HUMAN PAPILLOMA VIRUS (HPV) INFECTION AND HPV VACCINATION: A KAP STUDY AMONG ADOLESCENTS, ADULTS AND PARENTS

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HUMAN PAPILLOMA VIRUS (HPV) INFECTION AND HPV VACCINATION: A KAP STUDY AMONG ADOLESCENTS, ADULTS AND PARENTS

by

ABDUL NAZER ALI

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DEDICATION

to

my Belated Parents

for their exceptional confidence, and uncompromising life principles

they inculcated in me

my Wife

for her tolerance, patience and unfailing love and confidence rendered

my Children

for their support and participation for this study

my Colleagues

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LIST OF ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
AP	Attitude and Perception or Practice
HPV	Human Papilomavirus
CC	Cervical Cancer
CDC	Centre for Disease Control
HPV/ HPV vaccination	Human Papillomavirus infection and HPV vaccination
HR	High risk
IARC	International Agency for Research on Cancer
ICO	Information Centre on HPV and Cancer
IQR	Interquartile range
ICF	Informed consent form
IRB	Institutional review board
K	Knowledge
KAP (or)	Knowledge, Attitude and Perception (or)
KAP	Knowledge, Attitude and Practice
LR	Low risk
Mdn	Median
NR	No Response
PG	Post graduate
Ph	Phase
RA	Research assistant
STD	Sexually transmitted disease
STI	Sexually transmitted infection
UG	Under graduate
WHO	World Health Organization

JANGKITAN VIRUS PAPILLOMA MANUSIA (HPV) DAN VAKSINASI HPV: SUATU KAJIAN KAP KALANGAN REMAJA, DEWASA DAN INDUK

ABSTRAK

Maklumat asas tentang pengetahuan, sikap dan persepsi terhadap jangkitan Virus Papilloma Manusia (HPV) adalah penting untuk mewujudkan suatu prestasi amalan yang progresif mengenai program pelalian HPV bagi mengatasi segala cabaran-cabaran. Kajian ini bertujuan untuk membangunkan alat intervensi khusus (soal selidik) ke atas penduduk termasuk alat pembelajaan (risalah) dan menilai kesan alat-alat tersebut ke atas perubahan pada pengetahuan, sikap, persepsi dan / atau amalan (KAP) kalangan ketiga-tiga populasi kajian (remaja, dewasa dan induk). Suatu kajian prospektif, keratan rentas telah dijalankan di kawasan bandar dan luar bandar dalam negeri Kedah, Malaysia. Para peserta dipilih dengan menggunakan persampelan mudah dan data di kumpulkan dengan menggunakan soal selidik piawai yang telah disahkan. Data demografi, pengetahuan, sikap, persepsi amalan para peserta tentang jangkitan HPV dan pelalian HPV telah dinilai pada garis dasar, dan selepas intervensi dan pada tiga hingga enam bulan antara remaja (2928), orang dewasa (942) dan ibu-bapa (858). Hasil kajian menunjukkan peningkatan ketara dalam skor pengetahuan kalangan remaja dari 37% pada garis dasar ke 67% ($p < .001$), selepas intervensi dan 66% ke 88% ($p < .001$) pada ujian pra dan pasca selepas 3- 6 bulan intervensi. Skor KAP median juga meningkat dengan ketara dari [MDN = 47 (IQR = 12)] pada garis dasar kepada [MDN = 57 (IQR = 10)] di intervensi dan [MDN = 47 (IQR = 12)] di intervensi 3-6 bulan pasca. Di kalangan orang dewasa, skor pengetahuan meningkat daripada 63% pada garis dasar ke 89% ($p < .001$), selepas intervensi dan 66% kepada 90% ($p < .001$) pada ujian pra dan pasca selepas 3-6 bulan intervensi. Skor KAP median juga meningkat dengan ketara dari [MDN = 56 (IQR = 10)] pada garis dasar kepada [MDN = 88 (IQR = 18)] di intervensi dan [MDN = 87 (IQR = 17)] di intervensi 3-6 bulan pasca. Di kalangan ibu-bapa, skor pengetahuan

menjadi bertambah baik meningkat daripada 66% pada garis dasar ke 89% (p <.001), selepas intervensi dan 73% ke 94% (p <.001) pada selepas intervensi 3-6 bulan di ujian pra dan pasca. Skor KAP median juga meningkat dengan ketara dari [MDN = 50 (IQR = 22)] pada garis dasar ke [MDN = 62 (IQR = 11)] di intervensi dan [MDN = 73 (IQR = 5)] di intervensi 3-6 bulan pasca. Protokol ini meningkatkan skor pengetahuan dan KAP dengan ketara tentang HPV dalam kajian populasi tanpa mengira ciri-ciri sosiodemografi dan tingkah laku berisiko. Protokol-protokol yang berkesan, bermaklumat dan pembelajaran yang sesuai tentang jangkitan HPV dan pelalian HPV adalah sangat penting, dan kempen pendidikan berterusan dan tetap adalah perlu untuk mencegah tindakbalas buruk psikososial serta menggalakkan amalan seksual yang sihat dan tingkahlaku saringan Pap kalangan remaja dan orang dewasa. Tambahan pula, hasil penyelidikan ini memberikan kefahaman dalaman tentang penggunaan guru-guru kaunseling terlatih di sekolah menengah untuk mencegah penyakit berkaitan kesihatan demi kepentingan negara.

HUMAN PAPILLOMA VIRUS (HPV) INFECTION AND HPV VACCINATION: A KAP STUDY AMONG ADOLESCENTS, ADULTS AND PARENTS

ABSTRACT

Baseline information on knowledge, attitude and perception towards Human Papilloma Virus (HPV) infection is crucial to establish a progressive track of practice on HPV immunization program to defeat the challenges. The present study aimed at developing population specific intervention tool (questionnaires) including informative educational tool (pamphlet) and to assess the impact of these tools on knowledge, attitude, perception and/or practice (KAP) changes among the three study populations (adolescents, adults and parents). A prospective cross sectional study was conducted in urban and rural areas of Kedah state, Kedah Malaysia. The participants were selected using convenience sampling and data was collected using standardized and validated questionnaires. The participants' demographic data, knowledge, attitude, perception/ practice about HPV infection and HPV vaccination were assessed at baseline, and after intervention and at three to six months among adolescents (N=2928), adults (N=942) and parents (N=858). The research findings showed a significant improvement in knowledge scores among adolescents from 37% at baseline to 67% ($p < .001$), after intervention and 66% to 88% ($p < .001$) at pre and post-test after 3-6 months of intervention. The median KAP score also improved significantly from [Mdn = 47 (IQR =12)] at baseline to [Mdn = 57 (IQR = 10)] at intervention and [Mdn = 47 (IQR = 12)] at post 3-6 months intervention. Among adults, the knowledge score improved from 63% at baseline to 89% ($p < .001$), after intervention and 66% to 90% ($p < .001$) at pre and post-test after 3-6 months of intervention. The median KAP score also improved significantly from [Mdn = 56 (IQR = 10)] at baseline to [Mdn = 88 (IQR = 18)] at intervention and [Mdn = 87 (IQR = 17)] at post 3-6 months intervention. Among parents, the knowledge score improved from 66% at baseline to 89% ($p < .001$), after intervention and 73% to 94% ($p < .001$) at pre

and post-test after 3-6 months of intervention. The median KAP score also improved significantly from [Mdn = 50 (IQR = 22)] at baseline to [Mdn = 62 (IQR = 11)] at intervention and [Mdn = 73 (IQR = 5)] at post 3-6 months intervention. The protocol significantly increased knowledge and KAP scores about HPV in the study population, regardless of socio-demographic characteristics and risk behaviours. Effective, informative and appropriate educational protocols about HPV infection and HPV vaccination are particularly important and regular, booster education campaigns are required to prevent adverse psychosocial responses and promote healthy sexual practice and Pap screening behaviours in adolescents and adults. Furthermore, the research finding provides an insight into utilization of trained counselling teachers in secondary schools for prevention of health related diseases in nation's interest.

CHAPTER ONE

INTRODUCTION

1.0 Overview

Knowledge is one of the main treasures a person can ever possess in order to live his life complete and meaningful at all stages. Recalling an impressive quote from Confucius, "**knowledge is - When you know a thing, to hold that you know it, and when you do not know a thing, to allow that you do not know it**." Thus, knowledge is "to know what you know and what you do not know." When you know what you do not know, then a wise and intelligent person will be hungry to know what he does not know to have his/her wisdom. Further to strengthen the vision, another quote from Paul Tillich summarizes the expected outcome of this vision.

"Goodness without knowledge is weak; knowledge without goodness is dangerous.

We have to build a better man before we can build a better society.

All that is necessary for the triumph of evil is that good people do nothing.

Our purpose is not to make a living, but a life - a worthy, well-rounded, useful life.

Morality is not a subject; it is a life put to the test in dozens of moments."

With this morale strongly implanted in mind, an attempt to exploit the knowledge level of the study population to confer whether they violate the above moral, relating to the study topic – "Human Papilloma Virus (HPV) infection and HPV vaccination" since it is the most frequently encountered sexually transmitted disease (STD) as of today in the world (Gavillon *et al*., 2010).

In the quench to relate one's knowledge to their attitude, the Cambridge dictionary defines attitude as "a feeling or opinion about something or someone or a way of behaving towards certain situation." However, according to Allport (as cited in Richardson, 1996) "attitude is a mental and neural state of readiness, organized through experience, exerting a directive influence upon the individual's response to all situations with which it is related." Thus attitude plays an important role in one's acceptance to know what they do not know (knowledge). Thus attitude is defined as tendency or behaviour of a person, especially of the mind. Perception also plays an important role in how one understand to know, what they do

not know. Therefore, perception has a strong influence on one's attitude shift whether positive or negative, in decision making, in favour of or against any information.

At last, practice, what is believed to be the reflection of one's knowledge, attitude and perception, meaning "to carry out or perform a particular activity, habitually or regularly?" It is the reflection of the attitude regarding information of the knowledge provided which was not known or how does one react or respond to new unknown information. A positive and correct attitude reflects the person's decision to performance of activity. Thus, it is very motivating to carry out this Knowledge, Attitude and Perception or Practice (KAP) study (Kaliyaperumal, 2004; Bhagavathula, 2015) on 'HPV infection and HPV vaccination' and limiting the meaning of adolescent to the age they are eligible for HPV vaccination (9 years to 17 years), adults, the age eligible for HPV vaccination (18 years to 26 years) and parent population who are supposed to sponsor their children's vaccination decisions (9 years to 26 years).

Throughout the decade, more confirmation started to pour in, connecting more infection types to cervical carcinoma. To combine every one of the spots, in 1995, the committee for International Biological Study on Cervical Cancer was set up to address the issue more appropriately. Utilizing the test samples from 22 nations, they discovered HPV in more than 90%, among the vast majority of samples. However, this ended up being disparage. In 1999, a gathering of researchers, including Professor Julian Peto, UK researcher, Cancer Research, ambitiously re-tried the samples and found that for all intents and purposes; all cervical tumour test samples (99.7%) were HPV infected. They demonstrated HPV disease is the trigger for cervical carcinoma. This was, and stays right up to the present time, the most grounded connection between a solitary "cause" and a particular tumour.

Sexually transmitted infections (STIs) are one of the major health care problems that require the ultimate attention. HPV infection is one such STI that invades every human body invariably, at least once in their life time who are sexually active. Lack of knowledge about HPV/ HPV vaccination is the main concern for high prevalence of the disease. Though, HIV awareness campaigns have contributed to a certain extent in practising safe sex, the HPV

prevalence still remains challenging because its transmission is not restricted only through vaginal intercourse. Non-compliance to HPV vaccination among the sexually active adult population who are unaware or not covered by the national immunization scheme or unaffordable due to high cost will be the main contenders for cervical cancer in the next few decades to come, and thus the national health care burden is not going to change. The WHO suggested an arrangement of activities that incorporates intervention over the life course. It ought to be multidisciplinary, including segments from group instruction, social preparation, immunization, screening, management and curative care. Essential counteractive action starts with HPV immunization of young women at 9 - 13 years, before they have their sexual debut. Other prescribed preventive intercessions for both young men and women, that is suitable may be:

- instruction about safe sexual activity, including postponed sexual debut;
- use of condoms for those who are already having active sex;
- caution about tobacco use, which mostly begins at puberty that can cause both cervical and other tumours; and
- male circumcision (WHO Fact sheet, 2016).

1.1 History of HPV

In the year 1907, the human warts were first identified and in 1983, papillomavirus was first isolated from a rabbit (Faridi, 2011). In 2008, a review by Warren Levinson and Mc GrawHill stated that studies related to papillomaviruses moved forward only after cervical cancer's propinquity with HPV was proved (Faridi, 2011). Till date, over 150 HPV types are identified. Among them, 40 are anogenital and around 15 are oncogenic or cancer causing (Schiffman & Castle, 2003). Cervical cancer usually begins slowly and progresses gradually over a period of 10 - 20 years and is the most preventable cancer when treated early. Early detection of the disease is possible through regular Pap smear tests (Forman, 2012). Cervical cancer can affect women of any age, most common in mid-40s (IARC & WHO, 2015) and the world's major cause of death (Lee *et al.*, 2007 and Wong *et al.*, 2010). The actual link between HPV and cervical cancer was noticed in early 1950s. Cervical cancer was more

common in women with multiple sexual partners and those having sex in younger age (Durst *et al.*, 1983).

1.2 Burden of HPV Infection

HIV costs US$ 2.9 vs. $ 3 billion among 15–24 years aged individuals in US. In direct contrast, direct costs were 292.7 US$ and $5.8 million for all STD, respectively. Another observational study in US showed that the cost for screening and treatment of cervical cancer was highly significant (Mvundura & Tsu, 2014). About 17% attributed to pre-cancer management and 10% to invasive cervical cancer treatment (Guidelines for smear screening, MOH, Malaysia, 2004). The CDC studies using population-based data from cancer tissue reported annual diagnosis of about 38,793 HPV-related cancers among both females and males. The most common was 7.4 per 100,000 cervical cancer and 4.5 per 100,000 oropharyngeal cancer (Viens, 2016). The annual economic burden in Malaysia is reported as about RM 312 million towards prevention of invasive cervical cancer (Ezat & Aljunid, 2010).

1.3 Aetiology

A known human carcinogen, genital HPV infection leads to cervical cancer (Arends *et al.*, 1990; Schiffman *et al.*, 1993; Bouvard *et al*., 2009). The major risk factors associated include history of STDs, multiple sex partners, sex at young age and promiscuous male partners. There is a 5-fold increase in risk factors associated with cervical cancer, because of impaired immune response (CDC, HIV Infection and Cancer Risk, 2012).

1.4 Epidemiology

The annual international incidence of cervical cancer is more than 500,000, new cases of which about 4.5 cases per 100,000 reported from Western Asia and 35 per 100,000 in Eastern Africa (WHO/ICO information centre, 2012). Forouzanfar and team conducted age-specific assessment for cervical cancer among 187 countries and reported the global incidence inflated from 378,000 in 1980 to 454,000 cases in 2010. Though cervical cancer death rates are decreasing in developing countries, about 200,000 deaths occurred in 2010 of which 46,000 were in 15-49 years old and 109,000 among 50 years and older (Forouzanfar, 2011).

1.4.1 Prevalence and Incidence

Though HPV infection is self-limiting, about 10% remain infected over five years (Gavillon *et al*., 2010). It is mostly transmitted through skin contact over infected areas of hand, fingers, mouth, genitals or anus. Research indicates nearly 30-60% of sexually active male and female are HPV infected at some point in life (Bosch *et al*., 2008) and young adults are especially at higher risk (Wong *et al*., 2010) that contributes about 50% of the global cervical cancer cases in Asia Pacific region (Parkin *et al*., 2008). Proper use of condoms and limiting sexual partners can help reduce the risk (Forman *et al*., 2012).

1.4.2 HPV Prevalence Worldwide

The worldwide age-related prevalence is similar to that of the US cohorts. In central and south America, the prevalence has been reported to be as high as 64%, and interestingly many studies showed that women less than 25 years showed the highest prevalence which decreased with increase in age over 50 years. In Africa, the prevalence ranged from 12% to 55%, though most trials consisted of younger cohorts of women. The Canadian prevalence was lower than US, with a peak incidence of 25%. The Chinese trials showed a range of 6% to 53% while Japanese trials reported a lower prevalence of less than 15%. Studies of Indian women ranged from 0% to 45%. The European prevalence was almost consistent with the US with a peak of 20% in young women (Nagle *et al*., 2013).

Globally, cervical cancer in young women is the most prevailing and main cause of death. The most common high-risk (HR) genotypes accountable for 70% cervical cancer are HPV 16 and 18, with 530,000 and 270,000 related deaths (Bosch *et al*., 2008; Wright *et al*., 2008; Parkin *et. al*., 2008; Huh, 2009; Forman *et. al*., 2012; IARC & WHO, 2015). The western countries contribute a significantly high ratio, about 250,000 are observed to be fatal. These alarming situations lead the molecular virologists worldwide to study the pathogenesis in-depth and find solutions with therapeutic potential (Yasmeen *et al*., 2010). According to the most recent reports, the overall prevalence in women was 17.9%, while lower in men at 8% irrespective of races. People with multiple sex partners were on high risk to HPV infection (20.1%) compared to those with one (7%) life partner (Stone *et al*., 2002).

The largest US population–based HPV infection in men trial demonstrated a prevalence of 61% of any type of HPV infection. Specifically, HR-HPV infections in 23%, HPV 16 (7%) and HPV 51 (6%) were the most common. The "National Health and Nutrition Examination Survey" (NHANES) reveal men have a higher incidence of oral cancer (10% vs. 4%). In contrast, prevalence in women was not age affected. Only LR-HPV infections increased with age. Clearance of HPV infection seems to occur quicker in men, approximately six months. In another study, nearly 75% of HPV infections in men were cleared within one year. Male circumcision significantly reduced the genital prevalence, which led some to suggest circumcision as a method to reduce disease burden in endemic communities where vaccination and screening were not yet feasible (Barakat *et al*., 2009).

1.4.3 HPV Prevalence in Malaysia

Among the 11.5 million Malaysian women aged 15 and above, cervical cancer ranks 2nd among 15 - 44 years old women. About 2145 women are estimated to be diagnosed and 621 die every year due to cervical cancer (Abdullah, 2016). A South-East Asian study conducted using HPV detection test reveals, nearly 17% women are estimated to harbour HPV related cervical infection and 73% due to HPV 16 or 18 (ICO information centre on HPV and cancer). In Malaysia, the lack of resources, awareness and infrastructure led to low rates of screening in rural areas and hence the increase (Zaridah, 2014). Only about 6% of Malaysian women are screened for HPV says an estimate. Misperceptions and cultural inhibitions regarding screening procedure and the disease by itself have contributed to low Pap screening (Wong & Sam, 2007). Though cervical cancer deaths are rare among the young, the incidence enhanced from 30 and peaked at 60-69 years. However, nearly 50% of the cases involved 40-59 years. When the races are concerned, Chinese women (28.8/100,000) had the highest incidence followed by Indian (22.4/100,000) and Malay (10.5/100,000) women (Malaysian Cancer Statistics, 2006). As reported by Ministry of Health, Malaysia, there are about 2000 to 3000 hospital admissions per year due to cervical cancer of which most of them are in late stage of the disease (Devi *et al*., 2008) and death rate is 5.6/ 100,000 (Cervical Cancer Incidence and Mortality Rates, 2011; Zaridah, 2014). Even with the

national immunization and screening for cervical cancer introduced, the death rate still not decreased.

1.5 Transmission of HPV infection

1.5.1 Prenatal

Though HPV related disease in newborns is rare, can be transmitted during labour and juvenile-onset recurrent respiratory papillomatosis may be caused by types 6 and 11 (Sinal and Woods, 2005).

1.5.2 Genital infections

HPV infection is a prominently known STI and certain HPV types are mostly connected with cervical cancer. Among the HPV types, 51 species infect the genital mucosa of which 15 types are classified as high risk and 12 as low risk types (Cubie, 2013).

1.5.3 Sexual Transmission

Studies repeatedly proved that, the most important determining factor for HPV in women are (1) sexual partners, (2) sex debut and (3) sexual behaviour of male partner. A study conducted among virgins and monogamous women, reported women negative for HPV DNA and serum HPV-16 antibodies among virgins at enrolment and throughout the study period. The most crucial factor for HPV acquisition was number of sex partners (Brown *et al*., 2009; CDC, 2013). Several studies done for evidence of non sexual transmission of HPV types reported HPV infections may occur in sexually naive populations; horizontal transmission of low-risk types possible; vertical and perinatal transmission is also possible; HR-types have been detected in mouth, oropharynx and the conjunctiva (CDC, 2013).

1.6 Signs and Symptoms of HPV Infection

Most people do not develop HPV symptoms or health problems early because before two years, the immune system itself clears infection (CDC, 2013).

1.7 Clinical Features of HPV Infection

Often, HPV is asymptomatic and transient in women, present clinically as warts, detected by Pap or HPV test with or without abnormal cytology (Egendorf and Laura, 2007). Most men who get HPV never develop symptoms and the infection usually goes away completely by

itself. However, if persists, can cause genital warts or certain kinds of cancer (CDC - Fact Sheet, 2015).

1.8 Risk Factors

Apart from factors mentioned earlier, chronic inflammation, immune suppression, multiple parity and STIs due to chlamydia and herpes virus all contribute (Koutsky *et al*., 1997; Moscicki *et al*., 2001; Richardson *et al*., 2003; Sellors *et al*., 2003; Baseman and Koutsky, 2005). Furthermore, risk factor profiles were inconsistent and differ depending on HPV types. Researchers found association of HR-HPV type with frequency of intercourse and oral sex partners, whereas LR-types was invariant (Richardson *et al*., 2000). Overall, strong association was found with all types and sexual activity (Rousseau *et al*., 2000).

1.9 Duration, Persistence and Clearance of HPV Infection

Though the duration for clinical symptoms is still unclear, it is likely, for genital warts - three weeks to months, cervical abnormalities - months to years and cancer - decades. The median duration for cervical infection varies but probably eight months. Persistence does occur but duration unknown. 70% of infections clear within one year and 90% in two years.

1.10 Prevention

There is no treatment available for the infection by itself and therefore antibiotics or other currently available medicines cannot treat HPV infection. However, the most effective methods of avoiding problems are by:

A. Primary prevention (prevention of infection)

B. Early detection (abnormal cells screening)

C. Early treatment (harm minimization)

Some primary prevention methods associated with less transmission of HPV include:

- being faithful to partner (having a monogamous relationship)
- limiting the number of sexual partners
- consistent protective sex (if not in monogamous relationship)

1.10.1 Abstinence

“Abstinence from sex is the only best way to prevent HPV” at all times.

1.10.2 Use of condom

Condom use can reduce but not eliminate HPV transmission. A 2003 study reported adjusted hazard ratio 0.3, with consistent condom use by partners among female university students. Other studies have demonstrated a significant reduction among women when condoms were used consistently and correctly. However, since HPV infection can be transmitted by other than vaginal penetration by exposure to infected areas, hands etc. and abstinence is the best way to prevent infection (Bleeker, 2003; Hogewoning, 2003; Winer *et al*., 2006).

1.10.3 Pap Smear and Bethesda System

Early detection and treatment strategies can help reduce HPV infection by Pap smear screening around the globe.

1.10.4 HPV Vaccines

The US, FDA approved a bivalent vaccine for HPV in 2006 for girls (Cervarix®, GSK) and a quadrivalent vaccine for both genders (Gardasil®, Merck). Of late, 9-valent HPV vaccine (Gardasil-9) was approved. All the vaccines are administered at 0, 1 and 6 months.

1.11 Statement of the problem

Many investigations have showed a tremendous lack of knowledge about HPV disease despite the increased prevalence of HPV infection and its possible consequences (Vail-Smith & White, 1992; Ramirez *et al*., 1997; Yacobi *et al*., 1999; Dell *et al*., 2000 and Gerhardt *et al*., 2000). When a young college girl has more than one sex partner for four years annually, the probability for her to get HPV infection is more than 85% (Laura Egendorf, 2007). In another research involving 263 college-aged women who were questioned for their knowledge on HPV, 87% replied either never heard or not sure about HPV (Vail-Smith & White, 1992). Another study supported the findings among university students, only 38% had heard of the infection (Yacobi *et al*., 1999). It further revealed that nearly 59% of respondents were ignorant of how HPV was transmitted. Adults in family clinic had comparable constrained information on HPV. The clinicians use to distinguish those with minimal information about HPV was to ask patients how informed they were about HPV before turning out to be sexually dynamic. Notwithstanding, it stays misty whether

instructive intercession or information changes the hazardous practices (Laura Egendorf, 2007). Does the sexually active adult population have a similar level of awareness and information about HPV is the question to be pondered and addressed along with many others.

1.12 Rationale and Significance of the Problem

Till date, no studies have reported the knowledge, attitude and perception or knowledge, attitude and practice among the Malaysian adolescent, adult and parent populations (all three together) regarding HPV/ HPV vaccination. Thus, an exploration of KAP among the potentially, at risk population for HPV infection was warranted. The primary objective is to estimate KAP levels among the participants and evaluate the intervention tool in contributing to create awareness among study population. The study findings could provide the health care system with a better understanding on the status of KAP on HPV infection and formulate appropriate approaches to address the national demon.

As evident by the WHO - Fact sheet (2016), cervical carcinoma, the fourth common women cancers with an expected 530,000 new cases leading to 7.5% of all global female mortality. Of the evaluated, more than 270,000 are deceased annually due to cervical malignancy, over 85% reported in under developed nations. In developed nations, a program for early detection and management averts up-to 80% of cervical diseases. In developing nations, constrained access for successful early screening and prospects for treatment at the late-phase of ailment might be poor, bringing about a higher rate of death from cervical tumour. The high global death rate from cervical tumour (52%) could be comprehensively lessened by viable screening and management programs (WHO Fact sheet, 2016).

1.13 HPV Vaccination in Malaysia

In Malaysia, the cervical cancer screening programme was established in 1969 to ensure early detection among the target group aged 20–65 years through state-level health centres, Family Development Board clinics, Family Planning Association clinics, private and university/teaching clinics/hospitals. The Pap screening programme was planned, organized and evaluated by the Ministry of Health, Malaysia (Guidebook for Pap smear screening, 2004). In 2012, the government allocated RM 50 million for the free HPV vaccination

program for women who are eligible (The borneo post, 2013). This move is to encourage the vaccination of women in Malaysia and make sure the cervical cancer incidence decreases in Malaysia (Malaysian Cancer Statistics, 2006).

1.14 Research Question

Will education by intervention improve the KAP of the study population with regard to HPV infection and vaccination? If yes, to what extent?

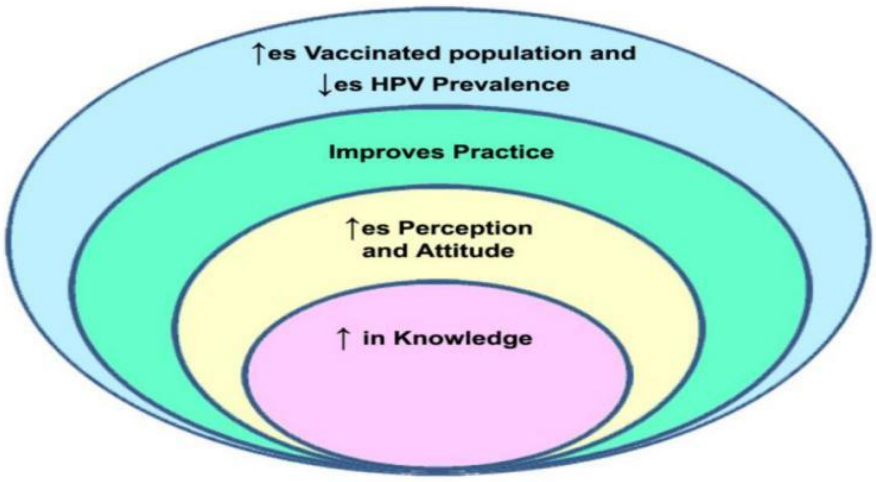

Figure 1.1: The conceptual relationship between KAP; ↑ - Increase, ↓ - Decrease.

1.15 Objectives

1.15.1 General Objectives

The studies primary objective is to estimate the KAP level among the respondents and evaluate the intervention tool in contributing to create awareness among the study population.

1.15.2 Specific Objectives

The studies specific objectives were

1) to develop and validate the study questionnaires regarding HPV infection and vaccination among the study population.
2) to develop and validate the effectiveness of 'educational pamphlets' in influencing the knowledge and KAP regarding HPV infection and HPV vaccination among the study population.
3) to evaluate the differences of total knowledge and KAP scores among demographic characteristics of each study population.

4) to evaluate the extent of knowledge gained and knowledge retained among each study population.

5) to assess the total KAP scores differences among the adolescents, adults and parents (a comparison among the three study populations).

CHAPTER TWO

LITERATURE REVIEW

2. Introduction

The chapter 2 introduces research studies connected to "knowledge, attitude, perception or practice towards HPV infection and HPV vaccination" among the adolescent, adult and parent participants. Significant findings, strength and weakness of the various studies are discussed in this chapter. This chapter combines the information related to the above mentioned factors in order to identify the measured questions and to analyse the subjects that could further enrich the knowledge on HPV/ HPV vaccination.

The literature search was targeted for both published and unpublished articles from 2008 to 2016. The peer-reviewed articles in the following electronic databases was screened: PubMed, Cochrane Central Register of Controlled Trials, Scopus, Web of Science, World Health Organisation Library Information System, Africa Wide and CINAHL. The search strategies for electronic databases will incorporate both medical subject headings (MeSH) and free-text terms and will be adapted to suit each individual database using applicable controlled vocabulary. Reference lists of relevant reviews and all eligible papers will also be searched for relevant studies.

Despite HPV related cancers (cervical, oral etc.) being potentially preventable, cervical cancer is the second most common cancer among women in Malaysia. This review focuses on the various aspects of questionnaire and pamphlet development and validation with regard to KAP on HPV/ HPV vaccination. Further, focuses on the knowledge, attitude and perception or practice of HPV vaccination of various groups of Malaysian population that potentially contribute to reduce the incidence and mortality of HPV related cancers. Prevention by vaccination or early detection through screening is still an important aspect because even with HPV vaccination, screening still plays an important role as vaccination does not cover all high risk HPVs. There is a need to seriously consider a properly organized educational intervention programme, taking into consideration what we already know about the knowledge, attitude and perception of Malaysian population, their economic and psychosocial issues of vaccination and preventive screening approach. There

is also a large gap in clinical studies on the outcome of well-structured and targeted educational intervention among Malaysian population and hence is the focus of this study.

2.1 Studies related to Development and Validation of Questionnaires

KAP surveys are useful in evaluating the effectiveness of intervention programmes and capable of estimating the target group's current KAP on a specific health related topic. Global studies regarding personal hygiene, nutrition, diseases, knowledge, attitude and practice measures have reported to focus on community or clinical settings (Elaziz & Bakr, 2009, Abiola *et al*., 2012, Wall *et al*., 2012, Ho *et al.*, 2013, Gautam *et al*., 2015). As suggested by Parmenter and Wardle (2000). If the instrument is not tested for validity and reliability, it may not provide consistent and stable results. Moreover, existing instruments are mostly developed for specific populations; therefore they may not be suitable for other studies (Parmenter & Wardle, 2000). This study aims to develop KAP Questionnaires on HPV/ HPV vaccination for each study population and evaluate its reliability and stability for later studies and also develop educational pamphlet and validate its effectiveness as an intervention tool which ultimately aims to educate adolescent, adult and parent populations on HPV infection, focusing on preventing HPV related cancers and encouraging HPV vaccination.

In Canada, a pilot study was conducted to test, re-test reliability of questionnaire among the target population, pregnant or recent mothers (N = 71). The content validity of the questionnaire was examined using an expert panel (N = 7) and pilot testing items in a small sample of pregnant women and recent mothers as target population (N = 5). Reliability scores for all constructs (r and intra-class correlation (ICC) coefficients with a score of >.5 were considered acceptable. The content validity of the questionnaire reflects the degree to which all relevant components of excessive risk in women are included. Test-retest bivariate correlations for the questionnaire (21 items) ranged from poor to a perfect correlation (ICC .361 - 1) and low to perfect (r values .417 - 1) were observed (Ockenden *et al.*, 2016).

A randomized cross-sectional study was conducted in Malaysia among adolescents (N=36). One group was selected to determine face validity while the other groups to determine

construct validity and internal consistency reliability of the KAP questionnaire. Four attitude and six practice dimensions were identified through factor analysis in construct validity. The study reported significant correlations between knowledge, attitude and practice which showed adequate convergent validity. The questionnaire is reliable based on its internal consistency reliability (knowledge: α =.654, attitude: α =.845, practice: α =.636) and test-retest reliability (knowledge: r =.631; attitude: r =.358; practice: r =.481) respectively (Hiew *et al*., 2015).

In an Italian study using a 69 item questionnaire containing closed ended questions towards validation of questionnaire among 30 girls, the study reported the highest value of Cronbach's alpha resulted on 24 items (alpha .774), the addition of other items and one at a time, decreased the value. Cronbach's alpha on all the 3 sections together resulted in a value of .059. Young women generally knew that HPV can cause cervical cancer (93.3%) and genital warts (16.7%) and 76.7% of them recognized Pap-test as a screening tool. The main sources of information about HPV vaccination were from magazines/ books (33.3%), TV (26.7%), and gynaecologists (23.3%). This literature information was very useful for the pilot studies conducted for the present study to validate the study questionnaires (Saulle *et al*., 2013).

A pilot study was conducted among high school Caucasian girls in Poland using 65 items questionnaire to develop and validate the questionnaire. After phase 1, the study generated a list of 65 issues concerning knowledge about cervical cancer and its prevention. Of 305, 155 were schoolgirls (mean age ± SD, 17.8 ± .5) and 150 were female students (mean age ± SD, 21.7 ± 1.8). The Cronbach's alpha reliability coefficient for the whole questionnaire was .71 (range for specific questionnaire sections, .60 to .81). Test-retest reliability ranged from .89 to .94 (Jaglarz *et al*., 2013).

A Irish pilot study conducted among cystic fibrosis patients (N = 100), both inpatient and outpatients at National Referral Centre, St. Vincent's University Hospital, Dublin reported a median age of 26 years (range 17–49 years; median FEV1:57% predicted, range 20–127% predicted). The level of knowledge was correlated with clinical and socio-demographic

characteristics. Questionnaire validation showed acceptable internal consistency (α = .75) and test - retest reliability (.94). Patients had a fair overall understanding of cystic fibrosis (M = 72.4%, SD = 13.1), with greater knowledge of lung and gastrointestinal topics (M = 81.6%, SD = 11.6) than reproduction and genetics topics (M = 57.9%, SD =24.1). Females and those with post-secondary education scored significantly higher (Siklosi *et al*., 2010).

Summary: Twelve articles related to questionnaire development and validation were found in a search through a database dedicated to indexing all original data between the years 2008-2015 were identified. Five articles were selected and reviewed which was found relevant for this study and is summarized in Table 2.1.

Table 2.1, Summary of the studies on Development and Validation of Questionnaires

No.	Study	Significance of the study	*Comments
1.	(Ockenden *et al*., 2016)	An electronic questionnaire related to women knowledge and perceptions of the current gestational weight gain guidelines and pregnancy-related health behaviour was validated.	The validation reported indifferent test correlations between poor and low to perfect.
2.	(Hiew *et al*., 2015)	Validity and reliability of KAP questionnaire among secondary school adolescent was found to show adequate convergent validity.	The study reported moderate to good reliability were as the results show moderate to poor correlations.
3.	(Saulle *et al*., 2013)	Assessed the reliability and validity of the questionnaire as a tool to examine knowledge, attitudes and behaviours towards screening and vaccination against HPV.	This literature provided an in-depth understanding on Cronbach's alpha values in reliability analysis. This was very useful for present study.
4.	(Jaglarz *et al*., 2013)	Aimed at development and validation of a knowledge questionnaire regarding cervical cancer, its primary and secondary prevention and identify sources of information about the disease among schoolgirls and female students.	This literature owns an understanding on questionnaire development process, generation of issues; construction and testing reliability, stability and validity of provisional questionnaire.
5.	(Siklosi *et al.*, 2010)	Assess the knowledge about cystic fibrosis in patients regarding the genetic and reproduction aspects.	This literature including criterion and face validation, test-retest and internal consistency was very useful.

* By this thesis author.

2.2 Studies related to Development and Validation of Pamphlet

This section of the review focuses on the various aspects of creating awareness and enriching the knowledge to address all answers to questions enlisted. The pamphlet development and validation with regard to KAP on HPV/ HPV vaccination focuses on the knowledge, attitude and perception or practice of HPV vaccination of various groups of Malaysian population.

A cross sectional survey was conducted among 418 Hispanic mothers in California to evaluate the clarity of educational material informing Hispanic mothers about HPV, cervical cancer and the HPV vaccine; to determine vaccination acceptability and identify predictors of vaccine acceptance in an under-served health setting. The study reported about 91% of participants understood most or all of the information provided. A 77% of participants reported vaccine acceptance for their children; this increased to 84% when only those with children eligible to receive vaccination were included. Significant positive predictors of maternal acceptance of the HPV vaccine for their children were understanding most or all of the provided information, older age and acceptance of the HPV vaccine for themselves. Concerns about safety and general dislike of vaccines were negatively associated with HPV vaccine acceptance. Prior knowledge, level of education, previous relevant gynaecology history, general willingness to vaccinate and other general beliefs about vaccines were not significantly associated with HPV vaccine acceptance. The majority of participants reported understanding of the provided educational material. Vaccine acceptability was fairly high, but was even higher among those who understood the information. The study concluded a well-structured educational material should be provided to parents for their better understanding so that they take informed decisions for their children regarding HPV vaccination (Brueggmann et al., 2016).

A cross-sectional study funded by the Bill & Melinda Gates Foundation was conducted in a project called “the Low-Cost Molecular Cervical Cancer Screening Study (LCMCCSS)” in a cervical cancer high risk provinces in China. The study focused to assess the short-term effectiveness of a hospital-based, brief, HR-HPV-focussed session among rural Chinese women knowledge and attitudes. Women from 22 cities were randomly selected (N = 4230).

Among them, 3241 responded for cervical cancer screening, 1829 attended intervention and 1412 were assigned control group. The study reported following intervention, significant increases were detected in awareness regarding HPV (5.9% vs. 59%, $p < .001$) and cervical cancer (63% vs. 89.2%, $p < .001$). Changes were also observed regarding women's intention to vaccinate themselves (82% vs. 89%, $p = .001$) and their daughters (82.9% vs. 88%, $p = .011$). Although the impact was more modest compared with the impact on change of awareness, women who were aware of HPV, 60.3% knew that cervical cancer is related to HPV, while only 5% knew the relationship between HPV and genital warts after the educational intervention. The study concluded educational campaigns, targeting women with limited education and poor access to public media or other educational channels needed focus to improve knowledge regarding HPV. The study concluded intervention produces positive outcome (Jing *et al*., 2015).

A cross-sectional telephonic survey with parents of vaccine-eligible girls from randomly selected schools, Fiji, Japan was conducted among 560 vaccine-eligible girls attending a campaign and 293 of their parents agreeing to participate in the study. The outcome measures included parents knowledge, experiences and satisfaction with the campaign; the extent to which information are needed for vaccine decision- making and factors associated with vaccination consent. The study reported there was broad acceptance and uptake of HPV vaccine, with almost 80% (230/293, 79%) of survey respondents having consented to vaccination, and over half reporting their daughter had received all three doses (58%). This is consistent with the coverage recorded by the vaccine campaign of 62%, 56%, and 55% for doses 1, 2, and 3 respectively. The high level of vaccine acceptance and uptake was observed in Fiji. The vaccine acceptance was good in this study population; however negative media reporting may give a wrong idea to parents about HPV vaccination (La Vincente *et al*., 2015).

A study embraced a quality improvement venture to figure out whether evidence based instructive pamphlet and reminder system can improve HPV immunization and completion rates. HPV vaccination rates were analysed between groups. Low national HPV antibody

rates exhibit the requirement for hypothesis based immunization conveyance programs. The review detailed that a noteworthy distinction in HPV immunization uptake ($\chi 2 = 11.668$, $p = .001$; OR = 9.429, 95% CI = 2.686-33.101) and measurements finishing ($\chi 2 = 16.171$, $p < .001$; OR = 22.500, 95% CI = 4.291-117.990) rates were found. Parents who got the intervention were 9.4 and 22.5 times more inclined to uptake HPV vaccine and complete the dose. These outcomes demonstrate that evidence based pamphlets with reminder system seemed to enhance HPV vaccine uptake and completion of doses (Cassidy *et al*., 2014).

A cross-sectional study using pre- and post-test intervention among parents (N=74) attending the healthcare clinic was conducted in Malaysia. The study reported "Sixty four valid survey forms were retrieved among 74 participated mothers (N = 64, 87.7%). Knowledge of child vaccination significantly increased post intervention ($p < .001$). There was a significant difference between educational level and monthly income with parents knowledge ($p < .001$ and $p = .005$), individually. Wilcoxon test and McNemar's test were used for comparison between pre- and post-intervention scores. The study concludes that educational intervention has increased the knowledge level substantially using animated movie and educational seminar as the intervention tool (Awadh et al., 2014).

In Australia, eligible women for cervical cancer screening were randomly chosen to receive standard intervention along with a control group around Yaounde´ and surrounding country side. About 302 women aged 25 to 65 years old were enrolled among 4 health care centres. The educational intervention consisted of video about HPV, cervical cancer, Self-HPV test and its relevancy as a screening test. Among 301 women (149 were in control group and 152 in intervention group) completed the full process and were included into the analysis. Participants who received the educational intervention had a significantly higher knowledge about HPV and cervical cancer than the control group ($p < .05$), but no significant difference on Self-HPV acceptability and confidence in the method was noticed between the two groups (Sossauer *et al*., 2014).

A multi-centred, cross-sectional study across five cities in China was conducted among a sample of 1146 employed women and 557 female undergraduate students. The study

reported that the baseline knowledge was poor among both groups. Only 28% and 12% of employed women and students had heard of HPV, while 21% and 7.2% of employed women and students knew the relation of HPV to cervical cancer. At post education, the knowledge significantly increased to 89% and 59% among employed women and students regarding the relationship between HPV and cervical cancer ($\chi 2 = 1041.8$, $p < .001$ and $\chi 2 = 278.5$, $p < .001$), respectively. Post-intervention, vaccine acceptability also significantly increased from 77% to 90%, ($p = <.001$) among employed women and 73% to 82% among students ($p < .001$). Respondents from both groups raised concerns about the safety, efficacy and limited use of vaccine as reasons for unwilling to vaccinate. Women willing to vaccinate their children increased from 44% to 81% after intervention, $p < .001$ (Chang *et al.,* 2013).

An educational intervention study among 394 male and female adolescents, aged 14 and 19 years was conducted using self-administered anonymous questionnaire in Baranya County, Hungary. Half of the students had an educational intervention while the other was control group. Both groups were retested post three months using the same questionnaire. There was a significant increase in cervical cancer awareness post intervention: causal relationship between HPV and cervical cancer (8 → 22%, $p < .05$), or perception of HPV vaccination (61% → 86%, $p < .05$). Similarly, health-related beliefs also increased, e.g. HPV may cause cervical cancer (65% → 81%, $p < .05$) or cervical cancer may be prevented by vaccination (67% → 85%, $p < .05$). Nearly 50% of adolescents were engaged in one-night sexual relationship (41%) without any safety measures. In addition to providing adolescents with clear and health education focused awareness, knowledge for safe sexual practice and reducing the number of sexual partners is the key to limit the spread of HPV infection (Marek *et al*., 2012).

An educational intervention study in Guilford County, North Carolina, USA was conducted among parents (N = 376), health care staff (N = 118) and school staff (N = 456) who attended the one-time intervention session and completed the questionnaires. The participants had relatively low levels of HPV and HPV vaccine knowledge prior to intervention. The education intervention increased knowledge among all the three focus

groups ($p < .001$), and objectively assessed knowledge about many aspects of HPV and HPV vaccine among health care and school staff members ($p < .05$). Following the intervention, more than 90% of school staff believed HPV and HPV vaccine education is useful for school personnel and that middle schools are an appropriate venue for this education. Most parents (97%) and school staff members (85%) indicated they would be supportive of school-based vaccination clinics. Use of power point presentation as educational intervention is found to be potentially effective for increasing HPV vaccination. A description of other intervention methods will be useful. This study aims to evaluate pamphlet as intervention tool and could provide a comparative knowledge on various tools (Reiter et al., 2011).

In the USA, a study was conducted in a hospital-based urban teen health centre at Cincinnati Children's Hospital Medical Centre**.** A total of 252 adolescent girls and boys participated in three study phases. The study intended to develop an educational protocol for HPV and Pap tests; to evaluate the protocol for understand-ability, clarity and effectiveness in increasing knowledge about HPV; to evaluate whether baseline knowledge improved significantly after the educational protocol was administered and whether the increase in knowledge was retained two weeks later. The study reported that the scores on HPV knowledge scale increased significantly ($p < .001$) among adolescents who participated in phases 2 and 3 after they received the protocol. Initial differences in scores based on race, insurance type and condom use were not noted post-protocol. This study aims at assessing knowledge post six months which will give a better understanding on knowledge retention capacity of the participants (Wetzel *et al*., 2007).

Summary: Fifteen articles related to pamphlet development and validation were found in a search through a database dedicated for indexing all original data between the years 2007-2016. Ten articles were selected and reviewed which was found relevant for this study and summarized in Table 2.2.

Table 2.2, Summary of the studies on Development and Validation of Pamphlet

No.	Study	Significance of the study	*Comments
1.	(Brueggmann et al., 2016)	Evaluate the clarity of educational material, determine vaccination acceptability and identify predictors of vaccine acceptance.	Well-structured educational material should be provided to parents for their better understanding so that they take informed decisions.
2.	(Jing *et al*., 2015)	Focused to assess the short-term effectiveness of a hospital-based, brief, HPV-focused session among rural Chinese women's knowledge and attitudes.	Educational channels needed focus to improve knowledge regarding HPV. Intervention produces positive outcome.
3.	(La Vincente *et al*., 2015)	Knowledge, experiences and satisfaction with the campaign, the extent to which information are needed for vaccine decision-making, and factors associated with vaccination consent.	The vaccine acceptance was good in this study population; however negative media reporting may give a wrong idea to parents about HPV vaccination.
4.	(Cassidy *et al*., 2014)	Weather evidence based instructive pamphlet and reminder system can improve HPV immunization and completion rates.	Evidence based pamphlets with reminder system seemed to enhance HPV vaccine uptake and completion of doses.
5.	(Awadh et al., 2014)	Changes in total knowledge score pre- and post-educational intervention were assessed.	Though done as a pilot study, population representative sample would be more appropriate.
6.	(Sossauer *et al*., 2014)	Evaluated whether an educational intervention would improve women's knowledge about HPV, cervical cancer and confidence in Self-HPV test method.	Video intervention produced knowledge gain among the study participants.
7.	(Chang *et al*., 2013)	Assessed knowledge regarding HPV/ HPV vaccine, and evaluated the effect of brief educational intervention on HPV knowledge and vaccine acceptance.	The intervention using group lecture had a significant improvement in HPV knowledge and vaccination. This study is encouraging for intervention studies.
8.	(Marek *et al*., 2012)	Impact of the educational intervention on adolescents' knowledge, beliefs and attitudes.	Intervention had a significant improvement in HPV related knowledge and vaccination.
9.	(Reiter *et al*., 2011)	Effect of educational intervention among three focus groups, parents, healthcare staff and school staff.	Education using power point or pamphlets is useful and middle schools are appropriate platform.
10.	(Wetzel *et al*., 2007)	Develop and validate educational protocol for HPV and Pap tests among adolescents.	Effective, appropriate educational protocols about HPV and Pap tests are particularly important.

* By this thesis author.