

SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Evaluation of cervical cancer prevention policies in East African countries

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INTRODUCTION

All over the world, cancer is a major public health burden. 19.3 million was the estimated number of new cases of cancer and nearly 10 million deaths from cancer globally. Cancer burden is apparent all over the world; however, the low middle income countries (LMICs) have an upward prevalence in the number of new cases and deaths from cancer for example the Sub Saharan countries. The occurrence of cancer is characterized by unregulated proliferation of cells after the failure of the mechanisms that regulate normal cell growth in so doing invading and destroying the tissues and organs that are adjacent then dissemination to the other parts of the body. World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) have enumerated obesity, alcohol consumption, family history of cancer, Human Papilloma Viruses (HPV), Human Immunodeficiency Virus/ Acquired Immunodeficiency syndrome (HIV/AIDs), lifestyle and tobacco smoking have been linked as the major risk factors for cancer Among the leading cancers that have been implicated to have a high morbidity and mortality worldwide in women of all ages are cancer of the breast, cancer of the lung and cancer of the cervix. Inadequate primary health care, compromised screening procedures, delayed histology results, little or no resources, follow up hitches, lack of awareness and limited treatment opportunities have marred the diagnosis and detection of cancer in the developing countries hence the cancer is discovered late and at an advanced stage. Ineffective implementation of policies for control of cancer, overwhelmed health demands and poor monitoring through population registries is a great contributor to the long term problem of cancer of the cervix facing sub-Saharan Africa(SSA) This has been the typical picture in most of these developing regions[13]. In contrast, the incidence and mortality from cervical cancer have decreased in developed countries, attributable to organized and consistent cervical screening programs rather than opportunistic screening programs and HPV vaccination [2], well-structured national health care systems, affordable high quality cancer treatment for all and prioritized health care spending hence the low mortality to incidence ratios. Cancer of the cervix has been linked to HPV and evidence strongly shows that it is the main causative agent, 99% of cervical cancers are caused by HPV. HPV types 16 and 18 cause approximately 70% of cervical cancers worldwide. Invasive cervical cancer is more frequently related with high risk Human Papilloma Virus (HR-HPV) types 16 and 18 than with other types. Of all the diseases transmitted sexually by mucosa to mucosa contact in the reproductive tract, HPV is the most frequent infection. There are a variety of HPV genotypes. These group of viruses

are sexually transmitted. There are oncogenic and non-oncogenic types. Their prevalence ranges from different geographic locations and populations. The diversity among continents and countries and the heterogeneity of the HPV types has affected the efficacy of HPV vaccination, hence these two factors ought to be taken into account when developing of vaccines and of screening tests. Based on this heterogeneity, no one HPV vaccine has the ability to provide full protection against all the HPV types. Effective programs and interventions facilitating early screening of women and increased availability of HPV vaccinations will greatly contribute to reduction of mortality from cervical cancer as it is preventable; this will maximize the chances of successful treatment of precancerous lesions.

The burden of cervical cancer (CC)

Globally, in 2020, cancer of the cervix was ranked fourth as the cancer with high incidence among females of all ages, with a total of 604,127 new cases which translates to 6.5% of the total percentage of new cases. Comparing these global statistics to the African continent, in 2018, a significant proportion is from African countries with 19 of its countries being amongst the 20 top countries globally with the highest incidence of CC. Narrowing it down to SSA, cervical cancer incidence is on the rise, and currently the second most frequent cancer and responsible for women deaths. The highest age standardized incidence rate of CC worldwide is from the south of Africa, Malawi (43.1 per 100,000). In the SSA, CC has been implicated for the cause of death among women in SSA as evidenced by its high (21.7%) percentage as compared to other mortalities from the other types of cancers. This alarming morbidity and mortality in the low resource settings has left countries desperate for an intervention. The WHO has made strategies that will hasten the eradication of CC as a public health concern by setting targets for countries to achieve by 2030; 90% full vaccination for girls before their 15th birthday, high precision screening for 70% women and 90% women diagnosed with CC to receive treatment and care. High level advocacy translated to vaccination against HPV and routine mass screening is the intervention urgently needed in SSA to curb this public health burden[33,36]. Underscreening and inadequate follow up are some reasons for the increasing burden of CC in some populations.

Public health policies for reducing disease burden

Policy mapping is a process of examining the prevalence, distribution and characteristics of adopted policies across jurisdictions to provide evidence on some effective interventions and

highlights the modifications of health policies. For a while now, it has been noted that policy mapping applies a methodology towards bringing clarity to the laws in health and it has become a popular practice. Mapping policy is essential because it provides very useful perspectives and reveals conceptual gaps in laws that affect health and can facilitate starting points to make amendments. Countries cannot be able to achieve their public health program goals effectively without laws; it is mandatory that legal and regulatory instruments are established and executed. Under legal mapping studies, laws, regulations and policies are the frequent legal instruments utilized. National policies, strategies and plans are fundamental legislative tools for protecting populations against threats from health calamities like cancer of the cervix among other diseases. In the past decade, international health commitments have been established enabling countries to legally bind themselves to oblige to implement national health policies. It is crucial to set up national cancer control policies as it is a demonstration of the state's commitment to facilitate and provide the direction for the implementation and realization of the cancer control programs which have proved that indeed public health policies enhance positive clinical outcomes. In the management and control of cancer, cancer policies provide the visibility that elevates interventions to address the burden of cancer leading to tangible gains, for instance lung cancer incidences reduction due to strengthening the implementation of smoke free laws and tobacco control policies.

Cervical Cancer policies and guidelines

Policies and guidelines for CC should address the affected population which is girls and women, the programs and structures crucial in the control of CC covering the full continuum from prevention to treatment and management of CC. In 2018, the WHO made a worldwide call to action to eliminate and end the suffering from curable and preventable cancer. The comprehensive CC control guideline by WHO broadly outlines the components for effective CC programs. The main objective of this international guide was to provide a uniform direction to governments to enable them establish, implement and update their CC guidelines and protocols. There have been great public health achievements whose success can only be pointed to policy amends. National policies on cervical cancer ought to be tailored for countries especially the LMICs recognizing the social disparities among the populations. Specifically, the national cervical cancer screening programs have fallen short because they have failed to favor different groups of disadvantaged and marginalized women because evidence has shown that in SSA, the huge gaps in health care systems have hindered implementation of cervical cancer policies. These countries have the

highest CC burden, lowest rates of crude and effective CC screening, lowest availability of skilled personnel and inadequate diagnostic and treatment facilities in contrast with the countries that have established guidelines whose screening rates are high with low disease burden. Effective CC policies are a fulfilment of the human rights of women and are a foundation for their empowerment.

Prevention of cervical cancer

Early detection by early screening for HPV, Pap smear testing, HPV vaccination and the treatment of precancerous lesions are the strategies to control and prevent CC. In order to identify cervical precancerous deviations, CC screening is recommended for all women aged between 25 and 65 years. Age appropriate high quality cytology test the Papanicolaou test (Pap smear) is the ideal screening examination highlighted in the guidelines for prevention and early detection of CC. Although cytology tests produce a false negative result for conventional smears, they are the most common used method for cervical cancer screening in many countries. Currently, the HrHPV testing is the most effective way for detecting precancerous cervical lesions and age appropriate cytology testing is recommended. detecting precancerous cervical lesions and age appropriate cytology testing is recommended [69]. Primary HPV screening has several advantages, including increased sensitivity in detecting precancerous lesions, improved reassurance with a negative test, and the ability to reasonably prolong screening intervals. The existence of cytology false negatives and inadequate screening contribute to the failure of cervical cancer screening. The use of primary HPV testing will greatly reduce the rate of false negative rate of cytology. Vaccination against the high risk and most common HPV types 16 and 18 prevent the problem of CC amongst women in SSA in the future. Affordable, effective screening programs designed based on the poor resource settings' needs will greatly lower the incidence of CC as data shows that screening has been associated with reduction in the incidence and mortality of CC in United Kingdom (UK) and Australia. The screen and treat approach is more practical, safe and reduces the chances of having increased prevalence of high grade CC precursor lesions in low resource setting because of its high sensitivity of 100%, its ability to give immediate results and requires less intense training. HPV DNA testing has been found to have higher sensitivity as compared to cytology tests. It is however pricier and as such due to the inadequate infrastructure in the low resource settings the cytology testing is more efficient as the primary method of screening. Although evidence shows screening rates are low, there is proof that screening provides substantial protection against CC.

Human Papilloma Virus Vaccine

2006/2007 was the year HPV vaccines were first launched worldwide. Quite a number of countries expressed remarkable interest and embraced the idea by adopting it in their national immunization schedules. WHO recommends Cervarix, Gardasil and Gardasil 9 HPV vaccines. Cervarix is a bivalent vaccine targeting the high risk HPV types 16 and 18, while Gardasil offers protection against both HPV 6 and 11 in addition to HPV 16 and 18. Gardasil 9 is a nonavalent HPV vaccine (9vHPV) which protects against more cancer causing HPV types 16, 18, 31, 33, 45, 52, and 58, and also prevents genital warts caused by HPV types 6 and 11. Gardasil 9 is the only HPV vaccine that provides protection against HPV types causing cervical cancer in women and other HPV-associated anogenital cancers in both men and women. HPV vaccination provides prophylactic efficacy against cervical pre-cancer in vaccinated adolescent girls and women consequently reducing the incidence of cervical cancer. It is predicted that high vaccine coverage of girls will eliminate CC in most LMICs. The HPV vaccines according to literature can provide nearly 100% protection against the HPV types included in the vaccines if they are given in adolescent age for prevention [96]. HPV vaccination may offer the added benefit of lowering the prevalence of HPV infection caused by types not covered by the vaccines though there is some evidence of cross protection. HPV vaccination has been handled as a public health priority by many countries as studies provide evidence of its gains and efficiency. The recommended age for vaccination is girls between 9 and 14 years since it is assumed that at this age the girls are not sexually active nor prior exposure to HPV and also because higher immunity can be generated in this age group. In developed countries where CC incidences are reduced like UK, United States of America (USA), Australia and Europe which have achieved high vaccination coverage, there have been recommendations for gender neutral vaccinations since there have been occurrences of HPV attributable cancers in men. It is also presumed that these gender neutral vaccines would provide significant cost-effective benefits. There is an urgent need to introduce HPV vaccination in the developing countries due to the high burden of CC. Globally, the uptake of HPV vaccines is suboptimal and available research shows that low levels of awareness, poor compliance to the HPV vaccination program, irrational parental reservations and misinformation, cultural and religious reasons. Kenya conducted a HPV pilot program in 2013-2015 whose success influenced the introduction of HPV vaccine countrywide in October 2019 with an objective to immunize 800,000 girls annually. Through the support of Global Alliance for Vaccines and Immunizations

(GAVI) and the WHO the vaccines were available at no cost. The United Nations Children’s Fund (UNICEF) publicized relevant public health messages highlighting the advantages, safety and effectiveness of HPV vaccine. As with any undertaking, increasing awareness and publicizing the HPV vaccine will improve the knowledge on all aspects of HPV and its prevention, this includes addressing the concerns of parents and children who are involved in HPV vaccination as this will enhance the uptake. In Kenya, communities’ opinions regarding HPV vaccination are related to apparent mistrust towards new vaccinations, deficient knowledge about the HPV infections and the vaccination, insufficient information due to fragmented training of stakeholders.

OBJECTIVES

Little is known about the uptake of HPV vaccine in different regions of Kenya. The views of the populace are fragmented and marred with a lot of misinformation. This is what informed this research as it sought to bring an insight on the progress of the HPV vaccination program and the opinions towards the introduction of the vaccine for the 10 to 11-year-old boys and girls two counties at the coast of Kenya (Mombasa and Tana-River).

1. To identify and content analysis of policies for prevention and management of cancer of the cervix of East-African countries
2. To determine the compliance of the policies from East-African countries with the comprehensive cervical cancer control guide to essential practice by WHO.
3. To assess the knowledge and attitude of HPV vaccination among school boys and girls, parents and other key informants comprising of head teachers, health workers and community leaders regarding HPV vaccination.

METHODOLOGY

Part 1: National Policies to Prevent and Manage Cervical Cancer in East African Countries: A Policy Mapping Analysis

A thorough systematic document search for health policies on CC prevention and management from East African countries i.e. Burundi (BI), Comoros (KM), Democratic Republic of Congo (DRC), Djibouti (DJ), Eritrea (ER), Ethiopia (ET), Kenya (KE), Madagascar (MG), Rwanda (RW), Somalia (SO), Uganda (UG), and Tanzania (TZ) [111] [112]. The search was uniformly conducted from the 12 national or government websites, national health ministry/department or

related websites, national cancer institute sites, international LexisNexis and Westlaw legal databases, national legal databases, the African legal information institute, the international cancer control partnership portal, and the WHO non-communicable disease document repository. A comprehensive list of all the websites and databases is found in the appendix 1. Depending on the filtering options of the different websites, different search terms were used. For the national databases, cervical cancer or cancer was used without any restrictions. This was because different countries had different titles for the documents. For the international databases, country name and cervical cancer or cancer were used. The comprehensive search was conducted from February to June in 2019.

Document screening

The documents of interest were any legal instruments i.e. guidelines, strategies, plans, policies, regulations, and acts of parliament. The eligible documents included; all national legal documents published under the health ministry, health-related ministries, governmental institutions, national cancer institutes, or parliaments. All national legal instruments that described the aspects of the prevention, management, and control of cervical cancer. The documents that were excluded lacked information on cervical cancer e.g. national non-communicable disease policies because they contained generalized information about cancer instead of highlighting the particular aspects of cancer of the cervix. Documents that were non-legal texts like articles or grey literature were also excluded.

Data coding and analysis

The data found were in English, Kiswahili, and French. The documents that were in Kiswahili and French were translated into English. The QRS Nvivo 12 Plus software was used for data processing. Data was coded using a content analysis approach. Inductive thematic analysis was used to analyze the data while identifying key themes emerging from the data following the coding process. The data categories were coded in two stages, with the second stage taking a more refined approach. A series of consensus discussions were undertaken to review, refine and confirm the main themes and codes; data that was related was selected and put into nodes.

Part 2: Knowledge, Attitude and Practice of Main Stakeholders towards Human Papilloma Virus Infection and Vaccination in Mombasa and Tana-River Counties in Kenya: A Qualitative Study

Study setting

Kenya is a country in East Africa with an approximate 52.5 million people. The study population was from Mombasa and Tana River counties which are located on the Indian Ocean coast. To the best knowledge, there is no similar survey that has been carried out in this region before. The two counties are distinct in that they have diverse socio-economic outlook which can permit a comparison of the results. Mombasa is situated in an urban locality. Tana River county is in a rural locality.

Study design and sampling

Individual interviews were conducted by purposively selecting the participants using a maximum variation sampling strategy. The inclusion criteria were composed of at least a boy or a girl aged between 9–13 years, a parent, a head teacher, a community leader and a health worker who was engaged in the HPV vaccination exercise.

Data collection

A total 103 interviews were conducted. Semi-structured interviews were used to collect data. The semi-structured interview guide was developed with questions that were related across the different groups of interviewees, with slight modifications to suit each of the participant groups. The interviews were held uniformly in a friendly environment that was convenient to the participant. The interviews were captured by recording using a digital voice recorder, observations and notes were taken. Data collection was conducted between September 2020 and February 2021. The interviews were conducted in both English and Kiswahili depending on the interviewee's preference. On average the interviews lasted for 30 minutes.

Data transcription, coding and analysis

All the audio files were transferred from the digital recorder to the computer in an MP3 format. Then uploaded into the QRS Nvivo 12 Plus software. Audio files were assigned different numbers in a randomly to assure confidentiality of the participants. Transcription was done verbatim by two researchers. Content was analyzed in themes, then indexed and then coded inductively for emerging similar themes. The initial open codes were sorted into sub-themes based on their

similarity. These subthemes were clustered and refined to form broad themes. Open discussions were carried out to arrive at agreements regarding the themes. Based on current evidence, knowledge node responses were categorized into three. These were: accuracy of the response either it was correct, lacked an answer or severe misunderstanding. Under attitude nodes, the opinion of others was classified depending on the nature of the attitude as supportive, opposing or neutral. During the preparation of the protocol, creation of the coding system, interrater reliability and data analysis, consistency was observed guided by the Guba and Lincoln's criteria for determining rigor in qualitative research. For each group, two interviews were coded by two researchers to determine the degree of similarity by doing an interrater reliability statistic using the Nvivo software. The Kappa score result per theme was: knowledge 0.79, attitude 0.83, and practice 0.75.

Ethical issues pertaining human subjects

University of Eastern Africa, Baraton (UEAB) Research and Ethics Board in Kenya approved the study and a research permit granted by National Commission for Science, Technology & Innovation (NACOSTI) the License number was NACOSTI/P/20/6514. All the adult participants gave a written informed consent prior to the start of the interview while the parents and teachers signed the informed consent on behalf of the minors.

RESULTS

Part 1: National Policies to Prevent and Manage Cervical Cancer in East African Countries: A Policy Mapping Analysis

The documents obtained were policies, plans, guidelines, acts and strategic documents from Kenya, Uganda, Tanzania, Burundi, Rwanda, Eritrea, Ethiopia, Madagascar, DRC and Comoros with the exception of Somalia and Djibouti where no relevant documents were found. 24 documents were included and the comprehensive list. There were only 4 acts of parliament which are legally binding. Kenya had the most documents with Uganda having the second most. Using the SPSS software package, the Cohen's kappa (k) inter-rater reliability statistic was calculated. The quality appraisal score was moderate and this was acceptable for evaluation.

Overview of themes

The emerging concepts were grouped into parent nodes. then the nodes were further categorized into themes. Global burden, justification for regulation, epidemiology, risk factors, validity period, edition year, target group, screening, treatment, mitigation efforts, diagnosis and prevention were the parent nodes. The child nodes were grouped into themes which were screening, prevention, diagnosis and treatment, challenges and solutions. The screening theme had 7 child nodes with 96 references (the number of relevant text parts that were coded at a node) from 15 files. These child nodes were: cytology using Pap smear test, early screening and detection, HPV DNA tests, single visit see and treat (SVA) approach, VIA combined with cryotherapy, VIA and VILI. Prevention theme had 11 nodes with 75 references from 13 files. This theme was mainly inclined towards providing modalities that would abate exposure to the causes of CC and reduce individual susceptibility to the consequences of these causes therefore offering the definitive potential public health control of cancer which are efficient and cost effective[151]. The prevention theme had 11 nodes which included: abstinence from sexual exposure, adoption of healthy lifestyle, advocacy, being mutually faithful, capacity building, consistent condom use, creating awareness on cancer and reproductive health education, promote male circumcision, discouragement of tobacco use, VIA combined with cryotherapy and HPV vaccination. The diagnosis theme had 4 nodes with 27 references from 10 files which included colposcopy (n=5), cervical biopsy(n=6), cervical cytology (Pap smear) (n=4) and staging (n=3). The treatment theme had 7 nodes with 104 references from 13 files which included chemotherapy (n=9), cone biopsy (n=8), cryotherapy (n=9), curative surgery (n=12), hospice care (n=8), radiotherapy (n=13) and loop electrosurgical excision procedure (n=7). The challenges theme had 100 references and 17 files under 11 nodes which included: late stage detection (n=15), high cost of treatment (n=9), chronic diseases (n=3), lack of information (n=7), poor infrastructure (n=10), long waiting time (n=1), scanty records (n=6), low screening rates (n=2), socio-cultural issues (n=3), poor funding (n=3), uncoordinated screening services (n=2), lack of capacity (n=8) and lack of regulation (n=1). Solutions theme had 77 references from 17 files incorporated under 8 nodes which included, initiation of prevention, screening and management of reproductive organ cancer at all levels (n=6), development and implementation of a national cervical cancer prevention and control programs (n=6), establishment of appropriate surveillance strategies and integration of other national policy documents (n=6), training up of health officers on screening and treatment and deploying them (n=6). There were

additional and unique nodes mentioned one or two times like the scale up of screening and treatment of cervical cancer (n=5), coordination of activities and resource mobilization (n=4), cancer education and community mobilization strategies (n=2), and the continuation of the previous strategy (n=1).

Comparison of the national policies from East-African countries to the WHO Comprehensive Cervical Cancer Control guide to essential practice.

A majority of the East-African countries to be precise, Kenya, Uganda, Tanzania, Madagascar, Rwanda, Ethiopia, Burundi and DRC had adhered to the requirements. However, it was noted that the countries are yet to include HPV vaccination into their national immunization programs. Somalia, Eritrea, Comoros and Djibouti did not have any information on HPV vaccination. In 2011, Rwanda was the only African country that had the HPV vaccination program included in its national immunization schedule. Majority (n=9) of the countries had regular screening programs, however the link to treatment was a challenge. Slightly more than half (n=7) countries regulate the procedures for the treatment for precancerous lesions while only 6 countries had mentioned the treatment of invasive cancer. Our findings highlight that only 6 countries had referral mechanisms for patients with cancer of the cervix.

Part 2: Knowledge, Attitude and Practice of Main Stakeholders towards Human Papilloma Virus Infection and Vaccination in Mombasa and Tana-River Counties in Kenya: A Qualitative Study

From the sample analyzed majority of the respondents were women. Out of the 76 adults who were interviewed, 53 were women. The age ranges of the boys and girls was from 10 to 13 years, parents and health workers between 30 and 45 years while community leaders between 35 and 60 years.

Cervical cancer, HPV and HPV vaccination knowledge

Knowledge was summarized by 7 nodes which predominantly answered questions about knowledge. These questions were what is HPV, what is the goal of HPV vaccination, how is CC and HPV prevented, risk of catching HPV or cervical cancer, what is cervical cancer, what is cervix and what is the goal of Pap smear. The responses to these questions were considered as correct, lack of an answer and severe misunderstanding. Health workers gave correct answers while the children had the highest percentage of lack of an answer or severe misunderstanding. It was quite noticeable that the children lacked suitable biological knowledge to respond to some of the questions. The questions on the risks of catching HPV and CC, prevention of HPV and CC and the goal of HPV vaccination had high percentages of correct replies from the groups combined. Substantial proportion of reactions had severe misinterpretation for instance the question on what is HPV, 37% of head teachers, what is the goal of the HPV, 26% of the community leaders and what is CC, 57% of the children. The question on how to prevent HPV and CC received satisfactory responses in most of the groups i.e. 99% and 74% from the health workers and community leaders respectively. Many respondents struggled to respond to what is HPV. On the knowledge on the threat of catching HPV and CC, the responses were acceptable across all the groups. On what is cervical cancer, answers received were correct from majority of the adult respondents. The children (78%) stayed silent and were shy to respond. A few (19%) of the head teachers did not give correct responses. The question on objective of a Pap smear, from the questioned groups, the responses showed a moderate reaction from parents (66%), head teachers (63%) and community leaders (30%). All the respondents with the exception of health workers for obvious reasons were asked what is a cervix. More than half (61%) of the community leaders provided an accurate answer. Majority (78%) of the children went silent while the proportion of accurate responses from the others were head teachers (43%), parents (36%) and children (20%)

Attitudes towards HPV vaccination

This theme had 6 nodes which included, access to information, efficacy, safety, opinion of others, cultural and religious beliefs. Except opinion of others, these child nodes were connected to the attitudes and perceptions of the individual participants. To define the magnitude of these opinions, there was a further classification according to the nature of the attitude i.e. supportive, opposing or neutral. When asked on how the community's perception towards the introduction of the HPV vaccination, its acceptance and the inclination to participate in the HPV vaccination exercise, different reactions sufficed. A minority (n=13) of participants made reference to having no confidence in the efficacy of the HPV vaccination to prevent CC: *"...am not quite sure if it can work, because I have heard many controversies about it. There have been uncertainties of whether it can actually work"* (Participant 60, a parent). A significant (n=72) number of participants have no faith in the ability of the HPV vaccine's efficiency in boys owing to the fact that boys have no cervix: *"...it doesn't relate to the boys or do they also have ovaries"*. (participant 20, a head teacher. Another interviewee reiterated: *"...it something that they cannot get because maybe they don't have a uterus"*. (Participant 2, a community leader). There were numerous concerns about safety which consequently heavily influenced the attitudes as evidenced by the high number of references to it. From both counties, there was a uniform pattern of significant percentages of mentions about birth control misconceptions from all the participants including the children. Referring to how the community reacted, the following quote captured this opinion: *"...they rejected and sent false messages that the vaccines are for family planning and it would affect their children in many ways"*. (Participant 6, a community leader). Just like the majority of the participants on the misconception on the association of HPV vaccine and birth control in reference to what other girls from her class said, a girl voiced that: *"...yes, some said they do not want to be injected. Others said, the vaccine spoils the womb of girls"*. (Participant, a girl). None of the participants gave an account of having observed actual side effects after vaccination. When participants gave their perspective on the opinions of the others, the cultural and religious beliefs received many references as being a contributor of the opposition towards the HPV vaccination exercise. This was consistent in both counties. There was an observation that the culture of the locals was a great obstacle to the success of the HPV program: *"...in our community, culture, that is, is the biggest factor that has hindered. Because, they believe, the HPV vaccine, is to limit children, child bearing, that is, as in a child when she is older, they give her the vaccine so that,*

she does not have more children in the future”. (Participant 37, a community leader). The concern about faith was uniform and acknowledged by the different religious groups: “...you know mostly the people who are living in this locality are Muslims, family planning is prohibited in the holy Quran that is their perception”. (Participant 58, a community leader)

Recommendations to improve the uptake of HPV vaccine

This theme was classified into 7 nodes which comprised of consent process, COVID-19 pandemic, inclusion into the national immunization schedule, pre-vaccination preparedness, building capacity for health workers and community leaders, community involvement and sensitization.

On involvement of children, health workers and parents in the procedure to obtaining an informed consent, 37 interviews confirmed that these groups participated autonomously well-versed giving their approval to participate in the HPV vaccine exercise. It was evident that the girls were given information and their parents were engaged in the consent process: “...the students were called and they were told to bring their parents and their parents were talked to and they were given consent forms to sign which there are others that refused.” (Participant 12, a head teacher). The COVID-19 pandemic gravely affected the continuance of the HPV vaccination exercise following the abrupt closure of schools as directed by the government. All scheduled vaccination calendars in the health centers and county hospitals in collaboration with the primary schools were interrupted leading to delays in the consequent dose for the girls that had received the first dose: “...the COVID pandemic drew us back again because when we were in top gear trying to do dissemination of information that's when lockdowns came in, people are basically afraid to come to the hospitals”. (Participant 66, a health worker) Recommendations to promote sensitization drives was a suggestion given by many participants. A concerned parent articulated this: “...it would be good for the community to be sensitized so that they know the importance of the vaccine”. (Participant 70, a parent). Some participants endorsed the inclusion of the HPV vaccination to the national immunization program. They emphasized that this would potentially increase the uptake of the HPV vaccine since it would be made compulsory for all the eligible children: “...the government make it compulsory for every child to receive this vaccination. So if after policy is in place it will be everybody abide by it to make sure that the child is given this vaccination”. (Participant 63, a health worker)

DISCUSSION

Part 1: National Policies to Prevent and Manage Cervical Cancer in East African Countries: A Policy Mapping Analysis

Comparison of findings with literature

Great strides have been made by the East-African countries in the effort to eradicate CC. This was as evidenced by the prevention and control policies for cancer of the cervix that this research analyzed. It is quite impressive to note that since 1996, there was already a cancer act of parliament in Tanzania. Eighty-three percent was the extent to which the countries addressed issues of CC as recommended by the WHO blue print for prevention programs for cancer of the cervix. Screening women is the primary means to detect if a woman has any suspicious lesions then refer them for follow up to further examine if it is indeed a case of pre-cancer or CC. Colposcopy, cytology with Pap smear test, HPV DNA tests, SVA, VIA and VILI screening and treatment techniques as recommended by the WHO guideline for essential practice for control of the cancer of the cervix were echoed and emphasized by majority of the policy documents from the countries. These practices have been proven to have effective and efficient ability to lower the incidence of pre-cancerous lesions and CC. Literature has severally recommended use of VIA and VILI, because of their simplicity and promptness of availing instant results and needing less training to be able to utilize in the disadvantaged settings that have limited resources. SVA relies on visual inspection and as such is part of VIA and VILI hence scalable by women. The characteristic prolonged and delay in results while using cytology tests and HPV DNA techniques resulting in fragmentation of the link between screening and treatment contribute to the wide use of VIA and VILI in low resource settings. In these settings treatment by cryotherapy is done immediately in the event there is a case of suspicious or precancerous lesions. Several researches conducted in Africa have demonstrated that HPV DNA testing is largely costly however it is highly recommended owing to its sensitivity which is far much better than the one produced by cytology. The fact that CC is a potential preventable NCD, its prevention should be accentuated in the LMICs and under developed countries grappling with the CC menace. As a primary prevention for CC, HPV vaccination has proven to significantly reduce the CC burden and as such WHO has fervently advised countries to prioritize HPV vaccination programs and consequently include it in the national immunization schedules along with the other childhood immunizations. Several researches have made suggestions to make HPV vaccination compulsory because there is evidence

of its efficacy as such with the mandatory directive, there is a guarantee in increased vaccine uptake, reduced healthcare costs, decline in HPV related disease, and also an opportunity to save lives. Madagascar, Tanzania, Kenya, Ethiopia, Uganda and DRC out of the 12 East African countries had plans to introduce the HPV vaccine to prevent cervical cancer. Building capacity of health workers is critical because it cushions from wastage and capitalizes on execution of cost-effective cancer prevention and control approaches. From the analysis, most legal documents from the data set underscored that empowerment is essential by means of conducting collaborative seminars and workshops, pursuing medical education, training health practitioners, continuous updates and conducting research. Promoting cancer awareness and prioritizing sensitization of CC by mobilizing the masses and lobbying were some of the means recommended by most of the countries as they are vital components in cancer control programs. The policies emphasized on improving the knowledge and perception of CC by creating public awareness aiding in motivation of the populations in taking action as it also plays a big role in prevention. Depending on the stage of CC the treatment options include surgery, radiotherapy and chemotherapy according to rising stages. The diverse infrastructure and scarce resources have led to a great discrepancy between the developed and Africa countries. The developed countries have accessible advanced technology and personnel to implement the recommended and ideal treatment for CC while the countries in Africa where CC burden is high, are contending with vaccination and screening. Diagnostic and treatment advancement is still a distant attainment. From the findings of this research indicate that the treatment for pre-cancerous lesions in Africa are curative surgery which is hysterectomy and cone biopsy whereas for invasive CC is radiation, surgery and palliative care; this aligns with the conclusions of a study on the perspective of CC in the SSA countries.

Challenges and solutions towards addressing the burden of cancer of the cervix

Lack of information about CC and the shortage of preventive services are the main causes of late stage diagnosis of CC in SSA and as such, the late stage diagnosis was linked to low survival rates despite interventions with radiotherapy and surgery. Poor infrastructure that is characterized by unapproachability to the health centers for preventive and curative services, insufficient drugs and poor screening facilities. The poor screening facilities have inadequate human resource hence the low percentage rates of screening seen in these developing countries. Further lack of information also contributed to the low screening rates. The advanced stage diagnosis has been associated with the prolonged cytology results which causes a lapse and ultimately a loss to follow up of patients,

effective referral systems prevent the many cases of loss to follow up. As seen in the legal documents and evidence from literature, most countries cited lack of funding as a barrier to measures geared at preventing and controlling CC. The solutions that were vastly highlighted by the East-African countries insisted on initiation of prevention, screening and management of reproductive organ cancers at all levels of health care. Concerted efforts to develop and implement national cervical cancer prevention and control programs and integration of other national policy documents will greatly contribute towards the reduction of CC burden. Establishment of surveillance systems and empowerment of health workers through comprehensive training on screening and treatment then deploying them is a key contributor in scaling human resource for health. All the countries echoed that training new and existing health workforce is very critical in the control of CC because the staff will be more competent to handle activities in the cancer control programs. Undoubtedly reversing the CC burden requires extensive advocacy to drive prioritization, allocation of budget, resource mobilization and collaborations with essential stakeholders for passably response to the cancer crisis.

Need for evidenced-based health policies on cervix cancer prevention

From the legal documents analyzed in this study, there were scanty binding policies and inconsistency with the international guide whose role is provide a basis for developing CC policy documents. Public health policies have a major function on provision of evidence based solutions to overcome burden of CC. There was a uniform nonexistence or very limited data on morbidity and mortality of CC cancer from these countries hence the gap in making of policies that would strengthen the programs for prevention and control of CC. Capacity building for policy makers on integration of evidence to the agenda for health policy making to better inform the priority budget items touching on CC reduction hence narrowing the gap between evidence and policy. Strengthened surveillance systems, detailed registries and data linkages contribute to prioritized resource allocation tailored to the needs of a particular population thereby improving cancer outcomes. The scarcity of data across the East-African countries illuminates the unavailability of reliable data to assess the burden of cancer in the populations. The policy makers in East-African countries need to urgently intensify transparency of legislature and give priority to developing and implementing CC policies and amending old policies that never worked and still remain in force in so doing widening the gap between what is necessary and what requires to be implemented. From the findings, there were few policies, some outdated which mirrored the weaknesses in

addressing the CC crisis, binding and non-binding policies are crucial in addressing the public health agenda, therefore there is need for scientifically sound policies and their executive laws for there to be evident change.

Part 2: Knowledge, Attitude and Practice of Main Stakeholders towards Human Papilloma Virus Infection and Vaccination in Mombasa and Tana-River Counties in Kenya: A Qualitative Study

This study provides information on the factors that are leading to poor uptake of HPV vaccination in two counties in Kenya. It was worth noting with the exception of the health workers, a substantial percentage of the adult participants in this study had inadequate information and knowledge on the key issues that were being evaluated. Children had little or no knowledge about what CC and HPV infection and HPV vaccination however, it is important to note that the children were part of the process of obtaining a consent and making a choice on the vaccination. It was not surprising to hear of the numerous unreasonable and illogical fears and distorted information prevailing among the community members. A high proportion of the participants were not in favor and did not support boys being a target for the HPV vaccination. In general, the parents and community members who are great influencers for positive feedback to the vaccination exercise did not express solidarity. On the other hand, head teachers, health workers and community leaders voiced their full support and expressed recommendations to improve the uptake of the vaccine and mend the negative impression among community members. From both Mombasa and Tana-River counties, there was a uniform observation in most of the emerging themes such as scanty knowledge and intense opposing attitudes.

Integration with prior work, implications, transferability and contribution to the field

From a majority of the interviewees, their experience was that they had previously heard a thing or two about CC or HPV; but when it came to recalling and giving answers, they vaguely responded or said they do not recall what they had learnt. Some participants also uttered that they hardly heard about Pap smear. A good proportion of participants were cognizant of the fact that the HPV vaccine confers protection against cancer of the cervix. On the risk of catching HPV infection and CC, the participants were acquainted with the knowledge that there was a high probability of catching both, particularly for the reason that there is early onset of commencement of sexual activity and having several sexual partners. There is an urgent need to carry out

awareness drives and make the vaccines readily available to attain the desirable levels of vaccine acceptability; since the introduction of HPV vaccines in 2006/2007, great support has been accorded to the LMICs to empower women by educating them. Some health workers demonstrated gaps in knowledge, however from our findings, there was proof of information that was obtainable through seminars and workshops that the health authorities facilitated. The information provided to the parents and girls was substandard. For the effective implementation of the HPV vaccination program, it is commended that a series of trainings and information dissemination campaigns be accelerated. Promoting training and communication of health workers significantly contributes to the effectiveness of the vaccination campaigns. A high proportion of the participants implied and associated the HPV vaccine as a means of birth prevention or depopulation purporting that it was laced with contraception to sterilize the young girls. This was the most common misinformation about the HPV vaccine among the community members and highly hindered the uptake of the vaccine. Some religious leaders who are highly influential in the community propagated this erroneous information initiating extremely hostility when it came to passing the accurate information on HPV vaccination to the community members; this finding is in line with Otieno et al. These ambiguous and biased information is detrimental as it gives the health workers the double task to drive the correct HPV vaccination messages to the populace. A number of children were not vaccinated or did not complete the doses. Diverse explanations were fronted comprising of unreasonable fear of the unknown vaccine, deviance from culture, non-conformity to traditional customs, negative influence from the community members, husbands giving stern warnings to their wives not to vaccinate the girl child, bizarre beliefs for example the vaccine was an indoctrination to illuminati. This study concluded that the HPV vaccination landscape has extremely been informed by the religious and cultural beliefs and endorses wiggle et al. and Grandahl et al. A substantial proportion of the participants articulated their disapproval in vaccinating the boys citing the anatomy of the boys has no cervix nor CC a disease affecting men therefore it was useless to vaccinate the boy child. Some participants responded with a question whether the boys had a cervix or a uterus. These responses portrayed insufficient knowledge base concerning HPV infections and the diseases it causes as revealed in a research in the UK probing on HPV vaccination in boys. Another proportion recommended the HPV vaccination to be prioritized to the girls then at a later opportunity expand the program to involve the boys; this finding corresponds with an exploration on the knowledge and intentions among parents of boys

and girls in US shared their thoughts that it was crucial to vaccinate girls than the boys. Generally, the responses on vaccination in boys were opposing and many participants connected the HPV vaccination with the girls owing to its goal being to exclusively prevent cancer of the cervix; as indicated in literature, this is a common observation among the community members. By and large in both counties, the parents and members of the community uniformly opposed the HPV vaccination exercise. This trend has commonly been observed in some studies where the vaccination controversy was conspicuous among community members have alluded their disapproval to inexplicable fears and apprehensions. Addressing these concerns and arguments by competent health workers by steering vigorous community discourses heavily involving the community members, these dialogues will be successful only after building the capacity of health workers and community leaders as these stakeholders are the drivers of distributing health messages to the community another reason is that they are already known in the community and have built trust and created rapport with the members of the community. The findings of this research indicated that the parents and children were actively part of the consent process. The nurses reported that the adolescent girls displayed no hesitancy on being vaccinated; this somewhat is in agreement with a South African study on factors influencing vaccine uptake however in contrast the nurses had no struggles starting conversations surrounding sex with the adolescent girls as compared to the findings of this research. The COVID-19 pandemic severely interfered with the implementation of the HPV vaccination exercise. The challenges affecting the acceptability of the COVID-19 vaccine because of the safety concerns were a great contributor. The HPV vaccine is yet to be incorporated into the national immunization schedule. The health workers expressed it as a concern that would greatly drive the HPV vaccine agenda in the community curtailing the forgetfulness to return for the second doses and hostile reception. From literature it was recommended that nations expand their national immunization budgets to cater for the adoption of the HPV vaccine to the routine immunization programs. Vaccine acceptancy will highly benefit from involving the community and organizing pre-vaccination preparedness. This was highly recommended by the participants especially the community leaders and health workers whose responsibility was to enlighten the population about the HPV vaccination exercise.

Implications and limitation of the study

From this study findings, the hurdles that are ailing the HPV vaccination acceptability from two counties in Kenya. The uniform patterns observed from the two counties can be generalized to the

entire country because the sample was a representative of the composition of the Kenyan population which is not too diverse. The recommendations by the health workers and community leaders to have concerted strategies to sensitize the community and also involve them in the HPV vaccination awareness drives was an optimistic gesture. Having conducted the interviews in only two counties of Kenya owing to budget and time constraints this was a limitation of this study. Selection bias is a characteristic of this study due to the nature of the methodology used hence the may affect the interpretation of the data. The groups had a handful number of interviewees and this is because a minimum sample of 12 reaches saturation of data.

RECOMMENDATIONS AND CONCLUSIONS

This research adds its voice to the existing body of knowledge on the state of CC policies in East African countries and the low HPV vaccination uptake in Kenya. Governments make knowledgeable decisions for health on the basis of gaps identified from policy mapping. Legal mapping in the health sector is crucial as it is a pointer of the gaps in the health system impeding the realization of the objectives to reduce the burden of cancer in SSA and also provides beneficial information to the stakeholders of policy making. There is an urgent need to perform periodic reviews of old and outdated cervical cancer policies to incorporate new innovations and latest evidence based best practices additionally, guaranteeing transparency to legal information in the East African countries. Lack of capacity remains an important challenge to implementing the programs to prevent and control cancer of the cervix in these countries and as such the mismatch between policy and practice needs to be looked into. East African countries need to combine their efforts in fighting the CC scourge by prioritization in budgeting, enhanced accountability and pooling of funds to sustain the HPV vaccination and CC prevention and control programs. HPV vaccination drives will be successful with rigorous community involvement in creating awareness by modifying the negative attitudes and promoting vaccine perceptibility. Campaigns to reach the children, parents and teachers are vital because they are the implementers and promoters of the HPV vaccine; their perception is very important as it shapes the vaccination landscape and they are the point of contact to the children and often they are in opposition of the vaccination based on the many fears. Studies in the future should pay attention to large scale awareness creation and education on HPV infections, HPV vaccination and CC and innovative techniques to deliver the critical information to the populace.



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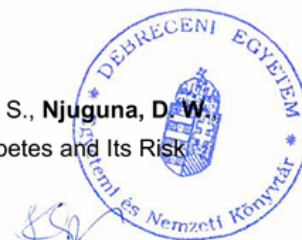
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List of publications related to the dissertation

1. **Njuguna, D. W.**, Mahrouseh, N., Isowamwen, O. V., Varga, O.: Knowledge, Attitude and Practice of Main Stakeholders towards Human Papilloma Virus Infection and Vaccination in Mombasa and Tana-River Counties in Kenya: a Qualitative Study.
Vaccines. 9 (10), 1-16, 2021.
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IF: 4.422 (2020)
2. **Njuguna, D. W.**, Mahrouseh, N., Onisoyonivosekume, D., Varga, O.: National Policies to Prevent and Manage Cervical Cancer in East African Countries: a Policy Mapping Analysis.
Cancers (Basel). 12 (6), 1-16, 2020.
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List of other publications

3. Mahrouseh, N., Andrade, C. A. S., Kovács, N., **Njuguna, D. W.**, Varga, O.: Diabetes Mellitus and Associated Factors in Slovakia: results from the European Health Interview Survey 2009, 2014, and 2019.
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4. Lovas, S., Mahrouseh, N., Bolaji, O. S., Nellamkuzhi, N. J., Andrade, C. A. S., **Njuguna, D. W.**, Varga, O.: Impact of Policies in Nutrition and Physical Activity on Diabetes and Its Risk Factors in the 28 Member States of the European Union.
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