UPTAKE OF THE HUMAN PAPILLOMAVIRUS VACCINE AMONG YOUNG MALAYSIAN WOMEN: DOES A PHYSICIAN'S RECOMMENDATION PLAY AN IMPORTANT ROLE?

By

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ABSTRACT

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With a high incidence of cervical cancer and a low prevalence of screening for the disease, mass vaccination of the human papillomavirus (HPV) vaccine has the potential to reduce the burden of cervical cancer in Malaysia. While much of the focus has been on vaccinating school-aged girls, the factors that drive vaccination among eligible young women in Malaysia have not been extensively studied. The purpose of this study is to determine the proportion of the sample that received a vaccination, among those who recall having a recommendation for the vaccine during a visit with a physician in the past two years. A survey was carried out in a private university in Malaysia, which recruited a convenience sample 223 participants who were female Malaysian students, aged between 18 and 26 years old. 70.9% of the respondents reported that they had at least one visit with the physician in the past two years, among which 20.9% recalled that they received a recommendation for the HPV vaccine during their visit. 66.7% of respondents who recalled a recommendation were vaccinated with the HPV vaccine. The prevalence of HPV vaccination in this study population is 18.4%. A physician's recommendation may serve as an introduction and/or encouraging factor for HPV vaccine acceptance among young women in Malaysia. However, further research is required to understand the role physicians can play in increasing vaccination rates in this population.

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INTRODUCTION

As of 2006, a vaccine that protects girls against persistent infection with the common types of human papillomavirus (HPV) was licensed for use.[1] It marks an important era in public health; not only do we now have a vaccine against a common sexually transmitted infection, we also have a vaccine that could substantially reduce the global burden of cervical cancer. This is an important milestone in our goal to reduce the morbidity and mortality associated with this disease in women; such a clearly established mode of prevention is rare in the realm of cancer epidemiology.

In Malaysia, widespread vaccination of girls could help decrease future cervical cancer rates in the country, especially in view of the low uptake of screening in this population, as will be discussed in the following chapter. Starting in 2010, girls aged 13 years old were provided with free HPV vaccination through the school immunization program throughout the country. The concern, then, remains for those older than 13 in 2010, who are still eligible for, and may greatly benefit from, HPV vaccination.

Therefore, the factors that increase the uptake of the vaccine in this population need to be identified and amplified. One such factor of interest in this thesis is the influence of a physician's recommendation. This thesis will take a closer look at the relationship between a physician's recommendation and HPV vaccination among a subset of eligible young women in Malaysia.

CHAPTER 2

BACKGROUND

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BACKGROUND

2.1 Global burden of cervical cancer

Cervical cancer is one of the most common cancers in women worldwide, second only to breast cancer.[2] In 2008, the World Health Organization (WHO) estimated that the global incidence of cervical cancer was a little over 500,000 cases and it claimed more than 270 thousand lives that year alone.[2] Furthermore, it showed that 86% of these cases occurred in developing countries.[2] For example, the age-adjusted incidence rate of cervical cancer in North America in 2008 was 5.7 per 100,000 women per year, while Eastern Africa observed rates of up to 34.5 per 100,000 women per year.[2] The age-adjusted incidence rates in Asia are also much higher than in the US; South Asia has rates as high as 25 per 100,000 women per year.[2]

Globally, peak incidence rates are seen among older women, specifically in the 55 to 64 age group.[2] While the overall age trend is similar across countries, the highest cervical cancer incidence rates were seen in a younger age bracket in developing countries.[2] The previously mentioned WHO report also predicts that by 2025, the incidence of cervical cancer in developing countries would increase by 40% among those younger than 69 years old, while the developed world is expected to see a 2% decrease in incidence.[2]

2.2 The human papillomavirus (HPV)

2.2.1 Introduction

The relationship between persistent infection with the Human Papillomavirus (HPV) and cervical cancer is, perhaps, one of the better established causal factors in cancer epidemiology. Bosch et al conducted a review in 2002 to determine if the existing knowledge about this relationship is supported by the Bradford Hill's causal criteria, and concluded that "the causal role of human papillomavirus infections in cervical cancer has been documented beyond reasonable doubt."[3] They found that there was strong, consistent evidence that persistent infection with HPV is a necessary, although not sufficient, cause of cervical cancer.[3] Therefore, steps to prevent persistent infection of HPV is an excellent starting point in the aim of reducing the burden of cervical cancer. The following sections will briefly introduce the virus, its epidemiology, and the vaccines developed for it.

2.2.2 Microorganism

HPVs have non-enveloped circular double-stranded DNA, and belong to the family *Papillomaviridae*.[4] There are 150 HPV genotypes; 40 of these genotypes affect the squamous epithelium of the ano-genital tract,[5] and are members of the *Alphapapillomavirus* genus.[6] Of this subset, 15 HPV genotypes have been implicated in cervical cancer development, with types 16 and 18 causing up to 80% of all cervical cancer cases.[5] HPV also causes a multitude of other diseases, such as benign genital condyloma, dysplasia, respiratory tract papillomatosis, warts, and other ano-genital cancers.[5]

2.2.3 Natural history

The natural history of HPV infection and the development of cervical cancer have been extensively discussed in the literature. Acute infection occurs primarily through sexual intercourse, where abrasions to the epithelium allow the virus to be deposited in the cervix.[5] The virus enters the host cells through endocytosis and takes residence in the nucleus.[5] This makes it difficult for the immune system to detect and respond to the active infection.[5]

After infection, the disease can take several courses; asymptomatic disease, low-grade squamous epithelial lesions (LSIL), or high-grade squamous epithelial lesions (HSIL).[6] In asymptomatic disease, the infection typically resolves without symptoms.[5] LSIL is usually associated with infection of low-risk HPV types; oncogenic HPV type 16 and 18 only causes approximately 35% of LSIL.[5] Also, progression from low-grade disease to high-grade disease is rare.[6] Spontaneous clearance of the virus in this type of disease is common, up to 90% of cases resolve without treatment, typically within 6 to 24 months.[6] The virus is cleared by the host's cell-mediated immune system, leaving the host with partial or full immunity to that specific HPV genotype.[5]

HSIL, on the other hand, is usually associated with persistent infection of high-risk HPV types, such as type 16 and 18.[5] In this course of disease, the viral DNA integrates into the host DNA, disrupting the E2 gene, which causes circular viral genome to become linear.[5] This triggers the deregulation of the E6 and E7 oncogenes, which inhibits p53 and the retinoblastoma gene respectively.[5] These inhibited tumor suppressor genes may lead to genetic

instability, uncontrolled cellular proliferation and the prevention of natural cell death,[5] which are precursors to the development of malignancy.

2.2.4 Epidemiology

Global prevalence of HPV infection is 11.7%.[7] However, there are large disparities of HPV prevalence across countries. The majority of the burden is carried by lower income countries such as those in Central America, Africa, and Asia, with prevalence of up to 36% among women with normal cytology.[7] In Northern America, this proportion is 4.7%.[7]

2.2.5 Risk factors

HPV is a sexually transmitted virus; the primary route of transmission is through unprotected penetrative intercourse.[5] Age is an important risk factor for HPV infection. The prevalence of HPV peaks in women younger than 25 years old, after which there is a dramatic decline.[8] In some studies, there appears to be an increase in prevalence among peri-menopausal women; the reasons for which have not been clearly established.[8] More importantly, however, it appears that women who have the infection later in life are more likely to have persistent infection, which puts them at higher risk for progression to cervical cancer.[6]

The risk of persistent infection is also amplified by smoking, long term oral contraceptive use, and increased parity.[5,6] Co-infection with other pathogens, such as the human immunodeficiency virus (HIV), herpes simplex virus (HSV) or chlamydia trachomatis, also puts one at risk for persistent HPV infection.[5] In general, any mechanism that works to suppress the

immune system from dealing with the active infection will increase the risk of persistent HPV infection, which in turn increases the risk of cervical cancer.[5]

2.2.6 Vaccination

Given the relative stability of the HPV viral DNA,[4] effective vaccines for HPV were created by 2006, and are licensed for use in over 100 countries.[1] These vaccines were created using viral-like particles (VLP), which are non-infectious and non-oncogenic.[9] These particles assemble to form the L1 structural protein of the viral capsid,[4,9] which, in turn, stimulates an immune response in almost all vaccinated persons.[10] Due to its novelty, the duration of immunity has not been clearly established. A recent 2010 study by Paolini and Venuti showed that the vaccine provided sufficient immunity at 6.5 years after vaccination.[11] Furthermore, antibody titers as a result of vaccination was higher than that of natural infection,[10] up to 13-fold at 6 years post-vaccination.[11]

Presently, there are two vaccines available for use. The bivalent vaccine, Cervarix®, confers immunity for the oncogenic types 16 and 18.[9] The quadrivalent vaccine, Gardasil®, protects against the four most common types of HPV; types 6, 11, 16 and 18.[10] According to a 2012 review of clinical trials, the quadrivalent vaccine has been recorded to be approximately 95 to 100% efficient in protecting young women against genital disease, and approximately 95% efficient in preventing genital warts.[9] In this same review, there was a 47% reduction in cumulative incidence of CIN 3 and adenocarcinoma in situ (AIS) in the vaccination arm at 42 months into the study, compared to the placebo arm.[9]

Both these vaccines are given in a 3-dose regimen; with the second and third dose given at month 2 and 6, respectively, after the first dose.[12] The current guidelines in the US strongly encourage the vaccination of 11-12 year old girls, with catch up vaccination available up to 26 years of age, preferably prior to sexual debut.[12] Thus far, the vaccine has been shown to be safe; the most common side effects are pain and swelling at injection site.[10] Serious adverse events reported in the Federal Drug Administration (FDA) clinical trial was less than 0.1%, and was similar between vaccine and placebo groups.[12]

The HPV vaccine provides an opportunity to prevent persistent HPV infection by priming the immune system to respond to an acute infection. This is expected to reduce the incidence of pre-cancerous lesions, and consequently, cervical cancer incidence. Therefore, vaccination of adolescents prior to sexual debut may be a necessary complement to cervical cancer screening later in life. A 2004 study by Goldie et al. showed that the lifetime risk of cervical cancer may reduce by 92% if women were vaccinated at age 12 and received cytologic screening every 5 years after that.[13] In settings where regular cervical cancer screening programs are hard to establish, widespread HPV vaccination may help reduce the burden of cervical cancer.

2.3 Cervical cancer in Malaysia

2.3.1 Introduction to Malaysia

A brief introduction into the population characteristics in Malaysia is important in understanding the public health problems this country faces. Malaysia is a country in South East Asia, spanning over 300,000 square kilometers.[14] It is composed of two regions, a peninsular that lies between Thailand and Singapore, and East Malaysia that lies across the South China Sea from the peninsula, in Borneo. The population size is a little over 29 million people of various ethnic groups. In 2010, 43% of the population was of Malay heritage, 24.6% were of Chinese heritage, and 7.3% were of Indian heritage.[15] The median age of the population in 2010 was 26.2 years old, and approximately 51% of the population were males.[15] The crude birth rate in 2010 was 17.5 births per 1,000 persons, and the death rate was 4.8 per 1,000.[16] Using the same data, maternal mortality rate was 27.3 per 100,000 live births and infant mortality rate was 6,8 deaths per 1,000 live births.[16] Average life expectancy at birth is 77 years for females and 71.9 years for males.[16] The urban population makes up for 71% of the total population in this country.[15] The concentration of people was highest in urban areas, with up to 6,891 persons per square kilometers in the capital, Kuala Lumpur.[15] The GDP per capita was $16, 200 in 2011; 8% of which was directed towards healthcare.[14]

2.3.2 Cervical cancer & HPV burden in Malaysia

Cancer of the cervix uteri is the third most common cancer among Malaysian women, with an age-adjusted incidence rate of 7.8 per 100,000 women in 2007.[17] Data from the World Health Organization (WHO) report that there are approximately 2,100 new cases of cervical

cancer in Malaysia every year.[18] The Chinese and Indian ethnic groups share a higher burden of cervical cancer, with age-adjusted incidence rates of 9.5 and 10.3 per 100,000 women in 2007, respectively.[17] The Malay ethnic group observed an incidence rate that was almost half of that seen in the other two major ethnic groups, approximately 5.3 per 100,000 women per year in 2007.[17] The incidence of cervical cancer is rare under 25 years of age, after which the incidence rate steadily increases and peaks between 55 to 65 years old,[17] as shown in Figure 2.1. There is also great variation across states, ranging from 4.1 to 13.4 per 100,000 women per year.[17] This could be due to combination of various factors, such as varying urbanization levels, health care access, and racial composition across states. Furthermore, the WHO expects that there will be a 50% increase in the annual number of new cases by 2025.[18]

There isn't much information readily available on national HPV infection prevalence in Malaysia, perhaps due to lack of regular cervical cancer screening among Malaysian women, as will be discussed later. A recent study of 200 women attending a health screening in Selangor, the most populous state in Malaysia, found that 46.7% of this population had HPV-DNA present in their cervical swabs, out of which 93% were the oncogenic types 16 and 18.[19] Another study of Southern Malaysia and Singapore found that 25.6% of the study population were positive for the high-risk HPV-DNA, and peak prevalence occurred in women aged 20-24 years old, approximately 49.1%.[20]

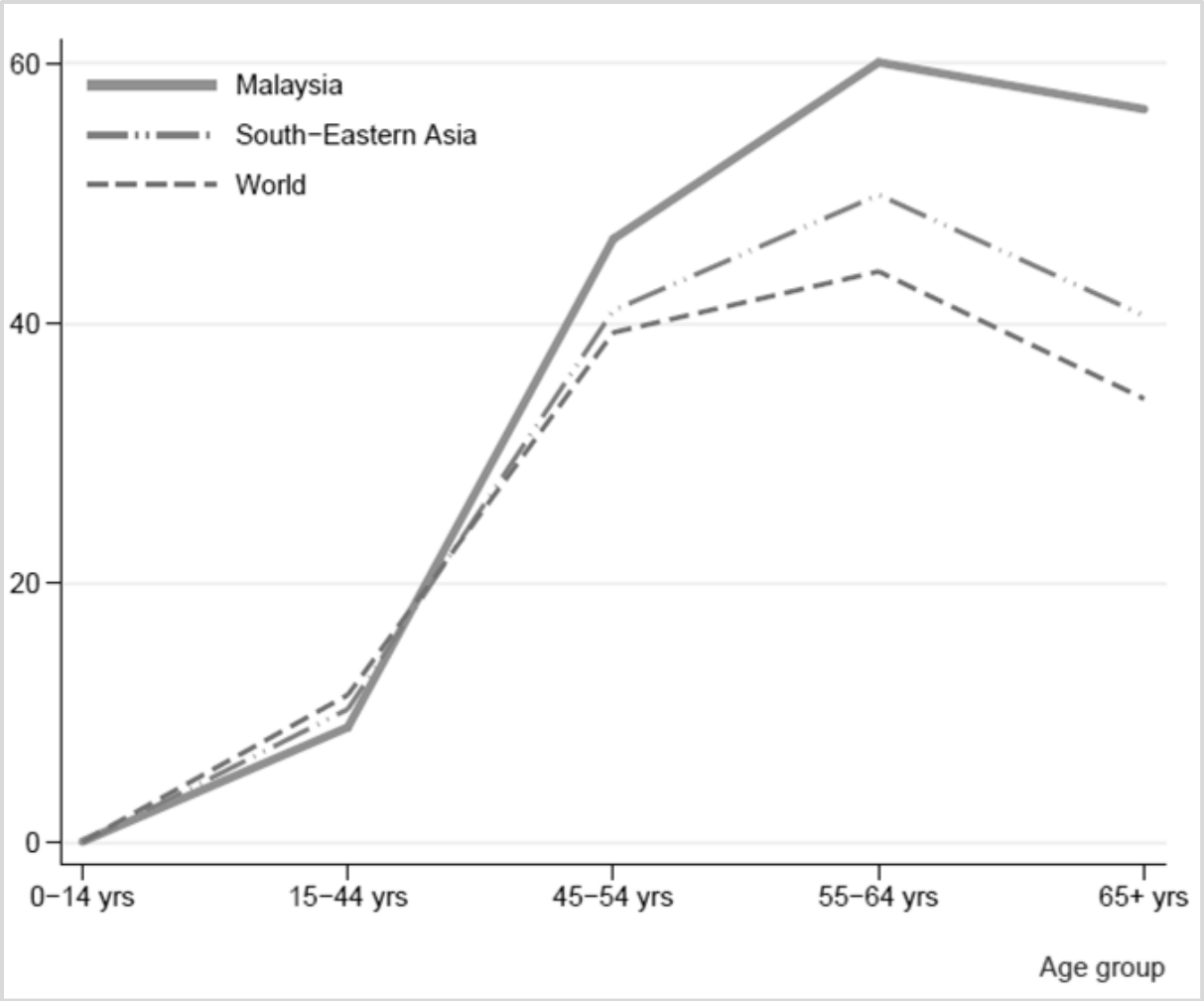

Figure 2.1: Age-specific rates of cervical cancer per 100,000 women per year[24]

2.3.3 Cervical cancer screening in Malaysia

In the industrialized world, the use of effective screening programs has resulted in dramatic declines of cervical cancer incidence rates.[5,21] In a recent review by Wright et al., they claimed that regular screening and treatment of precancerous lesions have been the "single most successful cancer prevention program."[21] However, such programs are often not affordable in low income countries. While the cost of the test itself is relatively low, these countries may not have the resources to establish the infrastructures necessary for widespread

screening.[21] Furthermore, successful implementation of such programs are complicated by sociocultural issues[22], given the relative invasiveness of a Pap smear and the social stigmas in some of these cultures. A 2008 study of cervical cancer screening coverage across 57 countries showed that prevalence of effective screening was very low in developing countries, averaging at about 19%.[23]

Cervical cancer screening has been provided in Malaysia since 1969.[24] Despite this, there hasn't been a significant reduction in cervical cancer rates since then.[24] This suggests that cervical cancer screening is not optimally utilized in this population. Furthermore, the majority of cervical cancer cases were diagnosed at later stages, with almost half of the cases diagnosed at Stage 3 and 4,[17] pointing to a lack of early detection in this population. In a 2009 study by Othman et al., approximately half of patients diagnosed with cervical cancer did not have a pap smear test in 3 years before diagnosis, and close to 40% were not aware of this screening test.[25]

There has been an increase in the percent of the population screened, from 26% in 1996 to 47.3% in 2006[26], but this is still considerably low, given the high risk of cervical cancer for women in this country. Furthermore, most of the screening was opportunistic, performed during ante-natal or post-natal check-ups.[27] There are many reasons why uptake of cervical cancer screening is low in Malaysia. Cost is always a factor in low-resource settings. In view of this, the Malaysian government has provided the screening for free to women between 20 and 65 years old in government-based hospitals.[27] However, in private clinics/hospitals, patients

have to pay for the screening, which is approximately RM100 (~ USD$33) per visit. Furthermore, a study by Dunn and Tan in 2010 showed that rural women, who were more likely to utilize government-provided healthcare, were also more likely to get screened than women in urban settings.[28] It was also shown that the most common reasons for not getting screened was lack of awareness.[25,28] An interview with women who have not had a pap smear revealed that half of the participants did not think that they needed it, unless they experienced abnormal symptoms.[29] Moreover, there are also some socio-cultural issues that may prevent women from getting regular pap smears. The above mentioned Dunn and Tan study showed that "embarrassment" was the second most common reason for not getting screened.[28] Some women may find the pap test procedure embarrassing and an invasion of their privacy.[29] That study also showed racial differences in tendencies of getting screened; they reported that Chinese women were the most likely to get screened, while Indian women were the least likely.[28] There may also be social stigma, coupled with the lack of knowledge, that is attached to cervical cancer screening.[27] The study by Wong et al. suggested that some women did not get screened because they were not "sexually promiscuous".[29] Other factors included fear of pain from the procedure and lack of time, especially among young urban women.[24,28]

Given these shortcomings, a "Plan B" must be initiated if a reduction in cervical cancer rates is to be expected. Therefore, widespread vaccination of young girls to protect them against persistent HPV infection that could lead to cervical cancer may be a necessary step in reducing rates of this disease in Malaysia.

2.3.4 HPV vaccination in Malaysia

The Ministry of Health in Malaysia has taken action to implement a cost-efficient HPV vaccination program in the country. After negotiations with the vaccine manufacturers, a nationwide in-school vaccination program for 13 year-old girls was implemented, in which the vaccinations were provided for free to girls with parental consent.[30] Initially, there were mixed feelings about such a policy. While some were happy that their children would receive this vaccine without having to pay the approximately RM1, 200 (USD $400) for all three doses, there were others that opposed the implementation, citing it as "unnecessary, unscientific, and unsafe".[30] Some of the grounds for these accusations may have stemmed from the belief that "religious education", or in other words, abstinence, is the best way to reduce sexual activity among adolescent, and thereby reducing HPV transmission.[30]

Despite the arguments against it, the free vaccination program for all 13 year old girls was carried out in 2010. Since then, there have been many articles that looked at the efficacy of this program and public opinion about HPV vaccination of young girls. A recent survey of school girls aged 13 to 17 at a particular Malaysian state showed that 77.9% of participants had received the HPV vaccination, and the majority received them through the school program.[31] However, there has not yet been a report of national vaccination rates in this population.

The problem arises, then, for girls who were not eligible for the free vaccination as a result of being older than 13 years old in 2010. Even though the target age group for HPV recommendation is between 9 to 12 years old, catch-up vaccination is also recommended for

girls up to 26 years old.[12] One needs to keep in mind that this age range was instituted based on the average age of sexual debut in the United States.[12] While the probability of sexual debut in American Caucasian females by age 17 was 58% (data from 2009),[32] only 2.9% of female students aged 12 to 18 reported a sexual experience in a study in Negeri Sembilan, a Malaysian state, in 2006.[33] However, the rates here are likely an underestimation for two reasons. Firstly, this sensitive question was asked of adolescents at school in a relatively conservative population, and secondly, the rates may be much higher in larger, more urban states than the one studied here. Even so, it is safe to assume that sexual debut occurs later for the majority of Malaysian girls, and it may be beneficial to focus efforts in increasing vaccination rates in this group of girls.

There have been several reports, especially among college students, to determine the extent of knowledge about the vaccine and vaccine acceptance in this eligible population. These studies are summarized in Table 2.1. For example, a study by Al-Naggar et al. in 2010 revealed that 27% of the study population were HPV vaccinated.[34] Wong conducted a larger study in 2010 to evaluate the awareness of the vaccine among university students.[35] This study found that only 10% had ever heard of the vaccine, and older participants were more likely to have heard of the vaccine compared to younger participants.[35] Unfortunately, this study did not report a vaccination rate, but it may very well be under 10%. A more recent study in 2011 by Al Naggar of 233 women aged 17 to 30 years old reported that 51.5% of the study sample was vaccinated.[36] Yet another study of medical students in 2012 by Rashwan et al. revealed that only 3.6% of approximately 300 participants were vaccinated with the HPV vaccine.[37]

Author (year)	Sample	n	Age group	Prevalence (%)								
					Barriers			Sources of Information				
				Vaccinees	Lack of knowlegde	Lack of need	Fear of safety	Newspaper	Media	Education	Family/ Friends	Doctor
Rashwan et al. (2012)[37]	Third year medical & pharmacy students from a public university	305	21-23	3.6	5	38.3	11.7	13.2		38.7	11	12
Al-Naggar, Bobryshev (2011)[36]	Convenience sample of women from public places in Kuala Lumpur	233	≥ 17	51.5	17.6							
Al-Naggar et al, (2010)[34]	Judgement sample of public university students	30	19-26	27			17					
Wong, Sam (2010)[35]	Convenience sample of public university students	1083	21.5 (±2.0)	n/a	89.7	41.5	50.9	49.3	25.4		31	1.5

Table 2.1 List of studies on HPV vaccination among young Malaysian women. Grey cells in the table represent information that was not collected in the respective study.

Clearly, there are inconsistencies in the results across the studies, which could be an effect of the convenience-based sampling scheme applied in most of these studies.

The consistent thread across all these studies is that there is a lack of awareness about the existence and benefits of the HPV vaccine among young Malaysian women. In the previously mentioned 2012 study by Rashwan et al., the most common reason for not getting vaccinated was perceived lack of necessity (38.3%), followed by concern about efficacy and side effects (11.7%).[37] This study of medical and pharmacy students revealed that only 5% never heard about the HPV vaccine.[37] In contrast, almost 90% of the participants in the study by Wong and Sam in the same year reported that they did not know about the vaccine.[35] In this study, over half were concerned about the safety and efficacy of the vaccine and 41.5% said that they did not get vaccinated because they were not at risk.[35] Also, 11.3% of those who refused to get vaccinated felt embarrassed to receive the vaccine because of its association with a sexually transmitted infection.[35] Cost is also important barrier to vaccination. Even though the government has provided free vaccinations to select groups, most of the eligible young women who were older than 13 years old in 2010 have to pay full price for this 3-dose vaccine, amounting to approximately RM1,200 (USD$400). The 2012 Rashwan et al. study showed that 13% of those who did not get vaccinated reported that it was not "cost-effective".[37]

Given the general lack of knowledge about the HPV vaccine, it is important to identify effective sources of information for the vaccine. In the study by Wong and Sam in 2010, the

primary source of information for the HPV vaccine among college students was the newspaper (49.3%).[35] In the Rashwan study, however, the main source of information was through education, as the participants were mostly medical students.[37] In this study, only 13.2% had heard about the HPV vaccine from public media, such as the radio, television or the newspaper.[37] Family and/or friends were also deemed as important sources of information in both these studies for 11%[37] and 31%[35] of the participants, respectively. Fewer still had heard of the vaccine from a healthcare professional; 12% of the participants stated that a healthcare professional was their source of information in the Rashwan et al. study[37] and 1.5% did so in the Wong and Sam study.[35]

There has not been a study looking at the influence of these sources of information on the decision to get vaccinated in this population. In this paper, the influence of a physician's recommendation on the uptake of HPV vaccination among young Malaysian women will be investigated.

2.4 Physician's recommendation as a proponent of HPV Vaccination

2.4.1 Current evidence

In North America, a physician's recommendation has been shown to be a strong predictor of HPV vaccination.[38-43] Rosenthal et al., who studied women aged 19 to 26 years old, and found that discussion and recommendation by a doctor was significantly associated with vaccination, with every unit increase in strength of the recommendation resulting in a 40% increase in odds of vaccination.[38] Another study in Canada found that those who did not intend to get vaccinated with the HPV vaccine were significantly less likely to have been given a recommendation by a doctor (odds ratio = 0.8).[39] Even prior to the development of the vaccine, a study by Zimmet et al. predicted that recommendation by a health care practitioner was an important factor in HPV vaccine acceptability.[44] Table 2.2 shows the results from previous studies that directly or indirectly assess the relationship between having a physician's recommendation and the decision to get vaccinated with the HPV vaccine among young women.

It is interesting to consider the reasons why a physician's recommendation is an important predictor of HPV vaccination. In a systematic review by Brewer et al., they concluded that a physician may play a crucial role in addressing some of the perceived barriers, such as misinformation and fear of the "unknown".[45] Since this vaccine is relatively new, a physician's recommendation may instill confidence in the vaccine as helpful, instead of harmful, to the individual. Furthermore, the association between a doctor's recommendation and vaccination has been seen with other vaccines, such as the influenza vaccine[46] and the Hepatitis B

Studies reporting a measure of association for the question of interest

Author (Year)	Design	N	Country, source	Sampling scheme	Age Group	Odds ratio
Juntasopeepun et al. (2012)[49]	Cross-sectional (online)	747	Thailand, college students	Convenience and chain-referral sampling	18-26	2.12 (1.22-3.68)
Krawczyk et al. (2012)[39]	Cross-sectional	447	Canada, undergraduates of McGill University	Convenience sample of students from psychology and non-psychology classes	18–43	0.81* (0.70, 0.94)
Bednarczyk et al. (2011)[40]	Cross- sectional	588	US, students at New York State University	Convenience sample of classrooms and women visiting clinics	18-22	1.18 (1.01, 1.39)
Rosenthal et al. (2011)[38]	Case-Control	345/ 185	US, medical & pharmacy claims database	Random selection from the database	19-26	93.50 (39.1, 223.6)
Young et al. (2010)[50]	Cross-Sectional	435	Philippines, community members	Convenience sample from three communities	18-26	2.08 (1.02-4.25)
Caskey et al. (2009)[41]	Cross Sectional	1,011	US, Knowledge Networks	Random selection from an existing research panel	18-26	14.67 (3.33-64.66)

Studies reporting a proportion to describe the question of interest

Author (Year)	Study design	N	Country, source	Sampling scheme	Age Group	Percent %	Comment
Marchand et al. (2012)[42]	Cross-Sectional	15,037	US, community college in LA	Convenience sample	18-26	70.3%	Proportion of vaccinees among those who received recommendation
Bendik et al. (2011)[43]	Cross-Sectional (Online)	1,975	US, college students	All women in sampling frame	18-24	35.4%	Physician's recommendation as main reason for vaccination
Mortensen (2010)[51]	Cross-Sectional	794	Denmark, geographically representative households	Randomized calls were made	21-26	11%	Physician's recommendation as main reason for vaccination

Table 2.2 Past studies that looked at the relationship between physician's recommendation and HPV vaccination.

vaccine.[47] In a study by Gurmankin et al about the influence of a physician's recommendation on treatment decisions, it was found that a physician's recommendation strongly influenced a patient's treatment choice, even when it was against the maximum health benefit.[48] In this study, 41% of the participants who complied with the physician's recommendation did so because they believed that the physician had more insight to the matter, while 17% believed that the physician would have tailored the recommendation based on their personal medical history.[48]

Does this mean that this relationship is a causal one from an epidemiological standpoint? From the pool of literature described above, it appears that the association between being recommended the HPV vaccine by a healthcare professional and vaccine uptake is consistently strong,[38-41,49-50] follows a somewhat dose response relationship,[38] and is analogous to that seen for other vaccines.[46,47] Time order is harder to prove, especially since most of these studies were cross-sectional in nature; however, it may be safe to assume that an individual may have to discuss the vaccine with their physician prior to being vaccinated. We cannot rule out the possibility that intention to get vaccinated was present prior to the discussion with the physician, and how this may have affected their receptiveness to vaccination during the conversation with their physician. However, even though the evidence is limited and highly reliant on self-reported behavioral variables, there is some evidence that a physician's recommendation may be a causal factor in the decision to get vaccinated among young women.

2.4.2 Evidence from Malaysia

There has not been much investigation into the role of physicians in the uptake of the HPV vaccine in Malaysia. In a 2011 study among high school students in Sarawak, a state of East Malaysia, 18.5% of those who were vaccinated or were willing to get vaccinated said that it was because of a recommendation by a healthcare professional.[52] In a large survey of four countries, including Malaysia, 78% of mothers indicated that a doctor's recommendation would increase their likelihood for getting their daughters vaccinated with the HPV vaccine.[53] In this same study, 91% of those with vaccinated daughters aged between 10 and 26 years old said that their main source of information when considering the vaccine was a doctor.[53] In a 2009 focus group study by Wong, however, the verdict was split; some agreed that a physician is an important channel for HPV vaccine promotion, whereas others disagreed due to the "sexual nature of [the] vaccine" and potential for misuse by the physicians as a money-making tool.[54] Wong conducted another study in 2010 which reported that only 1.5% of college students had heard about the vaccine from a healthcare professional.[35]

There were a couple of studies that interviewed physicians about their practice of recommending the HPV vaccination in Malaysia, and the results were not encouraging. One study by Wong in 2011 found that 80% of physicians in their sample reported that they recommend the vaccine at least occasionally; however, this sample consisted of physicians who they described as "HPV Prescribing Physicians" [55] and therefore may not be generalizable to the general population of physicians. Wong conducted a similar study in 2009, in which 11.3%

of physicians reported that they were "successful" in recommending the HPV vaccine to their patients.[56] In the previously mentioned study of four Asian countries, the proportion of general practitioners who actively recommend the vaccine was 25%, and this proportion was only slightly higher among OBGYNs and pediatricians, 39% and 37% respectively.[53] In the search of the existing literature, there was no report found on recommendation rates among the general population of physicians in Malaysia, and how this affects the decision of vaccination among eligible young Malaysian women.

2.4.3 Malaysian healthcare system: Does it promote regular contact with physicians?

Prior to determining if a physician's recommendation is an important factor in encouraging HPV vaccination in Malaysia, one must examine its' feasibility. In other words, do young women have sufficient contact with the health care system, which could lead to a discussion about the HPV vaccine with their doctor? If contact is rare, then the investigation into whether or not a physician's recommendation could increase vaccination rates in the population seems futile. Therefore, a brief review of the Malaysian healthcare system is warranted.

Health care in Malaysia is divided among two systems, the public sector and the private sector. In both these branches, the infrastructure ranges from small clinics to large hospitals. Healthcare in the public sector is heavily subsidized to serve persons from all socioeconomic strata, whereas the private sectors see mostly middle to higher income groups.[57] Considering both sectors, over 90% of the Malaysian population have access to some form of health

services within a 3 kilometer radius from their homes.[15] In 2008, the public sector had in its employment 15, 096 doctors, while 10,006 doctors worked in the private sector.[15] According to a recent interview with the current Health Minister of Malaysia, the ratio of doctor to patient in this country is 1:800, and is expected to increase to 1:600 by 2015 in accordance to WHO recommendations.[58]

The amount of contact young adults have with the healthcare system is of special interest in this discussion. In a population-based study conducted in 2009, 41% of the population was estimated to utilize health care services in the 3 months prior to the study, and there were no significant differences across the age group, except for those 50 years and above, who were more inclined to use healthcare services.[59] According to another study, those aged 18-25 years old were more likely than other age groups to seek medical attention if deemed necessary.[60] In addition to that, the percentage of young adults, aged between 18 to 27 years old, who undergo routine annual wellness checks was estimated to be 32.1%.[61] Stronger data on health-seeking behaviors of young adults was hard to find. However, the evidence displayed above may be enough to suggest that young adults have at least moderate contact with the health care system in Malaysia.

Another factor that needs discussion is the availability of the HPV vaccine in primary care settings in Malaysia, where most of the interface between physicians and young adults are expected to occur. HPV vaccines are readily available in government-run health facilities, while private-based clinics purchase the vaccines directly from the manufacturers, typically based on

demand.[62] Therefore, physicians who have the vaccine on stock may be more inclined to recommend the vaccine than physicians who do not have the vaccine readily available in the clinic. Both the quadrivalent (Gardasil®) and bivalent (Cervarix®) vaccine are licensed for use in Malaysia.[18]

Having established that the vaccine is available to physicians, either through the public sector or through purchase from the manufacturers, and that young adults have at least moderate amount of contact with the health care system, it becomes important to determine if a physician's recommendation of the HPV vaccine encourages vaccination among young Malaysian women. If this is seen as an important predictor of vaccination, steps can be taken to increase the quantity and quality of the HPV vaccine recommendation by physicians. The study carried out here was designed to add to existing knowledge about the association between a physicians' recommendation and the decision to get vaccinated with the HPV vaccine among young adult women in Malaysia.

CHAPTER 3

RESEARCH OBJECTIVES

CHAPTER 3

RESEARCH OBJECTIVES

Do young women in Malaysia who recall having a recommendation for the HPV vaccine during their visit to the doctor's office have an increased probability of getting vaccinated? This is the question that needs to be addressed in order to determine the potentially causal influence of a physician's recommendation on HPV vaccine uptake in this population. To answer this question in its entirety, a well-designed, randomized, prospective study with a nationally representative sample should be conducted. However, a study of this magnitude is will require a substantial amount of financial and logistical resources, which is presently not available to the study. Given these constraints, the study that could be feasibly conducted was a descriptive study using a sample of young women from a private university in Malaysia.

The main objective of this study, then, is to determine the proportion of respondents who were vaccinated with at least one dose of the HPV vaccine among those who recall having a recommendation for the vaccine during their visit with a physician.

3.1 Primary Research Objectives

To achieve the main objective, the following questions were asked in sequential order:

1) What is the proportion of respondents who consulted with a physician within the last two years?
2) What is the proportion of respondents who recall having a recommendation for the HPV vaccine during their visit with the physician within the last two years?
3) What is the proportion of respondents who were vaccinated with the HPV vaccine, among those who recall having a recommendation for the vaccine during their visit with the physician within the last two years?

3.2 Secondary Research Objectives

The secondary objectives that are of interest to this study as contributing to the understanding of the proponents and barriers of HPV vaccination in the study population are:

1) What is the proportion of those who have been vaccinated with at least one dose of the HPV vaccine in the study population, regardless of recall of recommendation or the two year time frame?
2) What are the common barriers to vaccination with the HPV vaccine in this population?
3) What are the common sources of information for the HPV vaccine in this population?

CHAPTER 4

METHODOLOGY

CHAPTER 4

METHODOLOGY

4.1 Study design and population

4.1.1 Original study design

As mentioned under "Research Objectives," the study that could feasibly be conducted was a descriptive survey. The study recruited participants from INTI International University, a moderate-sized private tertiary institution in Subang Jaya, the most populous city in Malaysia. The institution was selected based on convenience; personal ties with the university made it possible to gain access to the student population. At this campus, there were 3,807 students enrolled in 2012, out of which 14% were international students. There were 1,415 Malaysian female students enrolled at this campus during the time of the study. *(Data collected directly from university administration)* The plan was to obtain a list of students from the university, either a listserv of all female students or a list of students of a certain class year, so that sampling could occur within a defined sampling frame. This lends to the generalizability of the study results, at least to the female student population enrolled at the university during the study period, assuming that the sample who chose to participate were representative of all female students. The calculated sample size was 241, with a 90% confidence level and a 13% margin of allowable error. The sample size assumptions and calculations are in the Appendix.

4.1.2 Actual study design

A descriptive survey was carried out among a convenience sample of young women from the university, since a sampling list of students was unobtainable from the university. A

convenience sample is a form of non-probability sampling; that is, when some members of the source population have no probability of being selected. While this form of sampling is easy to implement, especially in situations where there isn't a clearly defined sampling frame, the results obtained from a convenience sample is restricted in generalizability.[63] Since we cannot be sure that the sample collected is representative of the larger, target population, the results from this study cannot be appropriately extrapolated beyond the study sample, as will be discussed in more detail in Chapter 6. The use of convenience sampling will also restrict the utility of inferential statistics, such as confidence intervals and p-values, since the results obtained from the convenience sample cannot be appropriately extrapolated to a target population, as described above. Furthermore, the assumptions that went into the sample size calculations are now no longer valid. Having said that, having an estimated sample size will help ensure that sufficient participants were recruited to answer the main question of interest, given the hierarchical structure of questioning.

Female Malaysian student, aged between 18 to 26 years old, were invited to participate in this study. In the Malaysian education system, the last year of secondary education is typically when the student is 17 years old, after which the student may choose to pursue tertiary education. The cut-off point at 26 years old was chosen because of the indication of the more common HPV vaccine, Gardasil, which does not recommend vaccination to women above that age.[64] The study excluded international female students; the factors that influence HPV vaccination among international students may differ greatly according to their nationality, and therefore, may not have been comparable to the local statistics.

4.2 Questionnaire

The questionnaire was entirely in English, as was the language of instruction at most private tertiary institutions in Malaysia. The questions were mostly closed-ended. Open-ended questions were limited to the "Other" option of close-ended questions, to allow for answers that were not accommodated for in the choice of answers. Components of the questionnaire included:

- The front matter, which is composed of an introduction of the study, contact information of the investigators, and terms of participation
- The back matter is the actual questionnaire. This included questions on demographic variables, which were considered important confounders in previous studies,[34-37] and specific objective-oriented questions. There were several terms that were consistently used in the questionnaire and are worth defining here:
    - The term 'doctor' was used to represent any health-care practitioner that the participant met with in the duration of two years prior to the study. The term 'doctor' was expected to be better understood by this population, compared to the term 'physician'.
    - The term visit or consultation refers to any contact with a doctor of health-related issues.
    - The HPV vaccine includes both commercial brands, Gardasil® and Cervarix®, as explained in the front matter

4.2.1 Pretesting of questionnaire

After the questionnaire was designed, it was pretested on a group of 5 young women who resembled the study population: Malaysians aged between 18-26 years old. On average, the respondents said that they took 3 to 5 minutes to complete the questionnaire. There were a couple of disparities among the pre-test group and the study sample. The individuals in the pre-test group were not students at the selected institution, although a few of them were alumni from this institution. Secondly, the questionnaire was sent electronically to the respondents for pre-testing. In the study sample, however, a hard copy of the questionnaire was directly handed to the participants.

Among the comments received from those who responded from the pre-test were:

- What was the HPV vaccine used for?

  This was an important change that needed to be implemented. If the individuals did not know what the HPV vaccine was prescribed for, they would not be able to answer the questions accurately. Therefore, a short sentence describing the vaccines indicated purpose was added to the front matter.

- Type of visit option was limiting

  It was pointed out by one of the respondents that participants may have visited the doctor for more than one reason in the past two years. She felt that allowing participants to select more than one option will provide them with some clarity in answering the question.

4.3 Study approval

4.3.1 Thesis committee approval

This study was designed with the assistance of the Thesis Committee. The proposal to conduct this study was submitted and approved in May 2012 by all three Thesis Committee members.

4.3.2 Michigan State University's Institutional Review Board approval

The proposal for this study was submitted to the Michigan State University's Institutional Review (IRB) Board for review. The study was approved as "Exempt" on May 8, 2012, after several changes were made to the protocol. The main change was the institution of a Drop-Box to ensure anonymity among respondents. Other changes were primarily in the language of the front matter of the questionnaire.

4.3.3 Malaysian National Medical Research Registry approval

Since this study was conducted in a region outside of the United States, research protocol in the country of interest must be taken into consideration. For Malaysia, any research study should be registered with the National Medical Research Registry (NMRR) prior to the start of the study. Apart from that, the investigator also has to be registered as a researcher with the NMRR. The degree to which review and approval was required depends on the nature of the study. For this particular study, there was no further action required except registration. A more invasive protocol would have required more in-depth review.[65] This study was officially registered with the NMRR on May 29, 2012.

4.3.4 INTI International University approval

There was no formal review board at the selected institution. Since the nature of the study was minimally intrusive, permission was granted for conducting the study in a common area of the university by the Vice President of the institution, Dr. Phillip Tan. Class-room outreach or roster-outreach, which was more “invasive”, was less attractive to the institution and required more review. Permission to conduct the study was granted for three consecutive days in June.

4.4 Data collection

Data collection occurred from Monday, June 4, to Wednesday, June 6, 2012. The dates were chosen based on the absence of university holidays. Different programs in the university took their vacation at different times of the year. During the selected dates, all programs were in session, as confirmed by a telephone call to the registrar's office. Data collection was conducted between 9am to 2pm daily for the three consecutive days. This timing was fine-tuned based on observations from the first day. The number of students was the greatest from approximately 9.45am to about 1pm. After 3pm, the number of students on campus dwindled considerably.

The booth consisted of a long table and 3 chairs. On the table were the questionnaires, pens, a drop box, signage and some instructions. A candy incentive was also placed on the table for participants. The booth was placed by the institution authorities at a convenient location that saw the most student traffic; across from the main building elevators. The schematic layout of the campus is displayed in Figure 4.2. The study booth was placed in the area marked "X". From this figure, one can see that students will most likely have to pass through the lift lobby to get to their classes in the main building. It may be worthwhile to point out that the larger area of the university was closed due to construction, which may have led to a bottlenecking of student traffic through the hallway where the study booth was located (see Figure 4.2). However, there is no method to verify the extent to which this phenomenon accounted for the selection bias introduced by convenience sampling.

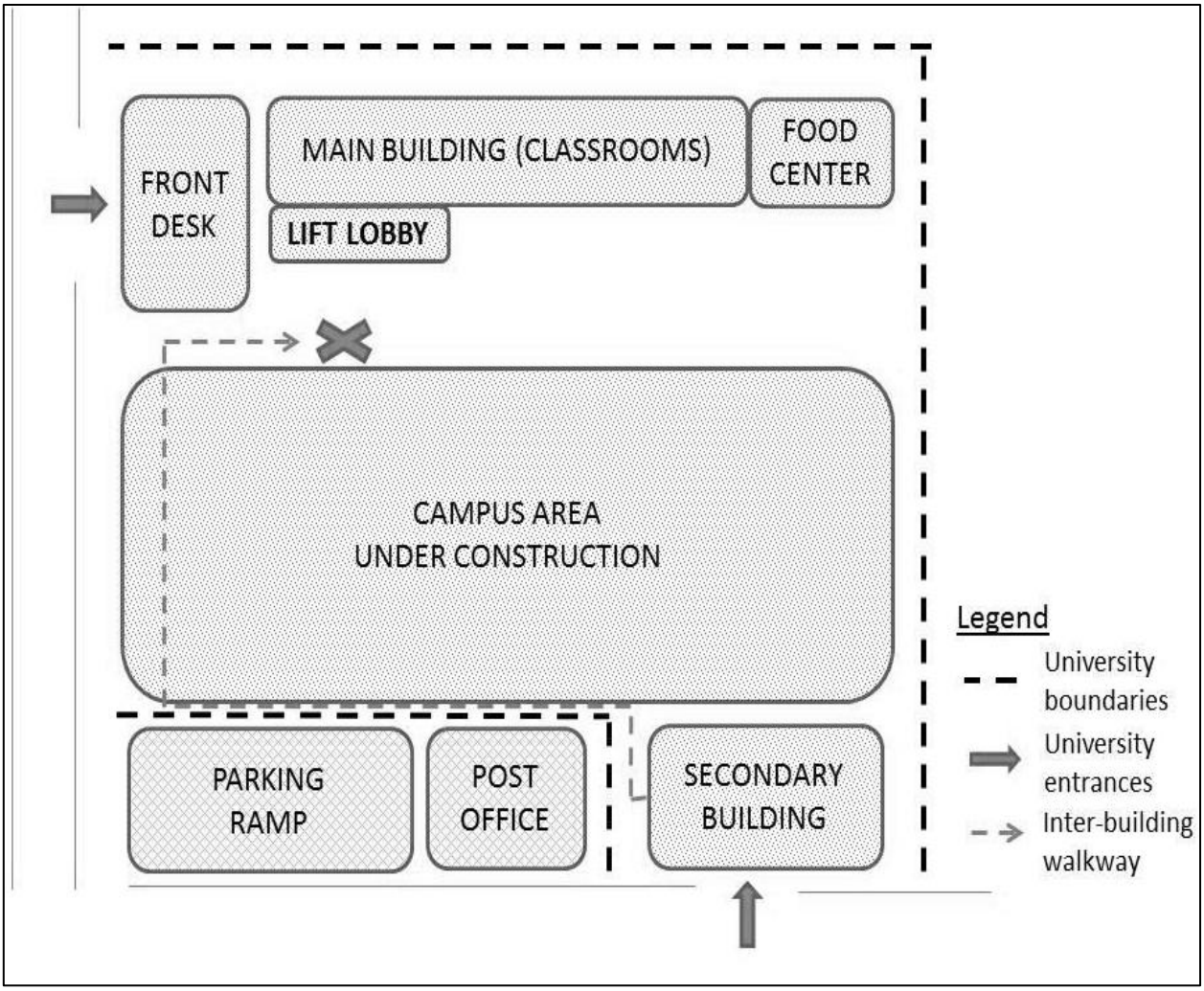

Figure 4.1 Gross layout of the campus. The study booth is marked “X”.

There is a subsidiary building, located south of the main building. This building was previously a separate private university, and was recently taken over by INTI University College. To maximize the number and type of students in the study, the investigator set up a booth in the second building on the last day of data collection. However, the student body there was very small and by afternoon, there were minimal prospects for participation. The investigator shifted the booth back to its original location so that the desired sample size could be achieved.

The questionnaire was offered to most female students who pass by the booth or were waiting for the elevator. They had a choice of filling it out at the table, or taking it with them to class, if they were in a hurry. This method was employed in hopes of increasing participation rates. Many students accepted the questionnaire upon learning that they could take it with them and return it at a later time. Most often, the following phrase was used when a student was approached: “Would you like to participate in a short survey? It’s about the HPV vaccine. It will only take a few minutes. If you are in a hurry, you can bring it back to me later, on your way out”. If they accepted the questionnaire, the investigator advised that they read the front matter, which consists of the introduction and consent information. They were also informed of the drop-off protocol; once they completed the questionnaire, they were to fold it in half and drop it in the box provided at the booth.

4.5 Data management

The data was coded and entered into an Excel spreadsheet. The code book is attached in the Appendix. Each question was entered as a variable in the Excel document. For questions where participants could select more than one option, each option was entered as a separate column. The Excel dataset was saved on a password-protected laptop, and a back-up copy was saved in a separate flash drive specific for this study. The completed questionnaires are kept in a hard-box folder, stored safely away from public eyes. There were some variables that were further recoded to facilitate data analysis:

1) Age was calculated from birth year to the year 2012. Among the 223 participants, only 200 provided a birthdate in the survey. 18 participants did not provide a birthdate, and 5 participants provided an erroneous birthdate; the year of birth was given as 2012. Given that the rest of the participants were in this age range, it was assumed that the individuals with missing birthdates also fell within this age range, and was included in the rest of the analysis.
2) Family income was re-categorized into 3 groups: Low (first category, <RM 2,500), Middle (second and third category, RM 2,500-5,000 and RM 5,000-10,000) and High (fourth category, >RM 10,000).
3) Those who answered “others” in the program of study were reclassified whenever possible, according to information obtained from the university website.[66]

4.6 Data analysis

All analyses were performed using the SAS 9.3® Statistical Software package. Each variable in the questionnaire was analyzed by calculating the proportions of responses, over the total number of respondents who were asked the question. For continuous variables, distribution characteristics were analyzed. Since the study population is a convenience-based sample, the assumptions that underlie the generalizability of the findings here are violated, making it inappropriate, and potentially misleading, to use confidence intervals to make assumptions about the "true" population proportion. Therefore, these calculations were not performed. Furthermore, hypothesis testing was not performed for comparisons of proportions, since it heavily relies on the assumption of random selection, which is not the case here. Therefore, proportions were reported on their own, without any measure of statistical significance.

CHAPTER 5

STUDY RESULTS

CHAPTER 5

STUDY RESULTS

5.1 The study population

There were 243 questionnaires completed in the series of three days. Of these 243 surveys, 20 respondents stated that they were not Malaysian citizens, and were therefore excluded from further analysis. This reduced the sample size to 223, 18 participants shy from the calculated sample size.

Table 5.1 describes the distribution of the study sample. The mean age of the respondents was 19.95 years old, with a standard deviation of 1.69 years. Most of the respondents were Chinese (74%, 165/223), with Buddhism as the predominant religion (59.2%, 132/223). All respondents were not married, and most of the participants were from low (40.4%, 90/223) and middle (35.4%, 79/223) income families. 61.4% (137/223) of the respondents were degree-seeking students and 62.3% (139/223) were Business majors.

Variable	Categories	Number	Percent, %	Mean (Standard deviation)
Age		200		19.9(1.69)
Relationship Status	Married	0	0	
	Single	204	91.5	
	In a steady relationship	19	8.5	
Race				
	Chinese	165	74.0	
	Indian	45	20.2	
	Malay	8	3.6	
	Others	4	1.8	
	Missing	*1*	*0.5*	
Religion				
	Buddhist	132	59.2	
	Christian	46	20.6	
	Hindu	25	11.2	
	Islam	8	3.6	
	Others	6	2.7	
	Missing	*6*	*2.7*	
Family Income				
	Low	90	40.4	
	Mid	79	35.4	
	High	20	9.0	
	Missing	*34*	*15.2*	
Program of study				
	Foundation	19	8.5	
	Diploma	59	26.5	
	Degree	137	61.4	
	Masters/PhD	1	0.5	
	Others	3	1.3	
	Missing	*4*	*1.8*	
Major of Study				
	Business	139	62.3	
	Mass Communication/Public Relations	35	15.7	
	Science	17	7.6	
	Engineering	7	3.1	
	Others	16	7.6	
	Missing	*8*	*3.6*	

Table 5.1: Characteristics of the study population

5.2 Primary Research Objectives

5.2.1 Consultation with a physician within the past 2 years

Approximately 70.9% (158/223) of the respondents had consulted with the doctor at least once in the past two years. Within this group, about two thirds had consulted with a doctor more than once in the last two years. These results are displayed in Table 5.2.

Consultation with a doctor in past 2 years (n=223)	Frequency	Percent, %
Yes	158	70.9
Once	*53*	*33.5*
More than once	*105*	*66.5*
No	62	27.8
Missing	*3*	*1.4*

Table 5.2 Consultation with doctor in the past 2 years

As shown in Table 5.3, the main reason for consultation with a doctor in this study population was reported as acute illness (39%, 62/158). About 8% (13/158) of the respondents reported that they consulted with a physician for an annual medical examination and vaccination, respectively, while 5% (8/158) visited the doctor for a follow-up examination. The majority of respondents (46.2%, 73/158) did not answer this question.

Type of visit (n=158)	Frequency	Percent, %
Acute Illness	62	39.2
Annual Medical Examination	13	8.2
Vaccination	13	8.2
Follow-up Examination	8	5.1
Other	1	0.6
Missing	*73*	*46.2*

Table 5.3 Reported type of doctors' visit. The denominator for these proportions are n=158, that is, those who had consulted with a doctor in the past two years (refer to Table 5.2). The total frequency and percent exceed 158 and 100%, respectively, because respondents were allowed to select more than one option.

5.2.2 Recommendation of the HPV vaccine by a doctor

Among those who had consulted with a physician, only 21% (33/158) reported that they recall having a recommendation for the HPV vaccine during their visit. An interesting finding in the present study is that only in 30% (10/33) of these recommendations did the respondent recall the doctor initiating the conversation about the vaccine; 36% (12/33) of the conversation was said to be initiated by the respondents and 24% (8/33) by a third party. Table 5.4 shows these results.

Recommendation of the HPV vaccine (n=158)	Frequency	Percent, %
Participant recalls being recommended	33	20.9
Initiated by doctor	10	30.3
Initiated by patient	12	36.4
Initiated by third party	8	24.2
Missing	*3*	*9.1*
Participant does not recall being recommended	121	76.6
Missing	*4*	*2.5*

Table 5.4 Recall of recommendation of the HPV vaccine during consultation. The denominator for these proportions are n=158, that is, those who had consulted with a doctor in the past two years (refer to Table 5.2).

Table 5.5 shows that respondents recall recommendation most often when the visit was for a vaccination (intended type of vaccination was not specified). Recommendation of HPV vaccination was also said to occur in 54% (7/13) of annual medical examination. It least frequently occurred when the visit was for an acute illness (25.8%, 16/62).

		Recall of recommendation of HPV Vaccination			
		Yes		No	
Type of visit	n	Frequency	Percent, %	Frequency	Percent, %
Acute Illness	62	16	25.8	46	74.2
Annual Medical Examination	13	7	53.9	6	46.1
Vaccination	13	12	92.3	1	7.7
Follow-up Visit	8	3	37.5	5	62.5
Missing	*73*				

Table 5.5 Type of visit during which recommendation may have taken place

5.2.3 HPV vaccination among those who recall being recommended

Among those who recall having a recommendation of the HPV vaccine during the consultation with a physician in the past two years, 66.7 % (22/33) said that they subsequently received the vaccine. The results are shown in Table 5.6. Vaccination typically occurred during the visit in which it was recommended; only in 18% (4/22) of the cases did vaccination occur at a later date.

HPV Vaccination (n=33)	Frequency	Percent, %
Vaccinated	22	66.7
During the visit	18	81.8
After the visit	4	18.2
Not vaccinated	9	27.3
Missing	*2*	*6.1*

Table 5.6 HPV vaccination for those who recall a doctor's recommendation. The denominator for these proportions are n=33, that is, those who recall having a recommendation for the vaccine during their consultation with a doctor (refer to Table 5.4).

Referring to Table 4.7, HPV vaccination most often occurred when participants visited the doctor for the purpose of vaccination (100%, 12/12); however it was unclear from this study whether or not the intended vaccination was the HPV vaccine. The trend here is similar to that seen for the recall of recommendation of the vaccine; it most frequently occurs during vaccination visits, followed by annual medical exam visits, follow-up visits, and lastly, acute illness. Interestingly, vaccination more often occurs when the respondent initiates the conversation about the vaccine (83%, 10/12).

Characteristics of visit	N	HPV Vaccination			
		Yes		No	
		Frequency	Percent, %	Frequency	Percent, %
Type of visit					
Acute Illness	16	8	50.0	7	43.8
Annual Medical Examination	7	5	71.4	2	28.6
Vaccination	12	12	100.0	0	0.0
Follow-up Visit	3	2	66.7	1	33.3
Missing	*2*				
Initiation by					
Doctor	10	6	60.0	4	40.0
Respondent	12	10	83.3	2	16.7
Third party	8	6	75.0	2	25.0
Missing	*3*				

Table 5.7 Characteristics of the visit in which HPV vaccination may have been received. The total number of HPV vaccinees by type of visit exceed n=22 because participants were allowed to select more than one type of visit.

5.3 Secondary Research Objectives

5.3.1 HPV vaccination rate in the study population

The vaccination rate in this sample population is 18.4% (41/223). The vaccination rate was defined as ever having at least one dose of the HPV vaccine, independent of whether or not the respondent consulted with a doctor in the past two years. These results are listed in Table 5.8.

HPV Vaccination	Frequency	Percent, %
Vaccinated	41	18.4
Not vaccinated	178	79.8
Missing	*4*	*1.8*

Table 5.8 HPV Vaccination in the study population

Table 5.9 displays some of the characteristics of the respondents by vaccination status. Respondents who were younger than 21 years old had a higher proportion of vaccinees than those who were older; 21% (28/135) compared to 13% (9/70). Respondents who admitted to being in a relationship had a higher proportion of vaccinees than those who are single; 42% (8/19) compared to 16% (33/204). Those of Malay race have a higher proportion of vaccinees than the other races. This variance is also reflected when looking at religion; Muslims, who are typically of Malay ethnicity, have a higher proportion of vaccinees than the other religions. Those who are from families with higher income status also have a higher proportion of vaccinated individuals, compared to those from low and middle income families. Another interesting factor to look at was health seeking behavior, potentially measureable from the frequency of consultation with a doctor in the past two years. The proportion of vaccinated respondents was only slightly higher among those who admitted to visiting the doctor more

than once in the past two year (24%, 25/105) compared to those who visited the doctor only once in the same time frame (21%, 11/53). However, these two proportions were much larger than those who did not visit a doctor at all in the past two years (6%, 4/62).

Characteristics of participants	n	HPV Vaccination			
		Yes		No	
		Frequency	Percent, %	Frequency	Percent, %
Age					
Under 21	135	28	20.7	104	77.0
21 and above	70	9	12.9	60	85.7
Missing	*18*				
Relationship status					
Single	204	33	16.2	167	81.9
In a relationship	19	8	42.1	11	57.9
Race					
Malay	8	3	37.5	5	62.5
Chinese	165	30	18.2	131	79.4
Indian	45	8	17.8	37	82.2
Others	4	0	0.0	4	100.0
Missing	*1*				
Religion					
Muslim	8	3	37.5	5	62.5
Christian	46	9	19.6	37	80.4
Hindu	25	5	20.0	20	80.0
Buddhist	132	21	15.9	107	81.1
Others	6	1	16.7	5	83.3
Missing	*6*				
Family income					
Low	90	16	17.8	71	78.9
Middle	79	14	17.7	65	82.3
High	20	6	30.0	14	70.0
Missing	*34*				
Consultation in past 2 years					
Yes, once	53	11	20.8	41	77.4
Yes, more than once	105	25	23.8	79	75.2
No	62	4	6.5	57	91.9
Missing	*3*				

Table 5.9 Characteristics of participants by HPV vaccination status (n=223)

5.3.2 Barriers to HPV vaccination

From Table 5.10, the main reason for not getting vaccinated was the lack of knowledge about the vaccine (57%, 104/182). The second and third most common reasons were the fear of needles (20%, 36/182) and price (13%, 29/182). Perceived lack of need was seen in a quarter of the respondents; 13% (24/182) admitted that they did not get vaccinated because they were not sexually active and 12% (22/182) said that they did not need the vaccine. Only 10% (18/182) were concerned with side effects, while only 2% (4/182) never considered taking it. Among the 4 respondents who did not respond to whether or not they were ever vaccinated with the HPV vaccine, 3 respondents said that they did not know about it and 1 person said that they did not need it (data not shown).

Reasons for not getting vaccinated (n=182)	Frequency	Percent, %
Don't know about it	104	57.1
Fear of needles	36	19.8
Price	29	12.9
Not sexually active	24	13.2
Don't need it	22	12.1
Fear of side effects	18	9.9
Never considered taking it	4	2.2
Not yet/No time	2	1.1
Parents did not discuss it	2	0.6
Missing	*12*	*6.6*

Table 5.10 Reasons for not getting vaccinated. The question was asked of 182 respondents, that is, those who were not vaccinated with the HPV vaccine or with missing responses to said question (refer to Table 5.8). The total frequency and percent exceed 182 and 100%, respectively, because respondents were allowed to select more than one option.

Another interesting aspect for analysis is the barriers to vaccination for those who recall having a recommendation from a physician. Among the 11 respondents that fell in this category, the most prominent barrier was price (54.6%, 6/11). 3 participants indicated that they

were afraid of needles and 1 of side effects. Even with a recommendation from a physician, 2 respondents indicated that they did not know about the vaccine and 2 indicated that they did not need it. These data are displayed in Table 5.11.

Reasons for not getting vaccinated (n=11)	Frequency	Percent, %
Price	6	54.6
Fear of needles	3	27.3
Don't know about it	2	18.2
Don't need it	2	18.2
Fear of side effects	1	9.1
Missing	*2*	*18.2*

Table 5.11 Reasons for not getting vaccination among those who recall having a recommendation. The total n is greater than 11 because the participants were allowed to select more than one option to answer this question. The total frequency and percent exceed 11 and 100%, respectively, because respondents were allowed to select more than one option.

5.3.3 Sources of information for the HPV vaccine

The last secondary objective of interest was the sources of information for the HPV vaccine, among those who did not recall having a recommendation from a physician in the past two years. Over 53% (65/121) of participants did not answer this question. Among the respondents who did not receive a recommendation from a physician, approximately 29% (35/121) of them heard about the vaccine from the media, which was defined in the questionnaire as information from newspaper, television or the radio. The second most common source of information was from family members (16.5%, 20/121), followed by friends (11.6%, 14/121), the web (9%, 11/121) and from places of education (5%, 6/121). These data are in Table 5.12.

Source of information (n=121)	Frequency	Percent, %
Media	35	28.9
Family	20	16.5
Friend	14	11.6
Web	11	9.1
School/College	6	5.0
Family doctor	1	0.8
Other(unspecified)	1	0.8
Missing	*65*	*53.7*

Table 5.12 Source of information for the HPV vaccine. The question was asked of 121 participants, that is, those who did not recall a recommendation for the HPV vaccine by their physician (refer Table 5.4). The total frequency and percent exceed 121 and 100%, respectively, because respondents were allowed to select more than one option.

CHAPTER 6

DISCUSSION

CHAPTER 6

DISCUSSION

6.1 Summary of findings

Among the respondents that completed the questionnaire, 71% (158/223) had consulted with a physician in the past two years, out of which only 21% (33/158) recall having a recommendation for the HPV vaccine during their visit. Among those who recalled having a recommendation, 67% (22/33) of respondents said that they were subsequently vaccinated with the HPV vaccine. The self-reported HPV vaccination prevalence in this sample is 18.4% (41/223), regardless of recommendation or the two year time frame. The main barrier to vaccination among those who were not vaccinated was identified as lack of knowledge (57%, 104/182). For respondents who were not vaccinated even with recall of a recommendation, the main barrier was price (54.6%, 6/11). The main source of information for the HPV vaccine among those who did not recall a recommendation is the media (29%, 35/121), which includes the newspaper, television, or the radio.

The main objective of this study was to investigate the role of a physician's recommendation on HPV vaccine uptake in this population. These data suggest that having a physician's recommendation may be positively associated with the woman's decision to get vaccinated with the HPV vaccine. The questionnaire did not specifically collect information on the proportion of vaccinees among those who did not recall a recommendation in the past two years. Using the data from the overall HPV prevalence, independent of recommendation or the two year time frame, one could estimate that this proportion lies between 0 % (0/121) to 16%

(19/121), which is still much lower than the proportion of vaccinees among those who recall a recommendation (67%, 22/33). However, the comparability of these two proportions are somewhat questionable, as the respondents that we are assuming to fall in this category may actually have been vaccinated prior to the 2-year interval, and may have also received a recommendation for it prior to this 2 years.

Interestingly, in this study population, only 30% (10/33) of respondents who recall a physician's recommendation remembered that the physician initiated the conversation; 60% (20/33) of the respondents recall that they or a third party, usually their mother, had initiated the conversation about the vaccine. Moreover, this data shows that vaccination was more common when the conversation was initiated by the respondent, compared to when it was initiated by the doctor. This may suggest that a physician's recommendation may not be the driving force behind the decision to get vaccinated among these women; prior knowledge of the vaccine or prior intention to receive vaccination may play an important role in this framework.

However, such conclusions about the variables investigated in this study and the population to which they can be appropriately applied to should be done with caution, given the less than desirable study design. The next sections will describe the comparability of the study results with what is found in existing literature, as well as an in-depth discussion about the limitations and strengths of the study, followed by some of the lessons learnt and possible future directions for this area of study.

6.2 Comparisons to existing literature

The present study showed that 67% (22/33) of the respondents who recall having a recommendation by a doctor reported that they were subsequently vaccinated, with over 80% (18/22) being vaccinated during the consultation in which recommendation was given. In the Chow et al. study of Southeast Asian populations, including Malaysia, 91% of mothers had their daughters vaccinated after getting a recommendation from a doctor,[53] which is much higher than that seen in the present study. However, the Chow et al. study asked these questions of mothers, who may have different responses to a physician's recommendation, compared to young adults. The 2012 study by Marchand et al. of young women in a community college in Los Angeles showed that 70.3% of participants who received a recommendation were vaccinated with the HPV vaccine,[42] similar to what was found in this study. Previously conducted studies on the relationship between having a physician's recommendation and HPV vaccination among young women have consistently shown a positive significant association, as seen in the summary shown in Table 2.2 (Chapter 2).[39-43,49-51]

There were other variables of interest in this study that should also be assessed for consistency, especially in the context of young women in Malaysia. For variables such as health-seeking behaviors and recollection of a physician's recommendation, no published data on such statistics in young Malaysian women were found during literature search. A population-based study by Krishnaswamy et al in 2009 showed that 41% of their sample of nationally representative households had used some form of healthcare service in the last 3 months, and

this proportion was similar across the age-groups.[59] A comparison to the present study is difficult given the differing populations and time periods. The prevalence of recollection of vaccine recommendation by a physician in the present study is 21%. This is similar to that found in the Chow et al. study of four Eastern countries including Malaysia, which stated that 25% of physicians admitted to actively recommending the vaccine to their patients.[53] Again, the comparison cannot be made linearly as the question was asked to the physician instead of the participant.

The prevalence of HPV vaccination in this sample regardless of a physician's recommendation or the two year time frame was 18.4% (41/223). This percentage fell in the lower range of previously reported vaccination rates among young Malaysian women, which ranged between 3.6% and 51%.[34-37] As mentioned previously, the majority of these studies were conducted using convenience samples,[34-36] and therefore may not be comparable to each other or representative of the "true" population value. Only in the Rashwan study in 2012 did they use a defined sampling frame, and this study reported the lowest vaccination rate, 3.6%.[37]

Many studies have also investigated the barriers to vaccination and sources of HPV vaccine information in young Malaysian women. However, as mentioned in Chapter 2, there is much heterogeneity in the findings across studies. In the present study, over 57% (104/182) of those who were not vaccinated did not know about the HPV vaccine. This greatly contrasts what was found in the 2012 study by Rashwan et al. who found that only 5% of their

participants, who were medical and pharmacy students, did not know about the vaccine.[37] The Wong et al. 2010 study of public college students showed a much higher percentage of uninformed participants, over 90%.[35] The main source of information in the present study is the media, namely, newspapers, television, and the radio. This finding is similar to that of the previously mentioned Wong et al. study, who found that 49% of students heard about the vaccine from the newspaper.[35] Family members were also an important source of information for this study and previous studies.[35,37] Only one respondent in the present study reported that the family doctor was their source of information. It is possible that this number is low because the option was not readily available on the questionnaire. However, the previously mentioned Wong et al. study also reported that only 1.5% of their participants cited a healthcare professional as their source of information about the vaccine.[35]

6.3 Limitations of study results

6.3.1 Limitations due to study design

The use of a descriptive survey severely restricted the ability to draw causal conclusions about the investigated relationship. Even though the questionnaire attempted to recreate the time order of the events, one cannot be sure that temporality is preserved in this study. Furthermore, this study did not report a measure of association, per se, due to the lack of a comparison group, i.e. vaccination rate among those who did not recall a recommendation. In the Marchand et al. study, for example, participants who did not recall a recommendation were all not vaccinated. However, it would have been beneficial in this present study to have recorded this information, as it may have allowed us to estimate the magnitude of this association.

6.3.2 Biases due to convenience sampling

This study recruited young female students who volunteered to participate in the study, which poses several problems in the study. Firstly, the investigator cannot be sure that all female students pass by the study booth during the study period. The campus is small, but there are a few other buildings that host classes that do not require students to pass through the study area. Secondly, among those who pass by the lobby, not all of them were approached. There were times of heavy traffic in the lobby when it was not possible to approach all the eligible students. Thirdly, there were students who were approached but were not willing to participate. It was not possible in this context to get information about the students who refused to participate; thereby making it impossible to determine if those who

participated were significantly different than those who did not. Also, participants were approached based on their "student-like" appearance. There could be instances where the investigator failed to approach a potential student who may not have "appeared" to be one. At each stage presented above, there is a possibility for selection bias.

Given the absence of a well-defined sampling frame and the lack of random sampling, it cannot be definitely said that the group of respondents in this study is representative of the student population at the university, let alone the general population of young women in Malaysia. Therefore, the results of this study cannot be appropriately assumed to apply to a larger population without making stretching assumptions about the semblance of the study population to the target population. Since no data is presently available about the demographic composition of the female students who were enrolled at this institution during the study period, making such assumptions about generalizability to the female student population may also not be possible. Also, the data from this study should not be assumed to apply to all eligible young women in Malaysia because the study only recruited women who were enrolled in a single private tertiary institution. According to the World Bank data on Malaysia, enrollment in tertiary education among 19 to 24 year olds was 40.2% in 2009.[67] Therefore, young women who attend tertiary education may express different health behaviors than those who did not attend tertiary education. Furthermore, young women who enroll in private tertiary education may also be different than those who enroll in public universities. Therefore, drawing conclusions about generalizability may be misleading and potentially erroneous.

Selection bias could also lead to a misrepresentation of the investigated relationships in this study. Those who did not participate in the study may have expressed different responses than the participants who did; that is, the responses from the respondents from this study may not reflect the average response of the female student body in this campus. Therefore, any assessment of the relationships seen in this study should be done keeping in mind that it was analyzed from a potentially biased sample.

6.3.3 Biases due to sample size

An important issue of note is the inadequate sample size. Based on apriori estimations, the desired sample size was 241 students. Over 240 questionnaires were successfully collected over the period of three days. However, after excluding the mistakenly approached international participants, the total sample size for the study was reduced to 223, 7% less than the desired sample size. Furthermore, the sample size calculation was made under the assumptions of a 90% confidence level and a 13% allowable error, which is far from ideal as a measure of precision. Given that, it allowed for an achievable sample size based on the resources available. Unfortunately, this severely restricts the extrapolation of the study findings to a larger, target population. This may not be an issue in this study, since the extrapolation of results to a larger population is already restricted by convenience sampling. However, the insufficient sample size could have skewed the proportions observed, leading to incorrect conclusions about the study population. In this study, only 15.8% (223/1415) of the eligible female student population was enrolled, lending to the possibility of great selection bias. This

condition is worsened in situations where conclusions were drawn from analyses with very small numbers, especially for the main question of interest here.

6.3.4 Other biases

There are several other biases that could influence the results of this study. Firstly, there was potential for misclassification bias. Given that a large percentage of the respondents reported that they did not know about the vaccine, there was a possibility that participants could have mistaken the HPV vaccine for some other vaccine. For example, the Hepatitis A and B vaccine is given in a similar three-course fashion, and may even sound similar to the HPV vaccine. Routine Hepatitis B vaccination for infants only begun in 1989 and the Hepatitis A vaccine is not part of the standard immunization program in Malaysia,[68] possibly leading to a later age of vaccination with these vaccines. Secondly, the sensitive nature of the questions could also lead to misclassification. The human papilloma virus is a known sexually-transmitted virus. Therefore, some respondents may be reserved to answer questions about such a vaccine for fear of insinuations that may follow. This condition may be worsened when participants travel in groups. This may also have been the case for the question on the respondents' relationship status, where only 8.5% admitted to being in a steady relationship. There is also concern that allowing students to take the questionnaire with them to class to complete at a later time would lead to less than accurate responses. This means that the investigator had no control over the environment in which the questionnaire was completed, which may have had an influence on the answers provided, possibly leading to misclassification. On the flip side, however, permitting the participants to complete the questionnaire at a later time may have

allowed them to do so in a more comfortable setting, given the lack of privacy at the study booth.

Recall bias could have also lead to misclassification of the variables of interest. All of the variables in this study were self-reported. Furthermore, the primary questions of interest asked respondents to remember incidents that occurred over the past two years. Capturing data on type of visit, whether or not one recalls a recommendation, or who initiated the conversation is particularly difficult. Respondents whose visit took place closer to the study period may impart more accurate information than those who had the visit earlier in the time interval. Unfortunately, this study did not collect data on the exact time point of the doctor's visit during which the recommendation was said to be given.

Another bias that may affect some of the results in this study is missing data. There were several variables that yielded high proportions of missing data. Firstly, approximately 10% of the respondents entered an erroneous birthdate. Since all of the other respondents fell within the desired age group, it was assumed that these 10% also fell in this range. Secondly, 15% of the respondents did not answer the question about family income. The question on type of visit also had a large amount of missing data; 46% of the respondents did not answer this question. It was interesting that when the analyses were restricted to respondents who remember receiving the recommendation, only 6% of the data on type of visit was missing. This may be indicative that the behavior of this subset of respondents may differ from the larger sample of respondents. The largest area of missing data was for the question on sources of information, with over 53% missing. This is rather unfortunate as the information to be gained

would have been very helpful to understanding how the HPV vaccine was introduced to this sample. The reason for this degree of missingness is not clear; perhaps the question was not well understood by the respondents or was “hidden” by the layout of the questionnaire.

6.4 Strengths of this study

The main objective of this study was to look at the impact of a doctor's recommendation on HPV vaccination among a subset of young women in Malaysia. In this study, 67% (22/33) of respondents who recalled having a recommendation subsequently received the vaccine. It could be interpreted, albeit cautiously, that the decision to get vaccinated with the HPV vaccine was positively influenced by the doctor's recommendation in this group of respondents. Despite its limited generalizability, the findings of this study can be used to generate research questions in investigating the role of a physician's recommendation in increasing HPV vaccination rates among eligible young women. Particularly, this study found that the majority of respondents who recalled having a recommendation had some knowledge of the vaccine prior to the conversation with the doctor. It also found that vaccination was more common when the respondents came to the doctor's office with knowledge of the vaccine. Therefore, there are several possible roles that physicians may play; they may be the ones who introduce the vaccine, which in this study was said to occur only 30% (10/33) of the time, or they may serve to encourage or discourage the vaccine among those enquiring about it. This study, then, suggests that a physician's recommendation may serve as an important effect modifier in the pathway between the introduction of the vaccine and the decision to get vaccinated (Figure 6.1).

Another possibility is that the increased proportion of vaccinees among those who were recommended is a mere artefact of knowledge of the vaccine prior to the doctor's visit. In other words, the association between a doctor's recommendation and HPV vaccination could be

confounded by the primary source of information that may have convinced these individuals to be more receptive towards the vaccine. Factors that facilitate the primary introduction of the vaccine, therefore, also need investigation. It was unfortunate that this study did not inquire about the main sources of information for those who had the conversation about the vaccine with their physician, as noted earlier. Among those who did not recall the recommendation, the main source of information was the media. Whether or not this source of information sufficiently convinced the individual to have a conversation with their physician should be investigated.

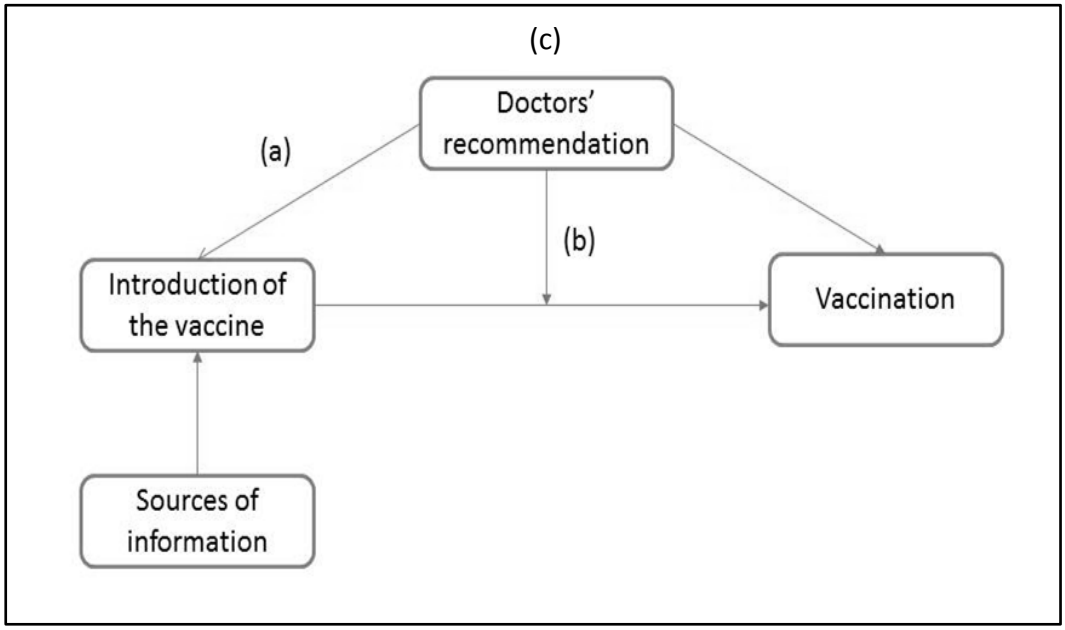

Figure 6.1 Hypothetical causal diagram on the role of a physician's recommendation as a) an introducer, b) as an effect modifier, or c) as a confounder.

Beyond its research generating properties, the findings from this study also seek to add new dimensions to existing knowledge about the factors associated with HPV vaccine acceptance in this group of respondents. While much effort has been focused on vaccinating 13-year old girls, there is a large group of eligible young adults who could greatly benefit from

being vaccinated. Factors that facilitate or hinder vaccination among eligible young women have been examined, but the populations of interest in previous studies in Malaysia were primarily high school students[31,52] and public university students;[34-37] this study looked at young women in a private university. Furthermore, studies in public universities were composed of predominantly Malay participants; [34-37] this study has a large proportion of Chinese respondents and moderate proportion of Indian respondents, whose risk for future cervical cancer is higher than their Malay counterparts.[17]

This study also provided some important information about this group of respondents, such as their health-seeking habits. This is not only important to this analysis, but it is also an indication of how much interface this group has with the health-care system. It suggests that the health-care setting could be a good avenue to promote the HPV vaccine and other public health messages that could potentially improve the lives of these young women. This study also identified barriers to vaccination in this group of respondents. It identified lack of knowledge as a major barrier of vaccination, indicating that the common sources of information about the vaccine may not be readily available to these respondents. This study also found differences in proportions of vaccinees based on age group, race and religion, relationship status, and health-seeking behaviors, which could be interpreted as potential confounders for future studies on HPV vaccination in a similar group of young women.

Moreover, this study was the first to ask young Malaysian women about whether or not they recall having a conversation about the vaccine with their physician. As mentioned

previously, there were several studies that asked doctors about their recommendation habits.[53,56] However, asking young women whether or not they have been given a recommendation has some advantages over asking the question to physicians. Firstly, a doctor may not be able to give an accurate number of how many people were given a recommendation or be able to characterize the type of people who received the recommendation. The doctor may not be able to inform us how many patients had actively inquired about the vaccine. Also, it gives an indication that the message was received by the patient, which gives the results of the present study an extended definition. Respondents who reported that they did not receive a recommendation could include two groups; the group that did not receive a recommendation at all and the group in which recommendation was given but inefficiently.

While the results obtained in the present study is fraught with threats to both internal and external validity, it can still lend some clues about the role that a physician's recommendation plays in the decision to get vaccinated with the HPV vaccine among young eligible women that could be built upon in future studies.

6.5 Lessons learnt and future directions for research

The limitations of the utility of the study results as a consequence of convenience sampling should be acknowledged and avoided in future research. It led to the uncertainty of the validity of the findings and the inability to generalize the results to the larger population of young Malaysian women, whom this research was intended to benefit. Future studies should randomly select their samples from a well-defined study base to uphold the applicability of their results. Furthermore, the questionnaire should have also been tested in a focus group, apart from pre-testing the questionnaire. While the pre-test helped to improve the comprehensibility of the questions, a focus group would have identified problematic questions as well as areas of interest that, in this case, were recognized post-data collection. An example would be the distinction between being given a recommendation and having a conversation about the vaccine. The questionnaire specifically asked if the respondents recalled having a recommendation of the vaccine. The problem arises for those who said no; are these individuals referring to the fact that they did not have a conversation about the vaccine with their doctor or to the fact that the doctor recommended them against the vaccine? The failure to separate this question into two, about conversation and recommendation respectively, may have compromised the interpretation for the respondents who said “no”. It would have been interesting in this study to see if there was a proportion of the respondents who received a recommendation against the vaccine. Another point of interest that was overlooked in the design of the study was the sources of information for those who recall having a recommendation for the HPV vaccine. This information would have been very helpful to the understanding of the introduction of the HPV vaccine, especially since 60% of the conversation

about the HPV vaccine in this study was said to be initiated by the respondent or a third party, not the physician.

Besides providing lessons to improve future research, this study provided important clues about studying this relationship in this population, as described in the earlier section on strengths of the study. To test this potentially causal relationship, a well-designed analytic study with a larger, more representative sample is required. Future studies should be designed to identify the role that physician's play in the complex behavioral model of decision making in these young women. Marchand et al. used the Health Behavior Framework to outline factors that influence a woman's decision to get vaccinated with the HPV vaccine, including personal factors, barriers and support systems, as well as health-care systems factor.[42] The use of such frameworks or models will increase the investigator's understanding of the factors that promote the acceptance of the vaccine. It will also provide a good understanding of some of the covariates that should be included in the analysis of future research.

For this group of respondents, there are other sources of information, apart from the physician, that seem to play an important role in the introduction of the vaccine. These sources should be investigated and amplified, if deemed important to the spread of vaccine awareness. In this study, the most common barrier to vaccination was the lack of knowledge about the vaccine; a problem that could be solved if we identify and intensify the more influential sources of information. Also, other common barriers of vaccination should be identified through more nationally representative research. Further investigation is required to identify barriers faced by physicians in recommending the vaccine to their patients, as well as research into the doctor-

patient relationship, especially the extent to which recommendation is acceptable in this multicultural society.

CHAPTER 7

CONCLUSION

CHAPTER 7

CONCLUSION

From this survey, about two thirds of the respondents who reported having a recommendation for the HPV vaccine during a visit with a physician in the past two years were vaccinated with the HPV vaccine. Also, participants with prior knowledge and/or intentions to be vaccinated were more likely to have received the vaccine after the conversation with the physician. Given the limitations set forth by the non-probability sampling scheme, the results from this study cannot be appropriately extrapolated to the general population of urban female young adults in Malaysia. However, the results of this study give an indication that a physician may play an important role in introducing and/or encouraging the vaccine to eligible young women. The conversation with the doctor about the vaccine is not only expected to inform people about the existence of the vaccine, it is also expected to help dispel some of the fears and misconceptions about the vaccine.

If the relationship between a physician's recommendation and HPV vaccination holds true, it has important public health consequences in Malaysia, such as the allocation of funds between avenues of vaccine promotion. Convincing a smaller group of doctors may be more feasible and cost effective, as compared to attempting to convince the general population. However, if the relationship is confounded, that is, if there is another factor or source of information that is driving individuals to have a conversation about the vaccine with their doctor, then increasing recommendation rates alone may not be beneficial. Unfortunately, this study did not collect information on all the pieces of this complex puzzle to put together a

complete picture. However, it lays the foundation for future studies on the role physicians can play in increasing HPV vaccination rates among young women. It implies that further investigations into the proponents and obstacles of HPV vaccine uptake is necessary if an increase in vaccination rates is expected, in the aims of reducing future cervical cancer incidence rates in Malaysia.

APPENDIX

A.1 Sample size calculation

The sample size was calculated based on a combination of apriori information and conservative estimations, as illustrated in the Figure A.1.

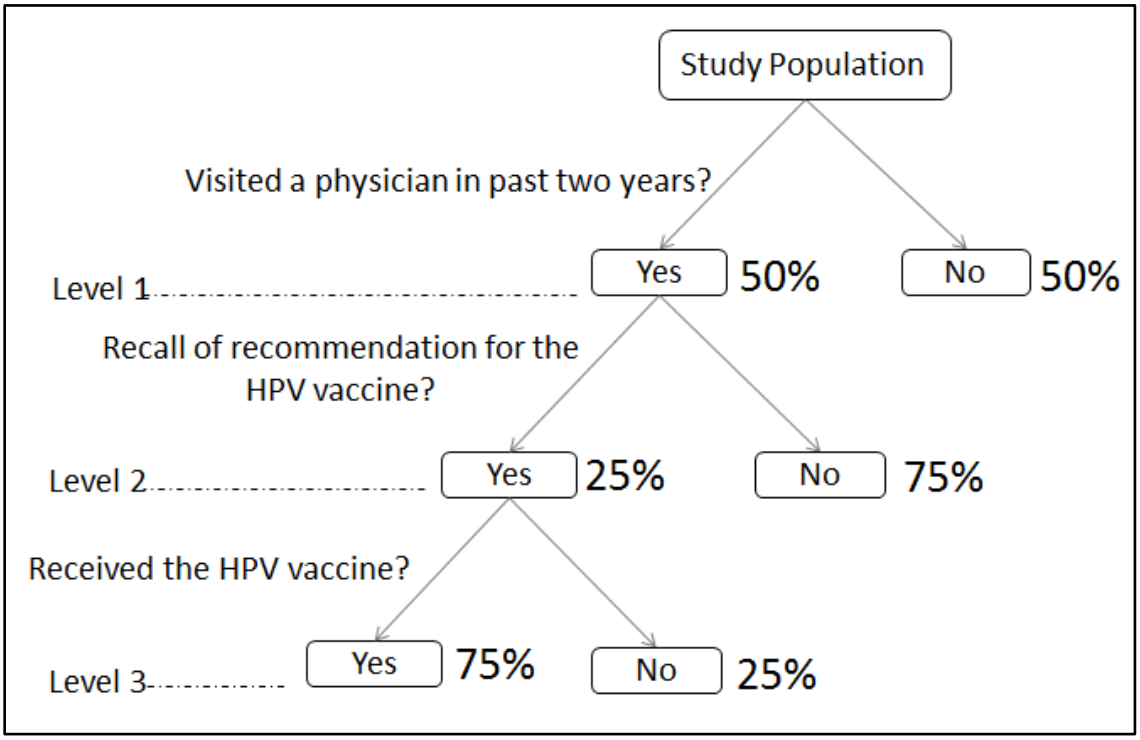

Figure A.1 Sample size calculation schematic.

Following Figure A.1, Level 1 proportions are based on a study conducted in 2009 that reported that approximately 41% of the population utilized health care services in the 3 months prior to the study.[59] Although one would expect that this proportion would be larger when the time interval is increased to two years, the investigator sought a conservative measure of 50% was taken. The Level 2 proportions were derived from the Chow et al. study of women in Malaysia, Taiwan, Thailand, and Singapore, which found that 25% of physicians admitted to actively recommending the HPV vaccine.[53] Finally, the proportion of those who were

vaccinated, having received a doctor's recommendation, was estimated to be 75%. This is a conservative estimate, based on the same study mentioned above, which revealed that 91% of those who were vaccinated or had their daughter vaccinated with the HPV vaccine did so after having a conversation with a physician.[53]

Table A.1 shows the calculated sample size for Level 3 based on simulated trade-off between the allowable error, that is, the difference between the calculated statistic and the true population proportion, and the level of confidence.

Allowable error	Level of confidence		
	0.85	0.90	0.95
0.05	156	203	289
0.10	39	51	72
0.13	23	30	43
0.15	18	23	32

Table A.1 Simulation of sample size calculation for Level 3.

However, to arrive at Level 3, participants must answer yes to both Level 1 and Level 2 questions (see Figure A.1). Therefore, the sample size has to be inflated to accommodate this hierarchical structure of questioning. The simulation of total sample size calculations is shown in Table A.2.

Allowable error	Level of confidence		
	0.85	0.90	0.95
0.05	1245	1624	2305
0.10	311	406	577
0.13	184	241	341
0.15	139	181	257

Table A.2 Sample size calculation simulation for total sample.

Based on these calculations, the ideal sample size for this study would be 2305, with 95% confidence and a 5% allowable difference between the calculated statistic and the true population value. However, a sample size of this magnitude is unachievable. Firstly, there were only 1,415

female students enrolled in the university during the study period. Secondly, the resources required for such a large study was not presently available to this study. Therefore, an achievable sample size for this study was 241, with 90% confidence and a 13% margin of allowable error.

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