CHAPTER ONE

INTRODUCTION

1.1 Study Background

Cervical cancer is the fourth most commonly diagnosed cancer and fourth leading cause of cancer death among females worldwide (Ferlay *et al*., 2010). Every year, about 530,000 women around the world are diagnosed with cervical cancer and about 275,000 women die from the disease (Ferlay *et al*., 2010).

The incidence rate in less developed regions (1708 cases per 100,000) is more than double the rate in more developed areas (9.0 cases per 100,000) (Ferlay *et al*.,2010). Cervical cancer ranks as the second most frequent cancer among women in Nigeria (ICO, 2014). About 47.72 million women aged 15 years and older are at risk of developing cervical cancer in the country (ICO, 2014). Also, about 14,089 women are diagnosed with cervical cancer and 8,240 die from the disease yearly in the country (ICO, 2014). The health and economic burden of cervical cancer is substantial. Deaths often occur in relatively young women, who are raising children, caring for families, and contributing to communities (Goldie *et al.*, 2008).More than 40 types of genital HPV are classified as either low risk or high risk types, depending on whether or not they are associated with cervical cancer (Brown*et a*l 2010). High risk HPV types cause virtually all cases of cervical cancer and also may lead to anal, penile, vaginal, vulvar, Oropharyngeal, and mouth cancers (Brown et al., 2010). Low risk HPV types may cause genital warts or recurrent respiratory papillomatiosis.

While cervical cancer screening programmes have been effective in reducing cervical cancer incidence in developed countries, screening in Nigeria is still unpopular (ICO, 2014). HPV screening is largely opportunistic with coverage estimated to be around 8.7 % (ICO, 2014).

There is currently no organized national screening programme in the country (ICO, 2014). The two types of vaccines that prevent cervical cancer - GSK's bivalent HPV vaccine (Cervarix®) and Merck & Co. Inc.'s quadrivalent HPV vaccine (Gardasil®) - are both licensed in Nigeria. The vaccines are highly effective in preventing persistent HPV infection and subsequent precancerous lesions due to infection with two types of HPV - types 16 and 18 – that cause about 70 % of cervical cancer worldwide [ICO, 2014]. In addition, quadrivalent HPV vaccine also protects against HPV types 6 and 11, which are responsible for genital warts (National Cancer Institute, 2011). Since the vaccines are not effective once a woman has been infected, and acquisition of HPV infection occurs relatively quickly after sexual debut, it is widely accepted that providing young adolescent girls with the vaccines before the onset of sexual activity will be the most cost-effective strategy (WHO,2015). WHO recommends vaccination for girls aged 9 -13 years as this is the most cost-effective public health measure against cervical cancer (WHO, 2015).

High prices have been a major barrier to introducing HPV vaccines in developing countries. The Vaccine Alliance (GAVI) and its partners provide the poorest countries with the access to sustainable supply of new and underused vaccines (GAVI, 2014). GAVI offers access to HPV vaccines for as little as N895.5per dose and provides support for HPV demonstration programmes and the national introduction of HPV vaccines (GAVI, 2014). The type of support provided however depends on a country's demonstrated ability to deliver vaccines to young adolescent girls (GAVI, 2014). GAVI's current vaccine support for Nigeria includes Pentavalent, Pneumococcal Conjugate, Yellow Fever, Meningitis A and Measles vaccines, as well as cash support for health system strengthening and immunization system strengthening (GAVI fact sheet, 2015).

The National Primary Health Care Development Agency (NPHCDA) in Nigeria recently announced commencement of plans for national HPV vaccination (Chukwu, 2015). The plan

involves a demonstration project in some selected states of the federation in order to determine cost, acceptance and best delivery method (Chukwu, 2015). A financially sustainable HPV vaccines delivery strategy is likely to require user financing to offset some percentage of the actual cost of vaccination. However, the viability of user fees as a financing mechanism for HPV vaccine depends on private demand for the vaccines (WTP).

Studies have assessed parental acceptance of HPV vaccination for their daughters in Nigeria and have reported high level of acceptance for the vaccine (Ugwu *et al.,* 2013; Perlman et al., 2014; Ezeanochie and Olagbuji, 2014). However, to the best of our knowledge no study has estimated the amount parents are willing to pay for HPV vaccine. Since HPV vaccines are targeted at young adolescents, parents will obviously play important roles in decision-making regarding their daughter vaccination. The focus on mothers was because the responsibility of family health in many families mainly falls to the mother(McGuigan, 2012).

1.2 Statement of the Problem

Currently, HPV vaccines are purchased 'out-of-pocket' and are not included among the vaccines offered for free under the National Immunization Programme (NIP) in Nigeria. Providing free HPV vaccination would further strain the government's tight health budget. Beside the cost of the vaccine, HPV vaccination requires the development of a new vaccine delivery service for adolescent girls in order to achieve the required dose. This is particularly due to the lack of an existing structure to support the adolescent vaccine delivery. Therefore, even with Gavi's support, HPV vaccination will require a substantial sum of money for its delivery. Therefore, a financially sustainable HPV vaccine delivery strategy is likely to require user financing to offset some percentage of the actual cost of vaccination. However, the viability of user fees as a financing mechanism for HPV vaccine depends on private demand for the vaccine (WTP).

WTP studies have been conducted in other nations to explore the viability of user fees to co-finance HPV vaccination program (Brown et al., 2009; Poulos *et al.,* 2011; Siraporn *et al.,* 2012). While there are studies on knowledge and willingness of parents to vaccinate their adolescent daughters in Nigeria (Ugwu *et al*., 2013, Iliyasu, Abubakar, Aliyu, & Galadanci, 2010, Ezeanochie & Olagbuji, 2014), to the best of our knowledge, no study has estimated amount parents are willing to pay for HPV vaccine. Secondly, probable cost per vaccinated girl with HPV vaccine has not been established in Nigeria.

1.3 Study Objectives

This study was aimed to assess Nigerian mothers' willingness-to-pay (WTP) for HPV vaccine using a contingent valuation method. The specific objective is to compare the average WTP amount for HPV vaccine with an estimated cost of vaccinating a pre-adolescent girl child (CVG) against HPV infection in Nigeria.

1.4 Justification

The results from this analysis can be used to assess whether fee-based HPV immunization services are a feasible way to achieve financial sustainability of HPV vaccination programme. Since the cost of HPV vaccines are high and not been subsidized like other vaccines under the national programme of immunization, it will be good establish mother's acceptance for the vaccine and the maximum amount they are ready to pay for the vaccine. This will help to establish the exact amount the government will place as fee for the vaccine in the event of HPV vaccine inclusion in the national immunization program.

1.5 Human Papilloma Virus

Human papilloma viruses are small, double-stranded DNA viruses that infect the epithelium. More than 120 HPV types have been identified (American cancer Society, 2015). They are

differentiated by the genetic sequence of the outer capsid protein L1. Each HPV virus in the group is given a number which is called an HPV type. Specific types of HPV tend to show some tissue tropism and depending on the type of epithelium infected, HPV types are often referred to as "cutaneous' or mucosal types. In general, cutaneous types infect the keratinizing epithelium (especially the skin of the hands and feet), while, mucosal types infect non-keratinizing epithelium primarily the anogenital tract epithelium, though they can also be found in the oral mucosa, conjunctiva and respiratory tract (Gomez and Santos, 2007).

As shown in table 1, HPV is associated with a variety of clinical conditions that range from innocuous lesions to cancer (Gomez and Santos, 2007). Most of HPV infections are benign. Infections of cutaneous epithelium can cause warts (Plantar warts, common warts and flat warts). Skin warts are transmitted by direct contact with an infected tissue or indirectly by contact with virus contaminated objects (Gomez and Santos, 2007). In general, they resolve spontaneously within one to five years. Recurrent respiratory papillomatosis is primarily a disease of the larynx in young children but can also occur in adults. The infection in young children is thought to be acquired by passage through an infected birth canal. Conjunctival papillomas associated with HPV infections has been described (Gomez and Santos, 2007). HPV-6 and HPV-11 are the etiologic agents of external anogenital warts (condylomas), which occur in sexually active individuals. Although they are benign, genital warts are a significant problem in sexually active individuals. Anogenital cancers are the most important disease associated with HPV infections.

HPV is one of the most common causes of sexually transmitted disease in both men women worldwide (Gomez and Santos, 2007). Of the many types of HPV, about 30 infect the genital tract through sexual contact. Genital HPV types infect primarily the cervix, vagina, vulva, penis, and anus. These genital HPV types are further divided into high risk and low

risk types according to association with genital tract cancer. Low-risk types include types 6, 11, 42, 43 and 44, and usually cause benign anogenital warts. High-risk HPV types include types 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and 70 and cause anogenital cancer (Munoz *et al*., 2003).Among the cancers attributable to high-risk HPV infection, cervical cancer has received the most attention. HPV 16, 18, 31 and 45 account for more than 90 % of cervical carcinomas (Munoz *et al*., 2003). Of these types HPV 16 is the most often found, accounting for about half of cervical cancer cases in the United States and Europe (Munoz *et al.*, 2003). Type 16 and 18 together account for about 70 % of cervical cancer (CDC, 2015). In addition, high – risk HPV types have been related with other genital cancers, such as carcinoma of vagina, vulva, penis and anus and their precancerous lesions (Anderson, 2002).

Table 1: Human Papillomavirus types and clinical manifestation (Gomez and Santos, 2007)

Clinical Manifestation	**HPV Types**
Plantar warts	**1, 2, 4,** 63
Common warts	**2, 1,** 7, 4,26,27,29,41, 57, 65, 77, 3, 10, 28
Flat warts	**3, 10,** 26, 27, 28, 38,41, 49, 75, 76
Other cuteneous lessons (e.g. epider moid cysts, Laryngcal carcinoma)	6, 11, **16,** 30, 33, 36, 37, 38, **41, 48, 60,** 72, 73
Epidermodysplasia verruciformis	**2, 3, 10, 5, 8, 9, 12, 14, 15, 17,** 19, 20, 21, 22, 23, 24, 25, 36, 37, 38, 47, 50
Recurrent respiratory papillomatosis	**6, 11**
Focal epithelial hyperplasia detteck	13**,** 22
Conjunctival papillomas/carcinomas	**6, 11, 16**
Genital warts (condylomas/carcinomas)	**6, 11,** 30, 42,43, 45, 51, 54, 55, 70
Low risk cervical intraepithelial neoplasis	**6, 11,** 16,18,13, 33, 2, 43, 44, 45, 51, 52, 74
High risk cervical intraepithelial neoplasia	**16, 18,** 6, 11, 31, 34, 33, 5, 39, 42, 44, 45, 51, 52, 56, 58, 66
Cervical carcinoma	**16, 18,** 31, 45, 33, 35, 39, 51, 52, 56, 58, 66, 68, 70
Other genital carcinoma (vagina, vulva, penis and anus	16, 18, 31, 45, 33, 35, 39, 51, 52, 56

Note|: *bold type indicates most frequent association*

1.5.1 HPV and Cervical cancer

Cervical cancer and premalignant lesions constitute a major problem in women's health. Cervical cancer is the second most common cancer in women worldwide and is the most frequent cancer in many developing countries (Gomez and Santos, 2007). Every year, 470,000 new cases of cervical cancer are diagnosed worldwide, and about half of the afflicted women will die (Franco *et al.,* 2001). Although cervical cancer screening had dramatically reduced the incidence of this disease in the developed world, it is still estimated that there will be 5,000 deaths from cervical cancer in US per year (Franco *et al*., 2001). Cervical cancer ranks as the second most frequent cancer among women in Nigeria (ICO, 2014). About 47.72 million women aged 15 years and older are at risk of developing cervical cancer in the country (ICO, 2014). About 14,089 women are diagnosed with cervical cancer and 8,240 die from the disease yearly in the country (ICO, 2014). In areas of the world where most women do not have access to regular gynecological care and screening, cervical cancer is second only to breast cancer as a cancer-related cause of death (Gomez and Santos, 2007).

The link between genital HPV infections and cervical cancer was first demonstrated in the early 1980's by Harold Zur Hausen, a German Virologist (Gomez and Santos, 2007). Since then the link between high risk HPV types and cervical squamous cell carcinoma has become well known. In 1996, the World Health Association recognized HPV as an important cause of cervical cancer (Gomez and Santos, 2007). HPV has been implicated in 99.7 % of cervical squamous cell carcinoma cases worldwide (Walboomers, 1999). The magnitude of association between HPV and cervical carcinoma is higher than that for association between smoking and lung cancer (Franco, 2001).

1.5.2 Epidemiology

Human Papilloma virus infection occurs throughout the world. Humans are the only natural reservoir of HPV. Human Papilloma Virus is transmitted by direct contact, usually sexual with an infected person. Transmission occurs most frequently with sexual intercourse but can occur following nonpenetrative sexual activity. Studies of newly acquired HPV infection demonstrate that infections occur soon after onset of sexual activity. In a prospective study of college women, cumulative incidence of infection was 40% by 24 months after first sexual intercourse.HPV 16 accounted for 10.4 % of infections (CDC, 2015). About 14,089 women are diagnosed with cervical cancer and 8,240 die from the disease yearly in Nigeria (ICO, 2014). There is no seasonal variation in HPV infections. Human papilloma virus is presumably communicable during the acute infection and during persistent infection. This issue is difficult to study because of the inability to culture the virus. Communicability can be presumed to be high because of the large number of new infections estimated occur each year.

1.5.3Pathogenesis

Transmission of HPV occurs primarily by skin to skin contact. Basal cells of stratified squamous epithelium may be infected by the HPV. Other cell types appear to be relatively resistant. It is assumed that the HPV replication cycle begins with entry of the virus into the cells of the basal layer of the epithelium. It is likely that HPV infection of the basal layer requires mild abrasion or microtrauma of the epidermis. Once inside the host cell, HPV DNA replicates and progress to the surface of the epithelium. In the basal layer, viral replication is considered to be non-productive and the virus establishes itself as a low-copy-number epitome by using the host DNA replication machinery to synthesize its DNA on average once

per cell cycle (Flores and Lambert, 1997). In the differentiated keratinocytes of the suprabasal layer of the epithelium, the virus switches to a rolling-circle mode of DNA replication, amplifies its DNA to high copy number, synthesize capsid proteins, and causes viral assembly (Flores *et al*., 1999).

The pathogenesis of cervical cancer is initiated by HPV infection of the cervical epithelium during sexual intercourse. Even though a high percentage of sexually active young women are exposed to HPV infections, only a very small percentage go on to develop cervical cancer (Elfgren *et al*., 2000). Several studies have suggested that most women successfully clear the HPV infection, presumably through the action of a competent immune system. Approximately 90 % of lesions regress spontaneously within 12 to 36 months (Chua and Hjerpe, 1996).

Other factors such as genetic predisposition, frequency of re-infection, intratypic genetic variation within HPV type, co-infection with more than one HPV type and hormone level may also influence the ability to clear an HPV infection. The evidence for the importance of the host immune system in preventing the development of cervical disease comes from the analysis of HPV infections in human immunodeficiency virus (HIV)-positive women. HPV infection with high-risk viral types, persistence of HPV infection and the presence of squamous intraepithelial lesions are more common within this immunocompromised group than in immune competent women (Cubie *et al.,* 2000).

The host cellular immune response is mediated by cytotoxic T cells and requires interaction with viral epitopes with histocompatibility class 1 molecules (Ostor, 1993). A hummoral immune response also develops but local levels of HPV-specific immunoglobulinG (IgG) and immunoglobulinA (IgA) in tissue do not correlate with virus clearance. In contrast, systemic

levels of HPV-specific IgG have been detected more frequently in patient with persistent HPV infection (Ostor, 1993).

The natural history of cervical cancer is a continuous disease process that progresses gradually from wild cervical intraepithelial neoplasia (CIN) to more severe degrees of neoplasia (CIN2 or CIN3) and finally to invasive cancer (Holowaty *et al.*, 1999). It is plausible that high-risk HPV infection occurs early in life, may persist, and in association with other factors promoting cell transformation, may lead to a gradual progression to more severe disease (Ho *et al*., 1995). A model for development of cervical cancer is presented in figure 1 (Gomez and Santos, 2007).

Mild and moderate dysplasias are associated with continued viral replication and virus shedding, and most of these lesions spontaneously regress. Progression to high grade lesions (CIN 2/3) and ultimately invasive cancer is usually associated with conversion of the viral genome from an episomal form to an integrated form, along with inactivation or deletion of Ez region and expression of the E6/E7 product genes (Holowaty et al, 1999). Some investigators have correlated HPV types with different decrees of CIN and have suggested that CIN1 and CIN 2/3 are distinct processes, with CIN1 indicating a self-limited sexually transmitted HPV infection and CIN2 or CIN3 being only true cervical cancer precursor (Holowaty et al, 1999), progression to cancer usually takes over a period of 10 to 20 years. Some lesions become cancerous more rapidly, sometimes within two years (Holowaty *et al*, 1999).

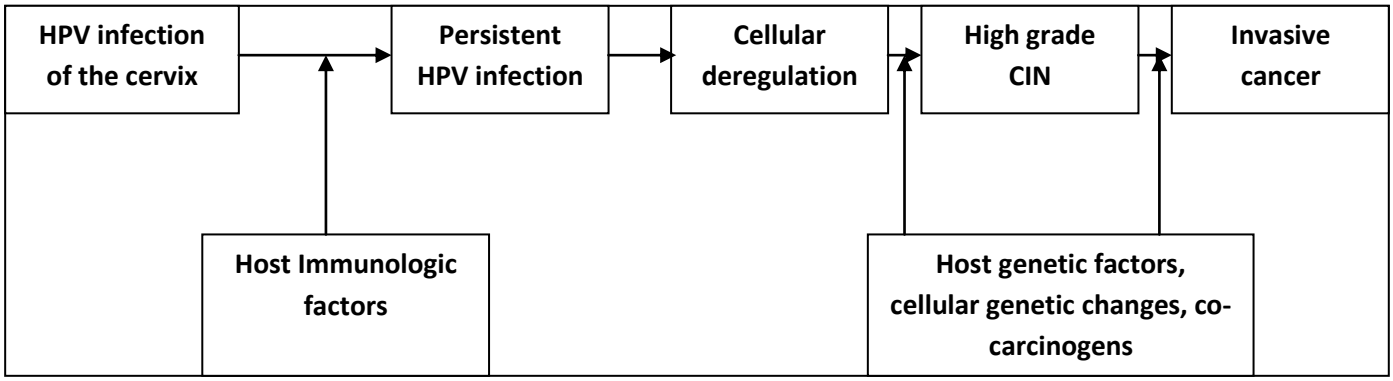

Figure 1: Model for the development of cervical cancer.

1.5.4 Risk Factors

Epidemiologic studies indicate that the risk of contracting genital HPV infection and cervical cancer is influenced by a variety of factors. High risk HPV infection is necessary but may not be sufficient for the development of cervical cancer. Cervical cancer depends on a variety of additional factors that act in concert with cancer associated HPV types.

1. Sexual factor

Numerous studies clearly indicate that the risk of contracting genital HPV infection and cervical cancer is influenced by sexual activity. An individual is at greater risk of becoming infected with HPV if he or she had multiple sexual partners (Peyton *et al* 2001). Sexual activity at an early age also has an increased risk of HPV infection, as does a history of other sexually transmitted disease, genital warts, abnormal pap sexual partner (Franco *et al* 2001). Condom usage may not adequately protect individuals from exposure to HPV since the virus can be transmitted by contact with infected tissues that are not protected by a condom.

In addition to sexual activity, age is an important determinant of risk of HPV infection. Most cervical cancers arise at the squamocolumnar junction between the epithelium of the endocervix and the squamous epithelium of the ectocervix. At this site, there are continuous metaplastic changes. The greatest risk of HPV infection coincides with greatest metaplastic activity. Greatest metaplastic activity occurs at puberty and first pregnancy and declines after menopause. The HPV prevalence reaches its peak in young adults (18 to 30 years of age) and declines at older ages (Burk *et al*., 1996). It has been shown that that as many as 46 % of college women, may have an HPV infection of the genital tract (Bauer, *et al* 1991). However, cervical cancer is more common in women older than 35 years, suggesting infection at a younger age and slow progression to cancer. (Gomez and Santos, 2007).

2. Viral factors

Persistent cervical infection (often defined as infection that is detected more than once in an interval of 6 months or longer) with an oncogenic HPV type (especially HPV – 16 and HPV – 18), is the most important risk factor for progression to high grade dysplasia and invasive cancer (Ho *et al,* 1995). The risk of progression depends on the HPV type. A 4 – 6 year follow-up of 1643 women with normal cytology showed that women with a positive PCR high – risk HPV DNA test at baseline were 116 times more likely to develop CIN3 than women with a negative DNA test (Rosendaal *et al*., 1996). The risk of progression for HPV – 16 and HPV – 18 is greater than for other HPV types approximately 40 % (Kiviat and Koutsky, 1993).

It has been proposed that the viral load correlates directly with the serenity of disease. Studies using quantitative type specific PCR for high-risk HPV and low-risk HPV has shown that HPV – 16 can reach much higher viral loads than other types, and that only for HPV-16 high viral loads correlate with increased severity of cervical disease (Swan *et al,* 1999). High-risk HPVs are able to induce malignant tumors even when they are present at low levels.

An important emerging factor in development of cervical neoplasia is the role of HPV variants. HPV variants differ in biological and chemical properties and pathogenicity (Giannoudis and Herrington, 2001). The oncogenicity of specific HPV variants appears to vary geographically and also with ethnic origin of the population studied. Based on sequence variation of L1, L2 and URR regions of HPV-16, five variants have been defined for HPV-16; European [E], Asian (As), Asian-American (AA), African- (AF1) and African 2 (AF2). Asian-American variants might have enhanced oncogenicity activity compared to European isolates due to increased transcriptional activity (Quint *et al*., 2001).

Several studies have shown that infections with multiple types of HPV can occur (Quint *et al* 2001). The majority of multiple infections contain two HPV types, but sample with two, three, four or five types were also seen (Quint *et al* 2001). The presence of multiple HPV types tended to increase with the severity of cervical disease. Multiple HPV types, usually with at least one type classified as high-risk, were found in 12 % of patients with normal cytology and in 35% of patients with mild to moderate dysplasia (Gomez and Santos, 2007).

3. Non-Viral Factors

The primary immune response to HPV infection is cell medicated; therefore, conditions that impair cell-mediated immunity such as renal transplantation or HIV disease increase the risk of acquisition and progression of HPV (Ho, *et al* 1995). The URR region of HPV contains sequences similar to the glucocorticoid response elements that are inducible by steroid hormones such as progesterone (the active component of oral contraceptives). Long term use of oral contraceptives is a significant-risk factor for high-grade cervical disease according to some studies (Gomez and Santos, 2007). Cervical cancer risk also seems to be independently influenced by other variables including smoking and parity, multiple pregnancies, alcohol consumption and diet (Adam *et al.*, 2000).

There have been suggestions that sexually transmitted viruses may serve as co-factors in the development of cervical cancer (Gomez and Santos, 2007) genetic predisposition was found to be a great component in cervical cancer. Genetic heritability was found to account for 27% of the effect of underlying factors for tumor development. Heritability could affect many factors contributing to the development of cervical cancer, including susceptibility to HPV infection, ability to clear HPV infection, and time to development of disease. The effect of shared familial environment was shown to be small at 2% and was found only between sisters and not between mothers and daughters (Gomez and Santos 2007).

1.5.5 Signs and Symptoms of HPV infection and Laboratory diagnosis

The majority of HPV infection does not cause symptoms or disease and resolved spontaneously. However persistent infection with specific types of HPV (most frequent types 16 and 18) may lead to precancerous lesions (WHO, 2015). If untreated, these lesions may progress to cervical cancer. Thus, progression usually takes many years. Symptoms of cervical cancer tend to appear only after the cancer has reached an advanced stage and may include:

- Irregular, intermenstrual (between periods), or abdominal vaginal bleeding after sexual intercourse.
- Back, leg or pelvic pain
- Fatigue, weight loss, loss of appetite
- Vaginal discomfort or odorous discharge; and
- A single swollen leg

More severe symptoms may arise at advanced stages.

HPV has not been cultured by conventional methods. Infection is identified by detection of HPV DNA from clinical samples. Assays for HPV detection differ considerably in their sensitivity and type specificity and detection is also affected by the anatomy region sampled as well as the method of specimen collection.

Several HPV tests have been approved by the food and Drug Administration (FDA)(CDC, 2015).The test detects 13-14 high-risk types of HPV(16, 18, 31, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68). Test results are reported as positive or negative for any of the types; some tests specifically identify HPV 16 and 18. These tests include:

- Conventional (pap) test and liquid based cytology (LBC)

- Visual inspection with acetic acid (VIA)
- HPV testing for high-risk types using nucleic acid amplification methods.
- Polymerase chain reaction

Epidemiologic and basic research studies of HPV generally use nucleic acid amplification methods that generate type-specific results. The polymerase chain reaction (PCR) assays used most commonly in epidemiologic studies target genetically conserved regions in the L1 gene. The most frequently used HPV serologic assay are virus-like particle (VLP)- based enzyme immunoassays. However, laboratory reagents used for these assays are not standardized and there are no standards for setting a threshold for a positive result.

1.5.6 Cervical cancer screening and medical management

There is no specific treatment for HPV infection. Medical management depends on treatment of the specific clinical manifestation of the infection (such as genital warts or abnormal cervical cell cytology.

HPV transmission can be reduced but not eliminated with the use of physical barriers such as condoms. Recent studies demonstrated a significant reduction in HPV infection among young women after initiation of sexual activity when their partners used condoms consistently and correctly (CDC, 2015). Abstaining from sexual activity (i.e., refraining from any genital contact with another individual) is the surest way to prevent genital HPV infection. For those who choose to be sexually active, a monogamous relationship with an uninfected partner is the strategy most likely to prevent future genital HPV infection.

Most cases and deaths from cervical cancer can be prevented through detection of precancerous changes within the cervix by cervical cytology using Pap test. Currently available Pap test screening can be done by a conventional pap or a liquid-based cytology. The Center for Disease control (CDC) does not issue recommendation for cervical cancer screening, but various professional groups have published recommendations. Cervical cancer screening recommendations were revised in 2012 after the U.S. Preventive Service Task Force (USPSTF) and a multidisciplinary group, including the American Cancer society (ASC), American Society for Clinical Pathology (ASCCP) reviewed new evidence. Previously, recommendations varied by organization. Since 2012, all organizations have recommended that screening should begin at age 21 years. While there are slight differences in other aspects of the recommendations, all groups recommend screening in women aged 21-65years with cytology (Pap test) every 3 years. For women aged 30-65 years who want to lengthen the screening interval, screening can be done with a combination of cytology and HPV testing ('co-testing) every 5 years. The use of HPV vaccine does not eliminate the need for continued Pap test screening, since 30% of cervical cancers are caused by HPV types not included in the vaccine.

Cervical cancer prevention programs aim to screen the largest possible proportion of women and ensure appropriate management for all those who have a positive or abnormal test result. Screening reduces cervical cancer by detecting and treating cases of pre-cancer before they progress to cancer. It can also detect cervical cancer in women at an early stage when the cancer can still be successfully treated.

High risk HPV infections are very common in young women, but most of these infections are transient. They are eliminated spontaneously by the woman's body. Only a small percentage of all HPV infections that persist for many years may lead to invasive cancer. Cervical cancer usually develops slowly, taking 10-20 years from early pre-cancer to invasive cancer. So,

cervical cancer is rare before the age of 30. Screening younger women will detect many lesions that will never develop into cancer, which will lead to considerable over treatment and is thus not cost-effective. World health Organization (WHO) therefore recommends that cervical cancer screening should not start before 30 years of age (WHO, 2014), this may be extended to young ages if there is evidence of a high risk for CIN2+. Among women who test negative with visual inspection with acetic acid (VIA) or cytology, the interval for rescreening should be three to five years. Among women who test negative with HPV testing, re-screening should be done after minimum interval of five years. Screening for cervical pre-cancer and cancer should be done in women and girls who have initiated sexual activity as soon as the woman or girl has tested positive for HIV regardless of age.

1.5.7 Human Papilloma Virus Vaccine

There are currently two vaccines which protect against both HPV 16 and 18 which are known to cause at least 70 % of cervical cancers (WHO, 2015). The vaccines are non-infectious subunit vaccines. The antigen for the vaccines is the L1 major capsid protein of HPV, produced by using recombinant DNA technology.

Quadrivalent HPV (HPV4) vaccine (Gardasil®, Merck) was approved by the FDA in June 2006 (CDC, 2015). The vaccine is approved for females and males aged 9 through 26 years of age (CDC, 2015). Each 0.5 ml dose of HPV4 contains 20 micrograms HPV6 L1 protein, 40 micrograms HPV 11 L1, protein, 40 micrograms HPV16L1 protein and 20 micrograms HPV18 L1 protein (CDC, 2015). The vaccine antigen is adsorbed on alum adjuvant. The vaccine also includes sodium chloride, L-histidine, polysorbate 80, and sodium borate. HPV4 does not contain a preservative or antibiotic. The vaccine is supplied in single-dose vials and syringe.

Bivalent HPV (HPV2) vaccine (Cervarix®, Glaxosmith Kline) was approved by the FDA in October 2009 (CDC, 2015). The vaccine is approved for females 9 through 25 years of age (CDC, 2015). HPV2 is not approved for males. The L1 antigen is adsorbed onto aluminum hydroxide. The unique adjuvant system ASo4 is composed of 3-o-desacy1-4'-monophosphory1 lipid a (MPL) adsorbed onto aluminum hydroxide. Each 0.5ml dose contains 20 micrograms of HPV 16L1 protein and 20 microgramms HPV18 Li protein. HPV2 does not contain a preservative or antibiotics. It is available in 2 types of prefilled syringes.

1.5.8 Immunogenicity and vaccine Efficacy

HPV vaccines are highly immunogenic. More than 99 % of recipient develops an antibody response to HPV types included in the respective vaccines 1 month after completing the three-dose series (CDC, 2015). However, there is no known serologic correlate of immunity and no known minimal titer determined to be protective. The high efficacy, found in the clinical trials to date has precluded identification of a minimum protective antibody titer. Further follow-up of vaccinated cohorts may allow determination of serologic correlates of immunity in the future. Both HPV vaccines have been found to have high efficacy for prevention of HPV vaccine type-related persistent infection, CIN 2/3 and adenocarcinoma in-situ (AIS). Clinical efficacy of HPV4 against cervical disease was determined in two double-blind, placebo-controlled trials. In women 16 through 26 years of age vaccine efficacy for HPV16 or 18-related CIN 2/3 or AIS was 97 % [CDC, 2015]. HPV4 efficacy against HPV 6, 11, 16 or 18-related genital warts was 99 %.

HPV2 efficacy was evaluated in two randomized, double-blind, controlled clinical trials in females aged 15 through 25 years. In the phase III trial, efficacy against HPV 16 or 18-related CIN 2/3 or AIS was 93 % (CDC, 2015).

Clinical trials results show that both vaccines are safe (WHO, 2015). Both vaccines work best if administered prior to exposure to HPV. Therefore, it is preferable to administer them before first sexual activity. The vaccine cannot treat HPV infection or HPV-associated diseases such as cancer.

Some countries have started to vaccinate boys as the vaccination prevents genital cancers in males as well as females, and one of the two available vaccines also prevents genital warts in males and females (WHO, 2015).

a. Vaccination schedule

WHO recommends vaccination for girls aged 9 – 13 years prior to initiation of sexual activity as this is the most cost – effective public health measure against cervical cancers (WHO, 2014). A two-dose schedule with an interval of six months between doses for girls aged < 15 years (including those girls aged ≥ 15 years at the time of the second dose). There is no maximum interval between the two doses; however, an interval of not greater than 12–15 months is suggested. If for any reason the interval between the two doses is shorter than five months, then a third dose should be given at least six months after the first dose. The three-dose schedule (0, 1–2, 6 months) remains recommended for girls aged 15 years and older and for immunocompromised individuals, including those known to be HIV positive (regardless of whether they are receiving antiretroviral therapy). It is not necessary to screen for HPV infection or HIV infection prior to HPV vaccination. These schedule recommendations apply to both the bivalent and quadrivalent vaccines (WHO, 2014).

HPV vaccines can be administered at the same time as other non-live vaccines.

Administering more than one vaccine at a single visit increases the likelihood that girls will receive all needed vaccines on schedule. All formulations of HPV vaccine should be kept cold at 2–8˚C. HPV vaccines are freeze-sensitive and lose efficacy if frozen. Therefore, HPV

vaccine cannot be placed in or near the freezer portion of the refrigerator nor directly on a frozen ice pack. If there are indications that HPV vaccines may have been affected by sub-zero temperatures, a shake test should be conducted to determine whether the vaccine can still be used.

Whenever feasible, the same HPV vaccine should be used for the entire vaccination series. HPV vaccines should be administered at the same visit as other age – appropriated vaccines. Each vaccine should be administered using a separate syringe of a different anatomic site. Because HPV vaccines are subunit vaccines, they can be administered to persons who are immune suppressed because of diseases or medications. However, the immune responses and vaccine efficacy might be less than that in persons who are immunocompetent. Women who are breast feeding may receive HPV vaccine (CDC, 2015).

b. Contraindications and precautions to HPV vaccination

A severe allergic reaction (e.g. anaphylaxis) to a vaccine component or following a prior dose of HPV vaccine is a contraindication to receipt of HPV vaccine. Anaphylactic allergy to latex is a contraindication to bivalent HPV vaccine in a prefilled syringe since the tip cap contains natural rubber latex. A moderate or severe acute illness is a precaution to vaccination and vaccination should be deferred until symptoms of the acute illness improve. HPV vaccine is not recommended for use during pregnancy due to limited data on vaccination during pregnancy.

c. **Adverse reaction following vaccination**

The most common adverse reaction reported during clinical trials of HPV vaccines were local reaction at the site of injection. No serious adverse events have been associated with either HPV vaccines based on monitoring by CDC and the food and drug administer (CDC, 2015).

d. Vaccine storage and handling

HPV vaccines should be maintained at refrigerator temperature between 35 ^{o}F and 46 ^{o}F (2 ^{o}C and 8^{o}C).

1.5.9 Cervical cancer prevention and control: A comprehensive approach

WHO recommends a comprehensive approach to cervical cancer prevention and control. The recommended set of actions includes interventions across the life course. It should be multidisciplinary including components from community education, social mobilization, vaccination, screening, treatment and palliative care.

Primary prevention begins with HPV vaccination of girls 9 – 13 years, before they become sexually active (WHO, 2015).

Other recommended preventive intervention for boys and girls as appropriate are:

- Education about safe sexual activity including delayed start of sexual activity.
- Promotion and provision of condoms for those already engaged in sexual activity
- Warnings about tobacco use, which after starts during adolescence, and which is an important risk factor for cervical and other cancer, and
- Male circumcision.

Women who are sexually active should be:

- Screened for abnormal cervical cells and pre-cancerous lesions, starting from 30 years of age
- If treatment is needed to excise abnormal cells or lesions, cryotherapy (destroying abnormal tissue on the cervix by freezing it) is recommended.
- If signs of cervical cancer are present treatment options for invasive cancer include surgery, radio therapy and chemotherapy.

1.6 Willingness-To-Pay using Contingent Valuation (CV) Approach

The contingent valuation(CV) method is a stated preference approach designed to directly estimate welfare gains/losses as appropriate (Mclntos, 2010). In carrying out CV, individuals are asked to consider a hypothetical scenario where they are asked to imagine that a market exists for the benefit or losses of a public programme. The CV can measure the value that consumers place on certain aspects or attributes of health care services. The CV model is utility based and people are asked how much money they would be willing to pay to maintain or improve services or activities. CV questions are used to estimate the demand function or the willingness to pay distribution of consumers.

Various design instruments can be applied to ask individuals to state their WTP to ensure that welfare can occur or their willingness to accept (WTA) to tolerate welfare loss from the programme. The WTP or WTA amount is then taken as a measure of the individual's perceived value of the programme (i.e. the demand) which is then aggregated across all individuals. If the individual, state high (low) WTP amount, then it is inferred that the demand for that programme is high (low). CV has (potential to offer) advantages over other methods of eliciting community values.

Contingent valuation method has been in use as far back as 1958 (Mclntos, 2010) and was first applied in health care context in a study to avoid heart attack. There has been steady growth in the number of published paper using CV methods within health care.

1.6.1 Designing CV study

The first stage of designing a CV study is the scenario description. This contains information on all relevant aspects of the product/services being valued and is what the respondents will read/listen to prior to the CV task. As respondents are typically asked to consider good or

services that are not routinely available in the market, there is often little or familiarity with the products being evaluated and thus (prior to the study), no opportunity to think about the product and form preferences and values. The scenario description therefore has to be realistic to the respondent and in a form, that is both informative and understandable. If the scenario is not presented correctly, then any subsequent analysis of the CV data will be meaningless as it is likely that the respondent will have misunderstood what it is that they have been asked to value (Mclntos, 2010).

1.6.2 Instrumentation techniques in CV approach

The choice of the instrumentation technique is a tradeoff between the ability to describe things in detail and gain reassurance that respondent has understood the task versus the ease and ability to achieve large sample size. Direct face to face interviews are generally regarded as the 'gold standard' (Mclntos, 2010) and it is usually beneficial if the health care intervention being valued is difficult to communicate. It can employ any of the elicitation formats.

The disadvantage of this instrumentation technique is that the respondents may become influenced by other aspects of the interview situation rather than on the relevant economic parameter. Telephone interviews provide an economical alternative to face-to-face interviews. It offers the opportunity to choose any elicitation format. Mail surveys provide the most economical option overall and scope to achieve a large sample size (relative to face-to-face interviews and telephone interviews), but are limited in that only certain elicitation formats can be used and there is minimal opportunity to describe the scenario in great detail.

1.6.3 Elicitation formats

The elicitation format refers to the style of questioning to elicit the WTP/WTA value. There are a number of different formats to choose from, each with its own strength and weaknesses

and there is little consensus in the health care literature concerning which is superior (Mclntos, 2010). The following are the available formats:

- Open-ended question

The open-ended question is the 'simplest' of the elicitation designs. This question asks for the WTP for a health care intervention without any prompts or cues from the questionnaire or interviewer. Usually the respondents are provided with a space (a line to write on) for their formal maximum WTP value.

- Iterative bidding technique

This format is termed the 'bidding game'. The question is designed so that it resembles an auction as the respondent enters a bargaining process with the interviewer. The respondent is presented with a first-bid and depending on whether they accept or reject that bid; it is either raised or lowered till eventually the respondent's maximum WTP is reached. The amount by which the bids are raised or lowered is governed by a predetermined algorithm to ensure that each respondent participates in the same bidding process.

- Payment card scale/card

The payment card scale question design was developed by Mitchelle and Carson in 1981 and 1984 as an alternative to bidding game approach (Mclntos, 2010). The scale present respondents with a range of values to choose from. If the maximum WTP is greater than the highest bid in the list, then the question defaults to open ended question design.

- Close ended dichotomous choice/ discrete question

Close-ended question are designed to lead to a yes/no response. In this method respondents are presented with a bid and are asked if they are WTP that amount. The bid levels are varied

across the sample so that it is possible to estimate the percentage of respondents who are WTP as a function of the bid.

- Close ended with follow-up question

This technique is an extension of the close-ended method, to obtain more information from each respondent; a follow-up open-ended question is inserted. Using a follow-up question lessens the need for such a large sample size as you get more information per respondents.

- Marginal approach

This approach involves asking individuals to firstly consider what treatment or service they prefer and then to reveal their maximum WTP value to have their preferred option over their less preferred option. This gives the relative WTP.

1.6.4 Strength and weakness of the Elicitation format

Each elicitation design comes with its own strength and weakness (bias) and the debate concerning the most appropriate format is far from resolved. The biases are as follows:

- Value cues bias

Apart from open ended elicitation format, all elicitation deigns provide respondents with value cues. This cues guides and encourage respondents to consider their maximum WTP, they have the disadvantage of overly influencing the respondents to reveal a WTP value that is more in accordance with the cues rather than their true maximum WTP value. This type of bias can be commonly classified as either the anchoring effect or range bias. The anchoring effect is usually seen iterative bidding design; the survey has the potential to be susceptible to starting point bias. The final maximum WTP value can be influenced by the starting bids used in the bidding algorithm. This can be detected by using randomly generated starting point bids across the respondents. Range bias is another type of cue bias, is usually

encountered in payment scale question designs. It is similar to starting point bias only instead of being influenced by the starting point bid, respondents are influenced by the range of values chosen for the payment scale question design. It is also plausible that respondent may be sensitive to the positioning of the values within the range. This effect has received limited empirical attention within the CV literature so the full impact of this effect is unclear. It is an important finding and should be borne in mind when considering the range of values to include within the payment scale design.

- Strategic bias

It involves the respondents deliberately overstating or understanding their true WTP value. Protest response can be classified as an extreme form of strategic bias and happen when respondents protest to the process of investigation by stating either zero response or unreasonably high or low response. The respondents may state no WTP value, even though they care about the intervention, if they feel that it is someone else's responsibility to pay e.g. Government or the health management organization. This can be curtailed by eliciting qualitative information about the intervention alongside the CV values.

1.7 Research Hypotheses

The null hypothesis is that mothers in Anambra state are not willing to pay for HPV vaccination of their daughters aged 9-13. The alternative hypothesis is that mothers in Anambra state are willing to pay some amount for HPV vaccination of their daughters aged 9-13.

CHAPTER TWO

LITERATURE REVIEW

2.1 Review of Similar Studies

A study carried out in Vinh Long province, Vietnam, in 2011, to access mother's preferences and willingness to pay for HPV vaccines, reported that the demand for HPV vaccines was high; increased with vaccine effectiveness and duration of effectiveness, and decreased with vaccine cost (Poulos et al., 2011). The predicted probability of respondents buying an HPV vaccine that was 70 % effective for 10 years varied by price, ranging from 30 % when the vaccine price was $353 per course, to 68 % when the vaccine cost was $6 per course (Poulos *et al*., 2011). The study also reported that the demand and predicted purchase probability were higher among groups with higher socio-economic status (Poulos *et al.*, 2011).

In a study carried out in Thailand to ascertain knowledge acceptance and willingness to pay for Human papilloma virus (HPV) vaccination among female parents, it was reported that knowledge regarding the HPV vaccine among parents was quite low. Nevertheless, vaccine acceptance was high if it was offered for free - 76.9 % for bivalent and 74.4 % for the quadrivalent. The proportion of respondents who were willing to co-pay for the vaccine if it was not totally free was also high; 68.9 % for bivalent and 67.3 % for the quadrivalent vaccine. No significance difference between bivalent and quadrivalent vaccines in terms of prevalence of acceptance and willingness to pay was found in the study (Siraporn *et al*., 2012). The study concluded that substantial effort should be made to educate parents prior to introduction of a national HPV vaccination program (Siraporn *et al*., 2012).

.A study carried out in Argentina to explore maternal HPV vaccination acceptance, willingness to pay for HPV vaccination and correlates of this willingness, awareness of HPV and HPV-associated disease and behaviors and attitudes associated with HPV vaccination

acceptance among 180 female parents of girls aged 9-15 years using quantitative, cross-sectional, survey-based study, reported that maternal HPV vaccination acceptance was 90%, and 60% of mothers were willing to pay for HPV vaccination. Mothers who were gainfully employed and had a higher disposable household income were significantly more willing to pay for HPV vaccination [odds ratio (OR)=2.54, 95% confidence interval (CI) 1.01-6.38; OR=3.28, 95% CI 1.36-7.94, respectively], as were mothers who were aware of cervical cancer prior to the study (OR=3.22, 95% CI 1.02-10.14). Only one in 10 mothers were informed that HPV vaccination does not offer complete protection against cervical cancer. The study concluded that there was high maternal HPV vaccination acceptance, although acceptance decreased when vaccination was not free-of-charge. Continuous public education campaigns were needed to improve knowledge of HPV, HPV vaccines and HPV-associated disease. (Alders, 2015)

A study conducted in United states using 307 US mothers of girls aged 13-17 years who had not received an HPV vaccine established that the mean maximum willingness-to-pay (WTP) ranges between $560 and $660. Mothers strongly valued greater cervical cancer efficacy, with 100% protection against cervical cancers as the most desired feature overall.(Brown *et al.*, 2009).

A similar study done in Hong Kong to provide a more representative and updated assessment on the acceptability of female adolescent HPV vaccination in Hong Kong using among 1022 mothers with daughters aged ≤ 18 years through random digit-dialing telephone interviewing showed that the willingness to pay for full-course vaccination among mothers had a median of US$128/HK$1000 (50% central range=US$64-192/HK$500-1500), i.e. substantially lower than the current market price. The study concluded that the gap between acceptability and actual uptake of HPV vaccination among mothers suggested that coverage is likely to be low

without an organized HPV vaccination program therefore policymakers should devise tailored, targeted and efficient vaccination strategies to achieve universal coverage for an effectively organized HPV vaccination program.(Choi, 2013).

A study conducted in Colorado State University (CSU) campus to address how likely college-age students in the Rocky Mountain West are to pay for vaccination programs Student's willingness to pay (WTP) or vote for a campus HPV vaccination program showed that only approximately 21% of female students would purchase the vaccine at the current price cost.

This study finds that, for all of the proposed vaccination programs, a personal belief that the community needs protection against HPV was associated with an increased probability of willingness to pay for the program. Therefore, in order to promote favorable attitudes toward such a program, efforts should be made to promote a sense of community within the student bodyi.e. educating the community about HPV (Ritten and Breunig, 2013).

A study carried out using cross-sectional contingent valuation method to assess the willingness to pay for Human Papillomavirus vaccination and factors influencing the willingness to pay among health professional students studying undergraduate health professional courses (Medicine, Dentistry, Pharmacy, Nursing) in a private medical University in Malaysia reported that the average amounts that the students were willing to pay were USD 108 • Among the participants who were not willing to pay, most of them felt that the cost should be paid by the government. • Age, gender, profession and the patient's perceived health status at baseline were not associated with willingness to pay. (Mari Kannan *et al.,* 2015).

CHAPTER THREE

METHODS

3.1 Study Area

The study was conducted in Anambra state, south east Nigeria, from February to August 2015. The state is located at latitude 6.20 degrees north and 7.00 degrees east with total area of 4,844 km,a population of 4.1 million and approximately 2.5million women(NPC, 2006). The main indigenous ethnic group in the state is Ibo with a small population of Igala. The inhabitants are mainly business people, government workers and students.Anambra state has some major cities and also many rural areas. There are also two main teaching hospitals in the state that handle cervical cancer cases.

3.2 Study Design

This study was a school-based cross sectional survey conducted in Anambra state using self-administered questionnaires. According to the State Ministry of Education record, there are 254 public secondary schools and 166 private secondary schools in the state.

Ten secondary schools five schools in Onitsha, three schools in Ekwulobia and two secondary schools in Isuofia) all in Anambra state were purposively selected for the study. Onitsha is an urban city while Ekwulobia and Isuofia are rural cities. Five schools were privately owned while the other five were public schools. The reason for selecting schools from both urban and rural area as well as from both private and public schools was to ensure inclusion of persons from all socioeconomic strata.

Eligibility for participation (i.e. to be given a questionnaire) was (1) female students aged between 9-13 years old and (2) their mothers being able to read and write in English language.

Using Anambra State with women population size of 2.5 million (NPC, 2006), confidence level of 95 % and margin of error of 5%, 385 respondents were determined to be appropriate for the survey. Fifty questionnaires were distributed to each of the 10 secondary schools to be distributed randomly to eligible girls.

The questionnaires were given to school teachers who distributed them to girls aged 9-13 years to take home to their mothers. The mothers were requested to return the completed questionnaire via their child back to the school teachers within 3 - 7 days. Contingent valuation approach using the payment card technique was used to estimate the average maximum willingness-to-pay (WTP) among the survey participants

3.3 Willingness-to-pay for HPV vaccine assessment

A 23-item self-administered questionnaire was developed for the WTP assessment. The questionnaire consisted of three sections. The first section included general information and socio-demographic characteristics such as age, number of daughters, level of education etc. The second section assessed awareness of HPV, genital warts, cervical cancer as well as HPV vaccines. Five questions examining causes of genital warts and cervical cancer were used to assess the knowledge of those aware of the diseases and HPV vaccine (i.e. knowledge index score). The third section presented facts about HPV and contained the payment card used to assess mothers' WTP for HPV vaccine.

- Vaccine rejection was measured based on the response to the following question: "If the vaccine is not free, and you have to pay 'out of pocket' by yourself, will you vaccinate your daughter against HPV"? The follow-up question was used to assess willingness to pay (WTP) of "vaccine acceptors". The question reads as follows: "If so, from the scale below mark '*x'* on the maximum amount you will pay (in Naira) to

have your daughter vaccinated against HPV". The parents who answered "no" or indicated zero in the payment card were classified as "vaccine rejecters", while the ones who answered "yes" and indicated a positive value in the payment card were classified as "vaccine acceptors". Offered WTP values in the payment card ranged from zero to more than 12,000 Naira (equivalent to US$ 60). The maximum price offered reflects the Nigerian market price for the vaccine. The maximum amount they were willing to pay was considered as their perceived monetary benefit of the vaccine. This is in accordance with welfare economic theory which states that the benefit to an individual of a service or intervention is defined as the individual's maximum willingness to pay for the service or intervention.

For content validity of the questionnaire, information on Willingness-to-pay assessment was obtained from textbooks on Health economics (Mclntos, 2010). While that of Human Papilloma virus was gotten from the internet.The questionnaire was face validated by two pharmacists: an experienced hospital pharmacist and an academic pharmacist.It was pilot tested using 10 mothers with at least a female child aged 9-13 years to assess feasibility and possible comprehension problems. Necessary adjustments were made.

3.4 Sample size calculation

Using Anambra State population size of women of approximately 2.5 million (Census, 2006), confidence level of 95% and margin of error of 5%, 385 respondents were determined to be appropriate for the survey. Sample size was determined by the formular below:

$$Sample\ Size = \frac{\frac{z^2\ x\ p(1-p)}{e^2}}{1+(\frac{z^2\ x\ p(1-p)}{e^2 N})}$$

Where population size (N) = 2.5million women; Margin of error(small amount that is allowed in case of miscalculation) (e) = 0.05 or 5%; z-score (how many standard deviations below or above the population mean a raw score is) (z) = 1.96; desired confidence level-p (range of likely values for the population parameter) = (0.95 or 9.5%).

3.5 Data Analysis

Responses to the willingness-to-pay (WTP) question were grouped into two categories: 'vaccine acceptors' versus 'vaccine rejecters'. The response to WTP question served as the dependent variables in multivariate binary logistic regression. The explanatory or independent variables were re-categorized into the following variables:

i. Socio-economic data: place of residence (urban or rural); age of respondents (3 dummy codes for 31 – 40 yrs, 41 – 50 yrs, and > 50 yrs); household size (3 dummy codes for 4 – 6 persons, 7 – 9 persons and ≥10 persons); occupation; average household income (4 dummy codes for ₦50000.00- ₦100000.00 versus others, ₦100000.00 – ₦250000.00₦250000.00 – ₦500000.00 and >₦500000.00); whether respondent is religious; whether respondent is a catholic; and whether respondent is a protestant.
ii. Awareness of HPV infection: ever diagnosed of infection, ever diagnosed of genital warts, and knowledge of HPV infection and consequences (summarized by differentiating those that answered all questions on knowledge of HPV infection correctly from those that did not).

Data were initially coded and transferred to Microsoft Excel (Microsoft Office 2010). Further re-categorization of data (i.e. creation of dummy variables) was done in Microsoft Excel before importing the data to SPSS (Version 14). Multivariate binary logistic regression used

the backward conditional as enter method and was performed with SPSS version 20. A two-tailed significance value of 0.05 was used.

3.6 Estimation of Average Cost per Vaccinated Girl

The Cost of vaccinating a girl (CVG) was estimated by adjusting cost of HPV vaccination delivery in Tanzania to the Nigerian setting (Quentin etal,2012). We adjusted the Tanzanian HPV delivery cost estimates by modifying cost items – social mobilization/information, training, procurement (except for vaccine cost), vaccination, cold storage, and administration/supervision – based on the difference in local purchasing power between Tanzanian and Nigeria. Difference in local purchasing power was computed with a web-based cost of living calculator (Cost of living calculator, 2015). In accordance with recent recommendations, vaccine procurement cost was modified to reflect the cost of two doses at ₦895.50 per dose instead of three doses at ₦995.00based on the original study(WHO,2015). Vaccine price of ₦895.50 reflects the price being offered by Vaccine Alliance (GAVI) for countries eligible for support, while vaccine price of ₦2587.00 represents the lowest public sector price offered by HPV vaccine manufacturers (GAVI,2014). Except for the vaccine cost, all other costs were inflated from 2012 (i.e. the year of publication) to 2015 naira value. This was done by converting adjusted cost in US$ to naira equivalent, inflating to 2015 value using the consumer price index. The exchange rates published by Central bank of Nigeria (CBN,2016) and consumer price index(CPI) published by World Bank (World bank, 2016)were used.

3.7 Ethical Consideration (NAUTH/CS/66/VOL8/73)

The research design and procedure were approved by theNnamdi Azikiwe University Teaching Hospital (NAUTH) Ethical Committee Nnewi, Anambra state. The study secured written informed consent from the respondents. Anonymity of participants' data was maintained by not including individual's name.

CHAPTER FOUR

RESULTS

4.1 Characteristics of respondents and their awareness of HPV infection

The overall response rate was 88%. More than half of the respondent (57.1%) resided in the rural areas. The majority of the mothers who participated in the survey were between the ages of 31 – 50 years and mainly of the Ibo tribe. Only 4.3% of respondents had no formal education. More than half of the respondents (57.6%) reported having a household monthly income of less than <₦50000.00. All the respondents except one had one form of religious belief or the other (Table 2).

Table 3 shows details of awareness of HPV infections and its consequences among the participants. Very few respondents (7.6%) had had or have been diagnosed with either HPV infection or genital warts. Similarly, very few of the mothers (19.1 %) had heard of HPV infection. Among the population that were aware of HPV infection, only very few (3.4%) had good knowledge of HPV infection and its consequences according to our knowledge index score.

Table 2: Socioeconomic characteristics of respondents (n = 438)

Variable	Frequence (%) or Average (± SD)
Place of Residence	
Rural	250 (57.1)
Urban	188 (42.9)
Age of mothers	
20 – 30 years	65 (14.9)
31 – 40 years	169 (38.8)
41 – 50 years	157 (36.0)
Above 50 years	45 (10.3)
Number of daughters	
One	314 (71.9)
Two	106 (24.3)
Three	12 (2.7)
Four	5 (1.1)
Average age of daughters	10.7 (± 1.4)
Tribe of respondent	
Ibo	422 (96.8)
Others	14 (3.2)
Level of Education	
No education	19 (4.3)
Primary education	131 (30.0)
Secondary education	167 (38.2)

Tertiary education	75 (17.2)
Post tertirary education	45 (10.3)
Monthly Income*	
Less than < (₦50,000)	251 (57.6)
₦50,000 – ₦100,000	109 (25.0)
-₦100,000 – ₦250,000	43 (9.9)
₦250,000 – ₦500,000	16 (3.7)
>₦500,000)	17 (3.9)
Occupation	
No occupation	28 (6.4)
Farming	57 (13.1)
House wife	40 (9.2)
Public servant	110 (25.3)
Private business	197 (45.3)
Others	2 (0.5)
Religious preference	
None	1 (0.2)
Traditionalist	48 (11.0)
Catholic	276 (63.4)
Protestant	101 (23.2)
Muslim	7 (1.6)
Others	2 (0.5)

**1 USD = 199 Nigerian Naira*

Table 3: Awareness of HPV infection and consequences (n = 438)

Variable	Frequency (%)
Diagnosed of HPV infection	33 (7.6)
Diagnosed of Genital warts	31 (7.1)
Ever heard of HPV infection	83 (19.1)
Sources of HPV infection knowledge	
Doctor, nurse or health professional	27 (32.9)
Family or friends	11 (13.4)
Newspaper or magazine	12 (14.6)
Television	11 (13.4)
Internet	7 (8.5)
Cannot remember	7 (8.5)
Multiple sources	7 (8.5)
Ever heard of cervical cancer	122 (27.9%)
Good knowledge of HPV infection and consequences	15 (3.4%)

4.2 Willingness to pay (WTP) for HPV infection

i. Average WTP

As shown in Table 4, 401 of the respondents (91.6%) stated a positive WTP amount. The average WTP amount stated by the respondents was ₦1,160 per dose while the most frequently stated amount was ₦500 per dose. Fifty percent of the respondents stated₦1000 as the amount they are willing to pay for a dose of HPV vaccine.

ii. Logistic regression predicting willingness-to-pay for vaccine

Thirty-three of the respondents (7.5%) rejected HPV vaccination of their daughters (Table 4). Logistic regression showed that mothers living in an urban area were less likely to demand for HPV vaccination for their daughters (odd ratio 0.27=). Also mothers that have been previously diagnosed with HPV infection were more likely to demand for HPV vaccination for their daughters. The predictive capacity of the model was 13%.

4.3Estimated Average Cost per Vaccinated Girl

Estimate of CVG was adapted from an HPV vaccine delivery pilot project in Tanzania and showed that if HPV vaccine is supplied at vaccine alliance's (GAVI) price, cost per vaccinated girl (CVG) in urban and rural area could cost as much as ₦3600 and ₦3800 respectively. However, CVG could be as high as ₦7000 and ₦7200 for urban and rural areas respectively, if vaccine is supplied at the lowest price which the vaccine manufacturers have offered the vaccine to the public sector. Details of estimated CVG are shown in Table 5.

Table 4: WTP amount for HPV vaccines and its predictors

Statistics	**WTP per dose (Naira)**		
Mean	1160		
Median	1000		
Mode	500		
Percentiles			
20	500		
90	1500		
Vaccine rejection, n = 33, vaccine acceptance,n= 401			
	Dependent: vaccine acceptance (=1)		
	B	S.E	b(exp)
Residence (urban)	-1.30	0.82	0.27
Diagnosed with HPV infection	18.76	8358.68	100000000
Constant	-2.83	1.04	21.50
Nagelkerke R^2	0.13		

Table 5: Estimated economic costs per fully-immunized girl (Naira)in a scaled-up regional school based HPV vaccination programme

Cost items	Source Data (Mwanza Vaccine Project, Tanzania) (US$)		Gavi vaccine price (₦895.5)		Lowest public sector price (₦2587)	
	Urban	Rural	Urban	Rural	Urban	Rural
Social Mobilization/IEC	0.5	0.5	87.56	87.56	87.56	87.56
Training	0.3	0.5	51.74	87.56	51.74	87.56
Procurement*	18.7	19.4	2479.54	2608.89	5862.54	5991.89
Vaccination	5.0	4.4	873.61	770.13	873.61	770.13
Cold Storage	0.2	0.3	35.82	51.74	35.82	51.74
Waste Management	0.0	0.0	0.0	0.0	0.0	0.0
Admin/Supervision	0.5	1.3	87.56	226.86	87.56	226.86
Total	*25.3*	*26.6*	*3613.84*	*3832.74*	*6996.84*	*7215.74*

**Vaccine procurement cost was modified to reflect the cost of 2 doses at US$4.5(₦895.5) per dose instead of 3 doses at US$5(₦995) as perthe original study.*

CHAPTER FIVE

DISCUSSION

5.1 Discussion

This study aimed to establish the amount that Nigerian mothers are willing to pay for vaccination of their daughters against HPV infection. The findings showed that majority of the mothers were willing to pay an average of ₦2300 to get their daughters fully vaccinated. Mothers that were previously diagnosed with HPV infection were more likely to demand for the vaccine. Mothers that live in urban areas were less likely to demand for the vaccine. The shortfall needed to augment the cost of vaccination ranges from ₦1300 to ₦4900 depending on the setting of vaccine delivery (rural or urban) and unit cost of HPV vaccine (GAVI's price or lowest price offered to public sector).

This study has useful implications for increasing uptake of HPV vaccine and planning HPV vaccination in Nigeria. Firstly, demand for HPV vaccine is quite high. A total of 91.6% mothers were willing to pay for HPV vaccination of their daughters. This is opposed to the fears of vaccine rejection that is speculated on due to cultural and religious sensitivities towards health interventions that target prevention of a sexually transmitted disease (Jumaan *etal*.,2013).For instance, it has been stated that mothers may be concerned about the vaccine being a 'license to premarital sex' (Jumaan *etal.*,2013). Other Nigerian based population studies have also reported high HPV vaccine acceptance. A study conducted among female health care workers in Enugu, South-Eastern Nigeria reported HPV vaccine acceptability rate of 91.0% (Ugwu *etal*,2013).HPV vaccine acceptance of 74% among female university students in northern Nigeria has been reported (Iliyasu,2010). Also, 70% accepted vaccination of their daughters in a cross-sectional survey of mothers attending the gynaecology clinic in a Nigeria University Teaching Hospital (Ezeanochie and

Olagbuji,2014). High acceptance and demand for the vaccine points to high likelihood of HPV vaccination programme success in Nigeria as fundamental to the success of such programme is the recipients' willingness to accept the vaccine.

The high demand for HPV vaccines could be emphasized in order to increase uptake of the vaccines in Nigeria. It could be possible to achieve higher vaccine uptake in Nigeria without relying on the government to provide the vaccine. A possible solution to achieving higher uptake of the vaccine is through is through education of the populace about cervical cancer and HPV vaccination. For example, those diagnosed of HPV infection were more likely to demand for HPV vaccination of their daughters. This group of persons will most likely have more in-depth knowledge of the disease and thus, explains their dispositions towards HPV vaccine. A systematic review by Kessel et al (Kessel *et al.*, 2012) also identified having higher vaccine-related knowledge, having a healthcare provider as a source of information and maintaining positive vaccine attitudes as correlates of HPV vaccine uptake in teenage girls. While waiting for national immunization, interventions that improve understanding of, and positive attitudes toward HPV vaccine could be applied. Educational interventions directed to parents or to adolescent/young adult have been shown to be moderately effective in increasing HPV vaccine acceptance and uptake (Fuly *etal.*, 2014). Simple educational interventions such as fact sheet about epidemiology and morbidity associated with HPV infection or few minutes radio novel about cervical cancer case willhelp increase vaccine uptake in Nigeria (Fuly *et al*., 2014).

Another solution to achieving high HPV vaccine uptake is to properly orient health professionals to inform patients and the public about HPV vaccination. Even if HPV vaccination is free under the national immunization programme, uptake of the vaccine will basically depend on whether health professionals are willingness to inform adolescent girls

about HPV vaccination. Provider-initiated model for improving health service utilization appears to be effective in developing countries. For example, increase in HIV test rates have been attributed to the rapid scale-up of the provider-initiated testing model (Njeru *etal*., 2011). The prescriber's ability to educate their patient's population on HPV vaccination must be supported and included as part of the national strategic plan for cervical cancer control. Denmark achieved a very high vaccination rates (3-dose coverage of over 80%) through administration by general practitioners (Baandrup *etal*., 2013).

The second important finding from the study is that co-payment for HPV vaccination could be a viable option to augment the cost of vaccination in a government funded vaccination scenario. HPV vaccination is a costly programme. Even at GAVI vaccine price, HPV vaccination requires substantial set up cost. Unlike new infant vaccines, which may be added to an existing infant vaccine delivery system, HPV vaccination requires the development of a new vaccine delivery service in order to achieve the required doses (Levin *etal*, 2014). This is particularly because of: (1) micro-planning defined as planning of vaccination activities at local levels that take into account issues of accessibility, geography, population movements, and cultural characteristics; (2) social mobilization/information, education and communication; (3) higher cold chain equipment requirements for delivery outside health facility; and (4) higher service delivery costs (Levin *etal*.,2014). With health expenditure of ₦22,885.00 per capita and considering other competing health services including nutrition activities and emergency aid (World Bank, 2015), it is important to consider other financing options to support HPV vaccination programme in Nigeria.

The caveat to co-payment as an option of financing HPV vaccination is that it may skew the vaccination programme to favour only those that can afford the vaccine. The ₦2300.00 could be a huge amount for many to afford in Nigeria considering that about 99 million Nigerians

or about 58% of the population live with less than ₦250.00 per day (World Bank,2015). In order to ensure equity balanced programme, HPV vaccination should be provided for free to the poor populace in Nigeria. As a suggestion, a practical way to achieve this is to stratify different secondary schools based on their school fees and offer free vaccination to schools in lowest stratum in school-based vaccine delivery system. Poor populations e.g. rural dwellers could be targeted for free vaccination in outreach vaccine delivery system.

5.2 Study Limitations

The WTP value obtained in the study has to be considered in the light of bias that is associated with open-ended elicitation format and WTP surveys in general. Respondents could have been influenced by the range of values chosen for the payment scale question design rather than their true maximum WTP values. It also possible that some respondents may have stated no WTP value or very low WTP value especially if they feel that vaccination should be paid by the government. The small sample size of respondents that rejected the vaccine could have induced a systematic bias, as logistic regression could over estimate odd ratios in studies with small to moderate sample size(Nemes et al 2009). Despite these limitations, this is the first study that assessed mother's WTP for HPV vaccination in Nigeria. The timeliness of this study makes the findings useful for HPV vaccination planning in Nigeria.

5.3 Conclusion

The findings showed that Nigerian mothers were willing to pay an average of ₦2300 for HPV vaccination of their daughters. At GAVI vaccine price, ₦1300 and ₦1500 extra are needed to augment the cost of vaccination in urban and rural areas respectively. At the lowest obtainable public sector vaccine price, ₦4700 and ₦4900 extra are needed to augment the cost of vaccination in urban and rural areas respectively. Demand for HPV vaccine was high and

this should present an opportunity for increased uptake of HPV vaccine in the country. Finally, we accept the alternate hypothesis that mothers in Anambra are willing to pay for HPV vaccine.

5.4 Recommendation

Educating the populace on cervical cancer and provider-initiated vaccination should be promoted as these could increase HPV vaccine uptake. In the event of government funded national vaccination, co-payment could be a feasible strategy to ensure sustenance of vaccination. However, free vaccination should be considered for the poor populace in order to ensure equity-sensitive vaccination programme.

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APPENDIX 1

A. WTP Questionnaire

This study is part of the requirement for my master's degree program in Clinical Pharmacy and Pharmacy Management, Nnamdi Azikiwe University. Below are some questions on Human Papilloma Virus infection. I plead that you give your candid opinion about the questions below. Thank you for your time.

Ifeoma Umeh

Section A: About You

This questionnaire is anonymous but it would be useful to have some background information about you. Please tick the correct answer.

1. How old are you? 20 – 30 [ ] 31 – 40 [ ] 41 – 50 [ ] above 50 [ ]
2. How many daughters aged 9 – 12 years old do you have? _____
3. Please state your daughters exact age(s) 1st _____; 2nd _____; 3rd _____; 4th _____; 5th _____; 6th_____; 7th_____; 8th _____
4. Please select your tribe from the list below: Igbo [ ] Hausa [ ] Yoruba [ ] Any other (specify) _____
5. What is your education level? No education [ ] Primary [ ] Secondary [ ] Tertiary [ ] Post tertiary [ ]
6. What is your average household income (in Naira) per month? Less than 50,000 [ ] 50,000 – 100,000 [ ] 100,000 – 250,000 [ ] 250,000 – 500,000 [ ] Greater than 500,000 [ ]

7. Please select your occupation from the list:

   No Job [ ] Farming [ ] House Wife [ ] Public servant [ ] Business [ ]

   Others (specify)

   _____

8. How many are in your household (including extended relations)?

   _____

9. Your religious preference is? None [ ] Traditionalist [ ] Catholic [ ] Protestant [ ] Muslim [ ] Others (specify)

   _____

10. How often do you attend your place of worship? Never [ ] Every week [ ] Few time a month [ ] Few times a year [ ]

Section B: Awareness of HPV infection and consequences

11. Have you ever been told by a healthcare provider that you had a human papillomavirus (HPV) infection? Yes [ ] No [ ] Not sure [ ]

12. At any time in your life, have you ever been told by a doctor or other medical care provider that you had genital warts? Yes [ ] No [ ]

13. Have you ever heard of Human Papilloma Virus (HPV) infection? Yes [ ] No [ ]

    If "Yes", answer question14, if "No" go to question 15

14. From which source did you hear about HPV infection? *Pease mark all that apply*

    Doctor, nurse or other health professional [ ]

Family or friends [ ]

News papers or magazines [ ]

Television [ ]

Internet [ ]

Cannot remember [ ]

Others (specify) _____

15. Do you know about genital warts? Yes [ ] No [ ]
16. Do you know about cervical cancer? Yes [ ] No [ ]

If you answered "No"to Numbers 15 & 16, please go to Section C, else continue with the questions below.

17. HPV infection causes genital warts? Yes [ ] No [ ] Don't know [ ]
18. HPV infection does not cause cervical cancer? Yes [ ] No [ ] Don't know [ ]
19. Can one get HPV infection through sex? Yes [ ] No [ ] Don't know [ ]
20. HPV infection can be treated if detected on time? Yes [ ] No [ ] Don't know [ ]
21. HPV infection can be prevented through vaccination? Yes [ ] No [ ] Don't know [ ]

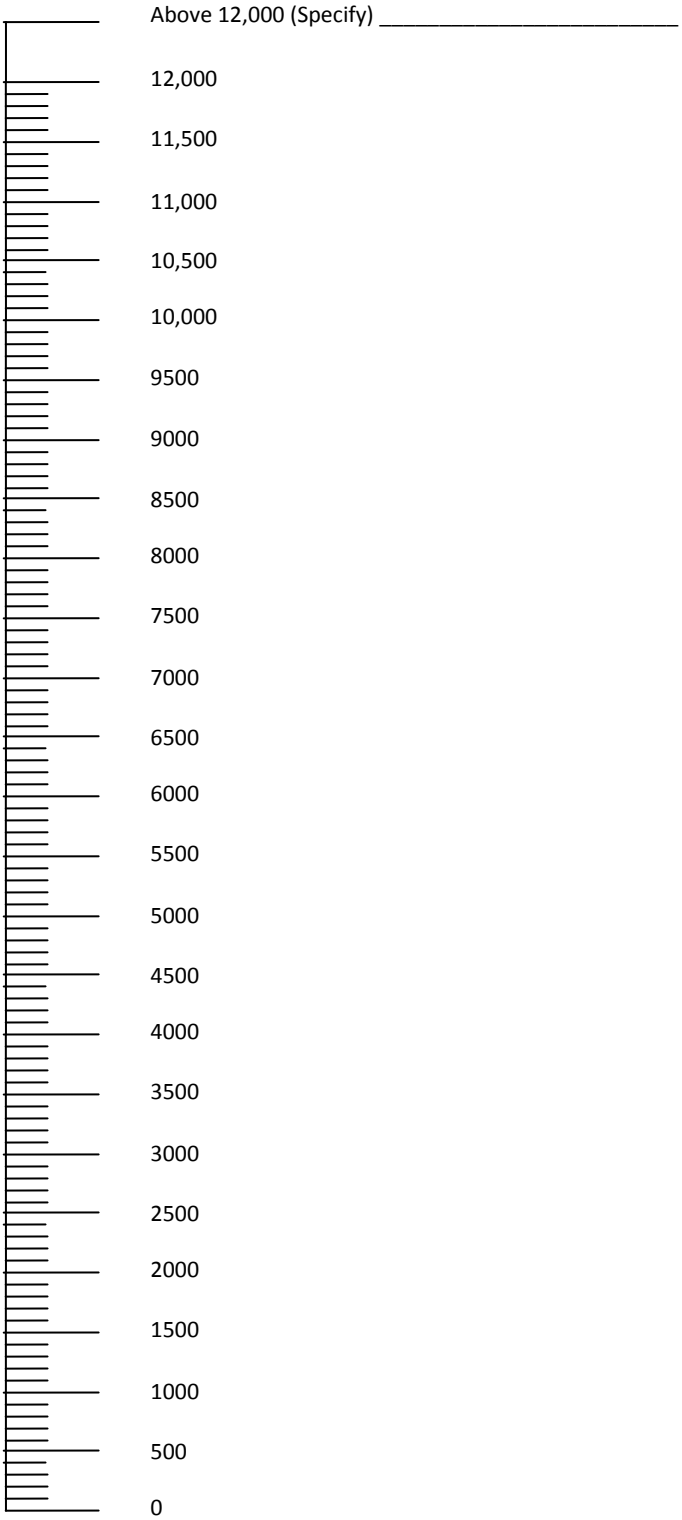
Section C: Facts about Human Papillomavirus (HPV)

- *HPV is spread by sexual activity*
- *HPV is very common (at least 50% of people who have sex will have HPV at some point in their lives)*
- *Most people who have HPV don't know they have it.*

- *There are many kinds of HPV and not all of them cause health problems.*
- *Only some kinds of HPV cause health problems like genital warts or cervical cancer.*
- *Most women who have HPV will **NOT** develop cervical cancer, and will likely get rid of the virus on their own without medical treatment.*
- *Condoms do not always protect against the spread of HPV.*
- *There is no cure for HPV, but there are treatments for problems such as genital warts and cervical cancer that caused by HPV*
- *There is a vaccine against the kinds of HPV that most often cause cervical cancer and genital warts. The vaccine protects one from getting the HPV virus and thus prevents cervical cancer. This vaccine is most effective if given before a person becomes sexually active. The HPV vaccine is now available for girls age nine and older*
- *The vaccines are very safe.*
- *The vaccine cannot cause disease because they don't contain live viruses.*
- *The vaccines are given as injections (shots) and require two doses for girls younger than 15 years old, and three doses for girls with low immunity (including those known to be living with HIV) and for girls aged 15 years and older*
- *The cost of the vaccine is 7000- 9000 Naira per dose*

Question

22. *If these vaccines are not free and you have to pay 'out of pocket' by yourself, will you vaccinate your daughter against HPV?* Yes [ ] No [ ]
23. *If you choose "Yes" in question 22, mark 'x' from the scale below the maximum amount you will pay (**in Naira**) per dose of the vaccine, to have your daughter vaccinated against HPV.*


Above 12,000 (Specify) _____
12,000
11,500
11,000
10,500
10,000
9500
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0

Raw Analysis Data

A. Logistic Regression predicting vaccine rejection

Case Processing Summary

Unweighted Cases(a)		N	Percent
Selected Cases	Included in Analysis	122	27.9
	Missing Cases	316	72.1
	Total	438	100.0
Unselected Cases		0	.0
Total		438	100.0

a If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
No	0
Yes	1

Block 0: Beginning Block

Classification Table(a,b)

	Observed			Predicted		
	Rejection of vaccine		Percentage Correct			
	No	Yes				
Step 0	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7

a Constant is included in the model.

b The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-3.384	.508	44.314	1	.000	.034

Block 1: Method = Backward Stepwise (Conditional)

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	19.178	17	.318
	Block	19.178	17	.318
	Model	19.178	17	.318
Step	Step	.000	1	1.000
2(a)	Block	19.178	16	.260
	Model	19.178	16	.260
Step	Step	.000	1	1.000
3(a)	Block	19.178	15	.206
	Model	19.178	15	.206
Step	Step	.000	1	1.000
4(a)	Block	19.178	14	.158
	Model	19.178	14	.158
Step	Step	.000	1	1.000
5(a)	Block	19.178	13	.118
	Model	19.178	13	.118
Step	Step	.000	1	1.000
6(a)	Block	19.178	12	.084
	Model	19.178	12	.084
Step	Step	-.064	1	.801
7(a)	Block	19.115	11	.059
	Model	19.115	11	.059
Step	Step	-.505	1	.477
8(a)	Block	18.609	10	.046
	Model	18.609	10	.046
Step	Step	-1.427	1	.232
9(a)	Block	17.182	9	.046
	Model	17.182	9	.046

Step	Step	-.913	1	.339
10(a)	Block	16.270	8	.039
	Model	16.270	8	.039
Step	Step	-.951	1	.330
11(a)	Block	15.319	7	.032
	Model	15.319	7	.032
Step	Step	-1.319	1	.251
12(a)	Block	14.000	6	.030
	Model	14.000	6	.030

a A negative Chi-squares value indicates that the Chi-squares value has decreased from the previous step.

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	16.031(a)	.145	.580
2	16.031(a)	.145	.580
3	16.031(a)	.145	.580
4	16.031(a)	.145	.580
5	16.031(a)	.145	.580
6	16.031(a)	.145	.580
7	16.094(a)	.145	.578
8	16.600(a)	.141	.564
9	18.027(a)	.131	.524
10	18.939(a)	.125	.498
11	19.890(a)	.118	.471
12	21.209(a)	.108	.432

a Estimation terminated at iteration number 20 because maximum iterations has been reached. Final solution cannot be found.

Classification Table(a)

	Observed			Predicted		
	Rejection of vaccine		Percentage			
	No	Yes	Correct			
Step 1	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 2	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 3	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 4	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 5	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 6	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 7	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 8	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 9	Rejection of vaccine	No		118	0	100.0
		Yes		4	0	.0
	Overall Percentage					96.7
Step 10	Rejection of vaccine	No		118	0	100.0

		Yes	4	0	.0
	Overall Percentage				96.7
Step 11	Rejection of vaccine	No	118	0	100.0
		Yes	4	0	.0
	Overall Percentage				96.7
Step 12	Rejection of vaccine	No	118	0	100.0
		Yes	4	0	.0
	Overall Percentage				96.7

a The cut value is .500

Variables not in the Equation(l)

			Score	df	Sig.
Step 2(a)	Variables	Dummy_noeducation	.000	1	1.000
	Overall Statistics		.000	1	1.000
Step 3(b)	Variables	Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	1.000
	Overall Statistics		.000	2	1.000
Step 4(c)	Variables	Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	.999
		Dummy_Prot	.000	1	1.000
	Overall Statistics		.000	3	1.000
Step 5(d)	Variables	Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	.999
		Dummy_Religious	.000	1	.995
		Dummy_Prot	.000	1	.995
Step 6(e)	Variables	Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	.999
		Dummy_Religious	.000	1	.996
		Dummy_Prot	.000	1	.997
		Ques12R	.000	1	1.000

	Overall Statistics		.000	5	1.000
Step 7(f)	Variables	Dummy_31_40	.064	1	.800
		Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	.999
		Dummy_Religious	.000	1	.996
		Dummy_Prot	.000	1	.997
		Ques12R	.000	1	1.000
Step 8(g)	Variables	Dummy_31_40	.064	1	.800
		Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	.999
		Dummy_Religious	.000	1	.993
		Dummy_Prot	.000	1	.994
		Ques12R	.275	1	.600
		Dummy_Knowledge	.313	1	.576
Step 9(h)	Variables	Dummy_20_30	.915	1	.339
		Dummy_31_40	.261	1	.609
		Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.240	1	.624
		Dummy_Religious	.240	1	.624
		Dummy_Prot	.240	1	.624
		Ques12R	.220	1	.639
		Dummy_Knowledge	.381	1	.537
Step 10(i)	Variables	Dummy_20_30	.739	1	.390
		Dummy_31_40	.386	1	.535
		Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.923	1	.337
		Dummy_100_250K	.634	1	.426
		Dummy_Religious	.157	1	.692
		Dummy_Prot	.157	1	.692
		Ques12R	.215	1	.643

		Dummy_Knowledge	.343	1	.558
Step 11(j)	Variables	Dummy_20_30	.701	1	.403
		Dummy_31_40	.638	1	.424
		Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	1.154	1	.283
		Dummy_100_250K	.000	1	.988
		Dummy_250_500K	.641	1	.423
		Dummy_Religious	.141	1	.708
		Dummy_Prot	.141	1	.708
		Ques12R	.237	1	.626
		Dummy_Knowledge	.333	1	.564
Step 12(k)	Variables	Residence	1.259	1	.262
		Dummy_20_30	.689	1	.406
		Dummy_31_40	.128	1	.720
		Dummy_noeducation	.000	1	1.000
		Dummy_50_100K	.000	1	1.000
		Dummy_100_250K	.476	1	.490
		Dummy_250_500K	.278	1	.598
		Dummy_Religious	.278	1	.598
		Dummy_Prot	.278	1	.598
		Ques12R	.192	1	.661
		Dummy_Knowledge	.244	1	.621

a Variable(s) removed on step 2: Dummy_noeducation.

b Variable(s) removed on step 3: Dummy_50_100K.

c Variable(s) removed on step 4: Dummy_Prot.

d Variable(s) removed on step 5: Dummy_Religious.

e Variable(s) removed on step 6: Ques12R.

f Variable(s) removed on step 7: Dummy_31_40.

g Variable(s) removed on step 8: Dummy_Knowledge.

h Variable(s) removed on step 9: Dummy_20_30.

i Variable(s) removed on step 10: Dummy_100_250K.

j Variable(s) removed on step 11: Dummy_250_500K.

k Variable(s) removed on step 12: Residence.

l Residual Chi-Squares are not computed because of redundancies.

B. Logistic Regression predicting zero WTP

Case Processing Summary

Unweighted Cases(a)		N	Percent
Selected Cases	Included in Analysis	118	26.9
	Missing Cases	320	73.1
	Total	438	100.0
Unselected Cases		0	.0
Total		438	100.0

a If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
No	0
Yes	1

Block 0: Beginning Block

Classification Table(a,b)

	Observed			Predicted		
	Willing to pay zero amount		Percentage Correct			
	No	Yes				
Step 0	Willing to pay zero amount	No		113	0	100.0
		Yes		5	0	.0
	Overall Percentage					95.8

a Constant is included in the model.

b The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-3.118	.457	46.548	1	.000	.044

Variables not in the Equation(a)

			Score	df	Sig.
Step 0	Variables	Residence	1.775	1	.183
		Dummy_20_30	1.399	1	.237
		Dummy_31_40	2.885	1	.089
		Dummy_41_50	.016	1	.898
		Dummy_50_above	1.135	1	.287
		Dummy_noeducation	.045	1	.833
		Dummy_Primary	.234	1	.629

	Dummy_Sec	2.142	1	.143
	Dummy_tert	.791	1	.374
	Dummy_50KLess	.022	1	.882
	Dummy_50_100K	2.292	1	.130
	Dummy_100_250K	.430	1	.512
	Dummy_250_500K	1.444	1	.230
	Dummy_500KMore	.894	1	.344
	Dummy_Religious	3.114	1	.078
	Dummy_Cath	.426	1	.514
	Dummy_Prot	.272	1	.602
	Dummy_Ques11	1.197	1	.274
	Ques12R	.132	1	.716
	Dummy_Knowledge	.760	1	.383

a Residual Chi-Squares are not computed because of redundancies.

Block 1: Method = Backward Stepwise (Conditional)

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	23.876	17	.123
	Block	23.876	17	.123
	Model	23.876	17	.123
Step	Step	.000	1	.986
2(a)	Block	23.876	16	.092
	Model	23.876	16	.092
Step	Step	-.007	1	.932
3(a)	Block	23.868	15	.067
	Model	23.868	15	.067
Step	Step	-.018	1	.894
4(a)	Block	23.850	14	.048

	Model	23.850	14	.048
Step	Step	-.063	1	.802
5(a)	Block	23.787	13	.033
	Model	23.787	13	.033
Step	Step	-.107	1	.744
6(a)	Block	23.681	12	.022
	Model	23.681	12	.022
Step	Step	-.282	1	.596
7(a)	Block	23.399	11	.016
	Model	23.399	11	.016
Step	Step	-.463	1	.496
8(a)	Block	22.936	10	.011
	Model	22.936	10	.011
Step	Step	-.346	1	.556
9(a)	Block	22.590	9	.007
	Model	22.590	9	.007
Step	Step	-1.194	1	.275
10(a)	Block	21.396	8	.006
	Model	21.396	8	.006
Step	Step	-.568	1	.451
11(a)	Block	20.828	7	.004
	Model	20.828	7	.004
Step	Step	-2.175	1	.140
12(a)	Block	18.652	6	.005
	Model	18.652	6	.005

a A negative Chi-squares value indicates that the Chi-squares value has decreased from the previous step.

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	17.522(a)	.183	.619
2	17.522(a)	.183	.619
3	17.529(a)	.183	.619
4	17.547(a)	.183	.618
5	17.610(a)	.183	.617
6	17.717(a)	.182	.615
7	17.999(a)	.180	.608
8	18.462(a)	.177	.597
9	18.808(a)	.174	.589
10	20.002(a)	.166	.560
11	20.570(a)	.162	.547
12	22.745(a)	.146	.494

a Estimation terminated at iteration number 20 because maximum iterations has been reached. Final solution cannot be found.

Classification Table(a)

	Observed			Predicted		
	Willing to pay zero amount		Percentage Correct			
	No	Yes				
Step 1	Willing to pay zero amount	No		112	1	99.1
		Yes		3	2	40.0
	Overall Percentage					96.6
Step 2	Willing to pay zero amount	No		112	1	99.1
		Yes		3	2	40.0
	Overall Percentage					96.6

Step 3	Willing to pay zero	No	112	1	99.1
	amount	Yes	3	2	40.0
	Overall Percentage				96.6
Step 4	Willing to pay zero	No	112	1	99.1
	amount	Yes	3	2	40.0
	Overall Percentage				96.6
Step 5	Willing to pay zero	No	112	1	99.1
	amount	Yes	3	2	40.0
	Overall Percentage				96.6
Step 6	Willing to pay zero	No	112	1	99.1
	amount	Yes	3	2	40.0
	Overall Percentage				96.6
Step 7	Willing to pay zero	No	112	1	99.1
	amount	Yes	3	2	40.0
	Overall Percentage				96.6
Step 8	Willing to pay zero	No	112	1	99.1
	amount	Yes	3	2	40.0
	Overall Percentage				96.6
Step 9	Willing to pay zero	No	111	2	98.2
	amount	Yes	3	2	40.0
	Overall Percentage				95.8
Step 10	Willing to pay zero	No	111	2	98.2
	amount	Yes	3	2	40.0
	Overall Percentage				95.8
Step 11	Willing to pay zero	No	113	0	100.0
	amount	Yes	3	2	40.0
	Overall Percentage				97.5
Step 12	Willing to pay zero	No	111	2	98.2
	amount	Yes	3	2	40.0
	Overall Percentage				95.8

a The cut value is .500

Variables not in the Equation

			Score	df	Sig.
Step	Variables	Dummy_noeducation	.000	1	.990
2(a)	Overall Statistics		.000	1	.990
Step	Variables	Dummy_noeducation	.000	1	.990
3(b)		Dummy_250_500K	.004	1	.951
	Overall Statistics		.004	2	.998
Step	Variables	Dummy_noeducation	.000	1	.991
4(c)		Dummy_50_100K	.010	1	.921
		Dummy_250_500K	.003	1	.956
	Overall Statistics		.014	3	1.000
Step	Variables	Residence	.064	1	.801
5(d)		Dummy_noeducation	.000	1	.988
		Dummy_50_100K	.015	1	.903
		Dummy_250_500K	.005	1	.941
	Overall Statistics		.073	4	.999
Step	Variables	Residence	.087	1	.769
6(e)		Dummy_noeducation	.000	1	.989
		Dummy_50_100K	.011	1	.915
		Dummy_250_500K	.004	1	.947
		Dummy_Cath	.062	1	.804
	Overall Statistics		.139	5	1.000
Step	Variables	Residence	.053	1	.817
7(f)		Dummy_noeducation	.000	1	.987
		Dummy_Primary	.261	1	.610
		Dummy_50_100K	.024	1	.876
		Dummy_250_500K	.006	1	.936
		Dummy_Cath	.084	1	.772
	Overall Statistics		.397	6	.999
Step	Variables	Residence	.039	1	.844
8(g)		Dummy_noeducation	.000	1	.986
		Dummy_Primary	.177	1	.674

		Dummy_50_100K	.031	1	.860
		Dummy_250_500K	.017	1	.896
		Dummy_Cath	.231	1	.631
		Dummy_Prot	.469	1	.493
	Overall Statistics		.766	7	.998
Step	Variables	Residence	.008	1	.929
9(h)		Dummy_20_30	.349	1	.555
		Dummy_noeducation	.001	1	.982
		Dummy_Primary	.246	1	.620
		Dummy_50_100K	.040	1	.842
		Dummy_250_500K	.028	1	.867
		Dummy_Cath	.113	1	.736
		Dummy_Prot	.240	1	.624
	Overall Statistics		1.057	8	.998
Step	Variables	Residence	.002	1	.964
10(i)		Dummy_20_30	.016	1	.901
		Dummy_noeducation	.003	1	.957
		Dummy_Primary	.189	1	.664
		Dummy_50_100K	.217	1	.641
		Dummy_100_250K	1.210	1	.271
		Dummy_250_500K	.152	1	.697
		Dummy_Cath	.119	1	.730
		Dummy_Prot	.181	1	.671
	Overall Statistics		2.256	9	.987
Step	Variables	Residence	.003	1	.957
11(j)		Dummy_20_30	.029	1	.864
		Dummy_noeducation	.005	1	.946
		Dummy_Primary	.093	1	.760
		Dummy_50KLess	.570	1	.450
		Dummy_50_100K	.345	1	.557
		Dummy_100_250K	.162	1	.687
		Dummy_250_500K	.246	1	.620
		Dummy_Cath	.132	1	.717

		Dummy_Prot	.239	1	.625
	Overall Statistics		2.397	10	.992
Step	Variables	Residence	.084	1	.771
12(k)		Dummy_20_30	.431	1	.512
		Dummy_noeducation	.005	1	.945
		Dummy_Primary	.022	1	.882
		Dummy_50KLess	.052	1	.819
		Dummy_50_100K	.409	1	.523
		Dummy_100_250K	.040	1	.842
		Dummy_250_500K	.279	1	.598
		Dummy_Religious	2.253	1	.133
		Dummy_Cath	1.400	1	.237
		Dummy_Prot	.076	1	.783
	Overall Statistics		5.131	11	.925

WTP

Statistics

Amount willing to pay

N	Valid	418
	Missing	20
Mean		1161.62
Median		1000.00
Mode		500
Skewness		5.089
Std. Error of Skewness		.119
Percentiles	20	500.00
	90	1500.00

Amount willing to pay

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	12	2.7	2.9	2.9
	12	1	.2	.2	3.1
	45	1	.2	.2	3.3
	100	2	.5	.5	3.8
	200	2	.5	.5	4.3
	250	1	.2	.2	4.5
	500	155	35.4	37.1	41.6
	550	2	.5	.5	42.1
	650	1	.2	.2	42.3
	900	1	.2	.2	42.6
	1000	151	34.5	36.1	78.7
	1500	51	11.6	12.2	90.9
	2000	17	3.9	4.1	95.0
	2500	2	.5	.5	95.5
	3500	1	.2	.2	95.7
	4000	3	.7	.7	96.4
	5000	6	1.4	1.4	97.8
	5500	1	.2	.2	98.1
	9500	2	.5	.5	98.6
	10000	2	.5	.5	99.0
	12000	4	.9	1.0	100.0
	Total	418	95.4	100.0	
Missing	System	20	4.6		
Total		438	100.0		