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Human papillomavirus (HPV) vaccine immunisation as an intervention programme for the prevention of cervical cancer and other similar HPV genotype-related diseases in South Africa: Some ethical and legal matters for consideration

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2014-08-22
http://hdl.handle.net/10539/15219

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Chapter 1 Introduction, Literature review, and Methodology

Introduction

Scientific research provides ample evidence that persistent Human Papilloma Virus (HPV) infection causes cervical cancer. Research has also led to the development of HPV vaccines, which have shown to prevent cancer of the cervix. With the high burden of cervical cancer in South Africa, I suggest that it is imperative that HPV vaccine immunisation (vaccination) be implemented as a Primary Health Care (PHC) intervention. In this chapter, I will present a synopsis of the burden of cervical cancer in South African women, the role of HPV in cervical cancer, as well as some public health considerations. I will conclude Chapter 1 with an explanation of my research report methodology. This will form the background of scientific and general information needed to inform the reader when discussing different ethical, legal and policy issues that arise in a proposed HPV prevention programme for South Africa.

1.1 The burden of cervical cancer

In 2010, The World Health Organisation (WHO) estimated that yearly about 500,000 women are diagnosed with cervical cancer and over 273, 000 women will die from the disease (WHO 2010; Ferlay *et al.* 2008; Parkin 2006a). When compared to industrialised countries, developing world countries carry a disparate portion of disease burden; eighty-six per cent of all cervical cancer cases and

88% of all cervical cancer deaths worldwide (Jemal *et al.* 2011; Ferlay *et al*. 2008). The reasons for this are multi-fold and include factors such as the overall low social status held by women, poverty, lack of education, mal-distribution or lack of resources, political will, as well as an absence of effective cytology Papanicolaou (Pap) smear screening programmes, a key to early cancer detection.

In an effort to address and reduce the burden of cervical cancer, South Africa introduced the *National Guidelines for a Cervical Cancer Screening Programme* in 2000. The main aim of the programme is to afford every woman over the age of 30 years, three free Pap smears during her lifetime at 10-year intervals. The goal was to screen at least 70% of women nationally within the target age group within 10 years of programme initiation (National Guidelines for Cervical Screening in South Africa, 2000). With the current coverage of this screening program it is unlikely that the screening will be adequate enough to make an impact on cervical cancer mortality figures, especially taking into consideration that rural South African women have limited access to health care (Denny 2008).

South African women have a high prevalence of HPV infection, the highest rates of which have been identified amongst the younger age groups (sexually active women under the age of 25 (Allan *et al.* 2001). About 15.5% of women in the general population are estimated to harbour cervical HPV infection at any given time and 63.0% of invasive cervical cancers in South Africa are attributed to HPV

types 16 and 18 (WHO, 2007).HPV type 16, which is oncogenic or high risk, is the most dominant type found in South Africa (Williamson *et al.* 2002).

Table 1.1.1 Burden of cervical HPV infection

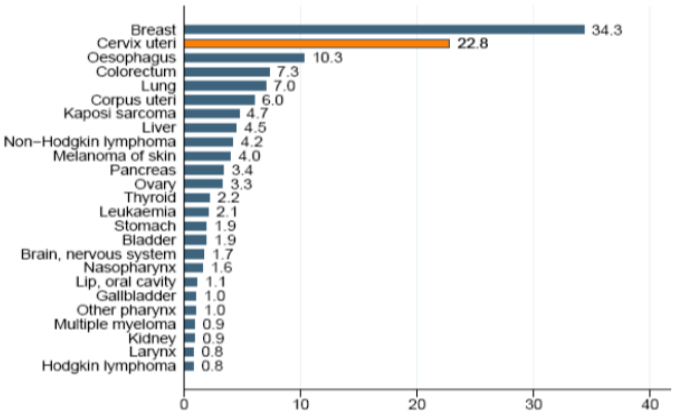
HPV prevalence (%) in the general population	21.0
Prevalence (%) of HPV 16 and/or HPV 18 among women with normal cytology	3.6
Low-grade cervical lesions (LSIL/CIN-1)	26.6
High-grade cervical lesions (HSIL/ CIN-2 / CIN-3 / CIS)	58.4
Cervical cancer (invasive)	62.8

Source: HPV and Related Cancers Summary Report Update (WHO). September 15, 2010. Calculated using estimated general population of women 15 years and older.

In 2002, Parkin *et al.* reported that the population of women in their reproductive years (ages 15 years and older) who are at risk of developing cervical cancer was estimated to be 16.48 million. Both the WHO September 2010 and Castlellsagué *et al.*(2007), report that in South Africa, cervical cancer is the second most frequently diagnosed cancer amongst women between 15 and 44 years of age.

1.2 South African cervical cancer statistics

Figure 1.2.1 Annual crude incidence rate per 100,000 South Africa: Female (All ages)

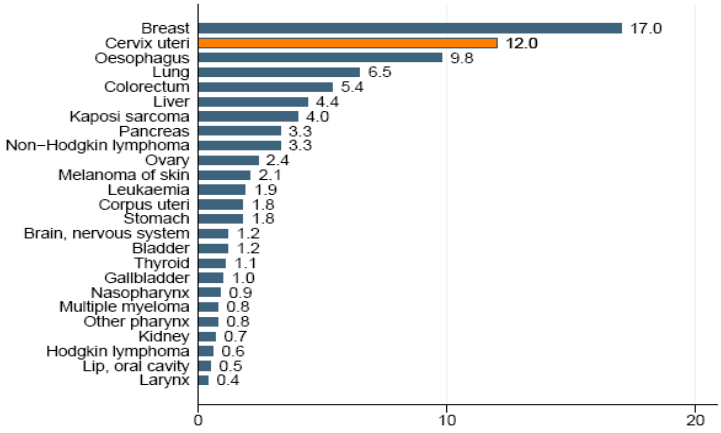


Source: WHO HPV and Related Cancers Summary Report Update. September 15, 2010. South Africa has 22.8 crude incidence rate compared to 15.8 world incidence.

Castlellsagué *et al.* (2007) state that the annual number of new cases reported per year was 6,742 with a mortality of 3,681, the highest mortality amongst those aged 55-64. It is to be noted here, that these figures might represent lower than the actual numbers due to under-reporting and the fact that the South African National Cancer Registry has undergone significant restructuring during the last few years. Prior to April 2011, new regulations made it mandatory for all healthcare personnel who diagnose cancer to notify the case to the National Cancer Registry as mandated by the National Health Act, 2003 (Act No 61 of 2003), and Regulations Relating to Cancer Registration, now making cancer a notifiable condition. It is therefore a probability that the number of cases reported

and the number of deaths prior to 2011 are much higher than reported. Nonetheless, the mortality rates due to cervical cancer in South Africa compared to the world are high. Compared to other types of cancer in women, cervical cancer is reported as the second-highest cause of mortality.

Figure 1.2.2 Cervical cancer mortality compared to other cancers in women of all ages in South Africa



Source: WHO HPV and Related Cancers Summary Report Update. September 15, 2010. In South Africa, cervical cancer is second cause of mortality in women with breast cancer being the highest.

The latest figures from Statistics South Africa (personal communication Dr D Kibuuka: Manager Health Statistics) for cervical cancer deaths for the period 2004 – 2008 are 2,576, 2,706, 2,728, 2,596 and 2,631 respectively. These latter figures are almost twice the number of deaths recorded for 1992 (1,105 deaths) and 1994 (1,497deaths).

1.3 Risk-factors for cervical cancer

There are a number of factors considered to increase the risk of developing cervical cancer. Some of these risk factors according to Walboomers *et al.* (1999) include 1) Age at first intercourse, 2) Sexual reproductive lifestyle (such as lifetime number of sexual partners), 3) High parity, 4) Smoking and other risky life-style habits, and 5) Sexually Transmitted Infections (STI) including viral infections such as HIV.

Table 1.3.1 Some risk factors contributing to cervical cancer

Smoking prevalence (%) women	7.7
Total fertility rate (live births per women)	2.9
Oral contraceptive use (%)	10.6
HIV prevalence (%), adults (15-49 years)	18.8

Source: Castlellsague *et al*. 2007: HPV and cervical cancer in the world 2007 report. HIV co-infection is the highest contributor to cervical cancer.

Relevant to developing countries, a major risk factor for many health problems, including cervical cancer, is low socio-economic status (Dos Santos and Beral 1997). This is because low economic status is linked to poor access to healthcare services, lower than optimum nutrition, and less access to health awareness programmes. Such factors can contribute to making women more vulnerable to diseases such as cervical cancer.

Venereal diseases and other types of viral infections

HIV-related immunosuppression is a significant risk factor for cervical and other types of cancer (De Vuyst and Franceschi 2007; Parkin and Bray 2006; Boshch *et al.* 2002; Schiffman *et al.* 2007 and Denny 2008). HPV disease is virtually unknown in celibates e.g. nuns and virgins but is relatively common in commercial sex workers (Williamson 1999). HIV immunosuppression generally results in opportunistic infections and it is to be expected that HPV infection will increase in individuals infected with HIV.

A study conducted by Rowhani-Rahbar *et al.* (2007), demonstrated that HIV infection based on CD 4 count reduces the likelihood of HPV clearance. In another study conducted by Mbulawa *et al.*(2009), in Senegalese women, women with HIV type 1 (which is more virulent) were not able to clear HPV infection than women with HIV type 2, which is less virulent (and only found in West Africa). These findings have direct implications for South African women, as South Africa's circulating HIV is type 1. Data from women treated in Johannesburg, South Africa 2000, 776 HIV-seronegative and 60 HIV-seropositive women reported a 7.2% seroprevalence Lomalisa *et al.* 2000. HIV-positive women presented with invasive cancer almost 10 years earlier than HIV-negative women with a mean age of 44 and 54 years respectively (Denny 2008).

Data from another South African study conducted to determine the risk of cervical pre-cancer and cancer among HIV positive women, showed that HIV-positive women were found to be 5 times more likely to have high-risk human papillomavirus infection (HR-HPV) present compared to HIV negative women (Moodley *et al.* 2006).In a similar study conducted in Uganda, HIV positive women showed a higher prevalence of HPV infection (Banura *et al.* 2008).

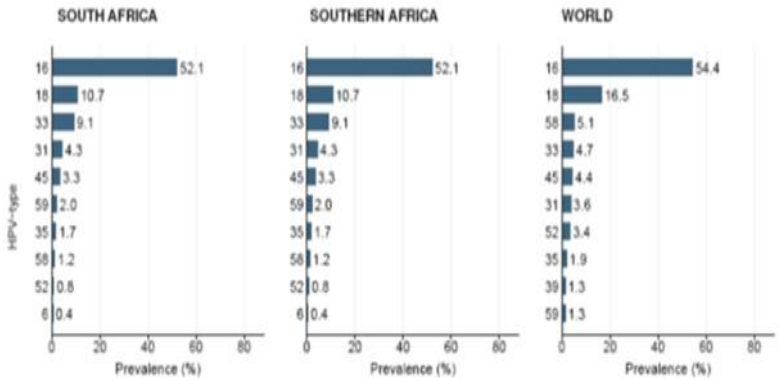
Moodley *et al.* (2006) report on a retrospective study conducted in Durban on 206 women with cervical cancer. These women tested for HIV and 21% of were found to be HIV-seropositive and were 13 years younger than were HIV-seronegative women. What is significant here is that the stage of the cervical cancer did not differ. HIV positive women demonstrated a five times higher rate of high risk HPV compared to HIV negative women and women with HPV and HIV displayed a forty times higher risk of developing squamous cell intraepithelial lesions (SIL) than women with neither.

1.4 Human Papillomaviruses (HPV) and Cervical Cancer

Over the last four decades, scientists have delved into the relationship between viruses and human cancer showing increasingly strong links between them (Lee *et al*. 2003). To date, scientists have completely described 118 papillomavirus types and higher numbers have been detected in preliminary studies but are not yet described (de Villiers *et al.* 2004). While many sexually transmitted viral agents were thought to be possible or co-aetiological agents for cervical cancer,

research has now clearly identified that nearly all cervical cancers are caused by human papillomaviruses (HPV). These types of HPV (called 'high risk' or 'oncogenic' types) cause cervical cancer if there is persistent infection by them in the genital tract (Munoz *et al.* 2006; Bosch& Munoz 2002).

Figure 1.4.1 Ten most frequent HPV types among women with and without cervical lesions in South Africa compared to Southern Africa and the World



Source: HPV and Related Cancers Summary Report Update (WHO). September 15, 2010. South Africa and Southern Africa have the same HPV types and prevalence with HPV 59 prevalence higher than in anywhere in the world WHO Sept 15, 2010).

The World Health Organization (WHO September 2010: IV) reports that 21.0% of women in the general population are estimated to harbour cervical HPV infection at any given time. Additionally, 62.8% of invasive cervical cancers are attributed to HPV types 16 and/or 18 (Clifford *et al.* 2003). HPV is primarily transmitted sexually and almost all individuals become infected with HPV within 2–5 years of initiating sexual activity (Munoz *et al.* 2006). Research also has indicated that

many HPV types may be transmitted vertically from mother to child (Rosi *et al*. 2005; Syrjänen & Puranen 2000; Puranen *et al.* 1995).

According to research published by Allan *et al*. (2008), presently there are more than 40 recognised human papillomavirus types that may infect the female genital tract. The strongest association has been found between specific HPV types and cervical cancer. These are sub-divided into different types according to their low, moderate or high oncogenic potential (Astbury & Turner 2009). High-risk DNA HPV types 16, 18, and 31 are considered oncogenic because they are directly implicated in cervical intraepithelial neoplasia (CIN) and cervical cancer (Alstbury *et al.* 2009; Allan *et al*.2008). HPV types 16, 18, 31, and 35 are most commonly found in cervical cancer biopsies (Markowitz, *et al*. 2000). HPV 16 was found in half of the cervical cancer cases worldwide (ibid). In South Africa, Allan *et al*. (2008) note that there is “a high prevalence of cervical HPV infection” and vaccination against the oncogenic HPV types 16 and 18 would therefore reduce or void the risk of acquiring HPV and thus cervical cancer.

1.5 HPV infection preventive strategies

It is established that well-organised cervical screening programmes can reduce cervical cancer incidence and mortality. Unfortunately in South Africa, these programmes have not been successful and in an effort to reduce the burden of cervical and related cancers an alternative strategy must be considered. A

vaccine to prevent oncogenic HPV infection, or premalignant cervical lesions from progressing to cancer, would clearly offer means of reducing the cervical cancer burden in South Africa.

1. 6 Vaccine development, efficacy, safety, in addition, cross protection of other HPV genotypes

Recombinant DNA technology is being used to develop vaccines against HPV. Two prophylactic HPV vaccines have been developed commercially and are approved for use in South Africa. Cervarix® is a bivalent HPV 16/18 vaccine developed by GlaxoSmithKline. It is given as an intra-muscular injection in a three-dose course, generally at zero, one and six months[5]. Gardasil®, developed by Merck and Co. Inc., is a quadrivalent HPV 16/18/6/11 L1 VLP vaccine delivered by an intra-muscular injection at zero, two and six months (Stanley M., Lowy D. R. *et al.* 2006).Recombinant L1 capsid protein from HPV has the useful property of self-assembling into virus-like particles. These particles contain no viral DNA and are therefore non-infectious. More importantly, these particles stimulate the production of antibodies that bind and neutralise the infectious (WHO 2011).

With the availability of effective vaccines against high-risk oncogenic HPV types, there is real hope for reducing the global burden of cervical cancer as well as other diseases related to HPV genotypes. Several researchers who have conducted clinical trials mainly in industrialised countries Joura *et al.* 2007;

Schiffman *et al*. 2007, Parkin *et al.* 2006; Keith *et al.* 2006; Harper *et al.* 2006; Mao *et al.* 2006; Villa *et al.* 2005; Harper *et al.* 2004, Galloway 2003; Koutsky *et al.* 2002 Bosch, *et al.* 2002; Walboomers *et al.* 1999, have shown that Gardasil ®vaccine, a quadrivalent, and Cervarix ®vaccine, a bivalent, have clinically demonstrated 100% protection against the HPV genotypes included in their vaccine formulas. GARDASIL, which is a product of Merk & Company, is the only human papillomavirus (HPV) vaccine that helps protect against 4 types of HPV. In females and young women ages 9 to 26, GARDASIL helps protect against 2 types of HPV that cause about 75% of cervical cancer cases, and 2 more types that cause 90% of genital warts cases (Merk & Company USA 1995-2010). CERVARIX, which is a product of Glaxo Smith Kline is a vaccine used in females from 10 to 45 years of age to prevent early stage cervical cancers (pre-cancerous lesions), pap smear abnormalities and cervical cancer caused by human papillomavirus (HPV) types 16 and 18 (Glaxo Smith Kline Australia, 2006).

1.7 Public Health Considerations in HPV vaccine immunisation Programmes: The Challenges

1.7.1 Basic issues in public health interventions

For any public health intervention the basic requirements are that, the intervention is safe and efficient. In the case of HPV vaccination, it is also important to highlight other relevant issues such as cross protection of the HPV types in the vaccine with other HPV types and the duration of protection/immunity. Some

standard issues include:" 'the costs of the available vaccines, questions about the long-term immunogenicity'… "efficacy in preventing cervical neoplasia, the efficacy of different vaccines, cross-protection against HPV infections not targeted by the vaccine antigens and the need for more logistically feasible dose regimes in inducing and maintaining immunogenicity and long-term protection against cervical neoplasia" (Sankaranarayanan 2009).

Another reason why a HPV vaccination programme presents a challenge is that the actual benefits of vaccination will not be recognisable immediately. The overall gain - that of preventing deaths caused by HPV infections that lead to cancer of the cervix - will be known only in the future. However, the history of vaccination viz. the eradication of vaccine-preventable diseases, lend support for such programmes.

1.7.2 Efficacy: Can the HPV vaccine stand up to the rule that vaccines be efficacious?

Castellsagué *et al*. (2009) report that between the years 2007 and 2009, "results indicate that HPV vaccines are highly immunogenic in inducing high levels of serum antibodies in almost all vaccinated participants, and have conferred a high degree of protection against HPV types in the vaccines and thus the associated precancerous cervical lesions in fully vaccinated individuals. The efficacies of the vaccines have been found to range from 98% to 100%, with higher immune

responses/geometric mean titres in younger age groups." Similar results were found in the PATRICIA (PApilloma TRIal against Cancer In young Adults) trials, which were conducted by Lehtinen *et al.* in 2012.

1.7.3 Cross protection: Can the HPV vaccines offer any cross-protection?

There is strong evidence that the current HPV vaccination can confer protection against other HPV types not included in the vaccines. Malagón and colleagues (2012) report that the quadrivalent vaccine would protect against infection and diseases caused by ten HPV types not included in the vaccine. The majority of known HPV types that infect the genital tract are members of the Alphapapillomavirus (or A) genus; of this group, 18 have been classified as oncogenic based on epidemiologic and/or genetic evidence.

In South Africa, the ten most prevalent HPV types are 18, 16, 33, 31, 45, 59, 35, 58, 52 and 6 (CDC 2012). The vaccines have been found to cross protect against HPV types 31, 45 and 52; while initial findings with the vaccine appear to show cross protection against twelve additional oncogenic HPV types including 31, 33, 35, 45, 52 and 58 (Sankaranarayanan 2009). The cross protection offered by the quadrivalent vaccine would thus protect vaccinated individuals protection for all the A9 (16, 33, 35, 52 and 58 types) species and two of the A7 species (18 and 45 HPV types) (CDC 2012).

1.7.4 Safety and duration of protection: How safe are the HPV vaccines? How long does one dose last?

The bivalent vaccine provides a high level of long-term protection against human papillomavirus (HPV) types 16 and 18, with minor side effects. The latest data published by Harper (2009), reveal that the HPV 16/18 vaccine offered sustained protection and long-term efficacy for up to 6.4 years for the bivalent vaccine and 5 years for the quadrivalent vaccine. In all studies conducted between the years 2004 to 2009, reports show rare serious adverse events. The side effects observed on injection site reactions for both bivalent and quadrivalent includes: pain, swelling, itching, redness, fever. Serious adverse events are nausea, and dizziness, but these too were also, observed in participants who received placebo (ibid).

1.7.4 Cost: Can the South African government afford the HPV vaccine *immunisation?*

The cost of HPV vaccination still represents an important barrier to implementation in many countries. The current price for the three doses of the vaccine is $130.00 per dose which is prohibitory by South African standards. The Global Alliance for Vaccines and Immunisation (GAVI), a public-private partnership focused on saving children's lives and protecting people's health by increasing access to immunisation in poor countries, has reduced the price of HPV vaccines to $ 4.50 per dose. This price is available to developing countries

that are eligible for the GAVI subsidy. For countries that do not qualify for GAVI, the WHO is working with partners to discuss different means to assist these countries (WHO 2013).

1.7.6 Challenges: What are some of the other challenges faced with introducing the HPV vaccine immunisation?

Because HPV is a sexually transmitted virus, objection was raised in the USA by some parents because they felt that vaccinating their pre- and adolescent female children would be sending a "wrong" message about sex and sexuality. As Lo (2006) writes, "Vaccination must be before HPV infection is acquired. It is most likely to be recommended for 11-12 year olds, because by the ninth grade (age 14-15) 28% of females in the US are sexually active. This has prompted some advocates of premarital abstinence to charge that HPV vaccination will condone or promote sexual promiscuity". This sentiment is also voiced by some USA religious groups saying that the vaccination is not suitable for young female-children and bases their argument on the practice of abstinence until marriage.

However, when this debate is 'stripped of its emotive response and the HPV vaccination is seen as prevention for cervical cancer and not a sexually transmitted disease, the debate over vaccination mandates can be framed as a contest between competing ethical values' (Field and Caplan, 2008).

The point Field and Caplan make is that the HPV vaccination debate is not just about sex, and the prevention of a sexually transmitted infection (STI), it is importantly about parents protecting their female-children from the oncogenic HPV types which result in cervical cancer. This calls for increased public awareness about how HPV *per se* is related to cancer.

Arising from this we may ask why female children are targeted as male children are also involved in the spread of HPV. Isn't a vaccination programme aimed at female children prejudicial? Questions such as these will be discussed in Chapter 2 and Chapter 3.

I now turn to an overview of the Methodology, objectives and outcomes of this research report.

1.8 Methodology, Objectives, and Outcomes

1.8.1 Design

This was a descriptive analytical study utilising ethical and legal analysis.

1.8.2 Methods

1) An extensive literature search was conducted using World Wide Web to access and Wits electronic journal library to retrieve references to relevant publications. Search engines included PubMed/ Medline, Google Scholar, Lexis Nexis and ProQuest.

2) Analysis of material from scientific and academic textbooks, ethics, Medical and Medico-legal journal articles published on the topic of HPV and adolescent vaccination/immunisation, ethics and public health.

3) Analysis of the current practices on HPV vaccination in other countries.

4) Analysis of the ethical and legal issues that arise from these sources, regarding policy implementation of HPV vaccination in South Africa.

1.8.3Objectives

1) Identify and discuss ethical and legal issues which are considered for the delivery of HPV vaccination in South Africa; and

2) Argue that the benefits of HPV vaccination programme for female children in South Africa outweigh the burdens.

1.8.4 Outcomes

1) This research report provides policy recommendations towards implementation of HPV vaccination in South Africa as a standard of care for adolescent female children in the country;

2) The research findings will be presented at national and international meetings/fora; and

3) The research report will be published in a peer-reviewed journal.

1.8.5 Limitations

Since the awareness of the role that certain Human papillomavirus's play as a necessary factor in the development of cervical carcinoma, there have been many new scientific developments. The development of vaccines that have been proven

to prevent certain HPV infections has led to further HPV vaccination research and drug-development. These facts limit the scientific facts included in this research report to the time of writing the report as scientific developments beyond September 2013 cannot be predicted.

Chapter 2 Ethical Issues in HPV Vaccine immunisation

2.1 Introduction

In this chapter, based on the data available at this time, I argue that an HPV vaccination programme for prevention of cancer of the cervix as well as other HPV-related cancers is warranted in South Africa. First, I will provide some information and the ethical basis of vaccination programmes in general, and then I will move to discuss some issues in HPV vaccination programmes aimed at female-children. I will also discuss some ethical issues in parental autonomy. To conclude the chapter I suggest that HPV vaccination programmes for female-children is ethically acceptable with the rider that it should be expanded to include male-children as soon as feasible.

2.1.1 Purpose of vaccine immunisation programmes

The purpose of any population immunisation/ vaccination programme is to prevent the acquisition of a communicable disease in individuals as well as the public (Malone and Hinman 2003). An immunised individual benefits the public, as she, due to her immunity, cannot serve as a source of X disease transmissible to others. Achieving population or 'Herd' immunity through the vaccination of a community serves to slow and may prevent the spread of a communicable disease in the greater population, thus reducing individual risk of contagion.

2.1.2 General controversies in immunisation programmes

Vaccination programmes have always raised some controversies as Morris (2008) states, "… [Vaccinations being] … Both poison and cure". Widely hailed as the eradicator of contagious diseases of human importance, such as smallpox, vaccinations have also been accused of causing autism and poisoning children with thimerosal, derived from mercury (Baker 2008).

Issues concerning the rights of parents to make decisions for their children, "in their best interests" come to the fore in vaccination debates. In such cases, the focus is on the parents' autonomy in raising their children versus what is believed to be in the best interests of society as a whole. Parents who are against vaccination programmes may make various claims. Some feel that the government or any of its organs do not have the right to interfere in a family's concerns. Such arguments are often framed in terms of Mill's Trieste "On Liberty" in which Mill makes the claim that the government should not interfere with the self-determination and liberty of an individual as long as that person's actions do not result in harm to others. The counter-argument is that in not vaccinating, potential harm is caused to society because herd immunity will be lost. If herd immunity is lost, then a population is vulnerable for disease acquisition. Therefore, certain liberties can be limited.

2.1.3 The individual and the public

Classic dilemmas in medical ethics usually involve an individual patient (Jonsen *et al.* 2010). In such situations, often a balancing of the "four principles" (respect for autonomy, non-maleficence, beneficence and justice) or application of a traditional ethical theory such as deontology guide the overall aim of medical efforts to promote the well-being of the individual patient. In such cases, the idea of serving the public good does not take prominence (Kass 2001). Conversely, ethics in a public-health perspective traditionally gives the needs of a group, such as a community or population priority over that of the individual.

Discussions concerning vaccination programmes identify differences between the ethics of individual care and the ethics of public health. Healthcare practitioners have an ethical responsibility to both individuals and the public's health. The ideal, of course is a healthy autonomous individual living within a healthy community or population. The problem is finding the right balance of interests, which is the core conundrum.

In 2002, the American Public Health Association (APHA) in conjunction with other public health groups developed a Code of Practice which, although primarily Western-based, serves to identify what ethical practice in public health should include (Thomas 2002). It is titled *Principles of the Ethical Practice of Public Health.* In this set of principles of practice, ethical ideals such as respecting autonomy, non-maleficence, beneficence and justice is entwined with

consequential overtones. Blending the rights and duties of individuals and the public good is a difficult task. The 'Principles of the Ethical Practice of Public Health' (APHA 2002) follow:

1. Public health should address principally the fundamental causes of disease and requirements for health, aiming to prevent adverse health outcomes.

2. Public health should achieve community health in a way that respects the rights of individuals in the community.

3. Public health policies, programs, and priorities should be developed and evaluated through processes that ensure an opportunity for input from community members.

4. Public health should advocate and work for the empowerment of disenfranchised community members, aiming to ensure that the basic resources and conditions necessary for health are accessible to all.

5. Public health should seek the information needed to implement effective policies and programs that protect and promote health.

6. Public health institutions should provide communities with the information they have that is needed for decisions on policies or programs and should obtain the community's consent for their implementation.

7. Public health institutions should act in a timely manner on the information they have within the resources and the mandate given to them by the public.

8. Public health programs and policies should incorporate a variety of approaches that anticipate and respect diverse values, beliefs, and cultures in the community.

9. Public health programs and policies should be implemented in a manner that most enhances the physical and social environment.

10. Public health institutions should protect the confidentiality of information that can bring harm to an individual or community if made public. Exceptions must be justified based on the high likelihood of significant harm to the individual or others.

11. Public health institutions should ensure the professional competence of their employees.

12. Public health institutions and their employees should engage in collaborations and affiliations in ways that build the public's trust and the institution's effectiveness.

Autonomy concerns self-governance; the ability and capacity to reason and make decisions concerning his or her own life (Kant 1993). Field and Caplan (2008) suggest that children do not have the same level of maturity and understanding as adults. Because autonomy involves the capacity for self-governance, the autonomy of children carries a lower weight than that of adults. Any directive for

children will thus directly affect the responsibility of the parent or guardian over the child. The decision-making capacity for this target age group for HPV vaccination differs from that of younger children, but it is not at the same level as adults. Since parental judgment can take account of the preferences of this group, the case to overrule parents' wishes with government directives is less compelling than when younger children are involved (Field and Caplan 2008).

The principle of beneficence guides the ethical theory to actively do what is good. In the case of a public health intervention, potential benefits to individuals should be maximised and potential harms be minimised, in other words, there should be balancing of potential harms and benefits for individuals and the public. In the context of the duties of public health officials, it is important that officials communicate any information to the public as quickly as possible (Coughlin 2006).

The principle of non-maleficence on the other hand, requires that harmful acts be avoided. Beneficence incorporates an obligation to avoid harm, but non-maleficence conveys an independent duty that relates to it notwithstanding attempts to create any benefit. If, however, a vaccine carries significant medical risk, the principle of non-maleficence would conflict (Field and Caplan 2008).

Stringent licensure requirements are in place for vaccines generally in all countries. South Africa has additional local safety requirements by the Medicines Control Council (MCC), which in 2008 approved the use of the two HPV vaccines. This requirement maybe seen to form part of fulfilling the non-maleficence

principle as it seeks to provide the community with an additional safeguard against harm.

The *Ethical Practice of Public Health* guidelines also include elements of the principle of justice calling for fair and equitable distribution of scarce goods (Kass 2001; Anand *et al.* 2004). Justice requires a sound system of allocating resources based on an underlying principle such as inequality or fair opportunity (Field and Caplan 2008). Healthcare is a scarce resource in South Africa, so justice demands a system of equity for determining access to it (Coughlin 2004).From this perspective, a just distribution of benefits from public health programmes or research is determined by the benefits to all affected.

Childress *et al.* (2002) note that public health activities are generally understood to be consequentialist in that the end result of every intervention is geared towards a better health for every member of the public. While this is certainly true, there is now a concerted effort made to, in as much as is possible, include many opinions from diverse communities and individuals.

On a micro-level, the rendering of the HPV vaccination services is based on the principle of justice. All female-children and adolescents in the targeted age group should be the beneficiaries of the programme irrespective of where they come from e.g. race, religion or socioeconomic circumstances. No one should be excluded from vaccination services, save only for the limitations of infrastructure and resources that render access to health services difficult in some

disadvantaged communities. The SA government, through the Expanded Programme on immunisation, has ongoing efforts and community collaboration to allow means to establish for health services to reach remote communities. These communities can be reached through the use of mobile clinics/services. Furthermore, the HPV vaccination programme will be structured such that no specific groups or individuals are made to bear an unequal burden in terms of risk or any other foreseeable burden; therefore, a just distribution of burdens will be assured (Field and Caplin 2008).

2.1.4 Ethical basis of most public health vaccine immunisation programmes

I will now outline the ethical basis of most public health vaccination programmes: Utilitarianism and Communitarianism.

Utilitarianism: Utilitarianism seeks to maximise the collective good, as such, it is the ethical theory that is used traditionally by public health to support vaccination programmes and other public health interventions (Coughlin 2006; and Beauchamp, 1994). Utilitarianism is based on the Principle of Utility, the provision of the greatest amount of utility (conceived as a good, happiness, or pleasure) for the greatest number of people (Beauchamp and Childress, 1994 and 2002). Since a vaccination programme can save lives, and saving lives is a good thing, the consequences of a vaccination programme are good. The success or failure of any vaccination programme relies on the level and extent of vaccine coverage. This is because the aim of vaccination programmes is to modify the epidemiology

of the disease or eradicate it at best (Schoub 2002). When applying the utilitarian theory, the singular focus on achieving the “greatest good” means that considerations such as a limitation on individual rights are justifiable. Societal good overrides the views of an individual.

In vaccination programmes, for the utilitarian theory to be applicable it relies upon someone or something, like a government, to believe that it will be an overall good. If the government perceives a vaccination programme to be negative or bad and fails to vaccinate, the consequences would be considered wrong because the overall consequences are bad. They are bad because the preventable disease will prevail causing society harm. A second ethical theory often used to justify vaccination programmes is Communitarianism.

Communitarianism: Communitarians support the idea that if acts benefit the community in terms of them being deemed valuable, and are supportive of traditional practices and the common good then they are right (Beauchamp and Childress 1994).In Communitarian thinking, individual freedom may be limited for the sake of the common good (Callahan and Jennings 2002). The common good is expressed by the community members. This may mean that practices valued by society can be enforced. Public protection, when available, against the ravages of disease may elicit a positive response to vaccination programmes. At the same time it must be noted that understanding the epidemiology of a given disease

process and good communication between public health personnel and the community are pivotal to any vaccination programme success.

Callahan and Jennings (2002) maintain that the Communitarian approach has merit writing,

" … We should enact public policy from a shared consensus about good society, not based on individual rights. Liberal assumptions about state's neutrality should be scrapped and society should be free to implement substantive concept of the good. Biomedical ethics should use communitarian values to implement or revise social laws and regulations governing the promotion of health, the use of knowledge ... In each case the question to be asked is: What is most useful to a good society? Not ... Does it violate autonomy?"

There are similarities between Utilitarianism and Communitarianism in that both seek the common good. The major difference lies on which particular party makes the decision (for or against a vaccination programme); in the case of Utilitarianism it is the government or other outsiders, in Communitarianism, it is the community which assigns (or does not) value to a (vaccination) programme.

Both the Utilitarian and the Communitarian theories focus on the important moral criterion of benefit to the whole of society, which sets them apart from other ethical theories.

Of the two, application of the Communitarian theory in developing world settings will assist in introducing procedural obligations to involve communities in decision-making whilst diminishing the use of Western models for contagious disease extinction. Concerning the current efforts to eradicate polio, Perkins (2013) notes, “This shift away from modelling global health campaigns on the West is likely to continue.” This may represent a significant step in current global approaches to contagion eradication. Receiving direction from and listening to the voices of communities can serve to address the element of trust and acceptability of vaccination programmes which in many countries has been absent.

Vaccination programmes aimed at the eradication of communicable diseases such as polio, diphtheria, whooping cough and measles are ethically supported as they seek the common good for all members of a population. All members of a population naturally include both genders: females and males.

2.1.5 Possible dominance of Pharmaceutical industry on HPV vaccine immunisation programmes

Pharmaceutical companies that manufacture vaccines are responsible for providing policy makers with scientific data to prove vaccines’ quality, efficacy, safety and protection. There are two HPV vaccines in the market for prevention of cervical cancer and related cancers: the guadrivalent gardisal and bivalent cervarix, products of Merck & Company and GlaxoSmithKline respectively. Merck

and Company has sponsored a number of Phase I, II and III clinical trials by FUTURE I & II groups.

The literature is abound with reference to studies conducted by these groups and in this report alone refers to four of their studies. In 2007, the FUTURE II study group conducted three studies: a) the study on the effect of prophylactic human papillomavirus L1 virus-like-particle vaccine, on the risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ which is a combined analysis of four randomised clinical trials; b) the study of the quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions; and c) the study of prophylactic efficacy of a quadrivalent human papillomavirus (HPV) vaccine in women with virological evidence of HPV infection. The FUTURE I study group, in the same year, conducted a study entitled: Females United to Unilaterally Reduce Endo/Ectocervical Disease (FUTURE) I Investigators, which looked at quadrivalent vaccine against human papillomavirus to prevent anogenital diseases.

Glaxo Smith Kline on the other hand sponsored the PATRCIA group. While there is only one reference to this group, it is because most of their other studies are in German. The study that is referenced in this report was on the efficacy of a prophylactic adjuvant bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial.

Reference is made to these studies so that it can be clear how the vaccines were eventually accepted/approved by different countries based on the outcomes of these studies. While it is acceptable for pharmaceutical companies to sponsor clinical trials it is the following role that Merck played in the implementation of HPV vaccination in the US that has raised speculation in the authenticity and transparency of these studies.

Mello *et al*. (2012) investigated the roles that Merck & Co., played in the US HPV immunisation policymaking in order to find out if Merck did not have conflict of interest. It is acceptable that legislators should rely heavily on Merck & Co., for scientific information, however, Merck's contribution towards drafting of the legislation included promoting school-entry mandate, mobilising female legislators and physician organisations, conducting consumer marketing campaigns and filling gaps in access to the vaccine. The study concluded that the involvement of Merck in the policymaking has undermined the transparency of their contribution and raised possible financial offers to legislators.

2.2 Some ethical issues in HPV vaccine immunisation

In 2006, with the advent of the US Federal Drug Administration's (FDA) approval of vaccination against certain types of HPV attributable as causes of cervical and other types of cancer, ethical discussions have arisen. Many articles focus on issues, which are nuanced to their particular socio-economic milieu (Omer *et al.*

2009; Charo 2007 and Bardley 1999). In industrialised countries, cancer of the cervix is largely prevented primarily due to their comprehensive PAP screening programmes. However, even within industrialised countries, disparities exist. For example, research conducted in the United States (US), identified that HPV disproportionately affects women based on race, social status and geographical location. This study identified that Black and Hispanic women had a greater cervical cancer mortality rate and underwent less-aggressive cancer treatment than did their White-women counterparts (Watson *et al.* 2008). In industrialised countries, those who argue against a blanket HPV vaccination programmes claim that better access and financial support for PAP screening as well as other women-focused heath programmes should be in place prior to or concurrent with HPV vaccination. The objective is to lessen the gap between access for the advantaged and limited access to healthcare for disadvantaged women. In developing countries where, for many reasons PAP screening programmes are inadequate, HPV vaccination may prove to have a positive impact on the mortality rates of cervical cancer in women.

Gender refers to the socially constructed roles, behaviours, activities, and attributes that a given society considers appropriate for men and women. One's sex refers to the biological nature of a person, for example, their biological, hormonal or chromosomal features (Nobelius 2004). As a member of the female sex, women have less control over sexual situations than do men do; they are

biologically not as strong as are males. When communicable diseases and other healthcare issues are considered, Doyal (2001) argues that the terms ‘gender’ and ‘sex’ are interrelated. This is important to consider in, for example, transmission of sexually transmitted infections (STIs). The prospect of vaccinating female-children against the HPV types responsible for cancer of the cervix raises ethical issues particularly that of gender equity, the ideal of being just, impartial, and fair to both genders.

To vaccinate females only at first glance would seem to be unfair. After all, it has been reported that virgin females and women apparently do not carry the carcinogenic HPV (Kejaer *et al.* 2001). Males transmit the majority of HPV infections to both females and other males through sexual intercourse or simply by skin-to-skin transfer (Burchell *et al.* 2006). Since the objective of vaccination programmes is herd immunity then it is reasonable to argue from gender equity that males should be immunised as well as females (Gostin and Powers, 2006). So what reasons can be given to prioritise female-children?

Whitehead (1990) defined inequity as, “differences in health that are unnecessary, unavoidable, unfair and unjust”. Globally, women carry a disparate burden of health problems. The impact of early death due to cancer of the cervix is multi-fold. Women play a central role in families and communities such as being wage earners, money-managers, caregivers of children, grandchildren and carers for the community’s ill (Knodel *et al.* 2003). In South Africa, the role of women as

carers for their HIV-infected children and grandchildren cannot be overemphasised (UN 2006).

When women die from cervical cancer, not only is there a massive social loss but the economy as well. According to Tsu and Levin (2008), women are the main income earners in about one-third of Sub-Saharan families. A compounding problem is that women diagnosed with cervical cancer, particularly those living in rural areas, often do not have access to tertiary health services such as chemotherapy or radiation. Such women may be compelled to travel far from their homes to support centres, which they often are reluctant to do. Poverty and a sense of familial obligation do play a major role in health seeking and delays in seeking treatment for diseases such as cervical cancer may result in catastrophic, painful and premature deaths.

The idea of social justice conveys the idea that persons who are the most vulnerable for living in a condition essentially out of their control where greater exposure to illness and disease exist should be given special concern (Braveman 2006). This may serve as a reason to prioritise the HPV vaccination to South African female-children when considered as a sub-group of health disparities.

Additionally, and as identified in earlier chapters, infection with high-risk HPV strains are the necessary yet not sufficient conditions for the development of cervical cancer. Co-factors associated with cervical cancer development include for example, “smoking, alcohol consumption, micronutrient deficiency in fruits and

vegetables, prolonged use of oral contraception, multiparty, uncircumcised male partner, low socioeconomic status, infection with HIV/AIDS or others including herpes simplex and Chlamydia trachomatis" (Branković *et al.* 2013). Cervical cancer is also linked to different types of sexual violence such as child sexual abuse and forced sexual experience (Coker *et al.* 2009). The physical trauma and psychological stress, negatively influence the body's immune system.

A South African study revealed that every six hours a woman is killed by her intimate partner (Mathews *et al.*2004). The lifetime prevalence of intimate partner violence (physical and/or sexual) or non-partner sexual violence or both among all women (15 years and older) in the African region is reported as 45.6 per cent (MRC 2013). As Khan *et al.* (2006) report, females are more likely to be the victims of a poor diet than males. These factors too may suggest that any act that serves to protect the health and well-being of female-children should be prioritised.

Yet, although there is a case to be made for prioritising the HPV vaccination for female-children, equity will only be seen when male-children are immunised as well and together, both female and male-children reach the level necessary for immunity or 'herd' immunity.

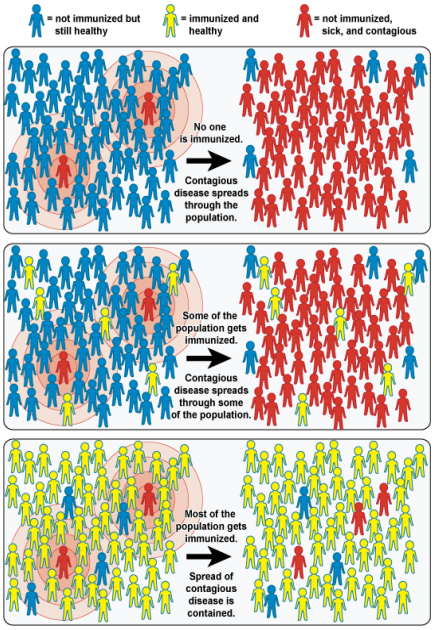


Figure 2.2.1 Herd or Community Immunity

Image Source: www.niaid.nih.gov/SiteCollectionImages/topics/communityImmunityGeneric.gif

A question yet to be addressed is “does the goal of herd immunity violate rights, such as those rights parents have concerning their children?” The rights that are involved in any vaccination programme include a child’s right to healthcare, parent’s right to raise their child in keeping with their own values and mores, and the right of the community to be protected against preventable communicable disease. These three rights may compete. The solution to competing rights is the view that not all rights are necessarily absolute and one right can be considered to outweigh or limit that of another.

Parental autonomy in matters relating to their children is particularly an issue raised by HPV vaccination in industrialised countries. This is because the subject

relates to a family's values concerning their children's sexual behaviour (Valmos *et al.* 2008). It is felt by such parents the provision of the HPV vaccination may contribute to sexual risk-taking and undermine efforts concerning abstaining from sexual intercourse (Ohri 2007). Articles that carry this concern come from industrialised countries where PAP screening programmes have been in place for over fifty years and as such had become the standard for cervical cancer prevention. Thus, it is likely that public education concerning HPV will allay some of their concerns. Industrialised societies, particularly the US are historically individualistic as opposed to many other societies, which have a more communitarian leaning (Bell D. 2013)

In South Africa, there is no current literature that identifies fears that the HPV vaccination will spark increased sexual activity. Should this occur, it might be helpful to turn to an ethical analysis of the benefits and burdens of implementing an HPV vaccination programme. In their South African study, Harries *et al.* (2009) identified that "opposition to the HPV vaccination was not anticipated if the vaccination was marketed as preventing cervical cancer rather than a sexually transmitted infection." They also suggested that educating communities concerning the relationship of HPV to cervical cancer as well as cervical cancer itself was very important noting that at community levels such information was sorely lacking. This relates to equity, viz. access to secondary healthcare services for better treatment and preventative options (ibid). Educating the public appears

to be the key as expectations may be high - such as the vaccination as a cure for present or advanced cervical cancer (Bloom *et al*. 2005). The benefit of the HPV vaccination lies in its use as an accepted biotechnology innovation that is capable of preventing serious disease. In this same vein, a burden would be any adverse drug side effects caused by the vaccination itself. Publications focusing on the administration of the cost-effective and appropriate public health initiative targeting a lifesaving problem are beneficial to public education. In public health, precedents' have been established when infringements of personal autonomy are imposed when the results will benefit the community. Should the HPV vaccination programme reach the level of a public debate concerning parental rights versus the public good, compelling argument can be made that in South Africa the benefits outweigh the burdens.

Daniel Callahan (2003) writes, "I hold that the first set of questions to be raised about any ethical problem should focus on its social meaning, implications, and context, even in those cases which seem to affect individuals only". His statement is relevant to the ethical issues rising in the HPV vaccination debate in South Africa. Contextualisation of the problem is vital, education of the South African population concerning cervical cancer is essential, healthcare resources should be allocated to support prevention and patient care, and communication with the community is non-negotiable for the vaccination programme to be a success.

In this chapter, I have discussed some of the ethical issues concerning an HPV vaccination programme. I have justified the initial phase of including female-children and suggest that the demands of health equity require that male-children be included as soon as it is feasible. In the next chapter, I will turn to some legal issues in HPV vaccination.

Chapter 3 Legal Issues in HPV Vaccine Immunisation

This chapter is based on the different pieces of legislation in the country. I argue that South Africa is legally bound to provide an HPV vaccination programme for prevention of cancer of the cervix as well as other HPV-related cancers. First, I will give a general background on what vaccination means in South Africa. Starting with the Constitution and covering all other legislation relevant to the youth and adolescent, I will show that the law supports providing the HPV vaccination for the target age group. Using the available data, I will also show that using the age of consent and sexual debut in the country, further supports youth and adolescent groups are highly susceptible to contracting the HPV and the need for protecting these groups using the HPV vaccination is thus imperative.

3.1 Legal issues in immunisation of South African children

It has been established that vaccination against common communicable diseases prevents suffering inflicted upon children by these diseases. Denying children this access to be vaccinated against these diseases can be regarded as an infringement of their basic human right. When viewed from this perspective, it is difficult to imagine a more basic infringement of children's rights than to deliberately put them at risk of suffering and dying, while a trusted intervention like a vaccination can prevent suffering. The WHO introduced the Expanded Programme on Immunisation (EPI) in 1974. The purpose EPI is to allow mostly developing countries the opportunity to combat communicable diseases, which

would otherwise result in high mortality of children. For example, an estimate of 2 million child deaths, were prevented by vaccination in 2003. It is in recognising this enormous impact of EPI that WHO and UNICEF have collaborated to provide support effective immunisation programmes. In South Africa, EPI is part of the essential package of Primary Health Care and is offered free of charge.

In line with the recognition of EPI is as a global health priority, the UN special sessions and the World Health Assembly (WHA) have adopted a number of resolutions on the control of diseases that are prevented by immunisation. The resolutions include: measles control, wild polio eradication and in 2005 endorsed, the Global Immunisation Vision Strategy (GIVS) (WHO 2005). The aim of GIVS is to increase global access to immunisation services. South Africa, as a member state of the United Nations, is mandated to implement these binding resolutions and ensure effective immunisation programmes.

Perhaps the other important legal point to address before discussing specific legislation on sexual consent and reproductive health is the rights of a child in relation to vaccination.

South Africa is obligated under Section 28(2) of The Constitution of the Republic of South Africa 1996, (Act No. 108 of 1996) to prioritise the best interests of the child in matters concerning children ‘A child’s best interests are of paramount importance in every matter concerning the child’. Argument could be made that because cervical cancer normally manifests at adult stage of human development,

the best interests of the child principle would not be applicable in this situation. Other factors being equal, it is known that HPV is transmitted at first sexual intercourse and takes ± 15 years to develop into a cervical cancer.

However, this principle must be read in conjunction with the United Nations Convention on the Rights of the Child, which has been ratified by 191 countries including South Africa. United Nations Convention on the Rights of the Child - adopted and opened for signature, ratification and accession by General Assembly resolution 44/25 of 20 November 1989. Entry into force 2 September 1990, in accordance with article 49. The Convention is quite clear that “every child shall enjoy special protection” and should be given the opportunity to ‘develop physically, morally, spiritually and socially in a healthy and normal manner”. Giving the child the VPV vaccination would allow her/him to develop in a health and normal manner. South Africa, through its Constitution, further affirms this right in Section 27(1) (a). According to this section on health care, food, water and social security, everyone has the right to have access to health care services, including reproductive health care. It is also stipulated that the state must take reasonable legislative and other measures, within its available resources, to achieve the progressive realisation of these rights. Section 28(2) is closely entwined with Section 27(1) (a) when it comes to the female-child and the adult woman.

It is on these constitutional imperatives that South Africa drafted a number of different legislation to address this matter, some of which are not necessarily relevant to the topic under discussion. The National Health Act 2003 addresses access to health services. This Act has devoted a full chapter 2, Sections 24 to 36: on rights and duties of users and health care personnel. This chapter stipulates conditions on access to health care services; responsibility for health care providers; and eligibility for free health services. Sub-section 2(c) (i) of the Act reaffirms the commitment of the State to the Constitutional mandate towards 'protecting, respecting, promoting and fulfilling the rights of the people of South Africa to the progressive realisation of the constitutional right of access to health care services, including reproductive health.

To fulfil this obligation, the National Department is to establish a National Healthcare System, which intends to encompasses public and private providers of health services; and provide, in an equitable manner to the population of the Republic with the best possible health services that available resources can afford.

3.2 Legal issues in HPV vaccine immunisation: Female and male children

Bridging studies of immunogenicity conducted amongst males and females aged between 9 and 15 years (FDA 2006) show that the HPV vaccine is immunogenic across a wide age-range, but the greatest immune responses were observed in pre-pubertal children (Rothstein and Marchant 2009). Numerous studies

confirmed the greatest immune responses in pre-pubertal female children as those aged 10-14 years (Block *et al.* 2006); 9-14 years (Giuliano *et al.* 2007); 10-18 years (Petäjä *et al.* 2009); and 10-14 years (Pedersen *et al.* 2007).

Prior to discussing legal issues concerning HPV vaccination in South Africa, it is important to examine one fundamental issue of who will be the target of HPV vaccination. If only female children are immunised, it is important to raise legal issues such as discrimination and equal protection.

If HPV vaccination is to be afforded to female children through a blanket public health intervention of preventing cervical cancer while male children are excluded from HPV vaccination, will this be considered as unfair discrimination?

Advocating female vaccination and excluding males, appears to deprive male children of equal protection and benefit of the law. Section 9(1) of the Constitution of the Republic of South Africa reads: “Everyone is equal before the law and has the right to equal protection and benefit of the law”.

It is, however, important that this case be analysed in terms of the cost involved if both females and males were to be afforded HPV vaccination and the difference in impact HPV between males and females. The vaccine is currently estimated to cost is R600 - R800 for three doses. While it may seem to be unfair discrimination on the ground of gender, the discrimination could be justifiable under Section 36 of the Constitution of the Republic of South Africa. It reads: “The rights in the Bill

of Rights may be limited only in terms of law of general application to the extent that the limitation is reasonable and justifiable in an open and democratic society. Based on human dignity, equality and freedom, taking into account all relevant factors, including the (a) nature of the right; (b) the importance of the purpose of the limitation; (c) the nature and extent of the limitation; (d) the relation between the limitation and its purpose; and (e) less restrictive means to achieve the purpose".

In the case of HPV vaccination, the limitation clause is applicable by weighing the mortality that would follow if legal mechanisms for regulation were not in place, against the resultant differentiation in treatment between males and females. HPV infections in males cause other cancers but the mortality rate is lower than when compared to deaths associated with cervical cancer in females. The South African courts have handled a similar case, discussed below.

In a landmark case, the "Minister of Health & Others vs. Treatment Action Campaign & Others (No. 2) 2002 (5) SA 721 (CC), the evidence showed that there is a minimum core of a particular service that should be taken into account in determining whether measures adopted by the state are reasonable.

Concerning socio-economic rights, Section 27of the Constitution, the ruling said, should not be construed as entitling everyone to demand that the minimum core be provided to them. This is because it is impossible to give everyone access even to a 'core' service immediately. The ruling identified that all that is possible,

and all that can be expected of the State is that it acts reasonably to provide access to the socio-economic rights identified in section 27 on a progressive basis.

Section 27(1) of the Constitution (providing for the right to health care services, food and water and social security) does not give rise to a self-standing and independent positive right enforcement irrespective of the considerations mentioned in section 27(2).

Importantly, Section 27(1) and 27(2) must be read together as defining the scope of the positive rights that everyone has, and the corresponding obligations on the state to respect, protect, promote and fulfil such rights.

In the case of HPV vaccination being afforded to male-children, it is expected of the state, as a democratic country, to progressively supply HPV vaccination to all who would need it.

3.3 Specific legislation dealing with reproductive health of children, age of sexual consent and age of sexual debut

Children's Act: The primary legislation addressing health issues and reproductive health services for children is the Children's Act 2005, (Act No. 38 of 2005). A number of issues are covered and include Section 129 on medical and surgical treatments; Section 130 on HIV testing; Section 12 on virginity testing; Section 134 on contraception; and Section 12 on circumcision. Some of these sections

are further, reiterated by additional legislation. These are Choice on Termination of Pregnancy Act 1996, (Act No. 92 of 1996); Sterilisation Act 2005, (Act No. 3 of 2005); and Criminal Law (Sexual offences and related Matters) Amendment Act 2007, (Act No. 32 of 2007). Some of these will be discussed further on the merit of their relevance to children's rights and HPV vaccination. Like with other communicable diseases the HPV vaccination can prevent suffering and dying of women with cervical cancer and other related cancers caused by the Human papillomavirus.

3.3.1Age of sexual consent

In South Africa, legislation-governing age of sexual consent and consent to related reproductive health intervention services for the age group being targeted for HPV vaccination is contained in several pieces of legislation. However, even with the guidance of specific legislation, there will be grey areas in the matter of consent to HPV vaccination of minors.

One of these concerns the maturity of the child concerned; and because the HPV vaccination is against a sexually transmitted virus, the wishes and opinions of the parents or guardian; cultural practices; and religious beliefs are of particular concern and need to be given special consideration and some of these may conflict.

The strongest argument from parents and other interested parties is that children should not be vaccinated on the grounds of medical opinion based on predictions of lifestyle choices that will be made during adulthood (Gwandure, 2011). However, unless these children abstain from sexual activities, there is a high possibility that they will contract human papillomavirus, and subsequently develop any of the cancers or genital warts associated with the virus. At this later age, the opportunity for protection that could be afforded by vaccination will be lost. The principle to bear in mind in such circumstances is that the child's best interests are paramount, as discussed herein.

The primary legislation governing the age of consent to sexual intercourse is the Criminal Law (Sexual offences and related Matters) Amendment Act 2007. According to this Act, the age of consent is 16, as stipulated in Sections 15 and 16 read with Section 1 of the Act. Section 15 on statutory rape, prohibits the engagement of "an act of sexual penetration with a child", while section 16 on statutory sexual assault prohibits the engagement of "an act of sexual violation with a child". Section 1 of the Act defines a "child" as a person under the age of 18 years; or a person 12 years or older but under the age of 16 years with respect to statutory rape and statutory sexual assault. The Act places the conditions that children are considered incapable of consenting to sex until the age of 12 years. Between the ages of 12 and 16 years, they are considered capable, but not

mature enough to consent to sex. Children at 16 years and older are thus considered capable and mature enough for consensual sex.

The Children's Act, 2005, Section 17, places the age of majority at 18 years. At this age, the law considers the person responsible and liable for acts or omissions. Anyone under 18 years needs their parents' or guardians' consent to bind them legally. At this age, for example, one can give consent to medical and surgical treatment. This Act does not have a definition for medical treatment, Prinslean *et al.* 2010 define medical treatment as a non-invasive and innocuous procedure, which include vaccination, and psychological treatment. Using this definition and the general understanding of what medical treatment entails, Section 129 of the Act states that a child at the age of 12 years can consent to medical treatment, if the child exhibit maturity and understands the implications of the procedure. Section 130 further reiterates, "the clinical and social implications of the medical treatment must be explained to the child". This view is applicable in the case of HPV vaccination. While the age of majority in the Act is 18, in the healthcare context, it recognises earlier ages at which informed consent to vaccination may be obtained from a child.

Because HPV vaccination is a reproductive intervention, other related legislation on reproductive health has relevance to this discussion. Of particular interest is the view of the Children's Act on reproductive health for children. Section 134 of

the Children's Act places the age at which a child can access contraceptives at 12 years. Section 134 stipulates that

"(1) No person may refuse – (a) to sell condoms to a child over the age of 12 years; or (b) to provide a child over the age of 12 years with condoms on request where such condoms are provided or distributed free of charge.

(2)Contraceptives, other than condoms may be provided to a child on request by the child without the consent of the parent or care-giver of the child if – (a) the child is at least 12 years of age; (b) medical advice is given to the child; and (c) a medical examination is carried out on the child to determine whether there are any medical reasons why a specific contraceptive should not be provided to the child.

(3) A child who obtains condoms, contraceptives or contraceptive advice in terms of this Act is entitled to confidentiality in this respect. However, it remains the responsibility of the health care providers to repost cases of physical or sexual abuse (Section 10 of the Act).

Other areas of reproductive health intervention include termination of pregnancy. According to the Choice on Termination of Pregnancy Act 1996, Sub-section 5(3), stipulates that no consent other than that of the pregnant woman shall be required for the termination of a pregnancy. For the purpose of the Choice on Termination of Pregnancy Act, woman means a female person of any age. Section 5(3) of the Act stipulates that … "in the case of a pregnant minor, a medical practitioner or a

registered midwife, as the case may be, shall advise such minor to consult with her parents, guardian, family members or friends before the pregnancy is terminated; provided that the termination of the pregnancy shall not be denied because such minor chooses not to consult them".

Interpreting this further is that, a female of any age can request a termination of pregnancy, but if she is a minor, she should be advised to consult with her parent or guardian, but she should not be denied a termination of pregnancy if she fails to consult a parent or guardian

The Sterilisation Act 1998, (Act No. 44 of 1998), places the age of consent to sterilisation, another reproductive health intervention, at 18 years. Section 2 (1) stipulates that no person is prohibited from having sterilisation performed on him or her if he or she is 18 years or above. Section 3 (1) (b) (i) stipulates that sterilisation may not be performed on any person who is incapable of consenting or incompetent to consent unless the physical health of the person is threatened. This mean that minors can only be sterilised if their life or health is compromised by not doing so.

According to the legislation discussed here, the age at which a child is considered independent varies from 12 to 18 years. The ideal age at which the HPV vaccination can be successfully be introduced, is below 12 years. Another important determinant for the age of introducing the vaccination depends largely on the sexual activities of the said children and this factor may be more pertinent

than ages of legal consent. The vaccines have been found to be more effective in those who have not been exposed to the virus (HPV-infection naive), and the key rationale for this approach is to intervene before sexual debut.

3.3.2 Age of sexual debut

Several studies conducted locally suggest that sexual debut in South Africa is less than 15 years with an average of 12 years. While most of these studies have been conducted to understand the risk behaviours of the youth in relation to HIV infections, the statistical results are relevant to HPV infection, as the two viruses are transmitted in the same way.

Earlier sexual debut is significantly associated with increased risk of HIV infection. Berry and Hall (2009) reporting on the data obtained from the South African Demographic Health Survey (SADHS) (1998-2003), found that "six percent of young women (15 – 24 years) reported having had sex by the age of 15 compared with twelve percent of young men". This suggests that males become sexually active earlier than do females. According to the SADHS data, by the age of 18, 42% of young females and 63% of young males had become sexually active.

A study by Anderson *et al.* (2005: 1-20) examined the relationship between HIV/AIDS risk perceptions and first intercourse amongst the youth in Cape Town. This research revealed that 50% of 4752 children in 2002 and 3536 children in

2005 perceive themselves to be at low risk of contracting HIV. This percentage was proportional to first intercourse. Although this study was conducted amongst youth 17 and over, it is a good reflection of sexual behaviours amongst youth.

A prospective population-based HIV and sexual behaviours survey conducted in the rural Kwa-Zulu Natal (2003 – 2007) was used to investigate the distribution and predictors of earlier first sex. The study population consisted of 4724 women and 4029 men aged between 12 – 25 years with emphasis on age of sexual début. The findings of the study were that out of the 4724 women who started as virgins 2051 (43%) reported having sex during the study period with the median age being 18.5 years (McGrath *et al.* 2009).

Wand and Ramjee, (2012) conducted a prospective study to investigate the impact of early sexual debut on HIV sero-prevalence and incidence rates among a cohort of women – between 2002 and 2005 in Durban South Africa. 3492 sexually active women consented to be screened in a HIV prevention trial during the study period, 1485 of the participants were followed-up for two years. During this period, 148 (6.8%) sero-converted. The highest sero-conversion rate was observed among women who had reported to have had sex at 15 years or younger.

An in-depth study was conducted by Harries *et al,* (2009) in the Western Cape Province, in an effort to find out the key challenges and opinions in preparation for HPV vaccination in South Africa. The study population involved two (2) doctors, 17 Primary Health Care (PHC) nurses, and 5 School Health nurses. In addition,

43 females from the community and 42 females recruited from PHC facilities (7 per facility) took part in the study. The results of this study indicated that sexual activity in South African females began between the ages of 9 – 15 years.

Perhaps the study that sums up the issue on age of sexual debut and sexual violence in South Africa is that conducted by Matthews *et.al* (2009). A prospective study conducted between 2004 and 2007 to determine predictors of early sexual intercourse among adolescent in Cape Town. This was a cluster-randomised controlled trial to investigate the effect of school-based HIV prevention programmes among grade 8 students (12 – 14 years). The study population was 1440 students with 836 females and 604 males. 12.9% of the females had their first sexual experience during the course of the study, while the percentage for males was 31.1%. Of all the females and males who had their first sex experience during this period, 76 females and 142 males reported being victims of violence in their intimate relationships. Of these, 52 (27.8%) females and 19 (17.8%) males reported forced sexual intercourse, underscoring the high level of sexual abuse in the country. While the study does not specify who are the perpetrators of the sexual abuse and violence, the high percentage of females (27.8%) indicate the scourge of sexual violence and re-iterates the need to protect these females before they are exposed to sexual intercourse and imminent infection by HPV.

From the above legal stipulations as regard age of sexual consent, should vaccination be to anyone under 12 years, this should be accompanied by

parental/caregiver consent. For children 12 years and older, the child's consent will suffice on condition that the child is of sufficient maturity and has the mental capacity to understand the benefits, risks, social and other implications of the vaccination.

The above studies point to the age of sexual debut in South Africa as between 12 and 15 years. It is on the basis of the above studies that it is recommended that the HPV vaccination be introduced before the age of ten - "with an underlying concern that high levels of sexual abuse has significantly decreased the age of sexual debut/exposure suggesting that vaccination should commence as early as nine years" (Harries *et al.* 2009).

From the above discussions, it is clear that introducing HPV vaccination in females from the age of 9 years will not be in violation of any existing laws in South Africa. Based on these it is thus ideal to vaccinate females between the ages of 9 -13 years.

Now that the ethical and legal issues have been discussed, it is clear that policy change towards respecting the rights of female children in the country with respect to the HPV vaccination is imperative.

Chapter 4 Policy recommendations and concluding remarks

This study has raised ethical and legal issues that strongly support the HPV vaccination intervention. There are few services for youth and adolescents health interventions. The HPV vaccination intervention is one area that specifically deals with this group. The recommendations that follow have bearing on policy and legislation issues for youths and adolescents. The main objective of the recommendations is to position the HPV vaccination in South Africa such that despite the challenges, it addresses ethical and legal concerns related to the intervention. The ultimate aim is to provide an HPV vaccination intervention that is practical in addressing the risk issues through a system that will avoid any legal suits from the public.

4.1 Policy development, recommendations, delivery strategies and monitoring & evaluation

The WHO (2009), in their position paper on vaccines against diseases caused by HPV, gives a number of recommendations on the introduction of the HPV vaccination for countries. The recommendations are:

1) “ HPV vaccination should be included in national immunisation programmes provided that: prevention of cervical cancer and other HPV-related diseases is a public health priority;

2) vaccine introduction is programmatically feasible, and sustainable financing can be secured;

3) the cost-effectiveness of possible introduction and vaccination strategies in the country or region be considered;

4) HPV vaccines should be introduced as part of a coordinated cervical cancer and other HPV-related diseases prevention strategy, including education on risk reducing behaviours, diagnosis and treatment of precancerous lesions and cancer;

5) HPV vaccine introduction should not undermine or divert funding from effective cervical cancer screening programmes and should not replace cervical cancer screening;

6) Programmes to introduce HPV vaccines should seek opportunities to link with other adolescent health services; and

7) HPV vaccination should not be deferred in countries because one or more of these interventions cannot be implemented at the time when vaccination could be introduced."

The introduction of HPV vaccination in developed countries has been successful and in line with the WHO recommendations, and is delivered through School-Health policy. Developed countries have been successful in implementing HPV

vaccination because they have the necessary infrastructure, and advanced school health policies (LaMontagne *et al.* 2011). Despite the success there are lessons learned which will apply not only to rich countries, but also to all countries implementing HPV vaccination.

Lessons learned and barriers to effective vaccination coverage in the developed world include:

(1) “partial vaccination for female children due to the vaccination schedule (the delivery of the vaccines is 0, 2 and 6 months period) and not necessarily opposition of the vaccination;

(2) the targeted females being absent from school on the scheduled dates of vaccination;

(3) limited awareness of the vaccination programme;

(4) insufficient information about cervical cancer, the HPV vaccine or the HPV vaccination programme;

(5) difficulty in determining a female’s eligibility; and

(6) insufficient information has also been found to contribute to vaccination refusal in developed countries.”

The key to avoid these challenges is to pay heed the problems, attentively plan and raise awareness amongst the communities concerned (LaMontagne *et al.* 2011).

Monitoring and evaluation of HPV vaccination is one of the key issues the WHO is placing emphasis. Because the progression of an HPV infection to any of the related cancers or other diseases takes a long time, in 2005 the WHO established a network of laboratories aimed to provide quality service for detection of HPV infections. These infections will assist in surveillance and determining the impact of HPV monitoring and training of laboratory personnel to build capacity (WHO 2005a). Other activities that are specific to HPV for monitoring is the annual review of delivery strategies in order to improve the strategies.

The biggest challenges in introducing HPV vaccination in developing countries are still the cost of the vaccine, cold chain, females not attending school and poor infrastructure for delivering of the vaccine (WHO April 2012). However, most of these developing /poor countries qualify for the Global Alliance for Vaccines and Immunisation (GAVI), which aims to reduce the prices on vaccines for EPI programmes (GAVI Policy 2009). Countries qualify for GAVI support if their Gross National Income (GNI) per capita is below or equal to US$1,550.The current GAVI price for HPV vaccines is $4.50 per dose (WHO May 2013).

South Africa, as a developing country faces additional challenges such as:

GAVI support SA does not qualifying for GAVI support, because the GNI was estimated at $7,610.00 in 2012 (World Bank 2012).

Integrated School Health Policy: South Africa launched the Integrated School Health Policy (which is a joint project between the Department of Health and Department of Basic Education) in October 2012. The policy does not provide the optimal school nurse and student ratio. Guttu *et al.*(2004) writing in the locale of the Southern US, reported on his study which covered twenty -one (21) counties with school nurse-to-child ratio ranging from 1:451 to 1:7,440. Schools with school nurse-child ratio below 1:750 provided better services than schools with high ratios.

The WHO estimates the number of 9-13 year old female children, in South Africa, eligible for HPV vaccination at 2,210 000 (WHO 2012). Currently, South Africa has 453 school health nurses (Personal communication Ms S Ngake: Deputy Director: Child Health at the National Department of Health. Pretoria). The ratio of school nurse-child is therefore 1:4,878, which is far above the 1:750 recommended in USA. The only way that the HPV vaccination programme can reach the target female children, with three doses of the vaccine, delivered within the space of six months will need an additional deployment of nurses. The nurses can be those who have retired or from PHC as recommended in the Policy as well as volunteers.

Because the HPV vaccination will be incorporated into the existing EPI programme, it is worth mentioning that the EPI coverage is also facing challenges. Staff shortage, poor supervision of nurses (Ngcobo 2008), and these challenges will influence the implementation of HPV vaccination.

4.2 Concluding remarks

The first chapter outlined the scientific background that deals with relationship between HPV infections and related cancers. Emphasise was made on the burden of cervical cancer. The current preventative strategies to cervical cancer, place with emphasis on providing a vaccine against oncological HPV types. It is from the relationship between the HPV and the cancers that recombinant technology was used to develop the available HPV vaccines. Challenges of an HPV vaccination programme were identified in the context of public health ethics. Relevant topics such as the HPV vaccines' efficacy, cross protection, safety, duration of protection and cost factors were also discussed in this chapter. Chapter one also dealt with the methodology, objectives and outcomes of the study. The limitations for this study were outlined and emphasis was placed on on-going scientific developments, which might affect this study.

Chapter 2 looked at the ethical issues in HPV vaccination, with emphasis on ethical theories that support vaccination: Utilitarianism and Communitarianism. The discussion in this chapter affirms the need for the HPV vaccination of female-children as a preventative measure for cervical cancer and not a sexually

transmitted virus. Community participation in the discussions and planning, delivery of the vaccines was reiterated as a measure of buying-in of parents and guardians.

Chapter 3 concerned some of the Legal issues regarding the HPV vaccination programme. Legislation and age of sexual debut placed the age for HPV vaccination at 9 years. It is based on sexual debut that the HPV vaccination is recommended for the age group of 9 – 13 years. While the legislation and discussion in this chapter excluded HPV vaccination as being in the best interest of the child, other reproductive health legislation concerning the target age group support HPV vaccination.

For the HPV vaccination to be successful, delivery strategy of the vaccination programme should include partners such as UNICEF, United Nations Fund for Population Activities (UNFPA) and the private sector to lobby for a reduced price of the vaccines. Further, as an additional reduction to the cost, a two-dose regimen instead of three should be considered. Implementation of the School Health Policy is to be improved in order to reach more children, with training of more nurses. Vaccination of out-of school female-children should be by campaigns as most of the areas affected are in the rural areas.

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