Awareness, knowledge and utilization of the Human Papillomavirus Vaccine

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I, Naseera Allie hereby declare that the work on which the dissertation is based on is original and is my own unaided work carried out by me under the supervision of Dr M Moodley. This work has not been submitted previously to this or any other university.

SIGNED……..

DATE:……..

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ABSTRACT

OBJECTIVES

To determine if health care workers are aware of the HPV vaccine and its availability, uptake of the vaccine and prescribing practices and reasons for non – uptake of the vaccine .

METHODS

Health care providers working in the private sector, in the Ethekweni health district in Kwazulu Natal, were interviewed. Health care workers included: 100 general practitioners, 50 gynaecologists, 50 paediatricians, 50 medical staff and 50 nursing staff. A questionnaire was designed for purpose of this study. Visits were be made to health care providers. All heath care providers who were willing to participate were interviewed.

STATISTICS

Comparisons of awareness among subgroups of health care providers was analysed using Chi-square tests. If significant, pairwise comparisons were made using a Bonferroni adjustment for multiple comparisons. Associations between awareness and other factors, such as demographic, uptake and beliefs were tested using a chi square test. Analysis was done by Stata v11 (StataCorp, 2009)

RESULTS

Three hundred health care workers were interviewed - 50 gynecologists (16.7%), 52 pediatricians (17.3%), 99 general practitioners (33%), 49 other medical doctors (16.3%) and 50 (16.7%) nurses. Two hundred and sixty seven health care workers (89%) were aware of the HPV vaccine and one hundred and eighty eight health care workers (70.4%) informed patients of the availability of the HPV vaccine. Most (77.9%) practitioners have only prescribed the vaccine less than ten times. Gardasil® was prescribed by 46%, Cervarix® by 6.5% and prescription of either vaccine of health care workers was 50.2%. Practitioners were generally unaware that Gardasil® could be prescribed to males (62.9%).

CONCLUSION

Health care workers were aware of the HPV vaccine and prescribed the vaccine on request. However even though practitioners were aware of the vaccine, most have prescribed the vaccine less than ten times since licensing in 2008. Knowledge with regards to the licensed use of the HPV vaccines is deficient.

CHAPTER 1

Cervical Cancer

Cancer of the cervix is the second most common cancer worldwide and accounts for approximately 80% of cases in developing countries.[1] In South Africa cervical cancer has an overall age standardized incidence rate (ASIR) of 22 per 100,000 cases per year and is the most common cancer amongst females.[1, 2] There are approximately 5743 new cases of cancer of the cervix diagnosed every year in South Africa and about 3027 women die of the disease each year.[2] Over the past few years the cervical cancer prevalence and mortality rates in the United States have decreased mostly as a result of cytological screening. Despite this, approximately 10 400 new cases of invasive cancer of the cervix and 3700 deaths occurred from the disease in 2005 in the United States.[3] This is contrary to the high incidence in the developing world of cervical cancer and is an indication of poor access to health care resources.[4] The incidence of cervical cancer in 2000 was 471,000 new cases; of which the mortality was 233, 000 cases worldwide.[5] Eighty per cent of cases occurred in developing countries although they have less than 5% access to the global cancer care resources. The age standardised incidence rates (ASIR) of cervical cancer in Southern African countries is shown in Figure 1.[2] South Africa has a rate of 26.6 cervical cancer cases per 100, 000 women per year; however Swaziland and Lesotho have the highest age standardized incidence rates of 50 and 35 per 100, 000

women per year of cervical cancer cases respectively. Differences can be attributed to different levels of cervical screening. Data collection is limited in numerous third world countries and the existing data is likely an underestimate of the true incidence of disease.

A pathology-based cancer registry was launched in South Africa in 1986. The information was obtained from laboratory reports in both public and private sectors. In 1986, the cancer registry showed that of all the cancers reported in women, 16, 559 were incident cases which comprised 2,897 (17.4%) of histologically confirmed cervical cancers.[6] In the South African cancer registry of 1993–1995, approximately 3,387 annual incident cases of cervical cancer were reported.[7] Mortality of women with cervical cancer for the year 1994 was reported to be 1,497. The age standardized incidence rate of cancer of the cervix in 1994 was 22/100,000. This figure was subdivided according to race groups - African females had a rate of 27/100,000. These represented the most disadvantaged women in South Africa in terms of health care access. Black African women had a lifetime risk of 1 in 34 for developing cervical cancer which is in contrast to 1 in 93 for White women.

A study performed in 2002 reflected the occurrence of cervical cancer in Black African women in Durban.[8] For women living in urban areas the age standardized incidence rate was 45/100,000 and two thirds of the lesions were stage III and IV, with a mean age of presentation of 52 years.

The figures will most likely change as data have shown that HIV (Human Immunodeficiency Virus) positive women have a higher risk of developing pre-cancerous lesions and cancer of the cervix.[9] Another study reported an accelerated clinical progression of premalignant cervical lesions to invasive cervical carcinoma in HIV-infected females.[10] In 1993 cervical cancer was included as one of the defining conditions of the acquired immune deficiency syndrome (AIDS).[11] A local study conducted in Durban, South Africa demonstrated a HIV prevalence of 21% in women with cervical cancer.[12] It was also found that women who were HIV-seropositive were about 15 years younger than women who were HIV-seronegative, however the stage of disease at presentation did not differ significantly. The available evidence suggests that the expression of HPV (Human papillomavirus) infection is greater in HIV infected women and the rate of progress is more rapid from initial HPV infection to the development of cancer of the cervix.[13] It has also been shown that women who are infected with high risk HPV subtypes and HIV have a 40 fold increased risk of developing a precancerous cervical lesion.[14]

CHAPTER 2

Human papillomavirus (HPV)

Human papillomavirus (HPV) is a small, double-stranded deoxyribonucleic acid (DNA) virus containing eight genes. HPV- related disease can occur at various locations in the body. In the female genital tract the most common association is cancer of the cervix and its precursor, cervical intra-epithelial neoplasia (CIN).[15] Other associations with HPV include anal, vaginal and vulval intraepithelial neoplasia (AIN,VAIN, VIN) as well as other cancers.Although these are not as common as CIN, they can also progress into invasive diseases at these sites. In the male genital tract HPV is associated with anal disease (AIN), penile cancer and penile intraepithelial neoplasia (PIN). HPV infection in males and females can also lead to genital warts which are benign. Other HPV related diseases can occur in epithelial tissues such as skin or mucous membranes of the head and neck where it can cause oro-pharyngeal cancers.[11]

The HPV types can be categorised into groups depending on the risk of oncogenicity. In 2003 described high risk (HR) and low risk (LR) groupswere described.[16] High risk HPV types include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68. Low risk types include HPV 6, 11, 42, 43 and 44.[16] HPV types 16 and 18 are the causative agent in approximately 70% of cervical cancers worldwide. About 20% of cervical cancers are caused by HPV types 31,

33, 35, 45, 52 and 58. Adenocarcinomas are largely associated with HPV 18 and HPV 45.[17] In South Africa HPV 16 and 18 has been found to be the most prevalent in cervical cancer. [18]

Infection with HPV is endemic in sexually active populations. After a sexual encounter the exposure to HPV peaks with a prevalence of 20-60%. By the age of 50 years approximately 80% of women who are sexually active would have been infected with HPV. HPV infection is transient as it has been shown by epidemiological studies that about 90% of infections do not cause major illness. Data have shown that after an infection, 50% of females will have a negative test at six months, 70% at one year and 80-92% at two years.[16] The body's natural immune response clears the infection. It is less likely that a transient infection will cause high grade CIN than a persistent infection. Infections which are transient can lead to low grade CIN (CIN 1) preceding the body's ability to clear the virus. Persistent infection is caused by high risk subtypes rather than low risk subtypes.

Infection which is persistent over a long period of time, can lead to high grade cervical intraepithelial neoplasia (CIN 2 or 3) and cancer of the cervix. Viral infection that persists with mainly high risk types (e.g. HPV 16 and 18), enhances the risk of high-grade CIN (CIN 2 or 3) and cancer of the cervix. Spontaneous regression can occur in high grade CIN; although the current management is to treat the lesions. High grade CIN lesions can progress to cervical cancer. In an unscreened population progression to cervical cancer is 5% for high risk

infections but in a population that is screened the risk is reduced to 1-2%. Immunocompromised patients e.g.HIV infected and immunosuppressive medication use, are at a higher risk of persistent infection resulting in high-grade dysplasia.

CHAPTER 3

Cervical Cancer Screening

Prevention of cervical cancer includes primary and secondary prevention. Decreased exposure by altering sexual practices (e.g., monogamy for life and the use of barriers contraception) and vaccination are included in primary prevention. Papanicolaou (pap) smears for precancerous lesions, screening for HPV, and removal of HPV-infected precancerous lesions by laser, cryosurgery, large loop excision of the transformation zone (LLETZ) and cervical cone biopsy are included in the concet of secondary prevention.[19]

Cervical cancer is the most prevalent cancer; however it can be prevented through screening and treatment of cervical intraepithelial neoplastic lesions.[20] Cervical cancer could very well be almost eliminated in South Africa if screening and treatment were sufficient.[21] Mortality related to cervical cancer has been decreasing in developed countires through screening programmes and treatment of early lesions. Implementation of nationwide screening in the 1960's in Nordic countries has shown a decrease in trend in cervical cancer. Iceland had the greatest fall (84% from 1965 to 1982) where there screening interval was the shortest and the target age ranges the widest.[22] In Norway 5% of the population were screened resulting in the smallest reduction of 11%.[22]

Screening programmes in resource- poor settings have been hard to introduce.[23] Barriers to implementation include: reduced awareness of the disease and the role of screening; failure of women to avail themselves for screening; low budget allocation for screening purposes and the demands of challenging health needs such as HIV infection, tuberculosis and other common diseases.

South Africa only implemented a national cervical cancer screening policy since the 1990's. Screening of the cervix, mainly in antenatal and family planning clinics were carried out opportunistically. This reached mainly women who were younger and who were not the target group who would most benefit from screening as they have reduced rates of diseases of the cervix than women who are older.[24,25] In 2000 the South African National Department of Health recognized cervical cancer as a national health priority. A national cervical screening policy was launched. The policy states that all women attending public sector services are allowed three free Papanicolaou smears in their lifetime starting at the age of 30, 10 years apart. The programme was expected to decrease the incidence by half of cervical cancer if it achieved over 75% coverage and this is assumed 100% coverage of the population.[24] In KwaZulu-Natal in 2005, 28 760 smears were performed, accounting for only 26% of the number of targeted smears for 2006 and 2007. In South Africa, during 2005–06, 100% of clinics offering primary health care had health care workers educated to perform pap smears, and still the rate of screening was only 1.3%[26]. The

economic load is considerable with treatment of cervical intraepithelial neoplasia lesions and the follow-up of false-positive cervical cytology.[27]

No statistics are available from the private sector of South Africa, although the impression is that women are over-screened. This practice is thus only available to those that can afford medical aid which represent less than 10% of the population.

CHAPTER 4

HPV Vaccine

Primary prevention of cervical cancer involves prevention of *de novo* HPV infection of the cervix. Vaccination against certain HPV types is potentially an effective method.

Two prophylactic HPV vaccines developed recently aims at primary prevention. These vaccines are recombinant adjuvant adsorbed and include a bivalent vaccine targeting HPV 16 and 18 (Cervarix®; GlaxoSmithKline) and a quadrivalent vaccine targeting HPV 16, 18, 6 and 11 (Gardasil®; Merck, Sharpe & Dohme). These vaccines have shown sustained efficacy and safety profiles up to 7 years. Three doses need to be administered over a six month period to ensure effective pharmocodynamics.[28, 29] The vaccines have been licensed in March 2008 for use in South Africa and are currently only available in the private health sector. It is recommended for girls 11 to 12 years old, but Gardasil® is approved for females 9 to 26 years and males 9 to 17 years. Cervarix® is approved for females aged 9 to 26 years. For maximal efficacy the vaccine must be given before sexual debut and thus before the possible exposure to HPV.[30] Recently (November 2010), the Food and Drug Association (FDA) approved a new indication for Gardasil® viz, it may be used to prevent cancer of the anus caused by HPV types 16 and 18 and for the prevention of anal intraepithelial neoplasia

(AIN) grades 1, 2, and 3 (anal dysplasias and precancerous lesions) caused by HPV types 6, 11, 16, and 18, in males and females aged 9 to 26 years.[30]

The vaccines have been extensively assessed in placebo-controlled trials and have shown to be effective and resulted in a more than 90% reduction in the number of persistent infections and HPV-associated genital diseases which are caused by the types of HPV included in the vaccines.[32] If a persistent HPV infection has already developed the vaccine may not be as effective. A major source of protection afforded by the vaccines is believed to be serum neutralising antibodies.[34, 35] After naturally acquired infection the concentration of antibodies are low.[36] Females who have acquired naturally HPV infection remain at risk for infection with the identical HPV type. This is possible since antibody concentrations after infection acquired naturally are insufficient to offer protection.[34] Poor antibody assay specificity could be attributed to these results.

A study has shown a sustained high concentration of IgG antibody to HPV 16 after infection acquired naturally resulting in a decreased risk of successive infection with HPV 16 and related types, but those with a lower concentration of IgG antibody did not have protection.[36] In the absence of a serological correlate of protection, higher neutralising antibody concentrations should be induced by vaccination than infection acquired naturally.[37,38] To date (>7 years) the vaccine has produced high antibody titres that have lasted with no need for booster doses.[39]

Quadravalent HPV 6/11/16/18 L1 Virus like particle vaccine (Gardasil®) has been evaluated in 2 large randomized control trials – FUTURE (Females United To Unilaterally Reduce Endo/ectocervical disease) II and I.[40,41] Findings from FUTURE II trial have shown that the HPV-16/18 AS04-adjuvanted vaccine in healthy females aged 15–25 years provided a high, sustained efficacy for the development of CIN 2 or 3, adenocarcinoma in situ and cervical cancer. The FUTURE I trial showed an efficacy of 100% in preventing anogenital disease in women who were HPV naïve. Vaccine efficacy was 100% in preventing CIN grades 1 to 3 or adenocarcinoma in situ. Secondary analyses of data from the FUTURE trials demonstrated partial protection against acquisition of the non vaccine HPV types (HPV31/33/45/52/58). In both FUTURE trials, no evidence was found that vaccination changed the course of disease or infection in women who had evidence of HPV infection at the time of receipt of the first dose of vaccine. This data reinforce the use of the HPV vaccine to prevent infection rather than treatment of pre existing HPV infection.

Cervarix® has been evaluated in one large, randomized clinical trial – PATRICIA (Papilloma trial against cancer in adults) [42] and an autonomous US National Cancer Institute (NCI).[43] In the PATRICIA trial vaccine efficacy for the prevention of CIN 2 or 3, adenocarcinoma in situ, or cervical cancer was 93%. Vaccine efficacies for the prevention of incidentally-detected 6 month and 12 month persistent infections by HPV 16/18 were 94% and 91%, respectively. Cervarix® demonstrated partial protection against acquisition of the non vaccine HPV types

(HPV31/33/45/52/58). The vaccine is used to prevent infection rather than as a treatment for pre- exsiting infections and related diseases. Excellent antibody responses have been reported with Cervarix®, with sustained high antibody concentrations after 6.4 years follow up. Assessment of the immunogenicity of the quadravalent and bivalent vaccines,[44] showed that immunization by Cervarix® induced titres of serum neutralizing antibodies 2.3 to 4.8 fold higher for HPV 16 and 6.8 to 9.1 fold higher for HPV 18. The long term duration of protection is however unknown.

A schedule for dosing which is a possible alternative to the standard schedule has been compared in healthy females aged 15 to 25 years. The results indicated that the third dose of the HPV-16/18 vaccine can be given any time between 6 and 12 months after the first dose resulting in immunogenicity which is adequate as well as having an acceptable clinical safety profile.[45]

There are concerns about an increase in unsafe sex practices and possible false impression that HPV vaccine would confer protection against other sexually transmitted infections (STIs). A possible theoretical risk of the HPV vaccine is a reduction of cytological screening for cancer of the cervix arising from the belief that screening is unnecessary. This might occur as a result of an inaccurate belief that prevention by screening is not needed or due to uncertainty about Papanicolaou smear schedules which may alter after extensive use of the vaccine. Cancer of the cervix will not be eliminated as some females are already

infected with HPV types 16 and 18. The vaccine is not 100% effective as other HPV types can also cause cervical cancer are not included in the vaccines.

Neither HPV vaccine should be routinely given during pregnancy. However if a patient is found to be pregnant and has already received a vaccine, the remaining doses should be given after pregnancy completion. Further studies are required to determine the actual risk.[46]

The effectiveness of the HPV vaccine uptake will depend largely upon whether providers advise the vaccine to patients and are able to attain high rates of immunization.[47] Health benefits will be likely with large-scale acceptance resulting in a decreasing morbidity and mortality associated with cervical cancer and by decreasing the psychosocial burden of both genital warts and abnormal cytological smear results.[48] An important step to establish an effective vaccine delivery program is to be aware of providers' intention to recommend and prescribe immunization.[49] There are several factors associated with the likelihood of providing the HPV vaccine i.e. characteristics of the provider, or that of the practice and knowledge and attitudes about HPV vaccination.[49] Despite studies revealing that clinicians are likely to recommend the HPV vaccine there are limitations with regard to recommendations for younger adolescents.[44] These are related to the physician's characteristics, knowledge, and attitudes about HPV vaccines.[50] Physician-attitudes regarding HPV vaccines may differ from those regarding childhood vaccines. This may be related to their prejudices against

immunizing children against sexually transmitted infections (STIs), or poor communication with preadolescents regarding sexually transmitted infections. Provider attitudes may be related to the disease targeted (cervical cancer vs. genital warts) or patient characteristics.[50]

Pediatricians' views regarding successful HPV vaccine delivery plans is important given their vital role in other vaccinations to children and their extensive clinical knowledge of vaccines in children. Pediatricians play an important role in HPV vaccine delivery to adolescents as they are more likely to seek medical care from a pediatrician than any other health care worker.[50] HPV vaccine uptake could be affected by factors associated with patient-provider communication. Studies show that the quantity and accuracy of the information presented by providers and patients' personal experience may persuade patient and caregiver acceptance of the vaccines.

Preventing cervical cancer with the HPV vaccine will only be realised if the vaccination is extensively implemented. HPV vaccines have received media support and health care physicians working in the private sector have approved its use. Immunization would be most beneficial to the developing countries, where women do not have access to clinics to have regular Papanicolaou smears. Challenges in developing countries could possibly be due to cost of the vaccine, distribution as well as access to the vaccine and personal beliefs with regard to vaccination against a sexually transmitted infection.[51] Cost and

availability represent important system-based factors that could prohibit vaccine uptake.[52] An important issue to address is the cost as at present in Durban, the Gardasil® vaccine is priced at R902 and Cervarix® R518 per injection. If the vaccine could be made available at a significantly reduced cost, uptake of the vaccine would be improved. The HPV vaccine has been shown to be a highly cost-effective health intervention especially when compared to cost of treatment of cervical cancer .[53] Treatment of cervical cancer may be required for many months after diagnosis, especially for women with late-stage cancers. The cost of diagnosis and treatment of stage I cervical cancer is R29,997 per woman vs. stage IV R55,997 per woman. [54]

The promotion of the HPV vaccine is important to its acceptance and compliance amongst young females and parents. The belief that a vaccine against an STI might promote unsafe sexual behavior has received interest in the media.[55, 56, 57] Currently it is uncertain whether vaccination would promote unsafe behavior. [55] The resistance to implementation of the vaccine could potentially be overcome with sufficient advice and information. The focus should be on the vaccines preventive properties against cervical cancer.[58] At present interventions such as providing adolescents with condoms and emergency contraception has not resulted in improved sexual behavior .[59,60]

Implementing the vaccine in developing countries is associated with a number of limitations. Countries mostly lacking the resources to attain effective screening programmes would therefore benefit from the extensive rollout of a preventive HPV vaccine. Interventions that do not have an immediate impact on health care can only be funded if the benefits are worth the expense. The reduction of cervical intraepithelial lesions over the next few years will be small and priority to vaccinate will therefore be low.[61]

As mentioned the high cost of the vaccine is concerning as this has implications for vaccination programs as cancer of the cervix is important among females from disadvantaged populations. In low income countries the HPV vaccines may not be affordable.[62] A South African study showed the addition of the HPV vaccine to the present cervical cancer screening policy can be cost effective.[62] HPV vaccines can most likely decrease the cost to the health system as well as reduce the cost to the patient.

It is still important to have a functional screening programme which is aimed at secondary prevention, as cancer of the cervix is not completely eliminated by vaccination against HPV, but instead the risk is decreased. In settings with low screening coverage like South Africa, where screening is less than 50% and treatment of cervical intraepithelial neoplastic lesions is well below 100%, the implementation of another preventative measure is beneficial.

The rationale for undertaking this research project was to establish the awareness, knowledge and utilization of the HPV vaccine amongst different health care workers. Practitioners in obstetrics and gynecology normally care for females who have developed the sequelae of HPV infection and they would therefore be critically involved in preventing HPV infection. General practitioners will play a major role in preventing HPV-related disease by the vaccination of girls and young women aged 9 to 26 years as well as provide primary care to children. Pediatricians will play a role in education of the HPV vaccine as girls and early adolescents are likely to visit a pediatrician. Their recommendation is likely to influence parent's or adolescent's decision to receive the vaccine. Nurses play a role in primary health care and therefore should provide valuable information to adolescents and parents with regards to the HPV vaccine. In addition other medical professionals may also be faced with the chance to recommend or prescribe the HPV vaccine when given the opportunity. It is therefore important to assess knowledge and uptake of the HPV vaccine amongst these different health care workers.

CHAPTER 5

STUDY: Awareness, Knowledge and Utilization of the Human Papillomavirus Vaccine

Aims

The aim of this study was to examine the knowledge, attitudes and utilization of the HPV vaccines amongst health care workers - gynecologist, pediatricians, general practitioners, nurses and other medical professionals.

Materials and Methods

The research protocol was approved by the University of Kwazulu Natal (UKZN) College of Health Sciences postgraduate committee and UKZN biomedical research ethics committee. (BE 118/09).

Study Sample

The study population consisted of a random sample of 300 health care providers. This included 100 general practitioners, 50 gynaecologists, 50 paediatricians, 50 other medical staff and 50 nursing staff.

A sample size of 256 health care providers was required to measure the awareness of the HPV vaccine to within ± 6% with a probability of 95% assuming an awareness of 50%. A stratified sample was selected. Awareness among general practitioners can be estimated to within ± 11% and to within ± 15% for the other groups. If a non-response rate of 15% is assumed, a sample size of 300 should be selected.

Study Design

Health care providers (pediatricians, general practitioners, obstetricians, medical staff and nursing staff) in the Ethekweni health district in Kwazulu Natal were interviewed. Other medical staff included specialists (excluding pediatricians and gynecologists) in other fields e.g. anesthetists and physicians. The interviews were conducted between July 2010 and December 2010. As the vaccine is currently only available in the private sector since March 2008, only private practitioners were interviewed. Interviews were conducted in clinicians' rooms as well as at various professional meetings which health care workers attended. All

participants in the study were asked to fill out a questionnaire at the time of the interview. The questionnaire was based on semi- structured and structured questions (see appendix A). The responses were anonymous. Participants were assured that individual information would be private and anonymity maintained. Important aspects explored included: knowledge of current cervical screening policy in South Africa, awareness of the HPV vaccine; target populations and profile of patient that the HPV vaccine would be prescribed to; and patient and prescribers beliefs.

Limitations of the study were that only practitioners practicing in the private sector were interviewed. Ethical considerations included: no direct patient interaction, only health care providers who consented to participate in the study were interviewed, the questionnaire had numbers for references and no names of practitioners were recorded and all the information obtained were kept confidential and solely for the purpose of the study.

DATA/ STATISTICAL ANALYSIS TECNIQUES:

Data regarding the number and reasons for refusals or non participation will be presented and where possible compared to those participating to determine any non-response bias. Frequencies and percents will be presented for all categorical data including 95% confidence intervals. All data was categorical and all comparisons were made using categorical data.

Comparisons of awareness among subgroups of health care providers were analysed using Chi-square tests. If significant, pairwise comparisons were made using a Bonferroni adjustment for multiple comparisons. Associations between awareness and other factors, such as demographic, uptake and beliefs were tested using a chi square test. A sub analysis of prescribing practices of those using the HPV vaccine will also be presented. Sub group comparisons and tests of association were done using Chi Square tests or exact tests as above. Reasons for not prescribing were collected in an open ended question, coded and reported.

Data was entered into Excel. All open ended questions were coded prior to data entry. Analysis was performed with Stata v11 (StataCorp, 2009).

CHAPTER 6

RESULTS

Three hundred health care workers were interviewed - 50 gynecologists (16.7%), 52 pediatricians (17.3%), 99 general practitioners (33%), 49 other specialists (16.3%) and 50 (16.7%) nurses. The provider characteristics in terms of age, gender, time practicing and patients being either medical or cash paying are shown in Table I. Most of the interviewed health care providers were in the age group 40-60 years (53%). The HPV vaccine was commonly prescribed by health care workers practicing for 10-20 years (46%). Most health care workers were treating patients who had medical aid, rather than cash-paying patients (65.7% vs. 34.3%).

The results indicated that 93% of health care workers were aware of the cervical screening programme in South Africa (Table II). One hundred and eighty one health care workers (60.3%) informed patients of HPV- related diseases. Most nurses (82%) and gynaecologists (76%) informed patients about the HPV-related illnesses.

Two hundred and sixty seven health care workers (89%) were aware of the HPV vaccine (Table II). One hundred and eighty eight health care workers (70.4%) informed patients of the availability of the HPV vaccine (Table II). There were 231 health care workers (86.5%) who prescribed the vaccine on request. If they did

not prescribe the vaccine reasons given were either that patients did not request the vaccine – 27%, they did not see patients that needed the vaccine – 30.6%, it did not come up in consultation – 22.2% and it was for the gynaecologist to prescribe – 11.1%. If they did prescribe the vaccine the target age group were females aged 9-26 (58.9%), sexually active patients – 8.2%, females of any age – 22.5% and on request only -10.4%. If health care workers were prescribing the vaccine, the number of times the vaccine was used was mostly less than 10 times (77.9%).

The specific HPV vaccine health care workers prescribed are shown in Table II. The results indicated that Gardasil® was prescribed by 100 health care workers (43.2%), Cervarix® by 15 health care workers (6.5%) and prescription of either vaccine (Gardasil or Cervarix) was 116 health care workers (50.2%). Reasons for choice of vaccine included HPV coverage - 42.86%, cost – 13.9% and patient choice – 12.1%. Two hundred and four providers (88.3%) indicated that patients returned for follow up doses. One hundred and thirty three health care providers (44.3%) indicated that patients requested the vaccine. There were 188 health care workers who were not aware that Gardasil could be prescribed to males (Table II).

Most health care workers (69.7%) believed that the vaccine was effective. Some indicated that more media coverage is needed (3.3%),2% feared the side effects, 3% believed it is expensive and 1% believed it promoted promiscuity.

Patient's beliefs with regard to the vaccine as determined by the health care worker: 46% were largely unaware of the vaccine, 39.7% believed it is effective and prevents cancer, 5.3% believed the doctor, 4% felt that media coverage was needed, 2.3% indicated the vaccine would promote promiscuity and 2.7% thought the vaccine was too expensive.

Demographics of healthcare workers awareness of the human papillomavirus vaccine are shown in Table III. Gynecologists, paediatricians and most general practitioners were aware of the HPV vaccine. Thirty seven other specialists (75.5%) were aware of the vaccine as well as 30 nurses (60%). The results indicated that there was no association between age and awareness, ($p = 0.2$). Males were significantly more aware than females of the vaccine, 96% vs 80% ($p < 0.001$). There was also no association between time in practice and awareness ($p = 0.2$). Health care workers who treated mainly medical aid patients were more likely to be aware of the vaccine than those who treated mainly cash-paying patients (84% vs. 91%) ($p = 0.07$).

Uptake of the vaccine among those health care providers who were aware of the vaccine is shown in Table IV. Most gynaecologists (96%), paediatricians (94%), general practitioners (90.8%) and nurses (100%) prescribed the vaccine. However, only 15 other specilaists (40%) prescribed the vaccine. There was no association between uptake of the vaccine and age ($p = 0.7$) or sex ($p = 0.2$),

time in practice ($p = 0.6$) or type of patients being treated either medical aid or cash paying ($p = 0.9$).

Utilisation of the vaccine amongst health care providers who prescribed the vaccine is shown in Table V. Results indicate that most health care workers prescribed the vaccine less than 10 times. Younger health care workers (< 40 years) were more likely to prescribe the vaccine 10-20 times, (20%) since licensing whereas health care workers 40-60 years of age tended to prescribe the vaccine more than 20 times (13%) ($p < 0.001$). The longer a health care worker was in practice (>20 years), the more frequent the vaccine was prescribed.

CHAPTER 7

DISCUSSION

Cervical cancer is the second most common cancer in women worldwide and the most common in developing countries. In Africa it is estimated that 78 897 women are diagnosed with cervical cancer annually and 61 671 (78%) demise from the disease. HPV types 16 and 18 account for 70% of cervical cancer cases worldwide and for 63% of those in South African women.[2] The main aim of HPV vaccines is primary prevention of HPV infections. Two prophylactic vaccines, with a sustained efficacy after 7 years and a good safety profile have been licensed in 2008 for use in South Africa for use. The vaccines currently available are a bivalent vaccine targeting HPV 16 and 18 (Cervarix®; GlaxoSmithKline) and a quadrivalent vaccine targeting HPV 16, 18, 6 and 11 (Gardasil®; Merck, Sharpe & Dohme).

Studies regarding knowledge about HPV disease and its prevention vary across specialties and seem to correlate with active involvement in screening and with the likelihood of having received education about HPV infection and its consequences. Gynecologists demonstrated the highest level of knowledge, followed by family physicians and paediatricians.[63] This study also showed that gynaecologists, paediatricians and general practitioners were mostly aware of the vaccine. This is understandable as they are the clinicians that treat the target

population – young males and females, and they are also involved in counseling and treatment about STI's. Other specialists seem to be aware of the vaccine but largely did not prescribe the vaccine. Nurses are least aware of the vaccine, but those that were aware have administered the vaccine to patients.

Health care providers who informed patients about the HPV vaccine comprised 70%, though 89% of providers were aware of the vaccine. This implies that even though they were aware of the vaccine they did not prescribe it. Reasons for this could be due to the fact that specialists in various disciplines are more likely to deal with specific conditions related to their specialty or that they may not have had enough knowledge about the vaccine to counsel patients and prescribe the vaccine. Practitioners may not be treating patients holistically but rather targeting care to the specific problem that patients present with. They might also expect the gynecologist, paediatrician or family practitioner to counsel and offer patients the vaccine.

Most physicians believe HPV vaccines should be administered to girls before the onset of sexual activity.[63] Similarly this study also showed that most physicians prescribed the vaccine to females aged 9-26 years. Some health care providers prescribed the vaccine to any female or to those who were already sexually active. For maximal effectiveness the vaccine must be given before initiation of sexual debut (and potential exposure to HPV).[37]This implies that even though some practitioners were aware of the vaccine and prescribed it, knowledge about

the vaccine is limited and the vaccine is prescribed to the incorrect target population.

Even though most clinicians were aware of the vaccine, the majority (77.9%) have only prescribed the vaccine less than ten times since licensing in South Africa. Only 7.3% of health care providers prescribed the vaccine more than twenty times. The health care providers who prescribed the vaccine more than twenty times were mostly gynaecologists and nurses. The latter may be due to patients with prescriptions from their doctor or that nurses may play a more effective role in counseling, screening and practicing preventative medicine. Younger practitioners (<40 years of age) mainly prescribed the vaccine less than 10 times which is surprising as it is assumed that the younger practitioners would have more knowledge about the vaccine since it has recently been approved and they should be more aware of the impact on cervical cancer morbidity and mortality. The longer the duration a clinician was in practice the more times the vaccine was prescribed. This could be due to the fact that these providers have busy practices or that a rapport has already been established with his/her patient and is therefore more comfortable discussing preventative measures. Clinicians that have established practices might also be more likely to treat the entire family and is thus able to recommend the vaccine to the patients' children and family.

Patients requesting the vaccine indicated patients' education and knowledge about the vaccine. Results showed that just under half of the health care

providers indicated that patients requested the vaccine. However, practitioners the private sector, treat patients from a higher socioeconomic status than those being treated in the public sector. These patients are thus more likely to be aware of the vaccines availability. These patients are also more likely to have regular Papanicolaou smears and are thus at a lower risk of developing cancer of the cervix.

Most practitioners believed that the vaccine is effective. However there were some who feared the side effects and who were unsure if it is effective. It is also believed by some practitioners that more media coverage is needed and that the vaccine is expensive. The bivalent vaccine Cervarix®, was chosen by some practitioners mainly because of the cost of the vaccine. A recent study has also shown that physicians identified cost as a barrier to patient acceptance.[66] The cost of the vaccine and availability represent important system-based factors that could inhibit vaccine uptake – cash paying patients may find the vaccine expensive. A study in South Africa showed that adding the HPV vaccine to the current cervical cancer screening strategy is cost-effective.[62] Vaccination can therefore reduce the cost of cervical cancer to the burdened health system and to the patient.[61] A few of surveyed health care workers (1%) believed that vaccination against HPV could unintentionally encourage risky sexual practices amongst patients vaccinated. This was more an anticipated concern among patients' with regard to their children.

Health care providers believed that patients 46% were largely unaware of the vaccine and 39% believed it is effective. Some also believed what the health care provider had told them. These results indicate that patients need to be counseled with regards to the vaccine. Health care practitioners provide patients with important information and parents value advice about preventative measure such as vaccines. The HPV vaccination programs success rely mostly on health care providers' willingness and ability to recommend vaccination against HPV to their patients. This includes the ability to give information with regards to the advantages of vaccination to adolescents and their parents.[18] Adequate counseling and information should be given to patients and parents of adolescents by health care workers as most are unaware or do not have enough knowledge with regards to the HPV vaccine since it is relatively new. Educational information to parents should be personalised taking into account the patients background knowledge and the information needs of the patient. The main emphasis should be that HPV vaccines do not cure cancer but prevent the most common HPV-related cancers and that they are most effective when given before the onset of sexual activity. In addition counseling is needed with regards to vaccine delivery i.e. three doses are required and it does not prevent Human Immunodeficiency Virus infection or other sexually transmitted infections. The importance of physician counseling is imperative as studies demonstrate that following counseling, more parents are in favor of vaccination.[59] HPV vaccine uptake may be affected by factors related to patient-provider communication. The amount and accuracy of the information offered by providers and patients'

personal experiences may influence patient and caregiver acceptance of vaccine.[64]

Most health care providers were unaware that Gardasil ® is registered for use in males as well. Practitioners that feel more comfortable vaccinating females than males might believe that vaccination against HPV will have a more important impact on female health. These beliefs are however not consistent with data which has shown that administering the vaccine to males and females is more successful in decreasing the load of disease with HPV than administering the vaccine to females only.[65] Health care worker education is needed about the importance of immunizing both genders. Promoting awareness of the association between HPV and cancer of the male genital tract, oral cavity, oropharynx, and larynx might be a more beneficial way to encourage vaccination. Although health care providers are aware of the vaccine and prescribe it, they are unaware of its recommended use.

CHAPTER 8

Conclusion/Recommendations

General awareness with regards to the vaccine amongst health care workers appears to be sufficient. Counseling of patients regarding the availability of the vaccine and practicing preventative medicine seems to be a concern amongst health care workers. This could be due to time constraints, inability to discuss a vaccine with adolescents and their parents, cost issues or simply that even though they are aware a vaccine exists they are not counseling patients about it. Many expect patients to request the vaccine and expect that patients should have some knowledge prior to the health care worker discussing the vaccine. Patients' may not see the long term need for the vaccine as there is no immediate gain and benefits are only detected later in life. Many health care workers believe that public education campaigns such as schools and the media should be in progress so that patients are aware of the vaccines availability.

Knowledge about the vaccine seems to be lacking (most are unaware the vaccine can be given to males and the vaccine seems to be prescribed to females of any age-group regardless if they were already sexually active). Health care providers need more education about the available vaccines and differences between the vaccines licensed, as well as the safety and efficacy.

APPENDIX

APPENDIX a - Questionnaire

Study No: _____

1. Designation: Gynaecologist =1 Paediatrician =2 General Practitioner =3 Other medical doctor =4 Nurse=5
2. Age: < 40 =1 40-60 =2 >60 =3
3. Sex: Male =1 Female =2
4. How long are you practicing? <10 years =1 10-20 yrs =2 >20yrs=3
5. Patients being treated mostly cash or medical aid? Cash =1 Medical Aid =2
6. Aware of cervical screening programme in SA : Yes =1 No =2
7. Aware that there is a vaccine for genital warts/precancerous cervical lesions/cancer caused by HPV? Yes =1 No=2
8. Do you inform patients of HPV related diseases? Yes =1 No =2
9. Do you inform patients of the availability of the HPV vaccine yes =1 No = 2
10. Do you prescribe the vaccine on request? Yes = 1 No = 2

a) If NO why?
_____

b.) If YES, target population: (eg. Sex, age)
_____

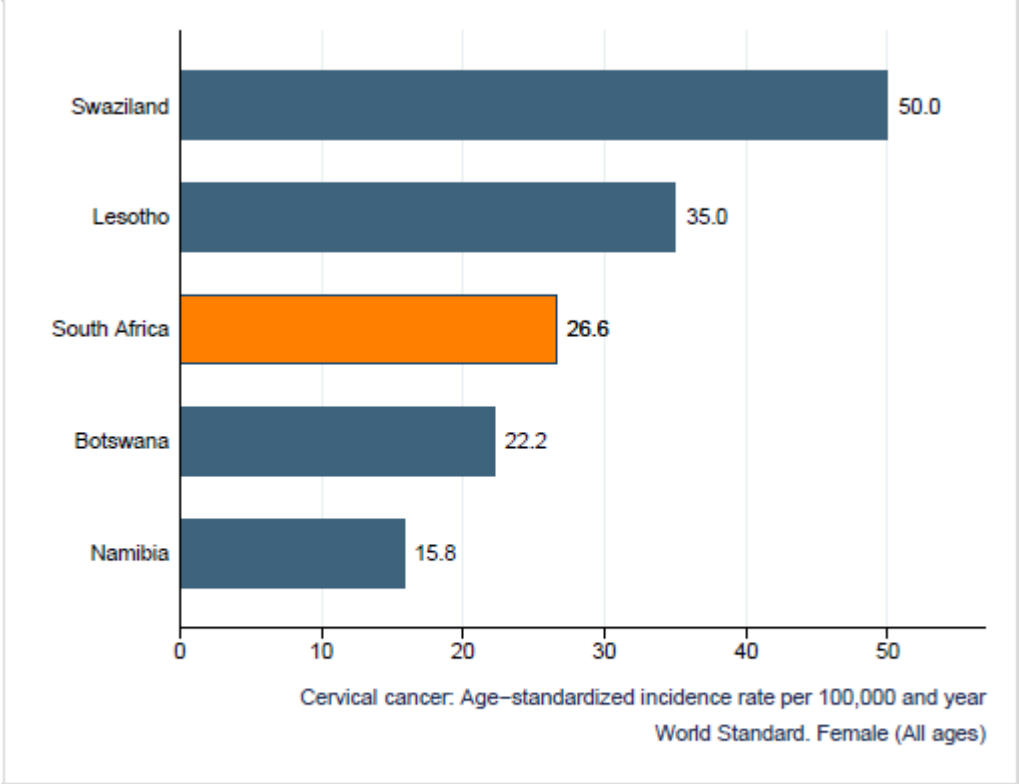
11. If using the vaccine, how many time have you prescribed the vaccine since licensing : <10 times =1 10-20 times =2, >20 times =3 N/A = 4
12. Are you aware that the vaccine (Gardasil) can be prescribed to males Yes =1 No = 2
13. Do patients request the vaccine? Yes =1 No =2
14. Which vaccine do you prescribe: Gardasil =1 Cervarix =2 Either =3 N/A=4
15. Reasons for your choice of vaccine: Cost =1 HPV coverage =2 Patient choice =3 All =4 Other =5 N/A =6
16. Are patients coming back for follow up dose: Yes =1 No =2 N/A =3
17. Beliefs regarding the HPV vaccine: (barriers/concerns/recommendations/comment)

a) (Own beliefs)
_____
_____

b) (Patients beliefs)
_____
_____

FIGURE 1

Age standardized incidence rates of cervical cancer in Southern African countries



Rates per 100,000 women per year. ** No rates are available
Data sources:
IARC, Globocan 2008. Age-specific data from GLOBOCAN 2008 were obtained from IARC, personal communication.
For specific estimation methodology refer to http://globocan.iarc.fr/DataSource_and_methods.asp.

TABLE 1: Demographics of Health Care Workers

	Frequency	Percentage (%)
Age: <40	94	31.3
40-60	159	53
>60	47	15.7
Sex: Male	167	55.7
Female	133	44.3
Time Practicing: <10 years	94	31.3
10-20 years	138	46
>20 years	68	22.7
Patients being treated: Cash	103	34.3
Medical Aid	197	65.7

TABLE II

Knowledge and awareness of the human papillomavirus vaccine among healthcare workers

	Frequency	Percentage (%)
Aware of cervical screening program: Yes	280	93.3
No	20	6.7
Aware of HPV vaccine: Yes	267	89
No	33	11
Inform of HPV vaccine: Yes	181	60.3
No	119	39.7
Prescribe vaccine: Yes	231	86.5
No	86	13.5
Vaccine used: Gardasil®	100	43.3
Cervarix®	15	6.5
Either	116	50.2
Reasons for choice: Cost	32	13.9
HPV coverage	99	42.9
Patient choice	28	12.1
All	65	28.1
Other	5	2.1
Patients request vaccine: Yes	133	44.3
No	167	55.7
Own beliefs: Effective	209	69.7
Unsure	37	12.3
Media coverage	10	3.3
Fear of side effects	6	2
Promotes promiscuity	3	1
Expensive	9	3
Not aware of vaccine	26	8.7

TABLE III

Demographics of healthcare workers awareness of the human papillomavirus vaccine

	YES	NO
Designation: Gynaecologist	50 (100%)	0
Paediatrician	52 (100%)	0
General Practitioner	98 (98.9%)	1 (1%)
Other medical doctor	37 (75.5%)	12 (24.5%)
Nurses	30 (60%)	20 (40%)
Age: <40	88 (93%)	6 (6.4%)
40-60	137 (86.2%)	22 (13.8%)
>60	42 (89.3%)	5 (10.6%)
Sex: Male	160 (95.8%)	7 (4.2%)
Female	107 (80.5%)	26 (19.6%)
Time practicing: <10 years	88 (93.6%)	6 (6.4%)
10-20 years	121 (87.8%)	17 (12.3%)
>20 years	58 (85.3%)	10 (14.7%)
Patients treated: Medical Aid	180 (91.5%)	17 (8.6%)
Cash	87 (84.5%)	16 (15.5%)

TABLE IV

Uptake of the human papillomavirus vaccine among providers who were aware of it

	YES	NO
Designantion: Gynaecologist	48 (96%)	2 (4%)
Paediatrician	49 (94.2%)	3 (5.7%)
General Practitioner	89 (90.8%)	9 (9.1%)
Other medical doctor	15 (40.5%)	22 (59.46%)
Nurses	30 (100%)	0
Age: <40	74 (84%)	14 (15.9%)
40-60	120 (87.6%)	17 (12.4%)
>60	37 (88.1%)	5 (11.9%)
Sex: Male	135 (84.4%)	25 (15.6%)
Female	96 (89.7%)	11 (10.3%)
Time practicing: <10 years	74 (84.1%)	14 (15.9%)
10-20 years	107 (88.43%)	14 (11.6%)
>20 years	50 (86.2%)	8 (13.8%)
Patients treated: Medical Aid	156 (86.6%)	24 (13.3%)
Cash	75 (86.2%)	12 (13.8%)

TABLE V

Frequency of vaccine prescription by healthcare workers

	Number of times prescribed vaccine		
	<10	**10-20 times**	**>20 times**
Designation: Gynaecologist	26 (54.1%)	14 (29.1%)	8 (16.7%)
Paediatrician	46 (93.8%)	2 (4.1%)	1 (2%)
General Practitioner	81 (91.1%)	3 (3.4%)	0
Other medical doctor	13 (86.7%)	1 (6.7%)	1 (6.7%)
Nurses	14 (46.7%)	7 (23.3%)	7 (23.3%)
TOTAL	*180 (77. 9%)*	*29 (12.6%)*	*17 (7.4%)*
Age: <40	59 (79.7%)	15 (20.3%)	0
40-60	92 (76.7%)	11 (9.2%)	16 (13.3%)
>60	29 (78.4%)	3 (8.1%)	1 (2.7%)
TOTAL	*180 (77.9%)*	*29 (12.6%)*	*17 (7.36%)*
Sex: Male	107 (79.3%)	15 (11.1%)	11 (8.2%)
Female	73 (76%)	14 (14.6%)	6 (6.3%)
TOTAL	*180 (77.9%)*	29 (12.6%)	17(7.4%)
Time practicing: <10 years	62 (83.8%)	12 (16.2%)	0
10-20 years	84 (74.5%)	13 (12.2%)	9 (8.4%)
>20 years	34 (68%)	4 (8%)	8 (16%)
TOTAL	*180 (77.9%*	*29 (12.5%)*	*17 (7.4%)*
Patients treated: Medical Aid	121 (77.6%)	18 (11.5%)	2 (2.7%)
Cash	59 (78.7%)	11 (14.7%)	15 (9.6%)
TOTAL	*180 (77.9%)*	*29 (12.6%)*	*17 (7.4%)*

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