

Health Disparity Concerns Associated with the HPV Vaccine

**Ralph J. Anderson, MD, FACOG, FRCS (C)
Chairman**

**Department of Obstetrics and Gynecology
University of North Texas Health Science Center
Fort Worth, Texas**

HPV Vaccine

■ Gardasil

- Approved by the FDA in June 2006
- Protects against
 - HPV 6,11
 - Genital warts
 - Pre-invasive cancer
 - HPV 16,18
 - Cancer of the cervix, vulva, vagina, anus and penis

■ Cervarix

- Final stages of development
 - HPV 16,18
 - Cancer of the cervix, vulva, vagina, anus and penis.

Human Papillomavirus (HPV)

Human Papillomavirus

- **More than 100 subtypes**
 - **Low risk types**
 - **High risk types**

Low Risk Viral Genotypes of Human Papillomavirus

■ Low risk viral types

– **6, 11**, 40, 42, 43, 44, 54, 61, 70, 72, 81

■ Low risk viral genotypes cause

– Genital warts (HPV 6 and 11 cause 90%)

– Preinvasive cancer of the vulvar, vagina, cervix, anus and penis

– Are not the cause of cancer of the cervix

High Risk Types of Human Papillomavirus

- High-risk types: **16,18,31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82**
- High-risk HPV types have been identified as the cause of cancer of the cervix (HPV 16, HPV 18 account for 70% of cases of cancer of the cervix).
- Most studies in young women show type 16 as the most common of identified types (7%-12% of positive HPV tests).

Human Papillomavirus (HPV)

- **HPV currently affects 20 million adults in the U.S.**
- **6.2 million sexually active adults acquire the infection each year.**
- **40% of young women will become infected with HPV in the 3 years following the onset of sexual activity.**

Human Papillomavirus Infection

- **Sexual behaviors are the most important risk factors for acquiring genital HPV infection.**
- **More than 7% of high school students have their first sexual intercourse before 13 years of age and 62% of girls and 70% of boys have had sexual intercourse by the end of 12th grade. By ninth grade, almost 11% have had more than four sex partners.**
- **Consistent condom use may or may not provide some protection against acquiring HPV – but condoms do protect against other sexually transmitted infections, some of which may relate to whether her HPV infection progresses to cervical cancer or not.**
- **By 50 years of age, 70-80% of women will have acquired genital HPV infection – often with more than one type of HPV.**
- **A woman can be infected with HPV by involuntary sexual exposure – such as date rape – as well as by her husband (or partner) if he was infected from a prior sexual partner, even if she were abstinent until marriage.**

Human Papillomavirus Infection

- **The vast majority (>90%) of cases of HPV infections are transient and will resolve spontaneously (10% persists).**
- **HPV is less prevalent as age increases but the amount of HPV that persists is much higher.**
- **Although the vast majority of women recover uneventfully from high-risk (cancer causing) genital HPV infections, some of these infections may lead to persistent infection, cause abnormal Pap tests, and progress to cervical cancer. Regular Pap screening and the treatment of any abnormalities that are detected prevent many HPV infections from causing cervical cancer.**
- **Persistent infection more common with**
 - Older age
 - Infection with multiple HPV types
 - Coincident vulvar condyloma

Estimated Annual Burden of HPV-Related Diagnosis in the United States

Infection with High Risk Oncogenic HPV Virus

- Infection with high risk “oncogenic” HPV is the cause of:
 - 100% of cancers of the cervix
 - 90% of anal cancers
 - 40% of vulvar cancers
 - 40% of vaginal cancers
 - 12% of oropharyngeal cancers
 - 3% of oral cancers
 - 3% of skin cancers

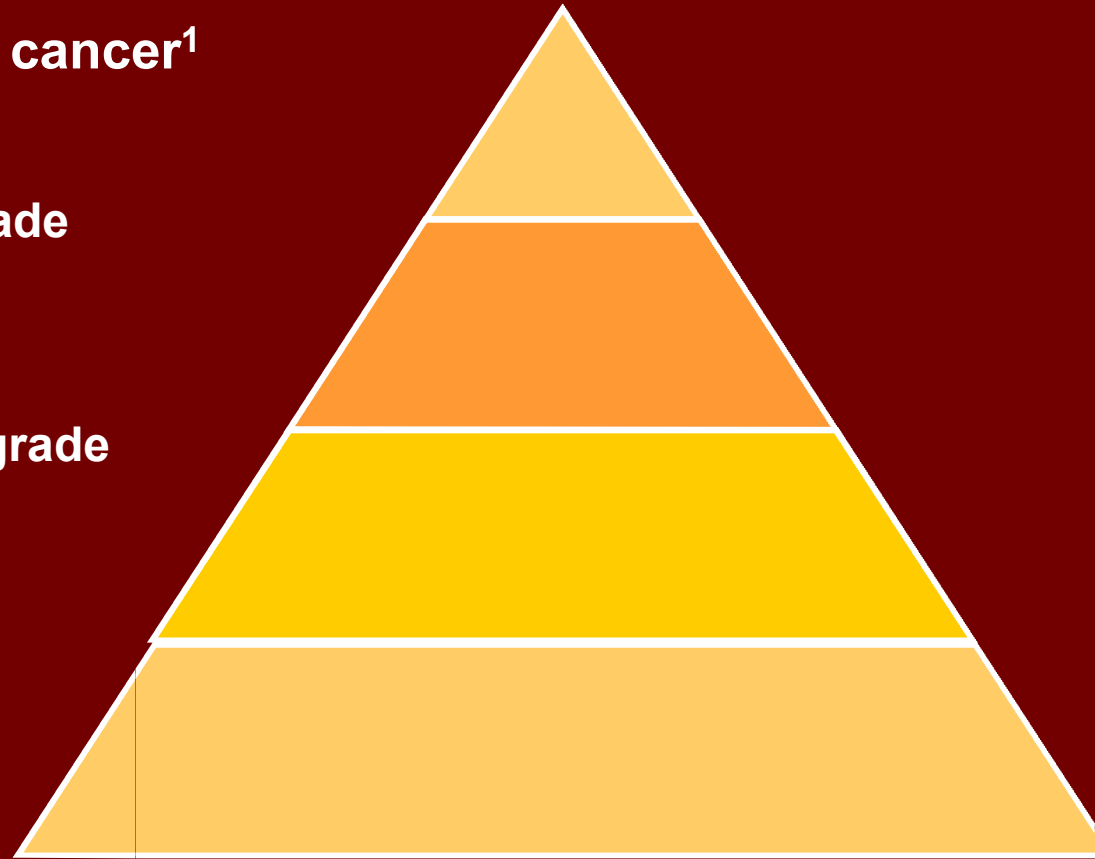
Estimated Annual Burden of HPV-Related Diagnoses in the United States

9,710 new cases of cervical cancer¹

333,000 new cases of high-grade cervical dysplasia (CIN 2/3)²

1.4 million new cases of low-grade Cervical dysplasia (CIN 1)²

1 million new cases of genital warts³



Cancer of the Cervix

Incidence

- **Cervical cancer is the second most common cancer among women worldwide.**
 - 493,000 cases
 - 274,000 deaths
- **80% of the cases occur in developing countries**
- **Highest rates are in Latin American and the Caribbean, Sub-Saharan Africa and South and South East Asia.**
- **Disproportionately affects underserved populations**

Cancer of the Cervix

Incidence in United States

- **3rd most common gynecologic cancer**
- **6th most common solid malignant neoplasm among women**
- **In the United States women have a 1 in 135 lifetime risk of developing cancer of the cervix.**
- **2007**
 - **11,150 new cases**
 - **3,600 deaths**
- **Afro-American women and women in lower socioeconomic groups have the highest age-standardized cervical cancer death rates.**
- **Hispanic and Latino women have the highest incidence rates**
 - **Probably results from financial and cultural characteristics affecting access to screening and treatment**
- **Incidence of cervical cancer in adolescents is essentially zero.**

Cervical Cancer Age-Standardized Incidence and Death Rates

Age – adjusted per 100,000 females

	All Races	White	Afro-American	Asian American	American Indian	Hispanic
Incidence (%)	8.9	8.7	11.1	8.9	4.9	15.8
Death (%)	2.8	2.5	5.3	2.7	2.6	3.5

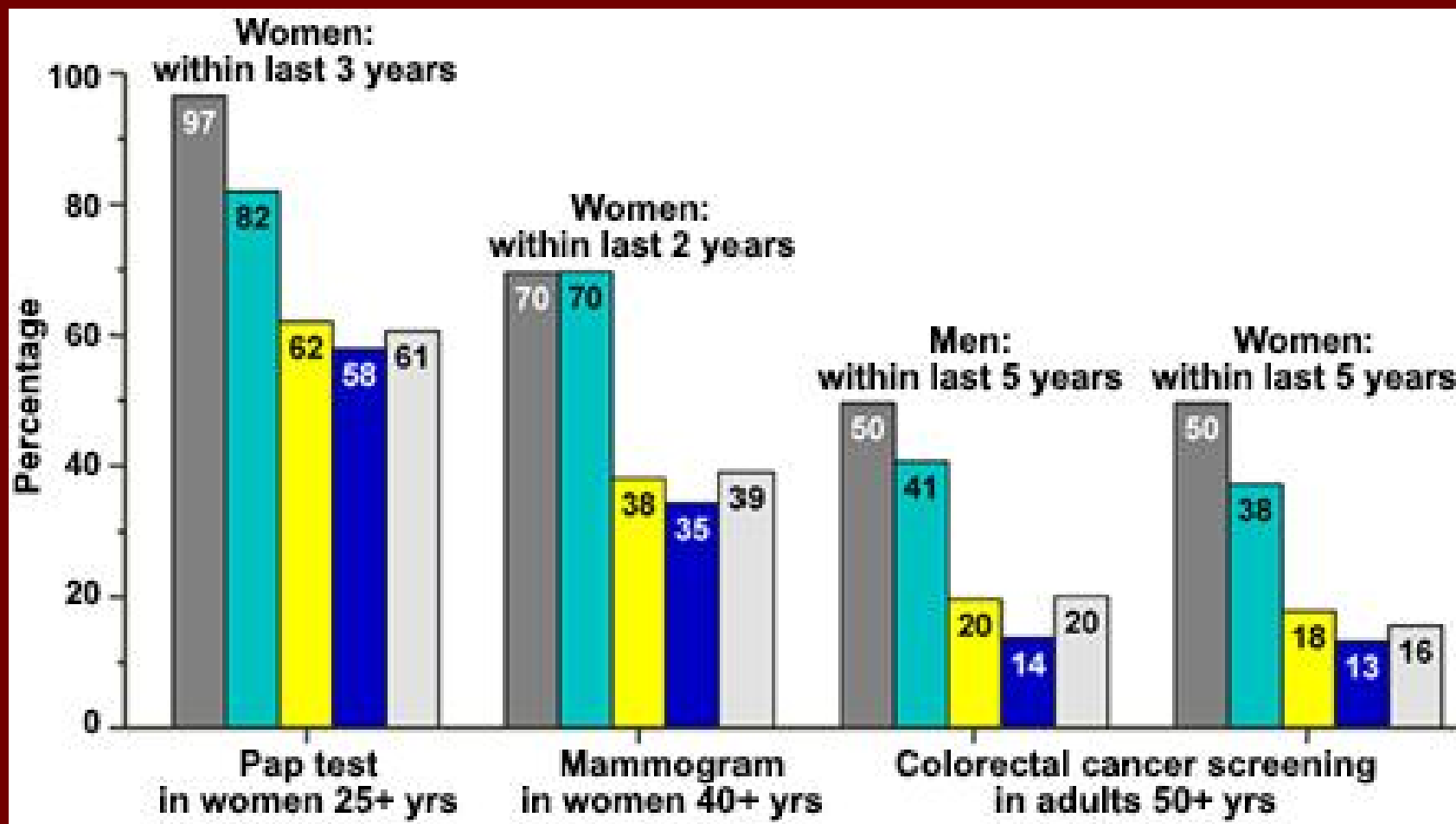
Jemal, 2006

Causes of Higher Age-Adjusted Mortality

Access to care

- **Although there has been an overall increase in the utilization of screening programs for the detection of cancer of the cervix, these gains have not been achieved in the groups who need the services the most.**
- **Largest gap in screening**
 - **Hispanic community**
 - **People with incomes below 200% of the poverty level.**

Greatest Disparities in the Use of Cancer Screening Tests: Uninsured, No Usual Source of Health Care, Recent Immigrants



Causes of Higher Age-Adjusted Mortality

Lack of Insurance

(Inability to Pay)

- **In a study that compared cervical cancer incidence stage at diagnosis and survival in Medicaid-insured and non-Medicare insured populations women who received Medicaid after a diagnosis was made were more likely to have late-stage disease and were more than 2 times more likely to die from cervical cancer than those who had insurance.**

Causes of Higher Age-Adjusted Mortality

Education Level

- Lower levels of education are associated with a higher incidence of cervical cancer and higher rates of death.
- Lower education is associated with poverty.
- Cervical cancer incidence and mortality rates increase with increasing poverty and decreasing education levels in all ethnic groups.
- Education affects health literacy and the ability to comprehend information and leads to lower participation in screening of cervical cancer.

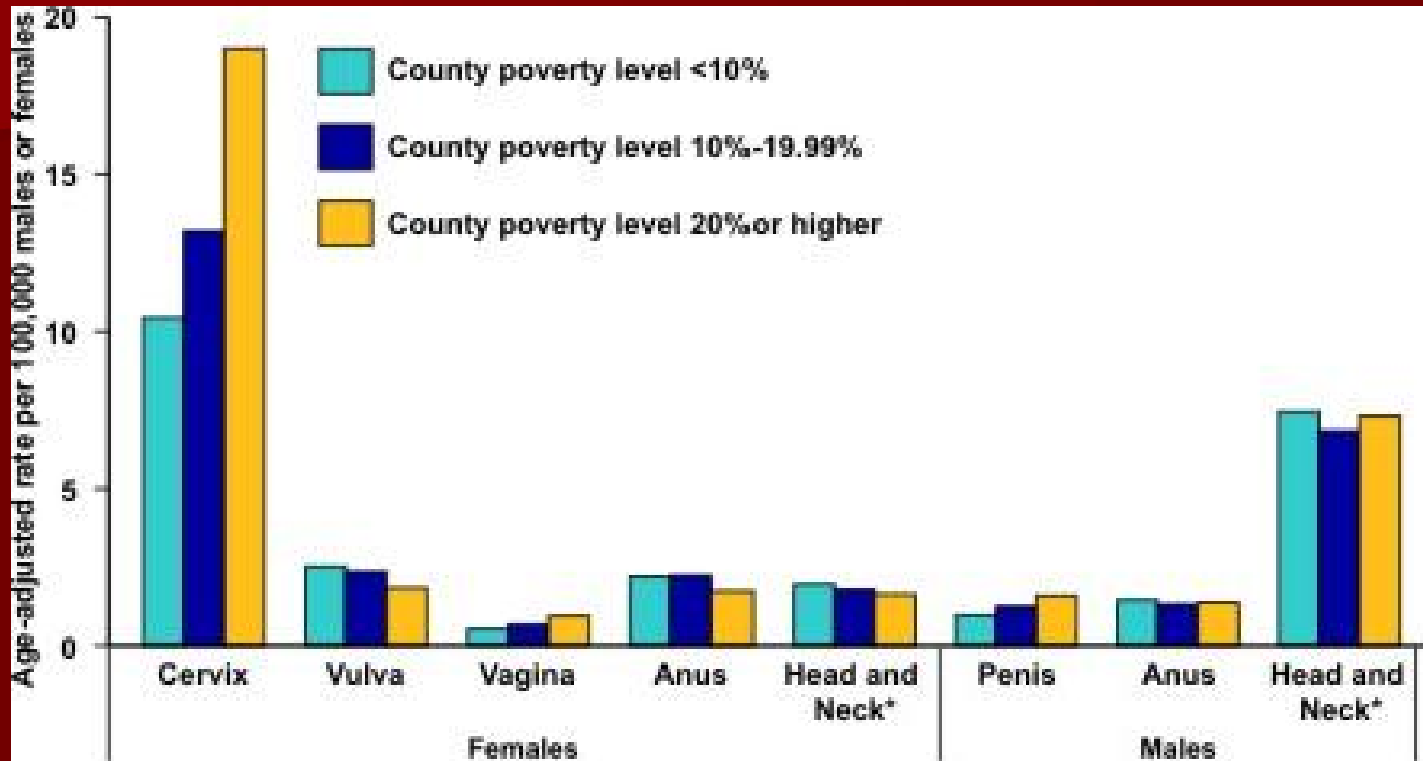
Causes of Higher Age-Adjusted Mortality

Poverty

- **Poor women seek care when they are symptomatic and more likely to have advanced disease.**
- **Poor women may experience humiliation due to her inability to pay.**
- **Poor women have diminished self-esteem and fatalistic feelings about the diagnosis of cancer.**

Parham et al, 1995

HPV-Associated Cancer Rates & County Poverty Levels in U.S.



Cervical cancer. About 10 out of every 100,000 women who live in counties in which fewer than 10% of residents have an income below the federal poverty level are diagnosed with cervical cancer each year. The rate climbs to about 13 women per 100,000 in counties in which 10% to less than 20% of residents are below poverty level, and peaks at about 19 per women 100,000 in poorer counties. These data suggest that the cervical cancer incidence rate is higher in poorer areas.

Causes of Higher Age-Adjusted Mortality

Cultural Beliefs

- **Austin et al used a Health Belief model to study cultural beliefs that affected cervical cancer screening in Hispanic women and found there was evidence of a fatalistic attitude towards cancer.**
- **Cultural influence can lead to an embarrassment about their bodies or discomfort with answering questions about sexual history.**
- **High levels of medical mistrust exist among some racial and ethnic minorities.**

HPV Vaccine

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Components of the Prophylactic Vaccine (Gardasil)

- **Active ingredients are virus-like particles that consist of 1 type of protein (L1), a major component of the viral shell.**
- **Neither vaccine contains viral DNA.**
- **Quadrivalent Vaccine**
 - **Each 0.5 cc dose contains**
 - 20 ug of HPV 6 L1 protein
 - 40 ug of HPV 11 L1 protein
 - 40 ug of HPV 16 L1 protein
 - 20 ug of HPV 18 L1 protein
 - 225 mg of aluminum sulfate
 - 9.56 mg of sodium chloride
 - 0.78 mg of L-histidine
 - 50 ug of polysorbate 80
 - 35 ug of sodium borate
 - **Contains no antibiotics, RNA, mercury or egg products**
 - **Uses latex free packaging**
- **Protocol for administration – 3 doses**
 - **0, 2, 6 months**

- **Recommendations of The Advisory Committee on Immunization Practices (ACIP)**
 1. **The vaccine is recommended for 13-26 year old females who have not received or completed the vaccine series.**
 2. **The vaccine can be administered to girls as young as 9 years of age.**
 3. **Ideally the vaccine should be administered before onset of sexual activity.**
 4. **In clinical trials antibody response was higher in 10-15 year old boys and girls than in 16-23 year old girls and boys**
- **The vaccine is administered through a series of 3 IM injections over a 6 month period (0, 2, 6 months)**
- **The list price of the vaccine is \$119.75 per dose (about \$360 for the full series)**

Recommendation For HPV Vaccination

- **Vaccine is recommended for females between age 14 and 26 even if they are sexually active.**
 - **Vaccine effective against HPV types to which they are naive**
 - **HPV testing is not indicated and not useful before vaccination.**
- **Vaccine recommended for females between age 14 and 26 even if they have had previous Pap Smear abnormalities or genital warts.**

Recommendations for HPV Vaccination

Boys and Men

- **Efficacy studies of the quadrivalent vaccine in boys and men are ongoing. The vaccine is not recommended for males at this time but probably will be recommended in the near future.**

Recommendations for HPV Vaccination

Pregnancy

- **The quadrivalent vaccine is not recommended for use in pregnancy.**
- **A woman can be vaccinated immediately after delivery.**
- **Breast feeding is not a contraindication to vaccination.**

Recommendations for HPV Vaccination

Immunosuppressed Patients

- **Quadrivalent vaccine can be administered to persons who are immunosuppressed. However, the immune response might be weaker than in immunosuppressed persons.**

Gardasil Vaccine

Effectiveness of Vaccine

- **The quadrivalent vaccine is almost 100 percent effective in protecting against four human papillomavirus types, which cause 70 percent of cases of cervical cancer and 90 percent of cases of genital warts.**

Gardasil Vaccine

Length of Time Vaccine Effective

- **Current research indicates (with 6 year follow up) that the vaccine is effective for at least 6 years. There is no evidence of waning immunity during that time period.**
- **Long term protection will be determined by data collected during ongoing long-term clinical trials.**
- **Indirect evidence based on immunological studies suggests durable protection.**

Long Term Safety of Gardasil Vaccine

- **As of June 30, 2007**
 - **2531 adverse events related to HPV vaccine have been reported**
- **95% non serious**
 - **Low grade fever**
 - **Mild nausea**
 - **Mild dizziness**
 - **Redness at injection site**
- **5% serious**
 - **Syncopal episodes**
 - **Seizures**
 - **Arthralgia**
 - **Joint pain**
 - **Fever**
 - **Guillain-Barré Syndrome (13 unconfirmed reports)**
 - **4 deaths – none caused by vaccine**
- **CDC has reported that the number of serious adverse events is no higher among the vaccinated than the non-vaccinated populations.**

Methods to Reduce Risk or Prevent Human Papillomavirus Infection

- Sexually active adults can reduce their risk by being in a monogamous relationship with someone who has had no other sexual partners. But even people with only one lifetime sex partner can get HPV if their partner has had previous partners.
- 14% of women in a monogamous relationship are infected with HPV
- Monogamy by both sexual partners could possibly assure a woman's protection – but only if both partners have been abstinent and they remain strictly monogamous.

Question: Will the vaccine eliminate cancer of the cervix?

- **Answer: No**
- **Even if the vaccine is universally accepted the true effect of the project will not be totally realized for several decades.**
- **During that time, because all people will not be vaccinated and because not all HPV types causing cancer are currently in the vaccine, women must be aware that the vaccination is not a substitute for cervical cancer screening and they should continue to have their Pap smears on a regular basis.**

Guidelines for Cervical Cancer Screening

	American College of Obstetrics & Gynecology	American Cancer Society
When to Start	Age 21 or within 3 years of sexual activity	Age 21 or within 3 years of sexual activity
Interval	Every year for women <30 or every 2-3 years for women >30 (except for high risk women with previous history of cervical dysplasia, or cancer, HIV, DES exposure, Immunosuppression)	Annually with conventional or every 2 years with liquid based cytology. >30 women with 3 adequate negative smears may be screened every 2-3 years. HPV negative – Pap smear – every 3 years
Thin Prep	Recommended	Recommended
Post hysterectomy	Discontinue except in high risk patients (previous history of cervical dysplasia or cancer, HIV, DES exposure or immunosuppression)	Discontinue if for benign reasons
When to Stop	AT the discretion of the physician	Age 70 or 3 or more negative tests within a 10 year period

Degree of Protection if Only Part of the Gardasil Vaccination Protocol Occurs

- **Protocols for vaccine administration: 3 doses**

Quadrivalent 0, 2, 6 months

Bivalent 0, 2, 6 months

- **Timing between 1st and 2nd dose very important.**
- **Timing between 2nd and 3rd dose less important (Information really not entirely reliable)**
- **Indirect evidence of antibody levels after administration of 2 doses indicates the levels may be sufficiently high to cause investigators to discuss value of a 2-versus-3 dose regimen.**
- **This is hypothetical and will require validation through clinical trials.**

HPV Vaccine Acceptability Study

Rachal Jackson

Kathryn Cardarelli

2009

Funded by FOR HER

HPV Vaccine Acceptability Study

- **To explain what female caregivers of African-American girls know about HPV and HPV vaccination**
- **Study consists of:**
 - **Brief survey**
 - **Focus groups**

Cardarelli and Jackson, 2009

HPV Vaccine Acceptability Study

Patient demographics

- Patients mainly 31-50
- Patients well educated

Cardarelli and Jackson, 2009

HPV Vaccine Acceptability Study

Results

- **Significant lack of knowledge of HPV**
- **Significant lack of knowledge about the HPV vaccine**
 - Unaware of guidelines
 - Unaware of side effects
 - Perceived as lacking adequate research to prove it is effective and safe
 - Perceived as being ineffective

HPV Vaccine Acceptability Study

Results

- **Concerned about whether the administration of the vaccine would promote sexuality.**
- **Prefer to wait until children are old enough to make their own decisions on vaccine.**
- **Wants patients to have enough knowledge to make their own decision.**

Cardarelli and Jackson, 2009

HPV Vaccine Acceptability Study

Results

- **Mistrust of medical community.**
- **Mistrust of social and political system**
 - **Governor's mandate.**

Cardarelli and Jackson, 2009



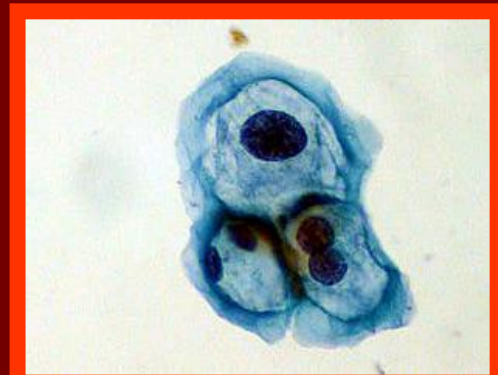
Knowledge and Acceptance of the HPV Vaccine in a County Hospital System

A System Based Problem

Lindsay McBride, DO

Ralph Anderson, MD, FACOG, FRCS (C)

2009



Knowledge and Acceptance of the HPV Vaccine In A County Hospital System

Patient Demographics	
Average Age	Late 20s
Race	%
Hispanic	64
Caucasian	20
Afro-American	16
Married	44
Employed	47
Spanish as 1st language	54
Graduated high school	65

200 patients

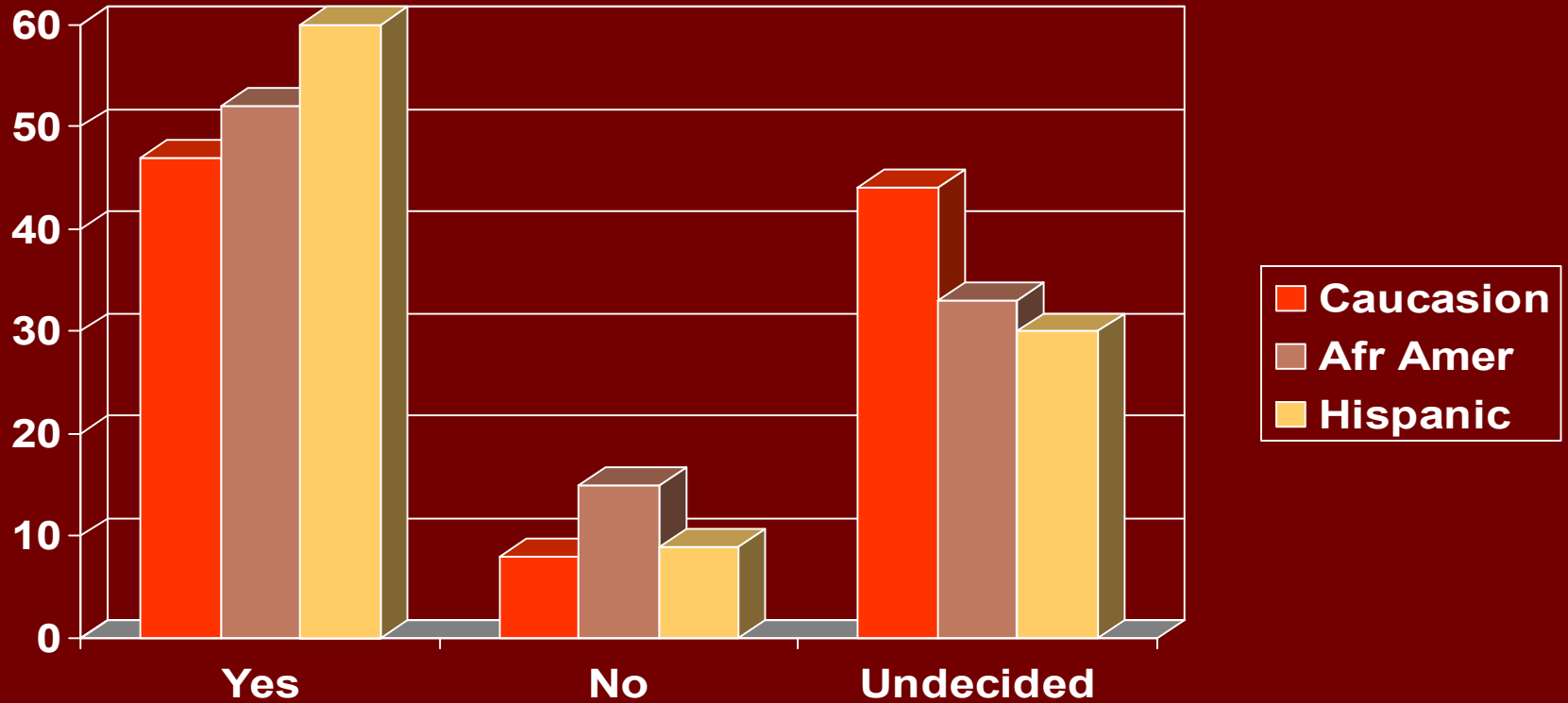
McBride and Anderson

Knowledge and Acceptance of the HPV Vaccine in a County Hospital Setting

Results

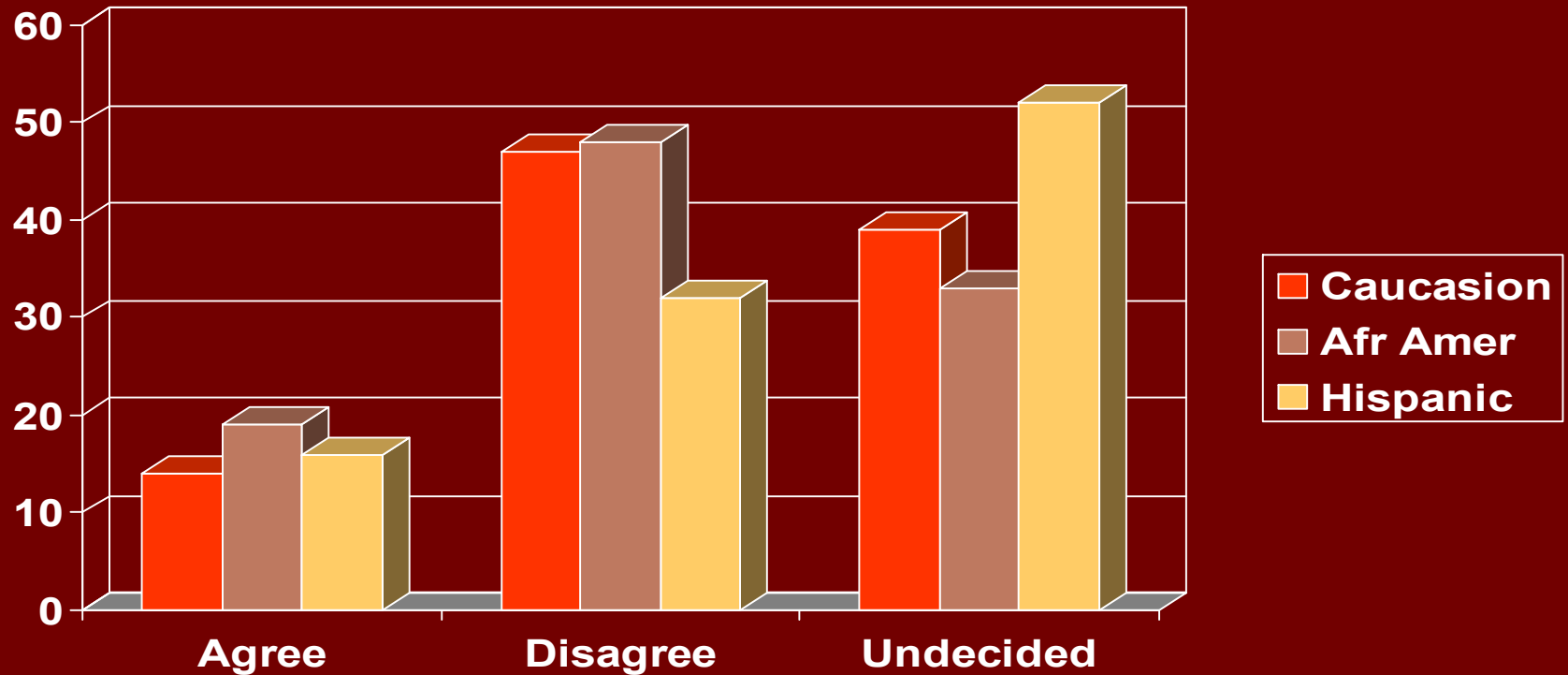
- 200 patients were surveyed
- Results were recorded in 3 categories:
 - Parental concern
 - Safety of the vaccine
 - Education regarding the vaccine

I would allow my child to receive the HPV vaccine? (RACE)



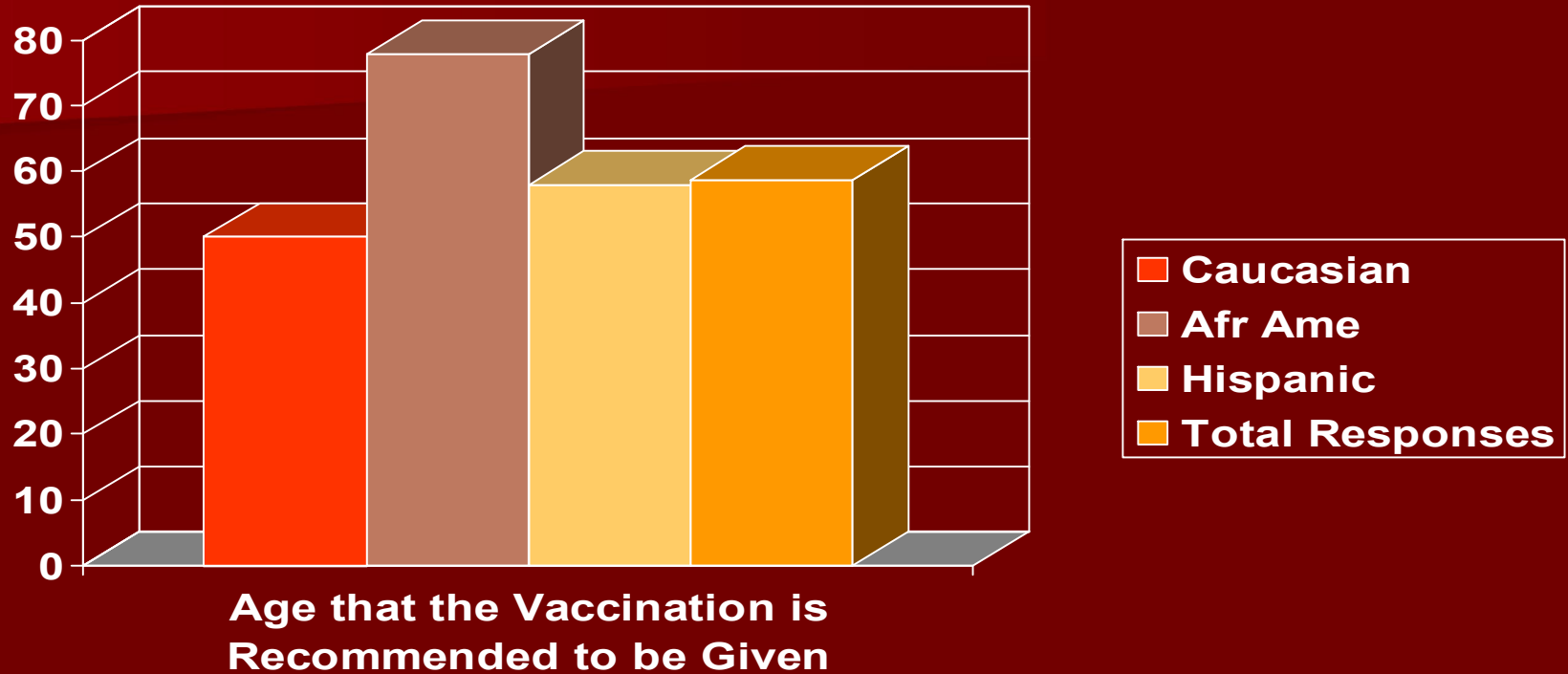
	Yes	No	Undecided
Caucasian	47.20%	8.30%	44.40%
African American	51.90%	14.80%	33.30%
Hispanic	60.20%	9.30%	29.60%

Will the Vaccine Encourage Sexual Activity? (RACE)



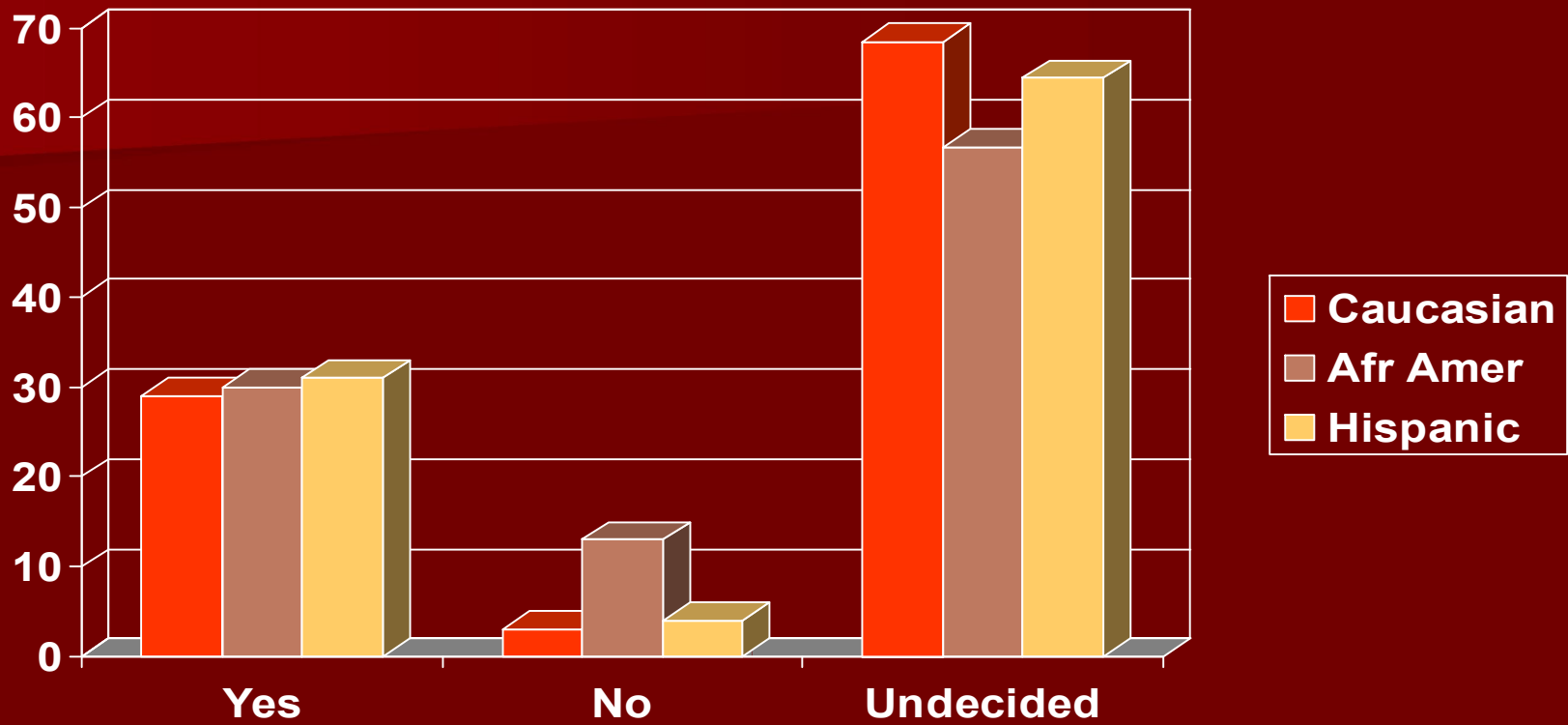
	Agree	Disagree	Undecided
Caucasian	14.00%	47.00%	39.00%
Afr Amer	19.00%	48.00%	33.00%
Hispanic	16.00%	32.00%	52.00%

Concern Regarding Age that the Vaccine is Recommended to be Given



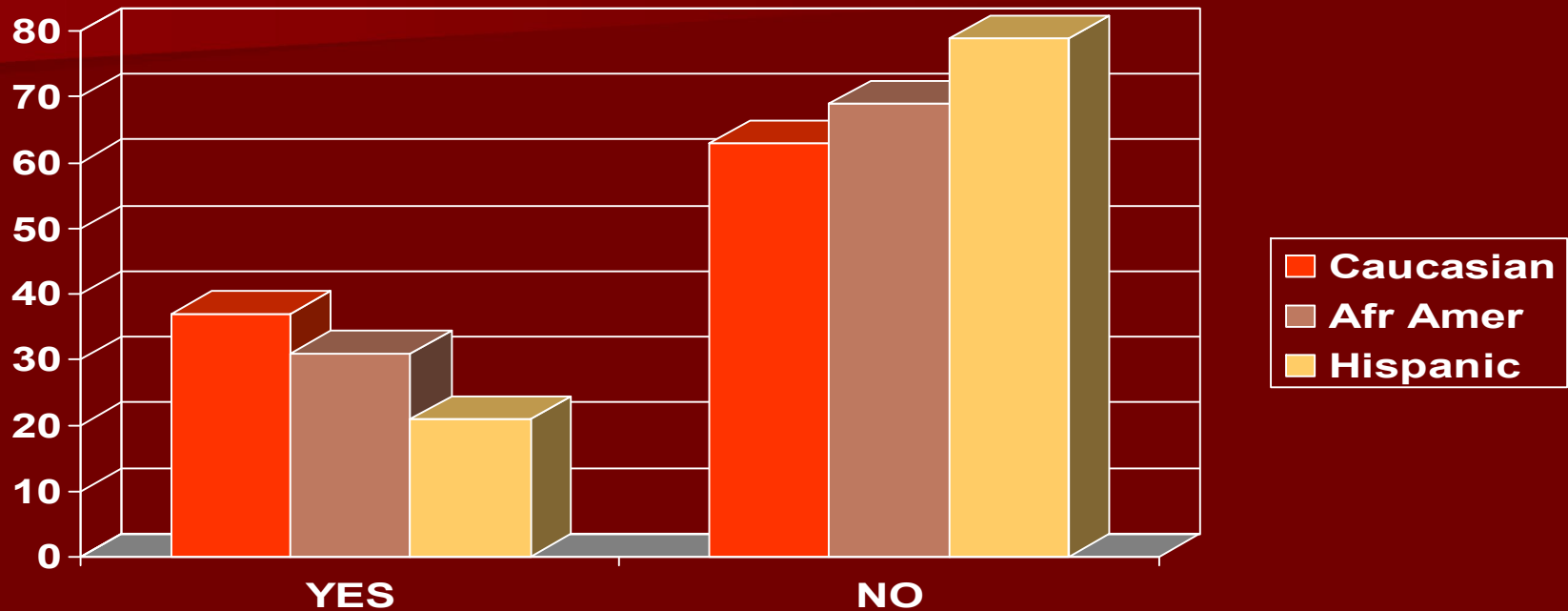
	Age that the Vaccination is Recommended to be Given
Caucasian	50%
Afr Amer	77.80%
Hispanic	58%
Total Responses	58.70%

Do you believe the vaccine is safe? (RACE)



	Yes	No	Undecided
Caucasian	29%	3%	68.40%
Afr Amer	30%	13%	56.70%
Hispanic	31%	4%	64.40%

Has a healthcare provider discussed HPV or the HPV vaccine with you? (RACE)



	YES	NO
Caucasian	36.80%	63.20%
Afr Amer	31%	69%
Hispanic	20.90%	79.10%

Major Findings of Survey

- **Patients did express some concerns about whether administration of the vaccine might encourage sexual activity.**
 - **Hispanics are less likely to believe it would encourage sexual activity.**
- **Patients did express some concern about the safety of the vaccine.**
- **Many parents, especially African American, were concerned that the vaccine was given at such a young age.**
- **The major concern expressed by the patients was the fact that they had not been appropriately educated about the vaccine by the provider. Therefore, they were undecided if it would encourage sexual activity, if it was safe or if it was medically important to them.**
- **Education level of the patient did not influence the patients' views on any of the parameters of the study**

Vaccine Recommendations and School Mandates

The individual states determine which vaccines should be required for school and daycare entry based on the public health needs of the state, usually based upon the Centers for Disease Control and Prevention (CDC) recommendations. States require that school children be immunized against certain diseases to protect both the vaccine recipient and his/her schoolmates from contagious illnesses. State requirements differ.

- School mandates have increased immunization levels and have reduced disease outbreaks, including among those who cannot receive the vaccine because of medical reasons.
- Most states permit religious and/or philosophical exemptions, in addition to exemptions from medical contraindications.
- Children who have been exempted from compulsory immunization for religious or philosophical reasons are many times more likely to both acquire and spread vaccine-preventable diseases.

Health Disparity Concerns Associated With The HPV Vaccine

Conclusions

- HPV vaccine if given universally will eliminate 90% of the genital warts and 70% of cases of cancer of the cervix.
- CDC has reported that the number of serious adverse events is no higher among the vaccinated than the non-vaccinated populations.
- The combination of administration of the HPV vaccine together with appropriate screening (Pap smear or HPV-DNA) will further reduce the incidence of cancer of the cervix.

Health Disparity Concerns Associated With The HPV Vaccine

Challenges

- **Lack of knowledge regarding the Human Papillomavirus.**
- **Lack of knowledge regarding the HPV vaccine**
 - **Benefits**
 - **Side effects**
 - **Safety**
- **Lack of patient access**
 - **Insurance**
 - **Patient desires**
- **Poverty**
- **Cultural beliefs**
- **Historical influences**
 - **Mistrust of society**
 - **Mistrust of government**
 - **Governor Perry's attempt to mandate vaccine**
 - **Mistrust of medical community**

Health Disparity Concerns Associated With The HPV Vaccine

Performance Improvement Plan

- **A major educational program to educate patients and their relatives regarding the benefits and problems of the vaccine and the underlying diseases the vaccine is designed to prevent.**
- **In view of the fact that the race of the patient does play a role in their perceptions regarding the vaccine and the diseases the vaccine is intended to prevent, the program must focus on cultural diversity.**
- **A study to determine the most effective manner to deliver the educational program.**

Health Disparity Concerns Associated With The HPV Vaccine

Performance Improvement Plan

- **Plan to improve access of patients to medical centers.**
 - Methodologies for payment of services.
 - Patient education to ensure patient safety care.

- **Plan to understand cultural beliefs and use that plan to attempt to reduce fears of disease, reduce mistrust of government and reduce distrust of the medical community.**
 - Community leaders