

**National Policies to Prevent and Manage Cervical Cancer in West African Countries:  
Policy Mapping Analysis**

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**Certification**

This is to certify that Evelyn Adejoke, ADEPOJU with matriculation number (LCU/PG/001586) carried out this research work titled “*National Policies to Prevent and Manage Cervical Cancer in west African Countries: A Policy Mapping Analysis*” in the Department of Public Health, Faculty of Basic Medical and Applied Sciences, Lead City University, Ibadan, Oyo State for the Award of Master of science Degree. In Public Health and that this has not been previously submitted.

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## **Dedication**

This research work is dedicated to God Almighty and my father Reverend J.A Adepoju.

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## **Acknowledgement**

I want to express my gratitude to this citadel of knowledge, Lead City University Ibadan, for making learning fun and also the management team for their scholarly assistance. I want to also appreciate the staff of lead city library.

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Even though the above mentioned institutions and persons have assisted in the process of this research work I alone stand responsible for the errors, if any found in the research work.

## Abstract

Cervical cancer is a significant public health challenge globally and it is more pronounced in the low and middle income economics to which West African countries belong.

WHO has guidelines which are the underpinnings of Countries National Policies towards prevention and management of cervical cancer. By using policy mapping, one may highlight the improvements that must be made to health policies while also presenting evidence for treatments that work. In order to identify and evaluate health policies for the prevention and management of cervical cancer in West African countries, this work mapped out the legal framework.

The majority of cancer-related deaths among women in West African nations are brought on by cervical cancer, a condition that is mostly avoidable. Legal records were uniformly searched from national cancer institute websites, government websites, and international and national legal databases. Results were put into tables and discussed. 35 documents which included plans, strategies, policies and guidelines from 16 West African countries were examined.

The topics that began to emerge included obstacles, screening, prevention, diagnosis, treatment, and mitigating attempts. The key findings include a lack of preventative vaccination against human papillomavirus inclusion into national immunization schedules, no binding rules, a considerable deviation from international norms (WHO guidelines) in most of the countries and insignificant screening registries. This study supports the connection between law and health and the requirement for open-book legislative and regulatory measures to further reduce cervical cancer mortality in West African nations.

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## **List of Acronym**

HPV: Human Papilloma Virus

WHO: World Health Organization

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## Chapter One

### Introduction

Persistent Human Papilloma Virus (HPV) infections are the main causes of cervical cancer. The International Agency for Research on Cancer has classified 12 of the 200 HPV varieties that have been found as carcinogenic, with HPV-16 being responsible for 50% and HPV-18 being responsible for 10%, respectively, of cervical cancer cases<sup>1</sup>. In comparison to a person who is not infected, the chance of developing cancer is increased by 435 and 248 times, respectively, by infection with one of these two HPV strains<sup>2</sup>. High-risk HPV genotypes are the primary cause of persistent viral infection, which is present in 99.7% of cervical cancer patients globally<sup>3</sup>.

About 80% of women will contract HPV at some point in their lifetime, many by the age of 45. It is worthy of note that HPV infection is sexually transmitted<sup>4</sup>. Since HPV infection is typically contracted during adolescence and the early stages of adulthood<sup>5</sup> it may take 10 to 15 years for abnormalities in the cervix to become apparent<sup>6</sup>.

Cervical cancer is the fourth most prevalent cancer in women worldwide, trailing only lung cancer (0.8 million cases), colorectal cancer (2.1 million cases), and breast cancer (2.1 million cases)<sup>7</sup>.

It affects both developed and developing countries. 528,000 new cases and 266,000 yearly deaths from cervical cancer were reported in 2012<sup>8</sup>. There were also 311,000 fatalities and over 570,000 new cases of cervical cancer in 2018<sup>9</sup>.

The primary reason for cancer-related fatalities among women in Eastern, Western, Middle, and Southern Africa in 2018 was cervical cancer. Controlling cervical cancer is a top global health priority, and it serves as an illustration of the significant differences between LMIC and HIC in terms of public health priorities, healthcare infrastructure and resources, cultural barriers,

technology, and the capacity to address prevention and treatment strategies. All three preventative tiers primary prevention with HPV vaccinations, secondary prevention with women's screening and treatment, and tertiary prevention with all diagnosed invasive malignancies being treated as necessary should be apart of a comprehensive prevention and control strategy. Two to four decades separate the peak of HPV infection from the peak of cancer incidence, giving screening plenty of room for advancement and innovation in the direction of better disease management<sup>10</sup>. While routine screening and vaccination campaigns have been quite successful in lowering cervical cancer rates in HIC, LMIC still face challenges in doing the same.

Cervical cancer rates have reduced by 1% to 1.9% annually since the introduction of HPV vaccines<sup>11</sup> demonstrating that prevention is a key component of managing cervical cancer as a whole.

Without laws, public health cannot be effectively regulated, and without designed and executed legal and regulatory mechanisms, nations cannot achieve their objectives. Policy mapping has become popular in recent years as a method of increasing the transparency of health regulations<sup>12</sup>. Laws, regulations, and policies are the three categories of legal instruments that legal mapping studies most frequently cover. Laws exist to control behavior, whereas regulation, in the context of public health, refers to the application of these socioeconomic policies or laws through the employment of various tools<sup>13</sup>. To achieve public health goals, such as lowering the burden of cancer by lowering its prevalence in a nation, law is crucial.

Although the establishment of national cancer control legislations/ policies is essential<sup>14</sup>. They represent a commitment by the government to lay the groundwork for the implementation and upkeep of cancer control programs<sup>15</sup>. Furthermore, research has shown that pertinent healthcare policies help to improve clinical outcomes<sup>16</sup>. Cancer policies increase awareness of the disease,

which leads to observable improvements in cancer management. Health regulations have resulted in a decrease in the incidence of some cancers, such as lung cancer<sup>17</sup>.

Despite the existence of numerous national and professional recommendations, the World Health Organization's (WHO) Thorough Cervical Cancer Control Guide to Essential Practice provides a comprehensive understanding of what a comprehensive strategy to cervical cancer prevention and control entails. This international handbook provides national decision-makers with evidence-based details on what works in cervical cancer prevention and control programs, which they may use as a foundation for updating their own policies, including recommendations and protocols<sup>18</sup>.

Figure 1.1: diagram illustrating cervical cancer



Source: Cervical cancer-Symptoms and Diagnosis IARC Technical publication no 45 Lyon: International Agency for Research on cancer; 2017

## 1.1 Background of the Study

It is possible to both prevent and treat cervical cancer. A method for obtaining data on successful treatments and identifying areas where health policies need to be improved is policy mapping. In order to identify and evaluate health policies for the prevention and management of cervical cancer, this project conducted legal mapping in West African countries. West African Country Profiles for Cervical Cancer, World Health Organization 2021 revealed that in 2019, Nigeria had the highest rate of cervical cancer deaths (10,600), followed by Ghana (2,200), Burkina Faso (2,100), and Mali (1,000). (1,700). Cervical cancer continues to be a major public health issue in places like the Benin Republic, where there is no information on the disease in the Cancer Registry. With 670 cancer-related deaths each year, cervical cancer is the second leading cause of death from cancer in the Benin Republic, according to data from IARC. Cervical cancer is the third most frequent cancer among women worldwide. Few West African Countries like Gambia, Cote d'Ivoire, Cameroon, Liberia, Mauritania, and Senegal included HPV in their National Vaccination Programs. In contrast, other West African countries, Nigeria, Niger, Burkina Faso, Benin, Ghana, Guinea, Guinea Bissau, Mali, Sierra Lone and Togo, did not make provisions for HPV National Vaccination Program, according to table 4.2 Column 5.

The cervical cancer mortality- to incidence ratio 2020 is contained in Table 4.2 Column 2, with Niger having the highest ratio of 0.76. Mortality-to-incidence ratio (MIR) is calculated by dividing the number of deaths for a selected cancer type in a given year by the number of newly diagnosed cases for that same year.

It is impossible for public health to function effectively without laws, and it will be challenging for nations to fulfill their health goals without putting the essential legal and regulatory

mechanisms in place and putting them into practice. With the aid of cervical cancer screening instruments, cervical cancer is extremely preventable.

## **1.2 Statement of the Problem**

As regards to table 4.1, cervical cancer is a serious public health concern in Africa. The prevalence is high. In 2019, Nigeria had the highest rate of cervical cancer deaths (10,600), followed by Ghana (2,200), Burkina Faso (2,100), and Mali (1,000). (1,700). Cervical cancer continues to be a major public health issue in places like the Benin Republic, where there is no information on the disease in the Cancer Registry. Cervical cancer is the second leading cause of death from cancer in the Benin Republic, according to data from IARC. Cervical cancer is the third most frequent cancer among women worldwide. Few West African Countries like Gambia, Cote d'Ivoire, Cameroon, Liberia, Mauritania, and Senegal included HPV in their National Vaccination Programs. In contrast, other West African countries, Nigeria, Niger, Burkina Faso, Benin, Ghana, Guinea, Guinea Bissau, Mali, Sierra Lone and Togo, did not make provisions for HPV National Vaccination Program.

Although due to excellent prevention efforts and legislation, the prevalence of cervical cancer has decreased in high-income nations <sup>19</sup> cervical cancer maybe wiped out by primary prevention (HPV vaccine) and secondary prevention (screening and treatment of precancerous lesions). Despite the difficulties that low-income nations have faced, where there are numerous resource constraints and implementation difficulties, there is still a growing interest in putting these strategies and policies into action and expanding them.<sup>20</sup>

This study aims to demonstrate the significance of law in healthcare and the requirement of policies in West Africa to further reduce cervical cancer mortality in light of the interest and commitment

of African policymakers to address the significant burden of cervical cancer. By evaluating the existence and content of laws/policies that prevent or manage cervical cancer in West African countries, the study seeks to address the issue of the lack of knowledge on these laws/policies in those nations and to offer recommendations on reviews where needed.

### **1.3 Justification of the Study**

The goal of this research project is to analyze the cervical cancer prevention and management strategies used in West African nations. To my knowledge, only three assessments have been done on this subject, one of which was done in 2020 by Njuguna<sup>21</sup> and the other in 2016 by T. Dutta.<sup>25</sup> with an emphasis on East African nations. In the rapidly evolving landscape of cancer control, Dutta's research is probably out of date. The most current study, carried out in January 2022 by Rifa Akanda.<sup>22</sup>, placed more emphasis on cervical cancer prevention than on its treatment. This study's main objectives are to assess the relationship between law and health, the need for policies to further reduce cervical cancer mortality in West Africa, to reduce illiteracy regarding the law that prevents and manages cervical cancer, and to compile publicly available data on cervical cancer prevention and management policies across West African nations. To the best of my knowledge, no analysis of national policy for the prevention and treatment of cervical cancer in West African nations exist; this study will fill that gap and open the door for additional research in the future.

### **1.4 Aim and Objectives of the Study**

The purpose of the project is to assess national policies in West African nations to prevent and treat cervical cancer. Specific Objectives are to:

- i. Identify the burden of cervical cancer in West Africa

ii. Determine the policies in the prevention and management of cervical cancer in West Africa countries

iii. Evaluate the effectiveness of policies and strategies on prevention and management of cervical cancer in West Africa countries.

iv. Assess the policies and strategies on prevention and management of cervical cancer adherence to the WHO guidelines on the management and treatment in West Africa countries.

### **1.5 Research Questions**

1. What is the burden of cervical cancer in West Africa?
2. What are the national policies on cervical cancer prevention and management in West African countries?
3. What role did policies played in the prevention and management of cervical cancer?
4. Did the West African Countries adhered to the WHO guidelines for the management and treatment of cervical cancer?

### **1.6 Significance of the Study**

This study will shed light on the existing legal frameworks for the prevention and treatment of cervical cancer in West African nations and identify those that don't have such policies. This analysis recommends out-of-date legislation and regulations and emphasizes their deficiencies.

This study will fill up the gaps in previous studies that only focused on cervical cancer prevention and did not consider West African nations or cervical cancer management practices. The results of this study will be used to inform the public about policies that can help them prevent and treat

cervical cancer, such as those that might make cervical cancer screening more widely available. This work will be useful to future researchers, policymakers, and the general public.

### **1.7 Scope of the Study**

This study's objective is to use policy mapping analysis to examine national cervical cancer prevention and management policies in West African nations. The study's main focus will be on the policies of the 16 West African nations, which will be covered in reviews, legal papers, official websites, National Cancer Institute websites, and other pertinent regulations.

This analysis only covers West African nations; it does not cover the policies of other African nations.

### **1.8 Purpose of the Study**

Examining the existence and content of laws and policies that address cervical cancer prevention or management in West African nations is the aim of the study. In order to further decrease cervical cancer mortality in West Africa, policies are required, and this study aims to show the significance of law in healthcare. It also aims to address the issue of West African nations' misunderstanding of the laws and regulations that are in place to prevent and treat cervical cancer.

### **1.9 Operational Definition of Terms**

**Cervical Cancer:** Cervical cancer is a type of cancer that starts in the cervix. Most cervical cancers begin in cells on the surface of the cervix.

**Cervix:** The cervix is a hollow cylinder that connects the lower part of a woman's uterus to her vagina.

**HPV:** Human papillomavirus (HPV) is the most common sexually transmitted infection (STI). It is an infection that causes warts in various parts of the body, depending on the strain. Many people with HPV don't develop any symptoms but can still infect others through sexual contact. Symptoms may include warts on the genitals or surrounding skin.

**Policy:** Policy is a deliberate system of guidelines to guide decisions and achieve rational outcomes.

**Prevalence:** prevalence is the proportion of a particular population found to be affected by a medical condition at a specific time

**Crude Incidence Rate:** A crude rate is defined as the total number of events, or count, divided by the mid-year total population of the selected geography and multiplied by a constant, which is a multiple of 10

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## Chapter Two

### Literature Review

#### 2.1 Conceptual Review

##### 2.1.1: History of Cervical Cancer

The first questions were how did the Human Papillomavirus (HPV) act and how significant was it expected to be in producing cervical cancer and precancer after Harald zur Hausen, Lutz Gissmann, and Matthias Durst discovered HPV6 and HPV16 in a sample of cervical cancers. Some researchers were thrilled by the finding, but others were skeptical due to their prior encounters with the Herpes virus<sup>1</sup>.

Aside from the low-grade and intermediate lesions detected by cytological screening that were unmistakably linked to HPV6 and HPV11, the nature of the remaining fraction of cervical neoplasia was unknown in the early 1980s. HPV16 and HPV18 appeared to be present in up to 50% of the small number of cancers and precancer studies by Southern blotting and later by radioactive methods like in situ hybridization<sup>2</sup>.

A Papanicolaou (Pap) test result that is abnormal is the most typical finding because many women are frequently checked. These people frequently show no symptoms. Abnormal vaginal bleeding, generally during a sexual act, is the earliest clinical sign of cervical cancer. Dysuria, offensive discharge, and vaginal pain are rather prevalent<sup>3</sup>The vaginal epithelium, squamous and glandular epithelial surfaces, and the lateral pelvic wall are all affected by the tumor's growth as it progresses upward to the endometrial cavity. It can immediately enter the rectum and bladder, causing obstruction of the ureter, fistula, hydroureter, and hydronephrosis, as well as constipation, hematuria, and hydroureter. Leg edema, discomfort, and hydronephrosis together point to

involvement of the pelvic wall. The extrapelvic lymph nodes, liver, lung, and bone are frequent locations for distant metastases<sup>4</sup>.

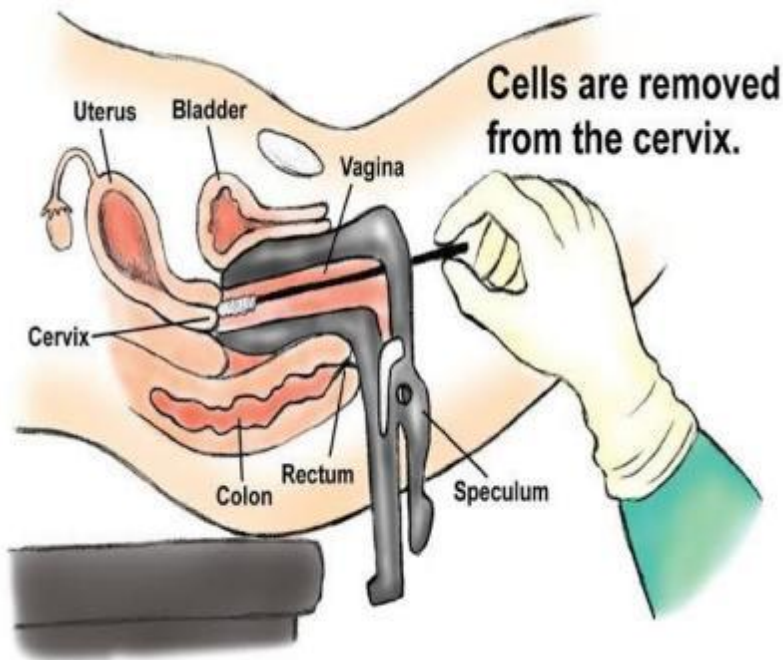


Figure 2.1: How A Pap Test Is Conducted By Inserting A Vagina Speculum To Hold The Vagina Wall Apart To See The Cervix, A Sample Cell From The Cervix Is Collected To Screen Cervical Cancer.

Source: Ministry of Health and wellness.

Physical examination results may be largely normal in people with early-stage cervical cancer. The cervix may start to seem odd as the condition worsens, including a tumor, ulcer, or severe erosion. The vagina may also be affected by these anomalies. An external lump or obvious blood from tumor erosion maybe found during a rectal examination<sup>5</sup>. Findings from abimanual pelvic examination frequently point to pelvic or parametrial metastases. Hepatomegaly may develop if the disease affects the liver. Unless pleural effusion or bronchial obstruction become apparent, pulmonary metastasis is typically difficult to identify on physical examination. Leg edema signals a tumor-related lymphatic or vascular blockage<sup>6</sup>.

The condition of cervical cancer carries a number of emotional undertones. It has represented the horror of cancer, the stigma associated with being a woman, the promise of screening for malignant tumors, and the optimism of innovative medical advances. Long-term incapacity and chronic pain, as well as physical deterioration, shame, and social isolation, were once associated with this illness, which was thought to have the most terrifying characteristics of all cancers<sup>7</sup>. The risks associated with being a woman were also demonstrated by cervical cancer. Radiation therapy and radium therapy, exfoliate cytology (Pap smear), homogenization of the "staging" of tumors, and widespread campaigns for the early detection of precancerous cervix lesions were innovations that were initially developed to control cervical cancer in the 20th century and set standards for the diagnosis, treatment, and prevention of other malignancies. Cervical cancer underwent a transformation in the late 20th century. The risk of stigmatizing patients grew as a result of this new knowledge of cervical cancer's connection to lifestyle choices, but it also created the opportunity for effective vaccination-based cervical cancer prevention<sup>8</sup>.

Subsequently, the Pap test is recommended to check for cervix lesions that are cancerous or precancerous<sup>9</sup>, as the natural history of HPV infection and subsequent cervical dysplasia has been clarified, the recommended age at which to begin cervical cancer screening has undergone significant change over time. Pap smear screening was previously advised to begin at age 18 or the start of sexual activity; however, in 2006, these guidelines were updated to advise waiting until age 21 or three years following the start of sexual activity. These were additionally updated in 2009 to advise starting cervical cancer screening at age 21, regardless of sexual history. In 2012 and again in January 2016, this suggestion was affirmed<sup>10</sup>.

Young women frequently have abnormal cervical cytology, and in teens, the majority of aberrant cytology resolves on its own<sup>11</sup>. Additionally, women under the age of 21 only represent for 0.1

percent of all cases of cervical cancer, and there is no proof that screening for the disease within this age group lowers incidence, morbidity, or mortality rates.

Given these details and the likelihood that cervical cancer screening would subject women at very low risk for cancer to unnecessary and potentially harmful evaluation and treatment, the 2009 ACOG guideline revision recommended starting cervical cancer screening at age 21, regardless of sexual history<sup>12</sup>.

Most scholars and practitioners consider the battle to understand the causes and effects of death, disease, and disability to be the essence of public health. When policymakers try to put that information to work, to translate knowledge into action for our common well-being, an even larger conflict often arises. Science can find solutions to major public health issues, but politics is the only way to make most of them a reality. "When we state that policies are selected by analysis," Lindblom clarifies, "By saying that policies are selected by analysis, we mean that an examination of the merits of numerous possible actions has shown reasons for selecting one policy over others." When we argue that politics dictates policy rather than analysis, we imply that policy is determined by the different ways in which people exert control, influence, or power over one another."<sup>13</sup>

A biomedical historian of Polish ancestry named Löwy authored a fascinating history of cervical cancer named "A woman's disease: The history of cervical cancer"<sup>14</sup>, that will enable readers to understand the significant advancements made in the diagnosis and treatment of this condition. Great strides have been made toward containing and, ultimately, eliminating this malignancy from the early nineteenth century to the twenty-first. Although there is still a long way to go before achieving these objectives in developing nations, it is hoped that with better planning, policies and more affordable technology, they will be able to tackle this potentially lethal disease.

Cervical cancer has been around since ancient times, according to historical records. Lowy, on the other hand, focused mostly on the nineteenth century, when significant attempts to identify and cure cervical cancer began. The history that Löwy presents in her work is one that is built on significant junctures. The ongoing development of new technologies and advancement of old ones opened the door to a greater comprehension of this disease's behavior, which therefore improved its management.

Women with cervical lesions received one of two treatments prior to surgical intervention. The first was palliative and involved drinking concoctions with 10% opium and 1% morphine in them. The second method was harsh and involved cauterization "with red hot iron" to practically burn the lesions.

According to lowy's "A woman's disease: The history of cervical cancer" In the eighteenth century some gynecologists were of the opinion that cervical cancer can be treated using a mix of chemical, physical, and mechanical techniques. In the latter, the doctor occasionally used just his hands. According to a French gynecologist, he "first scraped the damaged tissue with a curette then with his nails" in 1886 but all of those extreme steps were in vain. Women not only did not receive a solution for their illness, but they also had to deal with terrible side effects that left them with more devastating outcomes. Lowy describes how the frequent use of caustics and other harsh methods occasionally leads to the formation of fistulas, which are connections between a woman's vagina, urethra, and rectum. It had the effect of turning a woman's body into an "abominable cloaca through which women waste blood, pee, and feces." This result just made a lady feel more alone in society. Women who experienced this terrible fate preferred to spend their final days in hospices rather than return to their families.

The surgical removal of the uterus, or hysterectomy, has been practiced since ancient times. The surgery was performed on non-cancerous patients and was mostly utilized to remove a uterus that had prolapsed into the vaginal canal. The results of those operations were poor, and in the eighteenth century, such surgical interventions had a fatality rate of 90%. In 1812, a vaginal hysterectomy was performed for the first time to cure uterine cancer <sup>15</sup>, the surgeon mistakenly removed the entire uterus while trying to excise only the cervix. Three days later, the patient passed away from septic shock <sup>16</sup>.

Those who opposed surgical treatment for cervical cancer argued that those who did recover from their procedures didn't actually have the disease to begin with. Medical professionals were unable to discern between benign and malignant cervix conditions in the early decades of the nineteenth century. However, things quickly started to alter. Pathologists can now distinguish between cells of various anatomic sources as well as between normal and malignant cells thanks to the development of microscopes with higher resolution. This has two significant effects.

The first was that it is now possible to diagnose cervical cancer at the microscopic level before a woman receives treatment. The standard of care provided to women with cervical illness significantly improved as a result. The differentiation discovered between uterine body cells and cervix cells was the second significant result. This differentiation allowed the less specific words "carcinoma of the womb" and "cancer of the uterine body" to be used in place of each other

This distinction is important since uterine and cervical malignancies have different prognoses and treatment options<sup>17</sup>.

The development of X-rays by Wilhelm Roentgen (1845-1923) and radium by Pierre and Marie Curie (1859-1906) in the closing decades of the nineteenth century marked another significant

turning point in the history of cervical cancer treatment. Medical professionals began investigating the therapeutic uses of radiation treatment in both of its forms. The American gynecologist Barton Cook Hirst originally suggested using radiation therapy in 1903 in his Textbook on Diseases of Women to treat "tumors of the womb".

According to Ilana Lowe, an important turning point in the development of cervical cancer therapies was the adoption of radiation therapy. In her book she stated that Only one-third of women who had hysterectomy procedures were still alive and symptom-free five years following their procedure, making surgical involvement "dangerous" with an instant mortality rate that hovered around 10 - 15%. The treatment alternative of radiation therapy, which has a lower death rate, seemed more alluring. Furthermore, radiation therapy could be administered as an outpatient procedure. Additionally, unlike women who had hysterectomy surgery, those who had radiotherapy did not have incapacitating side effects that rendered them incapacitated and required them to be bedridden for weeks or even months at a time. While some women underwent "severe consequences and permanent mutilations," irradiation was far from a painless procedure<sup>18</sup>, as the book makes abundantly obvious, prevention has been the major narrative throughout cervical cancer history. At least in Western industrialized nations, a ground-breaking therapy did not contribute to the defeat of cervical cancer. It hasn't altered much over the past 150 years because receiving a diagnosis of an advanced cervical cancer is equivalent to receiving a death sentence. Experts concluded that the best opportunity for healing is through prevention. One of the rare human malignancies for which a precancerous stage can be detected and treated is cervical cancer. According to Löwy, the colposcope, Pap test, and later molecular identification of the human papilloma virus were important preventative measures that made cervical cancer a "barely apparent" disease in Western nations<sup>19</sup>. The book describes how doctors and gynecologists in the

nineteenth century came to the conclusion that telling women to see their doctors right away as soon as the first symptoms of the disease, such as irregular bleeding, pain, or discharge, appear is seldom beneficial. Physicians realized that many women would have advanced cancers by this point that were incurable. They understood that identifying cervical abnormalities before women had any disease symptoms would give them the best chance of preventing the cancer. It took over a century for this to become a reality. Women were receiving a variety of treatments in the meantime, but the results were highly unsatisfactory, and the majority of those affected eventually passed away from their illness.

The colposcope was created in 1924 by German gynecologist Hans Hinselmann with the goal of providing a magnified and illuminated picture of the cervix during visual examination to identify tiny abnormalities that are inaccessible to the naked eye. Hinselmann would administer acetic acid to the cervix during colposcopic examinations, turning any lesions into white patches. The latter would undergo a biopsy and microscopic examination. These lesions had malignant alterations, according to a histological analysis. Other types of lesions, however, indicated "precancerous changes," which were not true malignancies since they lacked one of the characteristics of cancer, which is the invasion of underlying tissues. The colposcope made it feasible to find those early cervical anomalies, which made cancer prevention more doable as a result. The cytological procedure developed by Greek American pathologist George Papanicolaou (1893-1962), later known as the Pap smear, was unveiled at this time.

The foundational publication "The Diagnostic Value of Vaginal Smears in Carcinoma of the Uterus," written by George Papanicolaou and American physician Herbert Traut (1894-1963), was published in 1941. This article established a solid foundation for cytological screening for cervical premalignant and malignant tumors. The sentence "If by any chance a simple and

inexpensive approach could be developed which could be used to vast numbers of women...we would be in a position to find the disease in its incipient stage" is arguably the most significant one in the essay. These were prescient statements because the Pap smears later widespread adoption as a cervical cancer screening tool can, in a very significant way, be linked to its ease of use and affordability.

There was a discussion on how to describe these "borderline" cervix lesions and what kind of care women with them should receive from the 1930s through the 1980s as pathologists and gynecologists got familiar with them. Opinions range from a radical response with hysterectomy or radiation, or a combination thereof, to a more cautious "watchful waiting," but as a better, if not comprehensive, understanding of the natural history of cervical cancer was attained, a consensus began to take shape.

Papanicolaou's pupil and renowned gynecological pathologist Leopold Koss (1920-2012), who is regarded as the founder of cytopathology, obtained biopsies from patients who had cervical lesions in the 1960s and discovered upon follow-up evaluation that those lesions had entirely disappeared. As a result, it was determined that cervical borderline lesions, or dysplasia, as they were later called, are delicate structures that can be conservatively treated with a modest surgical procedure. In the 1960s, there was "an era of prevention" for cervical cancer. The purpose of cervical screening was thus changed from exposing early uterine cervix malignant changes to "a method to detect and eradicate early precancerous lesions utilizing a conservative surgical approach." However, there was still a question that could not be answered with any level of certainty.

## **Why did cervical cancer develop?**

There were several hypothesized causes for this epidemic of women during the nineteenth century and the first few decades of the twentieth century. Cervical cancer used to be associated with a woman's promiscuous lifestyle. Some medical professionals thought that "sexual excesses and immorality" were related to cervical cancer. Other explanations like celibacy and sexual abstinence, venereal illnesses, menopause, or many pregnancies were put up. Some offered even stranger explanations, such as the perils of city living, fear, and extreme grief. In addition, the "Irritation Theory" of cancer was a widely accepted theory in the nineteenth century. The idea that cancer can be characterized as the unchecked growth of cells was reflected in this hypothesis, which was developed in the latter part of the century and is still true today. According to scientists, persistent inflammation can eventually cause uncontrolled cell division. The irritation theory of cancer was disproved with the introduction of the concept of mutation in the early 20th century and the growing acceptance of the role played by genetic mutation in causing unrestricted growth. However, the relationship between sexual behavior and cervical cancer was still a possibility. The condition was discovered by doctors in the middle of the 20th century in childless, sexually active women. Experts began to consider the possibility that cervical cancer might be a sexually transmitted illness. During the second part of the 20th century, efforts were made to identify the infectious agent responsible for infecting women and causing those potentially malignant lesions in their cervix.

A virus that may cause sarcoma, a cancer of the connective tissue of the body, in chickens was discovered in 1911 by American virologist Peyton Rous (1879-1970), who founded the field of tumor virology. Rous Sarcoma Virus was given to this virus (RSV). The results of Rous' study were contested, and many scientists thought that using chickens as a model for studying humans

was inappropriate. In spite of the availability of more sophisticated scientific knowledge and technical equipment, it took the scientific community more than 50 years to corroborate Rous's discovery. A virus with the potential to cause cancer was considered to be a "oncogenic virus" in the 1960s. Rous was awarded the Nobel Prize in 1966, four years before he passed away, for his work from 1911 and earlier studies, particularly his studies on the papillomavirus and its function in tumor initiation.

Herpes virus was among the suggested viral causes of cervical cancer.

The human papillomavirus (HPV), which causes warts, was found to be associated with cervical cancer in 1970, according to German virologist Harald zur Hausen (b. 1936). It was later determined that women were more likely to develop cervical lesions if they had the carcinogenic HPV versions 16 and 18. For his studies on the HPV virus, Harald zur Hausen was awarded the Nobel Prize in 1988. Currently, in settings with adequate resources, smears demonstrating atypical cells of unclear significance, or in cytopathological jargon, in women 30 years of age or older with an equivocal Pap test result are used as a triage tool to determine the urgency of HPV testing.

The viral etiology of cervical cancer gave rise to hopes for the creation of an HPV vaccine that would immunize women against infections and shield them from the dangers of cancer. The age of cervical cancer vaccination is discussed in Löwy's book. Throughout history, various social and political organizations have had disagreements about immunization and vaccines. Despite the fact that vaccination has significantly decreased morbidity and mortality from public health threats like polio, measles, and mumps, it continues to be the subject of intense debate over "safety, efficacy, individual rights, and the prerogative of government." The HPV vaccine is no exception, and the book reflects this debate.

The vaccine's effectiveness, "its effect at the population level," and "its possible hazards" were all hotly contested topics. The gender component is one of the main factors that set the HPV vaccination controversy apart from other vaccine-related issues in the past. After the first vaccine was introduced in 2006, several people argued that both sexes should have immunizations in order to create "herd immunity" and to be fair to women, who shouldn't have to "bear the dangers and cost of vaccination" alone.

The practice of medicine is hardly a totally scientific effort. It is where politics, economics, law, and public policy all converge. This interdisciplinary approach to the study of medical history is best illustrated in a book by Löwy. For instance, the author spends sometime discussing what she refers to as the "Scandal" at New Zealand's National Women's Hospital. A feminist and a lecturer in women's studies wrote an article in a magazine in 1987 in which they claimed that Dr. Herbert Green, a gynecologist, had purposely stopped providing conventional therapy to women who had cervical lesions, more specifically cervix cancer in situ.

According to the authors, the gynecologist subjected those women—without their knowledge or consent—to an experiment to evaluate his own traditional therapeutic strategy. Later on, some of the ladies experienced aggressive cervical cancer. According to the report, this affair exemplifies "male doctors' harsh and inconsiderate attitude of women." The Minister of Health established a panel to look into such claims within two weeks of the article's publication. The commission, led by Silvia Cartwright, a district court judge, came to the conclusion that "the medical profession had failed in its basic duty to patients" after six months.

Being a well-known feminist, Löwy's feminist views are readily apparent in some of the author's interpretations of this history. As an illustration, the author thinks that during a gynecological examination, a speculum is a tool that has been referred to as "one of the major emblems of the

power of male doctors over a woman's body." The author notes that in the 19th century, sex workers were compelled to submit to routine examinations by doctors, who were predominately male, in order to screen for sexually transmitted diseases like syphilis and gonorrhea. In contrast, women whose examinations revealed lesions were sent to a "lock hospital" and were not permitted to resume offering their sexual services until they had been declared free of any diseases.

Readers can now access a thorough, educational, and extremely readable history of cervical cancer thanks to Ilana Löwy. I am not aware of any English-language book that covers a history that goes back more than two centuries. The book does have some flaws, though. Sometimes while introducing specific information, the author forgets to cite sources. In one instance, the author claims that gynecologists invented the cone biopsy in the 1970s as a method to get rid of cervical lesions. The source of this information is not cited by the author.

Additionally, the author makes a historical error. It was reported in 1916<sup>10</sup> that the first description of cervical conization for the diagnosis and treatment of cervical lesions. The cone biopsy was already a well-established standard practice when it was first utilized in the 1950s and 1960s of the previous century<sup>11,12,13</sup><sup>20</sup>. (Another instance is when the author discusses the French gynecologist and orthopedic surgeon Jacques Mathieu Delpech (1777-1832), who performed a total of 21 hysterectomies on patients, all of whom died as a result of the procedure. Additionally, no citation was offered for this data.

Other minor factual errors also exist. For instance, the author claims that the atlas of pathology by British physician Matthew Baillie (1761-1818) was published in 1793. Actually, the first edition of this work was released in 1794. She also references Peyton Rous, who originally identified a virus that produced sarcoma instead of leukemia, giving rise to the term Rous Sarcoma Virus (RSV).

Since the 1960s, there has been much discussion on the role that the Pap smear and, by extension, population-based screening programs using the Pap test have played in the decline of cervical cancer morbidity and mortality. This debate is briefly discussed in the book. The majority of experts concur that the Pap smear was crucial in slowing the spread of cervical cancer. However, as the author correctly notes, it is unclear how significant that role was. To even attempt to respond to this question would be outside the scope of this work. Numerous studies have been published on this subject, but they are typically academic in style and filled with jargon, making them impenetrable to the average reader. It has been long overdue for a book that is accessible to readers, like Löwy's, to be written about the history of the Pap smear and its contribution to the fight against cervical cancer.

Harald Zur Hausen is said to be the first person to discover cervical cancer disease according to Grace Kim in her book that she named after him <sup>21</sup>.

According to Grace, In Europe during the twentieth and twenty-first century, Harald zur Hausen conducted virus research and found that some strains of the human papilloma virus (HPV), a sexually transmitted disease, can cause cervical cancer. In particular, cancer-causing viruses were the focus of Zur Hausen's research over his whole career (oncoviruses). He emphasized cervical cancer and HPV in particular. Two HPV strains, HPV 16 and 18, were found to cause cervical cancer. Zur Hausen postulated that HPV was carcinogenic. The development of the HPV vaccines Gardasil and Cervarix followed this discovery, which helped with the identification of cervical cancer. The Nobel Prize in Physiology or Medicine was awarded to zur Hausen in 2008.

Germany's Gelsenkirchen-Buer is where Zur Hausen was born on March 11, 1936. The regular bombardment of his hometown didn't stop him from living through World War II as a child with his family. In Germany's Gelsenkirchen-Buer, where Zur Hausen attended elementary school, the

frequent bombing in that year caused the closure of the local schools, which led to a halt to his schooling. At age ten, he started attending a high school in 1946, the year after World War II ended. He finished high school there in 1955 after his family relocated there in 1950, where he also received his diploma.

Zur Hausen enrolled in the University of Bonn in Bonn, Germany, in 1955 after completing his high school education to start his medical studies. He remained there until 1957, at which point he relocated to Hamburg, Germany, to pursue his studies at the University of Hamburg. Zur Hausen studied for a year at the University of Hamburg before transferring once again to the Medical Academy in Düsseldorf, Germany, in 1958. His medical degree was awarded to him in 1960 after he left the Medical Academy. The next two years were spent by Zur Hausen as a medical intern in order to obtain a German medical license. However, as an intern, he spent the majority of his time in obstetrics and gynecology. He also worked in surgery and internal medicine.

After completing his medical internship, zur Hausen chose to become a researcher instead of a doctor. In 1962, he started working at the University of Düsseldorf's Department of Medical Microbiology and Immunology. As a result of his investigation into the effects of the vaccinia virus in mouse cells, Zur Hausen gained fundamental scientific training in the disciplines of virology and bacteriology. Zur Hausen discovered that the virus changed the chromosomes, which are the DNA-carrying structures in cells, but he was unable to determine why. Zur Hausen later claimed that because research on bacteria and viruses was just being started in Germany in the 1960s, he had little means for furthering his knowledge. In 1964, as zur Hausen looked for research possibilities, he wed his first spouse; a year later, their son, Jan Dirk, was born.

Zur Hausen started working as a post-doctoral researcher in the US in 1965. Zur Hausen relocated to the US to work at Philadelphia, Pennsylvania's Children's Hospital. He worked there under the

direction of Werner and Gertrude Henle, virologists researching the Epstein-Barr virus (EBV). It can lead to a number of illnesses, including the infection mononucleosis, which is marked by a fever, sore throat, and exhaustion<sup>22</sup>, but in the 1960s, researchers had only found the virus in Burkitt's lymphoma cells. A malignancy of the fluid that contains white blood cells is called Burkitt's lymphoma (lymph). In addition to figuring out whether EBV caused Burkitt's lymphoma, the Henles and their research group were attempting to create serological tests that might be used to diagnose EBV using blood samples. The research team proposed that EBV maintained a continuous infection in the lymphatic cells, acting as an oncovirus, or a virus that promotes cancer. When a virus infects a cell and stays there for a long time, it is said to have established a persistent infection. Viruses multiply inside a cell before spreading to other cells. The Henles proposed that EBV persisted in a subset of lymphatic cells, progressively spreading to other cells.

While zur Hausen exhibited interest in researching EBV, he lacked knowledge of the necessary research techniques. Zur Hausen practiced lab techniques with the adenovirus, a distinct type of virus. The adenovirus most frequently results in respiratory sickness, although it can also cause bladder or digestive tract infections<sup>23</sup>. The Henle taught zur Hausen how to identify and analyze DNA using a technique called nucleic acid hybridization as well as how to discover viral DNA in sample cells using other techniques. Zur Hausen used such techniques to search for chromosome alterations in adenovirus-infected human cells. Additionally, he looked at chromosomal variations in human lymphoblastoids, which are developing cells that would eventually develop into several subtypes of white blood cells.

Zur Hausen started looking into EBV while he was still working on his adenovirus studies. Using an electron microscope, which creates a high-quality image of an object by bouncing electrons off it, he examined Burkitt's lymphoma cells. He found EBV in the malignant cells after doing this.

The concept that EBV had a significant role in Burkitt's lymphoma was further substantiated by Zur Hausen's investigation. Axel, the secondson of Zur Hausen, was born in 1967<sup>24</sup>.

Zur Hausen agreed to work as a researcher at the University of Würzburg's Institute for Virology in Würzburg, Germany, in 1969. He continued to study EBV while running a separate lab team. He proposed that, contrary to what the Henles had proposed, EBV DNA was present in every Burkitt's lymphoma cell but did not reproduce and distribute new viral copies. Zur Hausen suggested that only some cells were capable of activating the virus. Even though EBV was not causing illnesses like mononucleosis, zur Hausen discovered while working at the Institute of Virology that EBV DNA was present in the DNA of Burkitt's lymphoma cells. Instead, EBV-infected lymphatic cells had a longer lifespan than uninfected cells, which allowed them to multiply and expand more quickly than usual, an indication of malignancy. He demonstrated how viruses, which contain genetic material that can possibly change the host cells' genes, can start tumor growth in human tumor cells<sup>25</sup>. Zur Hausen agreed to become chairman of the Institute of Clinical Virology in Erlangen, Germany, in 1972.

In his capacity as chairman, zur Hausen started researching the origins of cervical cancer. Scientists had proposed that the sexually transmitted herpes-simplex 2 virus (HSV-2), which frequently causes genital warts, was the root cause of cervical cancer. The majority of genital warts are brought on by sexually transmitted illnesses, according to research. The discovery of HSV-2 DNA in cervical cancer tumor cell samples by researchers led some to postulate that HSV-2 was the cause of the disease. In his own research, Zur Hausen used nucleic acid hybridization to examine cervical cancer tumor samples for HSV-2 DNA.

However, zur Hausen discovered conflicting results when he examined cervical cancer tumor samples for HSV-2 DNA in 1976. HSV-2 DNA was not present in all tumor samples, which made

zur Hausen wonder if HSV-2 was a factor in the development of cervical cancer. After failing to find evidence of HSV-2 DNA in tumor samples, zur Hausen started looking into the human papilloma virus as a potential cause of cervical cancer (HPV). Zur Hausen looked at medical records of women who had genital warts caused by the HPV who later developed cervical cancer. Medical studies connected vaginal warts brought on by HPV to cervical cancer. In 1976, zur Hausen reported his notion that HPV causes cervical cancer based on those data. Zur Hausen relocated to the Institute for Virology and Immunology at the University of Freiburg in Freiburg, Germany, a year later, in 1977. Gerrit, zur Hausen's third son, was born in 1977 as well.

Seit 1977, zur Hausen has supported his hypothesis that HPV is the primary cause of cervical cancer. In 1976, zur Hausen published his theory that HPV infections resulted in genital warts, which later developed into cervical cancer. He and his research group cloned HPV DNA in 1980 and used it as a model to examine HPV DNA discovered in samples. Two new HPV strains, HPV 6 and 11, were found in genital wart sample analysis performed by zur Hausen and his research team between 1980 and 1982<sup>26</sup>.

zur Hausen and his study group looked for HPV 6 and 11 DNA in cervical cancer tumor samples after isolating and cloning HPV 6 and 11 DNA. The research team could come to the conclusion that HPV 6 and 11 caused cervical cancer if they discovered DNA from HPV 6 and 11 in cervical cancer tumor samples. While some HPV 6 and HPV 11 DNA was discovered by the research team in the cervical cancer tumor samples, the DNA was not in great quantities. Instead, two novel HPV strains, HPV 16 and 18, were found by Zur Hausen in cervical cancer tumor samples in 1983 and 1984<sup>27</sup> Zur Hausen relocated to the Deutsche in Heidelberg, Germany, in 1984. Additionally, he wed Ethel-Michele de Villiers, a member of his research team, after divorcing his first spouse. Zur Hausen and his study group kept looking into samples of cervical cancer and genital warts. They

discovered that samples of vaginal warts frequently contained HPV 6 and 11, while samples of cervical carcinoma frequently contained HPV 16 and 18.

In order to develop an HPV vaccination, zur Hausen contacted pharmaceutical companies in 1986. Later, Zur Hausen recalled that pharmaceutical companies had rejected his vaccination ideas over worries that the products might not be financially successful for the businesses and that there were more urgent health issues than HPV. Trotzdem, zur Hausen kept working on his HPV studies. He worked on new molecular DNA techniques while conducting clinical research to clarify how HPV forms and infects people. He also conducted molecular research on HPV. Additionally, he looked into the frequency and distribution of HPV DNA in cervical cancer patients from all around the world.

The polymerase chain reaction (PCR), a molecular technique, was developed by scientists in the late 1980s to more effectively extract genetic information from samples. Using those methods, numerous researchers from all around the world discovered HPV DNA in a variety of tissue samples. These results cast doubt on zur Hausen's contention that HPV led to cervical cancer. Later, Zur Hausen stated that since many of these approaches were novel, inadequate training and cross-contamination produced inaccurate results.

Few people agreed with zur Hausen's findings when he first presented his theory that HPV caused cervical cancer in the 1970s. The majority of scientists feel that HSV-2 is the true cause of cervical cancer. The academic community changed its research to focus on HPV rather than HSV-2 as zur Hausen continued his study of HPV and cervical cancer and as laboratory methods improved. *Infections Causing Human Cancer*, a book about the results of zur Hausen's investigation, was published in 2006.

After conducting extensive research on the relationship between HPV and cervical cancer, zur Hausen won numerous honors for his contributions to the field of oncovirus study. These included the William B. Coley Award for Distinguished Research in Basic and Tumor Immunology in 2006 and the Robert Koch Prize in 1975. In recognition of identifying the two HPV strains responsible for cervical cancer, zur Hausen received the Nobel Prize in Physiology or Medicine in 2008. Françoise Barre-Sinoussi and Luc Montagnier, the scientists who discovered HIV (the human immunodeficiency virus), also received an award. The Nobel Prize in Physiology or Medicine awarded to Zur Hausen sparked debate. In order to ascertain whether AstraZeneca, a pharmaceutical corporation engaged in the creation of the HPV vaccination, had any influence over two members of the Nobel Prize selection committee, Swedish police launched an anticorruption inquiry. A charge was never filed following the investigation.

He continues to undertake research at the German Cancer Research Center even after stepping down as director in 2003. He was researching the link between consuming red meat and colorectal cancer by 2016.

## The Human Papilloma Virus

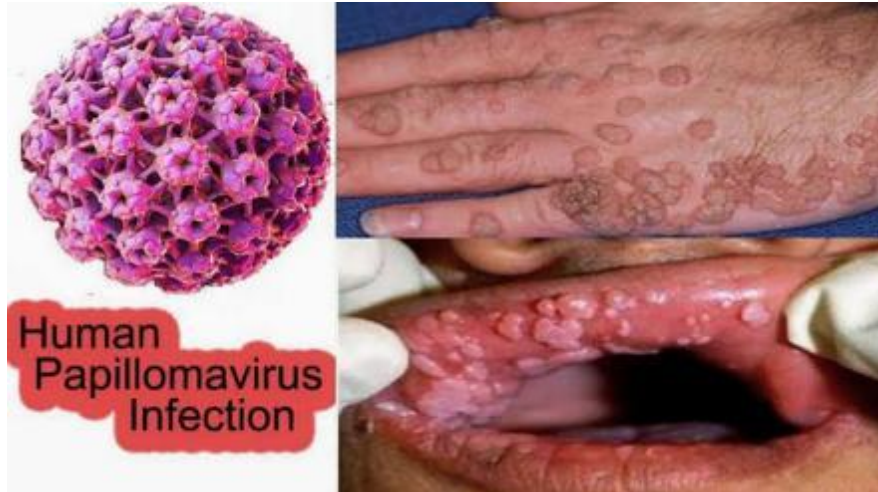


Figure 2.2: Human Papillomavirus and Infection

Source: Classified.com

The human papillomavirus (HPV) will infect almost everyone at some point in their lives. Fortunately, most cases have no symptoms and go away without any therapy after two years. Even though some HPV strains can result in the development of warts, these are typically rather innocuous.<sup>28</sup>

Unfortunately, HPV can also lead to major health problems. The virus is almost always to blame for occurrences of cervical cancer. Additionally, throat cancer and anal cancer risk are both increased by HPV infections.

While the association between HPV and cancer is now well understood, it wasn't always the case. Years of study were required to fully understand how HPV influences the body, particularly with regard to cervical cancer.

Scientists investigating cervical cancer's potential causes started investigating lifestyle factors that might be connected to the condition in the 1950s. They found that cervical cancer risks were greater in women who had several sexual partners or who started acting sexually younger. The findings showed a pattern resembling a sexually transmitted illness (STI).

Scientists at the time were perplexed by this, especially because cancer didn't seem to be a communicable disease<sup>29</sup>.

Harald zur Hausen, a German virologist, was intrigued, though. In his earlier studies on the cancer-causing Epstein-Barr virus, Zur Hausen had read findings from American researcher Richard Shope from the 1930s that described how a specific form of papillomavirus infection in rabbits resulted in the development of warts and later cancer<sup>30</sup>. He became aware of a possible relationship when examining medical cases when women with genital warts went on to get cervical cancer. The following stage was to determine whether his theory was accurate.

At the time, several researchers hypothesized that cervical cancer might be caused by herpes-simplex virus type 2 (HSV-2), a STI known to cause genital warts. Zur Hausen, however, desired to look into this further through his own studies. After discovering that HSV-2 was uncommonly absent from cervical cancer tumor samples, he moved his focus to HPV and first presented his theory in 1976.

Zur Hausen's research led to the identification of numerous novel papillomavirus species, including HPV-6 and HPV-11. He discovered that neither category had a very substantial association with cervical cancer. The link wasn't made obvious until Zur Hausen found two additional HPV strains (HPV-16 and HPV-18) in 1983 and 1984.

HPV-16 and HPV-18 were quickly identified by Zur Hausen and his team of researchers as being present in 50% of all cervical malignancies and 20% of cervical cancer samples, respectively. It was a significant finding that human papillomavirus infection, particularly HPV-16 and HPV-18, was closely associated with cervical cancer. Today, we understand that around 70% of cervical malignancies worldwide are caused by HPV-16 and HPV-18.

Since 1986, Zur Hausen has promoted an HPV vaccine while continuing his studies. Zur Hausen received the William B. Coley Award for Distinguished Research in Basic and Tumor Immunology in 2006, and he also earned the Nobel Prize in Physiology or Medicine in 2008.

Researchers from all around the world discovered more varieties of the HPV virus that may be connected to cervical malignancies following Zur Hausen's discovery in the 1980s. To put all of these discoveries together, the International Biological Study on Cervical Cancer group was established in 1995. They observed that 93% of the samples for cervical cancer contained HPV after combining the samples from 22 different nations.

These results were supported by additional research, which also demonstrated that the initial estimate was off. A team of scientists conducted a thorough investigation and retested the samples in 1999. They discovered that 99.7% of cervical tumors contained HPV, demonstrating that HPV infection is the cause of cervical cancer <sup>31</sup>

There are more than a hundred different kinds of HPV, but only 13 high-risk varieties have been related to cancer. Additionally, researchers found that other strains of HPV beyond the high-risk, cancer-causing ones are responsible for genital warts.

Fortunately, the majority of women with high-risk HPV infections won't get cervical cancer. Those who do develop cancer have a higher chance of surviving with the tests and treatments available

today. In fact, Australia is predicted to eradicate cervical cancer within 15 years as a result of the nation's robust screening and vaccination program. Cervical cancer rates are also continuing to decline as HPV vaccination becomes more widely available. Women today have a better chance than ever before of avoiding or overcoming cervical cancer because to decades of hard work by committed scientists.

The Papillomaviridae family of viruses includes the tiny human papillomaviruses (HPVs), which are DNA-carrying viruses. They can adapt to their hosts and are widely distributed. They have the capacity to successfully evade immunological responses. The majority of the more than 200 varieties of HPV that have been identified and divided into 29 genera have an effect on humans. These viruses, which mostly damage differentiated squamous epithelium, are associated with cutaneous infections and can infect mucous membranes as well as practically every area of the human body's skin. Because HPV infection plays a crucial role in carcinogenesis through the activation of its genetic products, it raises the risk of uterine cervix cancer <sup>32</sup>.

The upstream regulatory region (URR), the first area, and the second area are three distinctive regions that makeup the genome of all papillomaviruses. About 10% of the entire genome is made up of the URR, also known as the long control region (LCR) or the non-coding region (NCR) (IARC, 1995) <sup>33</sup>. The first region occupies roughly half of the genome and is divided into two large and several small reading frames. According to the IARC (1995), the large reading frames are E1-E2 and E4-E7, while the small reading frames are found in E6 and E7 and are involved in the development of cervical cancer <sup>34</sup>. The genes L1 and L2 are located in the second region, which makes up the remaining 40% of the genome (IARC, 1995).

Even while cervical cancer cases and HPV are regularly related, the virus has also been linked to other diseases. There are numerous HPVs that produce various lesions, and they may have similar

effects. HPV serotypes differ from one another genetically, and according to the standard classification scheme, a particular HPV type must possess a whole genome in which the L1 nucleotide sequence differs from that of any other HPV genome by at least 10%. Based on the date of their discovery, HPV types are assigned numerically in a chronological order<sup>35</sup>.

Currently, the Papillomaviridae family contains 39 genera. Alphapapillomaviruses, betapapillomaviruses, gammapapillomaviruses, mupapillomaviruses, and nupapillomaviruses are five of those genera that contain HPVs. The International Agency for Research on Cancer defined all the various HPVs in 2012 and classified them as either group 1 carcinogens (carcinogenic to humans), group 2A carcinogens (probably carcinogenic to humans), or group 2B carcinogens (maybe carcinogenic to humans)<sup>36</sup>. In high-pressure liquid chromatography, the group-1 HPVs (HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV59) are regarded as dangerous. Since there is no evidence to support HPV68 as being high risk, it is classified as probably carcinogenic and is put in category 2A. One of the 13 HPV varieties in groups 1 and 2A is responsible for 96% of all cases of cervical cancer<sup>37</sup> HPV26, HPV30, HPV34, HPV53, HPV66, HPV67, HPV 69, HPV70, HPV73, HPV82, HPV85, and HPV97 are additional alpha papillomaviruses that have been connected to sporadic cases of cervical cancer and are regarded to be group 2B carcinogens. It is more challenging to determine the carcinogenicity of group 2B HPVs because there are less incidences of cervical cancer linked to them. Research has however demonstrated that E6 mRNA and other markers of HPV-induced carcinogenesis increased the expression of p16 and decreased the expression of cyclin D1, p53, and Rb. All HPV carcinogen categories have been linked to cervical malignancies with this pattern<sup>38</sup>. A total of 98.7% of cervical cancers are HPV-positive malignancies if the 2.6% of instances connected to group 2B HPV-type carcinogens are combined with the 96% of cases associated to

group 1 and 2a type carcinogens. Additional information has shown that although uncommon, HPV68, HPV26, HPV66, HPV67, HPV73, and HPV82 are more frequently found in women with cervical cancer than in those with normal cervical cytology; as a result, an update to the carcinogen classification system should be taken into consideration <sup>39</sup>.

The majority of sexually transmitted infections (STIs) that occur in the United States are anogenital infections, which affect around 6.2 million people each year, mostly teens and young adults. According to clinical assessments, the prevalence of STIs in adolescent girls is normally around 30% but can rise to 64% in some groups. More than 50% of young women in the population had a cervical HPV infection at 4 years following their first sexual experience, according to a separate analysis <sup>40</sup>. The same study also showed that HPV could spread through non-penetrative sexual behavior, however this possibility is less likely than getting infected through penetrative sexual activity. Evaluations conducted in the United States have shown that individuals under 25 are also at risk for infection in addition to their sexual history. With the exception of one cohort research in Costa Rica, which found that the incidence increases once again beyond age 40, the incidence appears to be lower after this age in the majority of studies. Additionally, the rates of HPV infection in men and women seem to be comparable.

The discovery of high-risk HPV in newborns, kids, and virgins provides evidence that sexual contact is not the sole way HPV is spread. It is possible to spread both low- and high-risk HPV serotypes through non-sexual contact with others, communal bathing, and handling contaminated feces <sup>41</sup>. It appears that during parturition, as the newborn descends the contaminated birth canal, high-risk HPV is transferred from the mother to the child. Compared to women with less DNA, mothers with very high quantities of HPV DNA, particularly those with HPV-16, are more likely

to experience this. Additionally, it has been reported that two moms who had HPV-16 and 18 infections also had neonates who had the same co-infections <sup>42</sup>.

It suggests that getting pregnant increases your risk of getting genital HPV infections. In a study, this was demonstrated by the finding that 52.5% of moms tested positive for HPV DNA during the third trimester of pregnancy, as opposed to 17.5% after delivery <sup>43</sup>. Glucocorticoids and their response elements communicate with the non-coding region of HPV-16, which could explain why the hormone profile of pregnancy increases the transcription of HPV genes. Furthermore, immunosuppression is a condition that affects pregnant women. Additionally, HPV infections can spread during pregnancy through the placenta and amniotic fluid. One study found that 75% of the amniotic fluids taken from moms who tested positive for cervical HPV DNA contained HPV DNA<sup>44</sup>.

Cervical cancer affects roughly 35 out of every 100,000 women worldwide, making it the second most frequent cancer among women <sup>45</sup>. When HPV types 16 and 18 were found in cervical malignancies and preneoplastic dysplasia, the lesions that can make a woman prone to uterine cervix cancer, awareness of the connection between HPV and cancer was dramatically increased. More than 99% of cervical cancer cases have been shown to contain HPV DNA, however the most common high-risk serotypes vary between nations, racial groups, and socioeconomic levels. IARC found that of the most common HPV serotypes that cause cervical malignancy (16, 18, 58, 33, 45, 31, 52, 35, 59, 39, 51, and 56), HPV 16 causes more than 50% of cases of cervical cancer, while HPV 16 and 18 together cause more than 70% of cases worldwide<sup>46</sup>. Serotypes 18 and 45 of HPV are linked to cervical adenocarcinomas that are more aggressive.

It has been found that the main risk factor in the development of precursor lesions into cervical cancer is long-term infection with high-risk HPV serotypes. Identification of the same high-risk

HPV types at >2 visits spaced by 4-6 months is the standard definition of persistence<sup>47</sup>. Studies have revealed that these chronic infections can more than tenfold the risk of developing high-grade precursors of cervical cancer<sup>48</sup>.

#### Malignancies Associated with the Cervical Canal

The uterus and vagina are separated by a canal called the cervix, which has two openings: the superior internal os, which leads to the uterus, and the inferior external os, which leads to the vaginal cavity. Contrary to the vaginal cavity, which is bordered by stratified non-keratinizing squamous epithelium, the histology of the cervical canal is characterized by simple columnar secretory epithelium. The squamocolumnar junction, which corresponds to the region of the cervix at the external os, is where the epithelia that line the endocervix and exocervix unite<sup>49</sup>. Given that the squamocolumnar junction is a key cytological marker and the location of over 90% of lower genital tract cancers, it is also the region that is most susceptible to HPV infection<sup>50</sup>. Cervical dysplasia and cervical intraepithelial neoplasia (CIN), which frequently progress to cervical cancer due to a persistent infection with high-risk HPV, are known to be caused by HPV<sup>51</sup>.

Two distinct types of cancer can develop in the cervix because the transition zone contains two different types of epithelial cells (glandular and squamous cells). In 10-20% of cases, an adenocarcinoma is caused by an uncontrolled, rapid growth of glandular cells in the endocervix, albeit the incidence appears to be increasing recently<sup>52</sup>. Squamous cell carcinoma is brought on by a squamous cell malignancy. The latter is significantly more common (occurring in 80-90% of instances), usually asymptomatic in the early stages, but as it progresses, it can cause coital and pelvic pain as well as aberrant vaginal bleeding and discharge<sup>53</sup>.

## HPV Life Cycle

There is a substantial correlation between cervical carcinogenesis and the viral life cycle events. The basal layer-forming cells in a stratified squamous epithelium function as stem cells and divide when they take the place of surface layer-releasing cells. Two daughter cells are produced when a basal cell divides via mitosis: one rises and becomes a terminally differentiated cell, whereas the other cell remains in the basal layer to preserve the pool of dividing cells. The virus initially targets basal cells since they are weak due to microwounds. The process by which HPV virions enter cells involves connecting with certain receptors, like the alpha-6 integrin, which binds HPV-16<sup>54</sup>. The basal layers are where viral DNA replication begins, producing 50-100 copies of the genome in every cell. Following this, the E1 and E2 proteins are expressed, which are necessary for the replication process and for the separation of recently generated DNA, ensuring that infected stem cells remain in the lesion for along time. With the exception of the E1 helicase, the virus primarily exploits host technology to perform DNA replication. Early gene products, including E5-E7, are thought to provide an environment that is conducive for replication by promoting DNA replication in the host cell and stopping apoptosis.

### HPV's part in cervical cancer development

Although HPV is the biggest risk factor for cervical cancer, many experts contend that this infection is typically quickly cleared by the immune system because specific viral DNA integration does not frequently occur. While viral DNA can quickly transform infected cells into neoplastic ones once it is integrated, the mere presence of HPV DNA in the cell is probably insufficient to cause cancer because additional genetic and epigenetic events are required.

E6 and E7 are two of the key oncogenic proteins produced by the HPV virus; they function by altering how the cell cycle is controlled and by controlling apoptosis. Viral DNA insertion impairs the E2 protein's ability to function. Since it is known that the E2 protein can suppress the transcription of the oncoproteins E6 and E7, its disruption results in the dysregulated expression of these proteins. These proteins work together to immortalize cells, preserving their capacity to undergo mitosis and produce clones with the immortalized phenotype without going through terminal differentiation<sup>55</sup>. The fight against HPV infection and cervical carcinogenesis relies heavily on the immune response. However, by expressing the E5 oncogene, which controls a number of immunological systems, such as antigen presentation and inflammatory pathways, HPV is able to encourage immune evasion<sup>56</sup>.

#### Oncoprotein E7

E7's association with and consequent inactivation of pRb is its primary property that allows it to promote neoplastic transformation. As pRb is dephosphorylated in the G0 and G1 stages of the cell cycle, its phosphorylation status changes depending on the stage of the cell cycle. It is phosphorylated in the S-phase and remains phosphorylated until later in the M-phase when, as a result of the action of a specific phosphatase, it appears to be hypophosphorylated once more<sup>57</sup>.

When pRb and its associated proteins are dephosphorylated, they bind to transcription factors like E2F and inhibit them. This inhibits the expression of genes whose byproducts promote DNA synthesis and speed up the cell cycle. However, when pRb is phosphorylated by G1 cyclin D kinases (CDKs), it loses its ability to bind to E2F and its inhibitory effect is as a result eliminated, allowing the cell to enter the S-phase. As a result, it controls the G1/S checkpoint. When damaged DNA is detected, p53 is activated, which then triggers p21, a CDK inhibitor. This p21 restricts

cyclin E-CDK2 and connects to it. pRb can't be phosphorylated as a result. Therefore, pRb can prevent the G1/S transition by inhibiting E2F.<sup>58</sup>

The complex formed by pRb and E2F can be disturbed if the E7 protein links to the hypophosphorylated version of pRb. As a result, the cell enters the S-phase early, which triggers DNA synthesis and ultimately cell division. It's interesting to note that HPV replication and the completion of the entire life cycle depend on the actual generation of E7 and its effects on targets that include pRb<sup>59</sup>.

The Rb family of tumor suppressor proteins may play a role in the epigenetic modifications that the E7 oncoprotein may cause by modulating the DNA methylation mechanism to govern routes of cellular proliferation<sup>60</sup> A study revealed that HPV-16 E7 might link DNA methyl transferase DNMT1 to begin its enzymatic activities both in vitro and in vivo<sup>61</sup> The E7 oncoprotein can bind to DNMT1 directly and cause hypermethylation to silence genes<sup>62</sup> When E7 forms a close complex with Rb, E2F is released and binds to DNMT1, which results in the hypermethylation of CpG islands<sup>63</sup>.

#### Oncoprotein E6

According to Narisawasaito and Kiyono<sup>64</sup>, the E6 protein primarily manifests its carcinogenic effects on HPV-infected cells by promoting the ubiquitin-dependent proteosomal degradation of p53, a tumor suppressor gene product that prevents the accumulation of harmful mutations that can lead to the development of cancer. Such mutations may result from mistakes made during DNA replication, physical and chemical mutagens, or both. The cell cycle is stopped when aberrant DNA is found and p53 is activated, allowing DNA repair to take place before the cell splits.

Apoptosis, which is a mechanism for programmed cell death, can be triggered in specific circumstances, such as when the DNA cannot be repaired<sup>65</sup>.

Cervical cancer cells, among others, have p53 concentrations that are roughly two to three times lower than those of normal cells. Additionally, its half-life is significantly shortened. As a result, p53 does not react to DNA damage as it normally would. Unrepaired DNA mutations persist in the genome and are passed from one cellular generation to the next. Overtime, this buildup results in genomic fluctuations<sup>66</sup>. Therefore, cancer cells not only lack checkpoint vigilance for DNA damage but also have an inherent propensity to prefer mutagenesis<sup>67</sup>.

E6, an E3 ubiquitin protein ligase, does not automatically attach to p53; instead, E6-associated protein (E6AP) controls this process. E6AP belongs to a class of proteins that includes the E6-AP carboxyl terminus (HECT) E3 ligases, which identify substrates through ubiquitylation machinery intended for proteosomal destruction. It's interesting to note that the presence of E6 enhances the turnover of E6AP, perhaps due to its increased enzymatic activity in the cellular environment of HPV infection. Howley, 2006.

It has been documented how E6 mediates gene silencing. The procedure entails the breakdown of p53 and the release of the transcription activator specificity protein 1 (Sp1), which binds to the promoter of DNMT1 and increases the expression of this gene. The DNA is then hypermethylated as a result of the high level of DNMT1.

Viroporin classification for the oncoprotein E5 was proposed. This channel protein controls ion homeostasis, vesicle trafficking, virion production, and viral genome entry<sup>68</sup>. The E5 oncoprotein is essential for cell proliferation in HPV16-infected cells and disrupts a number of signaling pathways. Additionally, HPV16 E5 engages in pro-carcinogenic actions, such as promoting EGF-

mediated cell proliferation, inhibiting apoptosis brought on by tumor necrosis factor ligand (TNFL) and CD95 ligand (CD95L), and modulating genes related to cell adhesion and cell motility<sup>69</sup>. All of these actions affect the host's immune system in an indirect manner.

### **Burden of Cervical Cancer in Sub Saharan Africa**

Around 570,000 new cases of cervical cancer (CC) were recorded globally in 2018, with 80% of these occurrences occurring in low- and middle-income countries<sup>70</sup>. CC is the most prevalent cancer in half (23/46) of the SSA countries and the fourth most common cancer in women diagnosed worldwide (although second in frequency to breast cancer overall). (ibid) Due to higher incidence and mortality rates than anywhere else in the world, women in SSA bear a disproportionate share of the burden of CC. Southern Africa has the highest age-standardized incidence rate (ASR) of CC (43.1 per 100,000)<sup>71</sup>. Only 33% of women in SSA are still alive five years after being diagnosed with cervical cancer, according to a recent study involving 11 nations (Sengayi-Muchengeti, personal communication). CC was the leading cause of cancer death in the SSA in 2018, accounting for 21.7% of all cancer fatalities among female patients<sup>72</sup>.

In affluent nations like the United Kingdom (UK) and the United States (US), where population-wide screening programs have been in place since the 1960s, the prevalence of CC has dramatically dropped. These programs, which were initially based on cytology, now employ human papillomavirus (HPV) DNA testing<sup>73</sup>. A lack of effective population-level screening programs, low preventative awareness, unequal access to healthcare, poverty, and low socioeconomic position, on the other hand, are contributing to an increase in the prevalence of CC in developing countries<sup>74</sup>. As part of the country's national cancer control action plan 2010-2014, the Victoria hospital in Mauritius, a West African country, started a population-wide CC screening program. The country's transition from a low-income to an upper middle-income, diversified economy as

well as this screening program may have had something to do with the recent decrease in incidence<sup>75</sup>. The hospital serves around 30% of the island's population<sup>76</sup>. In Mauritius, there is a known incidence of CC, which is comparable to other high- and middle-income nations<sup>77</sup>. Women find it challenging to get the education they need to become educated consumers of cervical cancer services because the majority of SSA countries suffer from extreme poverty<sup>78</sup>. In SSA nations, it's common for even educated women such as those who work in healthcare to have a poor grasp of cervical cancer and its risk factors<sup>79</sup>. Furthermore, a lot of women in SSA are unable to access services for cervical cancer prevention and treatment because they lack the funds for transportation or medical bills<sup>80</sup>. Socio-cultural practices such polygamous marriages, immature sexual development, high parity, and teenage marriages<sup>81</sup>, enhance a woman's risk of developing cervical cancer in the SSA. Studies have demonstrated that there are cultural hurdles to cervical cancer screening even in locations where services are provided<sup>82</sup>, these women typically present late, at an advanced stage of the disease. Civil wars in SSA nations have resulted in the destruction, looting, and abandoning of medical facilities by medical personnel, making it hard to provide healthcare, including for cervical cancer. During war and other catastrophes, when vices such prostitution, multiple marriages and cohabitation, rape, and sexual promiscuity among males are common occurrences that cause HPV to be transferred to women<sup>83</sup>. People are uprooted and made to live in camps. Although CC has a high rate of morbidity and mortality, it maybe treatable, and it has significant public health concerns in SSA, where it accounts for 25% of female cancer diagnoses and fatalities<sup>84</sup>.

## Burden of Cervical Cancer in West African Countries



Figure 2.3: West African Countries Map

Source: Encyclopedia

Cervical cancer is Nigeria's second-leading cause of cancer burden, behind breast cancer, with an estimated 14,943 cases and 10,400 deaths in 2018<sup>85</sup>. Furthermore, it is currently predicted that over 53 million Nigerian girls and women over the age of 15 may face an increased risk of developing the disease if deliberate prevention and control measures are not put in place<sup>86</sup>. These estimates may just be a "tip of the iceberg" of the total burden of cervical cancer in Nigeria due to poor data quality and reporting, a lack of national prevalence research, and a dearth of cancer registries<sup>87</sup>. In Nigeria, cervical cancer continues to have a significant socioeconomic impact. Cervical cancer harms young, fertile women in Nigeria, slowing economic growth and increasing poverty<sup>88</sup>. The 90-70-90 goal, which needs to be accomplished by 2030, was chosen in response to the cervical cancer burden that is unbearable, especially in LMICs<sup>89</sup>. His objective urges governments to fully immunize 90% of young girls against HPV, screen 70% of women by the

ages of 35 and 45, and treat 90% of women who have pre-cancer or advanced cervical cancer<sup>90</sup>. To accomplish these objectives in Nigeria, a concerted health system policy and program driven by a strong political commitment would be required<sup>91</sup>. To reduce the prevalence of cervical cancer in Nigeria, creative and cheap policies are required that would scale up CCS services, especially for the most vulnerable women. A tripartite strategy is suggested to address missed opportunities for the delivery of CCS services and improve screening acceptance in Nigeria. The successful implementation of these interventions depends on a number of factors, including strong political will, the availability of resources, good institutional leadership and support, the amount of attention given to cervical cancer, and a qualified and motivated female nursing workforce<sup>92</sup>. Cervical cancer is also the leading cause of female cancer deaths in Senegal<sup>93</sup>, with an estimated 1,876 instances of the disease being discovered year, 1,367 fatalities, and an age-standardized mortality rate of 29.1 compared to 6.9 globally. With 7.6/100,000 women affected, North America has the 17th-highest age-standardized incidence rate of cervical cancer in the world, trailing only Senegal with 37.8/100,000 cases and Western Africa with 23/100,000.<sup>94,95</sup> Despite the fact that cervical cancer screening and therapy are effective in reducing incidence and 6.9% of all women between the ages of 18 and 69, the expected participation rate in Senegal is quite low<sup>96</sup>. Rural areas and older age groups, where participation rates are especially low (1.9 percent of women between the ages of 40 and 49 and 0% for women 50 and over)<sup>97</sup>, are two areas where this is the case. Cervical cancer screening has been made available in Senegal since 2014 thanks to the efforts of an ongoing collaboration in the Kédougou region, despite the fact that it is still unavailable in many rural sections of the country<sup>98</sup>. Social determinants of health include gender roles in decision-making, gender implications on discrimination and cancer stigmas, and other structural barriers like educational level and language all have a substantial impact on cervical cancer screening in

Senegal<sup>99</sup>. Although early detection of precancerous lesions through Pap smear testing can help prevent cervical cancer, its acceptance in Ghana is still comparatively low. The lack of a national policy on cervical cancer screening, the marital status of women, their satisfaction with healthcare, and their involvement in healthcare are all factors that contribute to the low patronage in Ghana. However, by developing and implementing a clear national policy on cervical cancer screening along with a planned national health education intervention program by the Ministry of Health/Ghana Health Service, the patronage may rise under certain circumstances<sup>100</sup>. The most common kind of cancer in Mali is cervical cancer, with most instances happening in people between the ages of 15 and 24<sup>101</sup>. A cervical cancer incidence rate of 37.7 per 100,000 females is predicted for Mali. The prevalence of high-risk HPV was between 12 and 14 percent; these numbers are congruent with those from other West African countries<sup>102</sup>. Cervical cancer screenings are generally very infrequent in Mali. 166 participants (82.5%) of a study who tested positive with either high-risk HPV type 16 or 18<sup>103</sup>.

In addition, much like many other SSA countries, the republic of Benin continues to face a serious public health problem with regard to cervical cancer<sup>104</sup>.

Cervical cancer ranks third in incidence and prevalence among Beninese people after breast cancer and prostate cancer in that order, with an annual new diagnosed cases of 783 and the second most common cancer and cause of cancer death, with an annual death of 652 among Beninese women. However, there are no data from the Cancer Registry in Benin available for cervical cancer<sup>105</sup>. The third highest overall cancer death rate is caused by cervical cancer<sup>106</sup>. In Liberia, 1.47 million women aged 15 or older who are at risk of having cervical cancer. The disease currently claims the lives of 469 women year, while 656 other people are diagnosed with it. Cervical cancer is the

most prevalent illness among women in Liberia and the second most prevalent malignancy among those between the ages of 15 and 44<sup>107</sup>.

It is unknown how common HPV is in Liberia's population as a whole. However, it is estimated that 4.3% of women in the general population in Liberia's neighboring Western Africa region are infected with cervical HPV-16/18, and that HPVs 16 or 18 are the cause of 55.6% of invasive cervical cancers. The risk of acquiring cervical cancer affects 1.47 million women in Liberia who are 15 years of age or older.

The disease currently claims the lives of 469 women year, while 656 other people are diagnosed with it. Cervical cancer is the most prevalent illness among women in Liberia and the second most prevalent malignancy among those between the ages of 15 and 44. It is unknown how common HPV is in Liberia's population as a whole. However, it is estimated that 4.3% of women in the general population in Liberia's neighboring Western Africa region currently have cervical HPV-16/18 infection, and that HPVs 16 or 18 account for 55.6% of invasive cervical cancers.) With a reported frequency of 19.6 and 24 percent among childbearing women in two different districts<sup>108</sup>, the disease is said to be the second most common malignancy in women nationally and the main cause of cancer-related fatalities<sup>109</sup>. In the SSA country of Cameroon, 50.1% of the population is female and at risk for the illness. It is the second most prevalent kind of cancer, with 15,700 new cases added year and a mortality-to-incidence ratio of more than 65 percent<sup>110</sup>. In the recent past, the country established the Cameroon National Committee for the Fight against Cancer, the National Cancer Control Plans for 2003-2007 and 2006-2010, and the National Strategic Plan for Cervical Cancer Control 2015-2020<sup>111</sup>. Despite this, the nation lacks a comprehensive screening program and instead relies on irregular cervical cancer examinations conducted by non-governmental and civil society organizations<sup>112</sup>.

3.85 million Women in Guinea, who are 15 years of age or older and at risk of developing cervical cancer, are listed by the ICO/IARC Information Centre on HPV and Cancer<sup>2021</sup>. Current estimates indicate that every year, 2068 women will be diagnosed with cervical cancer, and 1463 of them will die from the condition. According to Keita, in their article, *Hpv Infection in women with and without Cervical cancer in Conakry Guinea*, cervical cancer is the cancer that affects women most frequently in Guinea, and this is especially true for females between the ages of 15 and 44. It is estimated that cervical HPV-16/18 infection affects 9.8% of women in the general population, and that these HPVs are linked to 55.8% of invasive cervical malignancies.

### **2.1.2 Reducing Disease Burden through Public Health Policies and National Strategies**

The majority of population health maintenance takes place in people's homes, autos, communities, schools, and businesses. Health is significantly impacted by policies and county regulations<sup>113</sup>.

Without laws, public health cannot be effectively regulated, and without designed and executed legal and regulatory mechanisms, nations cannot achieve their objectives. Policy mapping has become popular in recent years as a method of increasing the transparency of health regulations<sup>114</sup>. Laws, regulations, and policies are the three categories of legal instruments that legal mapping studies most frequently cover<sup>115</sup>. Law is essential to achieving public health objectives, such as reducing the burden of cancer by reducing its prevalence in a country. Laws exist to control behavior, whereas regulation, in the context of public health, refers to the application of these socioeconomic policies or laws through the employment of various tools<sup>116</sup>. Policy can have a considerable impact on the intricate, multi-sectoral variables that influence this and other diseases' morbidity, death, and health inequalities at the population level. Public health policy may comprise legislation, norms, incentive systems, or other standardized procedures and practices in order to influence institutional and individual behavior to improve health and health equity.

Laws and regulations that weren't made with health objectives in mind can nonetheless significantly affect people's health, even though that isn't what they were intended to do. A thorough investigation of the connection between policies and population health is necessary to develop and execute health-promoting policy interventions that are practicable, effective, and minimize harms<sup>117</sup>.

Nations must establish realistic yet ambitious measures to prevent cancer. This is why having a National Cancer Control Plan (NCCP) or a plan related to cancer is essential (CRP). The CRP and NCCP have increased from 48 percent in 2000 to 87 percent in 2015<sup>118</sup>. Cancer is the leading cause of mortality not just in high-income countries (HIC), but also in middle- and low-income nations (MIC and LIC), according to these statistics<sup>119</sup>. The fourth most common cancer in women globally in 2018 was cervical cancer, with 569 847 new cases and 311 365 fatalities<sup>120</sup>.

The NCCP or CRP is not operationalized<sup>121</sup>. in nations where there are no immunization and screening programs, the health system is still fragile, and cervical cancer is a mammographically prevalent disease, despite the fact that it is one of the most preventable human malignancies and that its progression from HPV infection to invasive carcinoma is quite apparent and targetable. The majority of these deaths are preventable due to inadequate funding, a lack of expertise, or a lack of political will. Cervical cancer is actually the most common tumor in women and the leading cause of death in 38 LIC, mainly in Sub-Saharan Africa, Guyana, and Bolivia in South America. If nothing is done, LIC will be accountable for 95% of fatal cases of cervical cancer by 2030<sup>122</sup>. Since cervical cancer is a preventable tumor, the WHO has long viewed it as one of the top priorities to be treated through primary and secondary prevention, therapy, and palliation<sup>123</sup>. As part of the Global Action Plan for the Prevention and Control of Non-communicable Diseases 2013-2020, several suggestions were made in 2013 to assist member nations in pursuing clinically

effective cervical cancer treatments. These recommendations were designed to be included in any CRP or NCCP. In accordance with these WHO recommendations<sup>124</sup>, identified nine interventions as being part of the "Essential Cancer Package," such as vaccination, cervical screening, early diagnosis, pathology, radiation, surgery, chemotherapy, palliative care, and cancer registry. These interventions were considered to be crucial health services for cervical cancer. Non-Communicable Disease Country Capacity Surveys (NCD CCS) conducted by the World Health Organization over four time points evaluated how well each country was doing at accepting the aforementioned WHO recommendations (2010, 2013, 2015, and 2017).

Even the greatest offers have not yet been widely adopted in national plans, therefore only 158 of the 194 WHO member states had CRPs available in 2018. Only 85% of the 158 nations mentioned having a plan for HPV vaccination and only 67% for cervical cancer screening. Each of these distinct strategies is important and needs to be included in NCCPs in order to battle the increased incidence of cervical cancer<sup>125</sup>. Even more important than just scaling up each intervention is the symmetrical and coordinated extension of each service. In order to provide consistent services and obtain the greatest outcomes with the available resources in order to prevent and treat cervical cancer, national programs should be coordinated<sup>126</sup>. According to the WHO NCD CCS from 2015, little progress has been made even though the majority of HIC embraced HPV vaccination and cervical cancer screening into their national programs, only around 35 percent and 65 percent of LIC did so.

This is particularly concerning because, in LIC and MIC<sup>127</sup>, malignancies may soon surpass cardiovascular diseases as the primary cause of death. Cervical cancer is already the fourth most common malignancy in women worldwide at age<sup>128</sup>.

The desired cervical cancer control rates, as indicated by Simms<sup>129</sup>, are still very distant from being achieved in both LIC and HIC. By 2020, HPV vaccine coverage should reach 80 to 100 percent, and it should be mandated that 70 percent of women undergo cervical screening twice during their lifetimes. This will help prevent an additional 12.5 to 13.4 million cases of cervical cancer over the next 50 years, and it will also contribute to the eradication of cervical cancer as a public health problem by the end of the century. The new WHO "Global Strategy towards the Elimination of Cervical Cancer as a Public Health Problem" is being developed with the goal of lowering the age-adjusted incidence rate of cervical cancer to fewer than 4 per 100,000 women-years. The current range of age-standardized incidence rates is 80 per 100,000 in the countries with the highest risk and less than 10 per 100,000 in the countries with the lowest risk<sup>130</sup>. The new WHO guideline recommends that all nations complete the following significant projects by the year 2030: Between the ages of 35 and 45, 70% of women are checked with a high-performance test, and 90% of those who are identified with cervical illness receive treatment. 90% of the time, girls are fully protected against HPV by the age of 15.

In this sense, "therapy" refers to the management and care of 90% of women with invasive cancer and 90% of women with pre-cancer, respectively. A "high performance test" is defined as a test with performance at least as excellent as an HPV test. Both of these goals must be combined. According to this article's data based on the 2017 WHO NCD CCS<sup>131</sup>, only 23% of countries globally attain vaccine coverage rates of 70%. Government initiatives provide HPV vaccination in 82% of HICs but less than half of non-HICs. LMIC had the lowest availability rate, at 35%. Only 147 out of 194 nations (or 76%) offer cervical screening as a service. Of these, 57 had opportunistic programs, while 90 had population-based programs with organized services and higher participation rates (61.2%)<sup>132</sup>. Public monies are wasted and prevention from the disease is not

guaranteed if screening is done incorrectly, such as with insufficient population coverage, the wrong age cohort, or poorly organized programs<sup>133</sup>.

Throughout, the term "law" refers to both the public institutions such as courts, legislatures, and agencies charged with enacting, carrying out, and interpreting the law as well as the legal instruments such as legislation, treaties, and regulations that reflect public policy<sup>134</sup>.

Laws have a significant impact on all social and economic determinants of health by setting the guidelines and frameworks that govern social and economic interactions. Strong health systems, safe and nutritious food, safe and effective pharmaceuticals and vaccinations, safer and healthier workplaces, and better built and natural ecosystems can all be aided by well-designed legislation. Laws that are badly drafted, carried out, or applied, however, can hurt marginalized groups and strengthen stigma and discrimination.

To enhance population health, the government can use a variety of legal and political instruments<sup>135</sup>. Some are in places where public health agencies play a crucial or leading role and where policies are purposefully created to have an impact on health. These serve as the chapter's main topic. Taxation, financial incentives, and spending are examples of legal and public policy tools for the public's health. Other tools include changing the informational environment (such as food or drug labeling and disclosure of health information changing the built or physical environment such as zoning, toxic waste and changing the natural environment such as clean water, for example.

The majority of the aforementioned instruments are initiatives that are particularly intended to better or protect health, and some of them directly involve public health authorities. In some areas, especially the built/physical environment, where zoning and land use have become increasingly

health-focused, the lines between health-oriented and non-health policies are blurred (For the Public's Health: Revitalizing Law and Policy to Meet New Challenges (2011)

In addition to a strong commitment to the rule of law, the Lancet Commission in their article “ The legal determinants of health: harnessing the power of law for global health and sustainable development” articulates the critical role that law plays in achieving global health with justice through the use of legal tools, legal capabilities, and institutional reforms. The Commission's objective is to improve the understanding of law, regulation, and the rule of law as powerful tools for advancing equity and population health within the global health community.

Leaders from throughout the world in the domains of governance, law, and health are represented by this commission. They argued for stronger, more strategic ties between the legal and medical professions and the experts in each. They started by giving a brief overview of legal vocabulary, concepts, and the institutions and people who regulate health. Four legal factors that each have a significant impact on health outcomes make up the framework of their article, because it reveals the ability of law to address the underlying social and economic causes of damage and disease, we refer to these factors as legal determinants of health.

These four legal factors demonstrate how the law has a significant impact on equity and health. Instead of attempting a thorough analysis of law and global health, their goal was to promote and illustrate the law's critical importance to improving global health with justice. Finally, they provided seven specific recommendations for action, focusing on the reform areas that have been identified as well as the principles of good governance and the right to health.

Legal determinant 1 asserts that the law may turn a vision for sustainable development into concrete steps. The UN Sustainable Development Goals (SDGs) offer a vision for global

development and health that is audacious and unifying. To realize this aim, law provides the structures, accountability measures, and methods. In instance, the establishment of Universal Health Coverage (UHC), a vital component of sustainable development, can be accomplished through the employment of law. Through a case study of how law may create and implement UHC, they demonstrated how the power of law can be used to achieve health with justice. They provided two suggestions for practical action.

Legal determinant 2 asserts that the rule of law can improve the management of international and domestic health institutions. The intricate system of organizations, rules, and procedures that oversees global health can be organized and made clearer through the use of law. They highlighted three major governance issues that jeopardize coordinated health activity as well as means through which the legislation can guarantee sound governance. First, law can harmonize mandates and offer means to encourage cooperation where the missions of global health actors clash, overlap, or leave gaps. Second, creative approaches to law and governance can encourage state compliance and reinforce current international norms. Third, the legislation can foster greater openness, accountability, inclusivity, and transparency. They provided two suggestions for taking action.

Legal determinant 3 asserts that legislation is capable of enacting just, scientifically supported health solutions. Evidence-based laws that are properly applied and fairly enforced can foster a healthy environment. They offered a framework for assessing health laws and determining those that promote health while upholding justice. Infectious diseases, non-communicable diseases, and injuries were the three areas of health where they provided specific examples of such regulations. They talked about how domestic and international laws interact and influence one another in each of the respective fields. They also demonstrated how laws that are not based on facts or respect for

human rights can harm justice and health by entrenching inequality and prejudice. They offered just one piece of advice for action.

Building legal capacities for health was emphasized by legal determinant number four. A significant factor in the advancement of global health and sustainable development is having strong legal capabilities. But far too frequently, the fundamental legal framework or the capacity to create it is lacking in the respective nations. The commission argued for beneficial, mutually reinforcing connections between law and health and identified three areas of legal capacity-building for health: enhancing legal environments, expanding the body of evidence with high-quality effectiveness research, and educating key players in the creation and implementation of laws. Two suggestions for taking action were made.

The lancet commission recommended the following on each legal determinant they articulated:

Recommendation 1 urges the UN, WHO, and other international partners to establish benchmarks to promote the implementation of SDG 38 (UHC) and the planned UN political declaration on UHC in 2019, as well as to impartially assess compliance with these goals.

To ensure rights-based UHC based on the principles of equity and non-discrimination, including affordability, financial protection, transparency, accountability, participation, privacy, and sustainable financing, recommendation number two suggests that governments should strengthen or establish a legal framework, such as a constitutional or statutory right to health.

Recommendation 3 urges the UN, WHO, and other international partners to use their respective influence and power to establish or adopt good governance standards that uphold the highest ideals of equity, inclusive participation, transparency, and accountability in order to protect the health and safety of the general public.

A country-appropriate mechanism should be established to provide advice on legal interventions with high health impact, and legislation requiring health impact assessments for policies, programs, and projects that might negatively affect health should be adopted, according to recommendation 4. Recommendation 4 also urges governments to create legal frameworks that establish principles of good governance throughout national health systems and policy making.

According to recommendation number 5, WHO should strengthen its legal capabilities so that it can lead the creation of a worldwide evidence base for public health legislation and promote the adoption and implementation of efficient and long-lasting national and international health laws.

Governments are advised to strengthen national capacities for enacting and successfully implementing public health regulations in Recommendation 6.

In accordance with recommendation number 7, WHO and The Lancet should collaborate with legal and medical experts to establish an independent standing commission on global health and the law. This commission would promote the SDGs related to health by recommending evidence-based legal solutions for pressing global health issues, changes to international law and the global health architecture, and plans to develop and improve national and international health law capacities.

Law is all around us, even though it isn't always obvious. The definition of law that is used most frequently is a body of standards (or rules of conduct) that are stated and upheld by a recognized authority and have binding power and effect. Law establishes rights and obligations, which must be applied equally and uniformly across society. People are affected by the law every day once it is put into place because it molds their lives through the application of the laws and the related regulations. At the domestic level, when the sovereign state—the supreme authority in that

territory—is the recognized authority, this understanding of law is best represented. Nation states are able to make and uphold laws because they have sovereign power. Internationally, there is no sovereign authority, and to abide by the requirements of a legal agreement, states must agree. International accords can be challenging to enforce, even when nations formally agree to them. International legal standards are still crucial for improving health rights, nevertheless.

Health and justice are impacted in both a direct and indirect manner by both domestic and international law. High-impact litigation in one jurisdiction can enable advocates in other jurisdictions to take similar action. Innovations in domestic law and policy can serve as a model for other cities, nations, or regions to follow. International law also affects domestic law and policy by establishing generally regarded norms. International norms influence local and national laws, rules, and policies while domestic legal norms spread upward to other jurisdictions and down to international institutions.

The commission went ahead to differentiate domestic law from international law. Law is used to create standards, procedures, and frameworks. These laws should aim to equally lower or avoid injury and illness risks across communities in the context of health.

Law not only imposes obligations on people and organizations in a society, but it also grants rights. For instance, in many nations, every citizen has a right to equal justice under the law as well as to health care and public health services. The primary responsibility for granting these benefits rests with the state. The following areas of domestic law are all derived from various sources. The supreme law of the land is found in the constitution. Constitutional standards and principles must be followed by laws, regulations, and case law. Statutes, often known as legislation, acts, or laws, are adopted by legislative bodies like the Congress or the Parliament to convey public policy. The public's health and safety are protected through regulations, often known as delegated law, from

executive or administrative agencies (legislative bodies typically empower agencies to act). Case law, developed by courts and other tribunals, establishes judicial precedent by interpreting and applying the constitution, laws, and regulations to particular situations. Beyond specific instances, the impact of case law varies by nation based on its legal and constitutional traditions.

The supreme law of the land is frequently referred to as constitutional law. Varying jurisdictions may give the other three sources of law a different level of priority or relevance. The four sources—each of which has a significant impact on health—as well as their interactions are collectively referred to as "law."

The structure of domestic law differs from that of international law. A body of norms or standards that are generally viewed and accepted as binding in relations between states and other groups, such as international organizations, is the most basic definition of international law. Although it primarily regulates the behavior of nations, private parties like corporations for example, in regard to trade law and individuals can have a significant impact under international law eg, in relation to human rights law. The most authoritative explanation of the sources of international law is found in Article 38 of the Statute of the International Court of Justice, which lists the three main sources as treaties, customary international law, and general principles.

There is no separate international sovereign authority, unlike in domestic law, and no supranational organization governs international relations and transnational collaboration. Instead, a number of international organizations, like the UN, WHO, and the World Trade Organization (WTO), have the authority to pass laws or serve as platforms for member nations to negotiate treaties. States may also conduct their own bilateral, multilateral, or other transnational negotiations.

Trade is one area where different strands of international law are visible. The WTO is in charge of a number of multilateral agreements that its member nations abide by. States are also able to negotiate their own free trade agreements (FTAs), such as bilateral agreements or regional agreements like the United States-Mexico-Canada Agreement, which could establish extra standards beyond those established in WTO treaties. These agreements must adhere to WTO regulations even though they frequently take place outside of the WTO's purview.

International law confronts several governance issues, including ensuring effective implementation and compliance, in the absence of a sovereign authority and a distinct hierarchy of norms and regulations. International human rights, for instance, are a priority for many global health organizations and a significant commitment for nations. States' adherence to human rights has, however, varied greatly overtime, frequently being thwarted by strong political and economic interests.

Modern governance is characterized by an increase in the use of non-binding instruments enacted with a normative goal across all sectors. These tools are designed to encourage, direct, or prohibit certain behaviors. There are several names for soft legal instruments that deal with a wide variety of subjects, but we will refer to them as "soft rules" for the duration of this paper.

Any written international instrument, other than a treaty, that contains non-binding principles, norms, standards, or other assertions of expected behavior is included in the broad category of soft rules.<sup>136</sup>

Soft rules include recommendations, frameworks, and worldwide initiatives as well as codes of practice, declarations, and resolutions. Despite being approved through a formal legal process, UN and WHO resolutions typically do not impose legal duties on member nations. These instruments,

however, can have effects in practice that are comparable to those of binding law even though they are not legally required to do so. They are particularly crucial for benchmarking, monitoring, and transparency.

Compared to formal law, soft norms provide a number of advantages. They can reflect more ambitious goals and are typically quicker and less expensive both economically and politically to negotiate. They can also be less rigid, making amendments easier. When goals are presented as aims or declarations rather than responsibilities, governments are frequently more inclined to sign on.<sup>136</sup>

Additionally, methods to create soft norms might involve a broader coalition of parties beyond nation governments, such as civil society voices that are normally underrepresented in treaty discussions<sup>137</sup>. Hard law and soft law have a flexible connection. Formal international law can be developed on the foundation of informal rules, or foreign governments can include non-binding norms into their legal frameworks. For instance, the Codex Alimentarius Commission's non-binding rules, which are a collection of globally accepted standards, codes of conduct, and guidelines that apply to the entire food supply chain, are incorporated into the WTO's Agreement on Sanitary and Phytosanitary Measures<sup>138</sup>.

Another example of soft norms may be found in the United Nations Political Declaration on the Prevention and Control of Noncommunicable Diseases (September 2011). The Declaration, which was negotiated through the General Assembly, outlines member states' commitments to the prevention and management of non-communicable illnesses.

The ability to incorporate soft regulations into domestic legislation through a nationally recognized mechanism is perhaps most significant for instance through legislative or judicial decrees. The

Joint United Nations Programme on HIV and AIDS (UNAIDS) recommendations on HIV prevention and treatment as well as the WHO recommendations on salt and sugar consumption are only two examples of soft rules that are meant to be implemented at the national level. It is up to each nation to decide which soft regulations to enact domestically.

In almost every legal system, it is the responsibility of the government to protect the public's health<sup>139</sup>.

Domestic and international norms serve as the foundation for this power. The idea of sovereignty gives nation states their power since only sovereign governments may enact laws and regulations affecting the general welfare. This theory acknowledges that some dangers, including as infectious diseases, natural disasters, industrial hazards, tainted food and water, and others, are beyond the control of anyone person or organization. Nobody can guarantee the circumstances for health and safety by acting alone; only the State has the authority needed to act on behalf of the entire populace through coordinated action.

State obligations to protect rights connected to health are found in numerous international instruments, notably the constitution and treaties of the WHO. The fundamental definition of the right to health is found in Article 12 of the International Covenant on Economic, Social, and Cultural Rights (ICESCR), which was established in 1966<sup>140</sup>.

The Committee on Economic, Social, and Cultural Rights' General Comment No. 14 interprets and expands on Article 12 and is a body composed of 18 independent experts who oversee state compliance of the ICESCR by states parties<sup>141</sup>.

General Comments provide nations with direction by outlining treaty duties and how they should be carried out<sup>142</sup>.

The ICESCR and General Comment No. 14 state that everyone has a right to the "maximum attainable quality of health" that is necessary for leading a life of dignity and that this right to health is a "fundamental human right vital for the exercise of other human rights." <sup>143</sup>.

The availability, accessibility, affordability, and acceptability of health facilities must be ensured by the state.

The primary responsibility of the state is to ensure the health and safety of all of its citizens, including citizens and authorized residents as well as asylum seekers, refugees, and undocumented immigrants. States traditionally have no obligations to citizens of other countries. However, international treaties, human rights legislation, and humanitarian law may all suggest or even explicitly impose transnational obligations. For instance, states have a responsibility to uphold basic human rights and refrain from creating, storing, or using prohibited weapons (such chemical weapons). The International Health Regulations (IHR) include non-binding wording urging state parties to support the development of lower-income states' health systems. Soft regulations, like the Pandemic Influenza Preparedness (PIP) Framework, compel parties to exchange fresh flu virus samples and give incentives to neighboring governments in exchange.

States have the authority to impose limitations on private interests when acting to protect the public's health and safety<sup>144</sup>.

Public health initiatives have the potential to restrict economic freedom for enterprises as well as personal autonomy, privacy, or liberty. A recurring subject in public health legislation and ethics is striking a balance between ensuring individual freedoms and maintaining community health<sup>146</sup>.

Unbalanced solutions could lead to disproportionate personal costs, especially for marginalized communities. Individual and group goals frequently do not conflict, though. For instance, ensuring

the rights of people with HIV or AIDS enables them to get the care they need, improving their health and lowering the risk of transmission. Therefore, the purpose of law is to protect public health and safety while limiting personal freedoms only to the extent legally necessary to achieve public health goals.

Limitation and Derogation Principles of the Siracusa Convention the International Covenant on Civil and Political Rights (ICCPR) of 1985 contains provisions that help states strike the delicate balance between preserving liberties and ensuring the wellbeing of the populace

The Siracusa Principles were created in response to worries that governments would unjustifiably or illegally declare martial law or a state of emergency in order to restrict basic freedoms and rights. The principles were developed to specify the circumstances under which such departures from the ICCPR would be acceptable. When restrictions are legal, supported by a valid goal, strictly essential in a democracy, the least intrusive and restrictive method possible, and aren't arbitrarily, unjust, or discriminatory, they maybe justified<sup>147</sup>.

The Siracusa Principles are persuasive but not legally binding, which means that while states should strongly consider them, they are not obligated to abide by them.

Law can be applied to the creation, organization, and management of both public and private entities. In terms of scope and procedure, this role is most similar to the preceding two (creating norms and settling conflicts). In addition to corporations and non-governmental organizations, law also governs the activities of governmental institutions that are involved in establishing standards (such as parliaments, administrative agencies, and courts). The lancet commission provided (United Nations Economic and Social Council<sup>148</sup>.

A quick explanation of how the main actors and organizations in global health are established, organized, and governed by legislation.

By defining institutional mandates, laws can create institutions and limit the scope of their operations. The explicit, implied, and commonplace rights and obligations of an organization are referred to as a mandate. The constitution of a state outlines the duties of the government with regard to preserving public health and defending individual liberties and rights. Constitutions frequently create the three main branches of government, dividing up authority among them (and putting restrictions on it), and defining roles for each. The Ministry of Health is one of the essential institutions established by statutes, which also define its functions and allot funding for its activities. Institutions like the WHO are governed and established by treaties. The WHO constitution is a formal agreement that outlines the organization's goals, the range of its operations, and the duties of its several organs (assembly, executive board, regional and country offices, and secretariat). The mandate of a corporation, or the reason it was created, is stated in its charter or founding documents, such as a memorandum of association. Corporations are created in accordance with provincial or federal legislation that outline their fiduciary obligations, tax reporting and payment obligations, and other tasks. A not-for-profit organization with a global health mission can have its operations, organizational structure, and restrictions defined by statutes and regulations. Non-governmental organizations are required to operate within the bounds of the law. A new degree of complexity has been introduced by the growth of organizations dedicated to global health, including public-private partnerships, organizations with overlapping public, commercial, and non-governmental missions, and so on.

By establishing systems of checks and balances, law also controls institutions and processes. The traditional illustration is the system of checks and balances that helps prevent one arm of

government from overpowering the others—the legislative, executive, and judicial branches. Separate branches are "empowered to prohibit actions by other branches and are induced to share power" according to this theory of government. The law outlines each branch's authority as well as show each branch may restrict the authority of the others. Judges frequently review the conduct of legislatures and agencies, but the legislature has the power to overturn their judgments (other than with constitutional rulings). The rule of law depends on checks and balances.

Although essential, a legal right to healthcare is insufficient. To create, carry out, and judge a UHC framework, governments must adhere to the law. It will be challenging to use alternative legal tools to accomplish not only UHC but also more fundamental governance responsibilities if the rule of law is weak. It will be impossible to secure the funding necessary to guarantee the equity and efficiency of UHC if public authorities or healthcare professionals are corrupt.

Strong responsibilities created by international law reinforce domestic obligations of states to protect the right to health. State parties are required by the ICESCR to "take steps, individually and through international assistance and co-operation, especially economic and technical, to the maximum of its available resources, with a view to achieving progressively the full realization of the rights recognized in the present Covenant by all appropriate means, including in particular the adoption of legislative measures," according to Article 2 of the treaty<sup>149</sup>.

Particularly, states parties "recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health" and "undertake to take steps on concrete health goals, including the prevention, treatment and control of epidemic, endemic, occupational and other diseases," according to Article 12 of the treaty.

As previously mentioned, General Comment 14 (UN General Assembly International covenant on economic, social and cultural right of the UN Committee on Economic, Social and Cultural Rights provided a reliable interpretation of "the right to the greatest achievable quality of health." In addition to the ICESCR, a number of other treaties, such as the UN Convention on the Rights of the Child, the Convention on the Elimination of All Forms of Discrimination Against Women, and the Convention on the Rights of Persons with Disabilities, protect health rights, including the prohibition of discrimination in access. The right to health is a fairly universal standard because, despite the fact that states may be signatories to various treaties, the vast majority of nations are parties to at least one convention that upholds this right.

According to human rights conventions, governments are in charge of securing the right to health. However, under provisions like article 2(1) of the ICESCR, states are also required to offer international support to defend and advance the right to health. There is a "strong literary foundation" for the idea of shared duties for health. Tobin J The right to health in international law Oxford University Press, Oxford 2012

The Maastricht Principles on Extraterritorial Obligations of States in the Area of Economic, Social, and Cultural Rights as well as the guidelines from the Office of the UN High Commissioner for Human Rights (OHCHR) on maternal morbidity and mortality and human rights as well as the guidelines from UNAIDS and the OHCHR on HIV and AIDS and human rights all reaffirm the international duty to support UHC. Furthermore, the obligations of nations under so-called "hard law" and "soft standards" have been clearly stated by the UN Special Rapporteurs on the Right to Health<sup>150</sup>.

Numerous people contend that there is no legal way to address the glaring disparities between nations because states bear the major duty for establishing and maintaining UHC. They disagreed

with this assertion. International health assistance will continue to be a significant source of funding for efforts to minimize health inequities, which is a responsibility of the global community. Although low- and middle-income nations must invest a larger portion of their GDP in their health systems, they may still not be able to pay the anticipated US\$86 per capita (2012) and \$112 per capita (2014) needed to fulfill the SDG for health.<sup>151,152.</sup>

Paul Hunt, the first Special Rapporteur on the Right to Health, noted that "all international help and collaboration is inescapably predicated primarily upon charity if there is no legal requirement backing the human rights responsibilities of international assistance and cooperation." (Hunt P. Report of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health, Paul Hunt, Addendum, Mission to Sweden. Human Rights Council Fourth Session, 2007 despite the fact that such a stance could have been acceptable 100 years ago, it is now unacceptable.

International health assistance has a strong culture of charitable discretion, but sustainable funding necessitates a shared sense of accountability between those contributing and those receiving aid.

Ooms G, Hammonds R, Global constitutionalism, responsibility to protect, and extra-territorial obligations to realize the right to health: time to overcome the double standard (once again). If not, the international system fosters a scenario where states can hold each other accountable for not going far enough<sup>153.</sup> Furthermore, underdeveloped health systems can aggravate vulnerabilities that contribute to extremism and violence in low-income nations or those with unstable regimes.

Both the legal requirement for UHC and the means to realize it are provided. Although the mandate is global (based on the right to health), the methods used to implement UHC vary from nation to nation, depending on the available legal and regulatory frameworks as well as policy

considerations. Access, equity, quality, affordability, and choice are just a few of the key UHC metrics that will be impacted by these systems and decisions. All of these actions are crucial, but they also involve covert or overt political compromises. For instance, providing everyone with equitable access to high-quality services comes at a significant financial expense. Governments' treatment of measures like access, equity, quality, and affordability will change if they place a high priority on consumers' freedom of choice in the market<sup>154</sup>.

Of course, states have some flexibility in their decision-making; at the very least, they are bound by their duty to uphold human rights, including the right to health.

Additionally, improving governance and understanding UHC's practical and documented gaps possible "bottlenecks and weaknesses that prevent health systems from serving the entire population and from providing the full suite of priority services at a cost that is affordable and sustainable" are necessary for increasing coverage<sup>155</sup>.

importantly, UHC must be viewed as effective, accessible, and cheap access to high-quality healthcare (UHC in practice) rather than simply providing everyone with insurance, regardless of whether they can really get high-quality healthcare (UHC on paper). Effective access will depend on both the architecture of health systems (such as increasing primary health services) and the design of health insurance systems, especially for those with the least resources.

The word "universal" in UHC refers to a state's obligation to offer health services to everyone who falls within its purview. So-called universality may be little more than an ideal without proper legal structures to support it, doing little to alter "policies under which many countries either actively or passively refuse to offer access to health care to some people residing within their national borders." <sup>156</sup>.

Asylum seekers, refugees, undocumented immigrants, expatriate workers, indigenous peoples, nomadic people, or groups that have historically been marginalized due to sexual orientation, gender identity, sex characteristics, disability, political beliefs, or religious affiliation are just a few of the vulnerable groups that governments frequently exclude from high-quality services<sup>157</sup>.

These populations should be the focus of a UHC system because they are frequently already vulnerable and least able to pay for out-of-pocket medical expenses. For instance, Rwanda stratifies households based on their means-tested assets and income. The 25% of the population that has been deemed to be the most vulnerable then receives premium payments from the government<sup>158</sup>.

In a nation's UHC program, the law should comprehensively define the term "universal" and provide recourse in the event of discrimination or service rejection. Enshrining the right to health in a nation's constitution or legal framework can help achieve this, creating a framework for resolving disputes and a patient charter of rights to address complaints from individuals who are denied access to health services to which they are entitled, giving a health care ombudsman or commission the authority to look into violations of the State's obligation to provide health services; Decentralizing or delegating the management of health systems will allow people to access local services (including dispute resolution) without traveling; regulating the way public and private health insurance programs handle membership and coverage will prohibit insurers from discriminating against people with pre-existing conditions and require coverage of essential services like vaccinations, primary care, nutrition services, and child care.

The lancet authors did a beautiful job in exposing the impact and effects of lawson health relating it to the sustainable development goals, I must commend their work. It's true that a law remains a law regardless of when it's made till its repealed however the shortcoming of the lancet authors in

their article is the use of very old references, ranging from 1980's to 1990's they could have used more recent reference though like I earlier stated the law in 1996 remains the law in 2022 unless it is repealed in full or part.

### **2.1.3: Prevision of Cervical Cancer**

There are two complementary ways to prevent cervical cancer: primary prevention through vaccination to ward off the human papillomavirus (HPV) infection that causes this disease, and secondary prevention through screening. Cervical precancerous lesions can be identified and treated before they spread. While Papanicolaou cytology-based cervical cancer screening has been the cornerstone of cervical cancer prevention for at least 50 years, the widespread use of HPV vaccinations just began at the end of 2006<sup>159</sup>. Precision cervical cancer prevention and treatment: new ideas and clinical consequences. One of the most successful public health prevention projects worldwide, cytology screenings has considerably decreased cervical cancer incidence and mortality in those countries that have deployed it widely and with ongoing quality assurance as part of structured or opportunistic programs<sup>160</sup>. However, cytology has a number of disadvantages, the most significant of which are a low sensitivity and poor repeatability. The goal of cervical cancer screening has changed from detecting the disease to determining its cause<sup>161</sup>. This has made it possible to identify high-grade dysplastic alterations in the cervix that are associated with the disease more accurately and to prompt timely medical action. This trend has been influenced by knowledge of the biology and natural history of cervical HPV infection and carcinogenesis<sup>162</sup>. Among the many screening methods focusing on HPV detection that have emerged recently are commercial assays that detect women who have cervical infections with atleast one of 12- 14 high-risk HPV (HR-HPV) types, which are linked to the majority of cases of pre-invasive and invasive cervical neoplasia. Given the importance of HPV16 and HPV18 in terms of their etiologic

proportion in cervical cancer, further tests can also detect their presence apart from the other HR-HPVs<sup>163</sup>

Compared to classical cytology, clinically validated methods for identifying the presence of HPV nucleic acids have a number of benefits, the most important of which is the possibility to guide early detection further upstream in cervical carcinogenesis<sup>164</sup>. Other advantages of HPV testing have been noted, including its improved reproducibility and sensitivity compared to cytology, which is dependent on the expertise of cytotechnicians. When compared to cytology, it offers the following benefits: (i) the capacity to easily automate, centralize, and quality-check samples for high specimen throughput; (ii) sufficient safety despite longer screening intervals; and (iii) being more cost-effective than cytology, if employed for high volume testing<sup>165</sup>. Another important advantage of HPV testing is the capability to use self-collected samples, which has the potential to increase cervical cancer screening coverage to remote places or to women who are not immediately accessible by primary healthcare in urban areas. In addition to the advantages listed above that would result from a shift in the screening paradigm from cytology to HPV testing<sup>166</sup>. It is reasonable to anticipate that HPV testing will be able to meet the needs of cervical cancer screening in the post-vaccination period more effectively than cytology.

### **Primary Prevention of Cervical Cancer**

This also entails avoiding HPV infection and spread through the use of safer sex practices. Primary prevention includes strategies that promote behavior change, such as abstention from sexual intercourse, mutual monogamy, and the use of barrier techniques (male or female condoms). However, there is limited evidence that condom use can prevent infection with HPV strains that cause cervical cancer<sup>167</sup> furthermore, because most infected individuals are asymptomatic and sexual behavior is difficult to manage, preventing HPV transmission is a serious public health

concern. Primary prevention is not an effective population-level prevention technique in this regard. Because it is an individual-based strategy, it will only result in a slight reduction in the incidence of cervix cancer. However, such an approach can be integrated into existing STI/HIV prevention behavior-change programs, but it must be used in conjunction with population-based techniques (such as screening). Researchers are now looking into the prospect of vaccines that could be used to prevent HPV infection due to the poor success of behavior change measures<sup>168</sup>.

Researchers have lately had progress with HPV vaccination research. The researchers discovered that giving an HPV vaccine to HPV-negative women lowered the risk of HPV infection and cervical dysplasia.

## **Secondary Prevention of Cervical Cancer**

### **Cytologic screening**

Until now, attempts to prevent cervical cancer have relied on screening sexually active women with regular cytological tests to find precancerous lesions and then treating those lesions. Cytological screening includes the collection of cervical cells, preparation of the slide, staining, reading, and reporting<sup>169</sup>. Thus, a laboratory infrastructure is required, along with skilled cytotechnologists and pathologists for processing slides and reporting, internal and external quality control, and a system for notifying women about the outcomes<sup>170</sup>. High-quality training, ongoing education, and people competency testing are necessary to ensure trustworthy testing. When all of these criteria are met, cytologic testing has been shown to be both highly specific and somewhat sensitive in the diagnosis of CIN 2/3 lesions<sup>171</sup>. However, it has been shown that the testing, with a wide sensitivity range, is useless in identifying cervical neoplasia under the majority of normal situations. Recent investigations have shown that the specificity and sensitivity for detecting CIN

2/3 lesions, respectively, ranged from 60% to 95% and 47% to 62%, respectively. In numerous cross-sectional studies from underdeveloped nations, the sensitivity of cytologic screening ranged from 44% to 78 percent, while the specificity ranged from 91 to 96 percent<sup>172</sup>. In the majority of developing nations, only a small minority of women have access to cytologic screening; they must rely on private-sector providers. For instance, fewer than 1,000,000 cervical smears are performed annually in a large nation like India<sup>173</sup>.

Lack of adequate financial resources, qualified staff, efficient referral mechanisms, adequate laboratory facilities, a properly developed infrastructure for diagnosis and treatment, as well as numerous competing healthcare priorities, have all hindered the organization of successful cytologic screening programs in resource-poor nations<sup>174</sup>. A recent study<sup>175</sup>, comparing visual screening tests to conventional cytologic evaluation was motivated by the need for more accurate cervical screening tests as well as the fact that the majority of precancerous and early cancerous lesions are visible to the naked eye after application of diluted acetic acid and Lugol's solution<sup>176</sup>. Visual inspection after injection of a 3-5 percent acetic acid solution (VIA), also known as direct visual inspection (DVI), the acetic acid test (AAT), or cervicoscopy, is the most frequently researched visual screening technique<sup>177</sup>. The higher intracellular protein concentration found in cervical neoplasia causes a dense acetol whitening effect following acetic acid therapy. One to two minutes after applying diluted acetic acid with a cotton swab or aspray, a VIA is a naked-eye inspection of the uterine cervix using a bright torchlight or halogen focus lamp<sup>178</sup>.

A positive VIA test result is indicated by the presence of clearly defined acetol white patches surrounding the squamocolumnar junction (SCJ), or by the white color of a cervical growth or the entire cervix. The absence of acetol white lesions, faint, poorly defined, translucent acetol white patches, faint acetol whitening of end cervical polyps, acetol white spots, and considerable SCJ

are among the negative findings. Acetol whitening can also occur in immature squamous metaplasia, inflammatory, or regenerative cervical epithelium, in addition to cervical neoplasia.

Acetol white areas associated with CIN are localized in the transformation zone and are often well-defined and dull white. Early malignant growths become extremely opaque in these areas<sup>179</sup>.

### **The Normal Cervix's Anatomy and Physiology**

The original tall (columnar) cells that border the vagina and cervix are gradually replaced by flat (Squamous) cells throughout the first 18-20 weeks of embryonic life. The squamous cells meet the remaining columnar cells at the squamocolumnar junction (SCJ), a narrow line well out on the face of the cervix, throughout early childhood and until puberty. The columnar cells inside the SCJ are gradually replaced by newly growing squamous cells beginning with the onset of puberty, which is marked by increased levels of female hormones (estrogen and progesterone) and lasting for the majority of the reproductive years<sup>180</sup>. The transformation zone (T-Zone), the area of the cervix between the original SCJ (before puberty) and the new SCJ, is where squamous metaplasia occurs. Several factors, including age, parity, prior infections, and female hormone exposure, can cause the T-zone to be either a wide or small area on the surface of the cervix. This section of the cervix is usually often affected by abnormal cervix changes such as dysplasia (CIN) and cancer. As a result, screening procedures like VIA cervicography and colposcopy are aimed at checking the T-zone, particularly the SCJ.

#### **2.1.4 Management and Treatment of Cervical Cancer**

Depending on the cancer's stage and genomic profile, a particular course of treatment for cervical cancer may involve surgery, radiation, chemotherapy, or specially formulated drugs for the disease. The cornerstone of early-stage illness treatment is surgery.

##### **Surgery**

Surgery to remove the uterus is frequently used to treat early-stage cervical cancer (hysterectomy). Early-stage cervical cancer can be treated with hysterectomy, which also stops recurrence. However, losing the uterus renders pregnancy impossible<sup>181</sup>.

Surgery is frequently used to treat precancerous cervical conditions. Depending on the patient's overall health, the presence of abnormal cells under a microscope, and whether or not the patient plans to have children in the future, the type of surgery needed to eliminate the precancerous condition will vary. Several surgical procedures can be used to successfully treat precancerous cervical disease. The majority of operations leave the uterus in place and can, if the patient so wishes, allow for future childbearing<sup>182</sup>. The uterus can be preserved through surgery using cryosurgery (freezing), laser surgery, the loop electrosurgical excision process (LEEP), and cold-knife conization. Cryosurgery, laser surgery, and LEEP can all be performed in a doctor's office or an outpatient short treatment center, typically with local anesthesia<sup>183</sup>. During a more complicated technique known as a cold-knife conization, a piece of the cervix is removed while the patient is asleep<sup>184</sup>. Not every patient responds well to LEEP, laser surgery, or cryosurgery. This decision is based on the disease's severity and external symptoms as determined by inspection. Women who undergo one of these surgical treatments run the risk of developing an infection, bleeding, or watery discharge as adverse effects. Additionally, they might have cramps or pelvic

pain. Watery discharge may persist for several weeks after cryosurgery. A woman may later in her pregnancy encounter issues with cervical function following a cold-knife conization. Even after receiving surgical therapy for a precancerous cervical disease, some people may still acquire invasive malignancy. For stage 0 cervical cancer, 85–90% of women who undergo cryosurgery, laser surgery, or LEEP are cured. Following treatment with these techniques, 2% of patients will develop aggressive carcinoma, and 10-15% of patients may experience a recurrence of precancerous cervical disease<sup>185</sup>. Women who have conservative surgery must continue to see their doctors in order to make sure that recurrence of cervical illness can be identified in the precancerous phase or early while the malignancy is still treatable.

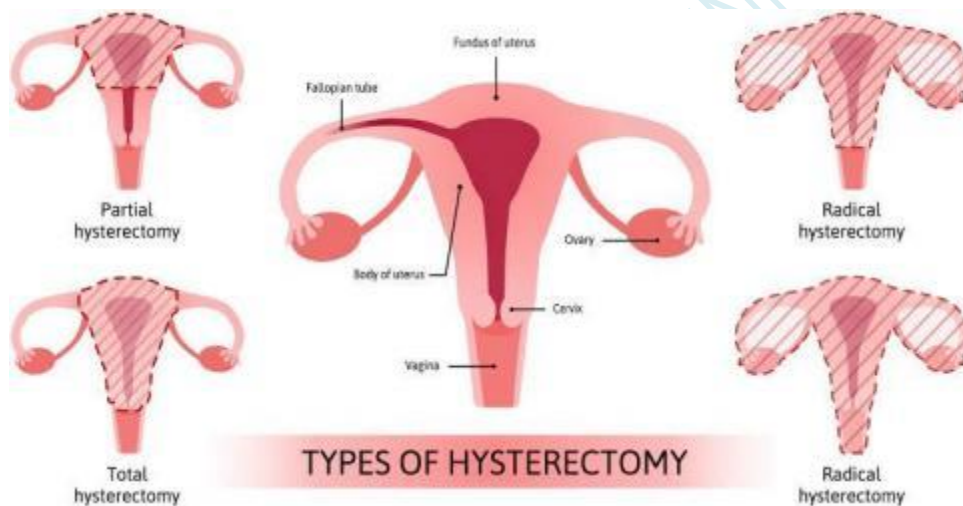


Figure 2.4: Types of Hysterectomy.

Source: National Women’s Health Network: Types of Hysterectomy

1. Simple hysterectomy: The malignancy is removed along with the cervix and uterus. Very early-stage cervical cancer typically has the option of a straightforward hysterectomy. Stage I cancer and precancerous cervix condition are frequently treated by hysterectomy<sup>186</sup>. The type of

hysterectomy performed to eliminate cervical cancer is determined by the cancer's stage. If the precancerous condition is more advanced and the patient doesn't want anymore children, a routine hysterectomy can be done<sup>187</sup>. Through a minor abdominal incision or the vagina, the entire uterus is removed along with the precancerous cervix and a surrounding patch of good tissue in an uncomplicated hysterectomy<sup>188</sup>. A simple hysterectomy is a very effective treatment if the cancer has not progressed past the cervix's surface cell layer. Medical practitioners can also do a bilateral salpingo-oophorectomy, which involves removing the ovaries and fallopian tubes<sup>189</sup>. The need for a bilateral salpingo-oophorectomy depends on the patient's age and whether or not her ovaries are still functioning<sup>190</sup>. Simple hysterectomy and/or bilateral salpingo-oophorectomy are the most complicated surgical procedures for precancerous illness, requiring general anesthesia and a hospital stay in each case. Some women may experience lower abdominal pain and urinary issues after having a hysterectomy. Hysterectomy patients cease their menstrual periods and are unable to get pregnant<sup>191</sup>.

2. Radical hysterectomy: The cancer is removed together with the cervix, uterus, portion of the vagina, and nearby lymph nodes. A radical hysterectomy is a more involved procedure that entails removing the entire uterus, along with the cervix, the cancerous tissue, and a portion of healthy tissue, through a small abdominal incision<sup>192</sup>.

This region of normal tissue, which includes the upper vagina, may cause vaginal shortening after surgery but infrequently causes sexual problems<sup>193</sup>. The ovaries and fallopian tubes are removed during a bilateral salpingo-oophorectomy, which is identical to a conventional hysterectomy<sup>194</sup>. The need for a bilateral salpingo-oophorectomy depends on the patient's age and whether or not her ovaries are still functioning.

A woman may experience lower abdomen incisional discomfort, bleeding, or infection following a radical hysterectomy. Additionally, some women may experience bladder control problems or difficulty urinating. Less commonly, some women could sustain rectum, ureters, or bladder injury. One type of harm could be a "fistula" or an inappropriate attachment to the vagina. Hysterectomy patients stop having their periods and are unable to get pregnant. After undergoing a radical hysterectomy and pelvic lymph node dissection alone or, more frequently, when combined with radiation therapy, women are more prone to develop lymphedema, a chronic swelling of the legs. Less than 1% of people die in the hospital following a radical hysterectomy<sup>195</sup>. A radical hysterectomy is most likely to be effective if the cancer has not spread past the cervix as determined by the surgical examination. Some people will have cancer that has spread to their pelvic lymph nodes from their cervix<sup>196</sup>.

Sometimes the doctor will perform a pelvic lymph node dissection before a hysterectomy<sup>197</sup>, which is a surgical operation to remove lymph nodes to check if they are cancerous. In most cases, the doctor won't do a radical hysterectomy if the lymph nodes are cancerous. A different kind of treatment, typically chemotherapy and radiation therapy, is generally suggested.

Even after having their cervical cancer surgically removed, some women may still contract the disease<sup>198</sup>. Cancer recurrence is more likely to occur in stage IB or stage II cervical cancers that are bulky<sup>199</sup>. It is important to realize that some cervical cancer patients have very small amounts of the illness that have spread outside the cervix and were left behind after surgery. These cancer cells cannot be found using any of the current assays<sup>200</sup>. Cancerous growths outside the cervix known as micro metastases are imperceptible. The presence of these tiny metastases causes recurrence following the initial therapy. In order to increase the likelihood that surgical excision

of the malignancy will be successful, chemotherapy and external beam radiation therapy, either with or without implant radiation, are usually recommended<sup>201</sup>.

### **Robotically- Assisted Hysterectomy Appears Effective for Cervical Cancer**

Robotically assisted hysterectomy (RAH) is at least as successful as and less problematic than open radical hysterectomy (ORH) in patients with early-stage cervical cancer. The robotically assisted radical hysterectomy (RAH) is carried out by a surgeon who is seated a distance away and watching a magnified 3D image of the surgical site<sup>202</sup>. From here, the surgeon can manipulate four little robotic arms within the patient. Because they perfectly mimic the minute movements of a surgeon's hands and wrists in realtime, these arms make it possible to perform intricate and precise treatments<sup>203</sup>, the technique uses specialized hardware and software components and even filters out natural hand tremors to increase accuracy<sup>204</sup>. Last but not least, a traditional hysterectomy requires a large incision<sup>205</sup>, whereas the robotic arms only make incisions the size of a dime<sup>206</sup>. Researchers from the University of North Carolina recently compared the outcomes of 49 patients who underwent a standard open radical hysterectomy with 51 individuals who underwent RAH (ORH). They found that patients who underwent RAH lost less blood and were hospitalized for shorter periods of time than those who underwent ORH. All RAH patients were discharged from the hospital the day after surgery, as opposed to the ORH group, which had an average hospital stay of roughly three days. Additionally, the ORH group experienced postoperative complications at a rate of about 16% vs the RAH group's approximate 8% rate<sup>207</sup>.

### **Complications of Surgery**

Bladder dysfunction — due to injured bladder nerve supply

Neuropathies — due to nerve injuries

Lymphocyst formation — Tissue fluid, Lymph and blood are collected to form the cyst following

Vesico Vaginal fistula

Urethric fistula

Rectal dysfunction

## **Radiation**

In radiation therapy, powerful energy beams like X-rays or protons are utilized to destroy cancer cells. To shrink a tumor before surgery or eliminate any cancer cells that could still be present after surgery, radiation therapy can be used alone or in combination with chemotherapy<sup>208</sup>. Radiation therapy, or radiotherapy, is a common treatment for cervical cancer. Medical doctors that specialize in using radiation to treat cancer are known as radiation oncologists. In radiation therapy, high-energy x-rays are used to kill cancer cells. External radiation therapy can be administered by firing x-rays at the body with a machine, or internal radiation therapy can be administered by inserting radioactive capsules into the cervix (internal or implant radiation or brachytherapy). Patients typically receive both radiation treatments. In stage I cervical cancer, radiation therapy maybe used in place of surgery or it maybe utilized following surgery to get rid of any cancer cells that persisted. Treatment options for cervical cancer in stages IB to IVA include chemotherapy and radiation therapy<sup>209</sup>.

## Methods

1. External beam radiation therapy
2. Implant Radiation Therapy/ Brachytherapy

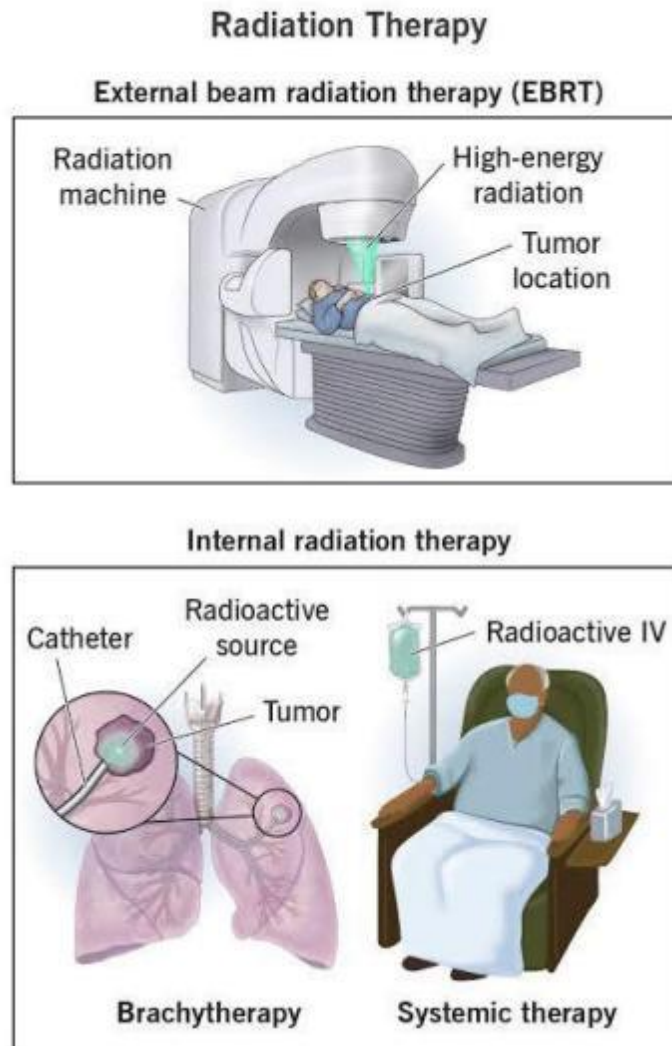


Figure 2.5: Radiation Therapy.

Source: Clevelandclinic

Primary Radiotherapy: This entails employing ionizing radiation and radium to treat cancer in an internal organ.

**External Beam Radiation Therapy:** Cervical cancer is treated for a few weeks using outpatient external beam radiation therapy (EBRT). Five days a week, it is presented. EBRT begins with a planning session, or simulation, during which marks are created on the body and measurements are taken in order to accurately align the radiation beam for each treatment.<sup>210</sup> After that, the patient is positioned on a couch to undergo daily radiation treatments to the pelvis. Cervical cancer patients receive outpatient external beam radiation therapy for 4 to 6 weeks<sup>211</sup>. External beam radiation therapy and implant radiation are coupled to deliver a larger dose of radiation to the cancer. More information on implant or internal radiation is provided in the section below<sup>212</sup>. When these two strategies are combined, after 4-6 weeks of external beam radiation therapy, the final "boost" of radiation to the cervix is administered using implant radiation<sup>213</sup>, although patients are unconscious during radiation therapy, the effects of radiation build up over time. As their treatments progress, many patients grow weary. Patients frequently have diarrhea or loose stools as well. Urination could become unpleasant or more frequent. Some people may report skin irritation or pubic hair loss. The vagina may become more rigid and restricted when the radiation therapy is finished. Sexual interactions may become uncomfortable as a result, and future pelvic exams may become challenging. To keep the vagina flexible, patients are frequently instructed on how to use a dilator. The ovaries may stop functioning as a result of pelvic radiation therapy, causing younger women to experience menopause earlier than usual<sup>214</sup>.

### **Implant Radiation Therapy/ Brachytherapy**

Implant radiation, sometimes referred to as brachytherapy, and involves injecting radioactive substance directly into the cervix. This method of radiation delivery gives the malignancy a high radiation dose while minimizing exposure to surrounding healthy organs like the rectum and bladder<sup>215</sup>. During a procedure in the operating room, a small device is put into the vagina and

cervix. Later, this apparatus is "loaded" with the radiation capsules while the patient is in a lead-shielded hospital room. The radioactive material is left in place for one to three days. Once the device is removed from the cervix, the patient is discharged from the hospital. This procedure may be used once or twice throughout the course of treatment<sup>216</sup>. Many hospitals are using "high-dose rate (HDR) brachytherapy," a somewhat different technique, to administer the implant radiation on an outpatient basis<sup>217</sup>. The patient only needs to be subjected to radiation for 30 to 60 minutes during this procedure, in which the radiation therapy department inserts a device into the cervix and vagina<sup>218</sup>. This procedure is frequently carried out three to five times each week while receiving treatment. HDR brachytherapy is a more recent technique, hence it is not yet widely available. According to preliminary data, HDR brachytherapy appears to be just as effective as traditional implant radiation while necessitating no hospitalization<sup>219</sup>. Implants placed interstitially (into the tissue) are a less common type of brachytherapy. This method involves general anesthesia being administered to the patient while tiny, tube-shaped needles are inserted into the tumor and surrounding tissue to try to match the shape of the cancer<sup>220</sup>. After the radioactive seeds are later "loaded" into the tube-shaped needles, the remaining procedures are similar to those for implants. For implant radiation therapy to be effective and secure, the device's positioning is essential<sup>221</sup>. Even though cervical cancer receives the highest radiation dose, other adjacent organs like the rectum and bladder are also exposed to radiation. It is possible for radiation to harm the rectum, bladder, or intestine, which can cause discomfort or bleeding when urinating or passing stools. Some people have a lower incidence of a fistula, or an inappropriate connection between the rectum or bladder and the vagina. It may occasionally be necessary to do further surgery for the treatment of fistulas or other radiation injuries<sup>222</sup>. Medical doctors that specialize in using radiation

to treat cancer are known as radiation oncologists. In radiation therapy, high-energy x-rays are used to kill cancer cells.

Both internal or implant radiation and brachytherapy, which involves injecting tiny radioactive capsules into the cervix, are routinely used to treat patients. External beam radiation is provided by a machine that shoots x-rays onto the body. For stage I cervical cancer, radiation therapy may be used instead of surgery, or it may be performed after surgery to get rid of any cancer cells that remained<sup>223</sup>. For cervical cancer patients in stages IB to IVA, chemotherapy and radiation therapy are frequently administered concurrently. Although patients are unconscious during radiation therapy, the effects of radiation build up over time. Many patients become fatigued as their treatments advance. In addition, diarrhea and loose stools are common. Urination can get worse or happen more frequently. Some persons may complain about pubic hair loss or skin irritation. When the radiation therapy is over, the vagina may become more brittle and constrictive. The ovaries may stop functioning as a result of pelvic radiation therapy, which can also cause younger women to go through menopause earlier than usual and lose their fertility.

As a conclusion, patients should investigate their alternatives, get a second opinion, and understand their roles and those of the medical team before beginning any cancer treatment.

It's crucial to consult a doctor before beginning treatment so that you are aware of the precise sort of radiation you will get as well as any potential adverse effects. This is because radiation side effects can sometimes be very severe.

### **Advantages of Primary Radiotherapy**

- a) Applicability in all phases of cervix Cacinoma
- b) Survival rate 85%, comparable with that of surgery in early stages

- c) Less primary mortality and morbidity
- d) Individualization of dose distributions/ requirements possible.

### **Complications of Radiation**

Radiation complications are mainly due to interaction with the normal tissues:

- . Vesicovaginal or Rectovaginal fistula
- . Menopausal symptom
- . Malabsorption syndrome
- . Radiation fibrosis

Surgery and radiation therapy are the most prevalent treatments for invasive cervical cancer. Chemotherapy and biological therapy are two more options. If the cancer is limited on the surface of your cervix, your doctor can use treatments like LEEP or cold knife conization to remove or eliminate the malignant cells. If malignant cells have slipped through the basement membrane, which divides the cervix's surface from the underlying layers, surgery will almost certainly be required. If the disease has advanced to deeper layers of the cervix but not to other regions of the body, a procedure to remove the tumor maybe necessary .If the cancer has gone to the uterus, the doctor would most likely recommend a hysterectomy. (I.e. the uterus is completely removed)

High-energy rays are used in radiation therapy (or radiotherapy) to harm cancer cells and inhibit their growth. Radiation, like surgery, only affects cancer cells in the treated area. An external source of radiation is a huge equipment that directs a beam of radiation at your pelvic. Such people will most likely receive treatments that last only a few minutes five days a week for five to six weeks. Finally, a "boost" dose of radiation maybe administered. Internal radiation (also known as

implant radiation or brachytherapy) is delivered through a capsule containing radioactive material that is inserted into the cervix by a physician. The implant directs cancer-killing rays toward the tumor while protecting the surrounding healthy tissue.

### **Precision Cancer Medicines**

Instead than categorizing or classifying malignancies purely according to their place of origin, precision cancer medicine aims to identify the genetic changes in the disease's DNA that are responsible for that particular malignancy<sup>224</sup>. To find mutations in a cancer's genome that are responsible for the cancer, precision cancer medicine uses molecular diagnostic tests, including DNA sequencing<sup>225</sup>. A unique targeted therapy can be created to target a particular mutation or other cancer-related change in the DNA programming of the cancer cells once a genetic defect has been detected<sup>226</sup>. Precision cancer medicine employs targeted medications and immunotherapies that are designed to attack the cancer cells directly while mostly sparing healthy cells. As precision medicines are being developed for the treatment of advanced stages of cervical cancer, patients should ask their doctor if testing is necessary<sup>227</sup>.

### **Chemotherapy**

Chemotherapy is a treatment that uses strong chemicals to kill cancer cells. It's commonly used by doctors to treat cervical cancer that's advanced locally or has spread to other places of the body. Chemotherapy is delivered in cycles of severe treatment and recovery<sup>228</sup>. The majority of patients receive it as an outpatient (at a hospital's outpatient clinic, a doctor's office, or at home). Biological therapy or immunotherapy works by turning on or off "checkpoints" in your immune cells that trigger an immunological response. Pembrolizumab (Keytruda) is a drug that inhibits a protein on

the surface of cells, causing tumors to shrink or develop more slowly. If chemo isn't working or the cancer has spread, doctors will use it. Every three weeks, it will be administered through a vein (intravenous, or IV) <sup>229</sup>.

### **Cervical Biopsy**

If a pelvic examination or Pap smear test suggests that cervical cancer may be present, the patient may need to have a biopsy. A biopsy is the only reliable method for figuring out if a patient has cancer. Using a tool, small pieces of cervical tissue are removed during a biopsy. The samples of cervical tissue are then examined under a microscope to look for cancerous cells. Sometimes, a cervical biopsy can be performed in the operating room while the patient is sleeping and is undergoing a more complete evaluation. In both cases, a colposcope, a specialized microscope used in medical offices, is used<sup>147</sup>.

### **Retroperitoneal Lymph Node Dissection and Scalene Lymph Node Biopsy**

Patients who have cervical cancer in an advanced stage or who are not candidates for surgery to remove the malignancy may receive radiation therapy, which is often administered in conjunction with chemotherapy. Before beginning radiation therapy, it's important to determine whether there are any microscopic malignant deposits in the lymph nodes in the pelvis and abdomen. This is determined by a surgery called a retroperitoneal lymph node dissection. During this surgery, a little incision is made in the middle of the belly, and the surgeon removes the lymph nodes that are situated underneath the abdominal contents. Most patients can leave the hospital and begin their radiation therapy treatment after a day or two. If the sampled lymph nodes have cancer, the radiation oncologist may modify the treatment to include these microscopic disease regions. In some women, cervical cancer is already advanced when it is first found. Identifying if the disease

has spread from the pelvis to other parts of the body in these patients is crucial. One method entails performing a little operation to divide the lymph nodes at the base of the left neck. The technique, known as a scalene lymph node biopsy, can be carried out without an inpatient setting. Depending on the results of this biopsy, more therapy might be required.

### **Combination Therapy**

Combination therapy: surgery, radiation, and chemotherapy may be administered one after the other.

Palliative care: Palliative care aims to provide comprehensive care for the relief of symptoms as well as the treatment of cancer in its advanced stages. Foul smell: Antimicrobial vaginal creams or suppositories are used to treat a purulent or unpleasant vaginal discharge. Bleeding-Symptoms of discomfort or bleeding may be relieved with palliative radiation therapy (180-200eGy/day) or chemotherapy. A tight vaginal pack soaked in Monsel's solution and placed on the cervix may temporarily stop bleeding.

Pain: Pain can be reduced or increased by lowering the pain stimuli or raising the pain threshold. Prostaglandin production is the primary cause of pain from bone metastases. Non-steroidal anti-inflammatory medicines (NSAIDs) are the most effective treatment (NSAIDS).

Palliative radiation with 2000c.Gy spread out over five treatments could be an option. Antidepressant medicines or anxiolytics (benzodiazepines) may help to enhance the pain threshold. To lower pain perception, opioids (oral morphine (3- 10 mg) mixed with paracetamol or aspirin, taken at a regular interval (4-5hrs) are extensively utilized.

Neuropathic pain is a challenging condition to deal with. In rare circumstances, regional block with local anesthetic procedures has been considered. Lower pelvic and perineal discomfort can

benefit from epidural block. Intrathecal (Spinal, Epidural) Opioids can be used to treat pain in any part of the body.

## **2.2 Theoretical Review**

There is a ton of material on cervical cancer, but the West African region suffers from a total of 31,955 new instances of the disease annually, with crude incidence and age-standardized rates of 16.8 and 29.6. (Cases of cancer per 100,000 women per year) <sup>230</sup>. The World Health Organization (WHO) revised its 2006 cervical cancer prevention and control recommendation and released it in 2014. This was to be accomplished through community mobilization, information and counseling, immunization of girls between the ages of 9 and 13 against the Human Papilloma Virus (HPV), the main known cause of cervical cancer, screening and treatment of cervical pre-cancer, diagnosis and treatment of invasive cervical cancer, and giving palliative care to cervical cancer patients <sup>231</sup>.

All member countries, especially those with little resources, are urged to adhere to this recommendation to ensure that the incidence of cervical cancer is significantly decreased. The Sustainable Development Goals 3 of the United Nations, which promotes healthy living and welfare for people of all ages, will be met if this recommendation is strictly followed<sup>232</sup>. The high prevalence of cervical cancer in SSA countries has been linked to a number of factors, including inadequate cervical cancer screening, a lack of awareness and knowledge of the disease, biological factors like malnutrition, HIV/AIDS, tuberculosis (TB), and malaria infections, socioeconomic and socio-cultural factors, as well as political inequities <sup>233</sup>.

## 2.3 Review of Empirical Studies

Previous research studies on cervical cancer, its prevention and management were carried out on the following subhead.

- a) Cervical Cancer Concept
- b) Cervical Cancer Risk Factors
- c) Cervical Cancer's Spreading Mode
- d) Cervical Cancer types and Staging
- e) Cervical Cancer Detection and Diagnosis

### **a) Cervical Cancer Concept**

When cells in a woman's cervix, which connects the uterus to the vaginal canal, change, cervical cancer occurs. The deeper tissues of their cervix can become damaged by this malignancy, which can also spread to other regions of the body, most frequently the lungs, liver, bladder, vagina, and rectum<sup>234</sup>. Human papillomavirus (HPV) infection is the most frequent cause of cervical cancer and is preventable with a vaccine<sup>235</sup>. Because cervical cancer spreads slowly, it can frequently be found and treated before it becomes a serious issue. Less and less women are dying from it every year because of improved screening through Pap smear exams. The greatest risk is among women between the ages of 35 and 44. However, more than 15% of new occurrences involve women over 65, especially those who have not undergone routine screenings<sup>236</sup>. The second most common malignant tumor in women globally is cervical cancer, which is extremely dangerous for women's health. The high-risk human papillomavirus is regarded to be the primary contributor to the

development of cervical cancer (HPV). The creation and execution of a thorough cervical cancer prevention and control strategy have been accelerated by the identification of a clear etiology. In May 2018, the World Health Organization (WHO) issued a global call for the eradication of cervical cancer, to which more than 70 nations and international academic groups swiftly expressed support<sup>237</sup>. The World Health Organization (WHO) then unveiled a global strategy to speed up the elimination of cervical cancer as a public health issue on November 17, 2020. This paved the way for cervical cancer prevention and control in the future, with 194 countries pledging to eradicate cervical cancer for the first time. In order to pave the way for the eradication of cervical cancer, they looked at the most recent developments in epidemiology, risk factors, and screening with regard to cervical cancer prevention and control. Theoretically preventable cervical cancer is the second most common cancer in women worldwide, the fourth most common tumor in women, and the most common malignancy of the female genital tract in low-income countries<sup>238</sup>. Cervical cancer, which may be curable, is the second most common cancer in women worldwide and the most prevalent malignancy of the female genital tract in low-income nations, according to Ferlay J. and Colombet M. Around the world, cervical cancer accounts for 500,000 new diagnoses each year and 273,000 fatalities; 80% of the new cases are found in low-income nations. In low-income nations like Nigeria, where the bulk of cases present in the late stages of the disease, about 85% of the 250,000 fatalities from cervical cancer annually are recorded. Cervical cancer has an incidence rate of 250 per 100,000 women in Nigeria. In Nigeria, roughly 10,000 women are diagnosed with cervical cancer every year, and 8,000 women pass away from it<sup>239</sup>.

4,100 women are expected to die from cervical cancer in the United States in 2016, which will affect 12,900 women.

Here in the United States<sup>240</sup> the disparity in cervical cancer incidence between these categories in low- and high-income countries, however, is mostly attributed to the lack of awareness and access to good cytological screening programs in low-income countries<sup>241</sup>. Another factor for this dual burden of illness is the attention given to diseases with conflicting health priorities, such as HIV/AIDS, TB, and malaria. Without a doubt, more than 85% of cervical cancer fatalities worldwide occur in low-income countries<sup>242</sup>. Programs for cervical cancer screening offer a comprehensive number of benefits. It is believed that the likelihood of successful therapy is significantly increased by widespread screening of women for precursor lesions and early detection of invasive illness. These discoveries have led to a 40% reduction in invasive cancer incidence and mortality<sup>243</sup>. The Papanicolaou (Pap) test, also referred to as cervical cytology screening, is a trusted, reasonably priced, and well-known early detection test for cervical cancer. Alternative screening techniques, particularly in locations with limited resources, include cervicography, visual inspection with acetic acid (VIA), and visual inspection with Lugol's iodine (VILI). Human Papillomavirus, a sexually transmitted infection, is the main cause of cervical cancer (HPV)<sup>244</sup>.

The women who are most likely to contract it are those who have had numerous sexual partners, as well as those whose partners have done the same or have previously been exposed to the virus. Early identification and treatment of precancerous diseases is the greatest method of cancer prevention. Early identification and treatment of precancerous diseases is the greatest method of cancer prevention<sup>245</sup>. In low-income countries with well-established screening programs, the incidence of cervical cancer has decreased by 70-90%<sup>246</sup>. The most common gynecologic cancer in Nigeria is cervical cancer. Cervical cancer is the second most common cause of cancer-related morbidity and mortality in Nigeria, despite being largely preventable through screening. Sporadic

screening is carried out using an opportunist approach for persons who frequent particular clinics. Furthermore, there are no standard guidelines or policies for cervical cancer screening in Nigeria. Cervical cancer screening options include the Papanicolaou (Pap) smear, visual examination of the cervix with acetic acid (VIA), HPV DNA test, and colposcopy. Colposcopy is carried out alongside other tests; it is not used as the primary screening procedure<sup>247</sup>. The high burden of cervical cancer is a result of both the high incidence of HPV infection and the dearth of efficient cervical cancer screening programs in low-income nations like Nigeria. The public's lack of awareness and unfavorable health-seeking behavior have led to low utilization of these services when effective screening programs are provided. A key technique for lowering the incidence and mortality of cervical cancer is to increase the screening rate among women who have not tested or who screen seldom<sup>248</sup>. Changes (mutations) in the DNA of healthy cervix cells are what lead to cervical cancer. A cell's DNA contains the instructions that specify what it should perform. Healthy cells grow and reproduce at a set rate before dying after a set amount of time. The cells do not die as a result of the mutations, which cause them to multiply and replicate in an unchecked manner. The accumulating abnormal cells take the form of a mass (tumor). Although the precise etiology of cervical cancer is uncertain, HPV is believed to play a role. Cancer cells can spread by infecting nearby tissues and rupturing away from a tumor that spreads to other areas of the body. Although HPV is fairly common, the majority of those who contract it never experience any symptoms. This indicates that other elements, like your environment and lifestyle decisions, may affect whether you develop cervical cancer.

The cervix, which joins the uterus to the vaginal canal, is a type of cancer that originates in the cells of the cervix. A sexually transmitted infection called the human papillomavirus (HPV) is the main cause of cervical cancer. When HPV enters the body, the immune system typically prevents

the virus from doing any damage. However, the virus can survive for years in a small percentage of people, which may help some cervical cells develop into cancer cells.

When cells in a woman's cervix, which connects her uterus to her vagina, change, cervical cancer develops. The deeper tissues of their cervix maybe affected by this cancer, which has the potential to spread to other parts of the body, most frequently the lungs, liver, bladder, vagina, and rectum. Human papillomavirus (HPV) infection is the most frequent cause of cervical cancer and is preventable with a vaccine. Because cervical cancer spreads slowly, it can frequently be found and treated before it becomes a serious issue.

#### **b) Cervical Cancer Risk Factors**

Numerous cervical cancer risk factors are linked to HPV infection. Up to 20 years may pass from the time that a sexually transmitted HPV lesion causes a precursor lesion before an invasive malignancy develops. There are, however, a variety of other risk factors for cervical malignancies, including as having sex when you're young (under 16), having multiple sexual partners, and smoking, having a high parity, and having a low socioeconomic position<sup>249</sup>.

#### **c) Infections That Are Spread By Sexual Contact (STI) HPV**

Sexual intercourse is regarded as the primary route of human papillomavirus (HPV) transmission. Infection with a high-risk or oncogenic HPV type is the leading cause of pre-cancerous and malignant cervical lesions. The majority of occurrences of cervical cancer are caused by HPV16 and 18. Human populations have been discovered to have a significant prevalence of high-risk kinds, particularly HPV16. The infection is spread by sexual contact and results in squamous intraepithelial lesions. Due to immunological intervention, the majority of lesions disappear after 6-12 months. A small fraction of these lesions, however, persist and can lead to cancer<sup>250</sup>

#### **d) Human Immunodeficiency Virus (HIV)**

Human papillomavirus (HPV)-induced carcinogenesis is accelerated by HIV. Cervical cancer burden at the population level has not been quantified in relation to HIV, nevertheless. We wanted to look into the cervical cancer risk among HIV-positive women and estimate the prevalence of cervical cancer worldwide due to HIV<sup>251</sup>. Women with HIV are considerably more likely to get cervical cancer. In southern and eastern Africa, where a sizable HIV-related cervical cancer burden has added to the existing cervical cancer burden, HPV vaccination and cervical cancer screening for HIV-positive women are especially crucial <sup>252</sup>.

24 studies that comprised 236 127 women living with HIV met the inclusion criteria in the findings of Dominik Stelzle. Women with HIV had a higher overall risk of developing cervical cancer (RR 6.07, 95% CI 4.40-8.37). In 2018, 33 000 new instances of cervical cancer (95% CI 26 000-42 000) were detected in women living with HIV globally. Of these cases, 58% (95% CI 4.6-7.3) were related to HIV infection (28 000 new cases, 20 000-36 000). Eastern and southern Africa were the area's most severely impacted. 63.8% (95% CI 58.9-68.1) of cervical cancer patients in southern Africa (9200 new cases, 9500-9800) and 27.4% (23.7-31.7) of those in eastern Africa were HIV-positive (14 000 new cases, 12 000-17 000). In six countries, all in southern and eastern Africa, there were more than 20 ASIRs of cervical cancer linked to HIV per 100,000 people.

The likelihood of contracting high-risk HPV strains is higher in females with HIV. Studies on the relationship between HIV and cervical cancer have found that those with HIV have higher rates of persistent HPV infection with a number of oncogene viruses, more abnormal Papanicolau (Pap) smears, and a higher risk of CIN and invasive cervix carcinoma. HIV-positive women have an increased chance of developing cervical cancer and HPV at a young age (13–18 years). Compared

to non-infected women, HIV positive women with cervical cancer are detected when they are younger (15-49 years old) <sup>253</sup>.

### **Sexual Partners**

Additionally, traits connected to sexual conduct have been linked to cervical cancer. One study found that people who have multiple sexual partners are more likely to develop cervical cancer. Additionally, numerous studies have shown that women who engage in multiple sexual relationships are more likely to catch HPV and develop cervical cancer. The meta-analysis found that both non-malignant cervical illness and cervical cancer risk is significantly higher in those who have multiple sexual partners than in those who have few partners. The connection persisted even after taking into account HPV infection, which is a major factor in cervical cancer. The age of the first sexual encounter is another risk factor for cervical cancer. <sup>254</sup>

### **Oral Contraceptive Pills**

Oral contraceptive tablets have been linked to a higher risk of cervical cancer. The relative risk of cervical cancer in current users increased as the length of oral contraceptive use increased in an international collaborative epidemiological study of cervical cancer. It has been stated that using an oral contraceptive for 5 years or longer can double your cancer risk. In a multi-center case-control study, women who tested positive for HPV DNA had a three-fold greater risk of cervical cancer if they had used oral contraceptives for five years or more. Furthermore, a recent systematic review and meta-analysis found that using oral contraceptive pills was linked to a higher risk of cervical cancer, particularly adenocarcinoma. <sup>255</sup>



Figure 2.6 : contraceptives

Source:Encyclopedia Britannica

### **Cervical Cancer's Spreading Mode**

**Hematogenous Spread:** Hematogenous spread in cervix carcinoma is more common in advanced stages and occurs mostly through the venous plexus or paracervical veins. The lung, liver, bones, and supraclavicular nodes are common sites of distant metastases. The heart, brain, muscles, and, on rare occasions, other organs are among the unusual places<sup>255</sup>.

The basement membrane is near to veins and lymphatic spaces. Direct blood vessel invasion, via lacerated capillaries and veins, through the thoracic or smaller lymphatic and venous channels, may cause hematogenous spread in patients with large lesions and severe disease. Veins, not arteries, are the most common sites of blood vessel invasion. Hematogenous spread affects about 5% of cervical cancer patients. Tumors with poor differentiation and aggressive cell types maybe more likely to spread through the bloodstream. At the time of death, 88 percent of patients with adenosquamous cell cancer had distant metastases<sup>256</sup>.

About 1% to 2% of patients with cervical carcinomas had lung metastases at the time of diagnosis, and 5% to 35% develop pulmonary metastases later. The liver (3%) is the most prevalent site of blood-borne metastases, followed by the bone (16%) and the bowel (16%). Local extension can cause bone metastases, but hematogenous dissemination is more commonly associated with distant metastases. Radiographically, these lesions are frequently lytic, and patients usually have recurring or advanced disease, as well as additional metastases. Small bowel metastases can occur as a direct result of para-aortic node involvement or as a result of intraperitoneal spread.

In this cost-conscious era, being aware of certain high-risk cell types for very early distant metastases can aid in more prudent test ordering. In most cases, information is disseminated in a logical order. Finally, between 10% to 30% of patients experience direct extension to the lower uterine region and/or endometrial cavity<sup>257</sup>.

#### **e) Cervical Cancer Types And Staging**

Cervical neuroendocrine cancer (NECC) is a rare and severe subtype of cervical cancer that accounts for less than 2% of all cervical malignancies. Tumors are classified as low-grade or high-grade. Human papillomavirus (HPV) 18 and, to a lesser extent, type 16 are linked to high-grade NECC. PIK3CA, KRAS, and TP53 mutations are the most prevalent molecular changes in NECC. CD56, synaptophysin, and chromogranin immunohistochemistry are useful tools in the diagnosis. Because of their aggressive nature, which is explained by their proclivity for early nodal and hematogenous dissemination, NECCs provide a considerable clinical and therapeutic challenge.

Their median survival time is 21-22 months, compared to 10 years for cervical squamous cell carcinomas. When compared to non-neuroendocrine cervical cancers, NECCs show a

homogeneous high T2 signal intensity, homogeneous contrast enhancement, and lower ADC values in MRI. A multimodality therapeutic approach including radical hysterectomy, systemic chemotherapy, and radiotherapy is indicated for the treatment of NECC<sup>258</sup>.

## **Staging**

The stage is one of the most important factors in deciding how to treat the cancer and determining how successful treatment might be. The International Federation of Gynecology and Obstetrics' (FIGO) staging method is the most extensively used for cervical cancer (FIGO). Previous versions of the FIGO system didn't include imaging as a tool for diagnosing or staging cervical cancer. The 2018 FIGO revision when imaging is available, it is used in the staging process. Local invasion was previously assessed only through physical examination, which excluded lymph nodes as a prognostic indication. These drawbacks emphasize the significance of imaging for correct cervical cancer staging, as defined by the new FIGO system. Despite the fact that physical examination remains the primary method of FIGO staging assessment, several studies have demonstrated that clinical staging differs from surgical staging in as many as 25% of early-stage illness patients and 40% of cases of more advanced disease<sup>259</sup>.

A significant rate of under staging is a well-known drawback of imaging techniques. Surgical staging, on the other hand, may provide more precise information on lymph node involvement

The clinical stage, which is used to identify cervical cancer, is determined by the outcomes of the patient's physical examination, biopsies, imaging exams, and a few additional procedures, including cystoscopy and proctoscopy, which may be carried out in specific circumstances. It is not based on what is found during surgery. Surgery does not affect your clinical stage, but the findings from the procedure can be utilized to determine a pathologic stage. Your treatment

strategy is determined by the clinical stage. The stages of cervical cancer vary from I (1) through IV (4). The lower the number, the less cancer has spread, in general. A higher number, such as stage IV, indicates that the cancer has progressed. An earlier letter inside a stage denotes a lower stage. Cancers in similar stages have similar prognoses and are frequently treated in the same way.

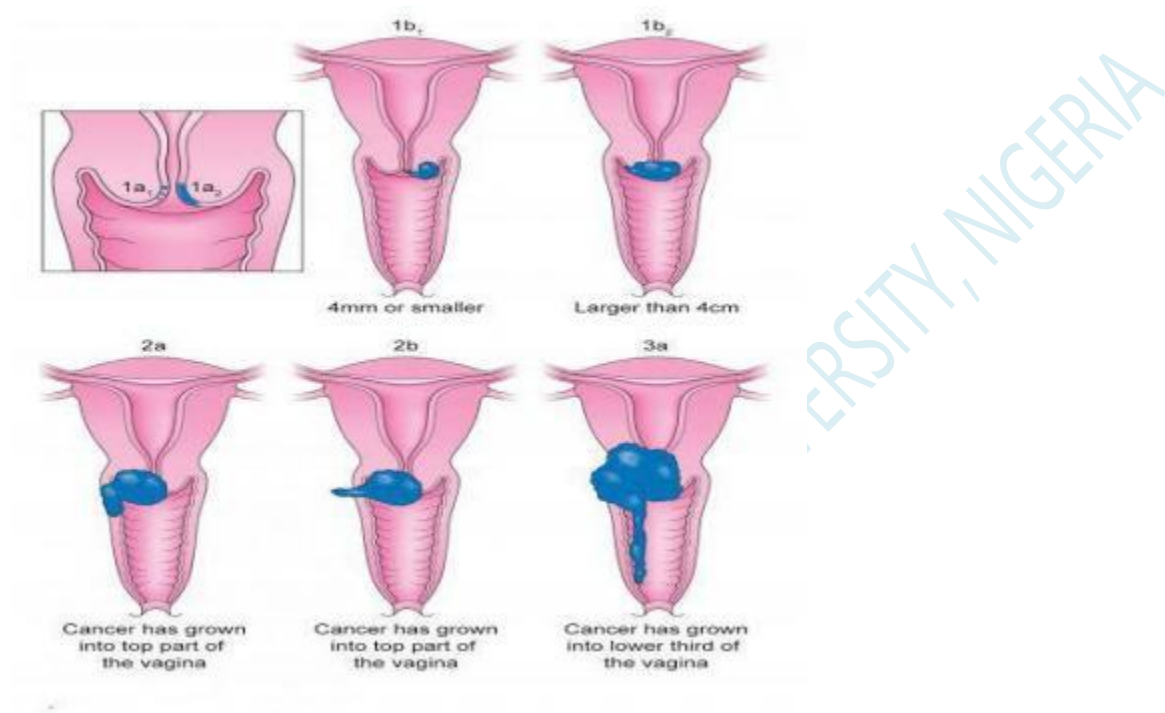


Figure 2.7: Cancer Staging

Source: Grading and Staging Cervical Cancer, Jo's Cervical Cancer Trust.

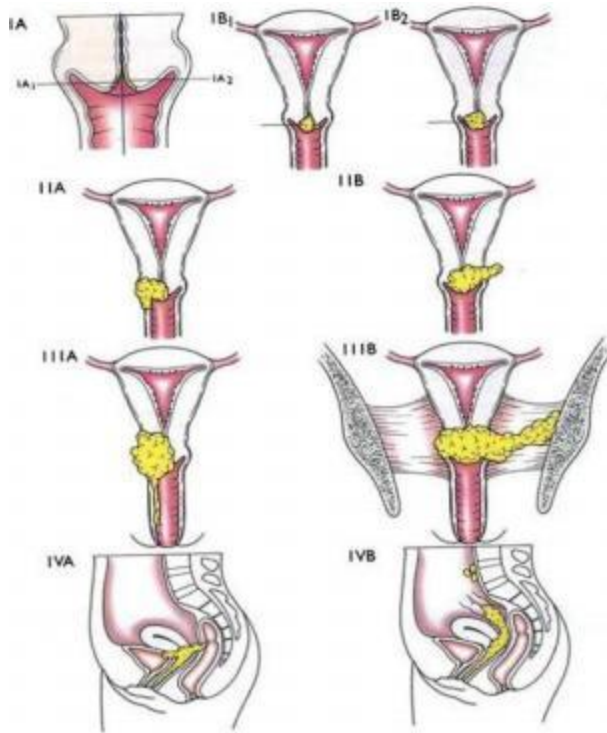


Figure 2.8: FIGO Cancer Staging<sup>260</sup>

Source: Wikimedia Commons

Stage I: Cancer cells have moved from the cervix's surface to its deeper tissues.

- Cancer has not migrated to adjacent lymph nodes
- The cancer has not spread to other locations.

Stage IA: There is very little cancer present, and it is only visible under a microscope.

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Stage IA1: The cancerous region is less than 3 mm (approximately 1/8 inch) deep and can only be spotted under a microscope.

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Stage IA2: The cancerous region is between 3 mm and 5 mm (approximately 1/5 inch) deep and can only be spotted under a microscope.

- It hasn't spread to the lymph nodes in the area.
- It hasn't spread to other areas far away.

Stage IB: This refers to stage I cancer that has only spread to the cervix and has penetrated deeper than 5 mm (about 1/5 inch).

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Stage IB1 describes cancer that is larger than 2 cm (about 4.5 inches) but not deeper than 5 mm (about 1/5 inch).

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Stage IB2: The cancer has a minimum diameter of 2 cm and a maximum diameter of 4 cm.

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Level IB3 The malignancy only affects the cervix and is at least 4 cm in size.

- It hasn't affected any lymph nodes close by.

- It has not spread to remote locations. Stage II: The cancer has gone through the cervix and uterus but hasn't reached the pelvic or lower vaginal walls.

- It hasn't affected any lymph nodes close by.

- It hasn't spread to other areas far away.

Cancer at stage IIA has gone past the cervix and uterus but hasn't yet reached the tissues nearby (called the parametria).

- It hasn't affected any lymph nodes close by.

- It hasn't spread to other areas far away.

Stage IIA1 refers to cancer that is less than 4 cm (1 3/5 inches) in size.

- It hasn't spread to the lymph nodes in the area.

- It hasn't spread to other areas far away.

- It has not spread to remote locations.

Stage II: The cancer has gone through the cervix and uterus but hasn't reached the pelvic or lower vaginal walls.

- It hasn't affected any lymph nodes close by.

- It hasn't spread to other areas far away.

Stage IIA cancer has spread beyond the cervix and uterus but has not yet affected surrounding tissues (called the parametria).

- No nearby lymph nodes have been impacted.
- It has not spread to remote locations.

Cancer that is smaller than 4 cm (1 3/5 inches) in size is considered to be at stage IIA1.

- The nearby lymph nodes have not been affected by it.
- It has not spread to remote locations.
- Neighboring lymph nodes may or may not have picked up the infection.
- It hasn't spread to other areas far away.

Stage IIIA: The disease has spread to the vaginal floor but not to the pelvic walls.

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Stage IIIB: The cancer has spread into the pelvic walls and/or is obstructing one or both ureters, which results in kidney issues (called hydronephrosis).

- It hasn't affected any lymph nodes close by.
- It hasn't spread to other areas far away.

Any size of cancer is considered in stage IIIC.

The malignancy has expanded to neighboring pelvic lymph nodes (IIIC1) or para-aortic lymph nodes, according to imaging studies or a biopsy (IIIC2).

- It hasn't spread to other areas far away.

Stage IV: The disease has spread to distant organs including the lungs or bones, the bladder, the rectum, or both.

Stage IVA: The cancer has spread to the bladder or rectum or it is growing out of the pelvis.

Stage IVB: The cancer has spread to distant organs outside the pelvic area, such as distant lymph nodes, lungs, or bones.

### **Cervical Cancer Detection and Diagnosis**

Broader adoption of the Papanicolaou test (Pap smear) and high-risk HPV testing is the most significant advancement in cervical cancer screening. A Pap smear is a test that is performed as part of a woman's regular pelvic exam. Your doctor extracts cells from the surface of your cervix, which are examined under a microscope by a technician. If anything unusual is found, your doctor will perform a biopsy on a small piece of cervical tissue.<sup>261</sup>

A colposcopy is similar to a pelvic examination. If a Pap smear reveals atypical cells, the doctor may use it. They use a nontoxic dye or acetic acid to stain the cervix, making it easier to see the cells. Then they seek for odd cells to biopsy with a colposcope, which magnifies the cervix by eight to fifteen times. If the colposcopy reveals symptoms of invasive cancer, there might be need for another biopsy<sup>262</sup>

A clinician uses an electrified loop of wire to extract a sample of tissue from the cervix during the loop electrosurgical excision technique (LEEP)<sup>263</sup>. While the patient is under anesthesia, the doctor can do a conization (removal of a portion of the cervix) in the operating room. A LEEP, a scalpel (cold knife conization), or a laser might be used. These procedures are usually performed as outpatient procedures, which means the patient can return home the same day<sup>264</sup>

## Mapping Policy

Health policy is legislation or other government action that deals with the influences that help, or interfere with, reaching health goals on a public level. Examples of health policies include Social Security regulations, labor policy, immigration laws, and standards related to national defense.<sup>264</sup>

Health policies affect organizations and individuals. Organizations include medical schools, health management organizations, medical technology companies, employees, and nursing homes. Individuals include medical doctors, as well as classes or groups of people like the elderly, the poor, and children.<sup>265</sup> National Health Policies, Strategies and Plans (NHPSPs) are crucial in defining a nation's vision, policy directions, and strategies for ensuring the health of its population. Evidence-based policy mapping plays a significant role in providing insight on the management of disease, allowing governments to make informed decisions for health<sup>266</sup>. Nearly all nations have NHPSPs that serve as a framework for addressing the wide variety of complex challenges necessary to improve health outcomes, including those connected to the Sustainable Development Goals and other national priority health issues, like noncommunicable illnesses. (WHO supports national health initiatives, programs, and policies)<sup>267</sup>

Legal mapping for cancer is particularly significant because it gives stakeholders in policymaking useful insight through the efficient application of cancer regulation<sup>268,269</sup>. It is urgently necessary to review out-of-date cervical cancer policy in order to update knowledge with evidence-based best practices.<sup>270</sup>

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## **Chapter Three**

### **Methodology**

#### **3.1 Research Design**

Documents pertaining to national cervical cancer policies from nations in the WHO West African area were gathered through review. The retrieved policies were those that have been published on the International Cancer Control Partnership ICCP, 2020, IARC (International Agency for Research on Cancer), databases. Utilizing key phrases like cervical cancer, HPV, mapping policy, and policy. Further cervical cancer policy documents were found using search engines like Google Scholar, PubMed, and others. Each websites were searched for general health policies and plans, as well as those particular to cervical cancer, HPV, cancer, non-communicable diseases (NCDs), mapping policy, and other topics. Relevant policy documents were located on each country's Ministry of Health or equivalent website, using both a manual search and search terms on search engines

#### **3.2 Population of the Study**

The population of the study was West African countries and sample was the policies in the 16 countries in west Africa namely: Benin, Burkina Faso, Cote d'Ivoire, Cape Verde, Guinea, Gambia, Ghana, Guinea- Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo that borders upon the prevention and management of cervical cancer.

### **3.3 Description of Research Instrument**

The search for data was a methodical approach, and websites for the national and state governments, the health ministry, the national cancer institute, and international and domestic legal databases were all searched for data. As a data-gathering method, document analysis was used in this study.

### **3.4 Data Collection and Analysis**

This research looked at policies across countries and activities, as well as compare policies across West African countries to see which ones are deficient in functionality and require revision. The West Africa regions cervical cancer burden, economics, health financing, and the policy environment were also be reviewed. Policy mapping analysis will be used to analyze all of the information gathered.

### **3.5 Ethical Approval**

The ethical approval for this study was obtained from Lead City University Research Ethics Committee.

## **Chapter Four**

### **Data Analysis and Presentation**

#### **4.1 Demographic Data Analysis**

Data aggregated from 16 West African countries, this research study carried out a detailed document search and analysis of health policies on cervical cancer prevention and/or management. These countries include Nigeria, Ghana, the Benin Republic, Togo, Côte d'Ivoire, Sierra Leone, Guinea, Guinea-Bissau, Senegal, Gambia, Liberia, Mali, Mauritania, the Niger Republic, Cape Verde, and Burkina Faso. The sample comprised policies, plans, guidelines, acts, and strategic papers from 16 West African nations.

**Table 4.1: 2021 World Health Organization Cervical West African Country Profiles.**

<b>Country</b>	<b>Crude Cervical Cancer Incidence Per 100,000 Women (2020)</b>	<b>Age Standardized Cancer Incidence Per 100,000 Women (2020)</b>	<b>Cumulative Risk Of Cervical Cancer, Ages 0-74 (2020)</b>	<b>Cervical Cancer Deaths (2019)</b>
<b>Nigeria</b>	11.9	18.4	1.9%	10,600
<b>Niger</b>	5.2	10.4	1.2%	490
<b>Burkina Faso</b>	10.8	18.2	2.0%	2,100
<b>Benin</b>	9.2	15.1	1.8%	670
<b>Gambia</b>	23.5	42.9	3.9%	140
<b>Ghana</b>	18.3	27.4	3.0%	2,200
<b>Guinea</b>	30.5	50.1	5.5%	1500
<b>Guinea Bissau</b>	23.8	39.6	4.4%	150
<b>Cote D’ivoire</b>	15.8	31.2	3.6%	1,400
<b>Liberia</b>	26.1	40.8	4.5%	470
<b>Mali</b>	19.1	36.4	4.2%	1,700
<b>Mauritania</b>	18.5	28.9	3.4%	330
<b>Senegal</b>	22.6	36.3	4.1%	1,400
<b>Sierra Leone</b>	12.6	21.2	2.5%	260
<b>Togo</b>	10.9	19.1	2.2%	420
<b>Cameroon</b>	20.9	33.7	3.6%	1,600

Source: World Health Organization

Table 4.2 WHO Cervical Cancer West African Country Profiles

Country	Cervical Cancer Mortality-To-Incidence Ratio (2020)	Did Population - Based Cancer Registry Existed In 2021?	Hpv Included In National Vaccination Programme?	Year Of Introduction/ Primary Target Cohort.	Screening For Cervical Cancer, 2019.
<b>NIGERIA</b>	0.66	YES	NO	-	1 in 10 women have been screened for cervical cancer in the last five years.
<b>NIGER</b>	0.76	YES	NO	---	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>BURKINA FASO</b>	0.74	YES	NO		Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.

<b>BENIN</b>	0.66	YES	NO	----	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>GAMBIA</b>	0.7	YES	YES	2019/9-13YRS	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>GHANA</b>	0.61	YES	NO	-----	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>GUINEA</b>	0.71	YES	NO	-----	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>GUINEA BISSAU</b>	0.72	NO	NO		Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.

<b>COTE D'IVOIRE</b>	0.69	YES	YES	2019/ 9YRS	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>LIBERIA</b>	0.71	NO	YES	2019/ 9YRS	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>MALI</b>	0.73	YES	NO		Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>MAURITANIA</b>	0.67	NO	YES	2021/ ND	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.
<b>SIERRA LEONE</b>	0.73	YES	NO		Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.

<b>TOGO</b>	0.68	NO	NO		1 in 10 women have been screened for cervical cancer in the last five years.
<b>CAMEROON</b>	0.65	NO	YES	2020/ 9YRS	Fewer than 1 in 10 women have been screened for cervical cancer in the last five years.

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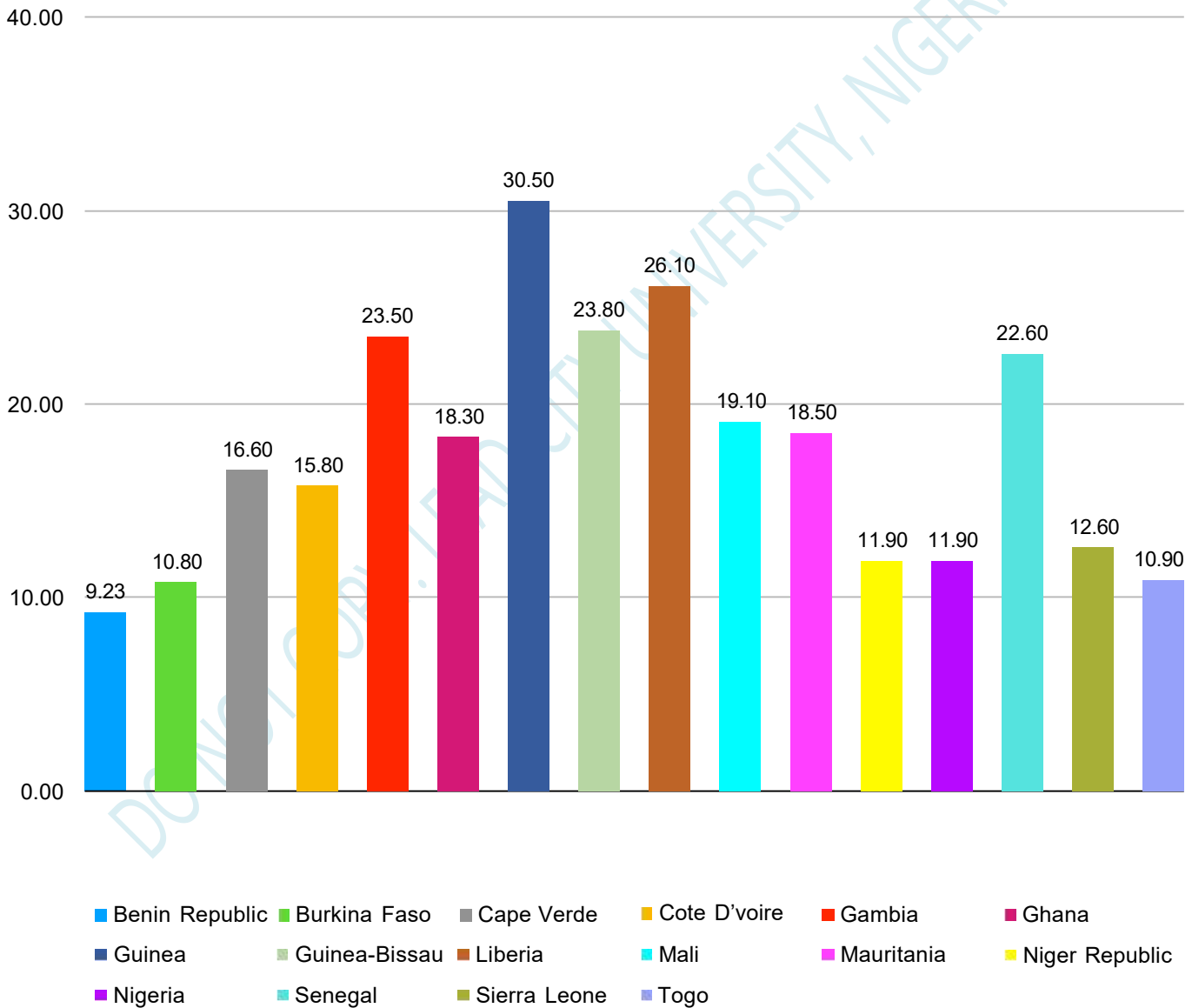
Source: WHO

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#### 4.2. Research Question (s)

Research question one sought to find out the burden of cervical cancer in West African Countries.

Figure 4.1 shows the crude incidence rate of cervical cancer in the 16 West African countries in this study



Source: Student's Research

From the figure above we can deduce that the incidence rate of cervical cancer is 9.23% in Benin republic, 10.8% in Burkina Faso, 16.6% in Cape Verde, 15.8% in Cote d'Ivoire, 23.5% in the Gambia, 18.3% in Ghana, 30.5% in Guinea, 23.8% in Guinea-Bissau, was 26.1 (9.25%) in Liberia, was 19.1% in Mali.

Crude incidence recorded was 18.5% in Mauritania, 11.9% in Niger Republic, 11.9% in Nigeria, 22.6% in Senegal, 12.6% in Sierra Leone and 10.9% inTogo. Mean incidence rate is 17.63 with a Standard Deviation of 6.30.

*Research question two sought to find out the policies available on cervical cancer*

The sample comprised policies, plans, guidelines, acts, and strategic papers from 16 West African nations in this study. Table 4.1 below presents a breakdown of the 35 included documents. No legally obligatory acts were recognized among the 35 legal documents.

**Table 4.3 List of Policy Documents by countries, title, and year of publication**

Country	Title of Policy	Type	Year of Publication	Reference
<b>Benin Republic</b>	Integrated Strategic Plan For The Fight Against Non-Communicable Diseases	Strategy	2018	16
<b>Burkina Faso</b>	Integrated Strategic Plan For The Fight Against Non-Communicable Diseases	Strategy	2016	17
	National Strategy for the Fight against Cancer	Strategy	2020	18
<b>Cape Verde</b>	Multisectoral Plan for the Prevention and Control of Non-Communicable Diseases	Plan	2014	19
	Cancer Prevention and Screening Guide	Guideline	2015	20
<b>Cote d'Ivoire</b>	Integrated Strategic Plan For The Fight Against Non-Communicable Diseases	Strategy	2014	21

	National Policy for The Prevention and Management of Chronic Non-Communicable Disease	Policy	2011	22
	National Health Sector Strategic Plan	Strategy	2014	23
<b>Gambia</b>	National Multisectoral Strategy and Costed Action Plan for Non-Communicable Disease Prevention and Control	Strategy	2022	24
	Strategic Plan for the Prevention and Control of Cervical Cancer	Strategy	2022	25
	National Policy Non-Communicable Diseases	Policy	2022	26
<b>Ghana</b>	National Health Policy	Policy	2007	27
	Strategy for the Management, Prevention and Control of Chronic Non-Communicable Diseases	Policy	2012	28
	National Cancer Control Policy	Policy	2015	29
<b>Guinea</b>	National Multisectoral Strategic Plan of the Fight against Non-Communicable Diseases	Strategy	2020	30
<b>Guinea-Bissau</b>	National Health Development Plan	Plan	2008	31
<b>Liberia</b>	National Cancer Policy	Policy	2018	32
	Integrated Strategic Plan For The Fight Against Non-Communicable Diseases	Strategy	2019	33
<b>Mali</b>	Integrated Strategic Plan For The Fight Against Non-Communicable Diseases	Strategy	2014	34
	National Policy for the Control of Non-Communicable Diseases	Policy	2013	35
	Integrated and Multisectoral National Strategic Plan for Prevention and Fight against Non-Communicable Disease	Strategy	2018	36
<b>Mauritania</b>	National Plan for the Fight against Cancer	Plan	2018	37

<b>Niger Republic</b>	National Multisectoral Strategic Plan for The Fight Against Non-Communicable Diseases	Strategy	2019	38
	Integrated National Strategic plan for Prevention and Fight Against Non-Communicable Chronic Diseases	Strategy	2012	39
	National Policy and Strategic Plan of Action on Prevention and Control of Non-Communicable Diseases	Policy	2013	40
<b>Nigeria</b>	Nigeria Cancer Plan	Plan	2007	41
	Nigeria National Cancer Control Plan	Plan	2018	42
	National Multi-Sectoral Action Plan For the Prevention and Control of Non-Communicable Diseases	Plan	2019	43
<b>Senegal</b>	Strategic Plan for cancer control	Strategy	2015	44
<b>Sierra Leone</b>	Non-Communicable Disease Strategic Plan	Strategy	2020	45
	National Cancer Plan Togo	Plan	2015	46
	National Cancer Plan Togo	Plan	2021	47
	Strategic Plan for the Prevention and Control of Cervical Cancer	Strategy	2016	48
<b>Togo</b>	Policy and Strategic Plan Integrated Fight Against Non-Communicable Diseases	Policy	2012	49
	Multi-Sectoral Policy and Strategic Plan For The Fight Against Non Communicable Diseases	Policy	2018	50

Source: Different countries Legal Database.

From the table above we can deduce that Benin Republic, Guinea-Bissau, Liberia, Senegal, and Sierra Leone have one policy each, while Burkina Faso, Cape Verde, Cote d'Ivoire, Guinea,

Mauritania, and the Niger Republic have two each, Gambia, Ghana, Mali have three policies each, Nigeria has 4 policies and Togo has 5 policies.

*Research question 3 sought to know the role policies played in the prevention and management of cervical cancer*

**Table 4.4 Showing the Cervical Cancer Preventive Measures Provided For By Each Country Policies**

No	Country	Name Of Policy	Primary Prevention	Secondary Prevention	Tertiary Prevention
1	Benin Republic	Integrated strategic plan for the fight against NCD 2018	Not Provided	Not Provided	Not Provided
2	Burkina Faso	Integrated Strategic plan For the control of NCDs, 2016	Not Provided	Not Provided	Not Provided
		National Strategy for the fight against cancer 2021-2025	Provided for vaccination against HPV between 2015 and 2017. Targeting 9 years old girls In two districts.	Provided for screening of precancerous lesions and visual inspection with acetic acid (VIA)	Provided for palliative care
3	Cape Verde	Multisectoral plan for the prevention and management of NCD 2014	Provided for the introduction of anti HPV vaccine.	Provided for screening and treatment program of cervical cancer precursor lesion,	a) Provided for the improved access to auxiliary means of diagnosis and treatment. b) Provided for palliative care program

		Cancer prevention and screening program: Prevention and control manual oncological diseases, 2015.	a) Provided for information and sensitization of the population on the risk associated with cervical cancer.  b) Provided for Vaccination against HPV	Provided for population based cancer screening	a) Provided for defending the rights of incurable patients  b) Provided for the ban on intentionally putting an end to the lives of incurable patients in the final stage of life.
4	Cote D’voire	Integrated strategic plan for the prevention and management of NCDs  National policy for the prevention and management of chronic NCDS			
5	Gambia	National health sector strategic plan 2014-2020  National multisectoral strategy and costed action plan for NCDs prevention and control 2022	Not Provided For  HPV vaccination	Not Provided For  Provided for cervical cancer screening	Not Provided For  NOT PROVIDED FOR

6	Ghana	Strategy for the management, prevention and control of chronic NCDs 2012-2016.	Provided for HPV vaccination	Provided for sensitization on cervical cancer screening	Provided for rehabilitation and palliative care.
		National Policy on NCDS 2022	Provided for HPV Vaccination	Provided for funding of treatment also provided for education on HPV	Provided for palliative care and rehabilitation
7	Guinea	National cancer control policy 2015	Provided for HPV vaccination, provided for cancer awareness programs.	Provided for screening and early detection	Provided for diagnosis and treatment, including palliative and psychosocial support services.
		National multisectoral strategic plan of fight against NCDs 2021-2025.	Provided for HPV vaccination	Provided for screening	Provided for palliative and rehabilitation care.
8	Guinea Bissau	National health development plan 2008-2017	Not Provided For	Not Provided For	Not Provided For
9	Liberia	National Cancer Policy 2018-2022	Provided for public awareness of risk factors of cancer, advocating for safe sex practice and HPV vaccination.	Provided for early detection and surveillance of cancer	Provided for pain management and palliative care
10	Mali	National Policy For the control of NCDs 2013	Not Provided For	Not Provided For	Not Provided For

		Integrated strategic plan for the fight against NCDs 2014-2019	Not Provided For	Not Provided For	Not Provided For
		Integrated strategic plan for the fight against NCDs 2019-2023	Provided for HPV Vaccination from 9-13 years	Provided for screening.	Provided for the creation of palliative care in the hospitals in Mali
11	Mauritania	Integrated and multisectoral national strategic plan for prevention and fight against NCDs 2018	Not Provided For	Provided For Screening	Provided for palliative care
		National plan for fight against cancer 2018-2022	Provided for vaccination against HPV in adolescents	Provided for screening	Provided for palliative care
12	Niger Republic	Integrated national strategic plan for prevention and fight against NCCDs, 2012.	Provided for HPV vaccination	Provided for screening	Recommended palliative care
		Integrated national strategic plan for prevention and fight against NCCDs, 2019 - 2021	Provided for HPV vaccination	Provided for early detection.	Provided for palliative care.
13	Nigeria	Nigeria cancer plan 2008-2013	Provided for HPV vaccination	Provided for creating awareness on cervical cancer and free cancer screening	Provided for quality cancer care, palliative care and pain control.
		National policy and Strategic plan of action on prevention and	Provided for HPV vaccination	Provided for cancer screening	Recommended the reenactment and revision of palliative care

		control ofNCDs, 2013			
		National cancer control plan 2018-2022	Provided for HPV vaccination for adolescents	Provided for screening and treatment	Provided for palliative care
		National multi sectoral action plan for the prevention and control ofNCDs 2019-2025	Provided for vaccination of girls from 9-13 years	Provided for Screening and treatment	NOT SPECIFICALLY PROVIDED FOR
14	Senegal	Strategic plan for cancer control	Provided for HPV vaccination of girls from 9-13 years	Provided for early diagnosis and treatment	Provided for palliative care
15	Sierra Leone	NCDs strategic plan 2020-2024	Provided for HPV vaccination	Provided for Screening	Provided for palliative care
16	Togo	National control program against NCDs 2012-2015	Provided for HPV vaccination	Provided for screening in women aged 35-65	Provided for palliative care
		National Cancer plan Togo 2016-2020	Provided for HPV vaccination	Provided for screening and sensitization on C.C	Provided for palliative care
		Policy and strategic plan, multisectoral disease control of NCDs 2018 - 2022	Provided for HPV vaccination	Provided for screening of C.C	Provided for palliative care.

Source: Different Countries Legal Databases.

Research question four sought to know the adherence to the WHO guidelines on prevention and treatment of cervical cancer

**TABLE 4.5 Adherence to the Who Recommendations by Countries**

No	Country Title	Hpv Vaccination	Screening	Treatment For Precancerous Lesions	Treatment For Invasive Cancer	Referral System
1	Benin Republic	No	No	No	No	No
2	Burkina Faso	Yes	Yes	Yes	Yes	Yes
3	Cape Verde	Yes	Yes	Yes	Yes	Yes
4	Cote D'voire	Nd	Nd	Nd	Nd	Nd
5	Gambia	Yes	Yes	Yes	No	Yes
6	Ghana	Yes	Yes	Yes	Yes	Yes
7	Guinea	Yes	Yes	Yes	Yes	
8	Guinea Bissau	No	No	No	No	No
9	Liberia	Yes	Yes	Yes	Yes	
10	Mali	Yes	Yes	Yes	Yes	Yes
11	Mauritania	Yes	Yes	Yes	Yes	Yes
12	Niger Republic	Yes	Yes	Yes	Yes	No
13	Nigeria	Yes	Yes	Yes	Yes	Yes
14	Senegal	Yes	Yes	Yes	Yes	Yes
15	Sierra Leone	Yes	Yes	Yes	No	Yes
16	Togo	Yes	Yes	Yes	Yes	Yes

Source: WHO

#### 4.3 Discussion of Findings.

Findings from this study revealed that the three countries in West Africa with the highest crude incidence of cervical cancer are Guinea, Liberia, and Guinea Bissau with a crude

incidence rate of 30.5%, 26.1%, and 23.8% respectively while Benin Republic, Burkina Faso and Togo had the lowest rates of cervical cancer with crude incidence rate of 9.23%, 10.8% and 10.9% respectively. This is inline with a study<sup>1</sup> which showed that cervical cancer is the most prevalent illness among women in Liberia and the second most prevalent malignancy among those between the ages of 15 and 44. It is estimated that 4.3% of women in the general population in Liberia's neighboring Western Africa region are infected with cervical HPV- 16/18, and that HPVs 16 or 18 are the cause of 55.6% of invasive cervical cancers. The risk of acquiring cervical cancer affects 1.47 million women in Liberia who are 15 years of age or older. The disease currently claims the lives of 469 women year, while 656 other people are diagnosed with it. The study is also in line with another study<sup>2</sup> which showed that the level of cervical cancer is high in Guinea and it ranks the 11<sup>th</sup> in the world as at 2020. This study is also inline with the study<sup>3</sup> that showed that cervical cancer is the second leading cause of cancer morbidity and mortality in Nigeria.

Findings from this study also revealed that the countries with the highest number of policies on cervical cancer are Togo and Nigeria with 5 and 4 policies each respectively. Most policies included information regarding the age range of females eligible for HPV vaccination, but this varied substantially.

Some of the west African countries do not have a distinct policy/strategy/plan/guidelines on cancer, rather they rely on strategies on fight against Non communicable diseases (NCDs), which mostly do not go into details on cervical cancer, however countries like Burkina Faso, Carpe Verde, Guinea, Mauritania, Nigeria, Senegal and Togo have distinct policy on cancers though none of the West African countries has a policy specifically on Cervical cancer alone.

Certain countries in Western Africa required vaccination of a certain age group (most frequently, 9-year-old females). While some of the nations did not establish an age range for vaccine

eligibility, this is not in line with the WHO recommendation for two vaccination doses for girls aged 9 to 14<sup>4</sup>.

The policies of only twelve nations included raising awareness of cervical cancer screening which was also not in line with the World Health Organization (WHO) recommendation using an HPV DNA test (or VIA in places with limited resources) to screen women aged 30 to 49 and treating precancerous lesions<sup>5</sup>

WHO recommended guidelines on the treatment and screening of cervical cancer<sup>6</sup> which areas follow: For both general population women and women with HIV, WHO advises using HPV DNA detection as the primary screening test rather than VIA or cytology.

Current programs using cytology as the primary screening test and with quality assurance should be maintained until HPV DNA testing is available; current programs using VIA as the main given the difficulties that quality assurance presents, screening tests should go quickly.

The WHO advises using either a triage-based or stand-alone HPV DNA primary screening test. Aim to protect all women from developing cervical cancer. Using HPV DNA detection as the main screening test in a screen-and-treat strategy. In the general population, WHO advises treating women who test positive for HPV DNA. Using HPV DNA detection as the primary diagnostic tool in a screen, triage, and treat strategy WHO advises utilizing partial genotyping for screening tests on women in general. Following a positive HPV DNA test, women are referred for colposcopy, VIA, or cytology. The triage based primary screening was not provided for by the countries policy.

All of the Country policies did not specifically make provisions for women living with HIV who has cervical cancer, which is not in line with the World Health Organization recommendation of

using either samples obtained from a health care samples of women from the general population or women who self-collected them having HIV/AIDS. Majority of the policies made provision for screening, which is in line with the World Health Organization which advises beginning routine cervical cancer screening among the general female population.

After the age of 50, the WHO recommends ceasing screening after two consecutive negative results. Screening outcomes in accordance with the suggested routine screening intervals among both the general female population and HIV-positive women. This was not provided for by the country policies.

The WHO advises using HPV DNA for routine screening every 5 to 10 years detection as the main screening procedure for women in general. WHO recommends a regular screening interval in cases where HPV DNA testing is not yet available. When VIA or cytology is used as the main screening test among both the general population of women and women with HIV, it should be performed every three years. When switching to a program that calls for routine screening intervals, screening the general population of women and even just twice in a lifetime are both ladies who have HIV.

## Endnotes

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## Chapter Five

### Conclusion

#### 5.1 Summary of Findings

Documents pertaining to national cervical cancer policies from nations in the West African area were gathered through review. The population of the study was West African countries and the sample was the policies in the 16 countries in West Africa namely: Benin, Burkina Faso, Cameroon, Cote d'Ivoire, Guinea, Gambia, Ghana, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo that borders upon the prevention and management of cervical cancer.

This research looked at policies across countries and activities, as well as compare policies across West African countries to see which ones are deficient in functionality and require revision. Data sourced from the West African Countries in this study revealed that the three countries in West Africa with the highest crude incidence of cervical cancer are Guinea, Liberia, and Guinea Bissau with a crude incidence rate of 30.5%, 26.1%, and 23.8% respectively while Benin Republic, Burkina Faso and Togo had the lowest rates of cervical cancer with crude incidence rate of 9.23%, 10.8% and 10.9% respectively.

Furthermore, this study revealed that the countries with the highest number of policies on cervical cancer are Togo and Nigeria with 5 and 4 policies each respectively. Most policies included information regarding the age range of females eligible for HPV vaccination, but this varied substantially. Certain countries in Western Africa required vaccination of a certain age group (most frequently, 9-year-old females). The majority of nations did not however, establish an age range for vaccine eligibility, this is not inline with the WHO recommendation for two vaccination doses for girls aged 9 to 14. The policies of only twelve nations included raising awareness of cervical

cancer screening which was also not in line with the World Health Organization recommendation using an HPV DNA test (or VIA in places with limited resources) to screen women aged 30 to 49 and treating precancerous lesions

We compiled, analyzed, and contrasted recent policy articles on primary, secondary, and tertiary cervical cancer prevention in West Africa. Each of the 16 countries had at least one policy addressing cervical cancer prevention, although most of these programs lacked crucial data. Although there has been a slight improvement in the comprehensiveness of policies over time, modern policies were not anymore extensive than older ones.

Policies addressed primary and secondary prevention more frequently than tertiary prevention. According to a prior scoping analysis West African cervical cancer policies give HPV vaccine less attention. The results thus point to an improvement in primary preventive programs, which may be brought about by better accessibility to vaccinations in the area.

The increased focus on prevention over treatment has been acknowledged in several recent African policy assessments and should be interpreted in light of West African countries' limited surgical access and lack of palliative care

However, it is crucial for cervical cancer strategies to address tertiary prevention, especially in low-income countries where cervical cancer survival rates are at their lowest and where many women with the disease are diagnosed too late due to a lack of access to primary and secondary prevention programs

Policies in Nigeria, Ghana, Togo, and Mali were more extensive than those in other nations. HIV-positive women acquire cancer more quickly, which is a crucial synergy, and preventative measures are required in contexts with high HIV prevalence; most of the policies did not make provision for this.

Countries with a larger share of their health budget from international donors tend to have more robust health policies. Donors sponsor several initiatives in West African nations to reduce the prevalence of cervical cancer, such as the HPV vaccination funded and supported by Gavi (which is an international organization that provides vaccines in poor countries) and the considerable assistance for screening programmes provided by USAID and other partners.

Since HIV is the primary target of donor funding in Sub-Saharan Africa, this maybe picking up an "HIV impact"

But in countries with a high HIV burden in West Africa, where donor funding is more common, comprehensive policies for cervical cancer may indicate a willingness to act in response to public health needs and a focus on the HIV response on the side of donors. The findings of this study call for more research to be conducted in order to get a deeper comprehension of the connection that exists between the quality of health policy and the source of its funding, such as donations from donors.

Surprisingly, there was no link between a nation's burden of cervical cancer and the breadth of its policy. However, due to incorrect identification and reporting, fatality estimates have substantial margins of error; as a result, this association should be treated with caution. The idea that nations with high cervical cancer mortality also have subpar healthcare systems and often have lower resources to undertake effective cancer control strategies is true.

This analysis also predicts a link between the breadth of policy and the percentage of women in government. Perhaps more would be done to advance women's health if more women had a voice in policy. However, based on the evidence at hand, it appears that the exact opposite is true. Previous studies from both high-income and low-income nations have shown a favorable association between female participation in government and population health outcomes, with the

enhanced financing for health being the proposed mechanism. The fact that most cervical cancer programs in West Africa receive outside funding, however, may lessen any possible benefits to health from female governance of cervical cancer policy. The findings imply that further study in this area is necessary, with an emphasis on how civil society women's perspectives and those of survivors of cervical cancer maybe strengthened in the context of policymaking.

Regardless of context or region, some policy elements were more common than others. For instance, it was more common to identify target vaccination and screening groups (91% of countries with primary prevention policies and 76% of countries with secondary prevention policies, respectively) and less common to address sensitization campaigns (40% and 21% of countries' primary and secondary prevention strategies, respectively) or education about risk factors (20% of primary prevention policies). The details of each policy, however, differed and weren't always consistent with the best information available. For instance, the WHO<sup>3</sup> strategy for eradicating cervical cancer proposes twice-lifetime screening (at ages 35 and 45) based on results from meticulous modeling analyses. The ages at which cervical cancer screening should start, however, were recommended in these policies to range from 20 to 35 years old (the age of 25 being the most popular proposal), and to end anywhere between 45 and 70 years old (the most common recommendation was age 50)

The West African region's cervical cancer burden, economics, health financing, and policy environment were also reviewed. Policy mapping analysis was used to analyze all of the information gathered. The screening intervals advised by West African nations ranged from annually to once every decade, with the most prevalent frequency being every two or three years. By deviating from worldwide guidelines for appropriate screening schedules, these policies may subject women to over-screening, resulting in the waste of scarce and important financial and

human resources. They can place an unnecessary strain on women (e.g., treatment complications and emotional distress).

In addition, although most cervical cancer screening policies in West Africa include visual inspection with acetic acid (VIA), as recommended by the World Health Organization for low-resource settings, only four countries reflect recent lesion treatment guidelines, i.e. thermocoagulation as an alternative approach in low-resource settings. In a prior examination of cervical cancer policy in Africa such discrepancies were discovered, indicating a minor improvement over time. These gaps and disparities indicate a potential for enhancing and harmonizing local policy with global principles.

## **5.2. Conclusion**

Comprehensive, evidence-based policies are crucial for enhancing population health outcomes, such as cancer control. Even though many West African nations have policies addressing the primary, secondary, and/or tertiary prevention of cervical cancer, many of these policies are incomplete, according to this study. When policies contain details, they vary significantly from country to country and may not reflect worldwide guidelines and contemporary scientific data. Given the current global policy climate, which places a greater emphasis on the prevention of NCDs, in particular the eradication of cervical cancer, which represents a substantial burden of cervical cancer in the West African area, these findings come as a surprise.

These findings simply that the comprehensiveness of cervical cancer policies may be influenced by factors such as the HIV load and donor funding for health. At the same time, other variables, such as cervical cancer mortality and female participation in government, may not be as relevant as questioned.

This research reveals potential for upgrading cervical cancer policy in the West African area, including often-overlooked themes, misalignments with global evidence that may be addressed, and "background" characteristics that may impact policy content and should be examined by individuals engaged in knowledge translation initiatives. Based on the results of the data analyzed it was concluded that the three countries in West Africa with the highest crude incidence of cervical cancer are Guinea, Liberia, and Guinea Bissau with a crude incidence rate of 30.5%, 26.1%, and 23.8% respectively while Benin Republic, Burkina Faso, and Togo had the lowest rates of cervical cancer with a crude incidence rate of 9.23%, 10.8%, and 10.9% respectively and these rates has nothing to do with the policies cause it is not enough to have policies, enforceable policies should be the goal as people don't obey rules that has no sanctions for its disobedience.

### **5.3. Recommendations**

1. Priority should be given to preventing cervical cancer by screening and immunization in West African nations, beginning with demonstration programs.
2. The WHO recommendations should be adapted to meet the specific needs of West African states.
3. Establishing national programs to control cervical cancer would offer the foundation for implementing the necessary policies to lower the incidence of cervical cancer in West Africa.
4. The national political will is essential to elevate cervical cancer prevention to the same degree of importance as other illnesses, such as HIV.
5. Policies should be made into Acts of parliament so it can be enforceable, people don't obey laws that are without sanctions for its disobedience.

#### **5.4 Contribution to Knowledge**

The findings and conclusions of the study lead to the below contributions to knowledge:

The study demonstrates that the persistent obstacles facing cervical cancer management initiatives in West Africa are not a result of a lack of solid evidence but rather the failure to implement these best practices. In addition to stressing that progress monitors are the real-time determinant of best practices in the cervical cancer management plan, the study noted that progress monitors are the key to identifying the most effective methods.

#### **5.5 Suggested Area for Further Research**

Future researchers are encouraged to examine two problems. First, there is a need for research that focuses on how cervical cancer is being improved and implemented in Africa and identifies explicitly what is being done to alleviate the bleak image that the current report paints of the situation. In addition, there is a need to focus on the role of governments and NGOs in offering solutions, particularly for rural community residents.

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## University Compliance Certificate

This is to certify that this thesis by Evelyn Adejoke ADEPOJU with Matric number: LCU/PG/001586 in the Department of Public Health, Faculty of Basic Medical and Applied Sciences, Lead City University Ibadan, is in full compliance with the approved university format

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