ACCEPTABILITY OF THE HUMAN PAPILLOMAVIRUS VACCINE AMONG RURAL AND URBAN WOMEN IN THE KILIMANJARO REGION, TANZANIA

by

Melissa Susan Cunningham

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Abstract

**Background:** Cervical cancer is a global disease with a disproportionate burden among low- and middle-income countries. In Tanzania, cervical cancer is the most common female cancer and a prophylactic vaccine offering protection against four human papillomavirus (HPV) strains is a promising prevention method. The targeted age and sex, as well as the sexually transmitted nature and novelty of the vaccine, support the need for formative research on the knowledge, attitudes, and barriers toward vaccination.

**Objectives:** The first objective of this thesis was to systematically review studies of HPV vaccine acceptability among African countries. The second and third objectives were to describe and determine the socio-demographic factors and HPV-related knowledge and attitudes associated with HPV vaccination and to identify the barriers to vaccination among a population-based sample of rural and urban women in the Kilimanjaro Region of Tanzania.

**Methods:** The literature was systematically reviewed by searching electronic databases, and a data abstraction form structured by the Health Belief Model was used to collect data and synthesize findings. For objectives 2 and 3, a cross-sectional study was conducted among rural (n=303) and urban (n=272) women aged 18-55. Differences in socio-demographic factors, knowledge, attitudes, and barriers were compared between groups, and multivariable models were used to identify associations among rural and urban women separately.
Results: Reviewed literature suggested that HPV vaccine-related knowledge was low, however predicted acceptance of the vaccine was high. Research on this topic was largely composed of cross-sectional studies in urban areas. Among rural women in the Kilimanjaro Region, independent associations with acceptance included variables related to cost, knowledge, access, and educational attainment. Among urban women, independent associations were related to social networks/norms and educational attainment. The most frequent perceived barriers to vaccination were cost, side effects, and safety.

Conclusion: Educational programs on the HPV vaccine and cervical cancer are needed in Tanzania and in other areas of Africa. This research suggests that vaccine campaigns in the Kilimanjaro Region should focus on emphasizing financial and physical accessibility, peer acceptance, and safety, in addition to highlighting endorsement of the vaccine by healthcare providers and the government.
Co-Authorship

This thesis represents the work of Melissa Cunningham in collaboration with her supervisors Dr. Kristan Aronson and Dr. Jennifer Carpenter.

Manuscript 1: “HPV vaccine acceptability in Africa: a systematic review of the literature”

The review was completed by Melissa Cunningham with guidance and editorial feedback from Dr. Aronson.

Manuscript 2: “Attitudes and socio-demographic factors associated with HPV vaccine acceptability among rural and urban women in the Kilimanjaro Region, Tanzania”

The “Prevention of Cervical Cancer in the Kilimanjaro Region of Tanzania” research initiative was led by five co-investigators (Drs. Karen Yeates, Jennifer Carpenter, Kristan Aronson, Christopher Booth and Olola Oneko) and four students (Melissa Cunningham, Emily Skrastins, Priya Jindal and Ryan Fitzpatrick). All co-authors assisted in the conceptualization and design of the cross-sectional survey. Supervision in Tanzania was provided by Dr. Olola Oneko. Fieldwork was executed by Melissa Cunningham, Emily Skrastins, Ryan Fitzpatrick and Priya Jindal with several Tanzanian research assistants. Data entry and database management was completed by Melissa Cunningham and Emily Skrastins. The statistical analysis, interpretation and writing of this manuscript was conducted by Melissa Cunningham with guidance and editorial feedback from Dr. Aronson and Dr. Carpenter.
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<tbody>
<tr>
<td>CHF</td>
<td>Community Health Fund</td>
</tr>
<tr>
<td>CIN</td>
<td>Cervical Intraepithelial Neoplasia</td>
</tr>
<tr>
<td>DHS</td>
<td>Demographic and Health Survey</td>
</tr>
<tr>
<td>EPI</td>
<td>Expanded Programme on Immunization</td>
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<tr>
<td>GAVI</td>
<td>Global Alliance for Vaccination and Immunization</td>
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<td>GNI</td>
<td>Gross National Income</td>
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<td>HBM</td>
<td>Health Belief Model</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>HPV</td>
<td>Human Papillomavirus</td>
</tr>
<tr>
<td>KCMC</td>
<td>Kilimanjaro Christian Medical Center</td>
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<tr>
<td>MoHSW</td>
<td>Ministry of Health and Social Welfare</td>
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<tr>
<td>OR</td>
<td>Odds Ratio</td>
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<tr>
<td>SAS</td>
<td>Statistical Analysis Software</td>
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<tr>
<td>STI</td>
<td>Sexually Transmitted Infection</td>
</tr>
<tr>
<td>TSH</td>
<td>Tanzanian Shillings</td>
</tr>
<tr>
<td>TRA</td>
<td>Theory of Reasoned Action</td>
</tr>
<tr>
<td>UN</td>
<td>United Nations</td>
</tr>
<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
</tr>
<tr>
<td>VIA</td>
<td>Visual Inspection with Acetic acid</td>
</tr>
<tr>
<td>VILI</td>
<td>Visual Inspection with Lugol’s Iodine</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Chapter 1

General Introduction

1.1 Scope of the introduction

The focus of this thesis is on the acceptability of the human papillomavirus (HPV) vaccine in the Kilimanjaro Region of Tanzania, if it were to be made available, and the factors associated with vaccine acceptance. This chapter is a brief introduction to the literature and study setting, presented in order to provide foundational knowledge for this thesis. The focus is on low-income countries and in particular, Tanzania, Africa. The section begins with some key definitions followed by background on cervical cancer, including the disease burden, risk factors and preventative methods, with an emphasis on human papillomavirus (HPV) vaccination. As an introduction to acceptability and vaccination intentions, health behavioral theory is presented. The section ends with an introduction to Tanzania including the demography, the health system and urban-rural contexts. Following this summary, the thesis rationale, objectives and organization are presented.

1.2 Key definitions

Countries that are referred to as low-resource, developing, or less-developed are to define areas that have a low national income (Gross National Income, GNI) and along with this, a lack of infrastructure including health and social services (e.g. education, investment in water, sanitation or energy), and high population growth (1). These
countries have low rankings on the United Nation’s Human Development Index, and generally consist of countries from Africa, South America and parts of Asia (2). Countries referred to as high-resource, developed or more-developed, are to define areas that have higher national incomes, robust health and social services, and lower population growth rates. Generally, countries from North America and Europe, and Australia fall into this category (2).

In this thesis, several comparisons are made between rural and urban areas and these will be described in the coming sections. In parts of this thesis, women have been labeled as ‘rural women’ or ‘urban women’, however this title is not meant as an all-encompassing definition or judgment. More accurately, ‘rural women’ refer to women living in rural environments, while ‘urban women’ refer to women living in urban environments; specifically, these are the two surveyed groups in the survey results. The descriptions of the women, rather than the labels, are used whenever possible.

Acceptability or acceptance of a vaccine in this thesis refers to a reported/predicted willingness and intention to receive a vaccination, and not actual uptake. This is a key concept for this thesis.

1.3 The burden of cervical cancer

According to the World Health Organization (WHO), cervical cancer is the third most common cancer among women worldwide, with approximately 500,000 cases occurring annually. Based on population growth rates alone, this number is expected to rise and reach 720,000 by 2025 (3). Around 86% of incident cases occur in low-
middle-income countries, representing a large inequity in the burden of this disease (3). Furthermore, 88% of the 275,000 women who succumb to cervical cancer live in low-income countries and die at ages younger than their developed comparators (3).

African countries have some of the highest rates of cervical cancer incidence and mortality in the world (4). In Tanzania, a country in East Africa, cervical cancer is the most common female cancer with an estimated age-standardized incidence rate of 51 per 100,000 women per year, a rate nearly five times higher than the rate of the next most common cancer among both sexes combined (5). Due to the late stage at diagnosis and lack of treatment, the age-standardized mortality rate is also high, at 38 deaths per 100,000 women per year (5).

Similar to other sub-Saharan African countries, Tanzania is now facing a double burden of disease with the rise in prevalence of non-communicable diseases such as cancer, competing for resources with communicable diseases (6). This can be quantified by comparing the causes of death using age-standardized death rates; in 2002 these were distributed in the following way (cause per 100,000 deaths): 1,344 communicable diseases (including 593 from HIV/AIDS), 847 non-communicable diseases (including 151 from malignant neoplasms and 435 from cardiovascular diseases), and 114 injuries (7).

1.4 Cervical cancer etiology

Development of cervical cancer can be considered the end result of a four-step process: human papillomavirus (HPV) infection/transmission, viral persistence,
progression of a clone of persistently infected cells to precancer, and invasion (8).

Infection with HPV is a necessary, but not sufficient, cause of cervical cancer. Over 100 variants of HPV have been identified, 40 of which infect the genital region, and these have been further divided into high and low-risk types on the basis of oncogenic potential (9–11). Type distribution has been shown to vary regionally, as well as between cervical cancer subtypes (squamous cell carcinoma and adenocarcinoma) (3). The eight most common HPV types detected in women with invasive cervical cancer, presented by decreasing prevalence are: HPV 16, 18, 33, 45, 31, 58, 52 and 35 (3). Importantly, HPV strains 16 and 18 are responsible for approximately 70% of invasive cervical cancer cases worldwide. HPV strains have also been implicated in other benign lesions, with HPV 6 and 11 responsible for 90% of genital wart cases. Although the various types have been identified, more research is needed on the modifying effects of HPV genotype, viral load, integration, and co-infection on risk estimates (8,12).

Infection with HPV can occur in both men and women via skin-to-skin or mucosa-to-mucosa contact, usually through sexual intercourse. Most infections are transient, and 90% will be cleared by a healthy host’s immune system or enter a latent phase within 1–2 years of exposure (13,14). The disease progresses slowly through precancerous conditions – cervical intraepithelial neoplasia (CIN 1, 2, 3) – and research suggests that it could take anywhere from 20–40 years to develop invasive cervical cancer once infected (15).

1.4.1 Risk factors for cervical cancer
Although necessary, HPV infection is not a sufficient cause for cervical cancer, as there are individual and behavioral risk factors that modify progression of the disease. The risk factors for cervical cancer are established in two areas: those that increase or decrease the probability of being infected with the virus and those that modify the probability that the infection will progress and develop into cancer. In terms of transmission of the virus, sexual behavior is a key determinant (16). A reduction in the risk of transmission can be modified through exposure-reducing behaviors, such as limiting the number of sexual partners, particularly those who would be considered high-risk, and a late age at first sexual activity. Other factors to reduce risk include male circumcision, condom use, and genital hygiene (12,17).

In addition to sexual behaviors, individual factors associated with increased risk of cervical cancer development include high parity, smoking, suppressed immune function and nutritional factors (12,17). The most convincing risk factor is for the multiplicative effect of smoking. Other risk factors, such as intake of micronutrients, is less convincing with literature presenting conflicting conclusions (12). Mechanisms for these risk factors have been postulated, invoking the modifiable nature of the cervix (e.g. changing through development or child-bearing) to explain how HPV can infect and persist, however more research is needed to explain this mechanism (8).

Suppressed or reduced immune function is especially important in developing countries where the high prevalence of HIV/AIDS and other sexually transmitted factors (i.e. herpes simplex virus 2, Chlamydia trachomatis) increase the contribution of these risk factors in comparison to the developed world (12,17). It has been shown that the HIV epidemic is a contributor to the burden of cervical cancer in sub-Saharan Africa (7). In
Tanzania, HIV prevalence among adults (age 15–49) was estimated at 5.8% in 2011 (18), which is a moderate proportion compared to the prevalence range of 0.61–25.86% across African countries (19).

1.5 Cervical cancer prevention

Cervical cancer prevention efforts can be categorized as primary, secondary, or tertiary. Primary prevention is focused on preventing disease from occurring, while secondary prevention prevents a covert disease from progressing. Finally, tertiary prevention aims to lessen the burden of disease once overt symptoms are present.

Organized, cytology-based screening methods using the Papanicolau (Pap) smear have diminished the burden of cervical cancer in much of the developed world by 50–70% over the past 50 years (20). The Pap smear screening method involves examining cells sampled from the cervix under a microscope for abnormalities. In high-resource countries screening rates are fairly high; a review among 57 countries estimated a crude screening coverage of more than 90% (21). In low-resource settings, cervical screening rates are much lower; in Africa, population screening coverage ranges from 0.2–20.2% (22). Unfortunately, the current technological and personnel resources do not support the widespread use of this prevention method in much of sub-Saharan Africa, including Tanzania.

There are two lower-resource screening tests available: visual inspection by acetic acid (VIA) or visual inspection by Lugol’s iodine (VILI). In low-resource countries, where patients are often lost to follow-up, a single-visit ‘see-and-treat’ approach is used
with these inspection methods. Health professionals are able to view precancerous/cancerous cells after application of a solution (acetic acid or Lugol’s iodine) followed by treatment with cryotherapy or excision, in eligible patients. VIA has been shown to have a sensitivity and specificity of 60–94% and 74–94%, and VILI, 90–97% and 73–91%, respectively (22). The ranges are indicative of the dependency on the health professional’s training and skills, and the variability on the choice and quality of reference standard used for comparison (23). The use of methods involving testing for HPV DNA have also been considered for low-resource environments. There are cost-effectiveness analyses in the literature weighing the potential of programs that use HPV DNA testing, VIA or cytology, or a combination of these methods (24,25); one analysis estimated a reduced lifetime risk of cancer by 25–36% with a single screening involving VIA or HPV DNA testing at age 35 (24). Promisingly, a trial of 132 000 women showed that a single round of HPV DNA testing significantly reduced cervical cancer incidence compared to those receiving VIA, conventional cytology, or standard care after 8 years follow-up (26). While these methods are clearly useful, the potential for reducing the burden of cervical cancer is expected to be greatly increased if it were combined with primary prevention measures – vaccination, abstinence and reduction of risk factors (27).

1.6 Human papillomavirus (HPV) vaccine

In 2006, two prophylactic vaccines became available: one bivalent (Ceravix®), immunizing against strains 16 and 18, and another quadrivalent (Gardasil®), providing additional immunity against two genital wart strains, HPV 6 and 11. These prophylactic
HPV vaccines work by priming the immune system to produce virus-neutralizing antibodies by mimicking infection with HPV using recombinant virus-like particles (28). They are indicated for use in three-dose schedule, usually over a period of six months (0, 2 and 6 months). As a prophylactic vaccine, the ideal time to vaccinate is before first sexual experience, although the vaccine has been approved for use beyond the average age of sexual debut (29). The vaccine has been licensed for use in more than 60 countries (30); in the US, Gardasil has been approved for use by the Center for Disease Control among females and males aged 9–26 for the prevention of cervical and penile cancers, and other HPV-related diseases including anal, and oropharyngeal cancers, and genital warts (31,32). In Canada, Gardasil is approved for use over a greater range of ages among females (ages 9–45), and similarly approved for use in males aged 9–26 (29).

Both vaccines have been shown in clinical trials to be nearly 100% efficacious in preventing the incidence of precancerous lesions (33), and a recent review reaffirmed safety of administration in females and presented arguments to refute safety concerns surrounding adverse reactions or chronic and autoimmune diseases (34). That said, controversies exist around slogans and campaigns that suggest these vaccines prevent cervical cancer, with adversaries citing that precancerous stages, CIN2/3, as study proxies for cervical cancer, are not sufficient (15). Furthermore, due to the short duration of studies, the lasting immunity and long-term effects are largely unknown. There are also concerns regarding safety of administering the vaccine in those who are already infected with HPV (15). From a social perspective, the vaccine has faced concerns from parents on its effect on teenage sexuality, and alignment with religious beliefs (35–37). These safety concerns should be made clear to all participants of vaccination programs. For
many low- and middle-income countries, routine health services that target this age group do not exist, and the targeted sex and sexually transmitted nature of the virus necessitates additional sensitivity and education.

1.6.1 Use in high-resource countries

The HPV vaccine is administered as part of national immunization programs in North America, Australia, Europe (19 of 29 countries in the European Union), and others (38). The age of vaccination is not uniform across countries, nor are the delivery models or financing methods. Immunization coverage with this vaccine has proven to be highly variable. In 2012, US coverage with the vaccine was 54% (≥1 dose, girls 13–17)(39), among countries in the European union, coverage ranges from 17–84% (various ages, 9–18)(40) and in Australia, in 2011, three dose coverage estimates were close to 70% for all states (41). In Canada, each province is responsible for administering the vaccine (42), and coverage with the first dose ranged from 85% in Newfoundland, to 53% in Ontario (43), in the first cohort of vaccination.

The lower expected benefit, and therefore cost-effectiveness of vaccination, in high-resource countries has been used in arguments by critics against widespread vaccination. Although media attention has recently driven an increase in perceived personal risk, with regular screening and typical behaviors the risk of cervical cancer is quite low (15). HPV infection has been shown to be higher among ethnic minorities that have low incomes and low levels of education (44), however uptake of the HPV vaccine has been largely among those who are of higher socioeconomic status and have high rates of health care utilization (45). Thus, it has been hypothesized that girls who are choosing
to be vaccinated are also those who will follow Pap testing guidelines, engage in less risky behavior, and are therefore likely to benefit the least from vaccination.

**1.6.2 Use in low-resource countries: Tanzania**

Implementation of any new vaccine requires consideration of both programmatic and policy issues (46). Introduction of the HPV vaccine in low-resource countries poses significant challenges for health service infrastructure, programming and presentation. The HPV vaccine will be the first vaccine to target an adolescent age group in Tanzania, since all current vaccines are administered during the first year of life (47). The age group targeted for vaccination, 9–13, represents a group that is often neglected, with few, if any, public health programs operating between childhood and adulthood. It has been noted that interaction with this group should also include other health education initiatives (i.e. HIV, nutrition, sexual and reproductive health) (35), and it may be an opportune time to promote cervical cancer screening and prevention methods for older women.

The Global Alliance for Vaccines and Immunization (GAVI), acts as a centralizing body for vaccination programs such as Tanzania’s, combining the financial and personnel resources of key stakeholders including the Bill and Melinda Gates Foundation, WHO, UNICEF and the World Bank. In June 2011, a deal was negotiated with Merck & Co to reduce the cost of the vaccine to GAVI-eligible countries (<$1500 USD Gross national income per capita) to $4.50/dose (48). With this price reduction, the financial barriers to implementation become less impactful, and through GAVI support the co-financing required by eligible countries can be as low as $0.20/dose (3). Still, the HPV vaccine would become the most expensive vaccine administered in Tanzania; costs
associated with current vaccines are as little as $0.25 for 10 doses (47). Total cost requirements have been enumerated and evaluated using the WHO’s Cervical Cancer Prevention and Control Costing (C4P) Tool for Tanzania (49); with a five-year phased, class-based introduction model the program is cost-effective and estimated to amount to 31.5 million US dollars.

The vaccine has been piloted on a small scale in parts of sub-Saharan Africa (38), with support largely provided by the Gardasil Access Program funded by Merck & Co. (50). Rwanda is the only African country with a national HPV vaccination program and has proven to be highly successful (93.2% three-dose coverage) in its first rollout of a school-based delivery program to 93,888 grade 6 girls (51). With the same reduction in price announcement, GAVI announced support for eight countries to pilot the HPV vaccine, including Tanzania, beginning within 2013–2014. The first of these projects was launched in May in Kitui County, Kenya with the targeted vaccination of 20,000 girls at primary schools (52).

Robust immunogenicity research among African populations are lacking, and this is concerning given the high prevalence of particular risk factors and other co-infections. Research in North America among HIV-infected children aged 7–12 suggested that the quadrivalent vaccine was safe and effective among this group, although differences were found in final antibody titer (53). HPV strain distribution has been shown to be slightly different in the Tanzania population, with HPV 52 as the most prevalent, followed closely by HPV16 (54). As a result, even with maximal uptake protection in this population may not be as high as that found in worldwide estimates.
1.7 The Health Belief Model (HBM) as a theoretical framework for vaccination behavior

The Health Belief Model (HBM) (55) is one of the most common theoretical frameworks used to explain health behaviors, including vaccination intentions, along with the Theory of Reasoned Action (TRA) and social cognitive theory (56). These frameworks have many similarities and can be shown to map onto each other, although there are important differences and some have been used more favorably to study particular health behaviors (57,58). Poss (2001) has suggested a synthesis of the HBM and TRA for understanding health behaviors in cultural settings that are distinct from the USA (59), and has outlined some of the differences between the HBM and TRA, for example, the TRA’s consideration of a normative component surrounding behaviors and beliefs.

The HBM is focused largely on individual perceptions and is divided among five constructs: perceived susceptibility, perceived severity, perceived benefits, perceived barriers and cues to action. Perceived susceptibility refers to the individual’s perception toward the likelihood or risk of the outcome, while perceived severity focuses on the perceptions of threat or seriousness. Perceived benefits can include perceptions of efficacy if a course of action were taken, while perceived barriers are negative beliefs or obstacles that impede a course of action (59). In this thesis, and as noted by experts on the Health Belief Model (55), perceived self-efficacy barriers may be included in the overall perceived barriers construct. Finally, cues to action include internal (e.g. symptoms) and external stimuli (e.g. media) that trigger performance of the behavior.
The HBM has been used and proven useful for predicting vaccination behavior for other vaccines such as influenza, swine flu and hepatitis B (60–62), in addition to being used review predictors of HPV vaccine acceptability from studies in the US (63). The systematic review presented in Manuscript 1 is similar to the latter, and is also structured by the HBM. The findings presented in Manuscript 2 from a cross-sectional study were based on a survey designed using knowledge of the HBM and TRA, in addition to other resources.

1.8 Introduction to the Kilimanjaro Region of Tanzania

Tanzania is a country with a population of approximately 45 million located in East Africa, bordered on the eastern side by the Indian Ocean (64) (Appendix A). Tanzania ranks 152 of 187 on the Human Development Index, a development measure by the UN that is composite of health, education and living standards.

The Kilimanjaro Region located in Northern Tanzania, is one of 30 regions with a population estimated at nearly 1.64 million (64). It is divided into six districts: Rombo, Mwanga, Same, Hai, Moshi Rural/District and Moshi Urban/Municipal. Moshi Urban is divided into 21 wards, with an estimated population of 184 292, while Moshi Rural has an estimated population of 466,727, divided among 31 wards (150 villages). Two hospitals serve this area, the private, Kilimanjaro Christian Medical Center (KCMC), and public, Mawenzi Regional Hospital, in addition to 18 smaller, regional hospitals and 32 health centers and 332 dispensaries (65).

1.8.1 Health system
Tanzania is composed of both public and private health facilities, from lowest to highest these include: dispensaries (serving 6,000–10,000 people), health centers (serving 50,000 people) and regional/district hospitals. Above this, there are four referral hospitals and four specialized hospitals. The majority of vaccines are stored at dispensaries (66) however it is clear that immunization infrastructure needs to be improved; an assessment of current facilities found that 46% did not have all the necessary components for adequate temperature monitoring, and the majority needed to improve stock monitoring (66).

Tanzania’s Ministry of Health and Social Welfare (MoHSW) implements its vaccination program through the Expanded Programme on Immunization (EPI), a program founded by the WHO in 1974. Through this program Tanzania has targeted six diseases since 1996, namely: diphtheria, measles, pertussis, poliomyelitis, tetanus and tuberculosis (49). Uptake of these vaccinations across Tanzania has been high, with 75% coverage of children aged 12-23 months (67). A small sample (n=33) on coverage in the Kilimanjaro Region indicated that vaccine uptake in this area was also very high (94%) (67). This can be considered an indication that the infrastructure for widespread vaccination is possible provided that there is a high acceptability rate. Of note, vaccination coverage in Tanzania was higher in rural areas compared to urban (86% vs. 73%, respectively), and among children whose mother was highly educated (88% More than Secondary vs. 63% No education) (67).

Healthcare spending is composed of public (28%), private (28%) and donor sources (44%) (68). Out-of-pocket spending as a percentage of total health spending for Tanzanians was 23.1% in 2005/6 (68). Health insurance options consist of community-
based programs such as the Community Health Fund (CHF) in rural areas, TIKA (Tiba Kwa Kadi) in urban areas, and the National Health Insurance Fund for civil servants, as well as private for-profit insurers, and other micro-insurance schemes (community and private)(68). The National Health Insurance Fund is mandatory for public servants, requiring a 3% salary contribution that is matched by a 3% government contribution. This insurance covers the employee’s spouse and a maximum of four dependents; 6% percent of Tanzanians are covered by this insurance fund, amounting to 1.63 million people in 2007 (68). Community-based programs (CHF and TIKA) are voluntary and contributions are matched by the government; typical premiums amount to 5,000-15,000 Tanzanian Shillings (TSH), per household per year (68). The included health services for these programs vary, and care is provided at selected facilities. Although the program has been available for nearly 14 years, uptake of the CHF among eligible households has been low (4-18%)(68). As alternatives to these programs, Tanzania has five private health insurance companies supervised by the Tanzania Insurance Regulatory Authority; less than 1% of the population is covered by this method. At the present time, it is unclear if the HPV vaccine will be covered by any health insurance scheme for those who are not in the targeted age range (9-13).

1.8.2 Rural and urban context

Importantly, over 70% of the population in Tanzania (nearly 30 million people), reside in rural areas that are poor (18). Although this is the majority of the population, an understanding of urban areas is also important, especially given trends of urban expansion, and an understanding that the rise in prevalence of non-communicable
diseases are found among urban areas first (69). In Tanzania, the urban population has been expanding, estimated at 5% in 1960, and 24% in 2005 (70).

The 2012 Population Census indicated that the Kilimanjaro Region had a population density of 124 people/km², however there was large variability within the region. Moshi Urban, encompassing 58 km², was estimated to have a density of 3177 people/km², a density similar to Tanzania’s capital (Dar es Salaam, 3133 people/km²)(64). Moshi Rural encompasses a much larger region (1713 km²), and was estimated to have a density of 272 people/km² (64).

Some general characteristics can be defined for rural and urban households in Tanzania using the 2012 Population and Housing Census (64). Urban residences are more likely to have an improved source of water suitable for drinking (81% urban, 46% rural), shorter travel times to obtain drinking water (>30 minutes, 27% urban, 53% rural), improved toilet/latrine facilities (22% urban, 9% rural), and households with electricity (45% urban, 3% rural). The majority of rural households have flooring made of earth, sand, or dung, and roofs made of grass/thatch/mud or iron sheets; urban households are more likely to have cement flooring with roofs made of irons sheets. Questions regarding the objects found in households indicated that most households have a radio (74% urban, 55% rural), while urban households are more likely to have a television (40% urban, 3% rural). There are also differences on other economic infrastructure measures (e.g. roads), and on measures of access and adequacy of resources within health and education sectors (65,68,71).

Rural and urban data are often stratified according to districts in national surveys (64), as they will be in this thesis, due to differing demographic, health and
socioeconomic profiles of these areas. It is also important to consider that there may be environmental and cultural components that differ, and these would be difficult to accurately measure and subsequently control for. Inclusion of both rural and urban samples in this study will not only allow for descriptive results from each area, but also comparisons, since the same study instrument and surveying methodology is used. As will be clear from the systematic review, few studies from Africa include rural populations, or population-based sampling, and so this warrants further study. We hypothesized that there may be differences in acceptability and different factors associated with acceptance between these rural and urban groups.

1.9 Purpose and study rationale

1.9.1 Manuscript 1

There has been much research on HPV vaccine acceptability among African countries in the last six years since the vaccine became commercially available. These studies have not been reviewed, as they have for studies originating from developed countries (63,72). The systematic review presented in Manuscript 1 is a synthesis of findings from HPV vaccine acceptability studies among African countries. This review is systematic in that a search strategy was devised, articles were screened based on specific inclusion/exclusion criteria, and the synthesis used a standard data abstraction form to evaluate each article. It follows then, that these results are replicable and updatable. Given that eight GAVI-supported African countries are expected to begin vaccine
demonstration projects throughout 2013-2014, this review is timely and may be informative to public health planners.

**1.9.2 Manuscript 2**

The aim of Manuscript 2 is to investigate the factors associated with acceptability of the HPV vaccine in Kilimanjaro Region of Tanzania, among a population-based sample of women from rural and urban areas. This study also addresses perceived barriers to vaccination, and provides descriptive findings on socio-demographic and health characteristics, and HPV-related knowledge and attitudes. The data for this study comes from a cross-sectional study conducted during July 2012, under the overarching project title Cervical Cancer Prevention in Tanzania. Additional information on Methods and additional tables not included within Manuscript 2 are presented in Appendix B.

**1.10 Thesis objectives**

1. Systematically review HPV-related knowledge and the associations of HPV vaccine acceptability among studies conducted within African countries
2. Describe the socio-demographic characteristics and HPV-related awareness/knowledge, attitudes and barriers, relating to HPV vaccination among rural and urban women in the Kilimanjaro Region, Tanzania.
3. Determine the socio-demographic, knowledge, and attitudes that are associated with HPV vaccine acceptability among rural and urban women in the Kilimanjaro Region, Tanzania using exploratory analyses.
1.11 Thesis organization

This thesis is organized and presented in the format of two manuscripts, in conformity with the framework provided by the School of Graduate Studies at Queen’s University. Chapter 2 (Manuscript 1) is a systematic review addressing Objective 1 and is being prepared for submission to Preventative Medicine: An International Journal Devoted to Practice and Theory. Chapter 3 (Manuscript 2) is original research addressing Objectives 2 and 3 and is being prepared for submission to Vaccine. Although these are presented in this order, Manuscript 2 was conceptualized and completed before Manuscript 1. Chapter 4 provides a general summary, discussion and conclusion of the thesis, including an outline of the strengths and limitations and implications for future research. Additional information on study methods and tables excluded from Manuscript 2 is presented in Appendix B. As partial fulfillment of the requirements of a Masters degree in Epidemiology, this thesis includes: conceptualization of thesis project, critical literature review, design and evaluation of a questionnaire, international fieldwork, database management, statistical analysis and interpretation of epidemiological data, consideration of strengths and limitations, and the preparation of manuscripts for submission for publication.
1.12 References


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Chapter 2

HPV vaccine acceptability in Africa: a systematic review of the literature

2.1 Abstract

**Objective.** The objective of this study was to provide a systematic review of peer-reviewed literature on the factors associated with HPV vaccine acceptability among adults and parents from African countries.

**Methods.** A search was conducted across five electronic databases: EMBASE, PsychINFO, CINAHL, Global Health and Ovid MEDLINE, in order to find all studies related to HPV vaccination in African countries. A data abstraction form structured by the Health Belief Model was used to collect data and synthesize findings.

**Results.** 14 unique studies representing ten countries from sub-Saharan Africa were identified and more than half were published within the last two years. Most studies were cross-sectional, and reported descriptive statistics from convenience samples. Acceptability of the HPV vaccine for daughters was high (range 59-100%); however, HPV vaccine-related awareness and knowledge was low. Perceived barriers including accessibility and cost concerns appeared to be important for acceptance, as were cues to action from healthcare providers and the government.
Conclusions. This systematic review demonstrates that educational and publicity campaigns should provide general information on the vaccine, including its relationship to cervical cancer. Campaigns could emphasize that the vaccine will be free for eligible girls, describe where the vaccine has been previously administered, and increase knowledge of the vaccination procedures including access and safety. Healthcare providers and the government could also be publically highlighted for their acceptance of the vaccine.

Keywords: Human papillomavirus, vaccination, Africa, review, acceptability, attitudes
2.2 Introduction

The quadrivalent human papillomavirus (HPV) vaccine is manufactured by Merck & Co. and has been available commercially since 2006. The cost of the vaccine is high (approximately $400 US for a three-series dose), and until recently this presented a significant barrier to implementation in low-resource countries. The Global Alliance for Vaccine Initiatives (GAVI) recently negotiated a $4.50/dose fee for GAVI-supported countries. At the same time, they have announced support for eight demonstration projects in African countries that will begin over 2013-2014 (GAVI, 2013). This is a significant and positive departure from historical trends of decades between the introduction of new vaccines and implementation in developing countries (Kane et al., 2006).

African countries carry the largest burden of cervical cancer worldwide. Globally, the prevalence of HPV infection is estimated at 11-12%, however in sub-Saharan Africa the estimate is substantially higher at 24% (Forman et al., 2012). In 2008, world estimates of new cervical cancer cases were 530,000, and 75,000 of these were from sub-Saharan African countries, representing almost 15% of the world’s burden (Forman et al., 2012). This burden is largely due to the deficiency of organized, preventative services, such as cytological screening (i.e. Pap smears), and the prevalence of risk factors for the disease (Bosch and Sanjosé, 2003; Sankaranarayanan and Ferlay, 2006). It is recognized that infection with HIV is a contributor to the problem, substantially reducing immunity and increasing the likelihood of infection and progression with HPV (Palefsky et al., 2006). Widespread vaccination with the HPV vaccine is expected to substantially reduce the
burden of cervical cancer, especially when combined with other preventative measures (Garnett et al., 2006). Formative research on the vaccine’s acceptability has been conducted among several developing countries including Latin America and the Caribbean (Winkler et al., 2008), Vietnam (Breitkopf et al., 2009; Dinh et al., 2007), Malaysia (Sam et al., 2009; Wong, 2008), China (Kwan et al., 2009; Li et al., 2009) and India (Madhivanan et al., 2009), however the focus of this review will be among African countries, as research on this topic has been growing in the past few years.

Although there are several conceptual frameworks to predict health behaviors, the Health Belief Model (HBM) is one of the most commonly used models for understanding vaccination behaviors; it has been used previously for studying other vaccinations as well as cervical cancer screening (Allen et al., 2010; Johnson et al., 2008; Prematunge et al., 2012). Furthermore, a previous systematic review of predictors of HPV vaccine acceptability in the US was structured by the HBM, and has proven useful for understanding and organizing the issues surrounding this vaccine (Brewer and Fazekas, 2007). As such, the HBM will be used in this review to divide and present research findings among the five HBM constructs that can be used to understand vaccination behavior (Janz and Becker, 1984). As an expectancy model, the HBM predicts that a person’s health behavior will depend on the value placed on achieving a goal and the belief that a certain behavior will achieve that goal (Poss, 2001). The perceived likelihood construct refers to the beliefs surrounding an individual’s susceptibility, or risk of disease. Perceived severity refers to beliefs that the disease represents a threat to the individual. Perceived effectiveness and benefit refers to beliefs that the behavior will prevent, or reduce the threat of disease. Perceived barriers include roadblocks to behavior
and these include: financial, physical, personal (e.g. fears), self-efficacy, safety, and side effects. Cues to action refer to external or internal stimuli to carry out the behavior. In addition to these five constructs, HPV vaccine-related awareness and knowledge, and other modifying factors previously found to predict acceptability, are included.

The purpose of this study is to provide a systematic review of peer-reviewed literature on the factors associated with HPV vaccine acceptability among adults and parents from African countries. This is the first systematic review of HPV vaccine acceptability of studies from African countries, and it is timely given recent project announcements. An understanding of the factors associated with acceptability among countries in Africa may be important for program planners for the promotion evidence-based practices.

2.3 Methods

2.3.1 Search Strategy

A trained health sciences librarian with experience conducting systematic reviews ran a search across five electronic databases: EMBASE, PsychINFO, CINAHL, Global Health and Ovid MEDLINE. A broad search was conducted in August 2013 to find all literature relating to HPV vaccination in African countries. The search consisted of database-specific vocabulary and use of Boolean operators for the search: human papillomavirus vaccin* and Africa. For example, the medical subject headings (MeSH) were used in the following way searching on MEDLINE: ‘papillomavirus vaccines’; OR [expanded]’papillomavirus infections’ and [expanded] ‘immunization’; AND [expanded]
‘Africa’. The small number of articles from test searches did not require the use of attitudes, beliefs, or barrier search terms to narrow results. In addition, no restrictions were placed on date or language. Reference sections of included articles were also examined and their journals were hand-searched for articles that may have been recently published. Authors were contacted for in-press publications if abstracts were identified. The complete search strategy is presented in Appendix C.

2.3.2 Study Selection

Inclusion criterion was the examination of HPV vaccine acceptability, and awareness, knowledge or attitudes related to HPV vaccines in an African country. Although the importance of the role of healthcare workers for HPV vaccine acceptance is recognized, the focus of this review was among adults and parents. No limits were placed on study’s selection of study participants, however studies examining the effects of educational interventions were not included. No limit was placed on study design; however, included articles are required to report original data (i.e. reviews, editorials and commentary were excluded). Articles examining actual HPV vaccine uptake were identified, but not included in this review. Titles and abstracts of all articles returned from the search were screened and those irrelevant were excluded. Remaining articles were given full-text review and further excluded if they did not meet any of the inclusion criteria above. Articles with multiple publications from the same data set were identified.

2.3.3 Data Collection and Abstraction

A standard data abstraction form was created based on preliminary research, the structure of a prior systematic review of HPV acceptability in the USA (Brewer and
Fazekas, 2007), and a review of measures used in systematic HPV vaccine acceptability studies (Allen et al., 2010). The HBM constructs were used to organize the data abstracted from articles, using the following headings: awareness and knowledge, perceived likelihood, perceived severity, perceived effectiveness, perceived barriers, cues to action and other factors. Data was collected using this form and these constructs were used to synthesize results in a qualitative manner, without statistical pooling of individual-level data. Study-level data for awareness and knowledge was summarized using article-reported statistics to calculate a summary percent. These were calculated by dividing the sum of affirmatory responses (numerators) by the sum of study sample sizes (denominators) for each variable common to studies.

2.4 Results

As shown in Figure 1, 229 unique articles were identified from the database search and of these 29 were relevant and given full-text review. Based on the inclusion criteria, 14 were included for this review. Excluded articles were those: examining uptake (n=5: Ladner et al., 2012; LaMontagne et al., 2011; Moodley et al., 2013; D. Watson-Jones et al., 2012; Deborah Watson-Jones et al., 2012), only available as abstracts (n=1: Adejimi et al., 2013), following a study-led community sensitization or communication campaign (n=3; Ayissi et al., 2012; Galagan et al., 2013; Wamai et al., 2012), were reviews (n=1; Bingham et al., 2009), or were studying healthcare workers only (n=5; Makwe and Anorlu, 2011; McCarey et al., 2011; Morhason-Bello et al., 2013; Nelson et al., 2010;
One article was identified by hand-searching methods (Ports et al., 2013). The final number of articles included in this review is 15, representing 14 unique studies (Table 1). The 14 studies span ten countries from sub-Saharan Africa: Botswana (1), South Africa (2), Nigeria (2), Kenya (3), Ghana (1), Uganda (1), Mali (1), Zambia (1), Tanzania (1) and Malawi (1).

All studies were conducted after 2006, when the vaccine had been approved and available commercially, and more than half of the studies were published within the last two years. One study is presented in two papers (Francis et al., 2011, 2010), with the second representing a sub-group of women who were interviewed following a survey among the entire sample. Ten studies were cross-sectional and reported quantitative results. Nearly all studies presented findings using descriptive statistics only, with one reporting results of a multivariable model. Of these ten studies, six were completed using a self-administered questionnaire, and the rest were administered by an interviewer. The remaining five studies presented qualitative results only, from focus groups or interviews. The age of participants ranged from 10–84, and all but three represented individuals from urban or semi-urban areas. The sample sizes ranged from 24–409 and most were conducted among females, although five studies included males. Response rates among studies were high, with seven reporting >93% response.

Eleven studies asked the participant’s willingness to vaccinate their daughters, however five studies not exclusive to parents required participants to imagine hypothetical daughters. Willingness among these studies ranged from 59–100%. Six studies questioned if the participants would vaccinate themselves, and willingness ranged from 58–100%. Of the three studies that asked participants about both themselves and
also about their child, only one reported differences in acceptability (Poole et al., 2013). In this study 100% of participants said they would accept the vaccine for themselves, and 75% would accept for their children. This question was hypothetical for those without children and was asked among a particularly young sample; 40% of participants of this study were between the ages of 12–17.

### 2.4.1 HPV-related awareness and knowledge

While overall awareness of cervical cancer was moderate, with 67% aware of the disease across nine studies (range 5%-100%), one study found that cervical cancer awareness for some participants meant that women had merely heard the word (Ports et al., 2013). Two studies conducting focus groups acknowledged that the terminology surrounding cervical cancer was not common, and that the disease was often understood only from its symptoms. In some instances, “cancer of the womb,” or “cancer of the opening or mouth to the womb,” was used to describe the disease (Francis et al., 2011; Katahoire et al., 2008).

Knowledge of the Pap smear test was moderate (45%, range 7%-74%), although an understanding of its use as a preventative, rather than diagnostic, test may have been unclear to participants. One study found that although 69% knew the Pap smear could be used to test for cervical cancer, only 18% thought this was a way cervical cancer could be prevented (Rositch et al., 2012). Focus groups reported additional misconceptions, with women suggesting that the test could be used to treat and “cleanse the womb” (Harries et al., 2009).
Awareness of HPV (26%, range 0%-36%, seven studies) and the HPV vaccine (15%, 0%-40%, six studies) was low across studies. Measures of additional HPV-related knowledge varied among studies. Across five studies, 24% knew HPV was a sexually transmitted infection (range 2%-52%) although one study found that 89% did not know infection could be asymptomatic (Iliyasu et al., 2010). Across nine studies, less than a third (24%, range 0%-66%) knew of a relationship between HPV infection and cervical cancer, and in studies conducted among university students (Iliyasu et al., 2010; Makwe et al., 2012) knowledge that HPV also caused genital warts was low (20% and 13%, respectively).

Three studies examined the relationship between acceptability and awareness. Awareness of HPV (Iliyasu et al., 2010), awareness of cervical cancer (Coleman et al., 2011; Iliyasu et al., 2010), and knowledge of the existence and purpose of the pap smear test (Coleman et al., 2011) had strong, positive associations with acceptance. These three variables were not significant in another study, which found a marginally significant relationship between knowing what may cause cervical cancer and acceptance (Omondi-Ogutu and M’Imunya, 2013).

2.4.2 Health belief model constructs

2.4.3 Perceived likelihood

Among university students, perceived personal risk of HPV infection or cervical cancer was low (6.3% and 6.9%, respectively) (Makwe et al., 2012). Some students (39%) thought it was an inherited disease (Iliyasu et al., 2010). While among parents and adults, perceived risk of HPV infection of cervical cancer for their daughters was high,
ranging 41%-78% considering both ‘very concerned’ or ‘high risk’ responses (Coleman et al., 2011; DiAngi et al., 2011; Francis et al., 2010; Harries et al., 2009). Personal risk among respondents for HPV infection or cervical cancer appeared lower, range 15%-37% (Coleman et al., 2011; Francis et al., 2010), and in studies that included measures of both personal and daughter’s risk, it appeared that adults rated their daughter’s risk higher than themselves (Coleman et al., 2011; Francis et al., 2010).

The relationship between acceptability and perceived likelihood was examined by two studies, with opposite findings. One study found insignificant relationships between their daughter’s perceived risk of HPV, genital warts, or cervical cancer and acceptance (DiAngi et al., 2011), while another found that those accepting were more likely to rate both their and their daughter’s cervical cancer risk as high (Coleman et al., 2011).

2.4.4 Perceived severity

Parents and adults recognized that cervical cancer was a severe and deadly disease among women (Becker-Dreps et al., 2010; Coleman et al., 2011; DiAngi et al., 2011; Francis et al., 2011; Ports et al., 2013; Remes et al., 2012). Of the thirty women interviewed in one study, eighteen knew someone who had died of the disease and this informed their view that a diagnosis of cervical cancer was a death sentence (Ports et al., 2013). Few studies examined the relationship between perceived severity and acceptability empirically. In the two studies that examined this construct, both found that those with perceived cervical cancer with higher severity were associated with acceptance of the vaccine (Coleman et al., 2011; DiAngi et al., 2011).

2.4.5 Perceived effectiveness and benefits
The benefits and effectiveness of vaccines in general were discussed positively among participants in focus groups (Francis et al., 2011; Katahoire et al., 2008; Ports et al., 2013; Remes et al., 2012). One study’s focus group were concerned that vaccines given to low-resource countries were inherently inferior (Harries et al., 2009). Another reported that protection against HPV infection was recognized as a benefit by parents concerned about sexual abuse among girls in their community (Francis et al., 2011). Another study found that half the women surveyed did not know the vaccine was effective for those not infected with HPV (Coleman et al., 2011), and a higher proportion thought that the vaccine should be given to those who were already sexually active, rather than before (Makwe et al., 2012).

In relation to acceptability, effectiveness was the fourth of five most important characteristic considered when deciding to vaccine in one study (Francis et al., 2010). Two studies citing the effectiveness of previous vaccinations (e.g. polio, measles) said that this influenced their acceptance of the vaccine (Katahoire et al., 2008; Ports et al., 2013). Finally, one study found that acceptance was associated with those concerned if the vaccine truly prevented HPV infection, but not among those concerned about prevention of cervical cancer (Coleman et al., 2011).

2.4.6 Perceived barriers

Several barriers were queried among participants including cost, safety, dosing, side effects, lack of information, accessibility, fear, and promiscuity. Although concerned, most of these did not deter participants from accepting the vaccine. Cost appeared to be an important barrier; some conditioned willingness on if the vaccine were
to be offered at no cost (Rositch et al., 2012), and some participants made it clear they thought the vaccine should be free (Francis et al., 2011; Harries et al., 2009), while others found a minority were willing to pay some amount, albeit substantially less than the commercial cost of the vaccine (Becker-Dreps et al., 2010; DiAngi et al., 2011; Poole et al., 2013; W Liu and Vwalika, 2012).

Associations with acceptability among studies were reported as cost concerns, safety and side-effects (Coleman et al., 2011), preference for lower dosing (Becker-Dreps et al., 2010) and vaccine message framing as cervical cancer prevention, rather than sexual transmitted infection (STI) prevention (Harries et al., 2009). In one study, male teachers were especially concerned with promiscuity and this negatively influenced their acceptance (Remes et al., 2012).

Concerns of access were a common barrier related to acceptance. Those who were more likely to accept thought the vaccine would be easy to obtain (DiAngi et al., 2011), felt self-efficacy in finding a doctor or clinic (Coleman et al., 2011), and were living further (i.e. more rurally) from healthcare services (DiAngi et al., 2011). In another study distances from health services were discussed as a barrier to vaccinations, but did not deter women from seeking vaccination (Ports et al., 2013).

2.4.7 Cues to action

Recommendation from a healthcare provider was important cue for acceptance (DiAngi et al., 2011; Francis et al., 2010; Makwe et al., 2012; Ports et al., 2013), although some indicated that they did not trust doctors (Omondi-Ogutu and M’Imunya, 2013). Recommendation and endorsement from the government was also important for
acceptance (Katahoire et al., 2008; Ports et al., 2013; Remes et al., 2012).

Acknowledgement that members of their communities, as well as other communities
where the vaccine had been implemented, held favorable attitudes towards the vaccine
was found to be important among study participants (Iliyasu et al., 2010; Katahoire et al.,
2008) and associated with acceptance (Coleman et al., 2011).

Mothers were recognized as key decision-makers for healthcare decisions,
including vaccinations, but spousal input was usually recognized. In one study, those who
thought they would be involved in the decision-making were more willing to accept
(DiAngi et al., 2011). One study reported that men had more autonomy in vaccine
decision-making for their children, however collapsing adolescent and adult categories
for comparisons may have been misleading (Poole et al., 2013). If adult women and men
are compared, the autonomy in decision-making appears more similar (75% and 85%,
respectively). Furthermore, this question may have been misunderstood by those who are
considered children themselves (40% of sample).

2.4.8 Other factors associated with acceptability

A previous history of pap smear testing was not related to acceptance in the single
study that examined this relationship (Coleman et al., 2011). A history of cervical cancer,
genital warts, HPV/STI infection and HIV-positive status were not found to be
significantly associated with acceptance (Coleman et al., 2011; DiAngi et al., 2011;
Rositch et al., 2012). Acceptors were found to have more life-time sexual partners
(Coleman et al., 2011), and two studies argued for a low age of vaccination due to
perceived earlier sexual debut among girls in their community (Harries et al., 2009;
Remes et al., 2012), although some were concerned about their maturity and understanding. Studies that included religious beliefs found mixed results. One study found that Christians were more likely to accept than those of Muslim faith, however this was not associated in a multivariable model (Iliyasu et al., 2010). Another study found that concerns of the vaccine’s alignment with religious beliefs was not associated with acceptance (Coleman et al., 2011). Finally, one study’s participants thought that God would protect their daughters from infection with HPV (Omondi-Ogutu and M’Imunya, 2013). No study examined the relationship between acceptability and specific tribal/cultural groups.

In terms of socio-demographic factors associated with acceptability, two studies found that older age groups were more likely to accept (Coleman et al., 2011; Iliyasu et al., 2010), and a third study found an insignificant relationship with age (DiAngi et al., 2011). The relationship between parental sex and acceptance was not found to be significant (DiAngi et al., 2011; Omondi-Ogutu and M’Imunya, 2013) and marital status was not important (Coleman et al., 2011; DiAngi et al., 2011). One study found that more education was associated with lower likelihood of acceptance (DiAngi et al., 2011), while another found that medical education was the strongest factor associated with acceptance (Iliyasu et al., 2010). Two other studies found no significant relationship (Coleman et al., 2011; Omondi-Ogutu and M’Imunya, 2013). No study specifically examined occupation, though a qualitative study that involved teachers noted that 5/14 male teachers were unaccepting due to fears of promiscuity and side-effects (Remes et al., 2012). In one study, acceptors were found to have higher incomes (Coleman et al., 2011).
2011) and in another, the relationship with income was insignificant (DiAngi et al., 2011).

2.5 Discussion

This systematic review found high acceptance of the HPV vaccine among young adults, adults, and parents in sub-Saharan African countries, despite low awareness of HPV and the HPV vaccine. This review was structured using the Health Belief Model (HBM), and demonstrates the utility of the HBM for integrating qualitative and quantitative research findings for the understanding of the factors influencing vaccine acceptance.

The reviewed studies were limited to cross-sectional studies of moderate size and qualitative syntheses of interviews and focus groups. Future studies could considering using higher quality designs, such as case-control or randomized clinical trial designs. Studies that reported quantitative relationships were not statistically advanced; nearly all presented descriptive statistics with only a single mode of measurement for acceptability. There was also variability in method of construct measurement between studies, thus limiting study comparability. Although response rates were high, there are limitations in the generalizability of findings since all were conducted among purposively selected samples (e.g. clinic attendees) or among specific sub-groups of the population (e.g. university students). Evaluating the quality of qualitative research can be difficult and quite subjective (Dixon-Woods et al., 2004); however, generally, the qualitative studies reviewed appeared to be of good quality with transparent presentation of their methods,
including themes used for discussion, and a method for synthesis of results. Studies outlined methods of selecting participants and described recruiting a number that was believed to reach saturation (i.e. data saturation, no new themes or unheard perspectives).

Rural populations were not adequately represented in the literature, despite the general recognition that these women are likely to be at higher risk. Further, no study was exclusively among males, and the studies that did include males may not have been sufficiently powered to make comparisons. The attitudes of fathers may be important to consider, especially if it appears they may hold differing opinions (Remes et al., 2012) and will likely be involved in decision-making. Inclusion of these two groups in future studies may be important for a more complete understanding of HPV vaccine acceptance.

In this review, we found that HPV-related awareness and knowledge was very low, however it appeared to be strongly associated with acceptance. Education and sensitization campaigns in communities within Cameroon successfully raised awareness of HPV, cervical cancer, and the HPV vaccine, to proportions higher than those reported among developed countries, such as the USA and Canada (Wamai et al., 2012). Campaigns such as these could be strategically adapted and duplicated across countries, as an important step for high uptake and ethical vaccination. Among parents, these campaigns could emphasize the relationship between HPV and cervical cancer, and highlight other cervical cancer prevention methods for their daughters, including promoting safe sexual behaviors. These campaigns are also an opportune time to emphasize the use of Pap smear screening tests for women, and to raise awareness for adolescents that may wish to seek screening in the future. The recognition that there were
local phrases and terms used to describe the disease is also an important finding for knowledge translation initiatives.

The relationship between perceived likelihood of HPV infection or cervical cancer and vaccine acceptance was unclear and this may be, partially due to low awareness and understanding. As pointed out by others, for many, perceived likelihood of this disease may be based upon an individual’s perceived likelihood of cancer in general (Sudenga et al., 2013). Perceptions that daughters may be at higher risk may be a result of the general belief that children are at higher risk for vaccine-preventable diseases. It is concerning that university students reported the lowest perceived risk, and knowledge gaps are evident from their belief that cervical cancer is heritable and that the vaccine is more appropriate for the sexually active.

Many respondents recognized cervical cancer as a threat to health, and perceived severity was related to vaccine acceptance. Perceived severity may be related to knowledge of the disease through personal experience. The high prevalence of cervical cancer along with the late-stage at diagnosis among sub-Saharan African countries has resulted in many women knowing at least one woman who has suffered from the disease. It is possible that women who are unaware of the cervical cancer may be familiar with cancer in general, and thus responding based on their perceived severity of any cancer diagnosis. Severity of the disease, and fears of a perceived fatal diagnosis, has historically deterred preventative behaviors, such as Pap screening (Birhanu et al., 2012). Thus, it will be important to emphasize the link between HPV and cervical cancer, and the substantial reduction in risk conferred with vaccination.
Perceived effectiveness and its positive relationship with acceptance were rooted in experience with previous vaccinations. Thus, it may be beneficial to frame vaccine messages and advertisements with comparisons to these positive past experiences. However, it will be critical to emphasize to individuals that the vaccine does not completely protect against cervical cancer, as the vaccine does not immunize against all oncogenic strains of HPV. Maintaining public trust in immunizations is key to the success of these programs (Cooper et al., 2008), and there has been some hesitation in implementing this vaccine due to fears that controversies or negative experiences with this vaccine will adversely affect positive attitudes towards other vaccines (Katahoire et al., 2008). HPV vaccinations in India were suspended after concerns of safety, efficacy and cost-effectiveness were raised by advocacy groups (Larson et al., 2010). Vicarious experience is important in formulating the perceived self-efficacy of individuals to carry out a health behavior, and so it may be important to introduce positive examples of HPV vaccination projects (Bandura, 1977). This review reveal misconceptions surrounding the timing and effectiveness of the vaccine for those already sexually active, which could also be included under the perceived likelihood construct. These misconceptions would be important to address in order to ensure uptake among all those who would benefit from vaccination.

The vaccine is likely to be administered freely to participants, and so addressing financial barriers could be accomplished by minimizing the indirect costs incurred by individuals (e.g. costs of travel or missed work). This is particularly key if a parent is required to accompany their daughter when the vaccine is administered, as occurred in Rwanda (Binagwaho et al., 2012). It is possible that individuals who are not age-eligible
to receive the vaccine for free will purchase the vaccine privately, and thus further reductions in the cost of the vaccine would increase access for these individuals. Physical access barriers could be mitigated by wide advertisement of vaccination dates and locations, increasing the perceived ease of vaccination and availability.

Public endorsement of the vaccine by a healthcare provider and the government may be important for acceptance. Physicians have been recognized as a strong influence for vaccine uptake in the US (Rosenthal et al., 2011), however the differing health roles in low-income countries requires other healthcare workers also be educated and approving of the vaccine. Nurses are an important source of cervical cancer awareness among adolescents (Ayissi et al., 2012), and studies from Uganda and Tanzania have suggested that cervical cancer education is also required among this group (Mutyaba et al., 2006; Urasa and Darj, 2011). The social cohesion and strong networks of communities, as well as the value placed on the attitudes of family and friends for health seeking behavior (Marmot and Wilkinson, 2009; Poss, 2001), can be used as evidence to promote the involvement of community leaders or use of a peer education process.

Among the other factors associated with acceptance, it may be important to involve religious leaders in the campaigns of some countries, especially those with significant variability in religious groups. It also appears that those of higher socioeconomic (i.e. income, education) status may be less accepting, possibly due to hesitation towards accepting something they have never heard of or have no additional knowledge of. Unfortunately, no studies simultaneously examined education, income and knowledge/awareness to discern these results.
This review has strength in its novel review of recently published literature and it is timely given the recent announcement of vaccine demonstration projects within this region. This review is structured similarly, and may be compared and contrasted to results from a previous review conducted using studies from the US (Brewer and Fazekas, 2007). Furthermore, it is believed that inclusion of both quantitative and qualitative research studies has increased the depth and explanatory nature of the findings. Although use of the HBM is considered a strength of this review for its explanatory power and structure, the model itself does have limitations. Constructs used for evaluation have not been standardized, and as a psychosocial model focused on the individual, there are likely other factors that may be important but not explicitly analyzed in the model. This includes factors affecting access beyond an individual’s control (e.g. public policy) (Poss, 2001). Since these are not considered, some of the findings are decontextualized, and it is important to note that the review is not generalizable to all African countries. As noted in the US review by Brewer and Fazekas (2007), the presentation of qualitative data may be misleading in highlighting attitudes or beliefs that may not be widespread. Another limitation is that it is unknown if the interviewed participants were necessarily from each urban, semi-urban or rural region, and thus may be misclassified. Women may travel up to four hours to receive health services (Ports et al., 2013), and several of these studies were among selected clinic or hospital attendees. A final limitation is the possibility that there are other eligible studies not identified in the search, or studies that were not published (publication bias).
2.6 Conclusion

Implementation of the HPV vaccine in African countries is an important step towards reducing the high burden of cervical cancer in these countries, and recent announcements from GAVI of HPV vaccine demonstration projects beginning in Kenya, Malawi, Tanzania, Ghana and among others, represent an important step toward this goal. In general, HPV vaccine acceptability appears to be quite high, however there are gaps in knowledge and misconceptions that should be addressed before these programs begin. There are aspects of the HBM constructs presented here that could be emphasized during planning programs, and these may be adapted for specific contexts, and changed as the program unfolds in the public domain. Future studies could focus on examining acceptability among sub-groups of the population, such as those living in rural areas or males, and using higher quality study designs, although given that acceptability is predicted to be very high, these may not be a good use of financial resources. Uptake or non-uptake studies may be more informative.

2.7 Acknowledgements

We would like to thank Amanda Ross-White for her assistance and expertise in electronic literature searches.

2.8 Conflict of Interest

The authors declare no conflicts of interest.
2.9 References


Figure 1. Selection of articles for inclusion in the systematic review.
Table 1. Characteristics of included studies.

<table>
<thead>
<tr>
<th>Year of study</th>
<th>Country</th>
<th>Study design</th>
<th>Study instrument</th>
<th>Location</th>
<th>N</th>
<th>Age</th>
<th>Sex</th>
<th>Statistics for acceptability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker-Dreps et al., 2010</td>
<td>2007</td>
<td>Kenya</td>
<td>Cross-sectional</td>
<td>Interview-administered questionnaire</td>
<td>SU</td>
<td>147</td>
<td>A</td>
<td>F</td>
</tr>
<tr>
<td>Coleman et al., 2011</td>
<td>2009</td>
<td>Ghana</td>
<td>Cross-sectional</td>
<td>Self-administered questionnaire</td>
<td>U</td>
<td>264</td>
<td>A</td>
<td>F</td>
</tr>
<tr>
<td>DiAngi et al., 2011</td>
<td>2009</td>
<td>Botswana</td>
<td>Cross-sectional</td>
<td>Self-administered questionnaire</td>
<td>U, SU</td>
<td>376</td>
<td>A</td>
<td>F, M</td>
</tr>
<tr>
<td>Francis et al., 2010&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2008</td>
<td>South Africa</td>
<td>Cross-sectional</td>
<td>Self-administered questionnaire</td>
<td>U</td>
<td>86</td>
<td>P</td>
<td>F</td>
</tr>
<tr>
<td>Francis et al., 2011&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2008</td>
<td>South Africa</td>
<td>Qualitative</td>
<td>Focus groups</td>
<td>U</td>
<td>24</td>
<td>P</td>
<td>F</td>
</tr>
<tr>
<td>Harries et al., 2009</td>
<td>2007-2008</td>
<td>South Africa</td>
<td>Qualitative</td>
<td>Focus groups</td>
<td>U, SU</td>
<td>43</td>
<td>P</td>
<td>F</td>
</tr>
<tr>
<td>Iliyasu et al., 2010</td>
<td>—</td>
<td>Nigeria</td>
<td>Cross-sectional</td>
<td>Self-administered questionnaire</td>
<td>U</td>
<td>375</td>
<td>CS</td>
<td>F</td>
</tr>
<tr>
<td>Katahoire et al., 2008</td>
<td>2007</td>
<td>Uganda</td>
<td>Qualitative</td>
<td>Focus groups, interviews, workshop</td>
<td>U, R</td>
<td>—</td>
<td>A, Y</td>
<td>F, M</td>
</tr>
<tr>
<td>Liu et al., 2012</td>
<td>2009</td>
<td>Zambia</td>
<td>Cross-sectional</td>
<td>Interview-administered questionnaire</td>
<td>U</td>
<td>310</td>
<td>A</td>
<td>F</td>
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<tr>
<td>Makwe et al., 2012</td>
<td>2010</td>
<td>Nigeria</td>
<td>Cross-sectional</td>
<td>Self-administered questionnaire</td>
<td>U</td>
<td>368</td>
<td>CS</td>
<td>F</td>
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<tr>
<td>Omondi-Ogutu et al., 2011</td>
<td>2011</td>
<td>Kenya</td>
<td>Cross-sectional, Qualitative</td>
<td>Self-administered questionnaire, interviews</td>
<td>U</td>
<td>332, 50</td>
<td>P</td>
<td>F, M</td>
</tr>
<tr>
<td>Poole et al., 2013</td>
<td>2011</td>
<td>Mali</td>
<td>Cross-sectional</td>
<td>Interview-administered questionnaire</td>
<td>SU</td>
<td>51</td>
<td>A, Y</td>
<td>F, M</td>
</tr>
<tr>
<td>Ports et al., 2013</td>
<td>2011</td>
<td>Malawi</td>
<td>Qualitative</td>
<td>Semi-structure interviews</td>
<td>U, R</td>
<td>30</td>
<td>P</td>
<td>F</td>
</tr>
<tr>
<td>Remes et al., 2012&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2010</td>
<td>Tanzania</td>
<td>Qualitative</td>
<td>Interviews, group discussion</td>
<td>U, R</td>
<td>151</td>
<td>P, Y</td>
<td>F, M</td>
</tr>
<tr>
<td>Rositch et al., 2012</td>
<td>2007-2009</td>
<td>Kenya</td>
<td>Nested cross-sectional within cohort (HIV-discordant couples)</td>
<td>Interview-administered questionnaire</td>
<td>U</td>
<td>409</td>
<td>A</td>
<td>F</td>
</tr>
</tbody>
</table>

Age: A=adults, P=parents, CS=college students, Y=adolescents. Location: U=urban, SU=semi-urban, R=rural. * = data not available or applicable
<sup>a</sup> Francis et al., 2011 were a subgroup of women from Francis et al., 2010
<sup>b</sup> This review studied the parents (n=60), female students (n=54) and teachers (n=37) of this study
Table 2. Awareness and knowledge of HPV among studies conducted in African countries.

<table>
<thead>
<tr>
<th>Study</th>
<th>Heard of HPV</th>
<th>Heard of HPV Vaccine</th>
<th>Heard of cervical cancer</th>
<th>Knowledge of Pap smear test&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Know HPV is an STI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Aware of relationship between HPV and cervical cancer&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker-Dreps et al., 2010</td>
<td>—</td>
<td>0%</td>
<td>15%</td>
<td>—</td>
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<td>—</td>
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<tr>
<td>Coleman et al., 2011</td>
<td>—</td>
<td>40%</td>
<td>87%</td>
<td>72%</td>
<td>52%</td>
<td>66%</td>
</tr>
<tr>
<td>DiAngi et al., 2011</td>
<td>35%</td>
<td>9%</td>
<td>71%</td>
<td>—</td>
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<td>—</td>
</tr>
<tr>
<td>Francis et al., 2010</td>
<td>29%</td>
<td>—</td>
<td>61%</td>
<td>74%</td>
<td>22%</td>
<td>19%</td>
</tr>
<tr>
<td>Francis et al., 2011</td>
<td>—</td>
<td>—</td>
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<td>—</td>
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<tr>
<td>Harries et al., 2009&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>—</td>
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<tr>
<td>Iliyasu et al., 2010</td>
<td>36%</td>
<td>—</td>
<td>54%</td>
<td>28%</td>
<td>23%</td>
<td>18%</td>
</tr>
<tr>
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<td>—</td>
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<td>—</td>
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<tr>
<td>Liu et al., 2012</td>
<td>—</td>
<td>—</td>
<td>72%</td>
<td>—</td>
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<td>—</td>
</tr>
<tr>
<td>Makwe et al., 2012</td>
<td>18%</td>
<td>14%</td>
<td>56%</td>
<td>7%</td>
<td>—</td>
<td>11%</td>
</tr>
<tr>
<td>Omondi-Ogutu et al., 2011</td>
<td>26%</td>
<td>—</td>
<td>79%</td>
<td>48%</td>
<td>—</td>
<td>14%</td>
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<tr>
<td>Poole et al., 2013</td>
<td>—</td>
<td>—</td>
<td>5%</td>
<td>—</td>
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<tr>
<td>Ports et al., 2013</td>
<td>—</td>
<td>0%</td>
<td>100%</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Remes et al., 2012&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>0%</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Rositch et al., 2012</td>
<td>18%</td>
<td>—</td>
<td>—</td>
<td>69%</td>
<td>12%</td>
<td>22%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Summary<sup>d</sup>  

<table>
<thead>
<tr>
<th>Heard of HPV</th>
<th>Heard of HPV Vaccine</th>
<th>Heard of cervical cancer</th>
<th>Knowledge of Pap smear test&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Know HPV is an STI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Aware of relationship between HPV and cervical cancer&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>26%</td>
<td>15%</td>
<td>67%</td>
<td>45%</td>
<td>24%</td>
<td>24%</td>
</tr>
</tbody>
</table>

HPV = human papillomavirus, STI = sexually transmitted infection

<sup>a</sup> Indicates the question was not measured quantitatively in the study

<sup>b</sup> Percent frequency is calculated using each study’s sample size as the denominator

<sup>c</sup> Among parents only (Harries et al., 2008, n=43 and Remes et al., 2012, n=60)

<sup>c</sup> Considered STI/virus/HPV

<sup>d</sup> Summary percent is calculated by dividing the sum of affirmatory responses (numerators) by the sum of study sample sizes (denominators) for each column. This summary measure should be interpreted with caution given that the measurement of these outcomes may have been different across studies.
Chapter 3

Attitudes and socio-demographic factors associated with HPV vaccine acceptability among rural and urban women in the Kilimanjaro Region, Tanzania

3.1 Abstract

Objective: The objective of this study was to describe and determine the socio-demographic factors, knowledge, and attitudes associated with HPV vaccine acceptability and to identify the barriers to vaccination among a population-based sample of rural and urban women in the Kilimanjaro Region of Tanzania.

Methods: A cross-sectional study was conducted using a multistage sampling technique among rural and urban women aged 18-55, with information obtained through interview-administered questionnaires. Bivariate and multivariable logistic regression models using generalized estimating equations were used to identify associations among rural and urban women separately, and barriers were assessed using Pearson’s Chi-square test.

Results: Women from both rural and urban areas had low vaccine-related knowledge; however, most indicated that they would be highly accepting of the HPV vaccine if it were available (93%). Among rural women, the independent associations with relative odds of HPV vaccine acceptance were: not having health insurance (OR=4.12, 95% CI: 1.43-11.88), willingness to pay for vaccines (OR=3.70, 95% CI: 1.47-9.32), knowing what the cervix was (OR=3.52, 95% CI: 1.67-7.42), believing they had access to a clinic or doctor to receive vaccinations (OR=3.23, 95% CI: 1.24-8.38), and lower educational attainment (OR=3.09, 95% CI: 1.49-6.42). Among urban women, independent
associations with relative odds of HPV vaccine acceptance were: believing their family or friends would support the vaccine (OR= 4.21, 95% CI: 1.74-10.18) and lower educational attainment (OR=3.84, 95% CI: 2.14-6.89). The most frequent perceived barriers to vaccination were concerns of cost, side effects, and safety.

**Conclusions:** According to this study, we expect that acceptance of the HPV vaccine in the Kilimanjaro Region of Tanzania would be high among women in both rural and urban areas. This study demonstrates that education on the vaccine and cervical cancer is needed, and vaccine publicity campaigns should emphasize financial and physical accessibility, peer acceptance, and safety.

**Keywords:** HPV, vaccine, Africa, Tanzania, cervical cancer, acceptability
3.2 Introduction

Cervical cancer is the third most common cancer among women worldwide, with approximately 500,000 new cases occurring annually (1). Nearly 86% of these cases occur in low- and middle-income countries, representing a large inequity in the burden of this disease (1). The introduction and widespread use of the Papanicolaou (Pap) screening test over fifty years ago for cervical cancer prevention has progressively reduced the incidence of disease by 50-60% in high-resource countries (2). Until recently, due to inadequate numbers of personnel and deficiencies in health system infrastructure, cervical cancer prevention in low-resource settings has relied on visual inspection methods using acetic acid (VIA), or Lugol’s iodine (VILI), with a ‘see-and-treat’ same-day approach (3).

Infection with human papillomavirus (HPV) is a necessary but not sufficient cause of cervical cancer. Development of invasive cervical cancer requires persistence of the infection and progressive development through precancerous stages. Most HPV infections are transient and 90% are cleared by a healthy host’s immune system or enter a latent phase within 1-2 years of exposure (4,5). Those that do persist may require 20-40 years to develop into invasive cervical cancer (6). There are individual and behavioral risk factors that increase the likelihood of infection and progression to invasive cervical cancer, which include: early sexual debut, having many sexual partners, long-term oral contraceptive use, high parity, smoking and co-infections causing suppressed immunity (e.g. HIV/AIDS) (7).

Over 100 genetic variants of HPV strains have been identified, 40 of which infect the genital region, and these have been further divided into high and low-risk types on the
basis of oncogenic potential (8,9). HPV strains 16 and 18 are responsible for approximately 70% of invasive cervical cancer cases worldwide while types 6 and 11 are responsible for 90% of anogenital warts cases. In 2006, a quadrivalent vaccine against these four strains became commercially available from Merck & Co. under the name Gardasil®. Gardasil is indicated for use in three-dose schedule, usually over a period of six months (0, 2 and 6 months). As a prophylactic vaccine, the ideal time to vaccinate is before first sexual contact, although the vaccine has been approved for use beyond the average age of sexual debut (10). Furthermore, it has been approved for use in both females and males, although in low-resource countries the vaccine is being targeting towards girls aged 9-13 among whom it is considered safe and effective (11–13). Organized cervical cancer screening and other educational campaigns are recognized as an important prevention methods, however the combination with prophylactic vaccination is expected to substantially reduce the future burden of disease in low-resource countries (11).

The cost of the three-dose series, nearly $400 US, has made the vaccine largely unavailable to individuals in low-resource countries that would be expected to benefit the most from vaccination. However, in June 2011, the Global Alliance for Vaccines and Immunization (GAVI) announced a negotiated $4.50/dose with Merck for vaccines in GAVI-eligible countries (<$1500 US Gross National Income per capita)(14). As a private-public partnership, GAVI acts as a centralizing body for vaccination programs such as Tanzania’s, combining the financial and personnel resources of key stakeholders including the Bill and Melinda Gates Foundation, WHO, UNICEF and the World Bank. With this price reduction, the financial barriers to implementation are less impacting, as
through GAVI support the co-financing required by eligible countries can be as low as $0.20/dose (1). GAVI is supporting demonstration projects in eight sub-Saharan African countries beginning in 2013-2014, including Tanzania. After successful demonstration of these programs, countries can apply to GAVI for national introduction support as was done for the national HPV vaccination program in Rwanda (15).

Similar to other sub-Saharan African countries, the health system in Tanzania faces a double burden of disease with communicable diseases competing for resources alongside non-communicable diseases such as cancer (16). In Tanzania, cervical cancer is the most common female cancer with an estimated age-standardized incidence rate of 51 per 100,000 women per year, a rate nearly five times higher than the incidence rate of the next most common cancer among both sexes combined (17). Cervical cancer screening in this region has been shown to be very low (18). The lack of existence and use of preventative methods in combination with risk factors have resulted in a high cancer-related mortality rate, with an age-standardized rate of 38 per 100,000 women per year (17).

The targeted age group and gender, as well as the sexually transmitted nature of the virus and novelty, have fueled a substantial amount of research on the knowledge, attitudes, and perceived barriers to vaccination. These factors have been well studied among high-resource countries. A 2007 systematic review of studies conducted prior to vaccine approval on the predictors of acceptability among young adults, adults and parents identified 28 studies from the US alone (19). This review was structured using the Health Belief Model (20) and found that respondents had high acceptability of the vaccine when they held beliefs of perceived effectiveness, perceived likelihood and were
cued to vaccinate by a physician. Acceptability was also higher among those with lower education. Common perceived barriers were cost, fears of promiscuity, safety, multiple dosing and side effects. In the years since the vaccine became available there have been reviews on the factors associated with uptake among teenage girls (21) and parental responses to the vaccine (22).

Within the last few years there has been a growing body of literature on this research topic in sub-Saharan African countries (23–37) and these studies have been recently reviewed [Manuscript 1]. Briefly, findings from 14 unique studies representing ten countries have revealed that HPV vaccine-related awareness and knowledge was quite low, however intention to vaccinate with the HPV vaccine was high. Most studies (11 of 14) were conducted in urban or semi-urban environments, and were convenience samples collected from clinics, communities, and schools/universities. Recommendation from a healthcare provider and endorsement by the government were two important cues to action for vaccine acceptance, and perceived barriers such as cost and accessibility appeared to be important.

Formative research on the knowledge and attitudes of vaccination is important for high acceptance of the vaccine (38) and may be informative for health planners. A case-control study following a social mobilization campaign conducted in northern Tanzania has examined the characteristics associated with vaccine uptake during a clinical trial (39). Among parents, factors associated with having a daughter who did not receive the vaccine included older age, owning fewer household items, not attending an education session and not knowing anyone who has had cervical cancer. This study has lessons for planning and education sensitization methods, and will be useful for preparation of a
national vaccination program. The formative research presented in the following study is among a population-based sample in Tanzania that has not been formally sensitized with an education campaign. As discussed, research in other countries have predicted high acceptance of the HPV vaccine should it become widely available, though most studies have presented results from selected samples, and none have compared population-based rural and urban samples within the same study. Furthermore, few studies have used statistical methods to explore the predictors of acceptability. Therefore, the purpose of this study was to determine the socio-demographic factors, knowledge, and attitudes that are associated with HPV vaccine acceptability using a population-based sample of rural and urban women living in the Kilimanjaro Region.

3.3 Methods

3.3.1 Study design and data collection

A cross-sectional survey was conducted among women aged 18-55 years old in Moshi Rural and Moshi Urban, two districts in the Kilimanjaro Region of Tanzania. These districts were chosen in order to provide representative samples of rural and urban living environments in the Kilimanjaro Region. The study questionnaire was designed in English and was translated and interviewer-administered in Kiswahili, the official language of Tanzania. The questionnaire was designed to be concise and practical for administration in a diverse population with varying levels of education. Questions included were either modified from previous studies, designed using best survey practices among the research team and guided by health behavioral theories to address the research
objectives (40–42). Back translation and cognitive interviewing with a translator was conducted after the questionnaire was translated to evaluate face validity and clarity. The questionnaire was pilot-tested among 60 women in Moshi Rural and revised to reflect the population’s socio-demographics, and refined for clarity. Surveying took place on weekdays from May to July 2012, using a stratified multistage sampling strategy. Within each district, five wards were randomly selected, followed by random selection of three villages and systematic sampling (with replacement) of houses. Every k\textsuperscript{th} household was chosen, depending on an estimate of village size, in order to sample 20 women representative of each village. If more than one woman was eligible in a house, a random selection was made. Trained Tanzanian female research assistants paired with study investigators gave a brief introduction to the purpose of the study before both voluntary oral and written consent was obtained. In the event that the participant could not write, verbal consent was considered adequate. Participants received no incentives to participate and the questionnaire took approximately thirty minutes to complete. Most questions were closed-response, consisting of Likert-type scales or Yes/No/Don’t Know response choices. Brief education on the location and function of the cervix was provided during the survey for women who said they had never heard of it before. The Kiswahili term for ‘cervix’ does not exist, described instead as the ‘neck of birth’ or ‘opening to the womb’, and this is common among other sub-Saharan African countries (25,31,43–45). However, the term for cervical cancer does exist, and can be understood though three variations (Saratani/Mdomo/Shingo ya Kizazi). The questionnaire was divided into nine sections, covering health and socio-demographic factors; cervical cancer awareness/knowledge, attitudes and barriers (18); and vaccination awareness, attitudes and barriers. In order to
clarify survey motives and reiterate confidentiality some sections had brief narratives that were read to participants. For example, before the vaccination sections the following was read: “Human Papillomavirus (HPV) can cause cervical cancer. HPV is not the same as HIV. Vaccines are medications given to prevent the development of disease or illness.”

Participants were considered to have an general understanding of cervical cancer if they answered ‘yes’ to “Have you heard of cancer?” and “Have you heard of cervical cancer?” and ‘women’ to “Who can develop cervical cancer?” (possible responses: men, women, both, don’t know). Vaccine awareness was queried by asking if they had ever heard of the HPV vaccine (possible responses: yes/no), and followed up with a question querying the source of this awareness. Vaccination attitudes were assessed by asking if the participant believed their husband or partner would support the vaccine, if they believed their friends/family would support the vaccine, if they thought vaccinations were beneficial, if they believed they could access a clinic or doctor to receive vaccinations and if they are willing to pay for vaccines (any amount). Identifying barriers consisted of a checklist of possible concerns or perceived barriers to vaccination of which the participant could choose multiple responses. Questions were also included on who participants thought should be involved in vaccination decisions, where the participant thought vaccination should occur and how long they would be willing to travel to receive a vaccination.

Acceptability of the HPV vaccine was evaluated by asking, “If the HPV vaccine became available in Tanzania, would you give permission for your daughter to receive it (or receive it yourself)?” (possible responses: definitely yes, probably yes, don’t know, probably no and definitely no). For the purpose of this study, the outcome was
conceptualized into a binomial response. Acceptors are those definitely accepting the vaccine (definitely yes (=1)) and those considered to be non-acceptors are those who gave less-accepting responses (all other responses: probably yes, probably no, definitely no, don’t know (=0)). The preamble to this question asked women to think of their daughters or hypothetical daughters/girls in the community, or if they were in the age range 10-25 they could answer thinking about themselves. At the time of survey design, an age group for targeted vaccination had not yet been decided upon for Tanzania. The age range 10-25 was chosen to reflect the age range used for HPV vaccine administration in high-resource countries.

The survey achieved a 97% and 98% percent response rate for rural and urban strata, respectively. Interviewer-reported validity and quality measures were collected for each survey, and those identified as invalid surveys by interviewers were excluded (n=11). Eight studies were excluded for being outside the targeted 18-55 age group, leading to a final study sample size of 272 urban and 303 rural women. Approval for this study was obtained from Health Sciences Research Ethics Board (Queen’s University, Canada), the Kilimanjaro Christian Medical Center Ethics Board and the National Institute for Medical Research (Tanzania).

3.3.2 Statistical analysis

Descriptive statistics were used to present measures on socio-demographic and health characteristics, cervical cancer and vaccination awareness/knowledge, and attitudes between rural and urban strata. Frequency tables were produced for categorical variables while means and standard deviations were calculated for continuous variables.
Comparisons for rural and urban strata were conducted using Pearson’s chi-square, Cochran-Armitage test for trend (modified chi-square for ordinal data) and Fisher’s exact test (n<5). Wilcoxon rank-sum test was used to compare between rural and urban continuous, non-normally distributed variables. Pearson’s chi-square and Fisher’s exact test were also used to test proportional differences between rural and urban strata in their barriers to vaccinations, sources of HPV vaccine knowledge, choice of vaccination site, and decision-makers for vaccinations. Sample clustering was not considered at the descriptive level of analysis as we were only interested in presenting sample proportions.

Rural and urban sample data were stratified a priori, and a purposeful selection strategy (46) was used to select exploratory multivariable models identifying covariates that were independently associated with vaccine acceptance in the samples. Generalized estimating equations with a logit link and exchangeable working correlation matrix were used to estimate odds ratios (OR) and 95% confidence intervals (CI) while accounting for the clustering within villages. First, bivariate associations were calculated between all covariates adjusted for age, and acceptance of the HPV vaccine. A variable indicating if the woman had a daughter aged 10-25 was tested to see if there was a difference between willingness based on real or imagined daughters, though we hypothesized there would not be based on previous studies (47,48). Variables associated at p<0.25 were included in preliminary models and were removed using backward selection until all remaining variables were significant p<0.05. Age was included in all models and variables removed from the model were re-considered as confounders if they changed the effect estimates by >10% when they were included again, as compared to the full model. No variable included in the multivariable models had more than 5% missing data. Collinearity
diagnostics and overall goodness-of-fit measures were assessed for each model. All statistical analyses were performed using SAS® version 9.3 (SAS Institute Inc., Cary, NC, USA).

3.4 Results

3.4.1 Socio-demographic and health characteristics of the sample

The study participants had a mean age of 34 years (SD: 9.7, range 18-55) and most were married (66%) and in monogamous relationships (96%). Participants in the urban stratum were significantly younger than those in rural (p<0.001) with nearly half under the age of 30. Most women were parents (85%) and 40% had a daughter between the ages of 10-25, though this was significantly different between rural and urban strata (49% and 30%, respectively, p<0.001). Overall, women from rural areas had significantly more children than urban women (p<0.001). Most women in the rural stratum belonged to the cultural group Chagga (85%) whereas urban women were distributed among Chagga (50%), Pare (20%) and other cultural groups (30%). Nearly all women in the rural stratum were Christian (95%) and urban women were either Christian (69%) or Muslim (30%). Women in the rural stratum were of low socio-economic status; the majority had completed Secondary (Form 4) education or less and lived in a household earning fewer than 20,000 TSH (US $12) per month. Women in the urban stratum were more distributed across monthly household earning categories, and 28% reported earning 100,000 TSH (US $61) or more per month. Women in this stratum also had a higher proportion that had completed Secondary (Form 6) or College/University education (33%
Form 6, 6% College/University vs. 12% Form 6, 3% College/University, rural and urban women respectively). Most rural women (77%) worked as farmers, while most urban women (65%) worked or owned small businesses related to tourism, dining/restaurants and tailoring. Approximately 14% of women said that they had health insurance, with no differences between strata.

In terms of health characteristics (Table 4), from a 5-point scale, most women rated their health status as ‘Fair’ or ‘Good’ (51% and 35%, respectively), few were smokers (0.9%) and 1.1% reported themselves HIV positive. More women in the rural stratum had ever had intercourse (p<0.001) although the mean age of sexual debut (20 years old, SD: 3.2 years) was not different between strata (p=0.79). The majority of women (69% rural and 59% urban) in both strata reported to only have had one sexual partner in their lifetime.

3.4.2 Awareness, knowledge, and attitudes among rural and urban women

Few women had heard of the HPV vaccine, with significant (p<0.03) differences in the proportion between rural and urban strata (12% and 6%, respectively (Table 5). Of those that had heard, the majority had awareness of the vaccine through the radio (70%), television (20%) or healthcare interactions (12%). Despite low awareness, most believed (80%) that their friends or family would support HPV vaccination. A similar proportion believed that they would have access to clinics or doctors to receive the vaccination and this was significantly different (p=0.03) between rural and urban women (75% and 83%, respectively). In terms of general vaccination attitudes, nearly all women (98%) believed that vaccinations were beneficial, and a moderate proportion (65%) were willing to pay
for vaccines if they were not offered free. Women were willing to travel to receive vaccinations, with many women agreeing to travel for longer than 2 hours (55% rural, 42% urban). When asked where they preferred their daughter to receive the vaccine, most women selected hospitals (53%), dispensaries (21%) or health centers (29%). Few women selected schools (7%) or family doctors (3%).

Significantly (p=0.004) fewer women in the rural stratum knew what the cervix was compared the urban stratum (10% and 18%, respectively). Women were considered to have an understanding of cervical cancer if they had heard of cancer and cervical cancer, and knew the disease only occurred in women. A moderate proportion (63%) had this understanding, with no significant differences between strata (p=0.64).

Cervical cancer attitudes and screening practices have been previously reported (18) from this sample of women. Few had ever been previously screened for cervical cancer (4% rural, 9% urban, p=0.04) and acceptance of screening among never-screened women was high (90%). Many thought that cervical cancer was fatal, with significant differences between strata (91% rural, 83% urban, p=0.004), and fewer thought that cervical cancer could be treated (63% rural, 67% urban, p=0.32). There were significant differences (p=0.02) in perception of personal risk for cervical cancer among strata (62% rural, 71% urban). Among the sub-groups that had daughters aged 10-25, the perception of their daughter’s risk for cervical cancer was similar (61% rural, 72% urban, p=0.12).

When asked to select from a list of possible HPV vaccination decision-makers, most women thought that parents alone should decide (49%). A smaller proportion thought that parents and daughters should decide together (26%), and fewer thought elder family members (7%), doctors (7%), mothers only (7%), daughters only (7%), fathers
only (6%), government (6%), or community leaders (6%) should decide. These responses were not significantly different between rural and urban strata, except more urban women thought mothers only (10%) should decide, as compared to rural women (3%), p<0.001.

3.4.3 Perceived barriers or concerns to HPV vaccination among rural and urban women

The greatest concern (50% rural, 46% urban, p=0.39) among women was the perceived costs associated with the HPV vaccine (Figure 2). This was followed by shared concerns among women in both strata regarding the unknown future side effects (41%), short-term side effects (20%), safety of administration (19%), social acceptability (15%), availability (13%), effectiveness (11%) and conformity with religious beliefs (6%). The concern of promiscuity/encouragement of early sex was significantly (p<0.001) different between strata, with more women in rural areas concerned (20% rural, 8% urban). Significantly more women in rural areas were also concerned about testing of the vaccine as compared to urban women (11% rural, 6% urban, p=0.03).

3.4.4 Acceptance of HPV vaccination

In both rural and urban strata, acceptance of the HPV vaccine among participants was very high with 93% of participants intending to definitely accept the vaccine if it were to become available in Tanzania. Willingness was not different among adults versus parents with daughters aged 10-25. Women were also asked to predict their husband or partner’s acceptance of the vaccine. There were no differences across strata but prediction that they would definitely accept the vaccine was lower (64%).
3.4.4.1 Bivariate associations between explanatory variables and HPV vaccine acceptance

Table 6 summarizes the associations between socio-demographic and health variables and HPV vaccine acceptance with adjustment for age. Among rural women, positive associations with relative odds of HPV vaccine acceptance included: working as a farmer or housewife compared to a professional occupation (OR 3.6, 95% CI: 1.05-12.17), primary school education or less compared to secondary school or more (OR 2.6, 95% CI: 1.09-6.32), having a monthly income of <40,000 TSH compared to ≥40,000 TSH (OR 2.3 95% CI: 0.81-6.53) and not having health insurance (OR 4.3, 95% CI: 1.66-11.29). Among urban women, positive associations with relative odds of HPV vaccine acceptance included: working in farming or business as compared to a professional occupation (OR 2.8, 95% CI:1.13-6.78) and primary school education or less compared to secondary school or more (OR 4.0, 95% CI: 2.13-7.69).

Table 7 summarizes the associations between knowledge and attitude variables and HPV vaccine acceptance with adjustment for age. Among rural women, positive associations with relative odds of HPV vaccine acceptance included: not having heard of the vaccine (OR 2.9, 95% CI: 1.20-7.16), believing family or friends will support the vaccine (OR 5.1, 95% CI: 1.79-14.61), believing they are able to access a clinic or doctor for vaccination (OR 4.4, 95% CI: 2.10-9.28), willing to pay for vaccines (OR 5.0, 95% CI: 2.37-10.52) and not knowing what the cervix is (OR 4.2, 95% CI: 1.91-9.26). Among urban women, positive associations with relative odds of HPV vaccine acceptance included: believing family or friends will support the vaccine (OR 3.1, 95% CI: 1.38-7.14) and not knowing what the cervix is (OR 3.1, 95% CI: 1.17-8.31). There were no
associations between cervical cancer screening status, having known someone with the disease, believing it was fatal, believing it could be treated, perceived personal or daughter’s risk of the disease and acceptance of the vaccine among either strata (additional Tables 10 and 11).

3.4.4.2 Multivariable models predicting HPV vaccine acceptance among rural and urban women

Exploratory multivariable models with the outcome of vaccine acceptance were conducted with all significant variables from bivariate models listed previously, along with additional variables significant at p>0.25. For the rural group, these additional variables included: having a daughter aged 10-25 and having known someone with the disease. For the urban group, these additional variables included: monthly household income, health insurance and parity.

Table 8 presents the results of a multivariable model showing the independent associations with HPV vaccine acceptance among rural women, adjusted for age, beliefs on if family/friends will support the vaccine, and other variables in the model. Those without health insurance had about 4 times the odds (OR=4.12, 95% CI: 1.43-11.88) of acceptance of the vaccine compared to those that had health insurance. Similarly, those who were willing to pay for vaccinations were had about 3.7 times the odds of acceptance (OR=3.70, 95% CI: 1.47-9.32) compared to those who were unwilling. Women who did not know what the cervix was were associated with 3.5 times the odds of accepting the vaccine (95% CI: 1.53-7.85) compared to those that did. Finally, Women who believed that they had access to a clinic or doctor to receive vaccinations were associated with about 3.2 times the odds of accepting the vaccine (95% CI: 1.24-8.38) compared to those
that did not, and those with lower educational attainment (Primary or less) were associated with about 3 times the odds of acceptance (OR=3.09, 95% CI: 1.49-6.42) compared to those with more (>Primary education).

Table 9 presents the results of a multivariable model showing the independent associations with HPV vaccine acceptance among urban women in the sample, adjusted for age, knowing or not knowing what cervix is, and other variables in the model. A belief that their family or friends would support the HPV vaccine was strongly associated with acceptance, with about 4.2 times the odds of acceptance (95% CI: 1.74-10.18) compared to those who did not believe they would support the vaccine. Furthermore, those who had lower educational attainment had about 3.8 times the odds of accepting the vaccine compared to those with more (OR=3.8, 95% CI: 2.14-6.89).

3.5 Discussion

This is the first study to present socio-demographic, knowledge, and attitudinal associations of HPV vaccine acceptability among a population-based sample of rural and urban women living in the Kilimanjaro Region of Tanzania. Despite differences on several measures, and findings of low vaccine-related knowledge, both rural and urban groups reported high acceptance of the HPV vaccine if it were to be available. This finding is consistent with other low-resource countries in sub-Saharan Africa [Manuscript 1], and due to low knowledge may represent a general attitude towards vaccinations, or an attitude toward a vaccine preventing cancer. Tanzania currently vaccinates against six diseases through the Expanded Programme on Immunization (EPI) and uptake of these vaccinations has been high, reaching 75% of children aged 12-23 months (49).
Our findings suggest that popular media sources, such as the TV and radio, are important sources for HPV-related knowledge dissemination and this is consistent with findings from other low-resource areas (33). The content or accuracy of these messages was not investigated in the present study and may be a future research direction; empirical studies examining message framing of the HPV vaccine have been studied mostly within the United States (50–53), and there may be different preferences as a result of cultural differences.

Although women themselves predicted high acceptance, prediction of their husband/partner’s acceptance of the vaccine was lower. Women may not have felt confident to speak on their behalf of their partner, however, in general it has been suggested that women make the majority of health decisions for their children in these contexts (24,26). Nevertheless, when asked about decision-making women expected that the decision to vaccinate would be made by both parents together, and so investigating vaccination attitudes among men may be of interest to future studies.

The strength and direction of associations of acceptability may be evidence of the relative importance of these variables to each group. Among rural women, variables related to cost, self-efficacy/access, cervical knowledge and educational attainment were independently associated with higher odds of acceptance. Not having health insurance was found to have a strong association with predicted acceptance and it is suspected that women without health insurance may be more willing, in general, to accept free health services due to a lack of financial resources including those for travel costs. This is consistent with other studies that have found health insurance as a significant barrier to HPV vaccination (54) and associated with use of cervical cancer screening (44). Not
having health insurance is also consistent with a willingness to pay for vaccinations, although it is unclear if insurers will cover this vaccine for women outside the targeted age group. The 2010 Demographic Health Survey indicated that the Kilimanjaro Region had the highest proportion (19.6%) of insured individuals in Tanzania, and incongruently to our results, found that those in urban areas were more likely to have health insurance (49).

A belief that they had access to a clinic or doctor for vaccination was associated higher odds of acceptance and this attitude could be understood as a perceived self-efficacy or access barrier. Self-efficacy barriers, originally proposed by Bandura (1977), hold that a person’s perception of their ability to successfully execute a behavior influences their initiation of the behavior (55). A similar finding was significant for vaccine acceptance among women in Botswana (29) and Ghana (28). This barrier may be largely mitigated if the vaccine is delivered through a school-based delivery model, as is being done in other countries such as Kenya (56). As further support for the school-based model, the Kilimanjaro Region has been shown to have a very high (91%) primary school attendance for children (ages 7-13). Notably, this proportion was found lower among lower-income households and in rural areas (49); for these areas, alternative delivery methods may be required concurrently.

Among urban women, independent associations with increased odds of acceptance were educational attainment and the belief that family or friends would support the vaccine. Health insurance and cost variables were not associated with acceptance in this group, and may be reflective of fewer monetary-related concerns due to the greater financial stability. Lower educational attainment was associated with
acceptance, and this was also true among rural women; this finding, along with other low knowledge/awareness associations with higher odds of acceptance warrant further research. The belief that family and friends also support the vaccine represents a normative social belief, and suggests that vaccine campaigns could increase acceptance by presenting the success and acceptance of the vaccine within other communities and foster peer-to-peer education programs.

Our findings on perceived barriers towards vaccination suggest that financial barriers are an important concern among both groups; this is consistent with other studies (25,28). Although the vaccine is expect to be administered for free, the financial burden associated with access to the vaccination should be minimized, and further reductions at the policy level may be important towards increasing access for those outside the age range who wish to vaccinate (14). Concerns of vaccine safety and side effects are also important barriers to address; history predicts that misinformation generated by publicity campaigns, such as that during the tetanus toxoid vaccination in Tanzania, present major barriers toward acceptance (57). The differences found in concern over encouragement of earlier sex and testing between rural and urban samples may be a true difference, however since socio-demographic, knowledge, and attitude variables were not concurrently considered it could be attributed to any number of the differences between these samples.

This study has strengths in reporting findings that are timely given the recent announcements of upcoming vaccine demonstration projects in Tanzania. In terms of design, the use of a multistage sampling strategy to collect a population-based sample that was powered to make rural and urban comparisons is novel for this region (Appendix
Comparison of the demographic characteristics of participants to findings from the nationwide Demographic Health Survey (DHS) conducted in Tanzania in 2010 illustrates that our sample has concordant findings on education, parity, smoking status and sexual behaviors such as contraception use (49). Although the sample is believed to be representative of the Kilimanjaro Region, the findings may not be generalizable to other regions with different socio-demographic differences. A final strength of this study is the use of multivariable modeling to identify associations with acceptance, and the consideration of clustered data. This is unique for an acceptability study from a sub-Saharan African country (Manuscript 1), with only one other study to date using a multivariable model among university students (23).

Although the survey was pilot-tested, a limitation of this study is the use of a survey that has not been tested for validity or reliability. Furthermore, the study’s analysis was exploratory in nature and may not have enumerated all the explanatory variables that identify the factors important for acceptance of the vaccine; the proportion of variance explained by either of these models was low (<10%). The survey results were self-reported and social desirability may have influenced answers to sensitive questions, such as those on sexual behaviors. The outcome measured in this study represents an intention to vaccinate may not necessarily translate into behavior (58), although strong correlations between vaccination intention and behavior have been found (59). This research was conducted before the vaccine had become publically available, without educational initiatives, and it is possible that attitudes may change as education programs and media sources disseminate information within the public domain. The survey was directed towards all adult females, and although having a daughter within the vaccination
age was not independently associated with acceptance, there may be different associations among parents only that this study did not investigate and was not powered to detect. Lastly, vaccination was queried for daughters, however given the findings of efficacy and indications for use of the vaccine among boys (60), research into these attitudes may be important to study since work in other countries have suggested that women may be less accepting of this vaccine for boys (47,48).

Recently announced demonstration project plans by GAVI represent an important step toward national introduction of the HPV vaccine in Tanzania. The current study examined the socio-demographic factors, knowledge, and attitudes associated with predicted acceptance of the HPV vaccine among rural and urban women, and the perceived barriers towards vaccination with in the Kilimanjaro Region. Our findings suggest that acceptance of the HPV vaccine will be high, however education is required, and there are particular concerns that could be addressed within educational and publicity campaigns in order to ensure high, widespread acceptance, including emphasis on financial and physical accessibility, peer acceptance, and safety.

3.6 Acknowledgements

We would like to acknowledge and thank the women who participated in this study. We also acknowledge the work of our research assistants and colleagues at Pamoja Tunaweza Women’s Center (Moshi, Tanzania). We also thank the Pure Art Foundation for contributing funding for this work.
3.1 Conflict of Interest

The authors have no conflicts of interest to declare.
3.2 References


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### 3.3 Figures and Tables

Table 3. Socio-demographic characteristics among rural and urban women in the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=575)</th>
<th>Rural (n=303)</th>
<th>Urban (n=272)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (+SD)</td>
<td>33.8 (9.7)</td>
<td>36.2 (9.7)</td>
<td>31.2 (8.9)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>&lt;30</td>
<td>38.0 (215)</td>
<td>27.5 (82)</td>
<td>49.6 (133)</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>30-39</td>
<td>32.9 (186)</td>
<td>34.2 (102)</td>
<td>31.3 (84)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>21.4 (121)</td>
<td>26.9 (80)</td>
<td>15.3 (41)</td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>7.8 (44)</td>
<td>11.4 (34)</td>
<td>3.7 (10)</td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>13.7 (78)</td>
<td>10.3 (31)</td>
<td>17.6 (47)</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Partner</td>
<td>8.6 (49)</td>
<td>4.3 (13)</td>
<td>13.5 (36)</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>65.6 (373)</td>
<td>74.2 (224)</td>
<td>55.8 (149)</td>
<td></td>
</tr>
<tr>
<td>Separated</td>
<td>6.7 (38)</td>
<td>4.6 (14)</td>
<td>9.0 (24)</td>
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<tr>
<td>Divorced</td>
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<td>0.7 (2)</td>
<td>0.0 (0)</td>
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<tr>
<td>Widow</td>
<td>5.1 (29)</td>
<td>6.0 (18)</td>
<td>4.1 (11)</td>
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</tr>
<tr>
<td><strong>Partnership type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monogamy</td>
<td>95.8 (406)</td>
<td>97.7 (31)</td>
<td>92.8 (47)</td>
<td>0.015&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Polygamy</td>
<td>4.3 (18)</td>
<td>2.3 (6)</td>
<td>7.2 (12)</td>
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<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christian</td>
<td>82.9 (474)</td>
<td>95.0 (287)</td>
<td>69.3 (187)</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Muslim</td>
<td>17.1 (98)</td>
<td>5.0 (15)</td>
<td>30.7 (83)</td>
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<tr>
<td><strong>Culture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Chagga</td>
<td>68.2 (391)</td>
<td>84.8 (256)</td>
<td>49.8 (135)</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
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<td>12.4 (71)</td>
<td>5.6 (17)</td>
<td>19.9 (54)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
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<td>9.6 (29)</td>
<td>30.3 (82)</td>
<td></td>
</tr>
<tr>
<td><strong>Monthly household income (TSH)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20,000</td>
<td>42.7 (241)</td>
<td>62.2 (184)</td>
<td>21.2 (57)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>20,000 - 39,999</td>
<td>22.5 (127)</td>
<td>22.6 (67)</td>
<td>22.3 (60)</td>
<td></td>
</tr>
<tr>
<td>40,000 - 59,999</td>
<td>11.2 (63)</td>
<td>7.4 (22)</td>
<td>15.2 (41)</td>
<td></td>
</tr>
<tr>
<td>60,000 - 79,999</td>
<td>4.4 (25)</td>
<td>0.7 (2)</td>
<td>8.6 (23)</td>
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<td>80,000 - 99,999</td>
<td>3.2 (18)</td>
<td>1.7 (5)</td>
<td>4.8 (13)</td>
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</tr>
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<td>≥100,000</td>
<td>16.1 (91)</td>
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<td><strong>Occupation</strong></td>
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<tr>
<td>Housewife/Farmer</td>
<td>51.0 (284)</td>
<td>76.6 (226)</td>
<td>22.1 (58)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Small Business</td>
<td>38.4 (214)</td>
<td>15.0 (44)</td>
<td>64.6 (170)</td>
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<td>Professional</td>
<td>2.0 (11)</td>
<td>1.4 (4)</td>
<td>2.7 (7)</td>
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<tr>
<td>Student</td>
<td>4.3 (24)</td>
<td>4.1 (12)</td>
<td>4.6 (12)</td>
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<tr>
<td>Teacher</td>
<td>2.3 (13)</td>
<td>1.7 (5)</td>
<td>3.0 (8)</td>
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<tr>
<td>Health Professional</td>
<td>2.0 (11)</td>
<td>1.0 (3)</td>
<td>3.0 (8)</td>
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</tr>
<tr>
<td><strong>Educational attainment</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>8.4 (48)</td>
<td>10.9 (33)</td>
<td>5.5 (15)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Secondary (to Form 4)</td>
<td>65.8 (377)</td>
<td>74.5 (225)</td>
<td>56.1 (152)</td>
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<tr>
<td>Secondary complete</td>
<td>21.6 (124)</td>
<td>11.9 (36)</td>
<td>32.5 (88)</td>
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<tr>
<td>College/University</td>
<td>4.2 (24)</td>
<td>2.7 (8)</td>
<td>5.9 (16)</td>
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<td><strong>Health Insurance</strong></td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>86.0 (485)</td>
<td>85.8 (254)</td>
<td>86.2 (231)</td>
<td>0.896&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Yes</td>
<td>14.0 (79)</td>
<td>14.2 (42)</td>
<td>13.8 (37)</td>
<td></td>
</tr>
<tr>
<td><strong>Number of births</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (+SD)</td>
<td>2.7 (2.1)</td>
<td>3.5 (2.2)</td>
<td>1.9 (1.5)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>None</td>
<td>14.7 (84)</td>
<td>7.6 (23)</td>
<td>22.6 (61)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1-2</td>
<td>36.8 (211)</td>
<td>30.7 (93)</td>
<td>43.7 (118)</td>
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</tr>
<tr>
<td>3-4</td>
<td>31.1 (178)</td>
<td>34.3 (104)</td>
<td>27.4 (74)</td>
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</tr>
<tr>
<td>&gt;4</td>
<td>17.5 (100)</td>
<td>27.4 (83)</td>
<td>6.3 (17)</td>
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<td><strong>Daughter aged 10-25</strong></td>
<td></td>
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<td></td>
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<tr>
<td>No</td>
<td>60.4 (347)</td>
<td>51.5 (156)</td>
<td>70.2 (191)</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Yes</td>
<td>39.7 (228)</td>
<td>48.5 (147)</td>
<td>29.8 (81)</td>
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</tr>
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<sup>a</sup> Wilcoxon rank-sum test
<sup>b</sup> Pearson’s Chi-square test
<sup>c</sup> Cochran-Armitage test for trend
<sup>d</sup> Fisher’s exact test

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Table 4. Health characteristics among rural and urban women in the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=575) % (n)</th>
<th>Rural (n=303) % (n)</th>
<th>Urban (n=272) % (n)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported health status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>3.2 (18)</td>
<td>2.7 (8)</td>
<td>3.7 (10)</td>
<td>0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Very Good</td>
<td>6.4 (36)</td>
<td>6.7 (20)</td>
<td>5.9 (16)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>34.7 (197)</td>
<td>26.3 (78)</td>
<td>44.1 (119)</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>51.3 (291)</td>
<td>58.6 (174)</td>
<td>43.3 (117)</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>4.4 (25)</td>
<td>5.7 (17)</td>
<td>3.0 (8)</td>
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</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>99.1 (564)</td>
<td>99.3 (298)</td>
<td>98.9 (266)</td>
<td>0.671&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Yes</td>
<td>0.9 (5)</td>
<td>0.7 (2)</td>
<td>1.1 (3)</td>
<td></td>
</tr>
<tr>
<td>HIV positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>99.0 (567)</td>
<td>99.3 (300)</td>
<td>98.5 (267)</td>
<td>0.429&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Yes</td>
<td>0.9 (5)</td>
<td>0.7 (2)</td>
<td>1.1 (3)</td>
<td></td>
</tr>
<tr>
<td>Currently using contraception (any)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>57.5 (319)</td>
<td>55.6 (164)</td>
<td>59.6 (155)</td>
<td>0.339&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Yes</td>
<td>42.5 (236)</td>
<td>44.4 (131)</td>
<td>40.4 (105)</td>
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</tr>
<tr>
<td>Ever had intercourse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7.0 (40)</td>
<td>3.3 (10)</td>
<td>11.1 (30)</td>
<td>&lt;0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Yes</td>
<td>93.0 (533)</td>
<td>96.7 (292)</td>
<td>88.9 (241)</td>
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</tr>
<tr>
<td>Age of sexual debut</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>19.8 (3.2)</td>
<td>19.6 (3.2)</td>
<td>19.9 (3.3)</td>
<td>0.794&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>&lt;16</td>
<td>6.4 (32)</td>
<td>6.5 (18)</td>
<td>6.5 (14)</td>
<td>0.973&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>16-23</td>
<td>82.1 (409)</td>
<td>82.4 (229)</td>
<td>81.8 (180)</td>
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</tr>
<tr>
<td>≥24</td>
<td>11.5 (57)</td>
<td>11.2 (31)</td>
<td>11.8 (26)</td>
<td></td>
</tr>
<tr>
<td>Lifetime number of sexual partners</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>7.2 (41)</td>
<td>3.3 (10)</td>
<td>11.7 (31)</td>
<td>0.201&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1</td>
<td>64.1 (363)</td>
<td>68.8 (207)</td>
<td>58.9 (156)</td>
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<tr>
<td>2-3</td>
<td>25.6 (145)</td>
<td>24.9 (75)</td>
<td>26.4 (70)</td>
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<tr>
<td>≥4</td>
<td>3.0 (17)</td>
<td>3.0 (9)</td>
<td>3.0 (8)</td>
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</tr>
</tbody>
</table>

<sup>a</sup> Cochran-Armitage test for trend  
<sup>b</sup> Fisher’s exact test  
<sup>c</sup> Pearson’s Chi-square test  
<sup>d</sup> Wilcoxon rank-sum test
Table 5. Human papillomavirus (HPV) knowledge and attitudes among rural and urban women in the study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=575)</th>
<th>Rural (n=303)</th>
<th>Urban (n=272)</th>
<th>p-value$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
<td></td>
</tr>
<tr>
<td>Heard of the HPV vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>91.0 (523)</td>
<td>88.5 (268)</td>
<td>93.8 (255)</td>
<td>0.027</td>
</tr>
<tr>
<td>Yes</td>
<td>9.0 (52)</td>
<td>11.6 (35)</td>
<td>6.3 (17)</td>
<td></td>
</tr>
<tr>
<td>Believes husband/partner will definitely accept HPV vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>36.3 (205)</td>
<td>37.9 (113)</td>
<td>34.3 (92)</td>
<td>0.375</td>
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<tr>
<td>Yes</td>
<td>63.8 (361)</td>
<td>62.1 (185)</td>
<td>65.7 (176)</td>
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<tr>
<td>Believes family/friends will support the HPV vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>19.9 (114)</td>
<td>21.6 (65)</td>
<td>18.1 (49)</td>
<td>0.294</td>
</tr>
<tr>
<td>Yes</td>
<td>80.1 (458)</td>
<td>78.4 (236)</td>
<td>81.9 (222)</td>
<td></td>
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<tr>
<td>Believes they are able to access a clinic/doctor for vaccination</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>21.0 (120)</td>
<td>24.6 (74)</td>
<td>17.0 (46)</td>
<td>0.027</td>
</tr>
<tr>
<td>Yes</td>
<td>79.0 (451)</td>
<td>75.4 (227)</td>
<td>83.0 (224)</td>
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<tr>
<td>Believes vaccines are beneficial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.6 (9)</td>
<td>1.0 (3)</td>
<td>2.2 (6)</td>
<td>0.319$^b$</td>
</tr>
<tr>
<td>Yes</td>
<td>98.4 (564)</td>
<td>99.0 (299)</td>
<td>97.8 (265)</td>
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<td>Willing to pay for vaccines</td>
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<td></td>
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<tr>
<td>No</td>
<td>35.2 (201)</td>
<td>33.9 (102)</td>
<td>36.7 (99)</td>
<td>0.488</td>
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<td>Yes</td>
<td>64.8 (370)</td>
<td>66.0 (199)</td>
<td>63.3 (171)</td>
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<td>Max. time willing to travel for vaccination</td>
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<td></td>
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<tr>
<td>&lt;30 min</td>
<td>25.7 (146)</td>
<td>20.8 (62)</td>
<td>31.1 (84)</td>
<td>&lt;0.001$^c$</td>
</tr>
<tr>
<td>1 hour</td>
<td>25.7 (146)</td>
<td>24.2 (72)</td>
<td>27.4 (74)</td>
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<tr>
<td>&gt;2 hours</td>
<td>48.6 (276)</td>
<td>55.0 (164)</td>
<td>41.5 (112)</td>
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<tr>
<td>Knows what the cervix is</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>86.2 (494)</td>
<td>90.1 (273)</td>
<td>81.9 (221)</td>
<td>0.004</td>
</tr>
<tr>
<td>Yes</td>
<td>13.8 (79)</td>
<td>9.9 (30)</td>
<td>18.2 (49)</td>
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<tr>
<td>Understanding of cervical cancer$^d$</td>
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<tr>
<td>No</td>
<td>37.5 (215)</td>
<td>38.4 (116)</td>
<td>36.5 (99)</td>
<td>0.643</td>
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<td>Yes</td>
<td>62.5 (358)</td>
<td>61.6 (186)</td>
<td>63.5 (172)</td>
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</table>

$^a$ Pearson’s Chi-square  
$^b$ Fisher’s exact test  
$^c$ Cochran-Armitage test for trend  
$^d$ Understanding assessed by (a) having heard of cancer and cervical cancer (b) knowing cervical cancer only occurs in females
Table 6. Bivariate associations of socio-demographic and health explanatory variables and HPV vaccine acceptance among rural and urban women in the study population

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Rural</th>
<th>Urban</th>
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<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
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<tr>
<td>Age</td>
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<tr>
<td>&lt;30 years</td>
<td>ref.</td>
<td>ref.</td>
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<tr>
<td>30-39</td>
<td>0.51 (0.16-1.66)</td>
<td>1.02 (0.42-2.47)</td>
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<tr>
<td>≥40</td>
<td>0.35 (0.10-1.20)</td>
<td>1.01 (0.31-3.31)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>0.73 (0.17-3.24)</td>
<td>0.91 (0.49-1.71)</td>
</tr>
<tr>
<td>Married/Partnered</td>
<td>ref.</td>
<td>ref.</td>
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<tr>
<td>Separated/Divorced/Widowed</td>
<td>1.76 (0.50-6.13)</td>
<td>——</td>
</tr>
<tr>
<td>Religion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christian</td>
<td>1.32 (0.22-8.02)</td>
<td>1.34 (0.39-4.64)</td>
</tr>
<tr>
<td>Muslim</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Culture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chagga</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Pare</td>
<td>1.27 (0.12-13.08)</td>
<td>0.82 (0.37-1.80)</td>
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<td>Other</td>
<td>2.02 (0.25-16.53)</td>
<td>1.28 (0.50-3.25)</td>
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<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmer/housewife*</td>
<td>3.57 (1.05-12.17)*</td>
<td>2.77 (1.13-6.78)*</td>
</tr>
<tr>
<td>Small business*</td>
<td>2.53 (0.24-26.83)</td>
<td>ref.</td>
</tr>
<tr>
<td>Professional</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Education</td>
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<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>2.63 (1.09-6.32)*</td>
<td>4.04 (2.13-7.69) *</td>
</tr>
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<td>≥ Secondary complete</td>
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<td>ref.</td>
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<tr>
<td>Monthly household income (TSH)</td>
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<td>&lt;40,000</td>
<td>2.30 (0.81-6.53)</td>
<td>2.44 (0.52-11.52)</td>
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<tr>
<td>≥40,000</td>
<td>ref.</td>
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<td>Health insurance</td>
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<tr>
<td>No</td>
<td>4.32 (1.66-11.29) *</td>
<td>2.35 (0.81-6.78)</td>
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<td>Yes</td>
<td>ref.</td>
<td>ref.</td>
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<tr>
<td>Self-reported health status</td>
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</tr>
<tr>
<td>Fair/Poor</td>
<td>ref.</td>
<td>ref.</td>
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<tr>
<td>≥Good</td>
<td>1.18 (0.36-3.90)</td>
<td>1.06 (0.19-5.92)</td>
</tr>
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<td>Currently using contraception (any)</td>
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<td></td>
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<tr>
<td>No</td>
<td>1.56 (0.72-3.35)</td>
<td>1.50 (0.62-3.64)</td>
</tr>
<tr>
<td>Yes</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Age at first intercourse</td>
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<td></td>
</tr>
<tr>
<td>&lt;19</td>
<td>1.34 (0.60-3.02)</td>
<td>1.61 (0.57-4.59)</td>
</tr>
<tr>
<td>≥19</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Lifetime number of sexual partners</td>
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<td></td>
</tr>
<tr>
<td>None</td>
<td>——</td>
<td>1.31 (0.49-3.49)</td>
</tr>
<tr>
<td>1</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>≥2</td>
<td>2.33 (0.66-8.26)</td>
<td>——</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never given birth</td>
<td>1.35 (0.24-7.67)</td>
<td>0.38 (0.10-1.46)</td>
</tr>
<tr>
<td>1-2 births</td>
<td>1.43 (0.40-5.03)</td>
<td>2.54 (0.53-2.45)</td>
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<tr>
<td>≥3 births</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Daughter aged 10-25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>2.03 (0.99-4.15)</td>
<td>0.89 (0.27-2.90)</td>
</tr>
</tbody>
</table>

HPV= human papillomavirus, OR = odds ratio, CI=confidence interval, ref.=referent group. Odds ratios are adjusted for age.

*p<0.05

Complete separation of covariate and outcome (all accepted)

These categories were combined for the urban strata.
Table 7. Bivariate associations of HPV knowledge and attitudinal explanatory variables and vaccine acceptance among rural and urban women in the study population

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Rural</th>
<th>Urban</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Heard of the HPV vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2.93 (1.20-7.16) *</td>
<td>1.05 (0.10-11.40)</td>
</tr>
<tr>
<td>Yes</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Believes family/friends will support the HPV vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>5.12 (1.79-14.61) *</td>
<td>3.14 (1.38-7.14) *</td>
</tr>
<tr>
<td>Believes they are able to access a clinic/doctor for vaccination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>4.42 (2.10-9.28) *</td>
<td>1.75 (0.57-5.33)</td>
</tr>
<tr>
<td>Believes vaccines are beneficial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>10.89 (0.73-161.7)</td>
<td>5.74 (0.76-43.37)</td>
</tr>
<tr>
<td>Willing to pay for vaccines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>4.99 (2.37-10.52) *</td>
<td>1.40 (0.43-4.59)</td>
</tr>
<tr>
<td>Knows what the cervix is</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>4.20 (1.91-9.26)*</td>
<td>3.12 (1.17-8.31) *</td>
</tr>
<tr>
<td>Understanding of cervical cancer ‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>1.40 (0.70-2.78)</td>
<td>0.79 (0.42-1.50)</td>
</tr>
</tbody>
</table>

HPV= human papillomavirus, OR = odds ratio, CI=confidence interval, ref.=referent group. Odds ratios are adjusted for age. *p<0.05.
‡ Understanding assessed by (a) having heard of cancer and cervical cancer (b) knowing cervical cancer only occurs in females
Table 8. Multivariable model presenting independent associations with HPV vaccine acceptance among rural women in the study population

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Adjusted OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Insurance</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.12 (1.43-11.88)</td>
</tr>
<tr>
<td>Yes</td>
<td>ref.</td>
</tr>
<tr>
<td>Willing to pay for vaccines</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>3.70 (1.47-9.32)</td>
</tr>
<tr>
<td>Knows what the cervix is</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.52 (1.67-7.42)</td>
</tr>
<tr>
<td>Yes</td>
<td>ref.</td>
</tr>
<tr>
<td>Believes they are able to access a clinic or doctor for vaccination</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>3.23 (1.24-8.38)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>3.09 (1.49-6.42)</td>
</tr>
<tr>
<td>≥ Secondary complete</td>
<td>ref.</td>
</tr>
</tbody>
</table>

*Adjusted for age, beliefs on if family/friends will support the vaccine, and the other variables in the table

Table 9. Multivariable model presenting independent associations with HPV vaccine acceptance among urban women in the study population

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Adjusted OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Believes family/friends will support the HPV vaccine</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
</tr>
<tr>
<td>Yes</td>
<td>4.21 (1.74-10.18)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>3.84 (2.14-6.89)</td>
</tr>
<tr>
<td>≥ Secondary completed</td>
<td>ref.</td>
</tr>
</tbody>
</table>

*Adjusted for age, knowing/not knowing what cervix is, and the other variables in the table
Figure 2. Perceived barriers or concerns of HPV vaccination among rural and urban women in the study population. *p<0.05
### 3.1 Additional Figures and Tables

**Table 10. Cervical cancer knowledge and attitudes among rural and urban women in the study population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=575)</th>
<th>Rural (n=303)</th>
<th>Urban (n=272)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever screened for cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>93.7(538)</td>
<td>95.7(290)</td>
<td>91.5(248)</td>
<td>0.040</td>
</tr>
<tr>
<td>Yes</td>
<td>6.8(39)</td>
<td>4.3(13)</td>
<td>8.5(23)</td>
<td></td>
</tr>
<tr>
<td>If not, would accept cervical cancer screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.2(55)</td>
<td>10.9(32)</td>
<td>9.4(23)</td>
<td>0.557</td>
</tr>
<tr>
<td>Yes</td>
<td>89.8(485)</td>
<td>89.1(262)</td>
<td>90.7(223)</td>
<td></td>
</tr>
<tr>
<td>Known someone with cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>73.8(417)</td>
<td>71.7(213)</td>
<td>76.1(204)</td>
<td>0.235</td>
</tr>
<tr>
<td>Yes</td>
<td>26.2(148)</td>
<td>28.3(84)</td>
<td>23.9(64)</td>
<td></td>
</tr>
<tr>
<td>Believes cervical cancer is fatal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12.8(73)</td>
<td>9.0(27)</td>
<td>17.0(46)</td>
<td>0.004</td>
</tr>
<tr>
<td>Yes</td>
<td>87.2(498)</td>
<td>91.0(273)</td>
<td>83.0(225)</td>
<td></td>
</tr>
<tr>
<td>Believes cervical cancer can be treated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34.9(197)</td>
<td>36.9(108)</td>
<td>32.8(89)</td>
<td>0.317</td>
</tr>
<tr>
<td>Yes</td>
<td>65.1(367)</td>
<td>63.1(185)</td>
<td>67.2(182)</td>
<td></td>
</tr>
<tr>
<td>Believes they are at risk for cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>33.4(192)</td>
<td>37.6(114)</td>
<td>28.7(78)</td>
<td>0.023</td>
</tr>
<tr>
<td>Yes</td>
<td>66.6(383)</td>
<td>62.4(189)</td>
<td>71.3(194)</td>
<td></td>
</tr>
<tr>
<td>Believes their daughter is at risk for cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>35.1(80)</td>
<td>38.8(57)</td>
<td>28.4(23)</td>
<td>0.116</td>
</tr>
<tr>
<td>Yes</td>
<td>64.9(148)</td>
<td>61.2(90)</td>
<td>71.6(58)</td>
<td></td>
</tr>
</tbody>
</table>

*Pearson’s Chi-square
Table 11. Bivariate associations of cervical cancer knowledge and attitudinal explanatory variables and HPV vaccine acceptance among rural and urban women in the study population

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Rural</th>
<th>Urban</th>
<th>OR = odds ratio (95% CI)</th>
<th>OR = odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever screened for cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>—*</td>
<td>1.71</td>
<td>(0.62-4.70)</td>
<td></td>
</tr>
<tr>
<td>If not, would accept cervical cancer screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.24</td>
<td>4.73</td>
<td>(1.64-13.60) *</td>
<td></td>
</tr>
<tr>
<td>Known someone with cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.82</td>
<td>1.07</td>
<td>(0.36-3.15)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Believes cervical cancer is fatal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.57</td>
<td>1.68</td>
<td>(0.39-7.23)</td>
<td></td>
</tr>
<tr>
<td>Believes cervical cancer can be treated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.62</td>
<td>1.05</td>
<td>(0.48-2.32)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Believes they are at risk for cervical cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.96</td>
<td>1.17</td>
<td>(0.36-3.83)</td>
<td></td>
</tr>
<tr>
<td>Believes their daughter is at risk for cervical cancer&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>ref.</td>
<td>ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.28</td>
<td>0.91</td>
<td>(0.40-2.10)</td>
<td></td>
</tr>
</tbody>
</table>

HPV = human papillomavirus, OR = odds ratio, CI = confidence interval, ref. = referent group. Odds ratios are adjusted for age. 

* p<0.05.  
<sup>a</sup> Complete separation of covariate and outcome (all accepted)  
<sup>b</sup> Of those who have daughters aged 10-25 (rural n=147, urban n=81)
Chapter 4

General Discussion and Conclusion

4.1 Summary and Discussion of Findings

The objectives of this thesis project were to describe and determine the socio-demographic, HPV-related awareness/knowledge, and attitudes associated with HPV vaccine acceptance, and to identify the perceived barriers to vaccination if the vaccine should become available. The populations of interest for these objectives were rural and urban women residing in the Kilimanjaro region of Tanzania (Objectives 2 and 3); however, we also explored current literature on this topic from other African countries (Objective 1).

These objectives were accomplished through a systematic review of HPV vaccine acceptability studies among African countries (Manuscript 1), and a cross-sectional study conducted in rural and urban areas in Tanzania (Manuscript 2). The survey design, sampling strategy, data collection, and analyses for the cross-sectional study were done to fulfill some research gaps, particularly the inclusion of both rural and urban samples, population-based systematic sampling methods, and the use of statistical modeling.

In the cross-sectional study, we determined that there were different socio-demographic, knowledge, and attitude factors associated with predicted HPV vaccine acceptance among rural and urban women. However, contrary to our initial hypothesis, we found that both groups predicted equally high acceptance of the vaccine if it were to become available. Among the rural sample, we found that variables related to vaccine
access (financial and physical) and awareness of the cervix were associated with acceptance. Among the urban sample, a variable related to social norms/peer acceptance was associated, along with the respondent’s educational attainment. These associations have been similarly found among other studies from Africa, as presented in systematic review sections: Cues to action, Perceived barriers and Other factors associated with acceptability. However, as noted in the review, these factors were considered separately in other studies, and modeling was not used where factors would be adjusted for each other. The systematic review is useful for understanding the breadth of factors associated with acceptance; however, it is difficult to draw conclusions on the factors that are most important or independently associated due to the descriptive nature of studies.

Nevertheless, cues to action from the systematic review indicated that endorsement by the government or healthcare providers were also important for acceptance: these cues were not explicitly examined in the cross-sectional study since individuals who were potential recipients of the vaccine, along with their daughters, were the focus. Given the number of studies suggesting the strength and importance of endorsement by the government or healthcare provider, it is expected that this may be important across all vaccination campaigns.

In addition to presenting the many factors associated with acceptance, the results of the systematic review and cross-sectional study can be compared for consistency. For example, research on the relationship between educational attainment and acceptance appears to be mixed in the literature from African countries(1–4). The inconclusive results on this issue in the systematic review could be due to the heterogeneity of study populations. In our study, low educational attainment was associated with acceptance,
and this is consistent with the majority of findings from the US (5). Future studies may need to further explore this relationship, as it may be important to knowledge translation initiatives. As an example of consistent findings, HPV vaccine-related knowledge was low in both Kilimanjaro samples, and this was also found in the pooled study-level findings from the systematic review. Variables that would be categorized under the Health Belief Model’s *Perceived likelihood* and *Perceived effectiveness and benefits* sections of the systematic review were found not to be associated with acceptance in the Kilimanjaro samples. This may be because knowledge of the HPV vaccine, cervical cancer, and the relationship between HPV and cervical cancer is very low. Alternatively, the perceived barriers/attitudes that were associated with acceptance may have simply been more important. In the same survey, we found cervical cancer screening acceptability among never-screened women to be high (90%); notably, perception of personal risk (perceived likelihood) was found to have a strong association with acceptability for both rural and urban groups (6). Overall, awareness and educational initiatives are required, and emphasizing the relationship between cervical cancer and HPV may be important for acceptance.

Studies included in the systematic review did not examine the relationship between health insurance and acceptance, however cost was frequently a concern. In the cross-sectional study, among rural women, health insurance status and a willingness to pay for vaccines were each independently associated with acceptance. At first this may appear contradictory, however, for those without health insurance, perhaps women that do not have the means to afford health insurance rely on out-of-pocket payments for healthcare. Those with health insurance may have been considering their payments
toward community-based insurance funds that could potentially cover these vaccines, or perhaps they were truly willing to pay.

4.2 Manuscript 2: Confounder Assessment

The statistical method for building models used in the cross-sectional study required that variables removed from the model during backward selection be re-examined as potential confounders. Confounder variables were included in final models if they resulted in change of any parameter estimate by >10%, compared to the full model. Using this method, one additional variable was identified for each of the rural and urban groups and included in the final models. Among rural women this variable was, ‘believes family/friends will support the HPV vaccine,’ and its impact was largely upon the variable ‘believes they are able to access a clinic or doctor for vaccination’. This may be explained by the use of social supports to provide (e.g. financial or physical) access to healthcare. The perceived support of the vaccine by family and friends has also been shown previously to be associated with acceptability (3,7–9). Among urban women, the variable ‘knows what the cervix is’ confounded the relationship between educational attainment and acceptability. A higher proportion of women in the urban sample may have had formal medical training as there was a higher proportion of healthcare providers compared to the rural sample; this would result in a relationship between educational attainment and ‘knows what the cervix is’, while knowledge of the cervix may be related to acceptability due to understanding the use or purpose of the vaccine. Within the rural model, ‘knows what the cervix is’ is independently associated with acceptance, in addition to educational attainment.
4.3 Strengths and Limitations

The Kilimanjaro region has substantial differences between rural and urban areas, thus the inclusion of both rural and urban population-based samples in a single study, using the same survey instrument and sampling methodology, is considered a major strength of the cross-sectional study. The use of a multistage sampling strategy that involved random sampling of wards and villages, and systematic sampling of houses, collected a population-based sample that is representative of this region. Selection bias is not believed to be present in the populations of the cross-sectional study due to the high response rates and the random sampling methods. Use of an interviewer-administered questionnaire and student participation during the survey allowed for immediate clarifications during the survey and monitoring of quality, and the experience of participating in fieldwork and speaking with participants was also useful for interpreting results. As identified in the systematic review, few studies have used advanced statistical methods to identify the associations to HPV vaccine acceptability in studies from Africa, and so an analysis using multivariable modeling, while taking into account the clustered sampling design, are also strengths of this research.

Although trained interviewers administered the survey, and participant anonymity was explained, there are limitations to this method. It is possible that the presence of an interviewer biased certain responses (interviewer or social desirability bias); respondents may not have felt comfortable reporting accurate answers to sensitive questions and this could have resulted in an underreporting (e.g. sexual behaviors) or over reporting (e.g.
income) on particular questions. Furthermore, participants may have indicated that they were aware or knowledgeable about cervical cancer or the HPV vaccine in order to please the interviewer. It is also possible that respondents felt pressured to predict that they would accept the vaccine; however, we suspect that those who were hesitant may have chosen a less definite answer such as probably yes. In the future, studies may wish to consider supplementing surveys with in-depth interviews or focus groups that will foster trust and engagement, in order to provide greater insight to the attitudes and barriers towards vaccination.

The modeling strategy was exploratory in nature, that is, we did not have a specific a priori relationship under investigation, and rather were interested in examining the associations of a number of potential factors that were purposefully chosen as the focus of the survey questions (10). We recognize the possibility of chance associations due to multiple comparisons; however, we chose not to use a statistical correction due to the exploratory nature of this work (11). In terms of potential limitations, it is likely that there are additional individual and external factors that are associated with acceptability but not considered in our study. This limits the explanatory power of the models presented, and the generalizability of our findings to other populations. Further, this study often uses only single variables to assess particular knowledge, attitudes, and barriers, and future studies may wish to explore multiple aspects of these factors.

The outcome variable, acceptance, represents a projected behavior and, as discussed in the cross-sectional study, this may not necessarily translate into action although acceptance of other vaccines in the region have been high (12). We did not find meaningful differences in acceptance between adults versus parents (i.e. hypothetical or
real daughters), or among those who may have answered considering themselves vaccination (those aged 18-25); however, there may be different associations with acceptance within these sub-groups that this study was not powered to detect. Given that communities within these regions are highly social and interconnected, the knowledge and attitudes of all women within communities, as presented here, is hoped to be useful.

The response categories were chosen carefully, to reflect the population’s demographics and comparability across studies, however it was necessary to collapse some categories for analyses (e.g. occupation) due to small numbers, and this may have masked potential differences and associations due to insufficient power.

4.4 Thesis Contributions

Manuscript 1 is the first to systematically review quantitative and qualitative literature on HPV vaccine acceptability among African countries. We hope this will be useful for public planners of upcoming vaccine demonstration projects, and of interest to other research teams conducting formative research on this topic in these areas. These research teams could consider conducting research among rural populations, and using population-based sampling methods rather than convenience samples, and collecting samples large enough that multivariable modeling can be conducted. Given that demonstration projects are expected to begin soon, research could shift toward examining the factors associated with uptake or non-uptake.

Manuscript 2 is novel in describing and determining the socio-demographic, knowledge, and attitudes associated with HPV vaccination in a population-based sample
of rural and urban women in the Kilimanjaro region. This study is robust methodologically, and has a sufficient sample size to draw confident conclusions for both rural and urban women. Knowledge generated from this research will of interest to public health planners (e.g. Ministry of Health) involved in the vaccination initiatives for this region and to other researchers in the region, including our colleagues at the Kilimanjaro Christian Medical Center (KCMC). Researchers wishing to continue this work may consider conducting in-depth interviews or focus groups, studying the attitudes of men or assessing the attitudes towards the vaccinations of boys; it may also be interesting to reassess attitudes and barriers once educational and social mobilization campaigns have occurred in these areas. Studying vaccine message framing and effectiveness in Tanzania may also be a future direction.

4.5 Knowledge Dissemination and Future Directions

Funding permitting, both of these manuscripts will be made available publically by publishing using the Open Access option. The results of the cross-sectional study will also be reported back to local collaborators in Tanzania, including Dr. Olola Oneko at the Reproductive Health Center at the Kilimanjaro Christian Medical Center (KCMC). Dr. Oneko has attended international meetings regarding the HPV vaccine in Tanzania, and he is an advisor to the Ministry of Health in Tanzania. Dr. Karen Yeates is continuing to pursue goals of the “Prevention of Cervical Cancer in the Kilimanjaro region of Tanzania” research team initiative by collaborating with Dr. Oneko on a related project investigating remote cervical cancer screening using cell phones. The principal
investigators on this project (KY, JC, CB and KA) are currently discussing projects for future students interested in joining the research team in the Kilimanjaro region.

4.6 Conclusion

Cervical cancer is a global disease, with a high burden distributed among low-resource countries in sub-Saharan Africa, including Tanzania. Within these countries, there are many challenges to overcoming the economic, physical, and social barriers to prevent and manage this disease. Cervical cancer screening programs that are affordable, acceptable, and effective remain a priority, and the ethics of implementing such programs should be considered in light of the availability of treatment. The introduction of a quadrivalent vaccine that protects against 70% of cervical cancer cases is a promising and important shift toward prevention of this disease. This thesis supports the need for cervical cancer and HPV vaccine-related education, within Kilimanjaro region and among other countries in Africa. The results of this thesis also suggest that acceptability of the HPV vaccine will be high in both rural and urban areas of Kilimanjaro region, and provides evidence that there are particular factors that should be addressed within education and publicity campaigns, such as financial and physical accessibility, peer acceptance, and safety.
4.7 References


6. Skrastins E. Determinants of Cervical Cancer Screening in the Kilimanjaro Region of Tanzania [Masters of Science in Epidemiology]. [Kingston, Ontario, Canada]: Queen’s University; 2013.


Appendix A

Map of Moshi Rural and Moshi Urban (Adapted from (73,74))
Appendix B

Manuscript 2: Additional Figures and Methods

This corresponds to the information presented descriptively in Section 1.4.2.

Table 12. Choice of HPV vaccination site among rural and urban women in the study sample.

<table>
<thead>
<tr>
<th>Choice of vaccination site</th>
<th>Total (n=575)</th>
<th>Rural (n=303)</th>
<th>Urban (n=272)</th>
<th>p-value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic/Dispensary</td>
<td>20.7 (118)</td>
<td>24.1 (72)</td>
<td>17.0 (46)</td>
<td>0.039</td>
</tr>
<tr>
<td>School</td>
<td>6.5 (37)</td>
<td>8.4 (25)</td>
<td>4.4 (12)</td>
<td>0.059</td>
</tr>
<tr>
<td>Family Doctor</td>
<td>3.3 (19)</td>
<td>3.0 (9)</td>
<td>3.7 (10)</td>
<td>0.646</td>
</tr>
<tr>
<td>Hospital</td>
<td>52.2 (297)</td>
<td>49.5 (148)</td>
<td>55.2 (149)</td>
<td>0.175</td>
</tr>
<tr>
<td>Health Center</td>
<td>29.4 (167)</td>
<td>29.1 (87)</td>
<td>29.6 (80)</td>
<td>0.889</td>
</tr>
</tbody>
</table>

$^a$ Note: multiple answers allowed.
$^b$ Pearson’s Chi-square

Table 13. Decision-maker for HPV vaccination among rural and urban women in the study sample.

<table>
<thead>
<tr>
<th>Decision-maker</th>
<th>Total (n=575)</th>
<th>Rural (n=303)</th>
<th>Urban (n=272)</th>
<th>p-value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Leader</td>
<td>5.8 (33)</td>
<td>6.6 (20)</td>
<td>4.8 (13)</td>
<td>0.354</td>
</tr>
<tr>
<td>Daughter/Parents Together</td>
<td>25.8 (148)</td>
<td>24.1 (73)</td>
<td>27.7 (75)</td>
<td>0.327</td>
</tr>
<tr>
<td>Parents</td>
<td>49.2 (282)</td>
<td>48.0 (145)</td>
<td>50.6 (137)</td>
<td>0.544</td>
</tr>
<tr>
<td>Father Only</td>
<td>5.6 (32)</td>
<td>4.6 (14)</td>
<td>6.6 (18)</td>
<td>0.292</td>
</tr>
<tr>
<td>Mother Only</td>
<td>6.6 (38)</td>
<td>3.3 (10)</td>
<td>10.3 (28)</td>
<td>0.001</td>
</tr>
<tr>
<td>Daughter Only</td>
<td>6.6 (28)</td>
<td>6.9 (21)</td>
<td>6.3 (17)</td>
<td>0.752</td>
</tr>
<tr>
<td>Government</td>
<td>5.8 (33)</td>
<td>5.9 (18)</td>
<td>5.5 (15)</td>
<td>0.835</td>
</tr>
<tr>
<td>Doctor</td>
<td>6.6 (38)</td>
<td>6.3 (19)</td>
<td>7.0 (19)</td>
<td>0.722</td>
</tr>
<tr>
<td>Elder Family member</td>
<td>7.2 (41)</td>
<td>8.6 (26)</td>
<td>5.6 (15)</td>
<td>0.158</td>
</tr>
</tbody>
</table>

$^a$ Note: multiple answers allowed.
$^b$ Pearson’s Chi-square
4.8 Non-manuscript: additional information on methods

4.8.1 Study questionnaire

The survey was developed as part of an independent study course in survey methods (EPID-815: Applied Survey Methods in Global Health) at Queen’s University. In addition to design evaluation via back-translation and cognitive interviewing, the survey was reviewed and modified before pilot testing by Dr. Olola Oneko, a gynecologist at the Kilimanjaro Christian Medical Center (KCMC). Dr. Oneko was familiar with the local terms/phrases used to describe the cervix and cervical cancer and these changes were incorporated into the final survey.

Pilot testing in Moshi Rural was conducted among 60 women using the sampling strategy that was designed for the study. Pilot testing resulted in changes to wording and response categories (e.g. education and income levels) to better represent the population’s socio-demographics. Ordering of questions was also modified, including first asking about household information in a smaller socio-demographic section at the beginning so that subsequent questions regarding children could be skipped.

4.8.2 Data collection

Six research assistants, fluent in English and Kiswahili, were hired by the student investigators (MC, ES, PJ and RF) and the research coordinator at Pamoja Tunaweza Women’s Center (Moshi, Tanzania). These assistants were females who had completed secondary school, or College/University, and had previous experience administering surveys in Tanzania. In order to prepare for this study, they underwent two days of
training covering the study’s purpose, procedures, general survey methods, sensitivity
issues and methods of obtaining ethical consent.

Surveying took place during weekdays, with each of the six interview-investigator
pairs completing 9–10 interviews per day. The survey was designed to be concise, and
took approximately 30 minutes to complete. It was administered verbally in Kiswahili by
the research assistants, with the student investigator following along using an English
version of questions. The literacy rate in Tanzania is 73% and so it was important that the
survey be interviewer-administered in order to include those who could not read or write.
This method was also chosen so that the interviewer and investigators could discuss
discrepancies or concerns about participant responses and record comments in a section
at the end of the survey. The comments section was also used to note the presence of
other individuals during the questionnaire. When possible, interviews were requested to
take place in private areas of the household or outside, however this was not always
possible. If other community members or family members were present this was noted on
the survey.

The villages that were randomly selected were visited one week before surveying
took place in order to introduce our team and gain surveying permission from the village
chairman. The community often anticipated our arrival, having heard of our visit through
community meetings and church announcements made by the chairman in the week
following our first visit. In rural communities there were no clear village boundaries or
streets from which to systematically sample every kth household. In these communities
the sampling strategy was adapted by relying on the village chairman to define his village’s boundaries, and lead interviewer-investigator pairs to different areas where they could define a linear path from which to sample households. In urban communities, streets were used to sample households. A large number of women work in the urban center of Moshi Town and in order to capture these women in our sampling, two of the five defined wards were purposely selected as streets in downtown Moshi. The women interviewed here were either living at their residences, or employed as small shop owners, fruit/vegetable sellers, or seamstresses. We asked women to indicate if they resided in Moshi Rural or Moshi Urban districts in order to account for women who may commute to work.

Ethical consent was obtained from all participants wishing to complete the questionnaire. A copy of the consent form was left with all participants and it included the name and number of Dr. Oneko, who oversaw the study and was available for participant inquiries.

4.8.3 Additional information on statistical methods

4.8.3.1 Data Management

All surveys were given a unique ID and entered into a password-protected database by the student investigators prior to departing Tanzania. The database is accessible in Canada by students with ethical clearance to complete analyses using the data. Hard copies of surveys and consent forms are stored in a locked cabinet accessible only by the research coordinator at Pamoja Tunaweza Women’s Center (Moshi).
4.8.3.2 Explanatory Variables

Presented here are details on the health and socio-demographic variables, cervical cancer awareness/knowledge and attitudes variables, and vaccination awareness and attitude variables as they were categorized for analysis. The conceptualization of the variables considered for multivariable analysis are shown in Figure 3; we believe these variables can be mapped onto constructs of the Health Belief Model (HBM) and Theory of Reasoned Action (TRA) as outlined by Poss (2001), however the survey variables included are not exhaustive in measuring aspects of each construct.

Knowledge/awareness and socio-demographic variables are conceptualized as modifying factors that inform attitudes and beliefs (HBM constructs). Acceptance or acceptability of the vaccine is conceptualized as a behavioral intention, informed by the HBM constructs, and intermediary before actual behavior (uptake).

Categorization was determined based upon on the mean and distribution of responses, and for comparability to previous knowledge, attitudes, and barrier studies conducted in sub-Saharan African countries. Questions with open-ended responses (i.e. occupation and ‘other’ responses) were translated into English and categorized \textit{a posteriori}. For analysis purposes, ‘no’ and ‘don’t know’ responses were collapsed.

Binomial variables with negligible responses (i.e. smoking status, HIV status, marriage type) were presented descriptively and not included in the multivariable analyses. Similarly, variables with almost perfect response were only presented descriptively (i.e. believes vaccines are beneficial).
Socio-demographic and health variables: location (urban or rural), age (<30, 30–39, ≤40), marital status (single, married/partnered, separated/divorced/widowed), religion (Christian or Muslim), cultural group (Chagga, Pare or other), occupation (Farmer/housewife, small business, professional), education (≥primary, secondary complete or college/university), monthly household income in Tanzanian shillings (TSH) (<40,000, 40,000–79,999 or ≥80,000), health insurance (yes or no), self-reported health status (fair/poor or ≥good), current use of contraception (any) (yes or no), age at first intercourse (≥19 or <19), lifetime number of sexual partners (none, 1 or ≥2), parity (never given birth, 1–2 births, 3–4 births, ≥5 births), daughter aged 10-25 (yes or no).

Cervical cancer knowledge/awareness variables: knows what the cervix is (yes or no) and known someone with cervical cancer (yes or no). The understanding of cervical cancer (yes or no) was a variable conceptualized prior to analysis. Those who have an adequate understanding had to answer ‘yes’ to “Have you heard of cancer?” and “Have you heard of cervical cancer” and answer ‘women’ to “Who can develop cervical cancer” (women, men, both or don’t know).

Cervical cancer attitude variables: ever screened for cervical cancer (yes or no), would accept cervical cancer screening (yes or no), believes cervical cancer is fatal (yes or no), believes cervical cancer can be treated (yes or no), believes they are at risk for cervical cancer (yes or no), of those that had daughters: believes their daughter is at risk for cervical cancer (yes or no).
Vaccine awareness and attitude variables: Heard of the HPV vaccine (yes or no), believes partner/husband will definitely accept the vaccine (yes or no), believes family/friends will support the HPV vaccine (yes or no), believes they are able to access a clinic or doctor for vaccination (yes or no), willing to pay for vaccines (yes or no).

<table>
<thead>
<tr>
<th>Potential explanatory factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Socio-demographic and health characteristics</strong></td>
</tr>
<tr>
<td>Age, marital status, religion, culture, occupation, education, monthly income, health insurance, health status, contraception use, age at sexual debut, lifetime sexual partners, parity, daughter aged 10-25</td>
</tr>
<tr>
<td><strong>Attitudes/Beliefs</strong></td>
</tr>
<tr>
<td>Believes family/friends will support the HPV vaccine</td>
</tr>
<tr>
<td>Believe they are able to access a doctor or clinic for vaccination</td>
</tr>
<tr>
<td>Willing to pay for vaccines</td>
</tr>
<tr>
<td>Ever screened for cervical cancer</td>
</tr>
<tr>
<td>Believes cervical cancer is fatal</td>
</tr>
<tr>
<td>Believes cervical cancer is treatable</td>
</tr>
<tr>
<td>Believes they or their daughter are at risk for cervical cancer</td>
</tr>
<tr>
<td><strong>Awareness and Knowledge</strong></td>
</tr>
<tr>
<td>Heard of the HPV vaccine</td>
</tr>
<tr>
<td>Understanding of cervical cancer</td>
</tr>
<tr>
<td>Knows what the cervix is</td>
</tr>
<tr>
<td>Known someone with cervical cancer</td>
</tr>
</tbody>
</table>

Map onto HBM and TRA constructs (Poss, 2001)

- Perceived likelihood
- Perceived effectiveness and benefit
- Perceived severity
- Perceived barriers, including self-efficacy
- Cues to action and normative beliefs

Intention to vaccinate

Figure 3. Conceptualization of cross-sectional study variables.
Appendix C

Search Strategies

Database Search (Queen’s University Health Sciences Librarian, Amanda Ross-White)
***************************
Database: Embase <1980 to 2013 Week 28>
Search Strategy:
1  Wart virus vaccine/ (6178)
2  exp wart virus/ (22848)
3  exp immunization/ (197006)
4  1 or (2 and 3) (7263)
5  exp Africa/ (203167)
6  4 and 5 (164)
***************************
Database: PsycINFO <1967 to July Week 2 2013>
Search Strategy:
1  human papillomavirus/ (516)
2  developing countries/ (3493)
3  africa$.mp. (51064)
4  1 and (2 or 3) (41)
5  vaccin$.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (3362)
6  immuni$.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (5883)
7  4 and (5 or 6) (31)
***************************
Database: CINAHL
#          Query                     Results
S11        S9 AND S10               23
S10        (MH "Africa+")          26,226
S9         S1 OR S8                2,111
S8         S4 AND S7               1,357
S7         S5 OR S6                27,797
S6         (MH "Vaccines+")        21,891
S5         (MH "Immunization+")   11,912
S4         S2 OR S3                4,485
S3         (MH "Papillomaviruses") 1,337
S2         (MH "Papillomavirus Infections+") 3,966
S1   (MH "Papillomavirus Vaccine")   1,543

***************************
Database: Global Health <1910 to 2013 Week 27>
Search Strategy:
1  exp human papillomaviruses/ (9026)
2  exp immunization/ or exp vaccines/ (90086)
3  exp Africa/ (168420)
4  1 and 2 and 3 (57)

***************************
Database(s): Ovid MEDLINE(R) without Revisions 1996 to Present with Daily Update
Search Strategy:
#    Search Results
1    Papillomavirus Vaccines/3430
2    exp Papillomavirus Infections/15784
3    exp Immunization/62056
4    1 or (2 and 3)/3657
5    exp africa/100684
6    4 and 5/66

***************************
Appendix D

Knowledge, Attitudes and Barriers Survey – English Version

Survey comments:

Date:

Location: □ Urban □ Rural

Interviewer: □ M □ F

Translator: □ M □ F

Thank you for participating in this study. With your answers we hope to be able to improve the health of women in Tanzania. Remember, there are no right or wrong answers to these questions. We would like to know what you think about these important topics.

To start I will ask about the people in your household.

Prevention of Cervical Cancer in the Kilimanjaro Region of Tanzania: A Survey of Knowledge, Attitudes and Barriers

SECTION 1: HOUSEHOLD INFORMATION

Including yourself, how many people live in your household: _____________

Daughters □ Sons □ Mother □ Father □ Grandmother □ Grandfather

Other (e.g. Neico, nephews...) __________

How many children have you given birth to? __________

*Is your daughter(s) between the ages 10-25? □ Yes □ No * Skip if they do not have a daughter

The next set of questions is about cervical cancer.

SECTION 2: CACX KNOWLEDGE

Do you know what the cervix is? □ Yes □ No

Have you heard of cancer? □ Yes □ No

Have you heard of cervical cancer? □ Yes □ No

If yes, where did you learn about it (Check all that apply)?

Community member or leader □ Church □ Family/Friends □ Government education program □ Radio

Healthcare provider □ Newspaper □ TV □ Other

Where would a woman go to be checked for cervical cancer? Ask participant to be specific (i.e. which hospital or clinic)

Do you know anyone who has/has had cervical cancer? □ Yes □ No

Who can get cervical cancer? □ Men □ Women □ Both

Can people die from cervical cancer? □ Yes □ No □ Don’t know

Is there a treatment for cervical cancer? □ Yes □ No □ Don’t know

Do you know how women are checked for cervical cancer? □ Yes □ No □ Don’t know

How do you think the following affect a women’s chance of getting cervical cancer?

Multiple partners □ More likely □ Less likely □ No difference □ Don’t know

Oral contraception □ More likely □ Less likely □ No difference □ Don’t know

Old age □ More likely □ Less likely □ No difference □ Don’t know

Unprotected sex □ More likely □ Less likely □ No difference □ Don’t know

HIV □ More likely □ Less likely □ No difference □ Don’t know

HPV □ More likely □ Less likely □ No difference □ Don’t know

Smoking □ More likely □ Less likely □ No difference □ Don’t know

Early age at first intercourse □ More likely □ Less likely □ No difference □ Don’t know
### SECTION 2.2: CACX ATTITUDES

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Don't know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you think you are at risk for cervical cancer?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Do you think your daughter is at risk for getting cervical cancer?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Skip if they do not have a daughter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you ever been checked for cervical cancer?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If no, would you accept screening if it was available to you?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How far would you be willing to travel?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 2.3: CACX BARRIERS

#### 2.3a - I have previously gone for screening because...

- I was experiencing symptoms
- I saw it in an advertisement
- Someone I know came for screening
- Someone told me to get screening
- Other __________________________

#### 2.3b - I do not want to go for screening (or I am unsure) because...

- I do not need a check-up if I have no symptoms
- I am not at risk for cervical cancer
- I am worried about the screening procedure
- I am worried my family will be upset if I have cervical cancer
- I do not trust the medical staff who performs screening
- I am too shy to be screened
- I do not want to be screened by a male doctor
- I cannot afford the treatment, so I do not get screened
- I want to let fate/god decide
- My doctor told me I do not need to go
- Other __________________________

#### 2.3c - I want to go for screening, but do not because...

- I did not know that this existed
- I have too many chores
- My husband would not want me to be screened
- Too many illness/problems in the family
- I will lose work or my job if I go
- I do not want to go alone
- My doctor told me I do not need to go
- If I have to pay, I can not afford to be screened
- It is too far to travel to be screened
- Other __________________________
Human Papillomavirus (HPV) can cause cervical cancer. HPV is not the same as HIV. Vaccines are medications given to prevent the development of disease or illness.

SECTION 3.1: VACCINE KNOWLEDGE

Have you heard of a vaccine that can help prevent HPV infection/cervical cancer? □ Yes □ No
If yes, where did you hear about this vaccine? (Check all that apply)
□ Community member □ Church □ Family/Friends □ Government education program □ Radio □ TV

SECTION 3.2: VACCINE ATTITUDES

Have you ever had vaccinations given to you? □ Yes □ No
*Has your child/children received routine childhood vaccinations? □ Yes □ No * Skip if they do not have a child
Do you think vaccinations are beneficial/useful? □ Yes □ No

The next questions ask about your daughter(s), if you do not have a daughter please answer these questions imagining that you do. If you do not have a daughter and you are in the age range (10-25) please answer thinking about yourself.

If a HPV vaccine became available in Tanzania, would you give permission for your daughter to receive it (or take it yourself)?
□ Definitely Yes □ Probably Yes □ Don’t know □ Probably No □ Definitely No
Do you think your husband/partner will approve of giving your daughter (or yourself) the vaccine?
□ Definitely Yes □ Probably Yes □ Don’t know □ Probably No □ Definitely No
Who should decide whether or not girls should receive the HPV vaccine? (Check all that apply)
□ Community leader □ Daughter and parents together □ Parents □ Father only □ Mother only
□ Daughter only □ Government □ Doctor □ Elder family member □ Other ______________

What do you think is the best way to deliver information about cervical cancer/HPV? (Check all that apply)
□ Schools □ Churches □ Public education program □ Radio □ Television
□ Healthcare providers □ Newspaper □ Other

Where would be the best place for your daughter (or you) to receive the vaccine? (Check all that apply)
□ Clinic/dispensary □ School □ Family doctor □ Hospital □ Other ______________
□ Health center

How far would you be willing to travel to receive a vaccine?
□ 30 minutes □ 1 hour □ 2-3 hours □ 4+ hours

If it was not paid for by the government, would you be willing to pay for the vaccine? □ Yes □ No □ Don’t know
Would your family and/or friends be in support of this vaccine? □ Yes □ No □ Don’t know
Do you think you could find a doctor or clinic to get the vaccine? □ Yes □ No □ Don’t know

SECTION 3.3: VACCINE BARRIERS

The following are potential concerns regarding the HPV vaccine. Which (if any) apply to you (Check all that apply):

Safety of the vaccine administration □
Short-term side effects □
Unknown future side effects □
Risk of encouraging early sex in young girls □
Vaccine conformity to religious beliefs □
The effectiveness of the vaccine at preventing cervical cancer □
Now I would like to ask some general questions about you, to help us better understand the study participants. Please remember that all questions are anonymous and confidential, and the information will not be shared with anyone outside this study.

SECTION 4: DEMOGRAPHICS

<table>
<thead>
<tr>
<th>Date of Birth</th>
<th>(Day, Month, Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td>□ Single □ Partnered □ Married □ Separated □ Divorced □ Widowed</td>
</tr>
<tr>
<td><em>Marriage type</em></td>
<td>□ Monogamy □ Polygamy</td>
</tr>
<tr>
<td>Religion</td>
<td>□ Christian □ Muslim □ Other ____________________</td>
</tr>
<tr>
<td>Cultural Group</td>
<td>□ Chagga □ Pare □ Wakhe □ Wakwavi □ Other ____________________</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Average monthly household income, in TSH</td>
<td>□ 0 – 20,000 □ 20,000 – 40,000 □ 40,000-60,000 □ 60,000-80,000 □ 80,000-100,000 □ 100,000 +</td>
</tr>
<tr>
<td>Highest level of education attained</td>
<td>□ None □ Primary (Incomplete) □ Primary (Standard 7) □ Secondary to Form Four □ Secondary to Form Six □ Tertiary (College/University)</td>
</tr>
<tr>
<td>Do you have health insurance/medical aid?</td>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

SECTION 5: HEALTH STATUS

| Height (inches) | ____________________ |
| Weight (kg) | ____________________ |
| Waist Circumference (inches) | ____________________ |
| Do you smoke? | □ Yes □ No |
| How many per day? | □ 1-2 □ 3-4 □ 5+ |
| How would you rate your current health? | □ Excellent □ Very good □ Good □ Fair □ Poor |
| Do you or have you ever had any of the following conditions? | □ HIV/AIDS □ Cancer (any) □ Schistosoma hematobium |
| Have you ever had sex? | □ Yes □ No |
| If yes, what age did you first have sex? | ____________________ |
| Have you ever used contraception? | □ Yes □ No |
| Are you currently using contraception? | □ Yes □ No |
| What kind of contraception do you use (or have you used)? | □ Pills □ Condoms □ Injectable □ Other ____________________ |
| How many people have you had sex with? | □ 1 □ 2-3 □ 4-5 □ 6+ |

To be completed by the surveyor, after completion of survey:

On a scale of 1 (Poor) to 4 (Excellent), overall, how would you rate the quality of this completed survey?  
□ 1 Poor □ 2 Fair □ 3 Good □ 4 Excellent

Do you feel this survey is an adequate representation of the participant’s knowledge, attitudes and barriers?  
□ Yes □ No

If no, comment:
Appendix E

Research Ethics Board Approval: Queen’s University

QUEEN’S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW
April 05, 2012

Miss Melissa Cunningham
Department of Community Health and Epidemiology
Queen’s University

Dear Miss Cunningham

Study Title: EPID-381-12 Screening and Early Diagnosis of Cervical Cancer in the Kilimanjaro Region of Tanzania: A Survey of Knowledge, Attitudes, and Beliefs
File # 6006780

Co-Investigators: Ms. E. Skrastins, Ms. P. Jinda, Mr. R. Fitzpatrick, Dr. K. Yeates, Dr. C. Booth, Dr. J. Carpenter, Dr. K. Aronson, Dr. O. Oneko

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol, survey and revised information/consent form for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair’s signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event forms: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # 6006780 in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file 6006780 in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair’s signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

[Signature]
Chair, Research Ethics Board
April 05, 2012

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete
Appendix F

Cross-sectional Study Consent Form

March 29, 2012

TITLE OF PROJECT:
Screening and Early Diagnosis of Cervical Cancer in the Kilimanjaro Region of Tanzania: A Survey of Knowledge, Attitudes and Beliefs

BACKGROUND INFORMATION:
You are being invited to participate in a research study directed by Dr. Olola Onoko and the Queen’s University School of Medicine to evaluate the knowledge, attitudes and beliefs regarding screening of cervical cancer. Students from the Queen’s School of Medicine and Department of Community Health & Epidemiology will read through this consent form with you, describe procedures in detail and answer any questions you may have. This study is being funded through financial support from Drs. Karen Yeates, Jennifer Carpenter, Chris Booth and the students’ own funding. This study has been reviewed for ethical compliance by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. It has also been reviewed by the Kilimanjaro Christian Medical College Research Ethics Board and the National Institute for Medical Research Tanzania (NIMR).

DETAILS OF THE STUDY:

1. Study aim:
The purpose of this study is to find the primary barriers related to access of cervical cancer screening and local beliefs surrounding cervical cancer. This knowledge will be used to guide the implementation of local screening programs for cervical cancer, in order to reduce the incidence of cancer among Tanzanian women. You will be considered for the study if you are a woman between 15-65 years of age.

2. Description of study procedure:
You were randomly selected to be invited to participate in this study. If you wish to participate, a survey will be administered by a student investigator working with a translator. The survey will ask questions about your knowledge, beliefs and attitudes of cervical cancer and screening procedures. The survey will take approximately thirty minutes to complete. All participants will receive the same survey.

3. Risks:
There are no physical risks associated with this study. However, please report immediately to the student investigator if you are experiencing problems at any time during the survey.

4. Benefits:
While you may not benefit directly from this study, results from this study may improve the understanding of the local knowledge, attitudes and beliefs regarding cervical
cancer and screening. This will help guide the implementation and monitoring of a local cervical cancer screening program. Educational seminars will also be held in selected villages in order to learn about other healthcare issues, such as high blood pressure and diabetes.

5. Exclusions:
Women who are not between 15-65 years of age at the time of survey will be excluded.

6. Confidentiality:
All information obtained during the course of this study is strictly confidential and your anonymity will be protected at all times. Your name will not be recorded and an ID number will be used to identify your survey. No new information will be collected without your permission. Completed surveys will not be shared with anyone outside the research team. Data will be stored in locked files and will be available only to the principal investigators. Any data input into a computer will be password protected and accessible only by the research team. No identifying information will be used in publication or reports.

7. Voluntary nature of study:
Your participation in this study is voluntary. You do not have to answer any questions that you find objectionable or make you uncomfortable. You may withdraw from this study at any time and your withdrawal will not affect your future medical care.

8. Withdrawal of subject by principal investigator:
The study investigators may decide to withdraw you from this study if they are unable to complete the survey due to unforeseen circumstances.

SUBJECT STATEMENT AND SIGNATURE SECTION:

10. The consent form will be provided in Kiswahili and discussed by the interpreter under the guidance of the student investigator.

Principal Investigators:

Dr. Olola Oneko
Gynaecologist & Obstetrician
Telephone Number: 0025527 275 4377
Address: Kilimanjaro Christian Medical Center, Moshi, Tanzania

Dr. Karen Yeates MD, FRCPC, MPH
Queen's University, Kingston, Ontario
yeatesk@kgh.kari.net
I have read and understand the consent form for this study. I have had the purposes, procedures and technical language of this study explained to me. I have been given sufficient time to consider the above information and to seek advice if I chose to do so. I have had the opportunity to ask questions which have been answered to my satisfaction. I am voluntarily signing this form. I will receive a copy of this consent form for my information. If at any time I have further questions, problems or adverse events, I can contact Dr. Olola Oneko or Drs. Karen Yeates and Jennifer Carpenter.

If I have questions regarding my rights as a research subject I can contact Dr. Albert Clark, Chair, Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at 1-613-533-6081.

By signing this consent form, I am indicating that I agree to participate in this study.

_______________________ _________________________
Signature of Participant Date

_______________________ _________________________
Signature of person conducting Date
the consent process
STATEMENT OF INVESTIGATOR:
I, or one of my colleagues, along with an interpreter, have carefully explained to the subject the nature of the above research study. I certify that, to the best of my knowledge, the subject understands clearly the nature of the study and demands, benefits and risks involved to participants in this study.

________________________________________  ________________________
Signature of Investigator                   Date
Appendix G

Preliminary Power Calculations

\[
\text{Power} = \Phi Z_{(1-\beta)} = \Phi \left\{ \Phi \left( \frac{[nr][1-p][1+r]}{p^2} \right)^{1/2} - Z_{a/2} \right\}
\]

Table 1: Estimated power for detecting associations between HPV vaccine knowledge and predicted willingness to vaccinate in rural women.

<table>
<thead>
<tr>
<th>n_1</th>
<th>% exposed</th>
<th>n_1 (exposed)</th>
<th>r</th>
<th>OR</th>
<th>p</th>
<th>p_0</th>
<th>p_1</th>
<th>d</th>
<th>Z_{a/2}</th>
<th>Z_{(1-\beta)}</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>353</td>
<td>0.09</td>
<td>31.8</td>
<td>10.11</td>
<td>1.3</td>
<td>0.88</td>
<td>0.8568647</td>
<td>0.9050633</td>
<td>0.0481986</td>
<td>1.96</td>
<td>0.698</td>
<td>75.70%</td>
</tr>
<tr>
<td>353</td>
<td>0.09</td>
<td>31.8</td>
<td>10.11</td>
<td>1.4</td>
<td>0.88</td>
<td>0.8494208</td>
<td>0.9112426</td>
<td>0.0618218</td>
<td>1.96</td>
<td>1.450</td>
<td>92.60%</td>
</tr>
<tr>
<td>353</td>
<td>0.09</td>
<td>31.8</td>
<td>10.11</td>
<td>1.5</td>
<td>0.88</td>
<td>0.8421053</td>
<td>0.9166667</td>
<td>0.0745614</td>
<td>1.96</td>
<td>2.152</td>
<td>98.40%</td>
</tr>
</tbody>
</table>

Table 2: Estimated power for detecting associations between HPV vaccine knowledge and predicted willingness to vaccinate in urban women.

<table>
<thead>
<tr>
<th>n_2</th>
<th>% exposed</th>
<th>n_2 (exposed)</th>
<th>r</th>
<th>OR</th>
<th>p</th>
<th>p_0</th>
<th>p_1</th>
<th>d</th>
<th>Z_{a/2}</th>
<th>Z_{(1-\beta)}</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>280</td>
<td>0.09</td>
<td>25.2</td>
<td>10.11</td>
<td>1.3</td>
<td>0.88</td>
<td>0.8568647</td>
<td>0.9050633</td>
<td>0.0481986</td>
<td>1.96</td>
<td>0.408</td>
<td>65.84%</td>
</tr>
<tr>
<td>280</td>
<td>0.09</td>
<td>25.2</td>
<td>10.11</td>
<td>1.4</td>
<td>0.88</td>
<td>0.8494208</td>
<td>0.9112426</td>
<td>0.0618218</td>
<td>1.96</td>
<td>1.077</td>
<td>85.92%</td>
</tr>
<tr>
<td>280</td>
<td>0.09</td>
<td>25.2</td>
<td>10.11</td>
<td>1.5</td>
<td>0.88</td>
<td>0.8421053</td>
<td>0.9166667</td>
<td>0.0745614</td>
<td>1.96</td>
<td>1.703</td>
<td>95.57%</td>
</tr>
</tbody>
</table>

n_1 is the sample size in the rural stratum
n_1 (exposed) is the number of women with the exposure (knowledge of the HPV vaccine) in the rural stratum
r is the ratio of unexposed to exposed
OR is the detectable odds ratio
p is the proportion of women who have the outcome (willing to vaccinate)
p_0 is the prevalence of those willing to vaccinate in those who do not have knowledge of the vaccine
p_1 is the prevalence of those willing to vaccinate in those who have knowledge of the vaccine
d is the difference between p_1 and p_0
Z_{a/2} is the level of significance (\( \alpha \) is 0.05)
n_2 is the sample size in the urban stratum
n_2 (exposed) is the number of women with the exposure (knowledge of the HPV vaccine) in the urban stratum