencies for Pap smear testing:**

I) Never
II) Yearly
III) Every 3 years
IV) Every 5 years

3. **Lifetime genital wart risk**

This feature refers to the number of individuals who will develop genital warts in their **lifetime**

HPV is a highly transmittable sexually transmitted infection which causes genital warts. Genital warts may appear within weeks or months after sexual contact with an infected person. Warts appear on the genitals or sexual organs of men and women and can also appear around the anus. Some people can have the wart virus present in their skin even though the warts cannot be seen. At least 1% and 2% of all sexually active men and women, respectively, have genital warts that require treatment.

**The levels below represent the number of individuals who will develop genital warts in their lifetime:**

I) 0 in 100
II) 2 in 100
III) 5 in 100
IV) 10 in 100

4. **Need for booster**

This feature refers to the frequency for vaccine booster.

A booster vaccine is a supplementary dose given after the initial administration of the vaccine series (in this case 3 doses) to enhance immune response. Although the HPV vaccines have shown to be protective against the precancerous lesions for up to 5.5 years, there is currently no booster recommendation due to the lack of knowledge on the long term length of immunity.

**The levels below represent the frequencies for receiving vaccine booster:**

I) Never
II) Every 5 years
III) Every 10 years

5. **Target group**

This feature refers to the gender to vaccinate.

In Canada, the vaccine is currently approved for girls only, but there are studies that support giving

the vaccine to boys as well. **Australia** has approved vaccination for boys.

**The levels below represent the gender to vaccinate:**

I) Girls only
II) Both girls and boys

6. **Frequency of side effects**

This feature refers to the number of individuals who will develop side effects. Like most vaccines, the HPV vaccines could have potential side effects. The most common of these are:
•Pain at the injection site
•Redness or swelling at the injection site
•Fever
•Itching at injection site
•Nausea
•Dizziness
•Diarrhea

**The levels below represent the number of individuals who will develop side effects:**

I) 2 in 100
II) 6 in 100
III) 10 in 100
IV) 14 in 100

7. **Vaccine Cost**

This feature refers to the cost of the HPV vaccine.

The government of Canada has allocated money to provinces and territories to help them implement a non-mandatory school-based HPV vaccination program. The program is paid for by the federal/provincial government using tax-payers dollars. Those who do not qualify for the "free" vaccine, will have to pay out of pocket for it.

**The levels below represent costs of the HPV vaccine:**:

I) $0= Insurance
II) $200
III) $400
IV) $600

**The table below is an example of a choice question**

Question 1

If you were asked to choose a Human Papilloma Virus (HPV) vaccine with the following characteristics, which option would you prefer?
**Choose by clicking one of the buttons below**:

| Features | Option A | Option B | |
|---|---|---|---|
| Lifetime cervical cancer risk | 2 in 100 | 5 in 100 | NEITHER |
| Pap smear frequency | Every 5 years | Every 3 years | |
| Lifetime genital warts risk | 2 in 100 | 5 in 100 | |
| Need for booster | Never | Every 10 years | |
| Target group | Both girls and boys | Both girls and boys | |
| Frequency of side effect | 6 in 100 | 10 in 100 | |
| Vaccine cost | Insurance | $400 | |
| | ○ | ○ | ○ |

**If you choose NEITHER, it means you prefer the baseline population risk (your current risk without the HPV vaccine) for cervical cancer and genital warts and the current recommended frequency for pap smear testing, which is every other year unless you have an abnormality detected.**

**NEITHER also means no vaccine side effects, vaccine booster and no one is vaccinated.**

**The table below shows the population baseline risk for cervical cancer, genital warts and the frequency for pap smear testing.**

| Attribute | Level |
|---|---|
| Lifetime Risk of cervical Cancer | 2 in 100 |
| Frequency of Pap smear testing | Every 2 years |
| Lifetime risk of genital warts | 10 in 100 |

**NOTE**:You may either benefit directly from the vaccine (i.e., yourself or a close family member e.g., mother or sister, may benefit from a lower risk of cervical cancer or genital warts) or indirectly (i.e., someone you know may benefit from a lower risk of cervical cancer or genital warts).
Please choose your best vaccine based your associated benefit.

**The 12 choice questions are hypothetical scenarios which may appear repetitive and similar but each question is different.**

**APPENDIX II**
**LETTER OF INITIAL CONTACT (CONSENT FORM)**

The University of British Columbia

**C**ollaboration for **O**utcomes **R**esearch and **E**valuation

# *Study Title: A Comparison of Societal Preferences for the Human Papillomavirus Vaccine*


## Principal Investigator:
Dr. Fawziah Marra, Vaccine and Pharmacy Services, BCCDC, 604-660-0386

## Co-Investigators:
Dr. Carlo Marra, Collaboration for Outcome Research and Evaluation, SPH, 604-806-3215
Dr Gina Ogilvie, STD/AIDS Control Division, BCCDC, 604-660-7484


**Background:** You are being invited by researchers at the University of British Columbia to participate in the above study because you expressed interest in doing research with IPSOS REID Canada. This study is about the Human Papillomavirus (HPV) vaccines. There are currently two of these vaccines. One of them has been approved by Health Canada for use and the second is currently going through the approval process. The vaccines protect females against Human Papillomavirus types 16 and 18 which cause 70% of all cervical cancer and types 6 and 11 which causes 90% of all genital warts. The vaccines are preventive, meaning it can only serve as protection for females who have not been infected with the virus. As such the vaccines have been recommended for girls as early as 9 years old.

**Objective: Given that** both vaccines protect against cervical cancer but only one vaccine protects against genital warts, our study is aimed at evaluating societal preferences and willingness to pay for Human Papillomavirus (HPV) vaccine. Your response to the questions will help us understand what is important to you in terms of the vaccines and their characteristics. This information may also guide policy makers to make better decisions with regards to money spent for our healthcare.

**Study Procedure:** You may participate in this study if you meet the following criteria:

- 19 years of age;
- Able to read and understand English;

Reside in Canada.

To participate, you will be asked to complete a questionnaire in which you will respond to questions related to your knowledge of the Human Papillomavirus, your occupation, your education, your total income. We have also identified some important characteristics of the HPV vaccines and formulated different scenario questions from them. For each question, we want you to choose the scenario you prefer the best or choose none as your option. It will take you approximately 10 minutes to complete the questionnaires for the study. Your participation is voluntary and therefore under no obligation to participate. If you decide to participate, you can withdraw from the study at any time without any consequence. We will not share your responses with anyone outside the study team.

**Risk:** There is no risk expected from this study as no medication or intervention is used. The information you provide is only used for research purposes.

**Benefit:** There is no direct benefit to you for participating in this research. However we hope the information obtained from this research would help us to study preference for HPV vaccines and how you trade-off between the vaccine attributes.

**Sponsorship:** This study in unfunded and not sponsored by government or the pharmaceutical agency.

## Confidentiality:

The information you provide is STRICTLY CONFIDENTIAL. By completing the questionnaire, we will assume that you have given us the consent to use your provided information. Your response to the questionnaires will be used to determine an overall understanding of societal preferences and willingness to pay for Human Papillomavirus vaccine as will be part of a Masters thesis.

Thank you for your time and co-operation. If you require additional information about the study, you are welcome to contact me via email at fawziah.marra@bccdc.ca or 604.660.0386.

If you have any concerns about your treatment or rights as a research subject, you may contact the Research Subject Information Line in the UBC Office of Research Services at 604-822-8598 or if long distance e-mail to RSIL@ors.ubc.ca

Yours sincerely

Fawziah Marra, Pharm.D., Principal Investigator

# APPENDIX III
# UBC BEHAVIOURAL RESEARCH ETHICS CERTIFICATE



*The University of British Columbia*
*Office of Research Services*
***Behavioural Research Ethics Board***
*Suite 102, 6190 Agronomy Road, Vancouver, B.C. V6T 1Z3*

## CERTIFICATE OF APPROVAL- MINIMAL RISK RENEWAL

| PRINCIPAL INVESTIGATOR: | DEPARTMENT: | UBC BREB NUMBER: |
|---|---|---|
| Fawziah Marra | UBC/Pharmaceutical Sciences | H08-00522 |

**INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:**

| Institution | Site |
|---|---|
| UBC | Vancouver (excludes UBC Hospital) |

**Other locations where the research will be conducted:**
There will be no other locations

**CO-INVESTIGATOR(S):**
Bridgette Oteng
Carlo Marra

**SPONSORING AGENCIES:**
N/A

**PROJECT TITLE:**
Evaluating Societal Preferences for Human Papillomavirus Vaccines using Discrete Choice Experiment.

**EXPIRY DATE OF THIS APPROVAL: April 17, 2010**

**APPROVAL DATE: April 17, 2009**

The Annual Renewal for Study have been reviewed and the procedures were found to be acceptable on ethical grounds for research involving human subjects.

**Approval is issued on behalf of the Behavioural Research Ethics Board**

Dr. M. Judith Lynam, Chair
Dr. Ken Craig, Chair
Dr. Jim Rupert, Associate Chair
Dr. Laurie Ford, Associate Chair
Dr. Anita Ho, Associate Chair