Missed Clinical Opportunities
for HPV Vaccination

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In my opinion this Dissertation is good enough to be awarded at least a PASS by the MSc Public Health Examining Board.

CHARMAINE GAUCI
Name of Supervisor

Signature of Supervisor

Date 26/10/2015
I dedicate this thesis to
my husband, Robert,
my parents, Victor and Dolores
and
my children, Michaela and David.
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Researching and writing this thesis has been an emotional rollercoaster, filled with apprehension and fear but also with excitement, pride and relief. I was fortunate enough to have the help and support of numerous people who shared this journey with me and helped to make it that little bit easier and more manageable.

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To all above, thank you.
Summary

Background: The introduction of vaccines against human papillomavirus (HPV) has essentially rendered cervical cancer a vaccine-preventable disease. Yet the uptake of the HPV vaccines has been much lower than anticipated all over the world, mainly due to missed clinical opportunities. These may be a consequence of gaps in the knowledge, attitudes and practices of healthcare professionals towards the HPV vaccines as doctors are known to play an important and influential role when it comes to patients deciding whether to accept vaccines or not. Identifying the barriers which prevent doctors from recommending these vaccines may help improve their recommendation practices and the uptake of the HPV vaccines.

Method: The study consisted of both quantitative and qualitative methodologies. The quantitative aspect was a cross-sectional study performed by means of a postal questionnaire sent to doctors specialised in family medicine, paediatrics and obstetrics and gynaecology in the Maltese Islands. The questionnaire assessed the knowledge, attitudes and practices of these doctors with regards to the HPV vaccines and identified any perceived barriers they reported. The data gathered was analysed statistically to identify significant differences in the above-mentioned factors depending on physicians' age, gender and specialty as well as the patients' age and gender, amongst other things. The qualitative methodology consisted of three focus groups carried out with members of the three specialties referred to during which a set of recommendations was drawn up according to the main themes which emerged and which can help local doctors in their recommendation of the HPV vaccines to patients.
Results:

Quantitative: Of the 412 doctors to whom the questionnaire was posted 175 eligible participants returned a completed questionnaire (46.7%). The final respondent population was analysed and found to be representative of the original sample of doctors. The level of knowledge was found to be good although a significant difference was observed in level of knowledge according to physician's age (p=<0.001) and specialty (p=<0.001). Younger doctors and obstetricians and gynaecologists were found to have the highest level of knowledge about HPV and its vaccines. While doctors' attitudes towards the vaccines appeared positive these were more positive when it came to recommending the vaccines to females than males. Recommendation of the vaccine, however, was very low. Doctors were found to recommend the vaccine least to young adolescent females (11-12 years old); obstetricians and gynaecologists were most likely to recommend the vaccines to the two younger female age groups and had 9.3- (95% CI, 2.8-30.7), 7.2- (95% CI, 2.7-18.8) and 5.5- (95% CI, 2.2-14) fold greater odds of "always" recommending the vaccines when compared to family doctors. The majority of physicians claimed that they "never" recommend the vaccines to male patients. The main barriers encountered by physicians in recommending the vaccines were related to cost and lack of parent education and understanding about HPV infection.

Qualitative: The main barriers faced by physicians to recommending the HPV vaccines were vaccine cost and lack of parent education - effectively reiterating the same findings made in the survey. Recommendations for actions to improve recommendation of the vaccines included improving health literacy and
patient education, methods to reduce the burden of the cost of the vaccines, lowering the recommended age group for vaccination and providing more education for the health care providers.

**Conclusion:** While the level of knowledge of participants about HPV and its vaccines is good, and the attitudes towards the vaccines are positive, recommendation practices leave much to be desired. The cost of the vaccines seems to be a major barrier, something which is perhaps reflected in the fact that while uptake of the vaccine in Malta where it is available for free is very good, its uptake in other sectors where it needs to be bought out of pocket is very low. This, and a lack of patient knowledge, seem to impact uptake of the HPV vaccines the most in the Maltese Islands, and are amongst the main issues which need to be addressed in order for the full benefits of the HPV vaccines to be enjoyed by all those eligible to receive them.
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Abbreviations

ACIP - Advisory Committee on Immunisation Practices
ASMR - Age-standardised mortality rate
ASR - Age-standardised rate
BASHH - British Association for Sexual Health and HIV
CDC - Centers for Disease Control and Prevention
CI - Confidence Interval
CIN - Cervical Intraepithelial Neoplasia
CMI - Cell-Mediated Immunity
CPD - Continuing Professional Development
DHIR - Directorate for Health Information and Research
DNA - Deoxyribonucleic acid
EASR - Age-standardised rates using European Standard Population
ECDC - European Centre for Disease Prevention and Control
EMA - European Medicines Agency
EU - European Union
FDA - U.S. Food and Drug Administration
GP - General Practitioner
HCCA
HIV - Human Immunodeficiency Virus
HPV - Human papillomavirus
HrHPV - High-risk human papillomavirus
HSIL - High-grade squamous intraepithelial lesion
IARC - International Agency for Research on Cancer
ICC - Invasive Cervical Carcinoma
IgG - Immunoglobulin G
LrHPV - Low-risk human papillomavirus
LSIL - Low grade squamous intraepithelial lesion
MMR - Measles, Mumps and Rubella
NCI - National Cancer Institute
NIS - National Immunisation Schedule
OC - Oral Contraceptive
OR - Odds Ratio
PSD - Personal and Social Development
RRP - Recurrent Respiratory Papillomatosis
SPSS - Statistical Package for the Social Science
STD - Sexually Transmitted Disease
UK - United Kingdom
US/A - United States (of America)
VLP - Virus-like particle
WASR - Age-standardised rates using World Standard Population
WHO - World Health Organisation
Chapter 1

Introduction
Chapter 1 - Introduction

1.1 Background

Human papillomavirus infection (HPV) of the genital tract is one of the most common sexually transmitted infections worldwide (Bruni et al., 2010, de Sanjosé et al., 2007) and most sexually active individuals (c. 75%) will acquire HPV infection at some point in their lives (Baseman & Koutsky, 2005). Most infections are asymptomatic and are cleared within around 2 years; however, genital HPV infection can cause clinical disease. This can include anogenital warts, neoplasia of the uterine cervix and other anogenital cancers.

For both females and males, the commonest time for becoming infected is soon after becoming sexually active (WHO, 2014), and the prevalence of HPV is highest among young people within the first few years after the first sexual encounters (Revzina & Diclemente, 2005, Tarkowski et al., 2004, Winer et al., 2003). Those at greatest risk of becoming infected with HPV are young, sexually active women. (Dunne et al., 2007).

Although the association of risk of cervical cancer with sexual behavior has been considered since around the mid-1800s, the central causal role of HPV infection was only identified around 35 years ago (zur Hausen, 2002, Boshart et al., 1984, Durst et al., 1983). Indeed, in almost all cases of cervical cancer, persistent
infection with HPV occurs (IARC, 2007). Bosch and de Sanjosé state that "...[c]ervical cancer has been recognized as a rare outcome of a common Sexually Transmitted Infection" (F Xavier Bosch & de Sanjosé, 2007). Similarly, Ibeanu declares that "...[c]ervical cancer is a sexually transmitted disease that results from infection with oncogenic types of human papillomavirus (HPV)" (Ibeanu, 2011).

Cervical cancer is the most common disease associated with HPV and almost all cases of cervical cancer can be attributed to HPV infection (Bonanni et al., 2014). Cervical cancer is the fourth most common cancer in women worldwide and the sixth most common cancer for females in Europe. In 2012 it was estimated that there were 528,000 new cases of cervical cancer globally, of which 58,400 were diagnosed in Europe (Ferlay et al., 2014), and 266,000 deaths globally (IARC, 2015). In Malta, in 2012, there were 7 new cases of cervical cancer diagnosed (Malta National Cancer Registry, DHIR, 2012) whilst there were 4 deaths in 2013 (DHIR, 2015). More than 100 types of HPV viruses have been described; at least 13 of these are "cancer-causing" and are known as "high risk type" (Handisurya, et al., 2009). HPV types 16 and 18 are the two most common HPV types and are responsible for 70% of cervical cancers and precancerous cervical lesions. HPV infection has also been linked with anal, vulvar, vaginal and penile cancers. (Handisurya et al., 2009). In Malta, a study carried out between May 2011 and February 2015 in women with abnormal cervical cytology indicated that the commonest HPV type was HPV type 16 with 21% of women with abnormal cervical cytology showing signs of infection with this high-risk type of HPV (Molecular Diagnostics Department, 2015).
Three prophylactic HPV vaccines have been licensed by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). These include a bivalent vaccine, a quadrivalent vaccine and the latest, a 9-valent vaccine. The safety profile of all three is good and they protect against the high-risk HPV types 16 and 18 (Merck Sharp and Dohme, 2011, GlaxoSmithKline, 2015, Merck Sharp and Dohme, 2015), and are indicated for use in individuals between 9 and 26 years of age. The quadrivalent and the 9-valent vaccines are licensed for administration to males as well as females. Since they do not cure existing infections they should be given before sexual activity begins. It is also important to bear in mind that HPV vaccination will not replace cervical cancer screening (Forman et al., 2012).

By August 2014 the HPV vaccine had been introduced in the national immunisation schedule of 58 countries, for girls. Some countries, such as Austria and Liechtenstein, have also introduced it for boys (European Centre for Disease Prevention and Control, 2015, WHO, 2014). In Malta the HPV vaccine has been administered for free by the Maltese National Health service to 12 year old girls since 2012, who are the main target group for these vaccines. Up till 2014 three doses were given and the coverage rate was very good - 87.5% for the 1st dose, 90.9% for the 2nd dose and 92.3% for the 3rd dose. (National Immunisation Services, 2015). As of 2015 the schedule consists of 2 doses given at a 6 month interval as indicated in the latest WHO position paper (World Health Organisation, 2014).
There is, however, a larger section of young men and women who are not eligible for the vaccine on the free national programme yet who would still benefit from taking the vaccine, and who would, therefore, need to buy it and have it administered privately. In Malta, currently, the 9-valent vaccine is not yet available on the market. Sales figures for the bivalent and quadrivalent vaccines, however, indicate a very low uptake, with figures decreasing as time goes by (personal communication). It is therefore this group of patients who would benefit most from improved doctor recommendations for these vaccines and in whom a higher rate of HPV vaccination should be sought.

Doctors are known to play an important and influential role when it comes to parents deciding whether to vaccinate their children or not. It is especially important that they express a clear opinion to parents that vaccines are beneficial while at the same time being directive in their recommendations for early childhood vaccinations (Opel et al., 2013, CDC, 2013). In fact, parents consistently cite their health care provider as playing an influential role in their decision-making concerning vaccines (Kennedy et al., 2011) and these have been shown to positively influence parents to vaccinate their children, including those who believe that vaccinations are unsafe. Thus it is important that health care providers enhance their efforts to develop good relationships with parents, particularly when they are concerned about issues of vaccine safety or may have the wrong idea about the benefits and risks of immunisation (Smith PJ et al., 2006).
Indeed, one way in which patients would be made aware of the HPV vaccine, and have it administered, is through recommendations being provided by their medical practitioner. Yet, despite recommendations encouraging HPV vaccination, the coverage rates in EU countries and the United States have proven to be lower than expected (Vadaparampil et al., 2014, ECDC, 2012). Possible reasons considered for this include the knowledge, attitudes and practices of healthcare professionals towards HPV vaccination about which, in Europe, studies are very scarce (ECDC, 2012).

A number of factors have been attributed to hesitancy of providers in recommending the HPV vaccine to patients. Among these are inadequate understanding of vaccine associated illnesses and benefits, cost of the vaccines, concerns about safety, insufficient time and motivation to educate parents and patients about HPV and the vaccine and personal attitudes and beliefs (NCI, 2013). Facilitators include "normalising" the HPV vaccine, encouraging co-administration of the vaccine with other vaccines, focusing on the advantages of cancer protection, and emphasising vaccine safety (Opel et al., 2013). Another facilitator for vaccine recommendation is the use of a "strong" recommendation which has been shown to improve vaccine acceptability and uptake by patients and parents alike (Holman et al., 2014, Rosenthal et al., 2011).

According to a recent report from CDC, "missed clinical opportunities are the most important reason why the U.S. has not achieved high rates of HPV vaccine uptake" (CDC, 2013). Any clinical visit by a patient who would benefit from the
vaccine, where a recommendation is not made, or is not made strongly enough, is considered to be a missed opportunity. This can result in the patient acquiring an infection, with potentially serious consequences, and for which an opportunity to prevent it was available but missed. Although most missed clinical opportunities regarding the HPV vaccine seem to involve the decision to delay vaccination rather than outright opposition to it, ultimately, delays often result in permanent failure of vaccination (Rebecca B Perkins et al., 2014).

The development of the HPV vaccines essentially means that cervical cancer has become a vaccine-preventable disease (Centers for Disease Control and Prevention, 2013b). Thus, it is important that efforts are made to address the main barriers to recommending the vaccines that health care providers face whilst simultaneously identifying the facilitators. Doing this could reduce considerably the number of missed opportunities in relation to the HPV vaccines.

Locally the only study that has been carried out with regards to the HPV vaccines looked at the attitudes towards HPV vaccines amongst students of health care professions (Z. Farrugia, 2011). Other than that there is a great dearth of information concerning the understanding and acceptance of the HPV vaccines, both by the general public as well as by the health care professionals who should be recommending their use. Vaccinated patient cohorts have shown a notable reduction in the prevalence of HPV infections, genital warts and precancerous lesions, indicating clearly that HPV vaccination is effective (Bonanni et al., 2014). It was therefore felt that having strong recommendation practices for HPV
vaccination, especially for adolescent girls, is a priority in public health, thus justifying the concept behind this study.

With this in mind this study sought to assess the knowledge, attitudes and practices of family doctors, paediatricians and obstetricians and gynaecologists with regards to the two HPV vaccines available on the Maltese Islands, and their practice and perceived influence on recommendation of the said vaccines. It also attempted to measure and assess a number of variables in physicians practising these specialities, including identifying barriers or facilitators which influence their recommending the HPV vaccines. Other variables measured included any significant differences in recommendation practices between male and female medical practitioners, to female and male patients and in different practice settings. The study also sought to identify sources from where the said medical practitioners are obtaining information about the HPV vaccines and whether they feel the need for more information/education sessions to address any queries they may have and how these can be transmitted to them.

The results of this study were analysed and compared with those of international studies to determine whether there are any differences or similarities in recommendation practices with the aim of providing a basis to understand where any issues may arise and how to address them. A set of recommendations was developed to enhance HPV vaccine recommendation practices by medical practitioners through discussion with the practitioners themselves in order to
ensure that the suggestions made were suitable to the requirements of local doctors.
Chapter 2

Literature Review
Chapter 2 - Literature Review

2.1 Identification and Eligibility of Relevant Studies

The literature was reviewed by searching a number of databases including PubMed, EBSCO, Google Scholar and the University of Malta search database, Hybrid Discovery (HyDi). Literature reviewed included journal articles, dissertations, reports and extracts from books. Local dissertations as well as direct communications with various experts were also referred to. Keywords used included human papillomavirus, HPV, cervical cancer, prevalence, epidemiology, natural history, burden and pathogenesis.

Where the review focused on the human papillomavirus vaccine the words HPV, human papillomavirus, vaccine, efficacy, safety, profile, perceptions, coverage and uptake were included in the search. The words knowledge, attitudes, practices, recommendations, physicians and providers were used when searching for literature which looked at recommendation practices by doctors.

Where possible information sources dated from the year 2010 onwards were selected. However, articles which were older yet considered to be relevant to the study were included, as were any references which were quoted in retrieved articles and found to be suitable. Since this study sought to be a nationally representative survey of Maltese provider recommendation of the HPV vaccine studies that looked
at populations other than those which were nationally representative where
excluded from the review. A table outlining the main studies and findings referring
to the knowledge, attitudes and practices of health care professionals regarding the
HPV vaccines and which were referred to in this literature review can be found in
Appendix G.

2.2 Pathophysiology of human papillomaviruses

The papillomaviruses are small viruses containing double-stranded DNA. They cause infections in squamous epithelia and require fully differentiating squamous epithelium in order to undergo a complete infectious cycle (Stanley, 2010). They only establish productive infections within stratified epithelia of the skin, the oral cavity and the anogenital tract (IARC, 2007).

2.2.1 HPV types

Over 100 types of human papillomaviruses (HPV) have been identified. These infect skin and mucosal squamous epithelium and usually cause benign papillomas. They are also, however, associated with malignant neoplasms of the skin and mucous membranes (Table 2.1) (Handisurya et al., 2009).

The major significance of HPV infection is its potential for carcinogenicity which has been most convincingly established for carcinoma of the cervix (IARC,
Approximately 40 types of human papillomavirus have been detected in the mucosa of the anogenital region (Sotlar et al., 2004, Ciesielska et al., 2012). They are classified as low or high risk types according to their association with the development of cervical cancer (Narisawa-Saito & Kiyono., 2007). Persistent infection with high-risk HPV types is the cause of all cancers of the cervix, most anal cancers, and some cancers of the vulva, vagina, penis and oropharynx (Handisurya et al., 2009).


Globally, around 70% of cervical cancers are associated with high-risk HPV-types (Ciesielska et al., 2012), with HPV 16 accounting for around 55% of all cases (Schmitt & Pawlita, 2011, Durst et al., 1983), while HPV 18 is involved in another 10-20% of cervical cancer cases (Muñoz et al., 2003, Narisawa-Saito & Kiyono, 2007). HPV infection with a particular type does not exclude becoming infected with another type. (CDC, 2012)
Table 2.1: Types of HPV and associated clinical manifestations

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>HPV Type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin</strong></td>
<td></td>
</tr>
<tr>
<td>Benign warts on the skin</td>
<td>Most common: 1, 2, 4&lt;br&gt;Less common: 26, 27, 29, 41, 57, 60, 63, 65</td>
</tr>
<tr>
<td>Verrucae planae</td>
<td>Most common: 3, 10&lt;br&gt;Less common: 28, 29</td>
</tr>
<tr>
<td>Butcher's warts</td>
<td>Most common: 7&lt;br&gt;Less common: 1, 2, 3, 4, 10, 28</td>
</tr>
<tr>
<td><strong>Mucosal lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Condylomata acuminata (genital warts)</td>
<td>Most common: 6, 11&lt;br&gt;Less common: 40, 42-44, 54, 61, 70, 72, 81</td>
</tr>
<tr>
<td>High-grade squamous intraepithelial neoplasias and invasive carcinomas of the anogenital tract</td>
<td>Most common: 16&lt;br&gt;Less common: 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 62, 68, 73, 82</td>
</tr>
<tr>
<td>Cervical dysplasia and carcinoma</td>
<td>Most common: 16, 18 (70%)&lt;br&gt;Less common: 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 62, 68, 73, 82 (30%)</td>
</tr>
<tr>
<td>Laryngeal papillomatosis/recurrent respiratory papillomatosis (RRP)</td>
<td>Most common: 6, 11</td>
</tr>
<tr>
<td>Head and neck carcinomas (30% appear to be caused by HPV infection)</td>
<td>Most common: 16 (90 % of HPV-positive carcinomas)</td>
</tr>
</tbody>
</table>

Sources: (Muñoz et al., 2003, Handisurya et al., 2009)

2.2.2 Natural history of HPV infection

Because of the proven association of persistant high-risk HPV infection in women and the increased risk for development of cervical cancer (IARC, 1995, Muñoz et al., 1992), cervical HPV infections are the best understood and the most significant types (Moscicki et al., 2012).

Most women with a specific type of HPV infection will not demonstrate signs of that same type six to twelve months later, and the great majority (~90%) clear the infection within a few years after acquisition (Figure 2.1) (Rodriguez et al., 2010, Winer et al., 2011). It is unclear whether the oncogenic HPV types have a
longer duration of infection than those which are not oncogenic (Richardson et al., 2003, Franco et al., 1999, Ho et al, 1998), however HPV 16 seems to have a longer time to clearance when compared to other types (Richardson et al., 2003, Liaw KL, 2001).

One of the hallmarks of HPV infection is long-term persistence over many years and this is required for cervical cancer to develop. The occurrence of new infections with HPV, whatever the age, are "benign unless they become persistant" (Moscicki et al., 2012). Therefore, those most at risk to develop high-grade intraepithelial disease and invasive cervical carcinoma (ICC) are women who develop persistent infection with a high-risk HPV-type (Liaw KL, 2001).

The reason why HPV infection persists in certain individuals and not others is not yet entirely clear. However, it is known that situations resulting in deficits in cellular immunity can result in an increase in persistence and diseases associated with HPV infection (Ibeanu, 2011).

Progression to cancer is not "normal" for human papillomaviruses. Rather, it is a "non-productive dead end" which results only after a long period of infection with a small selection of virus types. For the most part, infections with HPV are "benign and self-limited" (Ibeanu, 2011).
2.2.3 Transmission of HPV

Transmission of HPV infection can occur through either horizontal or vertical transmission (Table 2.2) (IARC, 2007). The viruses are easily transmitted and the main mode of transmission is through direct skin-to-skin or skin-to-mucosa contact (Burchell et al, 2006).
2.2.4 Risk factors for infection

Behaviours associated with sexual activity are the major risk factors for acquiring HPV infection. In fact it is necessary to have sexual contact with an infected partner for transmission of anogenital HPV infection to occur (IARC, 2007).

The main determinant of anogenital HPV infection both in women and men is the number of sexual partners (Dunne et al, 2006), new, recent or lifetime. The timing when sexual partnerships occur is also significant, (e.g. serial monogamy or occurring concurrently), as is age at first sexual experience (Tota et al, 2011, Trottier & Burchell, 2009, Burchell et al., 2006).

2.3 Pathogenesis of HPV-associated disease

The most common, and most significant, clinical indication of persistent genital HPV infection is cervical intraepithelial neoplasia (CIN) (CDC, 2012). CIN
are low grade lesions which can develop within a few years of infection although they may resolve spontaneously; most HPV infections and low-grade CIN resolve due to the development of cell-mediated immunity (CMI) (Stanley, 2010).

A small number of women do not develop a successful cell-mediated immune response. They remain infected with a persistent HPV infection (Moscicki A, et al., 2006, Cuschieri K, et al., 2005) which may progress directly to CIN2 or CIN3. These are high-grade abnormalities which risk progressing to cancer and are thus regarded as cancer precursors. Some of the high-grade abnormalities regress spontaneously but, if left undetected or untreated for many years, CIN2 or CIN3 lesions can develop into cervical cancer (CDC, 2012).

2.4 Treatment of HPV-related infections and neoplasia

In order to clear HPV infection more quickly cytoreductive treatment is generally indicated with the aim being the removal of clinically visible lesions. This is done through either medical or surgical methods, which still, however, do not remove the virus so that transmission and recurrence are still possible.

Therapies for the management of HPV-related pathologies include the use of cytotoxic agents, cryotherapy, electrodesiccation, immuno-modulation, laser ablation, surgical excision and loop electrode excision. (IARC, 2007).
2.5 HPV and Cervical Cancer

The three HPV types most commonly found in women with invasive cervical cancer are HPV16, 18 and 45, and the type most frequently identified in every grade of cervical disease is HPV 16. HPV prevalence in women has been shown to increase as the level of cervical disease becomes more severe, with prevalence ranging from 12% in women with normal cytology to 89% in women with invasive cervical cancers (Guan et al., 2012).

The findings that persistent infection with particular HPV-types is known to be a cause of the development of cervical cancer and its precursors (Bosch et al., 2002, Walboomers et al., 1999) carry more significance since the introduction of vaccines which can prevent primary infection among eligible women who have not yet acquired infection with the vaccine-specific HPV types (zur Hausen, 2009).

The development of cervical cancer is practically impossible if there is no sexually transmitted HPV infection (Bosch et al., 2002), as well as in the absence of intermediate progression to precancer. However, it is not sufficient to be infected with high-risk HPV alone (Bosch et al., 2006).
Behavioural co-factors (Figure 2.2 & Figure 2.3) such as smoking and multiparity double the risk of CIN2 and CIN3 among HPV-infected women together with long-term oral contraceptive use (Appleby et al., 2006, Smith et al, 2003). Although these co-factors have been firmly established by large case-control studies and by prospective evidence it is not known why they are co-factors. Other less well-established co-factors for progression given HPV infection include chronic cervical inflammation and immunosuppression.
Fig. 2.3: HPV and non-HPV factors that contribute to HPV-induced malignant progression

Viral risk factors:
- high-risk type
- viral load
- virus variants

Mutagenic factors and oestrogen derivatives

Upregulation of viral gene activity and amplification of persisting viral DNA

Non-HPV risk factors:
- several sexual partners
- mutagens
- smoking
- mutagenic infections (herpes simplex, bacterial and protozoal infections)
- hormones
- immunosuppression
- genetic predisposition

Gene regulatory function by increasing E6/E7 gene expression

Source: Harald zur Hausen, 2002
LSIL - low grade squamous intraepithelial lesion
HSIL - high-grade squamous intraepithelial lesion

2.6 Epidemiology of HPV infection

2.6.1 Human papillomavirus infection

Infection of the genital tract with HPV is one of the most common sexually transmitted diseases worldwide (Bruni et al., 2010, de Sanjose et al., 2007). It must be pointed out that, for the most part, the situation is relatively unknown and
figures quoted reflect only cases that have been reported and therefore may not reflect the true incidence and prevalence of the infection in the various countries.

A meta-analysis of 194 studies including more than 1 million women with normal cytological findings showed that the estimated prevalence for HPV worldwide was 11.7% (Bruni et al., 2010), similar to the global prevalence of 10.4% found in a previous study (de Sanjosé et al., 2007). The highest prevalence was in Africa and in women aged less than 35 years (Maucort-Boulch et al., 2008). The 10 most common HPV types across the world regions included HPV-16, 18, 31, 52 and 58 (Bruni et al, 2010). Another more recent meta-analysis reported that 12% of women with no cervical abnormalities resulted positive for HPV (Guan et al., 2012).

Figure 2.4: Worldwide prevalence of HPV, by type, among females with normal cytological findings.

Source: (Tota et al., 2011)
2.6.2 HPV infection in Malta

During an ongoing study which is being carried out in Malta, women with abnormal cytology underwent testing for infection with HPV. Of the 1591 women tested between May 2011 and February 2015, a little more than a quarter (26.4%) had no HPV detected. In the remaining 1171 women who resulted positive for HPV infection, the most common type detected was HPV 16 in 241 women (20.6%) (Fig. 2.5) (Molecular Diagnostics Department, MDH, 2015).

As observed in the literature (Bruni et al, 2010), HPV types 16, 18, 31, 52 and 58 are also within the top ten most common types found in the Maltese Islands. All the viruses detected are of the high-risk, oncogenic type (Nubia Muñoz et al., 2003).
2.6.3 HPV infection in men

HPV infection in men must not be ignored. Apart from the fact that men infected with HPV can transmit the infection to women, it places a significant disease burden on men themselves with the development of genital warts, recurrent respiratory papillomatosis (RRP) (Dominiak-Felden et al., 2013, Shi et al., 2012, Palefsky, 2010) and a number of cancers.
In the developed world HPV infection related cancers in men stand on a level much like that of cervical cancer in women (Kreimer et al., 2005, Daling et al., 2005, Ryan & Mayer, 2000). HPV infection in men may also increase their risk of becoming infected with HIV (Chin-Hong et al., 2009).

Genital HPV infection is very common in sexually active men; the incidence remains high regardless of age. Compared with cervical HPV infection, however, relatively little is known about its epidemiology. Recent estimates show a range from an overall prevalence of >50% (Giuliano et al., 2011) to between 2% and 93% in sexually active men who are at high risk and between 1% and 84% in men who are low risk (Smith et al., 2011), with prevalence remaining same or falling declining slightly with age once peak prevalence is reached. In men there is a higher proportion of the lower-risk HPV types than there is in women (Giuliano et al., 2011).

2.7 Epidemiology of cervical cancer

2.7.1 Incidence

In Europe cervical cancer is the sixth most common cancer for females and the 16th most common cancer overall, whilst globally it is the fourth most common cancer in women and the 7th overall. There were an estimated 528,000 new cases globally in 2012, of which 58,400 were diagnosed in Europe (Ferlay et al., 2014).
A large majority (85%) of cases globally are found to occur in the less developed regions (12% of all female cancers) (IARC, 2015). In 2012, worldwide, Africa had the highest incidence of cervical cancer, with Malawi having the highest age-standardised rate/100,000 (ASR) at 75.9. The lowest incidence was found in North America and Oceania. In Europe the highest world ASRs occurred in Romania, and the lowest rates were found in Switzerland (Ferlay et al., 2014).

Trends in cervical cancer incidence in numerous countries have shown that ASRs have decreased in several countries (Vaccarella et al., 2013) yet, projections for the incidence of cervical cancer in 2030, based only on demographic characteristics, is estimated to increase the global burden of cervical cancer by 2% (Forman et al., 2012).

2.7.2 Mortality

In 2012 it was estimated that 266,000 deaths occurred due to cervical cancer worldwide (7.5% of all female cancer deaths). 87% of deaths occur in the less developed regions and the mortality differs significantly between the different regions of the world; rates range from <2 per 100,000 in Western Asia, Western Europe and Australia/New Zealand to >20 per 100,000 in Melanesia, Middle and Eastern Africa (Figure 2.6) (IARC, 2015).
A systematic analysis which was carried out by looking at annual age-specific assessments of cervical cancer in 187 countries between 1980 and 2010 determined that deaths due to cervical cancer have decreased in almost all countries during this time period (Forouzanfar et al., 2011).
2.7.3 Cervical cancer in Malta

2.7.3.1 Incidence

The trend in cervical cancer incidence in Malta (Figure 2.7) between the years 2003-2012 indicates that, overall, there has been an increase in the number of new cases of cervical cancer occurring in Malta. It must be noted, however, that the figures being discussed are very small.

In 2012 there were 7 new cases of cervical cancer diagnosed (Malta National Cancer Registry, DHIR, 2012). The age-standardised incidence rates for 2012 are significantly lower than the estimated ASRs for 2012 for Europe (13.4) and the EU 27 (11.3) (Ferlay et al., 2013) and can be seen in Table 2.3 below.
Fig. 2.7: Incidence in cancer of the cervix in Malta (2003-2012)

![Graph showing incidence in cancer of the cervix in Malta between 2003-2012](image)

Source: (Malta National Cancer Registry, DHIR, 2013)

Table 2.3: Age-standardised incidence rates, cervical cancer, Malta, 2012

<table>
<thead>
<tr>
<th>Rate</th>
<th>Rate/100,000</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude rate</td>
<td>3.32</td>
<td>1.46-7.18</td>
</tr>
<tr>
<td>EASR¹</td>
<td>2.81</td>
<td>2.59-3.03</td>
</tr>
<tr>
<td>WASR²</td>
<td>2.21</td>
<td>2.09-2.39</td>
</tr>
</tbody>
</table>

Source: Malta National Cancer Registry, DHIR, Malta

¹ EASR = Age-standardised rates using European Standard Population/100,000 population
² WASR = Age-standardised rates using World Standard Population/100,000 population
During the ten year period between 2003 and 2012 the highest number of new cases were diagnosed in the 50-54 year age group (n=15) (Figure 2.8).

Figure 2.8: Number of new cases of cervical cancer diagnosed in Malta, between 2003-2012, according to age group

![No. of new cases of cervical cancer according to age group (Malta, 2003-2012)](image)

Source: (Malta National Cancer Registry, DHIR, 2013)

**2.7.3.2 Mortality**

In Malta, in 2013, there were 4 deaths due to cervical cancer (Figure 2.9 & Figure 2.10) (DHIR, 2015). The trend for mortality indicates a decrease (Figure 2.11) and, overall, the age-standardised mortality rates (ASMRs) compare with those for Southern Europe (Figure 2.6).
Figure 2.9: Number of deaths due to cervical cancer in Malta, in all age groups, between 2000-2013

No. of deaths in all age groups
2000-2013

Source: Annual Mortality Reports, DHIR, Malta, 2000-2013

Figure 2.10: Number of deaths due to cervical cancer in Malta, by age group, between 2000-2013

No. of deaths by age group - 2000-2013

Source: Annual Mortality Reports, DHIR, Malta, 2000-2013
Figure 2.11: Age-standardised mortality rates (ASMR) due to cervical cancer in Malta, 2000-2013

\[ \text{ASMR from 2000-2013} \]

Source: Annual Mortality Reports, DHIR, Malta, 2000-2013

2.8 Prevention and screening for cervical cancer

Since cervical cancer poses such a major public health problem resulting in the death of around 250,000 women every year, it is important to know that there are effective primary and secondary preventive strategies available which offer the possibility of decreasing the morbidity and mortality from this cancer in all countries (M. Arbyn et al., 2011).

For more than 50 years the standard screening method used was cytology-based screening using the Papanicolau (Pap) smear test. The fact that HPV infection is necessary for the development of cervical cancer has, however, opened plenty of new opportunities for prevention. More recently developed strategies for
prevention include screening for infection, and immunising to prevent infection, with the high risk HPV types (Figure 2.12) (Tota et al., 2011).

Indeed, perhaps the most important advancement in the management of HPV infection is the identification of particular types of HPV as the major cause of cervical cancer. The development of HPV vaccines against these oncogenic types means that the primary prevention of most cases of cervical cancer is becoming a possibility (IARC, 2005).

Figure 2.12: The natural history, risk factors and opportunities for prevention of cervical cancer

Source: (Tota et al., 2011)
2.8.1 Primary Prevention

One of the first steps in primary prevention involves the prevention of initial HPV infection which should reflect that given for other STDs. Nowadays this goes beyond the original 'ABC' approach (Abstain, Be faithful, use Condoms) (Baseman & Koutsky, 2005, Cohen, 2003) and looks at empowering individuals to be positive and have a responsible attitude towards sex (ABCD-Autonomy, Building healthy relationships, Connectedness and Diversity) and giving advice about how to practice safer sex (J. Farrugia & Health Promotion and Disease Prevention Directorate, 2013).

2.8.2 The HPV vaccines

Since HPV infection is necessary for the development of cervical cancer, prophylactic vaccination targeting specific genotypes for primary prevention of this cancer is expected to significantly effect the impact of this disease (Tota et al., 2011, IARC, 2005).

There are three prophylactic vaccines currently available on the international market for the prevention of HPV and its related diseases (Figure 2.13). These consist of a quadrivalent vaccine (against HPV 6, 11, 16, 18; Silgard/Gardasil; Merck and Co, Inc. - first licensed in 2006), a bivalent vaccine (against HPV 16, 18; Cervarix; GlaxoSmithKline - licensed in 2007) and a recently licensed 9-valent vaccine (against HPV 6, 11, 16, 18, 31, 33, 45, 52, 58; Gardasil 9;
Merck and Co, Inc.). All three of them are directed against oncogenic HPV genotypes and should, where possible, be administered prior to the onset of sexual activity. This would thus precede the first exposure to HPV infection (Petrosky, 2015, WHO, 2014). Studies have shown that the most cost-effective and clinically effective strategy to prevent cervical cancer is most likely to be the vaccination of girls aged 9–12 years whilst achieving high coverage (Goldie et al., 2008).

Fig. 2.13: Characteristics of the three human papillomavirus vaccines licensed for use

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bivalent (2xHPV)*</th>
<th>Quadrivalent (4xHPV)*</th>
<th>9-valent (9xHPV)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand name</td>
<td>Cervarix</td>
<td>Gardasil</td>
<td>Gardasil 9</td>
</tr>
<tr>
<td>VLPs</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 59</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>GlaxoSmithKline</td>
<td>Merck and Co, Inc.</td>
<td>Merck and Co, Inc.</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>Insect cell line infected with L1 encoding recombinant baculovirus</td>
<td>Saccharomyces cerevisiae (Baker's yeast), expressing L1</td>
<td>Saccharomyces cerevisiae (Baker's yeast), expressing L1</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>500 μg aluminum hydroxide, 50 μg 3-O-desacyl-4′-monophosphoryl lipid A</td>
<td>225 μg amorphous aluminum hydroxysulfate</td>
<td>500 μg amorphous aluminum hydroxysulfate</td>
</tr>
<tr>
<td>Volume per dose</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Administration</td>
<td>Intramuscular</td>
<td>Intramuscular</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

Abbreviation: L1 = the HPV major capsid protein; VLPs = virus-like particles.

Source: Petrosky, E. et al. (2015)

### 2.8.3 The Bivalent and Quadrivalent vaccines

Randomized placebo-controlled trials carried out on these vaccines provide good evidence that they prevent not only persistent infection but also preinvasive lesions of the anogenital tract associated with the HPV types included in the vaccines (Harper et al., 2006, Harper et al., 2004). The bivalent vaccine contains purified viral proteins for two HPV types (16 and 18) and is indicated for use in females from the age of 9 years to prevent premalignant genital lesions and cervical
cancer that are related to certain HPV types. The quadrivalent vaccine also prevents the development of genital warts which are caused by HPV types 6 and 11 (Denny, 2012, Villa et al., 2007, Villa et al., 2005). It contains purified viral proteins for four HPV types (6, 11, 16 and 18) and can be used in females and males from the age of 9 years to prevent premalignant genital lesions, premalignant anal lesions, cervical cancers and anal cancers that are related to certain HPV types, and anogenital warts that are related to specific HPV types. For both vaccines, in individuals aged 9 to 13-14 years the suggested vaccination schedule consists of two doses while from the age of 14-15 years onwards three doses are recommended (Merck Sharp and Dohme, 2011a, Merck Sharp and Dohme, 2011b, GlaxoSmithKline, 2015).

The two vaccines appear to offer full protection against HPV types 16 and 18 and have been shown to be safe (Macartney et al., 2013), immunogenic, and highly efficacious (Schiller et al., 2012). There is also some data that indicates that cross-protection against types 31 and 45 (both important in the cause of cervical cancer) results following the immune response to vaccination against types 16 and 18, increasing the estimated protection from vaccination to 75%-80% (Harper et al., 2006).

Both vaccines function through empty viral shells which are known as virus-like particles (VLP) and which resemble the natural infectious virions strongly, yet they do not contain any live biological products or oncogenic viral DNA. Hence, they are not infectious, and cannot replicate, so even immunosuppressed patients
can be vaccinated without experiencing problems (Handisurya et al., 2009). Neither vaccine contains any antibiotics or preservative agents (WHO, 2014) and after administration high-titer IgG antibodies are formed which can neutralise any infectious viruses (Handisurya et al., 2009).

These vaccines have been shown to be up to 100% effective in preventing persistent infections and cervical dysplasia with HPV 16 and HPV 18 in women who had not already been infected with the HPV types found in the vaccines. The genital warts which are caused by HPV 6 and HPV 11 were found to be prevented in about 90% of cases by the quadrivalent vaccine (Lowy & Schiller, 2006). Even when vaccine uptake was low the prevalence of the HPV-types found in the vaccines had decreased among girls aged 14–19 years, whilst the estimated vaccine effectiveness was high (Markowitz et al., 2013).

Since the two vaccines target HPV-types 16 and 18, they can only prevent the cervical dysplasias associated with these types (about 70%). Infection with the other high-risk HPV types, and the remaining 30% of cervical dysplasia they cause, can only be effectively prevented in around 25% of cases. Thus it is essential that women who have received the vaccine continue having regular gynaecological visits and Pap smear tests (Handisurya et al., 2009).
2.8.4  **Gardasil 9 - the 9-valent HPV vaccine**

The 9-valent vaccine contains highly purified viral proteins from the same four HPV types (6, 11, 16, 18) in the quadrivalent HPV vaccine (Gardasil or Silgard) and from 5 additional HPV types (31, 33, 45, 52, 58) (Merck Sharp and Dohme, 2015). It is recommended for use in both females and males between the ages of 9 and 26 years in a 3-dose schedule (Petrosky, 2015). It was licensed for use by the FDA in December 2014 (Petrosky, 2015) and by the EMA in 2015 (European Medicines Association, 2015).

2.8.5  **The HPV vaccine in various countries**

There were 58 countries that had introduced the HPV vaccine in their national immunization programme for girls by August 2014. In some countries it has also been introduced for boys (WHO, 2014). Table 2.4 below gives a brief description of the way in which the HPV vaccine is administered in various EU countries (European Centre for Disease Prevention and Control, 2015). In some instances there are recommended catch up phases for older age groups.
Table 2.4: Description of mode of administration of HPV in National Immunisation Schedules of various EU countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Given to females</th>
<th>Given to males</th>
<th>Age group</th>
<th>Dose schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Yes</td>
<td>Yes</td>
<td>10-12 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>Belgium</td>
<td>Yes</td>
<td>No</td>
<td>10-13 years</td>
<td>3 doses</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>Yes - not on NIS but voluntary &amp; free</td>
<td>No</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Czech Rep</td>
<td>Recommended</td>
<td>No</td>
<td>13-14 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Denmark</td>
<td>Yes</td>
<td>No</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Finland</td>
<td>Yes</td>
<td>N/A</td>
<td>11-12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>France</td>
<td>Yes</td>
<td>N/A</td>
<td>11-14 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>Germany</td>
<td>Yes</td>
<td>No</td>
<td>9-17 years</td>
<td>9-14yrs - 2 doses 15-17Yrs - 3 doses</td>
</tr>
<tr>
<td>Greece</td>
<td>Yes</td>
<td>No</td>
<td>11-18 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Hungary</td>
<td>Yes - school based</td>
<td>No</td>
<td>12-13 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Iceland</td>
<td>Yes</td>
<td>No</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Ireland</td>
<td>Yes</td>
<td>No</td>
<td>11-13 years</td>
<td>3 doses</td>
</tr>
<tr>
<td>Italy</td>
<td>Yes</td>
<td>No</td>
<td>11-18 years</td>
<td>11 years - 2 doses 12-18 yrs - 3 doses</td>
</tr>
<tr>
<td>Latvia</td>
<td>Yes</td>
<td>N/A</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Liechtenstein</td>
<td>Yes</td>
<td>Yes</td>
<td>11-14 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>Recommended</td>
<td>No</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Malta</td>
<td>Yes</td>
<td>No</td>
<td>12 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Yes</td>
<td>No</td>
<td>12-13 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>Norway</td>
<td>Yes</td>
<td>No</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Portugal</td>
<td>Yes</td>
<td>No</td>
<td>13 years</td>
<td>3 doses</td>
</tr>
<tr>
<td>Romania</td>
<td>Recommended</td>
<td>N/A</td>
<td>11-14 years</td>
<td>3 doses</td>
</tr>
<tr>
<td>Slovakia</td>
<td>Recommended - partially reimbursed</td>
<td>N/A</td>
<td>12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Slovenia</td>
<td>Yes</td>
<td>No</td>
<td>11-12 years</td>
<td>N/A</td>
</tr>
<tr>
<td>Spain</td>
<td>Yes</td>
<td>No</td>
<td>12 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>Sweden</td>
<td>Yes</td>
<td>No</td>
<td>10-12 years</td>
<td>2 doses</td>
</tr>
<tr>
<td>U.K.</td>
<td>Yes</td>
<td>No</td>
<td>12-13 years</td>
<td>2 doses</td>
</tr>
</tbody>
</table>
2.8.6 The HPV vaccine in Malta

In Malta the HPV vaccine has been administered for free by the Maltese National Health service to 12 year old girls since 2012, as had been indicated in The National Cancer Plan 2011-2015 (Ministry for Health the Elderly and Community Care, 2011). Uptake of the vaccine in this group of girls - who form the main target group for the vaccines - has shown a very good coverage rate. Up till 2014 three doses were given and the coverage rate was very good - 87.5% for the 1st dose, 90.9% for the 2nd dose and 92.3% for the 3rd dose for the year 2014 (National Immunisation Services, 2015). As of 2015 the schedule consists of 2 doses given at a 6 month interval as indicated in the latest WHO position paper (World Health Organisation, 2014). There is however a larger section of young men and women who are not eligible for the vaccine on the free national programme yet who would still benefit from taking the vaccine and who would therefore need to buy it and have it administered privately, and it is this group of patients who would benefit most from improved doctor recommendations for these vaccines and in whom a higher rate of HPV vaccination should be sought.

At the time the research project was carried out the retail price of the HPV vaccines in Malta as provided by pharmaceutical agents and dispensing pharmacists was €108.84 per dose for the bivalent vaccine (Cervarix) and €142.56 per dose for the quadrivalent vaccine (Silgard). Gardasil 9, the nonavalent vaccine is not yet available on the Maltese market.
The figures for the sale of Cervarix and Silgard vaccine in the private market indicate that the uptake in this sector is low. During the first 4 years following its launch sales of the Cervarix vaccine averaged 300-400 vials per month. This would indicate that, with a 3-dose schedule, only approximately 1400 people a year were receiving the Cervarix vaccine privately. Recent figures have indicated that sales have dropped to 50-100 vials per month meaning that only around 400 people a year are buying the Cervarix vaccine. Similarly figures for the Silgard vaccine show sales of around 60 vials per month meaning that only approximately 240-360 people are buying it per year, depending on the schedule followed.

2.8.7 Secondary Prevention

Cervical cancer screening programmes aim to decrease the incidence and, mainly, the deaths caused by cervical cancer, through identification of women who have precancerous cervical lesions and early invasive cancers, and treating them appropriately (IARC, 2005).

While prophylactic HPV vaccines do offer great hope for future generations, screening still plays a crucial role as there is no indication, as yet, that these vaccines will eradicate the disease anytime soon. Indeed, currently, women who are already sexual active will, for the most part, have to continue undergoing screening to prevent cervical cancer, for the timebeing. Halting cervical cancer screening now could demolish all the gains made during the last fifty years (IARC, 2005).
Cytology-based programmes using the Papanicolau test (or Pap smear) continue to be the principal method of cervical cancer prevention. This screening method has led to major reductions in the incidence and mortality of cervical cancer in countries where national screening programs have been organised and implemented (Tota et al., 2011, Hakama & Louhivuori, 1988).

Lately, HPV DNA seems to be developing as a possible replacement for Pap cytology for primary screening (Tota et al., 2011), with the former test found to be only slightly less specific, but more sensitive, in detecting high grade cervical precancerous lesions (Sankaranarayanan et al., 2009, Arbyn et al., 2006, Cuzick et al., 2006). Other screening techniques involve various visual inspection techniques and cervicography (IARC, 2005).

Screening in most European countries is recommended from age 25 to age 64/65 (IARC, 2005), with screening intervals of 3 to 5 years, with the former interval being the most recommended between normal cytological tests is three years.

2.8.8 Cervical cancer screening in Malta

Currently there is no cervical cancer screening programme and most cervical cancer screening is opportunistic. Screening for cervical cancer is, however, targeted to commence in October 2015. Women born between 1980 and 1990, 25-35 year olds inclusive, will be invited to attend screening over a three year cycle.
representing an initial cohort of 32,000 women. The second cycle is planned to start in 2019. The method of screening to be used is HPV triage although for women aged 30-35 years co-testing with HPV is also a possibility (direct communication, National Health Screening Services, 2015)

Although the introduction of prophylactic HPV vaccines will effect screening, screening will have to carry on in both vaccinated and unvaccinated populations, since the current vaccines do not target all the oncogenic HPV types identified.

For some countries the implementation of an HPV vaccination program, in conjunction with cytological screening, could be a cost-effective strategy to prevent cervical cancer (Goldie et al., 2004, Kulasingam & Myers, 2003). Thus, it would seem, having a successful HPV vaccination program, together with screening, is the best method to decrease the morbidity and mortality that are associated with HPV-related pathologies (Forman et al., 2012, Bosch et al, 2012).

2.9 Knowledge, attitudes and practices of healthcare professionals

Research has demonstrated that it is important that physicians express a clear opinion to parents that vaccines are beneficial and at the same time that they are directive when giving their recommendations for early childhood vaccinations (Opel et al., 2013, CDC, 2013). In fact, parents regularly state that their health care provider is an important influence on their decisions where vaccines are concerned
(Kennedy et al., 2011), and these have been shown to have a positive influence on parents to vaccinate their children, even those who have doubts about the safety of vaccinations. Therefore, health care providers should improve and maintain their efforts to develop good relationships with parents, particularly when they are concerned about issues of vaccine safety or may have the wrong idea about the risks and benefits of immunisation (Smith PJ et al., 2006).

Despite recommendations encouraging HPV vaccination, the coverage rates in EU countries and the United States have proven to be lower than expected (Vadaparampil et al., 2014, ECDC, 2012). Possible reasons considered for this include the attitudes, knowledge and practices of healthcare professionals towards the HPV vaccination about which, in Europe, studies are very scarce. This justifies addressing the issue further throughout the EU (ECDC, 2012).

2.9.1 Knowledge

Research into the knowledge of medical practitioners about HPV and the HPV vaccines has indicated that there are some areas where doctors are quite lacking. Awareness also varies widely by specialty and training of physicians (Krupp et al., 2010). In-depth interviews with physicians also revealed that knowledge of benefits of HPV vaccines, especially for males, was quite limited (CDC, 2013).
Many physicians have been found to be willing to delay the administration of HPV vaccines beyond the recommended age of 11 or 12 years. Indeed in many cases delay (not refusal) is the most common cause of non-vaccination, with both providers and parents contributing to the reasons for delay (Perkins et al., 2014). Consequently many young adolescents are unintentionally left exposed to HPV infection.

There is a greater possibility that patients and parents will accept a vaccine if it is recommended by a physician (Zimet, 2005), and if the recommendation provided by the doctor is strong (Rosenthal et al., 2011). Therefore, the widespread education of physicians, as well as patients and parents, about the consequences and risks of HPV infection, and the benefits of vaccination, coupled with strong recommendations to patients, will also be very important to improve vaccine acceptance and to develop appropriate uptake (Rosenthal et al., 2011, Anhang et al, 2004).

2.9.2 Attitudes

Studies conducted in Europe show that general practitioners are likely to accept the vaccine mostly in relation to the associated public health benefits (Luttringer-Magnin et al., 2011, Piana et al., 2009). Some concerns need to be tackled, however, especially those focused on long-term vaccine efficacy and the possible effects of the vaccination on the sexual behaviour of adolescents.
While most physicians might express a positive attitude towards vaccination, many believe that most of their patients would react negatively to a vaccine recommendation (Krupp et al., 2010). Also, some physicians feel that vaccinating males is not worth the effort or cost, are not aware of serious HPV-related disease in males, or think that parents would not want to vaccinate their sons (Holman et al., 2014, R. B. Perkins & Clark, 2012). Yet, recent research has shown that, when given any amount of information about HPV in both genders, parental acceptance of HPV vaccination of their sons is as high as acceptance levels for girls (Lee Mortensen et al., 2015).

Because the target vaccination population is young the decision-making process about whether to take the vaccine or not will involve physicians, parents and patients. Thus, acceptance of the HPV vaccines by individuals and parents is necessary to ensure the success of HPV vaccination programs (Gross, 2007). Since patients and parents will more likely accept a vaccine if it is recommended by a physician (Holman et al., 2014, Rosenthal et al., 2011, Zimet, 2005), it therefore follows that the attitudes of healthcare providers and their recommendation of HPV vaccination play an important role. How strong a physician’s recommendation is can be very significant; women who received a strong recommendation were four times more likely to take the vaccine as opposed to women who received a weaker recommendation (Rosenthal et al., 2011). Indeed, parents have stated that the reason for not vaccinating their child was not having a physician’s recommendation (Holman et al., 2014).
2.9.3 Practices

While paediatricians in the US showed a high level of acceptance of HPV vaccination for older adolescent females, fewer than one half of participants expected to administer the vaccine to younger female patients (Daley et al., 2006). Similarly, a survey amongst paediatricians and family doctors found that the vast majority declared that they offered the HPV vaccine, although fewer physicians strongly recommended it for younger patients than for older ones. Most of the physicians surveyed were not using active strategies to ascertain that patients completed the course of HPV vaccines by taking 3 doses. Thus patients are achieving full immunisation at an older age (Daley et al., 2010).

Male physicians have been found to be less likely than female physicians to vaccinate young male adolescents. This difference was not found to be associated with their intention to vaccinate female patients (Daley et al., 2006).

2.10 Barriers and facilitators to recommending the vaccines

2.10.1 Barriers

Physicians who report high perceived barriers to vaccination are less likely to recommend the vaccine to early adolescents than physicians who report low perceived barriers to vaccination (Table 2.5) (Vadaparampil et al., 2011).
<table>
<thead>
<tr>
<th>Perceived barrier</th>
<th>Reason/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target age (9-13 years)</td>
<td>1. Need to discuss sexually transmitted infections with adolescent patients (Lutringer-Magnin et al., 2011)</td>
</tr>
<tr>
<td></td>
<td>2. Talking to parents about their adolescent children’s reproductive lives and sexuality (Krupp et al., 2010)</td>
</tr>
<tr>
<td>Financial issues and costs</td>
<td>1. Inaccessible to some patients (Vadaparampil et al., 2013)</td>
</tr>
<tr>
<td>Parent opposition</td>
<td>1. Moral or religious reasons (Daley et al., 2010)</td>
</tr>
<tr>
<td></td>
<td>2. Knowledge gaps and false perceptions (Holman et al., 2014)</td>
</tr>
<tr>
<td>Lack of knowledge (physicians, parents and patients)</td>
<td>1. Insufficient information provided (Lutringer-Magnin et al., 2011)</td>
</tr>
<tr>
<td>Dealing with patients' concerns about potential side effects</td>
<td>1. Inadequate training (Lutringer-Magnin et al., 2011)</td>
</tr>
<tr>
<td>Lack of interest in the vaccine by patients</td>
<td>1. Belief that it was not needed</td>
</tr>
<tr>
<td></td>
<td>2. Not knowing enough about it</td>
</tr>
<tr>
<td></td>
<td>3. Concerns about safety</td>
</tr>
<tr>
<td></td>
<td>4. Not being sexually active (Anhang Price et al., 2011)</td>
</tr>
<tr>
<td>Recommending immunization not appropriate in their work setting</td>
<td>1. Should be done by other specialities (Krupp et al., 2010)</td>
</tr>
<tr>
<td>Unsure of which vaccine to recommend</td>
<td>1. Lack of guidelines (Vadaparampil et al., 2013)</td>
</tr>
<tr>
<td>Safety and efficacy issues</td>
<td>1. Insufficient information, especially for male patients (Vadaparampil et al., 2013)</td>
</tr>
<tr>
<td>Time constraints</td>
<td>1. Busy clinics and high workload (Vadaparampil et al., 2013)</td>
</tr>
<tr>
<td>Vaccine’s effect on sexual behavior</td>
<td>1. Could give adolescents a false sense of protection resulting in “sexual disinhibition” (Holman et al., 2014, Forster et al., 2010)</td>
</tr>
<tr>
<td>Low perceived risk of HPV infection</td>
<td>1. Inadequate information (Holman et al., 2014)</td>
</tr>
<tr>
<td>Social influences</td>
<td>1. Media and social pressures (Holman et al., 2014)</td>
</tr>
<tr>
<td>Irregular preventive care</td>
<td>1. Irregular contact with health system (Holman et al., 2014)</td>
</tr>
<tr>
<td>Parents not vaccinating their sons</td>
<td>1. Perceived lack of direct benefit/knowledge gap (Holman et al., 2014)</td>
</tr>
<tr>
<td>Difficulty explaining to parents why vaccine is recommended to girls who are not yet sexually active</td>
<td>1. Knowledge gaps (Hughes et al, 2011)</td>
</tr>
</tbody>
</table>
The issue related to discussing adolescent's sexuality and sexual health is a major and complex one such that, in order for physicians to avoid delicate conversations, HPV vaccination becomes an issue of timing. Very often, delays that should be temporary result in a permanent failure to start vaccination, for various reasons. So, although parents and physicians may agree about the importance of vaccination, almost one-half of all teenage girls remain exposed to HPV infection (Perkins et al., 2014). One study reported that parents of younger patients refused the vaccines more when compared with older female adolescents (Vadaparampil et al., 2011). This is especially of concern because recent research indicates that vaccinating against HPV before the age of 14 years is twice as effective compared with vaccinating at age 15 years and over (Gertig et al., 2013).

The issue of the supposed negative effect of the vaccine on the sexual behaviour of adolescent girls, leading to “sexual disinhibition”, needs to be dealt with in order to improve vaccine uptake (ECDC, 2012). In fact, parents who endorse this belief have been found to be less accepting of the vaccine (Forster et al, 2010). Yet, HPV vaccination does not appear to bear any significant impact on the indicators of sexual behaviour in adolescent girls. Concerns about increased promiscuity after HPV vaccination are unfounded and should not stop doctors and parents from giving the vaccine to younger patients (Smith et al, 2015).
2.10.2 Facilitators

Providers with vaccination rates exceeding 80% state that effective and simple ways to achieve vaccination include normalising the HPV vaccine, encouraging co-administration of HPV vaccine as recommended with other vaccines (e.g. tetanus and meningococcal vaccines) (CDC, 2013), focusing on benefits of cancer protection, and emphasising vaccine safety (Opel et al., 2013).

Another facilitator for vaccine recommendation is the use of a "strong" recommendation. Research has, in fact, demonstrated the importance of physicians giving parents a clear opinion and directive recommendations about the importance and benefits of vaccination (Opel et al., 2013, CDC, 2013).

2.11 Missed Clinical Opportunities

Any clinical visit by a patient who would benefit from the vaccine, where a recommendation is not made, or is not made strongly enough, is considered to be a missed clinical opportunity. Although guidelines have been issued which recommend vaccinating all females aged 9-26 years, there are many missed clinical opportunities for HPV vaccination, especially for young, adolescent females. It is known that the recommendation of physicians is important and can be a consistent predictor of vaccine uptake, yet decisions about recommending the vaccine may be influenced by perceived barriers. Therefore, interventions need to be implemented in order to address these barriers, and to promote vaccination against HPV of
young adolescents, be they female or male (Vadaparampil et al., 2013, Vadaparampil et al., 2011).

Many "missed opportunities for HPV vaccination" have been noted to occur because parents and providers agree to postpone giving the vaccine until they feel that girls are about to initiate sexual activity. Since it is difficult to determine exactly the onset of sexual activity, many girls remain exposed to developing cancers that are vaccine-preventable (Perkins et al., 2014).

2.12 Interventions to improve HPV vaccination uptake

In order to improve vaccine delivery and uptake it is important that strategies are developed in order to encourage more effective physician-patient and physician-parent communication. These would involve addressing approaches which would help physicians to encourage reluctant parents to discuss with them, as well as to determine the effect of different clinician decision-making styles on the delivery of the HPV vaccine (Hughes et al., 2011).

It is important that the fear of adverse reactions to the vaccine is addressed by providing patients, parents and physicians with appropriate, evidence-based information on the risks and benefits of HPV vaccination (ECDC, 2012). It is also essential to encourage physicians to make strong recommendations for HPV vaccines as cancer preventing vaccines as well as to recommend administrating
them with other vaccines routinely at age 11 years; these interventions have the potential to greatly decrease missed opportunities (Perkins et al., 2014).

2.13 The local situation

As has already been mentioned, the coverage rates for the vaccine in EU countries and the United States have proven to be lower than expected (Vadaparampil et al., 2014; ECDC, 2012) with one of the possible reasons considered including the attitudes, knowledge and practices of physicians towards the HPV vaccination. The coverage rate in 12 year old girls in Malta, who are given the vaccine in the public health sector, where the vaccine is offered free, is known and is very good. But little is known about doctors' recommendation practices for the vaccines, and also about administration rates of the HPV vaccine to patients who are required to buy them out of pocket.

As far as studies concerning HPV vaccines in Malta are concerned, to the best of the researcher's knowledge, only one study has been carried out that looked at the attitudes towards HPV vaccines amongst students of health care professions (Farrugia, 2011). This study in fact compared the knowledge, attitudes and behaviours of first year students with final year students especially in view of the fact that health care providers are viewed as credible and trusted sources of information by the public and since their positive attitude is associated with higher rates of vaccine coverage. The students were studying to become doctors, pharmacists and nurses and results of this study showed that students from all
courses had a low level of knowledge before enrolling at university and gained little despite their training. However they had a positive attitude towards the vaccine which could be taken to indicate their attitude once they started practicing their profession.

Other than that there have been no studies looking at the knowledge, attitudes and practices of doctors in this area. Thus it was felt that the topic needed to be analysed in more depth in order to understand the situation better and, where necessary, to develop effective recommendations to address any issues which are identified.

Thus it was decided that the aim of this study would be to assess the knowledge, attitudes and practices of family doctors, paediatricians and obstetricians and gynaecologists with regards to the HPV vaccines available as well as any barriers or facilitators which influence their recommending the use of these vaccines.

This aim would be achieved by fulfilling the following objectives:

1. Measuring and assessing the following variables in a population consisting of family doctors, paediatricians and obstetricians and gynaecologists:
   - Level of knowledge, attitudes and practices with regards to the HPV vaccines and their practice and perceived influence on recommendation of said vaccines
- Identify barriers to their recommending the HPV vaccine
- Identify facilitators to their recommending the HPV vaccine

2. Identifying any significant differences in recommendation practices between male and female medical practitioners.

3. Identifying any significant differences in recommendation practices to female and male patients.

4. Identifying any significant differences in recommendation practices in different settings i.e. private GP practice, Health Centre GP clinic, Hospital and specialty clinic.

5. Identifying sources from where the said medical practitioners are obtaining information about the HPV vaccines and whether they feel the need for more information/education sessions to address any queries they may have and how this can be transmitted to them.

6. Analysing the results and comparing them with those of other international studies to determine whether there are any differences or similarities.

7. Developing a set of recommendations to enhance HPV vaccine recommendation practices by medical practitioners.

The methods used in order to achieve these aims and objectives are described in detail in the coming chapter.
Chapter 3

Materials
& Methods
Chapter 3 - Materials and Methods

3.1 Introduction

This chapter describes the aims and objectives of the study and explains which methods were chosen to carry out the research and how they were carried out. It describes the research tools used as well as any associated limitations and the details of the study population, the pilot study carried out, and the data collection and analysis procedures applied.

3.2 Aims and objectives

3.2.1 Aims

The aim of this study is to assess the knowledge, attitudes and practices of family doctors, paediatricians and obstetricians and gynaecologists with regards to the HPV vaccines available as well as any barriers or facilitators which influence their recommending use of these vaccines.
3.2.2 Objectives

In order to address the described aim the following objectives were developed:

1. To measure and assess the following variables in a population consisting of family doctors, paediatricians and obstetricians and gynaecologists:
   - Level of knowledge, attitudes and practices with regards to the HPV vaccines and their practice and perceived influence on recommendation of said vaccines
   - Identify barriers to their recommending the HPV vaccine
   - Identify facilitators to their recommending the HPV vaccine

2. To identify any significant differences in recommendation practices between male and female medical practitioners.

3. To identify any significant differences in recommendation practices to female and male patients.

4. To identify any significant differences in recommendation practices in different settings i.e. private GP practice, Health Centre GP clinic, Hospital and specialty clinic

5. To identify sources from where the said medical practitioners are obtaining information about the HPV vaccines and whether they feel the need for more information/education sessions to address any queries they may have and how this can be transmitted to them.
6. To analyse the results and compare them with those of other international studies to determine whether there are any differences or similarities. This will provide a basis to understand where any issues may arise and may help to develop a plan to address these issues where necessary.

7. To develop a set of recommendations to enhance HPV vaccine recommendation practices by medical practitioners.

### 3.3 Missed clinical opportunities

The title of the study refers to missed clinical opportunities, in this case missed vaccination opportunities with regards to the HPV vaccines. Missed vaccination opportunities occur when patients who are eligible for a vaccine are seen for care, yet remain unvaccinated. These occurrences have been proven to result in lower vaccination rates among both adults and children alike (Wong et al., 2013).

### 3.4 Research design

The research consisted of mixed methodology containing a combination of quantitative and qualitative techniques, methods which were both found in the literature to be used in order to gather more information about the recommendation practices of physicians with regards to the HPV vaccines.
3.4.1 The quantitative methodology

The quantitative aspect consisted of a cross-sectional survey which studied the knowledge, attitudes and practices of physicians. Once this information was gathered recommendations were made in order to enhance recommendation for vaccine uptake.

3.4.1.1 The study population

The participants in the study consisted of all family doctors, paediatricians and obstetricians and gynaecologists who were registered on the respective specialist register of the Medical Council of Malta (Medical Council, 2014) and practicing in the said specialities in the Maltese Islands at the time the study was carried out.

There was a total of 481 doctors listed in the three specialities (378 in Family Medicine, 50 in Obstetrics & Gynaecology and 53 in Paediatrics). Seventeen of these doctors were excluded from the study as they were listed as residing overseas, while 50 were uncontactable as their postal address was not available on the specialist or general medical register. Therefore the final number of questionnaires posted was 414. Two of these were returned as the address provided was incorrect.

A missing data analysis was carried out using Chi-squared tests wherein the distribution of age, gender and specialty in the final respondent population was
compared to that of the original sample. No significant differences were found and thus the final respondent population was assumed to be representative of the original sample of doctors.

3.4.1.2 The questionnaire

The tool used was a self-administered postal questionnaire which was derived from two questionnaires which were used in similar studies overseas (U.S and Canada) (Vadaparampil et al., 2011, Duval et al., 2007). These questionnaires were found after a thorough literature search was carried out and they were both found to be designed in a way which suited the aim of this study. They had both been utilised to carry out national surveys about the knowledge, attitudes and practices of medical practitioners in the United States of America and Canada and were developed using models which propose that "... patient, physician, and practice level factors impact a physician's decision to provide a preventive service (e.g. HPV vaccination)" (Vadaparampil et al., 2011). They were considered to be very comprehensive in the quantity and quality of information gathered from them. Both had been validated when the original study was carried out and written permission was obtained from the developers of these questionnaires so that they could be used in this research project (Appendix A).

The final questionnaire (Appendix B) contained 39 questions. The questions were derived from the two questionnaires referred to previously; they were left unaltered and retained in the same sequence as in the original questionnaires.
Questions which were omitted from the two original questionnaires were related to information about patient ethnicity and insurance status, which were considered to be irrelevant for the study in question.

It required approximately 15 minutes to complete. Face validation was carried out by a local expert to detect any possible issues but none were identified. The internal consistency reliability of the questions was determined by means of Cronbach's alpha coefficient in the pilot study as explained further below. There was no need for the questionnaire to be translated into Maltese as it was directed towards healthcare professionals. It contained items which assessed the demographic and practice characteristics of participants as well as their knowledge on HPV, what they perceived to be barriers in relation to HPV vaccination, and their practices and recommendation with regards to both the bivalent and the quadrivalent HPV vaccines.

The specialist register includes all doctors who are eligible to register without identifying who is retired or who is no longer practicing the said specialty. Since the participants were required to be currently practicing medicine in the three said specialties in the Maltese Islands, an option was included at the beginning of the questionnaire which asked responders to tick a box if they were retired or no longer practicing. They were still however asked to return the empty questionnaire so that they would not be included with the non-responders.
Knowledge on HPV was assessed using the same system as that of the study from where the questionnaire was sourced (Vadaparampil et al., 2011). 10 items were designed to determine participants' knowledge regarding HPV infection and vaccination. Options to reply included “true,” “false,” or “don't know.” The correct responses were added up to create a "total knowledge score" with a range between 0-10. This was then dichotomized into “high knowledge” (8-10 correct responses) and “low knowledge” (0-7 correct responses), based on a median split (Vadaparampil et al., 2011).

Similarly, the perceived barriers to HPV vaccination were measured using 14 items which looked at issues about vaccine safety and efficacy, discussing sexuality, riskier sexual behaviors in vaccinated adolescents, cost and ascertaining completion of the 3-dose series. Response options were on a 5-point Likert scale (1=strongly disagree to 5=strongly agree). For this question the items were added and averaged to create a mean barrier score. The results for the sample were divided into thirds so that participants were grouped according to whether they reported low, medium, and high barriers (Vadaparampil et al., 2011).

Participants were also asked to identify strategies they used to ascertain completion of the 3-dose series. These included providing the patient with a paper-based reminder, using reminder letters or telephone calls, flagging patient charts, scheduling patients for the next dose during their current office visit and using a computerized immunization database or registry amongst others. Participants could select all the options that applied and the responses were classified into 3
groups: no strategies, 1 strategy, or 2 or more strategies (Vadaparampil et al., 2011).

Together with the questionnaire participants were sent a covering letter (Appendix C) explaining all the details about the study together with contact details of the researcher and her supervisor, as all participants have a right for informed consent. The covering letter also assured the participants of their anonymity and confidentiality and specified that their participation was voluntary. As an incentive to participate all participants were invited to participate in a lottery. The lottery ticket was sent together with the questionnaire although, in order to maintain anonymity, two stamped, self-addressed envelopes were included so that the questionnaire and ticket could be returned separately.

Since the act of completing and returning the questionnaire implies consent to participate respondents were not required to sign a consent form. Prior to commencing the study a written proposal together with the questionnaire to be used were submitted for approval by the University Research Ethics Committee and permission to proceed with the study was granted (Appendix D).

3.4.1.3 The pilot study

The pilot study was carried out between November and December 2014. The population consisted of all the trainees in the three said specialties. They were given a two week period during which to reply to the questionnaire. No
suggestions for corrections were received and so the questionnaire did not require any adaptations. Cronbach's alpha coefficient was used to determine the internal consistency reliability of the questions (Table 3.1).

Table 3.1: Internal consistency reliability for question according to questionnaire from which they were derived

<table>
<thead>
<tr>
<th>Study and questionnaire from which questions were derived</th>
<th>Cronbach's alpha coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Missed Clinical Opportunities: Provider Recommendations for 11-12 Year Old Girls is Limited.&quot; (Vadaparampil et al., 2011)</td>
<td>0.86</td>
</tr>
<tr>
<td>&quot;Vaccination against human papillomavirus: A baseline survey of Canadian clinicians' knowledge, attitudes and beliefs.&quot; (Duval et al., 2007)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

In order to replicate the same level of contact between the researcher and participants during the pilot study as there would be during the actual study, the participants involved were provided with the questionnaire and covering letter by the secretaries of their respective departments. A box was left in the secretary's office in order to replicate the postal method of returning the questionnaire and these were collected once the test period had elapsed. This was done in order not to influence the response rate of the participants of the pilot study through having direct contact with the researcher which might make them feel more obliged to participate.
There were 32 trainees in the specialties of family medicine, obstetrics and gynaecology and paediatrics who were contactable and training in Malta at the time of the study and who were thus involved in the pilot study. Fifteen were trainees in Family Medicine, 7 were trainees in Paediatrics and 10 were trainees in Obstetrics and Gynaecology. Of these a total of 14 trainees returned the completed questionnaire; 7 from Family Medicine (47%), 4 from Paediatrics (57%) and 3 from Obstetrics and Gynaecology (30%), giving an overall response rate of 44%. During the pilot study no reminders were sent to the participants and there were no incentives included either.

3.4.1.4 Data Collection

The mailing addresses of the doctors practicing in the specialities of family medicine, obstetrics and gynaecology and paediatrics in Malta were obtained from the respective specialist registers. These are publicly available on the website of the Medical Council of Malta (Medical Council, 2014).

A package consisting of the covering letter, the questionnaire, the lottery ticket and two stamped, self-addressed envelopes were posted to all eligible participants. Participants were asked to return their completed questionnaires within a two week period from the date of receipt of the package.

The week after the deadline for returning the questionnaire a second reminder package was posted to the same participants. This reminder package
contained a reminder letter replacing the covering letter (Appendix E), as well as the questionnaire, lottery ticket and two stamped, self-addressed envelopes, as were sent in the first package.

Two electronic reminders were sent to doctors on the 21st March 2015 and 4th April 2015 by the editor of The Synapse website. The Synapse is a website with medical professionals as members and to whom it disseminates information and mail shots as requested, among other things. The reminder included a link to the covering letter as well as a link to the questionnaire itself ("The Synapse," 2015a, "The Synapse," 2015b).

3.4.1.5 Data Analysis

The quantitative data that was collected was coded and transferred to the statistical package, Statistical Package for the Social Science (SPSS) version 20. This statistical package was used to carry out the required statistical tests as well as to generate any tables and figures. The tests carried out included measurement of frequencies, cross-tabulations and Pearson Chi-square tests, which were used in order to evaluate the significance of any observed differences between categorical data sets.

In this project the variables studied included levels of knowledge, attitudes and practices with regards to the HPV vaccines and barriers and facilitators to recommending the HPV vaccine and their relationship to the gender and age of the
recommending physician, the gender and age of the patient, the physicians' specialty and the practice settings (private GP practice, Health Centre GP clinic, Hospital and specialty clinic) of the physicians concerned.

The null hypothesis for this study states that there are no significant differences in recommendation practices between physicians regardless of their gender, experience, specialty or practice setting. There is also no significant difference in recommendation practices according to the age and gender of the patient. In this case the null hypothesis would be accepted if the p-value exceeds the 0.05 level of significance, thus indicating that the differences observed resulted due to chance. The alternative hypothesis states that any differences observed in the above-mentioned variables are not attributable to chance and is accepted if the p-value is less than 0.05.

3.4.2 The qualitative methodology

3.4.2.1 The focus groups

The qualitative aspect of the study consisted of three mini focus groups (Krueger, 1994), each one made up of doctors from a particular specialty - family medicine, obstetrics and gynaecology and paediatrics. Each focus group contained 3-4 doctors from the particular specialty and met the researcher on one occasion for a session that lasted approximately 45 minutes.
The focus groups were carried out after the quantitative part of the study had been completed and the results of the data collected had been analysed. The participants in the focus groups were presented with a summary of the quantitative results obtained and these were discussed with the intention of developing recommendations based on the findings. Prior to participating in the focus group the participants were given a brief overview of the project. They were informed that their participation was voluntary, that they could withdraw their participation at any point during the study and that their anonymity and confidentiality were assured. They were also asked to sign a form, prior to commencement of the focus group, giving their consent to participate as well as to the use of the data collected (Appendix F). The discussion was recorded on an electronic device and handwritten notes were taken simultaneously during the session itself.

3.4.2.2 Data Analysis

The form of analysis of the data collected during the focus groups used was thematic analysis. This is the most common form of analysis used in qualitative research. It aims to uncover and understand the big picture by using the data obtained to describe the subject being studied and give it meaning (“Module 9: Introduction to Research”).

Thematic analysis focusses on identifying, analysing and documenting patterns or themes within the data, which then become the areas to be explored further. During thematic analysis a coding process is carried out in six steps:
"familiarisation with data, generating initial codes, searching for themes among codes, reviewing themes, defining and naming themes, and producing the final report" (Braun & Clarke, 2006). This helps to establish certain patterns which have significance and relevance.

3.4.2.3 Conclusion

This chapter has given an overview of the methods used to conduct the research. It also described the study population, the pilot study and the processes used in order to collect and analyse the data.

A wealth of data was collected both by the quantitative and the qualitative methods and the results of the analysis of this data are presented in the coming chapter.
Chapter 4

Results
Chapter 4 - Results

The study was carried out using quantitative methodology in the form of a postal questionnaire (Appendix B) and qualitative methodology in the form of focus groups. The results of the two methods used are described in further detail in their respective sections below.

4.1 Quantitative Results

This section describes the results of the quantitative data which was collected by means of a postal questionnaire.

4.1.1 Response rate

The total number of doctors specialised in Family Medicine, Paediatrics and Obstetrics and Gynaecology and registered on the respective specialist registers at the time that the study was carried out was 481. Of these, 17 doctors had foreign mailing addresses and 50 did not have their addresses publicly available on the register. Thus, 414 questionnaires were posted in February 2015. Of these, 2 questionnaires were returned as the mailing address was incorrect leaving a final number of 412 doctors who were contactable by mail and which thus made up the final target population. In total 210 questionnaires were returned by the end of April 2015, after a postal reminder and two electronic reminders had been sent.
This gives an overall response rate of 50.9%. However, of these, 34 responders were excluded as they were either retired or not practicing the relevant specialty, and 1 responder was excluded as the questionnaire was returned empty with a note stating that he/she disagreed with the HPV vaccine and therefore did not want to participate in the study. In the end the corrected response rate was 46.7%.

4.1.2 Representativeness

A missing data analysis was carried out using Chi-squared tests wherein the distribution of age, gender and specialty in the final respondent population was compared to that of the original sample and no significant differences were found. Thus the final respondent population was assumed to be representative of the original sample of doctors.

4.1.3 Participant Characteristics

The age of the respondents ranged from 29 years to 79 years with a median age of 52 years (Table 4.1). Of the 175 eligible responders 120 were male (68.6%), 54 were female (30.8%) and the gender of one participant was not listed (Fig. 4.1).
Table 4.1: Participant characteristics (N=175<sup>3</sup>)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>50.3 years</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>52 years</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>120</td>
<td>68.6</td>
</tr>
<tr>
<td>Female</td>
<td>54</td>
<td>30.4</td>
</tr>
<tr>
<td><strong>Specialty</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Medicine</td>
<td>131</td>
<td>% of total (n=175) - 74.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specialty specific - 40.9</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>20</td>
<td>% of total (n=175) - 11.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specialty specific - 39.2</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynaecology</td>
<td>23</td>
<td>% of total (n=175) - 13.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Specialty specific - 51.1</td>
</tr>
<tr>
<td><strong>Type of practice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>122</td>
<td>69.7</td>
</tr>
<tr>
<td>Health Centre</td>
<td>31</td>
<td>17.7</td>
</tr>
<tr>
<td>Hospital department</td>
<td>22</td>
<td>12.6</td>
</tr>
<tr>
<td><strong>No. of years of clinical experience</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>25.6</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>&lt;10 years</td>
<td>6</td>
<td>3.4</td>
</tr>
<tr>
<td>10-24 years</td>
<td>66</td>
<td>37.7</td>
</tr>
<tr>
<td>25-49 years</td>
<td>99</td>
<td>56.6</td>
</tr>
<tr>
<td>50+ years</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td><strong>Hours spent in direct outpatient care per week</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>5</td>
<td>2.9</td>
</tr>
<tr>
<td>7-21</td>
<td>44</td>
<td>25.1</td>
</tr>
<tr>
<td>&gt;21</td>
<td>126</td>
<td>72</td>
</tr>
<tr>
<td><strong>No. of patients seen in a typical day</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15</td>
<td>37</td>
<td>21.1</td>
</tr>
<tr>
<td>15-19</td>
<td>47</td>
<td>26.9</td>
</tr>
<tr>
<td>20-29</td>
<td>43</td>
<td>24.6</td>
</tr>
<tr>
<td>30 or more</td>
<td>48</td>
<td>27.4</td>
</tr>
</tbody>
</table>

<sup>3</sup> For some variables N=174 as one participant did not provide demographic details
The majority of participants (18.3%) had their main practice in localities around the Northern Harbour area, including Sliema, St. Julian's and Gzira, as described in the HCCA location map codes. These were closely followed (17.7%) by physicians with their main practice in the Southern localities including Birzebbugia, Marsascala and Marsaxlokk.

4.1.4 Characteristics of the study population

The study population consisted of specialists in Family Medicine, Paediatrics and Obstetrics and Gynaecology. The proportion of participants from these fields consisted of 74.9% in Family Medicine, 11.4% in Paediatrics and 13.1% in Obstetrics and Gynaecology (Table 4.1).
The majority of specialists had their main outpatients clinics located in private practice (69.7%). Of these, the majority of specialists in Family Medicine and Obstetrics and Gynaecology had their main outpatients clinics located in private practice (Family Medicine 77.1%, O&G 56.5%) whilst 60% of the paediatricians that replied were mainly based at the hospital outpatients department (Table 4.2).

Table 4.2: Type of practice by physicians' specialty

<table>
<thead>
<tr>
<th>Type of practice</th>
<th>Total (N=175) n(%)</th>
<th>Family Medicine (N=131) n(%)</th>
<th>Paediatricis (N=20) n(%)</th>
<th>Obstetrics &amp; Gynaecology (N=23) n(%)</th>
<th>Other (N=1) n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private</td>
<td>122 (69.7)</td>
<td>101 (77.1)</td>
<td>8 (40)</td>
<td>13 (56.5)</td>
<td>0</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Health Centre</td>
<td>31 (17.7)</td>
<td>30 (22.9)</td>
<td>0</td>
<td>0</td>
<td>1 (100)</td>
<td></td>
</tr>
<tr>
<td>Hospital department</td>
<td>22 (12.6)</td>
<td>0 (60)</td>
<td>12 (60)</td>
<td>10 (43.4)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

The number of years during which the doctors had been providing clinical care ranged from 5 till 50 years with a median number of years practicing of 27 years (Table 4.1). The majority of specialists (72%) stated that they spent more than 21 hours per week in direct outpatient care with the majority of specialists in the fields of Family Medicine and Obstetrics and Gynaecology spending more than 21 hours per week in outpatients clinics (80.2% and 60.9% respectively) (Table 4.3).
Table 4.3: No. of hours spent in direct outpatient care per week by physicians' specialty

<table>
<thead>
<tr>
<th>No. of hours</th>
<th>Total (N=175) n(%)</th>
<th>Family Medicine (N=131) n(%)</th>
<th>Paediatricis (N=20) n(%)</th>
<th>Obstetrics &amp; Gynaecology (N=23) n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7</td>
<td>5 (2.9)</td>
<td>3 (2.3)</td>
<td>1 (5)</td>
<td>1 (4.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>7-21</td>
<td>44 (25.1)</td>
<td>23 (17.6)</td>
<td>12 (60)</td>
<td>8 (34.8)</td>
<td></td>
</tr>
<tr>
<td>&gt;21</td>
<td>126 (72)</td>
<td>105 (80.2)</td>
<td>7 (35)</td>
<td>14 (60.9)</td>
<td></td>
</tr>
</tbody>
</table>

When it came to the number of patients seen on a typical day overall the majority of paediatricians (60%) claimed to see less than 15 patients per day whilst most Obstetricians and Gynaecologists (52.2%) saw 15-19 patients per day. With regards to Family Medicine 35.1% of participants stated that they saw more than 30 patients per day (Table 4.4).

Table 4.4: No. of patients seen in a typical day by physicians' specialty

<table>
<thead>
<tr>
<th>No. of pts.</th>
<th>Total (N=175) n(%)</th>
<th>Family Medicine (N=131) n(%)</th>
<th>Paediatricis (N=20) n(%)</th>
<th>Obstetrics &amp; Gynaecology (N=23) n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>37 (21.3)</td>
<td>22 (16.8)</td>
<td>12 (60)</td>
<td>3 (13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>15-19</td>
<td>46 (26.4)</td>
<td>36 (19.8)</td>
<td>8 (40)</td>
<td>12 (52.2)</td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>43 (24.7)</td>
<td>27 (28.2)</td>
<td>0</td>
<td>6 (26.1)</td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>48 (27.6)</td>
<td>46 (35.1)</td>
<td>0</td>
<td>2 (8.7)</td>
<td></td>
</tr>
</tbody>
</table>
4.1.5 Knowledge

Knowledge about the recommendations for HPV vaccination in females as well as knowledge concerning the pathophysiology of HPV infection was quite good, with correct responses on these topics ranging from 72% - 85.7% (Table 4.5). On the other hand, some other knowledge questions had very poor correct responses. The question concerning the reduction of lifetime risk of cervical cancer with a regular Pap test with a frequency of ≤3 years only scored 21.1% of the correct replies and the question concerning the proportion of cervical cancer related to HPV-16 and HPV-18 types only scored 26.9% of the correct responses.

Table 4.5: Percentage of correct replies for all knowledge questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Number of correct answers (N=175)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Most HPV infections resolve without medical intervention&quot;</td>
<td>90</td>
<td>51.4</td>
</tr>
<tr>
<td>&quot;Treatment of cervical dysplasia/cancer permanently eliminates the causative infection&quot;</td>
<td>145</td>
<td>82.8</td>
</tr>
<tr>
<td>&quot;Genital warts are caused by the same HPV types that cause cervical cancer&quot;</td>
<td>117</td>
<td>66.9</td>
</tr>
<tr>
<td>&quot;Almost all cervical cancers are caused by HPV infection&quot;</td>
<td>127</td>
<td>72.6</td>
</tr>
<tr>
<td>&quot;The FDA approved the quadrivalent HPV vaccine for use in females ages 9-26&quot;</td>
<td>128</td>
<td>73.1</td>
</tr>
<tr>
<td>&quot;The FDA approved the quadrivalent HPV vaccine for use in males ages 9-26&quot;</td>
<td>90</td>
<td>51.4</td>
</tr>
</tbody>
</table>
One of the knowledge question contained 14 responses. As was done in the original study the correct responses for this question were added to create a total knowledge score and then dichotomised into high knowledge and low knowledge, based on a median split. There was no significant difference observed in the level of knowledge (high vs low) of physicians according to their gender. Significant differences were observed in the level of knowledge, however, between physicians according to their age and specialty (Table 4.6 and Table 4.7).

Table 4.5: Percentage of correct replies for all knowledge questions cont...

<table>
<thead>
<tr>
<th>Question</th>
<th>Correct Responses</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Females who have been diagnosed with HPV infection should not be given the HPV vaccine&quot;</td>
<td>150</td>
<td>85.7</td>
</tr>
<tr>
<td>&quot;HPV causes vulvar, vaginal and anal cancers in women&quot;</td>
<td>126</td>
<td>72</td>
</tr>
<tr>
<td>&quot;HPV causes anal cancers in men&quot;</td>
<td>115</td>
<td>65.7</td>
</tr>
<tr>
<td>&quot;HPV causes some head and neck cancers&quot;</td>
<td>79</td>
<td>45.1</td>
</tr>
<tr>
<td>&quot;Proportion of girls in Malta that become sexually active by the age of 14&quot;</td>
<td>88</td>
<td>50.3</td>
</tr>
<tr>
<td>&quot;Reduction of lifetime risk of cervical cancer with a regular Pap test with a frequency of ≤3 years&quot;</td>
<td>37</td>
<td>21.1</td>
</tr>
<tr>
<td>&quot;Proportion of cervical cancer related to HPV-16 and HPV-18 types&quot;</td>
<td>47</td>
<td>26.9</td>
</tr>
</tbody>
</table>
67.7% of younger doctors (<40 years of age) and 55% of doctors aged 50-59 years had a high knowledge score. On the other hand only 30.1% of doctors aged more than 50 years achieved a high level of knowledge score (Table 4.6).

Table 4.6: Level of knowledge score (high vs low) by age of physician

<table>
<thead>
<tr>
<th>Level of knowledge score</th>
<th>Age group (years)</th>
<th>p-value = &lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0-7 correct responses) (%)</td>
<td>&lt;40</td>
<td>10 (32.3)</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>18 (45)</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>72 (69.9)</td>
</tr>
<tr>
<td>High (8-10 correct responses) (%)</td>
<td>&lt;40</td>
<td>21 (67.7)</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>22 (55)</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>31 (30.1)</td>
</tr>
</tbody>
</table>

With regards to physician specialty, specialists in the field of Obstetrics and Gynaecology showed a significantly higher level of knowledge than the other specialties. 91.3% of Obstetricians and Gynaecologists achieved a high knowledge score when compared to 40% of Paediatricians and 34.4% of Family Doctors (Table 4.7).

Table 4.7: Level of knowledge score (high vs low) by physicians' specialty

<table>
<thead>
<tr>
<th>Level of knowledge score</th>
<th>Specialty</th>
<th>p-value = &lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0-7 correct responses) (%)</td>
<td>Family Medicine (N=131) n(%)</td>
<td>Paediatrics (N=20) n(%)</td>
</tr>
<tr>
<td></td>
<td>86 (65.6)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>High (8-10 correct responses) (%)</td>
<td>45 (34.4)</td>
<td>8 (40)</td>
</tr>
</tbody>
</table>
4.1.6 Attitudes

The attitudes of the participants towards HPV vaccination and vaccine recommendation are elaborated further in Table 4.8. The results tabulated indicate the percentage of participants, as part of the total and by specialty, who somewhat agreed or strongly agreed with a particular statement. Almost all respondents (97.7%) agreed that girls should be vaccinated prior to becoming sexually active, with 100% of the Obstetricians and Gynaecologists agreeing strongly with this. On the other hand, less physicians agreed with the need for vaccinating boys before onset of sexual activity (90.2%).

The best age for a universal vaccination program was considered to be less than 14 years by 83.4% of respondents and the age of 14–17 years by 16% of respondents.

A large majority of the responders (94.2%) stated that they would recommend the HPV vaccine to their patients even if the patients had to pay for the vaccine themselves.

No significant difference was observed between the specialties for any of the items concerning attitude which were analysed (Table 4.8).
Table 4.8: Physicians' attitudes concerning HPV immunisation and vaccine recommendation by specialty

<table>
<thead>
<tr>
<th>Item</th>
<th>% of somewhat or strongly agree</th>
<th>(%) of strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&quot;HPV vaccination should be given&quot;:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;To girls before the beginning of sexually active life&quot;</td>
<td>97.7 (87.9)</td>
<td>96.9 (87)</td>
</tr>
<tr>
<td>&quot;To boys before the beginning of sexually active life&quot;</td>
<td>90.2 (53.4)</td>
<td>89.3 (51.1)</td>
</tr>
<tr>
<td>&quot;To all sexually active females&quot;</td>
<td>90.8 (65.5)</td>
<td>88.5 (65.6)</td>
</tr>
<tr>
<td>&quot;To all sexually active males&quot;</td>
<td>85.1 (46.6)</td>
<td>82.5 (46.6)</td>
</tr>
<tr>
<td>&quot;The best age for a universal vaccination programme would be: &lt;14 years&quot;</td>
<td>83.4</td>
<td>80.9</td>
</tr>
<tr>
<td><strong>&quot;I will recommend the HPV vaccine to my patients&quot;:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;If it is publicly funded&quot;</td>
<td>70.1 (48.3)</td>
<td>71 (48.1)</td>
</tr>
<tr>
<td>&quot;Even if my patients have to pay for the vaccine&quot;</td>
<td>94.2 (56.3)</td>
<td>93.9 (55)</td>
</tr>
<tr>
<td>&quot;If they have to receive 2 doses of the vaccine&quot;</td>
<td>71.8 (37.9)</td>
<td>74.1 (39.7)</td>
</tr>
<tr>
<td>&quot;If they have to receive 3 doses of the vaccine&quot;</td>
<td>83.9 (49.4)</td>
<td>87 (51.1)</td>
</tr>
<tr>
<td>&quot;If it protects against both cervical cancer and anogenital warts&quot;</td>
<td>82.8 (54.6)</td>
<td>84.8 (57.3)</td>
</tr>
<tr>
<td>&quot;If it protects against cervical cancer&quot;</td>
<td>92 (71.3)</td>
<td>91.6 (71.8)</td>
</tr>
</tbody>
</table>
Overall 82.8% of physicians indicated an intention to prescribe the HPV vaccine to their patients. In fact 75% of Paediatricians, 91.3% of Obstetricians & Gynaecologists and 82.5% of Family Doctors indicated that they were likely or very likely to prescribe the HPV vaccines to their patients. There was no significant difference observed between the different specialties for intention to prescribe the vaccines.

With regards to attitudes according to practice location, 87.4% of physicians whose main outpatient clinic is located in private practice and 86.4% of those whose main clinic is located in a hospital department stated that they were likely or very likely to prescribe the HPV vaccines to their patients. On the other hand only 64.5% of physicians whose main clinic is located in a Health Centre stated that they were likely or very likely to recommend the vaccine. There was a significant difference observed for this variable with a p value of 0.003.

No significant difference was observed in the intention of the physicians to prescribe the HPV vaccines to patients when compared by age and gender of the physicians.

4.1.7 Opinion

Some questions looked at the opinions of respondents with regards to their colleagues' support of HPV vaccinations as well as their opinion on parents' and patients' acceptance of the vaccines. Overall, 84.5% of physicians think that most
physicians will recommend the vaccine to their patients (Table 4.9) and the majority (91.4%) believe that parents prefer the HPV vaccine to be given at school. While only 69% of respondents felt that parents will accept the HPV vaccination for their children who are aged less than 14 years, 91.9% felt that adolescents and young adults would accept the HPV vaccination (Table 4.9). Most respondents (86.2%) believed that their patients would comply with counsel provided regarding HPV vaccination, as opposed to only 58% who believed that patients would comply with advice given about safe sexual behaviour (Table 4.9).

Table 4.9: Physicians' opinions about colleagues', patients' and parents' attitudes towards HPV immunisation by specialty

<table>
<thead>
<tr>
<th>Item</th>
<th>% of somewhat or strongly agree</th>
<th>Family Medicine (N=131)</th>
<th>Paediatrics (N=20)</th>
<th>Obstetrics &amp; Gynaecology (N=23)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;In your opinion most&quot;:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Physicians will recommend HPV vaccination to their patients&quot;</td>
<td>84.5 (42)</td>
<td>80.9 (39.7)</td>
<td>90 (30)</td>
<td>100 (65.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>&quot;Parents will accept HPV vaccination for their children less than 14 years of age&quot;</td>
<td>69 (23.6)</td>
<td>66.4 (21.4)</td>
<td>70 (25)</td>
<td>82.6 (34.8)</td>
<td>0.72</td>
</tr>
<tr>
<td>&quot;Parents will prefer HPV vaccination to be given at school&quot;</td>
<td>91.4 (38.5)</td>
<td>89.3 (42)</td>
<td>95 (30)</td>
<td>100 (26.1)</td>
<td>0.23</td>
</tr>
<tr>
<td>&quot;Adolescents and young adults will accept HPV vaccination&quot;</td>
<td>91.9 (31)</td>
<td>90.1 (32.8)</td>
<td>95 (25)</td>
<td>100 (26.1)</td>
<td>0.35</td>
</tr>
<tr>
<td>&quot;Adolescents and young adults will seek HPV vaccination&quot;</td>
<td>61.7 (11.4)</td>
<td>58.8 (13)</td>
<td>65 (0)</td>
<td>78.2 (13)</td>
<td>0.39</td>
</tr>
</tbody>
</table>
Table 4.9: Physicians' opinions about colleagues', patients' and parents' attitudes towards HPV immunisation by specialty cont...

<table>
<thead>
<tr>
<th>&quot;Your patients will comply with counsel about&quot;:</th>
<th>Specialty 1</th>
<th>Specialty 2</th>
<th>Specialty 3</th>
<th>Specialty 4</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Safe sexual behaviour&quot;</td>
<td>58 (14.9)</td>
<td>60.3 (15.3)</td>
<td>55 (15)</td>
<td>47.8 (13)</td>
<td>0.57</td>
</tr>
<tr>
<td>&quot;Regular screening&quot;</td>
<td>83.3 (20.1)</td>
<td>85.5 (20.6)</td>
<td>65 (5)</td>
<td>86.9 (30.4)</td>
<td>0.13</td>
</tr>
<tr>
<td>&quot;HPV vaccination&quot;</td>
<td>86.2 (20.1)</td>
<td>85.5 (20.6)</td>
<td>90 (25)</td>
<td>86.9 (13)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

None of the items assessed showed any significant difference when results were compared between specialty (Table 4.9).

4.1.8 Practices

The majority of respondents (57.1%) mostly recommended the bivalent HPV vaccine to patients. Sixty-five respondents (37.1%) stated that they recommend the quadrivalent vaccine the most whilst 3 respondents claimed that they recommend both vaccines in equal amounts (Figure 4.2).
There was no significant difference observed in the choice of vaccine recommended and the gender, the age, the number of years of clinical practice of the physician recommending the vaccine, the main location of the outpatients clinic nor with the specialty of the physician.

4.1.8.1 Recommendation practices according to patients' age and gender

Recommendation practices of physicians for early adolescent females (aged 11-12 years) showed that only 11.5% of all respondents reported "always" recommending the HPV vaccine to female patients within that age group. These 11.5% were composed of 3.5% Paediatricians, 4% Obstetricians and Gynaecologists and 4% Family Doctors. Within each specialty the percentage of physicians
"always" recommending the vaccine in this age group was 30% for Paediatricians, 30.4% for Obstetricians and Gynaecologists and 5.3% for Family Doctors. A significant difference was observed according to physician specialty (p=<0.001) (Table 4.10).

When it came to recommendation of the vaccines to early adolescent females according to the gender of the recommending physician only 9.2% of male physicians claimed to "always" recommend it while 18.5% of female physicians claimed to "always" recommend the vaccine to females in this age group. A significant difference was observed for prescribing and physician gender with a p value of 0.046 (Table 4.11).

For middle adolescents (13-17 years) 20.1% of all respondents claimed to "always" recommend the HPV vaccines. Of these 20.1%, 3.5% were Paediatricians, 6.9% were Obstetricians and Gynaecologists and 9.7% were Family Doctors. As percentages of each specialty, 30% of Paediatricians, 52.2% of Obstetricians and Gynaecologists and 13% of Family Doctors "always" recommended the HPV vaccines to patients aged 13-17 years. Even here a significant difference was observed between the different specialties (p=<0.001) (Table 4.10).

The final patient age group was 18-26 year olds. For this age group the Paediatricians were excluded as they do not see patients of this age. Thus the total percentage from Obstetricians and Gynaecologists and Family Doctors who always recommend the vaccine was 21.8% with 7.5% being Obstetricians and
Gynaecologists and 14.3% being Family Doctors. As a percentage for each specialty this consisted of 56.5% of Obstetricians and Gynaecologists and 19.1% of Family Doctors. A significant difference of $p=0.001$ was observed in this scenario too (Table 4.10).

Table 4.10: Percentage of physicians who claim to "always" recommend the HPV vaccine to female patients according to patient age group and physician specialty

<table>
<thead>
<tr>
<th>Physician Specialty</th>
<th>11-12 years</th>
<th>13-17 years</th>
<th>18-26 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Medicine</td>
<td>4</td>
<td>9.7</td>
<td>7.5</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>3.5</td>
<td>3.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynaecology</td>
<td>4</td>
<td>6.9</td>
<td>14.3</td>
</tr>
<tr>
<td>Total</td>
<td>11.5</td>
<td>20.1</td>
<td>21.8</td>
</tr>
</tbody>
</table>

| p value              | <0.001      | <0.001      | <0.001      |

No significant difference was observed in the recommendation practices for the vaccines of physicians according to their gender for female patients aged 13-17 years and 18-26 years. It was noted that the physicians "always" recommended the vaccines most for female patients in the oldest age group (Table 4.11).
Table 4.11: Percentage of physicians who claim to "always" recommend the HPV vaccine to female patients according to patient age group and physician gender

<table>
<thead>
<tr>
<th>Physician gender</th>
<th>11-12 years</th>
<th>13-17 years</th>
<th>18-26 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9.2</td>
<td>19.2</td>
<td>20</td>
</tr>
<tr>
<td>Female</td>
<td>18.5</td>
<td>22.2</td>
<td>25.9</td>
</tr>
<tr>
<td>p value</td>
<td>0.046</td>
<td>0.46</td>
<td>0.8</td>
</tr>
</tbody>
</table>

No significant difference was observed when comparing the recommendation practices for female patients of all age groups with the age of the physicians or the number of years of clinical practice they had.

Family Doctors were the least likely to recommend the HPV vaccinations for the two younger age groups of female patients. In contrast the Obstetricians and Gynaecologists were most likely to recommend the vaccines to the two younger female age groups. When compared to Family Doctors there was a 7.4- (95% CI, 2.2-25.1) and 3.6- (95% CI, 1.2-10.9) fold greater odds of Paediatricians "always" recommending HPV vaccination for early and middle female adolescents (Table 4.12). Obstetricians and Gynaecologists had 9.3- (95% CI, 2.8-30.7), 7.2- (95% CI, 2.7-18.8) and 5.5- (95% CI, 2.2-14) fold greater odds of "always" recommending the vaccines when compared to Family Doctors.
Table 4.12: Likelihood of "always" recommending HPV vaccination to female patients by provider specialty and patient age group

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Patient Age Group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11-2 years</td>
<td>13-17 years</td>
<td>18-26 years</td>
<td></td>
</tr>
<tr>
<td><strong>Family Medicine</strong></td>
<td>1.0 (Reference)</td>
<td>1.0 (Reference)</td>
<td>1.0 (Reference)</td>
<td></td>
</tr>
<tr>
<td><strong>Paediatrics</strong></td>
<td>7.4 (2.2-25.1)</td>
<td>3.6 (1.2-10.9)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Obstetrics &amp; Gynaecology</strong></td>
<td>9.3 (2.8-30.7)</td>
<td>7.2 (2.7-18.8)</td>
<td>5.5 (2.2-14)</td>
<td></td>
</tr>
</tbody>
</table>

When it came to analysing the recommendation practices for male patients it was noted that only 1 physician "always" recommended the HPV vaccines to male patients aged 13-17 years of age. The majority of physicians were in fact observed to have claimed that they "never" recommend the vaccines to male patients. Indeed, the total percentage of physicians who claimed to "never" recommend the vaccines was 73% for male patients aged 11-12 years, 67.2% for male patients aged 13-17 years and 55.2% for male patients aged 18-26 years.

4.1.9 Strategies

Table 4.13 summarises the practices of physicians by looking at the number of strategies employed in order to get patients into their office to take the first dose of the HPV vaccine, and analyses them according to the speciality. There was no significant difference observed with a p value = 0.2.
Table 4.13: No. of strategies employed to initiate HPV vaccination

<table>
<thead>
<tr>
<th>Strategies to initiate HPV vaccination</th>
<th>Total (N=174) n(%)</th>
<th>Family Medicine (N=131) n(%)</th>
<th>Paediatrics (N=20) n(%)</th>
<th>Obstetrics &amp; Gynaecology (N=23) n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>65 (37.4)</td>
<td>48 (36.6)</td>
<td>6 (30)</td>
<td>12 (52.2)</td>
<td>0.2</td>
</tr>
<tr>
<td>1</td>
<td>83 (47.7)</td>
<td>64 (48.9)</td>
<td>11 (55)</td>
<td>8 (24.8)</td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>26 (14.9)</td>
<td>19 (14.5)</td>
<td>3 (15)</td>
<td>3 (15)</td>
<td></td>
</tr>
</tbody>
</table>

No significant differences were observed between the number of strategies employed in order to get patients into their office to take the first dose of the HPV vaccine and the age and gender of the recommending physician and the location of main outpatient practice.

Similarly, Table 4.14 summarises the practices of physicians by looking at the number of strategies employed in order to ensure that the 3-dose series was completed in patients who had started HPV vaccination and analyses them according to the speciality. There was also no significant difference observed here with a p value = 0.5.
Table 4.14: No. of strategies employed to ensure completion of the 3-dose series

<table>
<thead>
<tr>
<th>Strategies to initiate HPV vaccination</th>
<th>Total (N=174) n(%)</th>
<th>Family Medicine (N=131) n(%)</th>
<th>Paediatricis (N=20) n(%)</th>
<th>Obstetrics &amp; Gynaecology (N=23) n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 (0.6)</td>
<td>1 (0.8)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.5</td>
</tr>
<tr>
<td>1</td>
<td>92 (52.6)</td>
<td>64 (48.9)</td>
<td>14 (70)</td>
<td>14 (60.9)</td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>82 (46.9)</td>
<td>66 (50.4)</td>
<td>6 (30)</td>
<td>9 (39.1)</td>
<td></td>
</tr>
</tbody>
</table>

No significant differences were observed either between the number of strategies employed in order to get patients to complete the 3-dose series of the HPV vaccine and the age and gender of the recommending physician and the location of main outpatient practice.

4.1.10 Barriers

There were two questions which addressed the issue of barriers to vaccination. One question dealt with the physicians’ perceived barriers and the other dealt with parental barriers which physicians encountered during their practice.

For the most part physicians did not perceive the suggested issues as barriers to recommending the HPV vaccines to patients. The issue which most participants felt posed a barrier to immunising patients with the HPV vaccine was
related to the cost of the vaccines where the patient was required to purchase it.

The responses can be viewed in Table 4.15 below.

Table 4.15: Physicians’ responses to which issues were mostly perceived to act as barriers to immunising patients with the HPV vaccines

<table>
<thead>
<tr>
<th>Issues regarded as barriers</th>
<th>Replies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Strongly Disagree</td>
</tr>
<tr>
<td>Vaccine safety</td>
<td>66.3%</td>
</tr>
<tr>
<td>Vaccine efficacy</td>
<td>53.7%</td>
</tr>
<tr>
<td>Discussing sexuality/STIs</td>
<td>52.6%</td>
</tr>
<tr>
<td>Vaccinated teens practicing riskier sexual behaviours</td>
<td>49.1%</td>
</tr>
<tr>
<td>Administering a new vaccine with a limited track record of safety</td>
<td>30.9%</td>
</tr>
<tr>
<td>Adding another vaccine to the schedule</td>
<td>48%</td>
</tr>
<tr>
<td>Lack of information about vaccine</td>
<td>46.9%</td>
</tr>
<tr>
<td>Cost of purchasing the HPV vaccine</td>
<td>10.3%</td>
</tr>
<tr>
<td>Time to discuss HPV vaccination with patients/parents</td>
<td>33.7%</td>
</tr>
<tr>
<td>Difficulty ensuring that patients will complete the 3-dose vaccination series</td>
<td>28%</td>
</tr>
<tr>
<td>HPV vaccination not required for school attendance</td>
<td>50.3%</td>
</tr>
</tbody>
</table>
Similarly, when it came to parental barriers encountered, the barrier encountered most often was the cost of purchasing the vaccine, with 47.4% of physicians stating they encountered this parental barrier, closely followed by lack of parent education and understanding about HPV infection with 46.9% of physicians saying they encountered this parental barrier.

When results were analysed by looking at the sum of the scores resulting in low, medium and high barriers and comparing them by specialty no significant difference was found (Table 4.16), neither was any significant difference found according to the physicians' age and gender.

A significant difference was however observed when analysing the sum of the scores and comparing them with the location of the main outpatient practice (p=0.039). In fact while only 28.7% of physicians whose main outpatient practice is located in a private clinic and 27.3% of physicians whose main outpatient practice is located in a hospital department claimed to face high barriers almost double the amount of physicians whose main outpatient practice is located in a health centre (54.8%) claimed to face high barriers to immunising patients with the HPV vaccine.
Table 4.16: Perceived barriers related to HPV vaccinations by physicians' specialty

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Family Medicine (N=131) n(%)</th>
<th>Paediatrics (N=20) n(%)</th>
<th>Obstetrics &amp; Gynaecology (N=23) n(%)</th>
<th>p-value = 0.763</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>40 (30.5)</td>
<td>8 (40)</td>
<td>9 (39.1)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>44 (33.6)</td>
<td>7 (35)</td>
<td>8 (34.8)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>47 (35.9)</td>
<td>5 (25)</td>
<td>6 (26.1)</td>
<td></td>
</tr>
</tbody>
</table>

No significant difference was observed between the level of perceived barriers and "always" recommending the vaccines for young, female adolescents (p value = 0.11) although a significant difference was observed for 13-17 year old and 18-26 year old female patients; it was observed that physicians who achieved a high perceived barrier score had a lower rate of "always" recommending the vaccine (13-17 year old patients - p value = 0.03; 18-26 year old patients - p value = 0.004).

4.1.11 Sources of information

One of the questions looked at what sources of information the physicians used to obtain information about the HPV vaccines. Sources of information included professional organisations, the Advisory Committee on Immunisation Practices (ACIP), national immunisation programmes and colleagues. Other sources included pharmaceutical representatives, internet websites and media and conferences as well as grand rounds or lectures. The results are presented in Table 4.17 below although, of note, is the fact that 66.8% of doctors claimed to "often" or
"always" obtain information about the vaccines from the pharmaceutical representatives. A large majority of responders (82.8%) "never" or "rarely" obtain information from the media while 65.1% "sometimes" or "often" use internet websites. Medical conferences are "sometimes" or "often" used as sources of information about the HPV vaccines for 78.3% of physicians.

Table 4.17: Sources used to obtain information about the HPV vaccines (N=175)

<table>
<thead>
<tr>
<th>Source of information</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>Professional organisations</td>
<td>10.9</td>
</tr>
<tr>
<td>Advisory Committee on Immunisation Practices (ACIP)</td>
<td>29.1</td>
</tr>
<tr>
<td>National immunisation programs</td>
<td>14.9</td>
</tr>
<tr>
<td>Colleagues</td>
<td>12.6</td>
</tr>
<tr>
<td>Pharmaceutical representatives</td>
<td>3.4</td>
</tr>
<tr>
<td>Internet websites</td>
<td>9.1</td>
</tr>
<tr>
<td>Media</td>
<td>45.1</td>
</tr>
<tr>
<td>Medical conferences</td>
<td>7.4</td>
</tr>
<tr>
<td>Grand rounds/lectures</td>
<td>19.4</td>
</tr>
</tbody>
</table>
No significant differences were observed when comparing the sources of information referred to and the physicians' age, gender and type of specialty.

The majority of responders (53.1%) felt that the information they have received about the HPV vaccines is "somewhat sufficient" and 29.7% felt that it was "sufficient". There was no significant difference between the level of satisfaction with the information received and the physicians' gender or specialty, but there was a significant difference observed with the level of satisfaction according to physicians' age (p=0.01). Indeed, while 25% of respondents aged 40-49 years and 36.9% of those aged more than 50 years felt that the information received was sufficient, only 9.7% of those aged less than 40 years felt the same way.

Almost all the topics suggested to be included in clinical training materials and clinical decision support tools to guide the prevention of HPV infection for doctors were considered to be "important" or "very important" (Table 4.18). The topic considered least "important" or "very important" was vaccine development (52.6%) whilst vaccine efficacy and effectiveness was felt to be "important" or "very important" by 97.7% of responders.
Table 4.18: Frequency of responders considering certain topics of information to be "important" or "very important" to be included in clinical training materials and clinical decision support tools to guide the prevention of HPV infection (N=175).

<table>
<thead>
<tr>
<th>Topic</th>
<th>Important (%)</th>
<th>Very important (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural history of HPV related disease</td>
<td>51.4</td>
<td>37.7</td>
<td>89.1</td>
</tr>
<tr>
<td>Epidemiology of HPV related infection</td>
<td>45.7</td>
<td>38.9</td>
<td>84.6</td>
</tr>
<tr>
<td>Vaccine development</td>
<td>30.9</td>
<td>21.7</td>
<td>52.6</td>
</tr>
<tr>
<td>Vaccine safety profile</td>
<td>41.7</td>
<td>52.6</td>
<td>94.3</td>
</tr>
<tr>
<td>Vaccine efficacy and effectiveness</td>
<td>31.4</td>
<td>66.3</td>
<td>97.7</td>
</tr>
<tr>
<td>Impact of the vaccine on screening policy and practices</td>
<td>50.3</td>
<td>28.0</td>
<td>78.3</td>
</tr>
<tr>
<td>Cervical cancer screening and management of Pap results</td>
<td>45.1</td>
<td>46.9</td>
<td>92.0</td>
</tr>
<tr>
<td>Genital warts management</td>
<td>49.1</td>
<td>37.7</td>
<td>86.8</td>
</tr>
<tr>
<td>HPV counselling</td>
<td>50.9</td>
<td>40.6</td>
<td>91.5</td>
</tr>
<tr>
<td>Psycho-social issues related to HPV</td>
<td>53.1</td>
<td>30.3</td>
<td>83.4</td>
</tr>
</tbody>
</table>

When analysing the importance of topics of information according to physicians' age, gender and specialty, a significant difference was observed in the importance given to the topic of the management of genital warts for all three variables.

With regards to the management of genital warts, 93.2% of physicians aged more than 50 years felt that this topic was "important" or "very important" when
compared to 80.6% of doctors aged less than 40 years and 75% of those aged 40-49 years (p=0.035).

Similarly a significant difference was observed in the importance given to this topic by gender of the physicians. While 96.3% of female doctors felt this topic was "important" or "very important", only 82.5% of male doctors felt that it merited the same level of importance (p=0.029).

A significant difference was also observed according to the specialty of the physicians and the management of genital warts. The topic was considered to be "important" or "very important" by 95.6% of Obstetricians and Gynaecologists and 90.1% of Family Doctors while only 60% of Paediatricians felt that it deserved this level of importance (p=0.001).

The specialty of the physicians was associated with significant difference for other topics namely cervical cancer screening and management of Pap results (p=0.013) and vaccine efficacy and effectiveness (p=0.002).

4.1.12 Summary of Quantitative Results

Table 4.19 below summarises the main findings resulting from the data collected in the postal questionnaire.
Table 4.19: Summary of main findings about knowledge, attitudes, practices and perceived barriers of family physicians, paediatricians and obstetricians and gynaecologists

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Pt. age group (years)</th>
<th>p-value</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of knowledge score</td>
<td>&lt;40</td>
<td>40-49</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Low (0-7 correct responses) (%)</td>
<td>10 (32.3)</td>
<td>18 (45)</td>
<td>72 (69.9)</td>
</tr>
<tr>
<td>High (8-10 correct responses) (%)</td>
<td>21 (67.7)</td>
<td>22 (55)</td>
<td>31 (30.1)</td>
</tr>
</tbody>
</table>

| Physician specialty                             |                      |         |        |
| Level of knowledge score                        | Family Medicine (N=131) | Paediatrics (N=20) | Obstetrics & Gynaecology (N=23) |
| Low (0-7 correct responses) (%)                 | 86 (65.6)             | 12 (60)  | 2 (8.7) |
| High (8-10 correct responses) (%)               | 45 (34.4)             | 8 (40)   | 21 (91.3) |

<table>
<thead>
<tr>
<th>Attitudes</th>
<th>% of somewhat or strongly agree</th>
<th>(% of strongly agree)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item</td>
<td>Total (N=175)</td>
<td>Family Medicine (N=131)</td>
<td>Paediatrics (N=20)</td>
</tr>
<tr>
<td>&quot;HPV vaccination should be given&quot;:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;To girls before the beginning of sexually active life&quot;</td>
<td>97.7 (87.9)</td>
<td>96.9 (87)</td>
<td>100 (80)</td>
</tr>
<tr>
<td>&quot;To boys before the beginning of sexually active life&quot;</td>
<td>90.2 (53.4)</td>
<td>89.3 (51.1)</td>
<td>90 (40)</td>
</tr>
</tbody>
</table>
Table 4.19: Summary of main findings about knowledge, attitudes, practices and perceived barriers of family physicians, paediatricians and obstetricians and gynaecologists cont...

| "To all sexually active females" | 90.8 (65.5) | 88.5 (65.6) | 100 (70) | 95.7 (60.9) | 0.58 |
| "To all sexually active males" | 85.1 (46.6) | 82.5 (46.6) | 90 (40) | 95.7 (52.2) | 0.62 |
| "The best age for a universal vaccination programme would be: <14 years" | 83.4 | 80.9 | 85 | 95.7 | 0.52 |

"I will recommend the HPV vaccine to my patients":

| "If it is publicly funded" | 70.1 (48.3) | 71 (48.1) | 70 (60) | 65.2 (39.1) | 0.8 |
| "Even if my patients have to pay for the vaccine" | 94.2 (56.3) | 93.9 (55) | 95 (60) | 95.7 (60.9) | 0.9 |

Practices

<table>
<thead>
<tr>
<th>HPV vaccine recommended most</th>
<th>Cervarix</th>
<th>Gardasil</th>
<th>Neither</th>
<th>Both equally</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number (N=175) n(%)</td>
<td>65 (37.1)</td>
<td>100 (57.1)</td>
<td>7 (4)</td>
<td>3 (1.8)</td>
</tr>
</tbody>
</table>

% of "always" recommend HPV vaccines to female patients according to patient age group

<table>
<thead>
<tr>
<th>Patient Age Group</th>
<th>11-12 years</th>
<th>13-17 years</th>
<th>18-26 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Medicine</td>
<td>4</td>
<td>9.7</td>
<td>7.5</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>3.5</td>
<td>3.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynaecology</td>
<td>4</td>
<td>6.9</td>
<td>14.3</td>
</tr>
<tr>
<td>Total</td>
<td>11.5</td>
<td>20.1</td>
<td>21.8</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Physician gender

<table>
<thead>
<tr>
<th>Patient Age Group</th>
<th>11-12 years</th>
<th>13-17 years</th>
<th>18-26 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9.2</td>
<td>19.2</td>
<td>20</td>
</tr>
<tr>
<td>Female</td>
<td>18.5</td>
<td>22.2</td>
<td>25.9</td>
</tr>
<tr>
<td>p value</td>
<td>0.046</td>
<td>0.46</td>
<td>0.8</td>
</tr>
</tbody>
</table>
Table 4.19: Summary of main findings about knowledge, attitudes, practices and perceived barriers of family physicians, paediatricians and obstetricians and gynaecologists cont...

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Likelihood of &quot;always&quot; recommending HPV vaccination to female patients by provider specialty and patient age group</th>
<th>% of &quot;always&quot; recommend HPV vaccines to male patients according to patient age group</th>
<th>% of &quot;never&quot; recommend HPV vaccines to male patients according to patient age group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient Age Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11-2 years</td>
<td>13-17 years</td>
<td>18-26 years</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Family Medicine</td>
<td>1.0 (Reference)</td>
<td>1.0 (Reference)</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>7.4 (2.2-25.1)</td>
<td>3.6 (1.2-10.9)</td>
<td>N/A</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynaecology</td>
<td>9.3 (2.8-30.7)</td>
<td>7.2 (2.7-18.8)</td>
<td>5.5 (2.2-14)</td>
</tr>
<tr>
<td></td>
<td>Total (N=175)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>128 (73)</td>
<td>118 (67.2)</td>
<td>97 (55.2)</td>
</tr>
<tr>
<td>Barriers</td>
<td>Strongly disagree</td>
<td>Somewhat disagree</td>
<td>Somewhat agree</td>
</tr>
<tr>
<td></td>
<td>Strongly agree</td>
<td></td>
<td>Strongly agree</td>
</tr>
<tr>
<td>Cost of purchasing the HPV vaccine</td>
<td>10.3%</td>
<td>13.7%</td>
<td>42.3%</td>
</tr>
<tr>
<td>Perceived barriers related to HPV vaccinations by physicians' specialty</td>
<td>Specialty</td>
<td></td>
<td>p-value = 0.763</td>
</tr>
<tr>
<td>Overall</td>
<td>Family Medicine (N=131)</td>
<td>Paediatrics (N=20)</td>
<td>Obstetrics &amp; Gynaecology (N=23)</td>
</tr>
<tr>
<td></td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
</tr>
<tr>
<td>Low</td>
<td>40 (30.5)</td>
<td>8 (40)</td>
<td>9 (39.1)</td>
</tr>
<tr>
<td>Medium</td>
<td>44 (33.6)</td>
<td>7 (35)</td>
<td>8 (34.8)</td>
</tr>
<tr>
<td>High</td>
<td>47 (35.9)</td>
<td>5 (25)</td>
<td>6 (26.1)</td>
</tr>
</tbody>
</table>
Table 4.19: Summary of main findings about knowledge, attitudes, practices and perceived barriers of family physicians, paediatricians and obstetricians and gynaecologists cont...

<table>
<thead>
<tr>
<th>Main sources of information</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutical representatives</td>
<td>3.4</td>
<td>3.4</td>
<td>26.3</td>
<td>55.4</td>
<td>11.4</td>
</tr>
<tr>
<td>Professional organisations</td>
<td>10.9</td>
<td>13.7</td>
<td>20.6</td>
<td>40</td>
<td>14.9</td>
</tr>
<tr>
<td>Medical conferences</td>
<td>7.4</td>
<td>7.4</td>
<td>35.4</td>
<td>42.9</td>
<td>6.9</td>
</tr>
</tbody>
</table>

4.2 Qualitative Results

The qualitative data was collected through three small focus groups carried out with members of the three specialities involved in the study.

Each focus group consisted of members of one specific specialty and the discussion lasted between 30-45 minutes. The doctors were given a brief summary of the study and its findings and then asked to suggest methods or modes of action which they felt would help them to be able to recommend the HPV vaccines more.

Although there were a few themes which were particular to certain specialties there were particular themes which cropped up in all three focus groups since they were felt to be of importance by all three specialties.
The results are described below according to the themes which evolved during the discussions.

1. Improving health literacy and patient education

The issue of lack of patient knowledge was felt to be a strong one as most of the participating doctors found that it impeded their recommending the vaccine successfully on numerous occasions. This can be achieved through various methods some of which, such as the development of educational brochures and the provision of more information about the vaccines, have been shown to improve vaccine acceptance and uptake significantly (Cassidy et al., 2014, Lee Mortensen et al., 2015).

Suggestions for tackling this issue included:

- Organising workshops/sessions for parents explaining in more detail about HPV and its associated diseases as well as the concept behind giving the vaccine to young adolescents and also to boys. Many doctors claimed to encounter many parents wanting to delay giving their children the vaccine and often felt they had to hold back from insisting on giving it earlier as parents might interpret this as a suggestion by the doctor that their children are promiscuous.

- Educating teachers of Personal and Social Development (PSD) so that they may know the correct information and also how to guide children and
parents should they have any queries. A number of doctors recounted how a number of young people would come to them completely misinformed with what the PSD teachers tell them about HPV and the vaccines.

- Producing clear and easy-to-understand leaflets which doctors may distribute to patients - these could be used to break the ice and introduce the topic to parents where they do not ask about the vaccines themselves.

- More cooperation between the Directorate of Health Promotion and Disease Prevention and the media about the vaccines in order to deliver correct and accurate information. The doctors described how many of their patients come with queries about topics they heard discussed on TV or the radio and felt that the media could be used in a positive manner to introduce the topic to patients and raise awareness about it as well as to address certain myths or misconceptions that are being spread about the HPV vaccines.

- Organising an "STD week" which would focus more on these diseases as a general topic and which might help to make discussing sexually transmitted diseases easier.

- Developing comprehensive sexual education programmes for children and parents so that sexual health is destigmatised and does not remain a taboo issue which people find so difficult to discuss, but can addressed with the same ease as other diseases such as meningitis and measles.

- Organising more campaigns addressing adolescent health and vaccinations, using methods to deliver the messages which are more appealing to a young audience. This would include effective and creative use of social media as well as sessions which are interactive.
• Organising campaigns/adverts specifically referring to boys as the target group. Some doctors felt that their patients might feel that vaccinating boys is not that relevant and that their doctor is only advising them to do so as he receives remuneration from the pharmaceutical companies for selling more of their vaccines. In this way parents would be aware that boys can be vaccinated too and that it is beneficial to them and would not view the doctor's recommendation so suspiciously.

2. Cost of vaccines

The cost of the vaccines was repeatedly mentioned as a major barrier which was stopping certain patients from getting vaccinated against HPV. Suggestions to address this included:

• Subsidising the cost of the vaccine for adolescents between 13-18 years of age who are not entitled to it for free. This way parents might be encouraged to give it to their middle adolescents at a stage in their lives when they are still less likely to have been infected by HPV.

• Encouraging insurance companies to reimburse the cost of a private visit for a vaccination as well as the cost of the vaccine which is not being done currently.

• Introducing tax incentives for parents who vaccinate their children as is done for those sending their children to sports and cultural activities.
3. Lowering the recommended age group for vaccination

Lowering the recommended age group to whom the vaccine is given free on the national health system to 9-10 years of age can help doctors recommend the vaccine more; rather than referring to sexual health it can be "sold" as a cancer-preventing vaccine which is more effective in a younger age group and so should be given without delay. This takes a more directive approach rather than a partnership approach, yet, many doctors felt that by avoiding the sensitive issue that is sexual activity in young adolescents, this system could prove to be more effective in convincing parents to vaccinate their children.

4. Education of the health care providers

The education of patients was not the only educational need identified. Doctors themselves felt that they needed more education and training in order to ensure that they understood all the key issues related to HPV, its diseases and the vaccines. Topics such as the young age of the target group for vaccination, vaccinating older patients, recommendations for male and female patients, risks of vaccination and side effects were all topics they felt merited more attention.

- Education sessions could be part of Continuing Professional Development (CPD) programmes and should be mandatory to ensure that most if not all doctors attended. This would also ensure that all doctors delivered the same
messages and advice reducing the conflicting information patients sometimes receive from different doctors.

- Doctors could also regularly be sent emails and updates with any new developments, changes in the vaccination programme, alerts or new evidence in order to ensure that they keep abreast with the latest information available.

- The family doctors requested workshops teaching them better how to deal with discussing sexually transmitted diseases (STDs), especially to provide some type of counselling or support to patients as they felt they were not well-equipped to deal with such situations. Interestingly the Obstetricians and Gynaecologists felt that discussing STDs was no issue at all for them, whilst the paediatricians rarely needed to have such discussions with parents or patients.

The results obtained through both methodologies give an interesting insight into the knowledge, attitudes and practices of Maltese medical doctors with regards to the HPV vaccines, with a number of findings echoing those observed in international studies, as will be discussed in more detail in the following chapter.
Chapter 5

Discussion
Chapter 5 - Discussion

5.1 Background

The development of vaccines against HPV infection which have been shown not only to be safe (Macartney, et al, 2013) but also immunogenic and highly efficacious (Schiller et al, 2012) is an important milestone in the prevention of a sexually transmitted infection which places a great burden on health globally (Guan et al., 2012, Bruni et al., 2010) both in females (Moscicki et al., 2012) as well as in males (Dominiak-Felden et al., 2013, Palefsky, 2010, Kreimer et al., 2005).

Cervical intraepithelial neoplasia (CIN) in women is the most common and clinically significant sign of persistent genital infection with HPV. So much so that cervical cancer has even been described as a sexually transmitted infection (Ibeanu, 2011, Bosch & de Sanjose, 2007). It was estimated that there were 528,000 new cases of cervical cancer (Ferlay et al., 2014), and 266,000 deaths from cervical cancer, globally, in 2012 (IARC, 2015), making it the sixth most common cancer for females in Europe and the fourth most common cancer in women worldwide.

Hence, essentially, the development of the HPV vaccines means that cervical cancer has become a vaccine-preventable disease (Centers for Disease Control and Prevention, 2013b) which could be defeated through the administration of an HPV vaccination program, together with cytological screening (Forman et al., 2012,
Bosch et al, 2012). This could, therefore, be a cost-effective cervical cancer prevention strategy, especially in certain countries (Goldie et al., 2004, Kulasingam & Myers, 2003).

However, screening programmes are often very difficult to set up, especially in developing countries (Bonanni et al., 2014). Even in the Western world there are large sections of the female population who do not undergo screening for cervical cancer detection regularly, if at all. Thus, perhaps, the only real hope of defeating cervical cancer is the implementation of universal immunisation for girls in all countries (Bonanni et al., 2014). This, together with other possible efforts, such as convincing actions to convince both parents and girls that accepting HPV vaccination, is a very important step to improve prevention in women (Bonanni et al., 2014). Vaccination in boys should also be encouraged, however. Although cervical cancer is doubtlessly the most important HPV-associated disease, it is not the only likely public-health objective of immunisation. Therefore, it is essential that Public Health authorities assess all the possible positive impacts that HPV immunisation can have on the population's health, and consider investing in a larger sector for vaccination programmes (Bonanni et al., 2014).

Yet, despite all the possible advantages of vaccinating patients against human papillomavirus infection, and despite recommendations encouraging HPV vaccination (World Health Organisation, 2014), the coverage rates both in EU countries and the United States have been lower than expected (Vadaparampil et al, 2014, ECDC, 2012). Several reasons for such a low uptake have been cited,
including poor knowledge of HPV and the HPV vaccine (Lutringer-Magnin et al., 2011), the high costs of vaccination where it is bought out of pocket by the patient and the belief that the vaccine has low efficacy and a poor safety profile (Vadaparampil et al., 2013), together with supposed and real adverse events to vaccines (Lutringer-Magnin et al., 2011). Other issues include a preference to postpone administration of the vaccine until their children are sexually active and, importantly, the attitudes, knowledge and practices of healthcare professionals towards the HPV vaccination about which there are very few European studies (ECDC, 2012). In fact, one way of increasing the coverage rates which are required to obtain the very important public health results of HPV vaccination is through the provision of more information and reassurance on the safety and effectiveness of the HPV vaccines to parents from healthcare workers (ECDC, 2012). Thus, the attitudes, knowledge and practices of healthcare professionals towards HPV vaccination should be studied further and addressed properly through the appropriate initiatives whenever they are required.

Locally there has only been one study concerning attitudes towards HPV vaccines which looked at the attitudes towards HPV vaccines amongst students of health care professions (Z. Farrugia, 2011). Other than that there is very little knowledge as yet about the attitudes of parents, patients or health care professionals towards the HPV vaccines in the Maltese Islands.
5.2 Health care professionals, surveys and response rates

This study attempted to understand the knowledge, attitudes and practices of Paediatricians, Obstetricians and Gynaecologists and Family Doctors with regards to the HPV vaccines by inviting all doctors specialised in these fields in the Maltese Islands to participate in order to have a nationally representative survey of Maltese provider recommendation of the HPV vaccine.

This was done by means of a self-administered postal questionnaire, which was sent to all eligible participants, and followed by one postal and two electronic reminders, and accompanied by a lottery as an incentive to participate.

Postal and electronic questionnaires are tools which are used widely for data collection. In this case the researcher opted for a postal questionnaire as the availability of mailing addresses on the publically available specialist registers was deemed more reliable, especially since there is no publically available source of all physicians' email addresses in Malta as yet. Also, although electronic questionnaires and online surveys have recently gained in popularity, research has indicated that postal surveys still have a higher response rate than electronic ones and thus postal surveys should still be the method used wherever possible (Crouch et al., 2011, Nicholls et al., 2011).

Postal surveys of various health professionals are a popular method for the collection of data which is then used to advise public health, health policy and
health services delivery across a variety of topics. Yet, surveys of health professionals can be challenging and studies involving physicians, specifically, are unfortunately characterized by low or falling response rates (Cho et al., 2013, Cook et al., 2009). In fact, a meta-analysis of techniques to improve response rates amongst health professionals showed an estimated overall survey response rate of 0.53 and that rates were declining significantly during the last 50 years (Cho et al., 2013).

The problem with having a low response rate is that this can result in bias since the non-responders may be systematically different from responders. This non-response bias can "...impact the generalizability or applicability of study results" (Curtis & Redmond, 2009). Therefore, where possible, non-response analysis should be carried out and is important when interpreting survey results (Cook et al., 2009). In the case of this study a missing data analysis was carried out wherein the distribution of age, gender and specialty in the final respondent population was compared to that of the original sample and no significant differences were found. Thus it is assumed that the final respondent population was representative of the original sample of doctors.

In order to increase the survey response rates among health professionals researchers have utilized various strategies. Interventions which have been found to increase survey response rates include financial incentives, using recorded delivery systems, having shorter questionnaires, the use of reminders and sending a prenotification letter (Edwards et al., 2009, McColl et al., 2001). Stamped, self-
addressed envelopes and survey personalisation have also been found to increase survey response (Field et al., 2002).

The use of electronic reminders in order to improve the response rates for postal questionnaires has yielded conflicting results, with some studies showing a significant increase in the response rate (Clark et al., 2015) and others showing no improvement at all (Man et al., 2011).

The authors of one of the original studies from which the questionnaire was taken indicated that most of the physicians appreciated that the survey was short which indicated that the researchers understood that their time was precious (Vadaparampil, S.Ph., Murphy, D., Rodriguez M., 2013). Hence, although being comprehensive, the questionnaire was not too time-consuming, in view of the knowledge that there is a lot of demand on physicians' time. As already mentioned, in order to improve the response rate for this study, various strategies were applied which included sending one postal and two electronic reminders as well as organising a lottery for all participants as an incentive to participate. Despite this the final response rate obtained was 46.7%, which was still described as "pretty good for a survey of physicians" by one of the authors of the original surveys in a personal communication with the researcher.
5.3 The objectives of the study and the study findings

This study had numerous objectives, which were addressed mainly through the questionnaire. These included the level of knowledge, attitudes and practices of family doctors, paediatricians and obstetricians and gynaecologists with regards to the HPV vaccines and the perceived influence of these on their recommendation of the said vaccines, as well as the identification of barriers and facilitators to their recommending the HPV vaccine.

Any significant differences in recommendation practices between male and female medical practitioners, to female and male patients, as well as in different settings i.e. private GP practice, Health Centre GP clinic, Hospital and specialty clinic were also studied and analysed.

Other data obtained from this study included the identification of the main sources from where the eligible participants obtain information about the HPV vaccines as well as a clearer understanding of whether they feel the need for more information/education sessions to address any queries they may have.

Finally, a set of recommendations to enhance HPV vaccine recommendation practices by medical practitioners was developed by means of three mini-focus groups carried out with members of the three specialties concerned in order to have recommendations which were suited to the requirement of local medical doctors.
5.3.1 Knowledge

Maltese doctors, on the whole, have a good level of knowledge about the pathophysiology of HPV as well as the indications for recommendation of the vaccines, although the knowledge about the topic concerning female patients was better than for male patients. This was consistent with findings reported by the CDC (CDC, 2013). As has been reported in the literature (Krupp et al., 2010), the level of knowledge also varied according to the age and specialty of the doctors participating in the study.

Indeed, as was observed in other studies (Duval et al., 2007), Obstetricians and Gynaecologists had the highest level of knowledge, followed by Paediatricians and Family Doctors. More doctors aged less than 40 years of age had a higher knowledge score than older doctors, perhaps reflecting an increasing emphasis on the importance of HPV and its associated diseases in medical education in recent years.

5.3.2 Attitudes

While the literature indicates that many physicians are willing to delay the administration of the HPV vaccine beyond the recommended age of 11 or 12 years, unintentionally leaving young adolescents exposed to HPV infection (Perkins et al., 2014), almost all respondents in this study agreed that girls should be vaccinated
prior to becoming sexually active, and the majority felt that the best age for a universal vaccination program was, in fact, less than 14 years of age. Although still in a majority, less physicians agreed with the need for vaccinating boys before they become sexually active. This seems to echo findings showing that the attitude of physicians towards vaccinating males is less positive than it is for vaccinating females (Holman et al., 2014, R. B. Perkins & Clark, 2012).

This finding is very interesting in the local setting as one of the main causes of non-vaccination, and, consequently, missed opportunities for HPV vaccination is delay, not refusal, of giving the vaccine, with both providers and parents contributing to this. Vaccination in girls is usually delayed with the intention to vaccinate when the girls are about to initiate sexual activity which, in practice, is difficult to ascertain; hence many girls remain at risk for cancers that are now vaccine-preventable (Perkins et al., 2014). In this case, local doctors seem to have understood the importance of vaccination prior to the onset of sexual activity (although for girls more than for boys). This factor is vital for the success of the vaccines against HPV-related diseases such that recent evidence shows that vaccination against HPV is twice as effective when given before the age of 14 years when compared with ages 15 years and over (Gertig et al., 2013). The discrepancy between the importance of administering the vaccine to girls as compared to boys continues to persist. However, it must be pointed out that the World Health Organisation itself, in its position paper on the HPV vaccines, prioritises recommending and administering the vaccine to 9-13 year old girls before boys,
especially where resource constraints are present. Most EU countries, in their administration of the HPV vaccines on their national schedule, follow this recommendation (ECDC, 2015) and it may thus be reflected in the individual practices of medical practitioners when they come to recommend it to patients themselves.

Studies have shown that although most physicians express a positive attitude towards vaccination many believe that few of their patients would react positively to a vaccine recommendation (Krupp et al., 2010). Similarly, in this study, the majority of physicians indicated a positive attitude towards recommending the vaccine, in various scenarios. A majority, albeit a smaller majority than in the first situation, also felt, however, that parents would accept HPV vaccination for their children aged less than 14 years while a much larger majority felt that parents would actually prefer that HPV vaccination is given at school. This latter finding means, however, that parents would be missing out on the opportunity to discuss sexual health with their children. Interestingly, one key finding in the 2012 National Sexual Health Survey carried out in Malta was that teenagers seem to want to have more involvement from their parents when it comes to acquiring their sex education, and especially in aspects that are not related to biology (Directorate for Health Information and Research, Department of Health, 2013). This was one reason why it was decided that the HPV vaccines given on the Maltese national schedule were to be provided in a community rather than a school setting. In this way parents could be more involved in sexual health communication and simultaneously encouraged to understand and accept the HPV
vaccine. This setting also created opportunities for parents and children to start discussing sexual health and sexuality.

The indications are that local doctors seem to have a more positive opinion of the attitudes of parents and patients towards the HPV vaccines than international studies have indicated. Indeed, a majority of participants also felt that adolescents and young adults themselves would have no issue with accepting and seeking the HPV vaccines.

These findings augur well for successful recommendation of the vaccines as the success of vaccination programs can only be ensured if the HPV vaccines are accepted by individuals and parents alike (Gross, 2007), who themselves are more likely to accept a vaccine if it is recommended by a physician (Holman et al., 2014, Rosenthal et al., 2011, Zimet, 2005). At present, in Malta, the figures for the uptake of the HPV vaccine given on the national schedule do indeed show a high acceptance rate with 87.5% of 12 year olds being vaccinated in 2014 for the 1st dose, 90.9% for the 2nd dose and 92.3% for the 3rd dose. (National Immunisation Services, 2015). As of 2015 the schedule consists of 2 doses given at a 6 month interval.
Despite the seemingly positive attitude of the participants with regards to the HPV vaccines, a look at their recommendation practices showed that, in reality, they are not recommending the vaccines as strongly as would be expected. Only a small percentage of physicians reported "always" recommending the vaccines to female patients aged 11-12 years, with double the proportion of female doctors recommending it to female patients in this age group than male doctors. This compares with a survey showing that fewer physicians strongly recommended the vaccine for younger patients than for older ones (Daley et al., 2010)

Although a larger proportion of the participants in this study indicated that they "always" recommend the vaccine to middle adolescents (13-17 years) and older patients (18-26 years) they still constituted less than a quarter of all participants for each patient age group. Interestingly, the Obstetricians and Gynaecologists were more likely to recommend the vaccine to the two younger age groups while Family Doctors were the least likely to do so.

One major and complex issue where the administration of the HPV vaccines to young adolescents is concerned is that of discussing a young individuals' sexuality and sexual health which can require delicate conversations. It may be that since family doctors often have a close relationship with patients and their families they feel awkward discussing such a sensitive topic, especially if it is not
brought up by the individuals themselves. On the other hand, the very nature of the specialty means that sexual health is a frequent topic of discussion between obstetricians and gynaecologists and their patients which may make the discussion of an adolescent's sexual health and activity, and hence the recommendation of the HPV vaccines, easier for obstetricians and gynaecologists to deal with.

With regards to vaccinating male patients, one study found that male physicians were less likely than female physicians to expect to vaccinate young male adolescents (Daley et al., 2006). While this study intended to look at any significant differences in recommendation practices to female and male patients only one (male) physician claimed to "always" recommended the HPV vaccines to male patients aged 13-17 years of age whilst the majority of physicians claimed that they "never" recommend the vaccines to male patients. This further strengthens the findings mentioned above that some physicians do not think that it is worth vaccinating males, are unaware of the fact that HPV-related disease in males can have serious consequences, or else think that parents would not want to vaccinate their sons (Holman et al., 2014, R. B. Perkins & Clark, 2012). Recent research has shown, however, that when given clear information about HPV vaccination in both genders, parental acceptance of HPV vaccination of boys is as high as acceptance levels for girls (Lee Mortensen et al, 2015).

It has been shown that younger physicians were more likely to "always" recommend the HPV vaccines when compared to older physicians (Vadaparampil et al., 2014), suggesting that this difference reflected "a greater emphasis on the
importance of HPV in disease aetiology in medical education for more recent graduates." It has also been implied that younger physicians may be more receptive to adopting new clinical practice innovations. This study however did not observe any significant differences in the recommendation practices of physicians according to their age or the number of years of clinical practice they had. When considering the rather low recommendation rates observed this could indicate that more education and training about HPV and its vaccines is required across the board, regardless of the age of physicians. Considering the different recommendation practices observed by the different specialties perhaps further emphasis should be placed on the importance of recommending the vaccine to younger patients for those specialties that are not currently doing so. The importance of recommending the vaccine more to male patients should certainly be emphasised more to all physicians.

5.3.4 Strategies

When asked about whether they employ any strategies in order to get patients into their office for the first dose of the HPV vaccine and then to ascertain that the 3-dose series is completed among patients who had started HPV vaccination, the majority of physicians, in both scenarios, claimed to employ 1 strategy only - namely to discuss the issue during a routine visit. Other options suggested in the questionnaire, which do not seem to be employed much by local doctors, included sending reminders, flagging patient records to use as a reminder
during a follow up visit and even scheduling the patient for the next recommended dose during a visit, which is a more directive approach.

While discussing the topic during a routine visit is a good start, it is important to ensure that the discussion is fruitful and encourages the parent/patient to take the vaccine. Simply discussing the topic and leaving the decision up to the individual is likely to result in a missed clinical opportunity. A successful recommendation is one usually classified as "strong". This means that physicians need to express to parents their unambiguous view that the vaccines are beneficial and also to make directive recommendations in order to encourage vaccine uptake (Opel et al., 2013, CDC, 2013).

Studies have indicated that a lack of implementation of active strategies is common (Daley et al., 2010). This is unfortunate as, for example, not utilising active strategies to ascertain that patients receive all 3 HPV vaccination doses could result in a delay by when patients are completely immunised.

5.3.5 Barriers

The barriers associated with recommending the HPV vaccines are numerous and various, ranging from cost, to age of the target group, sensitivity of the topic, concerns about vaccine safety and efficacy and lack of knowledge, especially on the part of parents and patients.
For the most part the majority of participants in the study did not feel that these suggested barriers constituted a major stumbling block to their recommending the HPV vaccines to patients. The issue considered to be most likely to be a barrier was the cost of the vaccine which was, in fact, observed to be a top barrier in other studies as well (Vadaparampil et al., 2011, Keating et al., 2008) and which emerged very strongly during the discussions in the focus groups held with the various specialists. Indeed most felt that it should not be limited only to twelve year old girls on the national schedule and that, where possible, it should be subsidised for certain population groups in order to encourage more uptake.

Research has indicated that consistent HPV vaccine recommendations are linked to physicians' perceived issues or barriers related to immunising patients against HPV and that having a high perception of vaccination barriers was associated with physicians not strongly recommending or offering the HPV vaccine (Vadaparampil et al., 2014). While this finding was not observed for young female adolescent patients (11-12 years old), it was paralleled in the findings observed for 13-17 year old and 18-26 year old female patients, which were the age groups for which most recommendations were made.

While the age, gender and specialty of physicians did not seem to influence the level of perceived barriers observed, the location of the main outpatient practice of the physician did appear to influence the perception of the level of barriers faced. Double the number of physicians whose main outpatient practice was located in a
health centre compared to those located in a private clinic or hospital department felt that they faced high barriers to immunising patients with the HPV vaccine. This finding could reflect the time constraints and demands felt by physicians working in health centres who might feel that they do not have sufficient time to explain in detail about the HPV vaccines to patients because of very busy clinics.

The main parental barrier encountered by physicians when recommending the vaccine was also deemed to be the cost of the vaccine. Yet, interestingly, despite the cost of the vaccines being perceived as the top barrier to recommending it, the large majority of participating physicians stated that they would still recommend the HPV vaccine to their patients even if they had to pay for it themselves. The fact that, in Malta, the uptake of the vaccine where it is free for 12 year old girls is very good, consolidates further the finding that cost of the vaccines may be a strong reason for parents not vaccinating older children and those who are not eligible for the HPV vaccines for free.

5.3.5.1 **Health Literacy**

Closely following cost as a main parental barrier was lack of parent education and understanding about HPV infection. This issue was also a main topic of discussion during the focus groups where most of the participants claimed that, from their experience, the level of health literacy among many patients was quite low and that many people found it difficult to understand the concept behind the vaccines.
The recently published results of the Health Literacy Survey (Office of the Commissioner for Mental Health, 2015) have shown that nearly half the Maltese population have problematic or inadequate levels of Health Literacy, which seem to echo the statements made by the doctors from their clinical experiences. This lends more weight to the finding that one of the main barriers is lack of patient knowledge, as doctors find it more difficult and time consuming trying to explain certain details to patients, especially since the topic can be quite complex for individuals to grasp and accept.

5.3.5.2 HPV and the media

The role of the media as a barrier or facilitator in the acceptance of the HPV vaccines must not be underestimated either way. Indeed, how the HPV vaccines are portrayed in the media can effect the understanding of the public about the vaccines and decisions whether to vaccinate or not. People may find it difficult to be able to determine which information being provided by the media is credible and which is not. In the Health Literacy Survey carried out in Malta in 2014 (Office of the Commissioner for Mental Health, 2015) 29.7% of the respondents said that they find it "fairly difficult" or "very difficult" to judge if the information on health risks in the media is reliable while 33.1% had difficulty deciding how to protect themselves from illness based on the information in the media.
The media is a popular source of information about HPV and is known to influence perception of health matters as was seen during the Measles, Mumps and Rubella (MMR) vaccine controversy. In the case of HPV vaccination, the fact that it deals with a sexually transmitted infection renders the situation more delicate which could make the HPV vaccine a controversial topic and which could negatively effect its uptake (Forster et al., 2010).

In a study analysing the impact of blog posts about the HPV vaccine on college students, those students who were exposed to the negative blog post perceived the vaccine as less safe than students in the control group did. They also had more negative attitudes to the vaccine and reduced intentions to receive it. On the other hand, those students exposed to the positive blog were not found to have any altered risk perceptions, attitudes, or intentions related to the vaccine (Nan & Madden, 2012).

A popular media topic is the issue that HPV vaccination might lead youngsters to practice risky sexual behaviours (Forster et al., 2010). This can increase parents’ concerns about vaccination and negatively influence vaccination decisions and must certainly not be ignored when considering interventions to improve vaccine uptake. It has in fact been shown that parents who believe this perception to be true are less willing to vaccinate their children (Forster et al, 2010). Indeed, the ECDC itself recognised that this issue needs to be tackled so that vaccine uptake will improve (ECDC, 2012). Having considered all this, however, for the most part, the doctors participating in this study felt that parental
concern about negative media reports about the HPV vaccine never or only rarely constituted a barrier to their immunising young patients against HPV.

Actually, media coverage of the HPV vaccine is likely to play an important role in increasing public awareness of the immunisation program, as well as in influencing public attitudes about vaccination behaviour. Thus, it is important to give it due consideration when looking at methods to improve HPV vaccine uptake, and, where possible, to utilise it in a positive, constructive manner.

5.3.6 Sources of information

Pharmaceutical representatives constitute a major source of information about the HPV vaccines for a majority of the respondents in this study. Other sources referred to include medical conferences and internet websites while a majority of physicians claim to avoid referring to the media. The physicians' age, gender and type of speciality did not seem to influence the preferred sources referred to for obtaining information about HPV and the vaccines.

A slight majority of respondents felt that they had received "somewhat sufficient" information about the HPV vaccines with just over one quarter of participants declaring it to be "sufficient". Younger doctors seemed to be particularly dissatisfied with the level of information provided while older doctors where less critical.
Vaccine efficacy and effectiveness was the major topic considered to require most attention and which should be included in clinical training materials and clinical decision support tools to guide the prevention of HPV infection for doctors. Almost all doctors deemed this topic to be "important" or "very important", followed by the vaccine safety profile as well as how to provide HPV counselling.

5.4 Relevance and significance of the quantitative results

These results start to give a better picture of the knowledge, attitudes and practices of physicians towards the HPV vaccines, thus indicating where certain issues might arise and where further action might be taken in order to improve uptake of these vaccines.

While the level of knowledge seems to be reasonably good and the attitude of physicians indicates a more positive approach towards the vaccines than was obtained in other international studies, when it comes to recommending the vaccines the physicians seem to be encountering some obstacles or difficulties to translate their opinions into actions.

The lack of recommendations to male patients is quite glaring, although the low recommendation rate for young adolescent girls is quite worrying as well. As was evident from the quantitative results, while there is a strong awareness of HPV-related issues in female patients, their effects in males are given much less consideration, so much so that some doctors did not even consider that whilst
recommending the HPV vaccines to a patient's daughter they could recommend it to her son too! The recommendations of certain authorities, such as the World Health Organisation itself, which prioritises vaccinating girls before boys (World Health Organisation, 2014), might play a role in influencing the recommendation practices of doctors.

Doctors working in Health Centres also seem to perceive a higher level of barriers than those working in private and hospital clinics. Since they encounter a large proportion of the population, and especially people from all backgrounds, it would be useful to try to address methods by which recommending the HPV vaccine in Health Centre clinics could be facilitated. This finding may also reflect the high barrier that cost plays in the uptake of the HPV vaccines. Since people of a lower socio-economic background may frequent Health Centres more, and consequently they may be less likely to accept a recommendation to buy this vaccine because of its high cost, this may explain the higher level of barriers perceived by doctors working in Health Centres.

One must also consider the possibility that while the replies to the questions on attitudes and opinions might reflect what doctors feel to be the more "acceptable" answers, the replies to their recommendation practices give a clearer picture of what is actually put into practice.

The implications of these results are important; through understanding how physicians feel about the HPV vaccines, as well as identifying areas where more
action may be required, effective strategies can be developed which would improve patient and physician education about the HPV vaccines. Hopefully these would have a positive impact on their uptake, and decrease the number of missed opportunities for vaccine recommendation with a consequent decline in the incidence of HPV associated diseases.

5.5 The focus groups

Focus groups are a type of group interview that makes the most of communication between participants in the study in order to obtain data. One of the main features and strengths of focus groups is that they specifically use the interaction within the group in order to collect data from people - the "group effect" (Carey & Smith, 1994). Therefore, people are encouraged to discuss together, ask each other questions and comment on each other's comments and not just to respond to a researcher's question in turn. This method is especially useful when one wants to explore the participants' knowledge and experiences. The reason why focus groups are used is that the group dynamics can help people to be more expressive and to explain their opinions better than they would in an interview. Thus, group discussion is particularly suited when the researcher has open-ended questions to ask and would like to encourage the participants to express the issues which are significant to them. They encourage the participants to use their own vocabulary, to create their own questions and to discuss what is of importance to them (Kitzinger, 1995). Indeed the idea behind the focus group is to make use of the participants' feelings, opinions and perceptions. It is usually better to have
several focus groups to obtain a more objective and wider picture of the situation. Usually it is recommended to have at least three focus groups, and the participants should share common interests which are of importance to the research in question.

In the case of this study three mini focus groups were carried out. Although having a focus group with mixed specialties would have certainly produced interesting discussions, the sessions held during this study were very interesting and informative in themselves.

Indeed, originally, the qualitative part of the study was intended to consist of one focus group with 10 health professionals (family doctors, paediatricians and obstetricians and gynaecologists) of mixed age and gender. Unfortunately, repeated attempts at having one group consisting of a combination of professionals from the three different specialities proved unsuccessful. It was, therefore, decided to have three mini focus groups (Krueger, 1994), each one made up of doctors from a particular specialty - family medicine, obstetrics and gynaecology and paediatrics. Each focus group contained 3-4 doctors from a particular specialty and met the researcher on one occasion for a session that lasted approximately 45 minutes. Such mini focus groups are usually suitable when the participants have specialized knowledge and/or experiences to discuss in the group, as was the case in this study (Onwuegbuzie et al., 2009).
5.6 Limitations and biases

This study was intended to be a national survey of the knowledge, attitudes and practices of Family Doctors, Obstetricians and Gynaecologists and Paediatricians with regards to the HPV vaccines in order to identify missed clinical opportunities for HPV vaccination and propose recommendations to improve their recommendation of the HPV vaccines. Although attention was given to avoid certain biases and limitations there were certain issues which could still have an impact on the outcome of the results obtained.

5.6.1 Limitations and biases of the quantitative method

5.6.1.1 Response Bias

Since the study was intended to be a national survey, all doctors on the respective specialist register who could be contacted were invited to reply to the postal questionnaire, and some incentives were utilised in order to improve the response rate.

While postal surveys of various health professionals are a popular means by which data is collected, surveys of health professionals, and, specifically of physicians, are unfortunately characterized by low or falling response rates (Cho et al., 2013, Cook et al., 2009). The problem with having a low response rate is that
this can result in bias since the non-responders may be systematically different from responders which can affect the "generalizability" or "applicability" of results (Curtis & Redmond, 2009). Although the response rate for this study was 46.7%, a missing data analysis which was carried out on the final respondent population showed that there were no significant differences when compared to the original sample. Thus, it is assumed that the final respondent population was representative of the original sample of doctors.

5.6.1.2 Information Bias

One of the aims of the questionnaire was to assess the level of knowledge about HPV and the HPV vaccines of the doctors concerned. There is a possibility however that doctors may have looked up some of the replies in order to give the correct answer. While this in itself may help to improve their knowledge, it is not actually a reflection of what their level of knowledge was when recommending the vaccines to patients prior to the survey.

5.6.1.3 Selection Bias

The study relied on the Registers of the Medical Council of Malta in order to obtain the list of specialists in the chosen fields as well as the publicly available contact details in order to be able to mail the postal questionnaires and reminders. Thus the researcher was dependant on whatever information was available on the registers and could not be entirely sure of its accuracy. Although the doctors'
information is updated regularly it is up to the individual doctors to inform the Medical Council of any changes in their details - hence, if an individual does not provide updated information the details available may be outdated and inaccurate. In fact 2 questionnaires were returned as the mailing address provided was incorrect. There is a possibility that other questionnaires were never received by the intended recipient who was then marked as a non-responder.

The Medical Council registers allow doctors to choose not to display their address - in this case there were 60 doctors who did not have available addresses and so were excluded from the study immediately.

The questionnaire was anonymous. While this may have encouraged some people to participate as they could not be identified it also meant that reminders had to be sent to all participants. This could have led to a possible duplication of returns as people might have thought, on receiving the reminder, that the first questionnaire was not received and so they would have sent the second one too, even though the reminder specified that it was for those who had not yet sent the first questionnaire. Should this duplication have occurred there was no way of verifying it due to the anonymity of the questionnaires.

Although the researcher used a postal reminder, two electronic reminders and a lottery as incentives to improve the response rate, more postal reminders could have been sent as well as a pre-notification informing participants of the
impending study as preparation. Unfortunately, this was limited due to expenses as the cost of printing and posting questionnaires and reminders was quite high.

The questionnaire contained 39 questions as it was required to be comprehensive in order to address all the objectives of the study. This length was quite "standard" and questionnaires of similar length were used in similar studies (Vadaparampil et al., 2014, Wong et al., 2013). It should be acknowledged, however, that the questionnaire consisted of 13 pages which might have put some doctors off participating.

5.6.2 Limitations and biases of the qualitative method

5.6.2.1 Focus groups

We have already seen that focus groups, as part of the qualitative methodology, have a number of strengths, not least the fact that participants have the opportunity to express themselves in more depth than they would be able to do in a survey and also the fact that they stimulate the "group effect" through use of the interaction within the group (Carey & Smith, 1994).

Yet focus groups, as do other forms of qualitative research, also have certain limitations which can influence the results obtained from them. One such limitation is observer dependency which can raise questions about the validity of
the data obtained. With observer dependency there is a risk that the results can be influenced by the researcher’s way of phrasing questions or the way in which he or she interprets the discussion of the group.

The small size of focus groups also means that there might not be good representation of the larger population while the discussion may be difficult to steer and control especially with an inexperienced researcher. The participants may also feel pressurised into agreeing with the rest of the group, even though they may have a different opinion, simply not to stand out, or else may be reluctant to share sensitive ideas and concerns publicly. Focus groups have also been accused of being artificial settings causing participants to express themselves unnaturally (Krueger, 1994).

Having said all this, however, they are still useful tools which can provide an insight to certain topics which may not be picked up with other methods.

5.7 Further studies on HPV vaccination

Most studies about HPV vaccination rates as well as about the knowledge, attitudes and practices of health care providers with regards to the HPV vaccines and the barriers they face to recommending it have been conducted in the United States of America. Studies on the subject in Europe and elsewhere are still quite scarce, although a few have been carried out in recent years.
In Malta there has only been one survey carried out which looked at the attitudes towards human papillomavirus vaccine amongst students of health care professions (Farrugia, 2011). Other than that very little is known about the perceptions and opinions of potential patients and their parents as well as other members of the health care professions, and certainly more research is required in this area. While the uptake of the vaccine where it is given free to 12 year old girls on the National Immunisation Schedule is very good, the little available data from the private sector shows that only a very small number of vaccines is being bought out of pocket by patients.

The questionnaires used in this study had been utilised to carry out national surveys and had been used to reveal similar issues in the United States of America and Canada. They were considered to be very comprehensive in the quantity and quality of information gathered from them. The results obtained from this survey indicate that doctors are not recommending the vaccine as strongly as would be expected, and perhaps this is reflected in the poor sales figures reported for the HPV vaccines.

Apart from attempting to understand whether there were any particular differences in the knowledge, attitudes and practices of doctors this study also tried to identify any issues they felt prevented them from recommending the vaccines to patients with the intention of addressing these issues and thus improving vaccine uptake. The set of recommendations which could help doctors recommend the
vaccines more were drawn up following three mini focus groups conducted with specialists from the three specialties participating in the survey.

It would further be of interest, should the introduction of certain interventions be considered, if pre-interventional and post-interventional studies were carried out to identify which interventions, if any, had a significant impact on improving the uptake of the HPV vaccines.

5.8 More qualitative research

What is certainly required is more qualitative information, not only about health care professionals and their approach to HPV, but also about the perception of parents and patients about the vaccines. It would be interesting to delve further into any concerns they have, as well as the impact of the media on their acceptance or rejection of the vaccine for themselves or their children.

The focus groups carried out in this study were used to gather information from the doctors themselves in order to develop a set of recommendations about what methods they felt could help them to address the perceived barriers to recommending the vaccine; these are explained in further detail in the coming chapter. Yet, certainly, there is a lot of rich data that could be collected from clinicians which could shed more light on the difficulties they face and the reasons why they are not recommending the vaccine as much as expected.
Chapter 6

Recommendations and Conclusions
Chapter 6 - Recommendations and Conclusions

6.1 Recommendations

The recommendations listed below were extracted following the three focus groups held with members of the three specialties involved in the study in order to create a list which reflected the true requirements of the doctors themselves.

There were only a few themes which were particular to certain specialties. For the most part the same themes and issues cropped up in all three focus groups indicating that they are felt to be of importance by doctors from all three specialties.

6.1.1 List of recommendations

1. Improving health literacy and patient education

- Organising workshops/sessions for parents explaining in more detail about HPV and its associated diseases as well as the concept behind giving the vaccine to young adolescents and also to boys.
- Educating teachers of Personal and Social Development (PSD) so that they may know the correct information and also how to guide children and parents should they have any queries.
• Producing clear and easy-to-understand leaflets which doctors may distribute to patients.

• More cooperation between the Directorate of Health Promotion and Disease Prevention and the media about the vaccines in order to deliver correct and accurate information.

• Organising an "STD week" which would focus more on these diseases as a general topic and which might help to make discussing sexually transmitted diseases easier.

• Developing comprehensive sexual education programmes for children and parents so that sexual health is destigmatised and does not remain a taboo issue which people find so difficult to discuss, but can addressed with the same ease as other diseases such as meningitis and measles.

• Organising more campaigns addressing adolescent health and vaccinations, using methods to deliver the messages which are more appealing to a young audience.

• Organising campaigns/adverts specifically referring to boys as the target group.

2. Cost of vaccines

• Subsidising the cost of the vaccine for adolescents between 13-18 years of age who are not entitled to it for free.
• Encouraging insurance companies to reimburse the cost of a private visit for a vaccination as well as the cost of the vaccine which is not being done currently.

• Introducing tax incentives for parents who vaccinate their children as is done for those sending their children to sports and cultural activities.

3. Lowering the recommended age group for vaccination

• Lowering the recommended age group to whom the vaccine is given free on the national health system to 9-10 years of age.

4. Education of the health care providers

• Education and training for service providers in order to increase their level of knowledge and competence has been addressed in the National Sexual Health Strategy, 2011. Training in sexual health would be provided at both undergraduate and postgraduate level and could consist of e-modules as have already been organised in conjunction with the British Association for Sexual Health and HIV (BASHH).

• Education sessions could be part of Continuing Professional Development (CPD) programmes and should be mandatory to ensure that most, if not all, doctors attended.
• Doctors could also regularly be sent emails and updates with any new developments, changes in the vaccination programme, alerts or new evidence in order to ensure that they keep abreast with the latest information available.

• The family doctors requested workshops teaching them better how to deal with discussing sexually transmitted diseases (STDs).

5. Research

• More research, both of a quantitative as well as of a qualitative nature should be carried out locally.

• Pre-interventional and post-interventional studies should be carried out, if interventions are introduced, in order to indentify which, if any, interventions have a positive impact on HPV vaccine uptake.

6.2 Conclusion

The uptake of the HPV vaccines has been lower than expected in most countries. In Malta, the vaccine is available for free on the national health system for 12 year old girls, and the uptake in this group of patients has so far been good. Very little is known, however, about the role of physicians in their recommendation practices for the HPV vaccines, both in the public sector to promote uptake of the vaccine where it is available for free, as well as in the private sector, where people
have to buy them out of pocket, and where acceptance of the vaccines is particularly dependant on the recommendations of health care providers.

The role of health care providers in influencing patients' vaccine-taking decisions is well-established, and patients who receive a positive and encouraging recommendation from their medical practitioner are more likely to accept a vaccine even when they originally were determined to refuse it.

Hence, one of the reasons for the low uptake of the HPV vaccines includes the attitudes, knowledge and practices of healthcare professionals towards the HPV vaccination.

The Family Doctors, Obstetricians and Gynaecologists and Paediatricians participating in this study showed a relatively good level knowledge about HPV-related diseases and the HPV vaccines, as well as a positive attitude towards them and their recommendation. Yet, their actual recommendation practices for the vaccine indicate that very few doctors are regularly recommending the vaccines to eligible patients, and that male patients are almost entirely being disregarded.

This is resulting in a number of missed clinical opportunities where the HPV vaccines are concerned, which is probably reflected in the low sales figures observed for the HPV vaccines. The attitudes of the doctors appear to be very positive, perhaps more so than has been found in international literature.
However, for some reason, when it comes to recommending the vaccines, there are certain obstacles being encountered which need to be addressed.

The cost of the vaccines seems to be a main barrier, both locally and internationally. This has important implications, not least because this particular barrier can be construed to be causing inequalities where accessibility to a cancer-preventing vaccine is concerned. The burden of HPV-related illnesses are significant, for both female and male patients, and are not only related to cervical cancer, even though it is the HPV-related disease which causes most concern. These vaccines can be regarded as the stepping-stone to drastically reducing the incidence of one of the most common sexually transmitted infections worldwide and its associated burdens.

The discussions with doctors during the focus groups indicated that they felt very strongly that this was the primary barrier impeding a better uptake of the vaccines, so much so that it was suggested a number of times that it should be subsidised for particular sectors of the population. In Malta, the degree to which the cost of the vaccines acts as a barrier may be determined from the fact that, where it is available for free the uptake has been shown to be very good, whereas where it is required to be bought out of pocket the uptake is very low.

The level of health literacy in Maltese adults has been shown to be quite low, and this is perhaps reflected in the fact that numerous times doctors cited patients'
lack of knowledge and understanding about HPV and the vaccines as making recommending the vaccines more difficult. Certainly, many patients are finding it difficult to discern which information about health risks and disease prevention provided by the media is reliable and which is not, adding more to their confusion.

The HPV vaccines, as perhaps many other vaccines before them, have faced their fare share of media controversy. The fact that they deal with sensitive topics such as sexual health, and, especially, the sexual health of young adolescents, attracts public attention readily, especially when it is negative. The influence of media stories on the perceptions and understanding of parents and patients is strong, and can greatly influence their decision to accept or reject a vaccine. It is, therefore, vital for the success of the HPV vaccines and related immunisation programmes that the general public is regularly provided with accurate, clear and up-to-date information which counteracts the sensationalist stories that sometimes hit the news and explains and allays any fears or misunderstandings.

Lack of parental education and misinformation about the HPV vaccines is, in fact, another barrier faced by doctors when it comes to recommending the vaccines, and the media can thus be utilised to facilitate the role of the doctor in explaining the concept of vaccinating young adolescents before they become sexually active.
The sensitive nature of the topic seems to be an issue for some specialties but not for others. While the obstetricians and gynecologists felt that they had no issue with discussing the topic with their patients, family doctors, in particular, claimed to find it difficult to bring up the issue with patients, especially when they do not ask about it themselves. Fears of being misunderstood, being accused of being judgemental or implying that their children are sexually promiscuous hold doctors back from discussing the issue. In fact most missed clinical opportunities arise from delaying giving the vaccine rather than deciding at the outset not to take it, or give it to their children, at all. Consequently, as the decision keeps being delayed it very often ends up being missed out on completely.

This difficulty emerges clearly in the recommendations suggested by doctors for ways in which they can be helped to recommend the vaccines more effectively. The request for workshops and training sessions which prepare them better to approach the subject tactfully, yet effectively, came up repeatedly during the focus groups, and is, therefore, something that should definitely be considered.

A commonly encountered suggestion was taking a more directive approach whereby the age at which the vaccine is given to girls on the national schedule should be lowered to around 10 years of age and the vaccine is simply addressed as "another one on the list to protect their children", so that the discussion about sexual activity could be skirted and does not remain an issue. Certainly, the fact that the vaccines address a sexually transmitted infection does seem to be drawing
a degree of negative attention to them and, possibly, to be contributing to their low uptake.

While cervical cancer may not be the most common cancer, the fact that there is now a way by which it can be avoided should be viewed as a positive aspect which should be celebrated rather than vilified because of the way by which the illness can be contracted. What certainly emerges from many of the studies is that people still feel uncomfortable discussing sexual health and issues about sexuality and would rather avoid the subject where possible, especially where young people are concerned. However, this is resulting in a great disservice to a large number of young people who can now be protected from a disease which can place such a heavy burden on them.

In truth, perhaps what is required, apart from just educating people about the HPV vaccines is developing comprehensive sexual education programmes for children and parents so that sexual health does not remain the taboo issue it still seems to be today, which people find so difficult to discuss, but can be dealt with with the same ease as one discusses other diseases such as meningitis and measles. It needs to be destigmatised as only once this happens will people be able to truly accept the value of the HPV vaccines, so that the burden HPV and its related diseases place on the population can start to be lightened.
References
References


References


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References


References


Appendices
Appendix A

Permission to use questionnaires from authors
Appendix A (1) - Permission to use questionnaires from authors

From: Vadaparampil, Susan T. [Susan.Vadaparampil@moffitt.org]

Sent: Wednesday, 28 May 2014 13:06

To: Cuschieri Liliana at MEH-Environmental Health-Health

Cc: Malo, Teri L.

Subject: Re: Qualitative study with regards to the HPV vaccination

Attachments: image006.jpg; image001.jpg; image003.jpg

Dear Liliana,

We are happy to give you permission to use/adapt our survey for your study. We look forward to hearing the results.

Best of luck with your project!

Sent from my iPhone

On May 28, 2014, at 6:23 AM, "Cuschieri Liliana at MEH-Environmental Health-Health" <liliana.cuschieri@gov.mt> wrote:

Dear Dr. Malo,

A few weeks ago you kindly sent me a questionnaire: HPV HINTS – Hearing Physicians’ Views – HPV Immunization National Trends Survey.

I would like to ask your permission to be able to use this questionnaire for my research project. It might be necessary, however, to remove or modify some questions slightly in order to make them more suited to the local health service (e.g. remove questions about uninsured patients as this is not relevant to the Maltese health system). Should you agree to this I will, of course, cite your study as the source of the questions for the questionnaire.

Thank you very much and regards,

Liliana

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Kindly consider your environmental responsibility before printing this e-mail

Ministry for Energy and Health
Hi Liliana,

No problem, you can use the questionnaire.

My suggestion would be to mention something like: The questionnaire we used was previously validated (ref). XX questions were updated and adjusted to local conditions.

Usually reviewers want to be sure the questionnaire was validated and well understood by responders.

Cheers

Vladimir

"Cuschieri Liliana at MEH-Environmental Health-Health"<liliana.cuschieri@gov.mt>

2014-05-28 06:18

Objet RE: Publication - Vaccination against human papillomavirus: A baseline survey of Canadian clinicians' knowledge, attitudes and beliefs

Dear Dr. Gilca,

A few weeks ago you kindly sent me a questionnaire: Prophylactic Human Papillomavirus Vaccines – How they should be used? – which you had used in a study.
I would like to ask your permission to be able to use this questionnaire for my research project – as you said it will have to be actualised since, since then, the vaccines have been placed on the market and are being administered to patients. Therefore, I might not use all the questions in your questionnaire but those which are relevant to today’s situation.

Should you agree to this I will, of course, cite your study as the source of the questions for the questionnaire.

Thank you very much and regards,

Liliana

Liliana Cuschieri
Basic Specialist Trainee
Health-Environmental Health
Continental Business Centre,
OLD RAILWAY TRACK,
SANTA VENERA,
MALTA

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Ministry for Energy and Health
Appendix B

Questionnaire
Missed Clinical Opportunities for HPV vaccination

Questionnaire for Family Doctors, Obstetricians and Gynaecologists and Paediatricians
as part of a research project for the Masters in Public Health

Your answers will be treated in strict anonymity. Thank you.

Kindly note that this questionnaire is to be completed by doctors who are currently practising in the specialities of: Family Medicine, Obstetrics & Gynaecology and Paediatrics.

If you are currently practising, or have only temporarily suspended your practice but intend to resume in the near future (e.g. currently on maternity leave, parental leave, study leave or similar) then please proceed with the questionnaire.

If you are enlisted as a specialist in these fields but have retired or are practising in a different speciality or for some reason are no longer practising then please tick the box below. There is no need for you to proceed with the questionnaire but kindly return it as it is in the larger enclosed self-addressed envelope and mail your lottery ticket separately in the smaller enclosed self-addressed envelope. Thank you.

1. Currently there are two HPV vaccines available. Which vaccine do you use/recommend the most?

☐ Gardasil® (quadrivalent HPV vaccine)  ☐ Cervarix® (bivalent HPV vaccine)  ☐ Neither

For the remainder of this survey “the HPV vaccine” refers to the vaccine you use/recommend the most.
2. How often do you use the following sources to obtain information about the HPV vaccine?

<table>
<thead>
<tr>
<th>Source</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Professional organisations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Advisory Committee on Immunisation Practices (ACIP)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) National immunisation programs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Colleagues</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Pharmaceutical representatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>f) Internet websites</td>
<td></td>
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<td></td>
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<tr>
<td>g) Media</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) Medical conferences</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i) Grand rounds/lectures</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Please mark the box for the response that best reflects your opinion of each of the following statements:

<table>
<thead>
<tr>
<th>Statement</th>
<th>True</th>
<th>False</th>
<th>Unsure</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Most HPV infections resolve without medical intervention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Treatment of cervical dysplasia/cancer permanently eliminates the causative infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Genital warts are caused by the same HPV types that cause cervical cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Almost all cervical cancers are caused by HPV infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) The FDA approved the quadrivalent HPV vaccine for use in females ages 9-26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) The FDA approved the quadrivalent HPV vaccine for use in males ages 9-26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Females who have been diagnosed with HPV infection should not be given the HPV vaccine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) HPV causes vulvar, vaginal and anal cancers in women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i) HPV causes anal cancers in men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>j) HPV causes some head and neck cancers</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4. How strongly would you agree/disagree that the following are barriers related to immunising your patients against HPV? (for each row please tick one box)

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Strongly Disagree</th>
<th>Somewhat disagree</th>
<th>Somewhat agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Your concerns about vaccine safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Your concerns about vaccine efficacy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Discussing sexuality/sexually transmitted infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Vaccinated teens practicing riskier sexual behaviours</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>e) Administering a new vaccine with a limited track record of safety</td>
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<td></td>
</tr>
<tr>
<td>f) Adding another vaccine to the vaccine schedule</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Lack of information about the HPV vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) The cost of purchasing the HPV vaccine</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>i) The time it takes to discuss HPV vaccination with patients and/or parents</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>j) Difficulty ensuring that patients will complete the 3-dose vaccination series</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>k) HPV vaccination is not required for school attendance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. How often have you experienced the following parental barriers to immunising 9-17 year old patients against HPV?

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Never (0%)</th>
<th>Rarely (1-25%)</th>
<th>Sometimes (26-50%)</th>
<th>Often (51-75%)</th>
<th>Always (&gt;75%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Parent concern about vaccine safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Parent concern about vaccine efficacy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Parental reluctance to discuss sexuality/sexually transmitted infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>d) Parent concern that adolescent will assume that a parent who agrees to HPV vaccination condones premarital sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Parent concern that vaccinated child will practice riskier sexual behaviours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) Lack of parent education/understanding about HPV infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Parent requests that HPV vaccination be deferred</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) Parent believes child is not at risk for HPV infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. How often have you experienced the following *parental* barriers to immunising 9-17 year old patients against HPV? cont...

| i) Parent won’t consent to vaccination | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| j) Parent believes child is too young for the HPV vaccine | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| k) Parent concerned about negative media reports related to the HPV vaccine | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| l) The cost of purchasing the HPV vaccine | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

Please answer the following questions with respect to your *primary* site of outpatient practice. If you practice at more than one outpatient site, please respond to this survey regarding the site at which you spend the most time.

6. Do you currently use any of the following strategies to get patients into your office for the first dose of the HPV vaccine? (✓ all that apply)

| a) I don’t administer HPV vaccine in my clinical practice | ☐ |
| b) Send patient reminder regarding need for preventive visit/check-up | ☐ |
| c) Send letter or call patient to prompt them about when the vaccine is due | ☐ |
| d) Place a reminder flag/tag in patient’s medical record | ☐ |
| e) Use a computerised immunisation database or registry to track when the first dose is due | ☐ |
| f) Other method (specify) | ☐ |
| g) I don’t use any strategies to get patients for the first dose | ☐ |

7. Do you currently use any of the following strategies to ensure completion of the 3-dose series among patients who have started HPV vaccination? (✓ all that apply)

| a) I don’t administer HPV vaccine in my clinical practice | ☐ |
| b) Record when the next dose is due on a paper-based card that the patient keeps | ☐ |
| c) Send reminder/recall letter or call patient | ☐ |
| d) Place a reminder flag/tag in patient’s medical record | ☐ |
| e) Schedule patient for the next recommended dose during their office visit | ☐ |
| f) Use a computerised immunisation database or registry to track when the next dose is due | ☐ |
7. Do you currently use any of the following strategies to ensure completion of the 3-dose series among patients who have started HPV vaccination? (✓ all that apply) cont...

<table>
<thead>
<tr>
<th>g) Other method (specify)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>h) I don’t use any strategies to ensure that patients complete the 3-dose series</td>
<td></td>
</tr>
</tbody>
</table>

8. In the past 12 months how often did you recommend the HPV vaccine to your female patients, in the following age groups?

<table>
<thead>
<tr>
<th></th>
<th>Never (0%)</th>
<th>Rarely (1-25%)</th>
<th>Sometimes (26-50%)</th>
<th>Often (51-75%)</th>
<th>Always (&gt;75%)</th>
<th>Do not see male patients in this age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Ages 11-12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Ages 13-17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>c) Ages 18-26</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

9. In the past 12 months how often did you administer, at least one dose of the HPV vaccine to your female patients, in the following age groups?

<table>
<thead>
<tr>
<th></th>
<th>Never (0%)</th>
<th>Rarely (1-25%)</th>
<th>Sometimes (26-50%)</th>
<th>Often (51-75%)</th>
<th>Always (&gt;75%)</th>
<th>Do not see male patients in this age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Ages 11-12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Ages 13-17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Ages 18-26</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

10. In the past 12 months how often did you recommend the HPV vaccine to your male patients, in the following age groups?

<table>
<thead>
<tr>
<th></th>
<th>Never (0%)</th>
<th>Rarely (1-25%)</th>
<th>Sometimes (26-50%)</th>
<th>Often (51-75%)</th>
<th>Always (&gt;75%)</th>
<th>Do not see male patients in this age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Ages 11-12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Ages 13-17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Ages 18-26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
11. In the past 12 months how often did you administer at least one dose of the HPV vaccine to your male patients, in the following age groups?

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Never (0%)</th>
<th>Rarely (1-25%)</th>
<th>Sometimes (26-50%)</th>
<th>Often (51-75%)</th>
<th>Always (&gt;75%)</th>
<th>Do not see male patients in this age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>d) Ages 11-12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Ages 13-17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) Ages 18-26</td>
<td></td>
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</tr>
</tbody>
</table>

12. In the past 12 months, how often did your male patients or parents of male patients, in the following age groups, refuse HPV vaccination (i.e. did not agree to vaccination currently or at a later date?)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Never (0%)</th>
<th>Rarely (1-25%)</th>
<th>Sometimes (26-50%)</th>
<th>Often (51-75%)</th>
<th>Always (&gt;75%)</th>
<th>Do not see male patients in this age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>d) Ages 11-12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Ages 13-17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) Ages 18-26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

13. During what type of patient visit do you mention HPV vaccination? (✓ all that apply)

- a) Acute care
- b) Preventive (e.g. well child visit or when patient is in for other vaccines)
- c) Other (specify) ____________________________

14. How often do you use HPV testing results to make a decision about whether to recommend the HPV vaccine to your female patients?

- □ Never
- □ Rarely
- □ Sometimes
- □ Often
- □ Always
15. Among your female patients age 26 years and younger, how often do you recommend HPV vaccination if they had an abnormal Pap test?

☐ Never  ☐ Rarely  ☐ Sometimes  ☐ Often  ☐ Always

☐ N/A - I don't perform Pap tests

16. Do you plan to change the frequency with which you provide Pap test screening to females who have received the HPV vaccine?

☐ Yes  ☐ No  ☐ Don't know  ☐ N/A - I don't perform Pap tests

17. In your opinion, what proportion of girls in Malta become sexually active by the age of 14? (Please √ only one)

☐ <10%  ☐ 10-25%  ☐ 26-50%  ☐ >50%

18. A regular Pap test with a frequency of 53 years reduces the lifetime risk of cervical cancer by: (Please √ only one)

☐ <50%  ☐ 51-70%  ☐ 71-90%  ☐ >90%  ☐ Not sure

19. The proportion of cervical cancer related to HPV-16 and HPV-18 types is: (Please √ only one)

☐ <40%  ☐ 40-60%  ☐ 61-80%  ☐ >80%  ☐ Not sure
20. Considering the proven efficacy and safety of the HPV vaccines, indicate your opinion regarding these statements: (for each row please mark one box).

<table>
<thead>
<tr>
<th>HPV vaccination should be given:</th>
<th>Strongly Disagree</th>
<th>Somewhat disagree</th>
<th>Somewhat agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) To girls before the beginning of sexually active lifestyles</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>b) To boys before the beginning of sexually active lifestyles</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>c) To all sexually active females</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>d) To all sexually active males</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>e) Only to individuals who have more than one sexual partner</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

| A vaccination program will eventually permit: | | | |
|-----------------------------------------------| | | |
| f) The beginning of screening later in life | □ | □ | □ | □ |
| g) The reduction of the frequency of screening interventions in vaccinated females | □ | □ | □ | □ |
| h) The reduction of the number of post-screening follow-up interventions | □ | □ | □ | □ |
| i) The abolishment of screening | □ | □ | □ | □ |

| I will recommend the HPV vaccine to my patients: | | | |
|-----------------------------------------------| | | |
| j) If it is publicly funded | □ | □ | □ | □ |
| k) Even if my patients have to pay for the vaccine | □ | □ | □ | □ |
| l) If they have to receive 2 doses of the vaccine | □ | □ | □ | □ |
| m) If they have to receive 3 doses of the vaccine | □ | □ | □ | □ |
| n) If it protects against both cervical cancer and anogenital warts | □ | □ | □ | □ |
| o) If it protects against cervical cancer | □ | □ | □ | □ |

| In your opinion most: | | | |
|----------------------| | | |
| p) Physicians will recommend HPV vaccination to their patients | □ | □ | □ | □ |
| q) Parents will accept HPV vaccination for their children less than 14 years of age | □ | □ | □ | □ |
20. Considering the proven efficacy and safety of the HPV vaccines, indicate your opinion regarding these statements: (for each row please √ one box) cont...

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Disagree</th>
<th>Somewhat disagree</th>
<th>Somewhat agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>r) Parents will prefer HPV vaccination to be given at school.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s) Adolescents and young adults will accept HPV vaccination.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t) Adolescents and young adults will seek HPV vaccination.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

21. The best age for a universal immunisation program is: (Please √ only one)

- [ ] <14 years
- [ ] 14-17 years
- [ ] >18 years

22. Please give your opinion about the following statements: (for each row please √ one box)

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Disagree</th>
<th>Somewhat disagree</th>
<th>Somewhat agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>My patients will comply if I counsel them about:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Safe sexual behaviour (condom, monogamy, etc)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Regular cervical screening (frequency ≥3 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) HPV vaccination</td>
<td></td>
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</tr>
</tbody>
</table>

23. Please indicate the importance of topics to be included in clinical training materials and clinical decision support tools to guide the prevention of HPV infection for doctors: (for each row please √ one box)

<table>
<thead>
<tr>
<th>Topic</th>
<th>Not at all important</th>
<th>Somewhat important</th>
<th>Important</th>
<th>Very important</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Natural history of HPV related disease</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>b) Epidemiology of HPV related infection</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>c) Vaccine development</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Vaccine safety profile</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) Vaccine efficacy and effectiveness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
23. Please indicate the importance of topics to be included in clinical training materials and clinical decision support tools to guide the prevention of HPV infection for doctors: (for each row please \( \checkmark \) one box) cont...

<table>
<thead>
<tr>
<th></th>
<th>Not at all important</th>
<th>Somewhat important</th>
<th>Important</th>
<th>Very important</th>
</tr>
</thead>
<tbody>
<tr>
<td>f) Impact of the vaccine on screening policy and practices</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>g) Cervical cancer screening and management of Pap results</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>h) Genital warts management</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>i) HPV counselling</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>j) Psycho-social issues related to HPV</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>k) Other (please specify)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

24. So far, the information you have received about HPV vaccines is? (please \( \checkmark \) only one)

- ☐ Not sufficient
- ☐ Somewhat sufficient
- ☐ Sufficient

25. How many hours do you spend in direct outpatient care per week? (choose one)

- ☐ <7 hours
- ☐ 7-21 hours
- ☐ >21 hours

26. Approximately what percentage of your patients is in each age group? (please specify for EACH age group)

|   | a) Under age 10 _____% | b) Age 10-14 _____% | c) Age 15-18 _____% | d) Over age 18 _____% |
27. Please indicate if it applies to your practice and how often: Please ✓ only one box for each row

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Sometimes</th>
<th>Weekly</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) I am directly involved in cervical cancer screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) I do colposcopies at my practice site</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Vaccines are given in my office</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Vaccines are given at the facility where I practice</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

28. Please indicate what you intend to do concerning HPV vaccination: Please ✓ only one box for each row

<table>
<thead>
<tr>
<th></th>
<th>Not all likely</th>
<th>Somewhat likely</th>
<th>Likely</th>
<th>Very likely</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) I will prescribe the HPV vaccine to my patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) I or my staff will administer HPV vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) HPV vaccines will be administered at the facility where I am practicing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

29. Which of the following describes your primary clinical specialty (choose one)

- [ ] Paediatrics
- [ ] Obstetrics/Gynaecology
- [ ] Family Medicine
- [ ] Other (specify) ________________

30. Where is your main outpatient practice located? Is it within? (choose one)

- [ ] Private practice office
- [ ] Health Centre
- [ ] Hospital department
- [ ] Other (please specify) ________________
31. Which of the following categories best describes your practice arrangement? (choose one)

- [ ] Full or part-owner physician practice
- [ ] Employee of physician-owned practice
- [ ] Government employee
- [ ] Other (specify) ____________

32. On a typical day in your primary practice, how many patients do you see? (choose one)

- [ ] <15
- [ ] 15-19
- [ ] 20-29
- [ ] 30 or more

33. Compared to your clinical peers you are often among the first to use a newly recommended vaccine.

- [ ] Strongly disagree
- [ ] Somewhat disagree
- [ ] Somewhat agree
- [ ] Strongly agree

34. You tend to wait to adopt new medications, vaccines or procedures until you hear about them from several trusted colleagues.

- [ ] Strongly disagree
- [ ] Somewhat disagree
- [ ] Somewhat agree
- [ ] Strongly agree

35. What is your gender?

- [ ] Male
- [ ] Female

36. What is your age?

[ ] years
37. How long have you been providing clinical care? ___________ years

38. In which town/village is your main practice located? ________________

Date of completion of questionnaire: ________________

Thank you for your participation in this survey. Please mail the survey in the larger postage-paid envelope (enclosed). Please mail your lottery ticket separately in the small postage-paid envelope (enclosed) so as to maintain your anonymity.
Appendix C

Covering Letter sent with postal questionnaire
28th January 2015

Invitation to participate in research project for dissertation for Masters in Public Health, University of Malta

Dear Doctor,

I am a trainee in Public Health Medicine who is currently reading for a Masters degree in Public Health at the University of Malta as part of my specialisation in this field. As part of the Masters course I am required to carry out a research project for which I am kindly requesting your assistance.

The title of my project is Missed Clinical Opportunities for HPV vaccination.

The main aim of this project is to try to understand what the knowledge, attitudes and beliefs of various medical practitioners with regards to the HPV vaccine are and what the barriers and facilitators for them to provide recommendations for it are.

I would therefore be very grateful if you could kindly complete this questionnaire, which should take around 20 minutes to fill in, and return it to me by the 21st February 2015 in the enclosed larger self-addressed envelope accompanying the questionnaire. Your anonymity throughout the study is guaranteed.

Respondents will be eligible to participate in a lottery for a small prize as a token of gratitude. The prizes consist of:

1st prize: €100 voucher at Quadro Restaurant, the Westin Dragonara Resort, St. Julian’s
2nd prize: €50 One4all voucher
3rd prize: €50 One4all voucher

Kindly complete the accompanying lottery ticket with your details and return it in the smaller SEPARATE self-addressed envelope which is also enclosed. This will ensure that your questionnaire is not identifiable.

The results obtained from this study will be published in my dissertation and may be used in any future publications pertaining to this same study. Once again I would like to assure you that no identifiable data will be used. Once the study is complete the questionnaires will be destroyed.

Should you have any queries, comments or need to contact me you may do so at the email address provided below.

Thank you very much in advance for your time and assistance,

Kindest regards,

Liliana Cuschieri

Researcher: Dr. Liliana Cuschieri MD FFPH
Email: liliana.cuschieri@gov.mt

Supervisor: Dr. Charmaine Gauci MD MSc PhD FRSPH
Email: charmaine.gauci@gov.mt
Appendix D

Ethics approval
Ms. Liliana Cuschieri
16
Triq tal-Grazja
Zebbug ZBG1058

Dear Ms. Liliana Cuschieri

Please refer to your application submitted to the Research Ethics Committee in connection with your research entitled:

**Missed Clinical Opportunities for HPV vaccination**

The University Research Ethics Committee granted ethical approval for the above mentioned protocol.

Yours sincerely,

Dr. Mario Vassallo
Chairman
Research Ethics Committee
Appendix E

Reminder letter
28th February 2015

Reminder for invitation to participate in research project for dissertation for Masters in Public Health, University of Malta

Dear Doctor,

A few weeks ago I sent an invitation requesting your kind assistance with my research project which is part of the Masters in Public Health which I am currently reading for at the University of Malta.

The title of my project is Missed Clinical Opportunities for HPV vaccination.

The main aim of this project is to try to understand what the knowledge, attitudes and beliefs of various medical practitioners with regards to the HPV vaccine are and what the barriers and facilitators for them to provide recommendations for it are.

I would first of all like to express my gratitude and appreciation to those doctors who took some time to reply to the questionnaire and return it.

I am also sending this reminder to those doctors who may have not yet had the time to complete it, or who may have misplaced the questionnaire, to kindly complete it and return it to me by the 14th March 2015 in the enclosed larger self-addressed envelope accompanying the questionnaire. Your anonymity throughout the study is guaranteed.

Respondents will be eligible to participate in a lottery for a small prize as a token of gratitude. The prizes consist of:

1st prize: €100 voucher at Quadro Restaurant, the Westin Dragonara Resort, St. Julian's
2nd prize: €50 One4all voucher
3rd prize: €50 One4all voucher

Kindly complete the accompanying lottery ticket with your details and return it in the smaller SEPARATE self-addressed envelope which is also enclosed. This will ensure that your questionnaire is not identifiable.

The results obtained from this study will be published in my dissertation and may be used in any future publications pertaining to this same study. Once again I would like to assure you that no identifiable data will be used. Once the study is complete the questionnaires will be destroyed.

Should you have any queries, comments or need to contact me you may do so at the email address provided below.

Thank you very much in advance for your time and assistance,

Kindest regards,
Appendix E - Reminder Letter

Liliana Cuschieri

Researcher: Dr. Liliana Cuschieri MD

Email: liliana.cuschieri@gov.mt

Supervisor: Dr. Charmaine Gauci MD MSc PhD FRSPH FFPH

Email: charmaine.gauci@gov.mt
Appendix F

Consent form to participate in focus groups
CONSENT FORM

I am a Maltese citizen and am over eighteen (18) years of age.

I have been asked to participate in a focus group for a research study entitled:

'Missed Clinical Opportunities for HPV vaccination'

The purpose and details of the study have been explained to me and any difficulties which I raised have been adequately clarified.

I give my consent to the Interviewer to make the appropriate observations based on my statements.

I understand that the results of this study may be used for medical or scientific purposes and that the results achieved from the study in which I am participating may be reported or published: however, I shall not be personally identified in any way, either individually or collectively, without my express written permission.

I am under no obligation to participate in this study and am doing so voluntarily.

I may withdraw from the study at any time, without giving any reason.

I am/ I am not receiving any remuneration for participating in this study.

In case of queries during the study I may contact Dr. LILIANA CUSCHIERI at liliana.cuschieri@gov.mt or Dr. CHARMAINE GAUCI at charmaine.gauci@gov.mt

Signature of participant ____________________________

Name of participant ____________________________

ID of participant ____________________________

Signature of Chief Investigator ____________________________

Name of Chief Investigator ____________________________

ID of Chief Investigator ____________________________

Date ____________________________
Appendix G

Summary of studies on Knowledge, Attitudes and Practices of healthcare professionals regarding the HPV vaccines
Table 2.6: Summary of studies on Knowledge, Attitudes and Practices of healthcare professionals regarding the HPV vaccines

<table>
<thead>
<tr>
<th>Author &amp; date of study</th>
<th>Study title</th>
<th>Country</th>
<th>Target group</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Lee Mortensen et al 2015&quot;</td>
<td>&quot;Parental attitudes towards male human papillomavirus vaccination: a pan-European cross-sectional survey&quot;</td>
<td>Europe (the UK, Germany, France and Italy)</td>
<td>Parents of sons in the UK, Germany, France and Italy</td>
<td>&quot;Parental acceptance of HPV vaccination of sons is as high as acceptance levels for girls when given brief information about HPV in both genders.&quot;</td>
</tr>
<tr>
<td>&quot;Smith et al 2015&quot;</td>
<td>&quot;Effect of human papillomavirus (HPV) vaccination on clinical indicators of sexual behaviour among adolescent girls: the Ontario Grade 8 HPV Vaccine Cohort Study&quot;</td>
<td>Canada</td>
<td>Adolescent girls</td>
<td>&quot;HPV vaccination does not have any significant effect on clinical indicators of sexual behaviour among adolescent girls; thus concerns over increased promiscuity following HPV vaccination are unwarranted and should not deter from vaccinating at a young age.&quot;</td>
</tr>
<tr>
<td>&quot;Perkins et al 2014&quot;</td>
<td>&quot;Missed Opportunities for HPV Vaccination in Adolescent Girls: A Qualitative Study&quot;</td>
<td>USA</td>
<td>Parents/guardians and health care providers</td>
<td>&quot;Missed opportunities result from assumptions about the timing of vaccination relative to sexual activity. Vaccination rates can be improved by routinely recommending HPV vaccination as cancer prevention to be coadministered with other vaccines at age 11 years; the most common reasons why parents do not vaccinate their daughters was lack of a physician recommendation.&quot;</td>
</tr>
<tr>
<td>&quot;Vadaparampil et al 2014&quot;</td>
<td>&quot;Physicians’ human papillomavirus vaccine recommendations, 2009 and 2011&quot;</td>
<td>USA</td>
<td>Physicians practicing family medicine, pediatrics, and obstetrics and gynecology in the USA</td>
<td>&quot;A modest increase in recommendations for HPV vaccination of girls aged 11 or 12 years over a 2-year period was observed; however, recommendations remain suboptimal for all age groups despite national recommendations for universal immunization.&quot;</td>
</tr>
</tbody>
</table>
| "Gertig et al" | "Impact of a population-" | Australia | Women age- | "A population-based HPV vaccination program
<table>
<thead>
<tr>
<th>Publication</th>
<th>Study Title</th>
<th>Country</th>
<th>Participants</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Opel et al 2013&quot;</td>
<td>&quot;The Architecture of Provider-Parent Vaccine Discussions at Health Supervision Visits&quot;</td>
<td>USA</td>
<td>Vaccine providers and parents</td>
<td>&quot;How providers initiate and pursue vaccine recommendations is associated with parental vaccine acceptance; parents had significantly higher odds of resisting vaccine recommendations if the provider used a participatory rather than a presumptive initiation format.&quot;</td>
</tr>
<tr>
<td>&quot;Vadaparampil et al 2013&quot;</td>
<td>&quot;Qualitative Responses to a National Physician Survey on HPV Vaccination&quot;</td>
<td>USA</td>
<td>Family Physicians, Pediatricians, and Obstetricians and Gynecologists in the USA</td>
<td>&quot;Physicians are developing various approaches to vaccine delivery within the context of their clinical practice; they are particularly attuned to specific vaccination issues including clinical practice guidelines and barriers to administration.&quot;</td>
</tr>
<tr>
<td>&quot;Perkins &amp; Clark, 2012&quot;</td>
<td>&quot;Providers’ Attitudes Toward Human Papillomavirus Vaccination in Young Men: Challenges for Implementation of 2011 Recommendations&quot;</td>
<td>USA</td>
<td>Physicians and nurse practitioners in community health centres</td>
<td>&quot;Majority of providers interviewed favoured vaccinating males yet only a small number offered vaccination. Providers who did not offer vaccination felt that parents would not be interested in vaccinating sons and were largely unaware of serious HPV-related disease in males.&quot;</td>
</tr>
<tr>
<td>&quot;Anhang Price et al 2011&quot;</td>
<td>&quot;Use of human papillomavirus vaccines among young adult women in the United States: An analysis of the 2008 National Health Interview Survey&quot;</td>
<td>USA</td>
<td>Women aged 18-26 years in the USA</td>
<td>&quot;HPV vaccine coverage among young adult women was low, especially among the uninsured. Public financing and care provision programs can help to expand vaccine coverage among uninsured women, who are at increased risk of cervical cancer; main reasons for lack of interest were belief that vaccine was not needed, not knowing enough about it, concerns about safety, and not being sexually active.&quot;</td>
</tr>
<tr>
<td>&quot;Farrugia, 2011&quot;</td>
<td>&quot;Attitudes towards human HPV vaccination program on cervical abnormalities: a data linkage study&quot;</td>
<td>Malta</td>
<td>First and final year</td>
<td>&quot;Students from all courses had a low level of</td>
</tr>
<tr>
<td>Study Reference</td>
<td>Study Title</td>
<td>Study Design</td>
<td>Study Population</td>
<td>Key Findings</td>
</tr>
<tr>
<td>-----------------</td>
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</tr>
<tr>
<td>Hughes et al 2011</td>
<td>&quot;HPV vaccine decision making in pediatric primary care: a semi-structured interview study&quot;</td>
<td>USA</td>
<td>Adolescent/mother/clinician triads</td>
<td>&quot;Programs to improve HPV vaccine delivery in primary care should focus on promoting effective parent-clinician communication. Strategies to help clinicians engage reluctant parents and passive teens in discussion need to be evaluated; teens considered themselves passive participants in decision making, even when parents and clinicians reported including them in the process.&quot;</td>
</tr>
<tr>
<td>Kennedy et al 2011</td>
<td>&quot;Vaccine attitudes, concerns, and information sources reported by parents of young children: results from the 2009 HealthStyles survey&quot;</td>
<td>USA</td>
<td>US parents of young children</td>
<td>&quot;To maintain and improve on the success of childhood vaccines in preventing disease, a holistic approach is needed to address parents' concerns in an ongoing manner; these include listening and responding in ways and with resources that address specific questions and concerns could help parents make more informed vaccination decisions; the most important sources of information on vaccines, for parents was a child's doctor or nurse.&quot;</td>
</tr>
<tr>
<td>Luttringer-Magnin et al 2011</td>
<td>&quot;Human papillomavirus (HPV) vaccination: Perception and practice among French general practitioners in the year since licensing&quot;</td>
<td>France</td>
<td>GPs in France</td>
<td>&quot;GPs in a major region of France showed a favourable opinion about the HPV vaccine and widespread use of it; there were some concerns that the recent introduction of the vaccine meant that the potential for side effects and the recommended target age of recipients were not yet fully understood.&quot;</td>
</tr>
<tr>
<td>Rosenthal et al 2011</td>
<td>&quot;Predictors of HPV vaccine uptake among women aged 19-26: Importance of&quot;</td>
<td>USA</td>
<td>Women aged 19-26 years</td>
<td>&quot;In women aged 19-26 years, those who discussed the HPV vaccine with their physician and received a recommendation were...&quot;</td>
</tr>
<tr>
<td>Study</td>
<td>Title</td>
<td>Country</td>
<td>Participants</td>
<td>Summary</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>---------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Vadaparampil et al 2011</td>
<td>&quot;Missed Clinical Opportunities: Provider Recommendations for HPV Vaccination for 11-12 Year Old Girls is Limited&quot;</td>
<td>USA</td>
<td>Family Physicians, Pediatricians, and Gynecologists in the USA</td>
<td>&quot;There were missed clinical opportunities for HPV vaccination; perceived barriers to vaccination may drive decisions about recommendation. There is a need for age and specialty targeted practice and policy level interventions to increase HPV vaccination among US females.&quot;</td>
</tr>
<tr>
<td>Daley et al 2010</td>
<td>&quot;Human papillomavirus vaccination practices: a survey of US physicians 18 months after licensure&quot;</td>
<td>USA</td>
<td>Paediatricians and family physicians in the USA</td>
<td>&quot;The vast majority of paediatricians and family physicians reported offering HPV vaccine. Fewer physicians strongly recommended the vaccine for younger adolescents than for older adolescents; the most frequently reported barriers to HPV vaccination were financial.&quot;</td>
</tr>
<tr>
<td>Krupp et al 2010</td>
<td>&quot;Factors Associated With Intention-to-Recommend Human Papillomavirus Vaccination Among Physicians in Mysore, India&quot;</td>
<td>India</td>
<td>Physicians from a range of specialties and practice settings in India</td>
<td>&quot;Knowledge about HPV infection and its relationship to cervical cancer was low among physicians across specialties; most physicians expressed positive attitudes toward vaccination in general, and HPV vaccination in particular, but the overwhelming majority believed that few of their patients would react positively to a vaccine recommendation; there were concerns about talking to parents about their adolescent daughters' reproductive lives. There is a strong need to provide more education for physicians about the relationship of HPV infection and cervical cancer and the benefits of vaccinating adolescent girls to prevent cervical cancer in the future.&quot;</td>
</tr>
<tr>
<td>Piana et al 2009</td>
<td>&quot;Standpoint and practice concerning the human Papillomavirus vaccine&quot;</td>
<td>France</td>
<td>French family physicians</td>
<td>&quot;The majority of family physicians were in favor of HPV; the ideal age for vaccination was felt to be between 14 and 15 years of age. Family...&quot;</td>
</tr>
</tbody>
</table>

*Appendix G - Summary of studies on KAPs*
<table>
<thead>
<tr>
<th>Study Reference</th>
<th>Title</th>
<th>Country</th>
<th>Population</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Daley et al 2006&quot;</td>
<td>&quot;A national survey of pediatrician knowledge and attitudes regarding human papillomavirus vaccination&quot;</td>
<td>USA</td>
<td>Paediatricians in the USA</td>
<td>Paediatricians expressed a high level of acceptance of human papillomavirus vaccination in older adolescent females yet fewer than one half anticipated giving the vaccine to younger female patients. Concerns focussed on parental vaccine acceptance which will need to be addressed to optimize human papillomavirus vaccination implementation.</td>
</tr>
<tr>
<td>&quot;Smith et al 2006&quot;</td>
<td>&quot;Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage&quot;</td>
<td>USA</td>
<td>Health care providers and parents of young children</td>
<td>Health care providers have a positive influence on parents to vaccinate their children, including parents who believe that vaccinations are unsafe.</td>
</tr>
<tr>
<td>&quot;Anhang et al 2004&quot;</td>
<td>&quot;Women's Desired Information about Human Papillomavirus&quot;</td>
<td>USA</td>
<td>Ethnically-diverse, low income women</td>
<td>Effective HPV education must include information about transmission, prevention, treatment, and cervical carcinoma risk as well as clarification about HPV strains and different types of tests and their results; it must be tailored according to patient age and risk profile; need to provide a balance between accurate discussion of cancer risk and reassurance that following recommended screening practices will reduce risk to negligible level.</td>
</tr>
</tbody>
</table>

Physicians most in favor of vaccination were those involved in screening for STDs, those who did not think that the vaccine would have a negative effect on the image of sexuality and on screening for cervical cancer, and those who were confident about the vaccine safety.