FACTORS INFLUENCING THE PROVISION AND UPTAKE OF VISUAL INSPECTION WITH ACETIC ACID (VIA) SCREENING FOR CERVICAL CANCER AMONG WOMEN ACCESSING ANTENATAL AND POSTPARTUM CARE AT A TERTIARY CENTER IN BLANTYRE, MALAWI

by
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Abstract

Background

Over 90% of cervical cancer mortality occurs in low and middle income countries where early screening and management services are not widely available. Malawi has the highest cervical cancer incidence and mortality rates globally. Visual Inspection with Acetic acid (VIA) is the screening of choice, management is limited to chemotherapy and palliative care.

This dissertation describes factors associated with provision of VIA during antenatal (ANC) and postpartum (PPC) care, and with acceptance of VIA during PPC clinics. We also describe the sociodemographic and health characteristics of women with labia minora elongation (LME) and examine their uptake of maternal health interventions.

Methods

The study sampled 529 women at a tertiary center in Malawi attending either ANC (pregnant 28+ weeks), or PPC clinic (postpartum 6 weeks). We conducted descriptive statistics followed by logistic regression models to determine the impact of sociodemographic, obstetric, clinical and relationship factors on rates of VIA offer and uptake. Then, we described the sociodemographic and health correlates of women with LME and explored their likelihood of being offered select diagnostic and management interventions when accessing maternal care.

Results

Women attending PPC clinics were more likely (AOR=5.19, p<0.001) to be offered VIA when compared to ANC.

Women who had no school through primary (AOR=0.55, p=0.04), those with LME (AOR=2.04; p=0.003) and with abnormal vaginal exam signs (AOR=0.33; p=0.06) were more likely to be offered VIA compared to their counterparts. Women reporting high degree of sexual satisfaction were less likely to refuse VIA in PPC clinic (AOR=0.34, p=0.02).

Women with LME were more likely to be illiterate or partially literate (12.4% v/s 6.2%, p=0.03) and to have travelled more than 30 minutes to reach clinic (74.3% v/s 62.2% p=0.007). They were less likely to have undergone ultrasound exams (AOR=0.41, p=0.002) or to have had instrumentation (including cesarean section) during their most recent pregnancy or delivery (AOR=0.49, p=0.06).

Conclusions

Healthcare providers may be influenced by women's sociodemographic, cultural and clinical characteristics while offering VIA screening during ANC/PPC clinics. Meanwhile, women's sociodemographic background and personal attitudes seem to be linked to uptake of preventive, diagnostic and management interventions during ANC/PPC.

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This dissertation is dedicated to my father, my earliest and most influential teacher, and a widely-cited marine biologist and researcher. It was his greatest desire to see me complete my doctoral degree, a wish that was upended by his unexpected demise last year. As his memories envelop me today, I like to imagine that he would approve of this work, and that he would be proud of this document dedicated to him.

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Acronyms

Adjusted Odds Ratio	*AOR*
Antenatal care	*ANC*
Anti-retroviral treatment	*ART*
Cervical intraepithelial neoplasia	*CIN*
Christian Health Association of Malawi	*CHAM*
Cold knife conization	*CKC*
College of Medicine Research Support Center	*COMREC*
Demographic and Health Survey	*DHS*
Department of Reproductive Health and Research	*RHR*
Ethics Review Committee	*ERC*
Family planning	*FP*
Female genital mutilation	*FGM*
Free Primary Education	*FPE*
Gender, Sexuality and Vaginal Practices	*GSVP*
General Anxiety Disorder	*GAD 9*
High income Countries	*HICs*
Human Immunodeficiency Virus	*HIV*
Human papillomavirus	*HPV*
Human Simplex Virus	*HSV*
International Agency for Research on Cancer	*IARC*
Intimate partner violence	*IPV*
Labia minora elongation	*LME*
Large loop excision of the transformation zone	*LEEP/LLETZ*
Low middle income countries	*LMICs*
Malawi Congress Party	*MCP*
Maternal Morbidity Measurement Tool Study	*MMMT*
Maternal mortality ratios	*MMR*
National Health Sector Strategic Plan 2011-2016	*NHSSP*

Negative Predictive Values	*NPV*
Non-communicable disease	*NCD*
Papanicolou	*Pap*
Personal Health Questionnaire	*PHQ 9*
Positive predictive values	*PPV*
Postpartum care	*PPC*
Private for profit	*PFP*
Queen Elizabeth Central Hospital, Blantyre	*QECH*
Reproductive, maternal, newborn, child and adolescent health	*RMNCAH*
RHR Research Project Panel	*RP2*
Sexual and Reproductive Health Research	*SRHR*
Squamocolumnar junction	*SCJ*
Squamous intraepithelial lesions	*SIL*
Total fertility rate	*TFR*
Visual Inspection with Acetic	*VIA*
WHO Disability Assessment Schedule	*WHODAS 2.0*
World Health Organization	*WHO*

Chapter 1: Introduction

1.1 Cervical cancer

1.1.1 Etiology and pathophysiology

The cervix is the lowest part of the uterus, connecting the uterine cavity to the vaginal canal. About 2-3 cm long, it consists of a uterine endocervix formed of mucus-secreting single-layer columnar epithelium and a vaginal ectocervix composed of nonkeratinizing stratified squamous epithelium. [1] The squamous cell layer consists of stratified, non-keratinizing glycogen-containing squamous epithelium that is 20-30 cells thick. In contrast, the columnar layer consists of tall, glandular, mucus-producing cells that are a single cell thick [2]. The squamocolumnar junction (SCJ) where the two layers meet is involved in intense cervical metaplasia and microglandular hyperplasia as columnar epithelium is constantly replaced by squamous epithelium. This process is regulated by blood estrogen levels and by the effects of commensal bacterial flora. The SCJ is the site of origin for cervical cancer and its precursors. The constant cervical remodeling at the junction creates a 'transformation zone' between the old and new SC junctions, which is the site for more than 90% of all squamous cell carcinomas. [3,4]

Cervical cancer refers to a series of invasive carcinomatous changes arising in the cervix, most commonly the transformation zone. The commonest forms of

cervical cancer are squamous cell (70-80% of all cases) and adenocarcinoma (10-15% of all cases) [5,6]. Although the pathophysiology of cervical cancer is poorly understood, current clinical consensus points to progressive epithelial changes following human papillomavirus (HPV) infection as a common etiology. [7,8] Following HPV infection, viral particles pass through a breach in the cervical mucosa to attack the basal layer, resulting in 'premalignant' cervical intraepithelial neoplasia (CIN). The virus enters through a breach in the cervical epithelium and affects the basal layer. The viral DNA, which undergoes episomal replication at first, eventually expresses specific genes that encapsidate the viral genome to form progeny viruses that are now capable of replication [9]. Fig 1 describes the progression of HPV infection to pre-cancerous and invasive cancer stages.

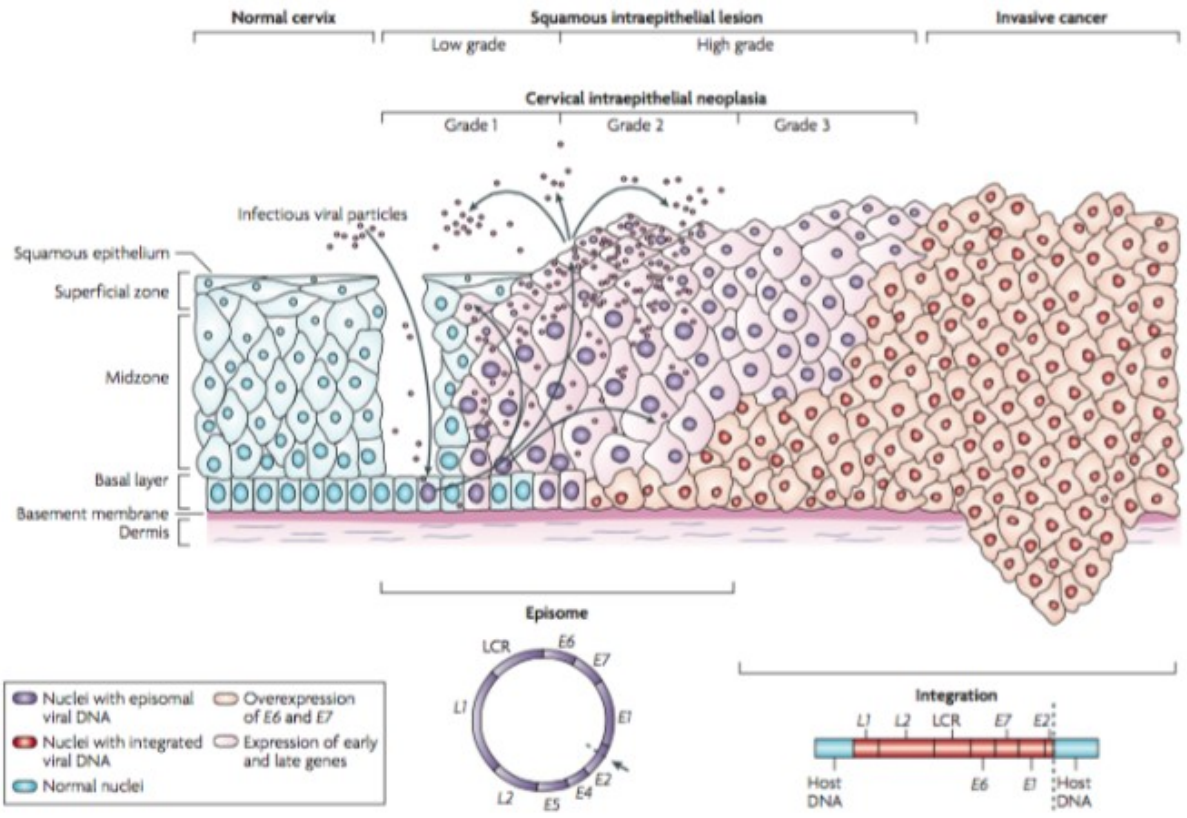

***Figure 1**: HPV–mediated progression to cervical cancer.*
(Source: Woodman CB, Collins SI, Young LS. The natural history of cervical HPV infection: unresolved issues. Nature Reviews Cancer 2007; 7(1): 11-22) [9]

The risk of developing cervical cancer is greatest in women aged 30-45 years. [6] At risk are women who show atypical cervical cytology (atypical squamous cell and atypical glandular cells) on examination, [10,11] who have been treated for CIN in the past 20 years [12,13] and who have persistent Human Papilloma Virus (HPV) infection. [8,14] Although the epidemiological association between cervical cancer and sexual activity was first described by Rigoni-Stern in 1842, [15] it took more than a century for researchers to establish HPV as the cause of cervical cancer. [16,17] Researchers erroneously linked Human Simplex Virus (HSV), another sexually transmitted viral infection, to cervical cancer in the 1960s. [18] However,

newer technologies like viral typing, polymerase chain reaction and hybrid capture assays confirmed HPV as the etiological agent in the late 1980s. The link between HPV and cervical cancer screening has gained currency only recently, with the expansion of HPV testing and screening and large-scale immunization programs [19].

Human Papilloma Virus (HPV) consists of a group of more than 160 identified species of DNA viruses that mostly cause infection of keratinocytes in the skin or mucus membranes in humans. Over 40 of them are known to be sexually transmitted, affecting primarily the anogenital region. [8] Castellsague et al. calculated the risk of developing adenocarcinoma associated with specific HPV types and found that the risk was highest for HPV 18 (OR = 410), followed by types 16 (OR = 164), 59 (OR = 163), and 33 (OR = 117). Other types strongly associated with adenocarcinoma include HPV types 35, 45, 51, and 58. [20] HPV 16 and 18 are thought to have roughly the same efficacy in causing cervical carcinoma, [21] and are associated with over 72% of all cases in Africa. [22] Recent studies analyzing HPV-16 variants across the globe suggest that the papilloma virus may have co-existed with archaic hominins up to 40 million years ago, and may trace their current patterns of distribution among different populations to the movement of prehistoric homo sapiens and other hominid species out of Africa into Europe, Asia and the American continent. [23] HPV infection is often self-limiting, and only a small proportion of cases go on to breach the cervical epithelium and result in intraepithelial neoplasia. CIN may spontaneously

resolve, especially in the absence of persistent HPV infection, or lower grade CIN (grade 1) that fails to progress. [7,8] The progression of CIN to cervical carcinoma can take more than 10 years [7]. Fig 2 describes the epidemiological model of cervical cancer carcinogenesis.

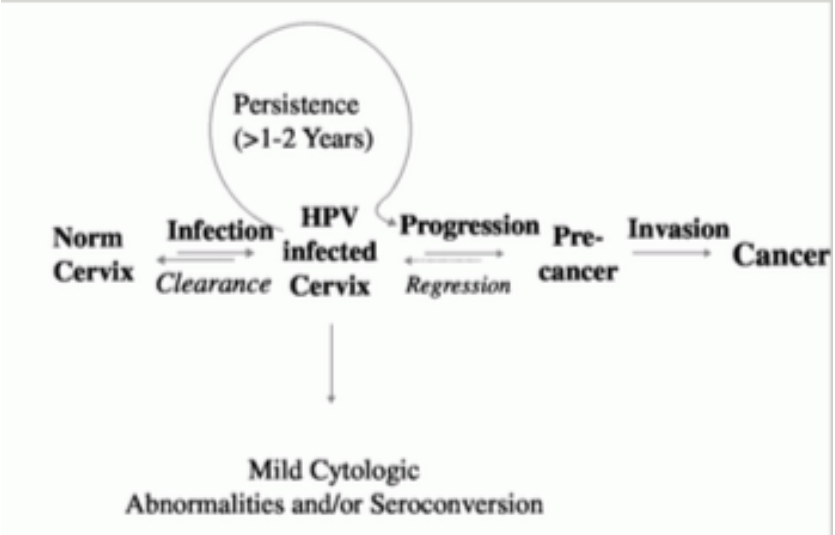

***Figure 2**: Epidemiological model of cervical cancer carcinogenesis.*
(Source: Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. The Lancet 2007; 370(9590): 890-907. [8]

For uninfected women, unprotected sexual intercourse with an infected partner is a major risk factor for contracting HPV, [14] as also an uncircumcised male sexual partner who has a history of multiple sexual partners. [24] Heavy smoking (</= 20 cigarettes/ day) among women with HPV-16 infection increases the risk of developing invasive squamous cell carcinoma. [25-27] Two meta analyses of case control and cohort studies report a possible link between cervical cancer and long term contraceptive use (>/= 5 years), but the risk was found to reduce on cessation of use. [28] Among women with HPV infection, multiparity (7+ full term

pregnancies) is associated with an increased risk of developing cervical cancer [29], although evidence suggests this effect is only restricted to adenocarcinoma. [20] Human Immunodeficiency Virus (HIV) positive women are also at increased risk of developing squamous intraepithelial lesions (SIL) following HPV infection compared to HIV-negative women, as well as have an increased risk of developing cervical cancer. The risk is greater in women with HIV and HPV co-infection than either HIV or HPV infection alone. [30]

1.1.2 Epidemiology of cervical cancer morbidity and mortality

Cervical cancer is the fourth most commonly diagnosed cancer and the fourth leading cause of cancer deaths among women worldwide, improving on its status as the second most lethal female cancer in 1975. [5,31,32] However, global distribution of cervical cancer deaths reveals dramatic differences between high-income countries (HIC) and low- and middle-income countries (LMICs). [33,34] Following an increasing trend over the past few decades, almost 90% of the estimated 311,000 deaths in 2018 occurred in LMICs, [31,32,35,36] especially countries in Sub Saharan Africa and South and Southeast Asia. [37,38] In addition, a greater number of cases of CIN progress to carcinoma in LMICs, age-standardized prevalence rates of cervical cancer are greater than 30 per 100000 (High-Risk) in Eastern, Southern, Middle and Western Africa but less than 7 per 100000 (Low-Risk) in Australia/New Zealand, Western Asia, North Africa, and North America. [36]

The reduction in cervical cancer prevalence and mortality in HICs has been largely due to the effect of regular screening and early management programs. [35,39] In the past several decades, population-based cervical cytology screening programs in North America, Western Europe and Oceania have resulted in a reduction in nationwide mortality due to cervical cancer by up to 80%. [40] An analysis of five Nordic countries from 1955 to 1980 (Fig 3) conducted by the International Agency for Research on Cancer (IARC) revealed a dramatic decrease in cervical cancer mortality rates in countries like Iceland and Finland (84% and 50% respectively) that had instituted countrywide screening programs in the mid 1960s. Meanwhile, countries like Norway that offered screening coverage only in few counties saw a more modest drop (11%) in mortality rates. [40] Even as new evidence suggests that previous estimates in HICs might have underestimated mortality, especially among minority populations, [41] current projections expect almost all cervical cancer deaths to occur in LMICs by 2030. [42] Differential access to early screening and follow-up of suspected cases through efficient, nationwide programs has contributed greatly to the increasing disparity in prevalence and mortality rates of cervical cancer globally. [39,43] Multi-pronged strategies combining Human Papilloma Virus (HPV) vaccination with routine population and clinic-based screen-and-treat programs have been found to improve detection and management of pre-invasive lesions in LMICs, thereby reducing overall risk of mortality. [44,45]

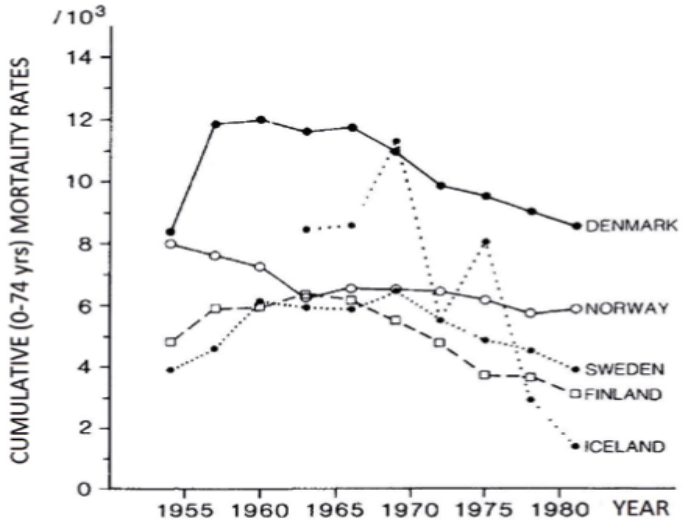

***Figure 3**: Trends in cumulative cervical cancer mortality rates (0–74 years) in five Nordic countries: 1965 – 1982.*
(Source: Saracci R, Wild C. International Agency for Research on Cancer: The First 50 Years, 1965-2015; 2015.) 43

1.1.3 Early detection, screening and management

The big breakthrough in the approach to cervical cancer screening at the end of the previous century had been to recognize carcinoma as one of the many sequelae of HPV infection and to propose screening strategies that include a combination of tests to identify and stage lesions as well as isolate the virus. [46] Cervical cancer is unique for the relatively early exposure to etiological agent (HPV), appearance of premalignant changes at affected site and long latency (and frequent resolution) before progression to carcinoma. [7] This makes it an ideal candidate for prevention programs involving routine screening of non-lethal sequelae and planned management of screening-positive women, in addition to detection of incident viral infection. Integration of routine cervical cancer prevention, screen and treat services into health systems has been shown to be

efficient and cost-effective in reducing disease burden due to cervical cancer in Rwanda, in a program that is widely considered the first national program for cervical cancer prevention, care and control in Africa. [44]

The World Health Organization (WHO) recommends routine cervical cancer screening for all women over the age of 30 (younger if HIV positive). Women with a negative VIA/ pap tests are advised to repeat screening in 3-5 years (3 years for HIV positive/high- endemic area/CIN1 or less women). HIV-negative women who are also HPV negative are advised to repeat HPV screening after a minimum interval of 5 years. [47] WHO recommends a 'screen and treat' approach to detect and manage CIN 1, 2 or 3 (CIN 3 and CIN 2 are often known together as CIN2+) in eligible women. Currently available screening tests include an HPV-DNA test, visual inspection with acetic acid (VIA), and examination of cervical cytology (Papanicolou/Pap test). In resource-constrained settings, VIA is recommended over HPV-DNA testing or examination of cervical
cytology. [47] For detected precancerous lesions, the treatment of choice is cryotherapy, if the entire lesion is visible, covering not more than 75% of the ectocervix, and the squamocolumnar junction is visible. [48,49] In cases where cryotherapy is contraindicated, loop electrosurgical procedure or large loop excision of the transformation zone (LLEEP/LLEETZ) is recommended. [47] WHO recommends cryotherapy and LEEP procedures over cold knife conization (CKC) wherever feasible (Strong recommendation, low quality evidence). [50] A randomized control trial conducted in South Africa reported 37% reduction

(p=0.002) in prevalence of CIN2+ lesions at 6 months following VIA screening and cryotherapy (screen – and – treat strategy) compared to a delayed evaluation group. [45] The management strategy of choice for cervical cancer is surgery or radiotherapy depending on tumor stage and patient status, with adjuvant chemotherapy as indicated. [51]

An additional approach to screening and treatment programs involves vaccination against HPV infection, currently recommended for girls aged below 15 years. [52] The past decade has seen significant advances in vaccine technology, and the latest iteration of the HPV vaccine in the US (trade name: Gardasil 9) protects against 90% of the viral strains that cause the disease in women. [53,54] The involvement of various governmental and non-governmental agencies has seen an expansion of immunization programs in developing countries over the past decade. [55] A demonstration project for HPV vaccine among girls aged 9-13 years was successfully completed in 2013 with support from the global vaccine alliance (GAVI). [56,57] Vaccines, however, do not prevent older women or women already infected with HPV from developing cervical cancer.

1.1.4 Visual Inspection with Acetic Acid (VIA)

Visual Inspection with Acetic (VIA) is a process of naked-eye visualization (without magnification) of the uterine cervix after application of 3-5% acetic acid to screen for cervical abnormalities. The method was first described by Ottaviano in 1982 [58] and subsequently tested and validated in different settings across the

developing world. [59-61] VIA relies on the interaction between 3-5% acetic acid and the squamous epithelial layer of the cervix, which is about 20-30 cells thick.

Acetic acid causes a reversible coagulation of the nuclear proteins and cytokeratins present in cervical epithelium. When acetic acid is applied to the superficial layer of the cervix, it removes the surface mucus, but has little effect on the underlying cell layer as these are sparsely nucleated with profuse cytoplasm. In cases where intraepithelial neoplasia is absent (i.e., normal cervical histology), acetic acid is unable to penetrate the superficial squamous cell layer to reach the deep basal layer. Epithelial cells infected with certain types of HPV undergo morphological changes that result in relatively large nuclei with less cytoplasm. Acetic acid applied to this layer desiccates the cell contents, concentrating it and making it reflect light and appear opaque. [2,49] A positive test is characterized by well-defined, opaque acetowhite lesions in the transformation zone or if the external orifice or entire cervix turns acetowhite. Invasive cancer is suspected when a cervical growth turns acetowhite, or on observing bleeding of the cervical wall following acetic acid application. [2,62]

The immediately available results of VIA and its comparatively low costs of operation make it a suitable screening tool in low-resource settings. When coupled with cryotherapy, the screen-and-treat approach offers immediate evaluation and management for suspicious cervical lesions. [62-64] VIA requires very limited laboratory support and health workers can be easily trained to

successfully perform the test. [2,65] The 4-10 -day long competency-based training programs are suitable for community health workers, midwives, nurses, paramedical workers and doctors. VIA, however, suffers from all the drawbacks of a provider-dependent subjective test, and inconsistent provider competence often results in wide variability in test-positive rates, detection of high- grade CIN and low reproducibility of results. [62]

In a review of more than 50 studies looking at accuracy of VIA, a wide range of sensitivity (14 – 95%) and specificity (14 – 98%) was reported. [66] A subsequent meta-analysis of 11 studies described pooled estimates of 72%, 79%, 10% and 99% for sensitivity, specificity, PPV and NPV respectively. [67] Pooled estimates from a similar meta-analysis of 26 studies were 80%, 92%, 10% and 99% [68] respectively. The variability in sensitivity and specificity can be attributed to the subjective, provider-dependent nature of the test and the different endpoints measured in the studies. [69] VIA was found to have better sensitivity but lower specificity than conventional cytology methods; [66 69] additionally, specificity was seen to decrease significantly with HIV co-infection. [70] HPV-DNA testing consistently reported higher sensitivity and specificity than both VIA and conventional cytology. [45,71] In spite of these limitations, VIA is the best method for early detection of precancerous cervical lesions in pre-menopausal women in low-resource countries with weak health systems. [72,73 70,74,75]

1.1.5 Factors influencing VIA uptake in low and middle income countries

Before the widespread acceptability of VIA as a population-level screening strategy, cervical cancer detection in LMICs relied on liquid cytology-based testing to detect precancerous cases. The relatively resource-intensive nature of pap smears and testing made cervical cancer screening unattainable for a large segment of the population, a barrier that has reduced considerably with the introduction of VIA in LMICs. [60,72,75] Multiple factors including greater educational, economic and employment attainment, higher parity, HIV+ status, equitable domestic gender power relations, and awareness of cervical cancer and screening predict an increased likelihood of women accepting cervical screening. [76,77] Misconceptions about the implications of screening, diagnosis and management options as well as cost, accessibility, quality of care and barriers to follow up negatively impact the rate of VIA uptake by eligible women. In the absence of appropriate treatment options like routine radiotherapy, women seem to be less motivated to access screening, even when it is available at the primary care level. [78,79] In general, awareness of cervical cancer and of screening methods exert greatest influence on women's decision to access testing. [80]

1.2 Malawi

1.2.1 General overview and demographic background

Malawi is a landlocked country in South-Central Africa with a population of 18.62 million (2017 census estimate). About 85% of its population is rural, and engaged in low-productivity subsistence farming. [81,82] Malawi's (primarily agricultural) economy depends disproportionately on tobacco, maize and sugar cultivation, with tobacco alone accounting for almost 60% of the country's exports. [83] Classified as a low income country by the World Bank, Malawi has a GNI per capita of $1180 (2017, PPP current international $); 71% of the population earns less than $1.90 (2011 PPP) per day. [84] Among the world's poorest non conflict-affected countries, Malawi's economy suffers from over-reliance on rain-fed agriculture, incomplete integration with the regional economy, out-migration of trained personnel and over-reliance on foreign aid to sustain a fragile macroeconomic stability. [81] Although real national gross domestic product has increased in recent years, the effects of unseasonal rains and extreme weather slowed economic growth most recently in 2015-16. [84] Globally, Malawi is one of the countries designated most vulnerable to the effects of climate change, [85] and repeated droughts in the North and floods in the South have hampered the economy's efforts to grow and flourish. [86]

Formerly a British protectorate called Nyasaland, Malawi declared its independence in 1964. Following the formation of a Republic in 1966, Malawi was a single-party state ruled by the Malawi Congress Party (MCP) till countrywide elections were held in 1994 following a referendum. [87] Malawi was

led by President-for-life Dr Hastings Kamuzu Banda from 1964 – 1994; Dr Banda's personal experiences as a physician in the US and the UK and autocratic style of functioning would come to have a lasting influence on many of the country's policy decisions, especially regarding population control and family planning. [88] Through the 1980's and 1990's, Malawi had among the highest fertility rates in Eastern Africa (after Uganda, Burundi) and the second highest under-five mortality rate in Sub Saharan Africa. [89] The neo-malthusian family planning policies advocated by international agencies in Sub Saharan Africa in the 1970's were resisted by the MCP government, which favored a more pro-natalist approach. [88] Access to modern contraceptive methods was severely limited in the country till 1994, although access began to expand in the final years of MCP rule. Consequently, family sizes were high, and permanent sterilization was the method adopted to limit family size. [89] Malawi's fertility rate was among the 10 highest in the world from 1975 to 1995 [90]. The universality of marriage and the higher rates of early marriage for girls (almost half of all women of reproductive age were married before the age of 18) [91] meant that age-specific fertility rates were high across all reproductive age groups during this time period. [92] Following the transition to a multi-party democracy, President Bakili Muluzi dramatically shifted the direction of Malawi's population policy and declared population control as a legitimate strategy to development. [88]

The HIV/AIDS pandemic struck Malawi just as it was emerging from the legacy of limited access to contraception and high fertility seen in the previous century.

Adult mortality was high still 2005, before effective ARV distribution programs were established by the government. In 2008, the probability of dying between the ages of 15-60 was 43% for men and women; 65.1% of adult deaths were due to HIV/AIDS. [93] Malawi has a population structure today that is typical for LMICs with high birth and death rates (see fig 4). Over 60% (64%) of the population is under the age of 15 years, 18% under the age of 5 and only 3% above 65 years. Early childbearing is common, almost 30% of women aged 20-24 had had their first child before the age of 18. [91,94]

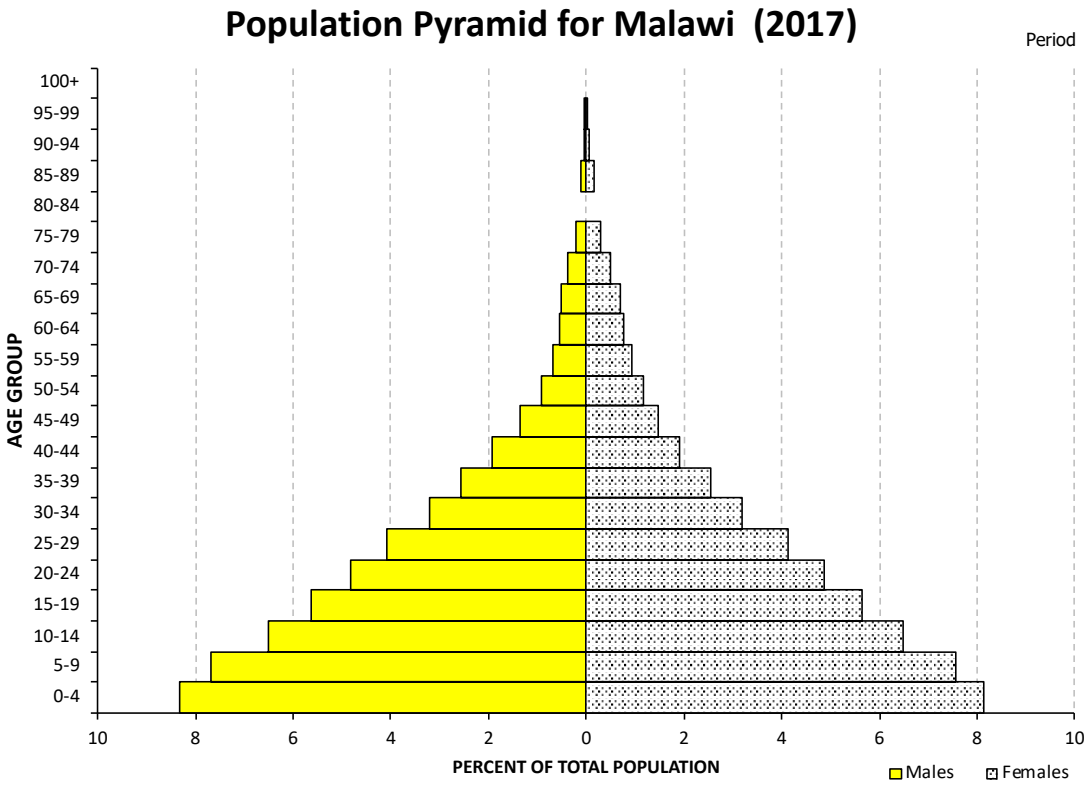

***Figure 4**: Malawi Population Pyramid, 2017.*
(Source: United Nations Population Division (2017). World Population Prospects: The 2017 Revision. Geneva). [95]

1.2.2 Women's reproductive health in Malawi

According to the results of the 2015-16 Demographic and Health Survey (DHS), total fertility rate (TFR) in Malawi is 4.4, down from 5.7 in 2010. [96,97] Malawi has among the highest maternal mortality ratios (MMR) in the world (439/100,000 births). MMR in Malawi, which was already among the highest in the world in 1980, [98] increased 1.81 times from 1990 to 2000, fueled at least partly by deaths due to HIV/AIDS. [99] High MMR in Malawi coexists with relatively high rates of skilled ANC coverage (51% of women attended at least four ANC visits, 95% at least one with a skilled provider) and institutional deliveries (91%). However, rates of skilled postpartum care (PPC) are low, only 42% of the population accessed PPC at a health center within the first 6 weeks after delivery. [91,100]

Following a transition from more pro-natalist policies to countrywide adoption of modern contraception in 1994, Malawi's access to contraceptive services has been fairly widespread and rapid. The modern contraceptive prevalence rate rose from 7% to 58% between 1992 and 2016, while the unmet need fell to 19% from a high of 37% in that same period. Between 2010 to 2016, the proportion of women aged 15-49 years accessing modern contraceptive methods rose by 39%, with almost 80% of those services accessed through the public sector. Injectables (22.5%), implants (9.0%) and female sterilization (8.3%) account for a majority of methods used. [88,97]

1.2.3 HIV epidemic in Malawi

The HIV/AIDS pandemic that swept across Sub-Saharan Africa in the last decade of the 20th century affected Malawi's health sector dramatically. Malawi's HIV/AIDS prevalence rates ranked among the ten highest in the world in 2003. [101] After peaking in 2001, deaths due to HIV/AIDS have recorded a steady decline, largely linked to nationwide distribution of anti-retroviral treatment (ART) through the public sector, beginning in 2005. [102,103] The government of Malawi mandated routine HIV testing of pregnant women in 2003, [104] and recommends provider-initiated testing and counselling services for all antenatal (ANC) and postpartum (PPC) clinic attendees. [105] However, HIV testing is widely viewed as a mandatory part of antenatal services by women in Malawi. [106] Evidence indicates that the HIV/AIDS pandemic has had a permanent impact on fertility choices and migration patterns in Malawi, resulting in situational uncertainty and disrupted parenting patterns. [107,108]

1.2.4 Cervical cancer in Malawi

Malawi has the highest age-standardized incidence rate of cervical cancer in the world (75.9/100,000 women/year), which accounts for over 78% of all diagnosed female cancers in the country. Diagnoses are predominantly of squamous cell carcinoma, and almost 30% of all cancer deaths (45.9/100,000 women/year) among women aged 15-49 in Malawi is due to cervical cancer. [109] [57]. With an estimated 2879 deaths in 2018, Malawi has the highest cervical cancer mortality rate in the world. [36,110]

1.2.5 Cervical cancer prevention, screening and management

Malawi instituted cervical cancer screening using VIA in 2004 as a pilot project in Mulanje district, which was subsequently expanded to cover the entire country. [111] Malawi's rates of pap smear testing for cervical cancer screening were among the lowest in the world (<5% in 2002-2003), [112] and the shift to VIA was seen as a way to expand access to screening while keeping costs down. As of January 2016, Malawi had 170 public VIA testing sites in the country, covering all the districts except Likoma Island. In 2015, 49,301 women were screened across the country, 91.2% of whom were screened for the first time. VIA coverage (calculated as 80% of eligible women over 5 years) almost tripled from 9.3% to 26.5% in the years 2011 – 2015. [111] Currently, screening is recommended every 5 years for women. [113] Although protocols recommend regular screening and follow up, in case only one-time lifetime screening can be carried out, the ideal age group of beneficiaries is 30-39 years. [114] The World Bank recommended expanded VIA screen-and-treat as the most cost-effective screening intervention (USD/ DALYs saved) for Malawi in the National Health Sector Strategic Plan 2011-2016 (NHSSP). [115] Building on the recommendations of the national reproductive health strategy, [116] routine cervical cancer screening was included in the NHSSP-2 (2016-2020), the only reproductive cancer screening to be thus included. The NHSSP-2 recommends primary prevention strategies (i.e., HPV vaccination for girls ages 9-13, education about sexual risk reduction-related strategies, promotion of condom use and male circumcision), and secondary prevention

(detection and treatment of non-cancerous lesions using VIA/ cryotherapy/ LLEEP and HPV-DNA testing). Recognizing the contribution of cervical cancer to female morbidity and mortality, in 2017 the Ministry of Health in Malawi released the national cervical cancer control strategy 2016-2020 that aims to incorporate emerging strategies from existing efforts at cervical cancer prevention and control, institute universal HPV vaccine administration and promote integration of cervical cancer screening into HIV care. [105] Tertiary prevention, or diagnosis and treatment of invasive cancer involves advanced technology for timely treatment and where not possible, palliative care. [117]

A demonstration project for HPV vaccine among girls aged 9-13 years was successfully completed in Malawi in 2013 with support from GAVI. [118,119] From 2013-2016, a school-based pilot HPV vaccination program 6 for girls aged 9-13 years using quadrivalent Gardasil vaccine against HPV subtypes 18, 16, 11 was carried out in the districts of Rumphi and Zomba. Almost 90% of the school-based cohort were comprehensively covered by the time of project completion. [120] Following the institution of the Free Primary Education (FPE) policy in 1994, Malawi has enjoyed high rates of enrolment at the primary school level (6-13 years), estimated at 94% of all girls aged 9-13 in 2016, although rates of recidivism and educational attainment seem to display concerning trends in recent years. [121] Nevertheless, the low rates of coverage for out-of-school girls represents a clear gap in universal coverage, and an indication for renewed

attempts to reach these populations through other means. A country-wide rollout of HPV immunization is anticipated in 2019. [122]

The lack of radiotherapy services in Malawi hampers provision of appropriate care for cervical cancer patients, making treatment options largely limited to palliative services. [123] Malawi also has a severe shortage of qualified oncologists – the country has only five oncologists and hematologists practicing full-time. [124] The paucity of appropriate management options for cervical cancer cases in Malawi underscore the importance of primary and secondary prevention strategies for cervical cancer control in Malawi. [125]

In spite of the impressive strides in recent years expanding cervical cancer screening, there are multiple barriers to access early screening and detection services for women in Malawi including cost, availability of services and lack of information regarding early screening and treatment options. [112,126] In a study assessing client satisfaction with VIA screening services in Malawi in 2013, Maseko et al. reported that knowledge of the screening test (VIA), confirmed appointment for screening, distance travelled to the health facility and waiting time were significant predictors of satisfaction [127]. In a 2012 assessment in 13 districts conducted through interviews with district co-ordinators and service providers, Munthali et al. identified lack of equipment, supplies and space, lack of supervision, irregular availability of services, long distances to health facilities,

staff shortage and absence of female providers as key system-level barriers to expanding screening access. [118]

1.2.6 Female genital modifications in Malawi: Labia Minora Elongation

Labia minora elongation (LME) is a form of female genital modification practiced by multiple communities across different African countries including Malawi, Zimbabwe, Uganda, South Africa, Mozambique and the Democratic Republic of the Congo. [128-133] Along with steatopygia, (accumulation and deposition of large amounts of fat over the gluteus maximus), LME was initially reported in western scientific literature as a morphological characteristic present from birth among the *khoi-san*. [134,135] LME has subsequently been established as a long-standing cultural practice in multiple communities across South Eastern Africa, either alone or part of a series of puberty initiation rites for pre-pubescent and adolescent girls. [136] Manual stretching of the labia minora begins among girls aged 7-11 years within gender-segregated groups overseen by older adolescent girls. [137,138] Although regular labial stretching in girls is encouraged only up to puberty, continuation of elongation practices in adulthood may be accompanied by the use of specific herbal oils, unguents, powders or poultices. [129,136,138,139] Although there is considerable heterogeneity among different communities, LME is commonly observed in matrilineal societies in Africa, and the practice is often guided and supervised by older female relatives. [140,141] WHO categorizes LME as a form of female genital mutilation (FGM) category 4, which includes all harmful

procedures to the female genitalia for non-medical purposes that are not included in categories 1-3 (this includes pricking, piercing, incising, scraping and cauterization of the genitalia) [142]

LME is practiced among different ethnic communities in Malawi, including the *Chewa,* the country's largest ethnic group, and communities like *Nyanja* and *Mang'anja* in the South, although specific rituals and practices vary within communities and even within the same community living in different parts of the country. [143,144] LME in Malawi is associated with rural communities that have lower educational attainment and who traditionally practice it in the context of puberty initiation rituals for both boys and girls. [145] Like in other parts of Africa, the significance of LME in Malawi is linked to fertility and marriage and often described as an essential pre-requisite for women desirous of entering matrimony. [146-148] The practice of LME in early adolescence and adulthood is linked to its role in enhancing sexual pleasure for men and women, as a signifier of fecundity in women, and for enlarging the introitus to promote easier childbearing. [131,137,149-151]

In Malawi, girls aged 7-12 years are encouraged by older female relatives to perform manual elongation of the labia minora (*"kukuna"* in Chichewa) in gender-segregated 'friend groups' ("*mansanje"*). Upon attaining menarche, these girls undergo a series of puberty initiation rituals (known as *chinamwali, chidototo* or *masesoto* in Central and Southern Malawi). The rituals include a

period of instruction by an older woman from the community (*anumkungwi*) on subjects like personal etiquette, community practices and rituals. The ceremonies culminate in a peri-pubertal period of separation from the family in gender-specific 'camps' known as *chiputu,* after which there is a public ceremony that welcomes new initiates into the community. *Chinamwali* rituals among some communities may include a period following the ceremony that is characterized by social acceptance of sexually risky or promiscuous behavior, in some cases, as a ritual act of intercourse with a shaman, referred to as the *fisi,* or hyena. [128,152] Initiation rituals for boys often involve circumcision and a period of instruction and confinement culminating in a ceremonial event, which may be followed by a period of apparent social tolerance for sexually promiscuous behavior. [128,130,140,152]

Labial elongation is currently practiced by multiple tribes in Malawi with different degrees of adherence, and it is widely recognized that the introduction of Christianity over the last two centuries has irrevocably changed traditional practices and imperatives among various groups, for eg the introduction of *chilangizo*, a Christianized alternative to traditional *chinamwali* ceremonies in the Baptist Synod of Malawi. [144,153,154]

1.3 Reproductive health service integration in Malawi

1.3.1 Health system overview

Malawi has a three-tiered health system, and services are provided by a combination of public (55%), private for profit (PFP 20%), faith-based (Christian Health Association of Malawi CHAM 14%) and non-governmental (6%) organizations, with public and private employer organizations accounting for the remaining share. [155] There are four tertiary hospitals and 26 district hospitals in the country, each district hospital overseeing a population of 140,000 to 1.4 million through 11-40 health centers located within its oversight area. The contribution of PFP facilities is mostly in provision of primary care, and there is widespread variation between urban and rural areas in both quality and coverage of services. [94] Rising disease burdens and disproportionate spending share continued to stretch an already overburdened public sector until 2013, when a wide-reaching corruption scandal in the health system (nicknamed "cashgate") resulted in widespread donor withdrawal and extraordinary stress on public health financing systems. [156,157] Nevertheless, external sources continue to account for a disproportionate share of Malawi's total health expenditure (74% in 2016/17), although this funding is often targeted towards specific disease prevention programs. [158] The majority (84%) of funds for Malawi's response to HIV/AIDS comes from international sources, however this share too, has shown a decreasing trend over recent years. [101,103] More recently, analysts warn that introduction of user-fees and "bypass fees" may have exacerbated inequity in access to healthcare, especially maternal health services in Malawi. [159]

1.3.2 Integration of reproductive, maternal, newborn, child and adolescent health services

In 2008, WHO described integrated health services as a package of preventive and curative health interventions for a particular population group, often (but not always) distinguished by its stage in the life cycle, with the goal of ensuring continuity of care. Integration may be achieved across different delivery points and across multiple levels in the healthcare system, as well as through involvement of distinct sectors of the government in health policy formulation. Integration does not need to provide fully comprehensive care at the same site, but it does require healthcare providers to have skills to provide appropriate basic services and refer patients onward for necessary services not provided at the site. [160,161] Most integrated public health programs in LMICs tend to address communicable diseases, most notably HIV/AIDS, tuberculosis and malaria. [161-165] However, successful integration of programs has proven challenging due to a variety of factors, including a lack of national integration policies, funding inequities and the tendency of programs to encourage enhanced collaboration absent shared responsibility. [166,167] Reproductive, maternal, newborn, adolescent and child health (RMNACH) services have been popular avenues for horizontal integration with other screening and diagnostic interventions, primarily because recipients are characterized by similar gender and background characteristics with specific health needs, much of it addressed through routine care and follow-up. [161]

1.3.3 Integration of primary care and VIA services in Malawi

Unlike HIV screening, which is well integrated into ANC screening in many settings, limited evidence exists concerning integrating VIA into other points of care where women are already at the facility. [168,169,] In a 2018 systematic review of randomized clinical trial and non-randomized intervention studies that examine the effectiveness of integrating gestational and non- gestational non-communicable disease (NCD) interventions with ANC among women and children in LMICs, Kikuchi et al. suggest that integration of VIA screening and RMNACH care has a clear positive impact on the uptake of screening services and identifying potential cervical cancer cases. The move from cervical cytology screening using pap smear to VIA has made integration more feasible and achievable for LMICs seeking to address low rates of cervical cancer diagnosis and prevention. [170]

Predictable barriers of cost, access and information about early detection and treatment continue to retard expansion of VIA coverage in Malawi. [112,126] To address system-level barriers to expanding screening access including longer commute and wait times, lack of supplies, space, equipment and gender-appropriate staff (discussed previously), the Ministry of Health has sought to integrate VIA screening with other points of primary care delivery. [118] [127] Malawi's National Service Delivery Guidelines for Cervical Cancer Prevention recommends that VIA be offered by trained nurses and health workers at family planning and STI clinics, and the national Sexual and Reproductive Health

Research (SRHR) policy advocates the integration of cervical cancer screening with primary care service provision. [171] [109] However, evidence indicates that women accessing maternal healthcare, including family planning services, are not offered VIA screening routinely by healthcare providers, who may choose to selectively offer screening based on the clinic setting, patient characteristics and findings elicited during examination. [79,119]

1.4 Hypothesis and specific aims

Antenatal and postnatal care represent an integral and unique point of contact with the health system for women in LMICs. The timing and nature of prenatal visits offers opportunities for systematic assessment and management of women's reproductive health. Cervical cancer screening is a routine preventive health intervention that helps in early detection and management of the disease. Recent advancements in early screening and management of suspected precancerous cases have reduced the barriers to conducting successful screening programs in LMICs. Barriers to screening access for women may be provider-driven and may be prompted by sociodemographic and cultural cues as well as clinical presentation during the visit. Access to VIA testing is also influenced by the women's decisions regarding screening and its implications. The objective of this dissertation is to better understand the factors that influence women's uptake of cervical cancer screening during routine ANC and PPC in Malawi and to offer direction for future research and implementation strategies designed to

integrate VIA screening and maternal health care. Data are drawn from a population of women seeking ANC and PPC care in a tertiary health facility in Blantyre, Malawi.

AIM 1: To describe the clinical factors associated with women being offered VIA screening during ANC and PPC.

AIM 2: To describe the sociodemographic and relationship factors associated with women's acceptance of VIA screening during ANC and PPC.

AIM 3: To describe the sociodemographic, health and wellness characteristics of women with labia minora elongation (LME) and examine provider treatment of these women when accessing maternal health care.

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Chapter 2: Methods

2.1 Study background and setting

2.1.1 Maternal Morbidity Measurement Study

Data for this study are drawn from a pilot study designed to test a maternal morbidity measurement tool in three countries (Jamaica, Malawi and Kenya) in 2015-16. The objectives of the pilot were to quantify the morbidities women experience during and after childbirth and validate the tool. The pilot included approximately 1500 women across the three countries, thus 250 women from antenatal (ANC) and postpartum (PPC) care clinics in each country (500 total in each country). Women attending either ANC clinic and more than 28 weeks pregnant, or attending PPC clinic at six weeks postpartum were invited to be part of the pilot in each of the sites.

2.1.2 Malawi study site – Queen Elizabeth Central Hospital, Blantyre

Queen Elizabeth Central Hospital, Blantyre (QECH) was the sole study site of study in Malawi. QECH is a 1120-bed public hospital serving the healthcare needs of Blantyre, Malawi's second-biggest city, and of Southern Malawi. It is a tertiary care center, one of four 'Central Hospitals' as well as the only teaching hospital in Malawi. [1] QECH caters to the primary care needs of the surrounding areas in addition to provision of tertiary care in all specialties. The Department of

Obstetrics and Gynecology at the hospital has had between three and six specialist physicians, two to three registrars and three to five intern medical doctors at different times over the past decade. There are between two and four nurse-midwives for each shift [2,3]. The gynecology department manages women diagnosed with precancerous lesions or suspected cervical carcinoma. The primary methods of management are surgery, chemotherapy and referral to palliative care services. [4] QECH is expected to house Malawi's first radiotherapy center for cancer care in 2019. [5]

2.1.3 Study protocol and sample

The measurement tool consisted of three main data collection activities:

- Questionnaire (face-to-face)
- Physical exam including a pelvic exam
- Medical record review.

a) Study Flow

Women accessing antenatal care or attending postpartum clinic at QECH were approached for enrolment in the study. Eligible women were briefed on the details of the study and administered informed consent. Women were free to refuse to participate in any of the data collection activities, and were free to discontinue the study at any time. Consenting participants were administered a questionnaire recording reports of clinical symptomatology and management, functional impact assessment (WHO Disability Assessment Schedule WHODAS

2.0, General Anxiety Disorder GAD-9 and Personal Health Questionnaire PHQ-9), [6-8] and maternal history and current health status. [9] Data were collected using into a digital device (electronic tablet) and study investigators were either nurses or female medical physicians who had recently graduated from QECH. The goal of this questionnaire was to learn from the women's perspective what their subjective experiences of the current or most recent pregnancy was.

b) Physical exam

The second part of the tool consisted of a physical exam (including vitals, general physical, breast and abdominal exam), followed by a pelvic inspection and internal exam. The physical exam was conducted by a clinical health professional in a separate location from the oral interview. The person doing the exam was asked to report on clinical findings and provide assessment of the overall well-being of the women. The clinician was not privy to the results of the detailed questionnaire, and was not required to review any health records. VIA screening was part of the study protocol for the Malawi site so all women seeking care were expected to undergo screening as part of the internal exam. That said, if the clinician felt the woman was 'ineligible' for VIA, the clinician would not offer VIA and record the reason. Women who were considered eligible were asked if they wanted VIA, and could either accept or refuse. These two decision points, the clinician's and the woman's, form the basis for the analyses for Aims 1 & 2 (see fig 5). In case a positive VIA exam was recorded, the woman was referred to the gynecology department for further evaluation and management. Following

assessment, the appropriate management strategy was discussed with the patient. Since QECH is a tertiary care center, the referral center is located within the same physical building.

c) Record review

The third part of the tool was a record review (the national health passport is used in Malawi) to assess the investigations and tests done prior to the current visit. The health passport in Malawi is a document that chronicles patient health records and health care visits. It is in the possession of the women themselves, and is required to be presented during public or private sector healthcare visits. [10] Women without a health passport are required to buy a new one at the time of the visit.

Study protocols and a majority of items in the questionnaire were the same for both ANC and PPC. In addition, both samples were simultaneously recruited at QECH during the course of the study. National screening guidelines in Malawi recommend regular VIA screening every 5 years for all women aged 30-49 years in the general population, aged 18-49 if at high risk of cervical abnormalities (including HIV+, early sexual debut, multiple partners, previous abnormal screening result). [11] The National Reproductive Health Service Delivery Guidelines (NRHSDG) recognize cervical squamous cell carcinoma as an AIDS defining illness, and requires yearly screening for women living with HIV, and for women reporting prior positive screening result (until resolution of lesions).

Screening is recommended for women who are currently pregnant, postpartum, or accessing post-abortion care, as well as women attending sexually transmitted infection (STI) and HIV/AIDS clinics. [11,12]

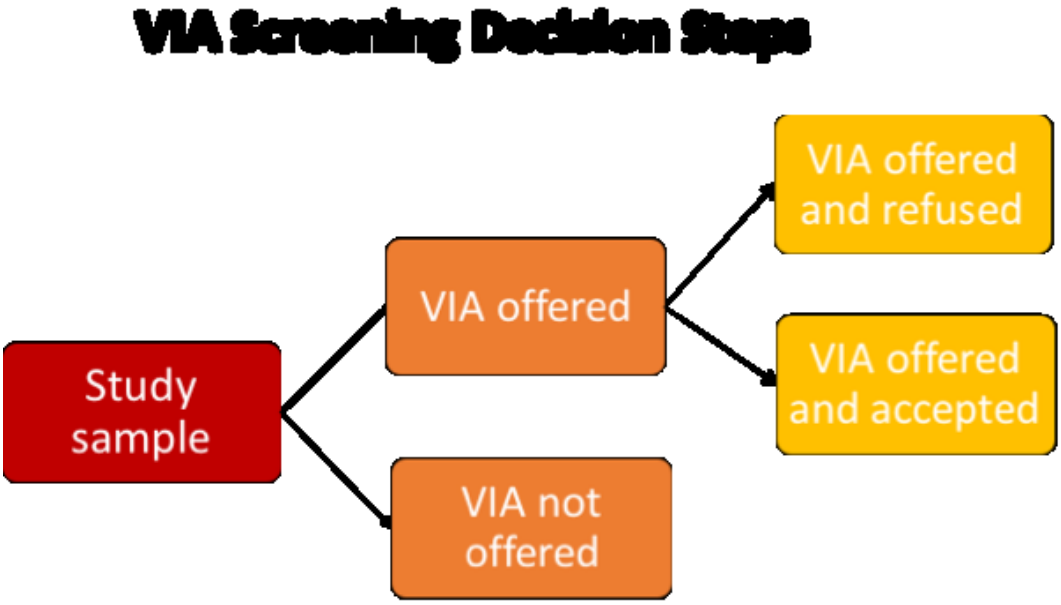

Figure 5: VIA screening study in QECH, Blantyre

2.2 Ethical considerations

This study uses secondary data from the Malawi pilot study which was conducted by WHO in collaboration with QECH. Ethical approval was provided by WHO's Research Ethics Review Committee (ERC). The study also cleared the ethics committees in each of the partner countries, including COMREC, (College of Medicine Research Support Center), the ethics and institutional review board at the College of Medicine, Blantyre, Malawi.

2.3 Dissertation overview

This dissertation addresses three aims related to provision of screening, diagnostic and management interventions for women accessing maternal healthcare in QECH. A detailed description of the methods used for each aim is presented in the corresponding chapter of the dissertation.

To address aims 1 and 2, we divided the clinical encounter into two component parts: whether VIA was offered by the clinician to eligible women, and if the screening test was accepted or refused by these women. For the first part, we considered all enrolled women who presented for antenatal or postpartum care at QECH during the study period (n=481, ANC=239, PPC=242). Among these women, we identified those who were offered VIA screening by the clinician during the physical exam, and analyzed the factors that might have contributed to this decision. On examining ANC and PPC sample separately, we decided to pool the samples as there were no significant differences in variables considered in the analysis between the antenatal and postpartum women.

Among women offered VIA during ANC clinic, 92% refused screening, making the resulting sample too small for meaningful analysis. Thus, to address aim 2, we analyzed only the women attending PPC clinic who were offered VIA by the clinician.

To address aims 1 and 2, we first conducted descriptive statistics, followed by bivariate and multivariate logistic regression models to determine the impact of sociodemographic, obstetric, clinical and relationship factors on rates of VIA offering and uptake.

To address aim 3, we considered all women who accessed ANC and PPC as part of the pilot study. Based on findings recorded during the pelvic exam (n=419, ANC=230, PPC=189), we identified women who had labia minora elongation (LME). We described the correlates of LME among women accessing maternal healthcare services and tested for differences in provision of screening, diagnostic and management interventions during the pregnancy, delivery and postpartum period. Specifically, we described sociodemographic, health and wellness variables for women with LME, the rates at which the women were offered ultrasound screening during ANC clinic, and the rates of cesarean section or other instrumentation during the most recent delivery. We also analyzed the rates at which VIA screening was offered for the entire sample. First, we conducted descriptive statistics of key covariates thought to be associated with LME, followed by a series of multivariate regression models, adjusting for key sociodemographic and health covariates.

2.4 References

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Chapter 3: Factors Influencing Offer of Visual Inspection with Acetic Acid (VIA) Screening to Women Accessing Maternal Healthcare in Blantyre, Malawi

3.1 Introduction

Cervical cancer is the fourth leading cause of cancer mortality among women worldwide with almost 90% of the estimated 311,000 deaths in 2018 occurring in low and middle income countries (LMIC), [1-4] especially those in Sub Saharan Africa and South Asia. [5,6] Current projections expect almost all cervical cancer deaths to occur in less developed countries by 2030. [7] This is largely attributable to a 'screening gap' between developed and developing countries. Historically, early screening and follow-up of suspected cases through efficient, nationwide programs have contributed greatly to reducing mortality rates in developed countries. [8,9] Multi-pronged strategies combining Human Papilloma Virus (HPV) vaccination with routine population and clinic-based screen-and-treat programs have been found to improve detection and management of pre-invasive lesions in developing country settings, thereby reducing overall risk of mortality. [10,11]

Between 80-90% of all cases of cervical cancer are either squamous cell or adenocarcinoma, a majority of which tend to be asymptomatic until later stages.

Frank carcinoma represents the final stages of a series of neoplastic changes within cervical tissue, almost always etiologically linked to HPV infection. [12,13] Unprotected sexual intercourse with an infected (especially uncircumcised) [14] partner represents the most important risk factor of contracting HPV for an uninfected woman. [15] Also, heavy smoking, long-term use of combined oral contraceptive pills, multiparity and presence of concomitant Sexually Transmitted Infections (STIs), including HIV are linked to increased risk of developing some forms of cervical cancer, both as independent risk factors as well as by accelerating disease progression in HPV-infected women. [16-21] Disease progression from incident infection to clinical manifestations takes an average of 18.5 months, and frank carcinoma in the absence of appropriate management develops in about 10 years. [13,22] The slow progression of pre-cancerous lesions to frank carcinoma allows effective screening strategies, currently done either through examination and analysis of cervical epithelium to detect early dysplastic changes following HPV infection (Papanicolou (Pap) screening and Visual Inspection with Acetic Acid (VIA)), or through laboratory detection of HPV DNA correlated with clinical symptoms. [23]

3.1.1 Visual Inspection with Acetic Acid (VIA) Screening for Cervical Cancer

Although HPV-DNA testing is widely regarded as the gold standard, in resource-constrained settings, VIA is recommended for population-level screening of women at risk. [24] VIA involves application of 3-5% acetic acid to the squamous

epithelial layer of the cervix to observe the resulting color changes, if any. A positive test is characterized by well-defined, opaque acetowhite lesions in the transformation zone or if the external orifice or entire cervix tns acetowhite. Invasive cancer is suspected when a cervical growth turns acetowhite, or on observing bleeding of the cervical wall following acetic acid application[25,26]. VIA is contraindicating for women allergic to acetic acid, those over 55 years, or who are currently experiencing heavy menstrual flow. [25] Multiple meta-analyses of studies on the efficacy of VIA conclude that the test tends to have better sensitivity but lower specificity when compared to conventional cytology-based methods of screening[27-29]. In addition, the subjective provider-dependent nature of the test may sometimes impact its reliability, in ways that may not be easily predictable. [30] In spite of these limitations, the immediate availability of results, low costs of operation, limited laboratory support and relative ease of training health workers to successfully evaluate and report VIA screening makes it ideal for developing country settings [26,31-33].

Existing cervical cancer screening strategies in developing countries rely largely on provision of cytology or visual-inspection tests as part of routine primary care for women aged 30-50 years. [10,34] Unlike HIV counseling and testing which has been offered as part of standard maternal healthcare for over two decades, cervical cancer screening is not currently integrated into routine antenatal (ANC) or postpartum (PPC) care in developing countries, despite the clear link between precancerous lesions, incident HPV infection and unprotected sexual activity.

The aim of this analysis is to understand uptake and potential barriers to VIA uptake in order to assess the feasibility of providing screening for cervical cancer during routine maternal healthcare in a developing country setting. By analyzing the factors associated with the clinician's decision to offer or deny screening to a woman accessing maternal healthcare within a monitored setting, this research study offers an opportunity to understand some of the barriers to mainstreaming VIA during ANC and PPC care.

3.2 Study Setting and Background

3.2.1 Reproductive Health in Malawi

Malawi is a land-locked country of 18.62 million (2017 census est) where more than 70% of the population earns less than $1.90 a day, [35] primarily employed in occupations dependent on rain-fed agriculture. [36] Malawi had among the highest fertility as well as under-5 mortality rates in Sub-Saharan Africa in the 1980s and 90s. [37] Currently, the total fertility rate (TFR) is 4.4, down from 5.7 in 2010 and almost a third of women aged 20-24 have had their first child before the age of 18. [38,39] The country also has among the highest estimated maternal mortality ratios (MMR) in the world (439/100,000 births), as well as relatively high rates of skilled ANC coverage (51% of women attended at least 4 ANC visits) and institutional deliveries (91%). [38,40] Malawi has the highest incidence of (predominantly squamous cell) cervical cancer in Eastern Africa (age standardized 75.9/100,000 women/year), which accounts for over 78% of all

diagnosed female cancers and almost 30% of all cancer deaths (age standardized 45.9/100,000 women/year) among women aged 15-49 in the country. [41] [42] With an estimated 2879 deaths in 2018, Malawi has the highest cervical cancer mortality rate in the world. [4,43]

3.2.2 Cervical Cancer Screening in Malawi

Pap screening rates in Malawi have traditionally been low (<5% in 2005)[44], but VIA screening was introduced in 2004 and expanded to cover almost the entire country by 2016. VIA coverage has tripled from 9.3% to 26.5% between 2011 to 2015 in Malawi[45]. However, predictable barriers of cost, access and information about early detection and treatment continue to retard expansion of coverage. [44,46] System-level barriers to expanding access in the literature include lack of supplies, space, equipment and gender-appropriate staff as well as long commute times to health facilities[47] while awareness of the VIA test, waiting time, time to travel to the testing center and confirmed appointment for screening were seen to greatly influence client satisfaction for VIA. [48] Although the ministry of health recommends integration of cervical cancer screening with primary care service provision in the national Sexual and Reproductive Health Research (SRHR) policy, [41] evidence indicates that women accessing primary care services are not offered VIA screening routinely by clinicians - due to a variety of factors. [49,50] Clinicians may choose to selectively offer screening based on the clinic setting, patient characteristics and clinical findings elicited during examination. Malawi's National Service Delivery Guidelines for Cervical Cancer Prevention recommend

that pregnant women may be safely screened by VIA, and suggests special attention be paid to women complaining of STI-related symptoms. [51]

The objective of this study is to assess the factors that influence clinicians' decisions to offer VIA screening to women attending ANC/PPC care in a study setting where integration of these services was part of clinical protocol. Based on what is known about VIA integration as well as cervical cancer in Malawi, we hypothesized that clinicians decision to offer screening might be influenced by sociodemographic factors like the woman's age, education, parity and marital status as well as clinical signs elicited during examination.

3.3 Methods

3.3.1 Study Design

Data for this study are derived from the Maternal Morbidity Measurement Tool (MMMT) study, a cross-sectional research study that was conducted in Jamaica, Kenya and Malawi in 2015-16 to assess and quantify morbidities experienced by women in the antenatal and post-partum period. The MMMT study consisted of a questionnaire, physical exam and medical record review. The questionnaire was administered by trained investigators, who were clinicians trained for the survey. The questionnaire recorded women's reports of clinical symptomatology and management as well as maternal history and current health status, including functional assessment and mental health screening[52-55] The questions attempted

to assess female respondents' subjective experiences of the current or most recent pregnancy.

The physical exam consisted of a general obstetric exam followed by a pelvic inspection and internal exam. It was conducted in a separate location, recorded on paper and the supervising clinician was not privy to the information gathered in the questionnaire. The pelvic inspection and internal exam was offered based on clinical correlation assessed by the clinician. During the physical exam, clinicians (either nurses or Ob/Gyn physicians), were required to offer Visual Inspection with Acetic Acid (VIA) screening to all eligible candidates, irrespective of the woman's screening history. In case VIA was not offered, clinicians were required to record the reason for ineligibility. Routine VIA screening is recommended as part of the national screening guidelines in Malawi. Participating women were free to refuse any part of the study or discontinue their participation at any time. Additional details of the study protocol are described by Say et al. [52] In all three sites, the MMMT was administered as part of routine ANC and PPC clinics. Ethical approval was provided by the WHO's Research Ethics Review Committee (ERC) as well as by the RHR Research Project Panel (RP2), the external review body of the Department of Reproductive Health and Research (RHR). The study also cleared the appropriate ethics committees in each of the partner countries, including the College of Medicine Research Support Center (COMREC), the ethics review board at the College of Medicine, Blantyre, Malawi.

3.3.2 Study Site

In Malawi, the Queen Elizabeth Central Hospital, Blantyre (QECH) was the study site. QECH is a 1120-bed public hospital serving the healthcare needs of Blantyre, Malawi's second-biggest city, and of Southern Malawi. It is a tertiary care center, one of four 'Central Hospitals' as well as the only teaching hospital in Malawi, catering to more than 45% of Malawi's population living in the Southern region. [56,57] Due to the often-unreliable public healthcare services in rural areas of Southern Malawi, QECH caters to the primary care needs of the surrounding areas in addition to provision of tertiary care in all specialties. The Department of Obstetrics and Gynecology at the hospital has had between 3 and 6 specialist physicians, two to three registrars and 3 to 5 intern medical doctors at different times over the past decade. There are between two and four nurse-midwives for each shift. [58,59]

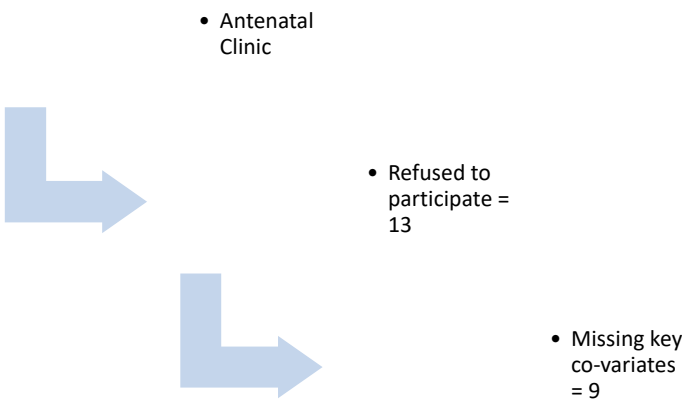
3.3.3 Study Protocol

Women attending ANC clinic and more than 28 weeks pregnant, or attending PPC clinic at 6 weeks postpartum were invited to be part of the study. Women who consented to participating in the survey were administered the questionnaire, physical exam and record review. All data was collected on site by study investigators using hand-held devices, collated and transmitted to a central data repository where it was entered and cleaned. As the data collected in the questionnaire was not immediately shared with the clinician, the reasoning behind deciding to offer VIA was based solely on what the clinician observed.

3.3.4 Study Sample

The final analytical sample of 409 women was drawn from a total of 529 (ANC=252, PPC=277) who were approached to participate in the study. Of these women, 481 (ANC=239, PPC=242) consented to enroll in the study. 239 women attending ANC and 229 attending PPC clinic (total N= 468) were considered for VIA screening. Women currently menstruating (12) and post-hysterectomy (1) were excluded to create an eligible sample of 455 women (ANC=239, PPC=216). Of the 455 eligible women, 46 (ANC=37, PPC=9) were missing key co-variates that were part of the hypothesis and analysis. The details of the sample selection are described in fig 6.

Antenatal clinic



Postpartum clinic

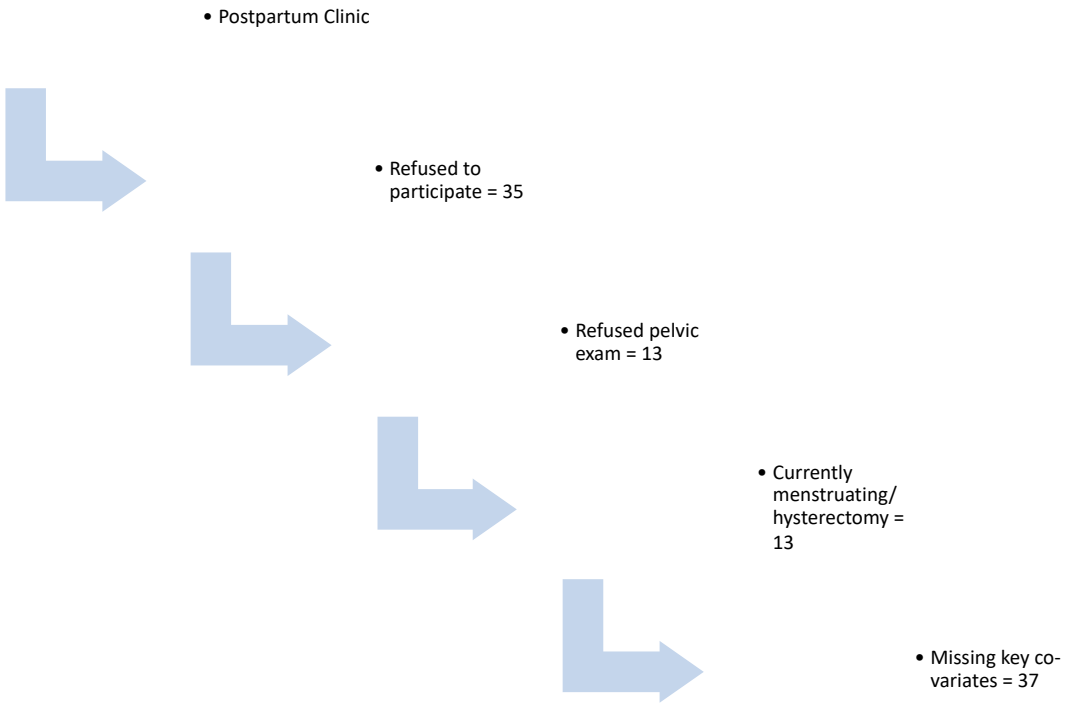


Figure 6*: Enrollment and selection into VIA testing, by clinic.*

Variables

To better understand the factors associated with the clinician offering VIA to women, this analysis focuses on the characteristics of the women (both sociodemographic and clinical) that could be directly observed or elicited by the clinician, or which could be inferred from the brief obstetric history educed during the clinical encounter.

Dependent Variable: The dependent variable for this study is whether the clinician offered VIA screening to the woman. It is important to note that study protocol in Malawi was designed so that all women were expected to be offered

VIA as part of the study. However, if, during the postnatal exam it was evident that women had had a hysterectomy (n=1) or were menstruating (n=13) (contraindications for VIA), [25] those women were excluded. Based on the clinical reports, a dichotomous variable was generated to indicate whether women were offered or not offered VIA.

Independent variables: Age, educational and marital status of the women were considered for analysis. Age was included as a continuous variable. Marital status was coded as a dichotomous variable (married or cohabiting versus single or divorced). Educational attainment was assessed using literacy status as well as through a binary variable (primary or less versus secondary or higher) and the variable that showed association with VIA offer was retained in the analytical model. Women were characterized by whether they reported being currently employed at the time of the survey or not.

Clinical variables: Labia Minora Elongation (LME) status (none versus present), abnormal vaginal exam signs (absent versus present) and first pregnancy (ongoing/ first delivery completed versus primigravida or recent first birth) were the clinical variables considered in the analysis. All three clinical variables are dichotomous. LME is a form of Female Genital Mutilation (FGM) that is seen in Malawi and is better described as a for of female genital modification. LME is classified by the WHO as FGM category 4. [60-62] The motivations, rituals and language associated with LME are markedly different from those of FGM

categories 1 through 3. In the absence of data collected that signifies religious or tribal status, LME recorded during physical examination may be a proxy indicator for ethnic background. [63] Abnormal vaginal exam signs included evidence of ulcers, lesions, excoriations or swelling in the external genitalia and the vagina as well as vaginal discharge seen upon examination. These may have influenced the clinician's decision to offer or not to offer VIA screening, although none of these are contraindications for performing VIA, per se. [25] It is also possible that clinicians may treat women experiencing their first pregnancy or who have just had their first delivery differently from multiparous women.

3.3.5 Analysis plan

This study analyses the provision of cervical cancer screening to pregnant women over 28 weeks gestation attending ANC clinic and women up to 6 weeks postpartum attending PPC clinic. Consenting women who underwent the complete study including the physical exam, pelvic inspection and internal exam were considered for the analysis. The final sample analyzed all eligible women who had completed the survey, general physical and pelvic internal exam.

To assess the similarity or differences between the antenatal and postpartum samples with the anticipation of conducting a pooled analysis, we first described key demographic characteristics of the sample potentially associated with attending ANC or PPC clinic. Next, we explored the relationship between each of our independent variables and the outcome—clinician offering VIA during the

clinical encounter - using t-tests and chi-square tests for significance. For analyses where individual cells had fewer than 10 observations, a Fischer's exact test was used. We conducted bivariate logistic regression to assess the association of each independent variable with the outcome and then conducted multivariable logistic regression to explore factors that may have impacted the clinician's decision to offer or not offer VIA. Finally, we conducted a descriptive analysis of the reasons clinicians reported for not offering VIA, stratified by visit type. All analyses were conducted using STATA ver14.1.

3.4 Results

A total of 481 women (ANC=239, PPC=242) were enrolled for the survey, of which 409 (ANC=230, PPC=179) are in the final analytic sample. Women excluded from this analysis include those who refused to undergo the pelvic exam (n=13), were ineligible due to menstruation or hysterectomy (n=13) or had incomplete or missing records for the variables of interest (n=46) considered in the analysis. Results of the comparison between the ANC and PPC are shown in Table 1.

Overall, there were very few significant differences between the two samples. A significantly greater proportion of the women in the ANC sample reported a past miscarriage compared to the PPC sample (23.9% vs. 17.3%, p=0.01).

***Table 1**: Sociodemographic, clinical and obstetric characteristics of women in antenatal (ANC) and postpartum (PPC) clinic visits at Queen Elizabeth Central Hospital, Blantyre*

Category	*Antenatal Clinic n=230*	*Postpartum Clinic n=179*	*Total n=409*	*p-value*
Sociodemographic Characteristics				
Age (years)				*1.00*
Mean	*27.7*	*26.6*	*27.2*	
Range	*15-43*	*15-50*	*15-50*	
Literacy				*0.10*
Illiterate/ Partially literate	*7.4 (17)*	*12.2 (23)*	*9.6 (40)*	
Literate	*92.6 (213)*	*87.8 (166)*	*90.5 (379)*	
Education				*0.35*
Primary or less	*26.5 (61)*	*30.7 (55)*	*28.4 (116)*	
Secondary or more	*73.5 (169)*	*69.3 (124)*	*71.6 (293)*	
Marital status				*0.46*
Single	*7.0 (16)*	*8.9 (16)*	*7.8 (32)*	
Married/cohabiting	*93.0 (214)*	*91.1 (163)*	*92.2 (377)*	
Employment Status				*0.07*
Currently unemployed	*53.5 (123)*	*62.6 (112)*	*57.5 (235)*	
Currently employed	*46.5 (107)*	*37.4 (67)*	*42.5 (174)*	
Time to reach clinic				*0.59*
<30 mins	*30.4 (70)*	*33.0 (59)*	*31.5 (129)*	
>/= 30 mins	*69.6 (160)*	*67.0 (120)*	*68.5 (280)*	
Expressed fear of intimate partner violence				*0.74*
No	*93.0 (214)*	*93.9 (168)*	*93.4 (382)*	
Yes	*7.0 (16)*	*6.2 (11)*	*6.6 (27)*	
Obstetric Characteristics				
Parity				*0.29*
Any previous births	*66.5 (153)*	*61.5 (110)*	*64.3 (263)*	
First delivery	*33.5 (77)*	*38.6 (69)*	*35.7 (146)*	
History of miscarriage				*0.01*
No	*76.1 (175)*	*82.7 (148)*	*79.0 (323)*	
Yes	*23.9 (55)*	*17.3 (31)*	*21.03 (86)*	
Clinical characteristics				
Abnormal vaginal exam signs [a]				*0.20*
No	*94.8 (218)*	*97.8 (175)*	*96.1 (393)*	
Yes	*5.2 (12)*	*2.2 (4)*	*3.9 (16)*	
Labia Minora Elongation				*0.32*
None	*48.3 (111)*	*41.9 (75)*	*45.5 (186)*	

Present	*51.74å (119)*	*58.1 (104)*	*54.5 (223)*	

[a] Due to small cell size, p-value determined with Fischer's Exact test

Most women (70.9%, n=290) attending ANC or PPC clinics were offered a VIA exam by the clinician; however, a significantly higher proportion of women attending PPC clinics were offered VIA when compared to women attending ANC clinics (87.7% versus 57.8%, p=0.001). Analysis of independent variables reveals that the proportion of women who were offered VIA did not vary by age, marital status or parity (Table 2). However, among women who were educated up to primary school, 80.2% were offered VIA as opposed to 67.2% of secondary school and higher (p=0.009). Slightly more than a third of 16 women who were diagnosed with abnormal signs on vaginal exam were offered VIA, as opposed to almost three quarters of the women who did not have any abnormal signs, and this difference was statistically significant. Among women who had undergone LME (greater than 55% of the sample), 78% were offered VIA, compared to 62.4% among women who had not undergone LME (p=0.001).

***Table 2**: Characteristics of women in antenatal (ANC) and postpartum (PPC) clinic visits, by clinician offering VIA (visual inspection with acetic acid) for cervical cancer*

Category	**VIA not offered % (n) (n=119)**	**VIA offered % (n) (n=290)**	**Total % (n) (n=409)**	**p-value**
Visit type				0.001
Antenatal care	42.2 (97)	57.8 (133)	100 (230)	
Postpartum care	12.3 (22)	87.7 (157)	100.0 (179)	
Sociodemographic characteristics				
Age (years)				1.00

Mean Range	27.3 15-43	27.2 15-50	27.2 15-50	
Literacy				0.38
Illiterate/ partially literate	23.1 (9)	76.9 (30)		
Literate	29.7 (110)	70.3 (260)		
Education				0.009
Primary or less	19.8 (23)	80.2 (93)	100.0 (116)	
Secondary or more	32.8 (96)	67.2 (197)	100.0 (293)	
Marital status				0.49
Single	34.4 (11)	65.6 (21)	100.0 (32)	
Married/cohabiting	28.7 (108)	71.4 (269)	100.0 (377)	
Clinical/ Obstetric characteristics				
Labia Minora Elongation (LME)				0.001
None	37.6 (70)	62.4 (116)	100.0 (183)	
Any	22.0 (49)	78.0 (174)	100.0 (226)	
Abnormal vaginal exam signs[a]				0.008
No	27.7 (109)	72.3 (284)	100.0 (393)	
Yes	62.5 (10)	37.5 (6)	100.0 (16)	
Parity				0.30
Any previous births	27.4 (72)	72.6 (191)	100.0 (263)	
First pregnancy/ delivery	32.2 (47)	67.8 (99)	100.0 (146)	

[a] Due to small cell size, p-value determined with Fischer's Exact test

Based on the significance levels and theoretically important variables, we conducted bivariate and multivariable logistic regression. As there were no major changes between the bivariate and multivariable models, we focus on the results of the multivariable analysis (Table 3, column 3). Women accessing PPC were more than five times as likely (Adjusted Odds Ratio (AOR)=5.19; 95% CI 3.04 - 8.85, p<0.001) to be offered VIA when compared to women attending the ANC clinic. Women with a secondary school education or higher were only half as likely to be offered VIA testing compared to women who had no school through

primary level (AOR=0.55, 95%CI 0.31-0.97, p=0.04). Women with LME were twice as likely to be offered VIA (AOR=2.04; 95% CI 1.28-3.26, p=0.003). Women with abnormal signs on vaginal exam were less likely to be offered VIA (AOR=0.33; 95%CI=0.11-1.04, p=0.06) compared to women with a normal vaginal exam.

Table 3: Unadjusted and adjusted odds ratios of clinician's decision to offer VIA (visual inspection with acetic acid) for cervical cancer, by the woman's sociodemographic, clinical and obstetric characteristics

	Unadjusted Odds Ratio n=409	***95% CI, p-value***	***Adjusted Odds Ratios[a] n = 409***	***95% CI, p-value***
Visit Type				
Antenatal care (ref)	*1.00*		*1.00*	
Postpartum care	*5.20*	*3.10-8.73 p<0.001*	*5.19*	*3.04 - 8.85 p<0.001*
Sociodemographic Characteristics				
Age	*1.00*	*0.96-1.03 p=0.78*	*1.00*	*0.95 - 1.05 p=0.92*
Education				
Primary or less (ref)	*1.00*		*1.00*	
Secondary or more	*0.51*	*0.30-0.85 p=0.01*	*0.55*	*0.31 - 0.97 p=0.04*
Marital status				
Single (ref)	*1.00*		*1.00*	
Married/Cohabiting	*1.30*	*0.61-2.80 p=0.49*	*1.15*	*0.45 – 2.94 p=0.78*
Clinical & Obstetric Characteristics				
Labia Minora Elongation				
None (ref)	*1.00*		*1.oo*	
Any	*2.14*	*1.39-3.31 p=0.001*	*2.04*	*1.28 – 3.25 p=0.003*
Abnormal vaginal exam signs				
No (ref)	*1.00*		*1.00*	
Yes	*0.23*	*0.08-0.65*	*0.32*	*0.11 – 1.04*

		p=0.005		*p=0.06*
Parity				
Any previous births	*1.00*		*1.00*	
First pregnancy/delivery	*0.79*	*0.51-1.23 p=0.31*	*0.79*	*0.43 - 1.46 p=0.46*

[a]Adjusted for all variables appearing in the unadjusted column

Although based on a relatively small sample, the reasons for not offering VIA screening to women attending the clinic are helpful to analyze the clinician's stated motivations for offering or not offering screening. The top three reasons for not offering VIA among ANC clinic attendees were 'not done/not indicated (69.1%)', 'VIA was done recently or will do later (7.2%)' and 'client is pregnant' (4.1%). In contrast, the top three reasons clinicians did not offer VIA to PPC clients were 'client had had an episiotomy (22.7%)', 'VIA was done recently or scheduled for later (22.7%)' and no supplies/ equipment (13.6%) (see Table 4).

***Table 4**: Recorded reason (clinician) for not offering VIA (visual inspection with acetic acid) screening for cervical cancer, by visit type*

Stated reason	***ANC***	***PPC***	***Total***
Not done/ not indicated	*69.1 (67)*	*4.5 (1)*	*57.1 (68)*
No supplies/ no equipment	*2.1 (2)*	*13.6 (3)*	*4.2 (5)*
Cervicitis/ other abnormal vaginal discharge	*2.1 (2)*	*4.6 (1)*	*2.5 (3)*
Done recently/ scheduled for later	*7.2 (7)*	*22.7 (5)*	*10.1 (12)*
Episiotomy	*N/A*	*22.7 (5)*	*4.2 (5)*
Pregnant	*4.1 (4)*	*N/A*	*3.4 (4)*
Missing	*15.5 (15)*	*31.8 (7)*	*18.5 (22)*
Total	*100.0 (97)*	*100.00 (22)*	*100.0 (119)*

N/A=Not applicable

3.5 Discussion

We studied the clinical encounters of 409 women accessing antenatal or postpartum care at the Queen Elizabeth Central Hospital in Blantyre to detect patterns in provision of VIA services. Although the integration of VIA with ANC and PPC care was an explicit part of the study protocol in Malawi, in practice women accessing maternal health services at QECH were only screened about 70% of the time with a significantly higher rate of screening in PPC clinic (87.7% versus 57.8%).

Women attending ANC clinics were roughly similar to women attending PPC clinics based on their sociodemographic background, clinical and obstetric history. However, ANC attendees were far more likely to have had a history of prior miscarriage as compared to PPC. This suggests that women attending ANC clinics have a riskier obstetric history than PPC attendees, possibly because women with history of adverse pregnancy events would be more likely to seek antenatal care from a tertiary center like QECH for subsequent pregnancies, as compared to postpartum clinic attendees.

Woman's education was associated with the decision to offer VIA, and secondary school or higher educated women were significantly less likely to be offered screening as compared to women educated up to primary school. It is possible

that clinicians had an idea of the woman's level of education based on conversation and other social cues, but the clinicians did not have access to data collected on the woman's educational status at the time of the encounter. Women who presented with abnormal signs during vaginal exam were also significantly less likely to be offered VIA screening. These included ulcers, swellings and abnormal vaginal discharge, none of which are contraindications for VIA. [25] This result is somewhat counter-intuitive as the presence of abnormal vaginal exam signs, while not definitive, might be indicative of incident STIs or increased risk of contracting them. [64] Excluding such women from screening could potentially miss out on a population at increased risk of developing HPV.

We found that the odds of being offered VIA were significantly higher if the patient had undergone labia minora elongation as compared to women who had not. This result remained consistent even when adjusted for age, education, marital status, clinical exam signs and obstetric history. FGM in Malawi is different from more well-known and widely documented forms of female genital mutilation (categories 1-3) seen in Northern and Eastern parts of Africa and thus may be indicative of a very specific marker signifying tribe, regional identity or religion. [61] Women who have undergone the process of labial elongation (known as "*chiputu*" in Chichewa)[65] and are sexually active would be seen as having participated in a series of puberty initiation ceremonies surrounding the "*chinamwali*" or 'coming-out' ritual. This attaches a specific set of assumptions to these women, primarily related to their tribal status, rural/ urban status,

educational attainment and sexual behavior. [66] It is possible that clinicians considered the sample to be at greater risk for developing cervical cancer due to culturally-specific behaviors like early sexual debut and multiple sexual partners.

An analysis of the stated reasons for not offering VIA reveals an overwhelming majority as "not done/ not indicated", especially among ANC clinic attendees. This gives an indication of the challenges that a program designed to mainstream cervical cancer screening services with maternal health provision would potentially face. Clinicians also recorded 'ongoing pregnancy' and 'recently screened' as reasons for not offering VIA. It is possible that clinicians, being unsure of standard procedure for VIA screening during ANC care, preferred to err on the side of caution, particularly for pregnant women.

The results of this analysis should be considered against some of the limitations of the study. First, the MMMT study used convenience sampling of women accessing ANC or PPC care during the study period at QECH, a tertiary teaching hospital. Malawi has both an early age of first pregnancy and a high total fertility rate, thus the sample of women accessing maternal health care is generally younger than the ideal age range for VIA screening (30-50 years). The study sample is probably not exactly representative of women who should be most urgently targeted for VIA screening. Additionally, the study was not designed to specifically consider barriers or facilitators to integrating VIA screening into routine ANC or PPC. Therefore, several key variables were not collected. For

example, we do not have data on clinician characteristics or data on the availability of supplies or equipment for VIA, nor do we have a direct observation of the encounters. Ideally, qualitative follow-up with clinicians could help provide the needed context and highlight barriers they experienced. Further work is needed before making recommendations on the feasibility of scaling up VIA screening in routine ANC and/or PPC care.

Despite these limitations, there are number of important findings from this pilot study. First, while there was an explicit requirement in the protocol to offer all women VIA, clinicians seeing pregnant women offered VIA just over half the time. Furthermore, women exhibiting symptoms suggestive of STI were less likely to be offered screening, despite potentially at greater risk of developing cervical cancer. While we cannot know all of the reasons for clinicians not offering VIA consistently, the data suggest that attempts to integrate cervical cancer screening with maternal care in Malawi should be accompanied by comprehensive training of providers, including VIA eligibility requirements and risk factors for cervical cancer. Lastly, consistent adherence to clinical protocol by practicing clinicians cannot always be pre-supposed, even under closely monitored study settings. The variation in the rate at which women are offered services while accessing routine maternal care at a tertiary health center underscores the challenges of integrating opportunistic screening programs with primary care provision.

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Chapter 4: Factors Influencing Visual Inspection with Acetic Acid (VIA) Testing Uptake Among Postpartum Clinic Attendees In Blantyre, Malawi

4.1 Introduction

In 2008, the World Health Organization (WHO) defined successful integrated programs as those in which healthcare service delivery is organized so that patients can access "the care they need, when they need it, in ways that are user-friendly, achieve the desired results and provide value for money". Integration does not need to provide fully comprehensive care at the same site, but it does require healthcare providers to have skills to provide appropriate basic services and refer patients onward for necessary services not provided at the site. [1,2] Most integrated public health programs in low- and middle- income countries (LMICs) tend to address communicable diseases, most notably HIV/AIDS, tuberculosis and malaria. [2-6] Reproductive, maternal, newborn, child and adolescent health (RMNCAH) services have been popular avenues for horizontal integration with other screening and diagnostic interventions. RMNCAH services typically provide care to a specific population subgroup characterized by specific gender and age distribution who have different health status. [7,8,2,9] The intuitive rationale favoring integration assumes greater significance in LMICs with limited health budgets and inconsistent health coverage. However, operationalization of

integrated programs has proven challenging due to a variety of factors. These include a lack of national integration policies, funding inequities, increased burden on providers and the tendency of programs to encourage enhanced collaboration absent shared responsibility. [10,11] In recent years, amid growing recognition of the contribution of non-communicable diseases (NCDs) to the mortality burden in middle-income countries, [12] integration of NCD prevention and control within routine programmatic areas like RMNCAH has been widely promoted. [3]

4.1.1 Cervical cancer screening in LMICs

Cervical cancer is largely attributable to clinical sequelae following human papillomavirus (HPV) infection, especially HPV types 16 and 18. [13] It is the fourth most commonly diagnosed cancer and the fourth leading cause of cancer deaths among women worldwide. [14-16] Over 85% of cervical cancer deaths occur in LMICs located in sub-Saharan Africa and South Asia, [15,17-20] where inadequate screening and inequitable access to treatment for women has resulted in a disproportionately high mortality burden. [21-23] Meanwhile, population-based cervical cytology screening programs and timely management of suspected precancerous lesions has contributed significantly to the reduction in disease burden in high-income countries in recent decades. [24-26] Programs providing routine screening, early detection and appropriate management of premalignant lesions in eligible women are central to efforts to reduce cervical cancer incidence in LMICs. [18,22,27,28] Currently, Visual Inspection with Acetic Acid (VIA) screening

followed by emergent treatment with cryotherapy is seen as the most effective and efficient method to manage premalignant lesions in poorer countries, preventing disease progression to malignancy needing surgical intervention – which is often inaccessible and expensive. [29] [30,31] Despite these advances, screening rates in LMICs remain as low as 4.1%. [32] The scarcity of prevention services within the healthcare system and unresponsive policies coupled with multiple barriers to accessing screening results in under-screened populations that are nevertheless at high risk of developing cervical cancer. [33]

4.1.2 Factors influencing uptake of cervical cancer screening in LMICs

Before the widespread acceptability of VIA as a population-level screening strategy, cervical cancer detection in LMICs relied on liquid cytology-based testing to detect precancerous cases. The relatively resource-intensive nature of pap smears and testing made cervical cancer screening unattainable for a large segment of the population, a barrier that has reduced considerably with the introduction of VIA in LMICs. [29,34,35] Sociodemographic factors including greater educational, economic and employment attainment, higher parity, HIV+ status, equitable domestic gender power relations, and awareness of cervical cancer and screening predict an increased likelihood of women accepting cervical screening. [36,37] Personal factors like misconceptions about the implications of screening, diagnosis and management options are seen to influence screening uptake by eligible women. [38] In general, awareness of cervical cancer and of screening

methods exert greatest influence on women's decision to access testing, along with service delivery issues like cost, accessibility, quality of care and barriers to follow up. [39] Mindful of the link between sexually transmitted infections and cervical cancer, women are often reluctant to undergo an internal exam for screening, especially when a positive diagnosis offers few avenues for timely and appropriate management. [40] Additional factors like dyspareunia and a history of sexual abuse may contribute to a general discomfort with internal exams in the clinical setting. [41,42]

Malawi has the highest cervical cancer incidence in Eastern Africa, accounting for the highest proportion of cancer deaths among women in the country. [43-45] The national cervical cancer screening policy targets testing 80% of all eligible women (aged 30-45 years, comprising 6.74% of the total population) within 5 years. Coverage rates have shown an encouraging increase from 9.3% to 26.5% from 2011-2015, but far greater efforts are needed to ensure effective diagnosis and management of affected women. Malawi's screening program continues to face issues of cost, availability, and lack of political support for aggressive expansion of early screening and treatment options. [32,46-48]. Furthermore, case series studies at tertiary centers indicate an inordinate amount of delay between the onset of symptoms and screening, as well as between positive VIA test and follow up. [49] In Malawi, awareness regarding testing, greater accessibility of health facilities and shorter waiting times were linked to greater acceptance of cervical cancer screening by eligible women. [50,51]

In addition, perceived inadequacies of the health system leading to irregular care and absence of female providers were seen as barriers to access. [52] Very few trials have rigorously tested the efficacy of integrating cervical cancer screening with routine RMNCAH care. Successfully evaluated programs report screening trends that exceeded official targets, while test positivity rates remained comparable to previous districtwide numbers. [53] Rates of emergent treatment and follow-up also showed a steady increase, with constraints on the program's success imposed largely by logistical inadequacies at the testing site. [54]Our paper analyzes the factors influencing uptake of integrated VIA screening for cervical cancer among women attending postpartum clinic at a tertiary public healthcare facility in Blantyre, Malawi in 2015.

4.2 Methods

4.2.1 Study Design

This paper studies women accessing postpartum care (PPC) at a tertiary hospital in urban Malawi. Data for the study is derived from the WHO Maternal Morbidity Measurement Study (MMMS) study, a cross-sectional research study conducted in 2015-16 to assess and quantify morbidities experienced by women in the antenatal and post-partum period. The MMMS study consisted of a questionnaire, physical exam and medical record review and was administered to consenting women during their antenatal and postpartum clinic visit. The

questionnaire recorded women's sociodemographic background, relationship details, obstetric history, clinical symptoms and management, current health status, functional assessment and mental health screening [55-59] This was followed by a general obstetric exam, pelvic inspection and internal exam by the assigned clinician (either nurses or Ob/Gyn physicians). During the exam, eligible women were offered Visual Inspection with Acetic Acid (VIA) screening, and reasons for ineligibility (if any) were recorded. Integration of VIA screening with primary care is one of the stated objectives of Malawi's National Reproductive and Sexual Health and is recommended as part of the national screening guidelines in Malawi. The record review assessed the national health passport carried by the women that detailed their past medical and obstetric history. All data was collected on site by study investigators using hand-held devices, collated and transmitted to a central data repository where it was entered and cleaned. Ethical approval was provided by the WHO's Research Ethics Review Committee (ERC) in addition to COMREC, (College of Medicine Research Support Center), the ethics and institutional review board at the College of Medicine, Blantyre, Malawi.

4.2.2 Study Site

The study was conducted at the Queen Elizabeth Central Hospital (QECH), a 1120-bed public hospital in Blantyre, Malawi's second-biggest city. QECH is a tertiary care center, one of four central hospitals as well as the only teaching hospital in Malawi [60]. The hospital's catchment area includes the surrounding

districts of Southern Malawi in addition to the city of Blantyre and its suburbs. The Department of Obstetrics and Gynecology at QECH has between three to six specialist physicians, two to three registrars and three to five intern medical doctors, as well as up to four nurse-midwives for each shift [61,62].

4.2.3 Study Sample

For this analysis, we focus on women receiving PPC at six weeks postpartum, who were invited to be part of the study. Participating women were screened to determine eligibility and women who consented to the study were administered the questionnaire, physical exam and record review. A total of 277 women attending PPC clinic were approached to participate in the study. Of these women, 242 women consented to enroll in the study, of whom 229 were evaluated by the clinician during the physical exam. A total of 194 eligible women were offered VIA screening by the clinician.

4.3 Variables

The dependent variable for this study is the woman's decision to accept or refuse VIA after being offered screening by the clinician. The independent variables, grouped as sociodemographic, relationship, self-reported health and clinic visit factors, are described below.

4.3.1 Sociodemographic characteristics

Age (years), marital status (married or cohabiting versus single or divorced), educational attainment (primary or less than primary, secondary school and higher), and employment status were explored. Education was assessed using both literacy and actual years of schooling, and the variable that was significantly associated was retained in the final model. Parity was coded into three categories (1, 2-4, 5 or more)

4.3.2 Relationship characteristics

Marital status, satisfaction with current sex life and fear of partner were evaluated as relationship factors that could possibly influence the woman's acceptance of screening. Almost 90% of first births in Malawi occur within marriage, and a woman's age at first childbearing and fertility are higher when women's education is higher. [63] [64] Satisfaction with sex life is a proxy indicator for relationship quality. Similarly, women reporting fear of their current partners might be reluctant to accept screening, even though they might be at higher risk of contracting HPV infection. [65]

4.3.3 Self-reported health

Women were asked to assess their overall health status on a scale of five, from very good to very poor. With limited variation in scores, we created a binary variable (very good and good versus neutral, poor, and very poor). In addition, the General Anxiety Disorder GAD-7 and Personal Health Questionnaire PHQ-9

questionnaires were administered to assess mental health status. [57,58] The GAD-7 scores anxiety disorder based on the response to seven questions with response categories ranging from not at all (0) to nearly every day (3). The PHQ-9 is used to measure depressive symptoms. Each of the nine items are scored between 0 (not at all) to 3 (nearly every day). As the incidence of clinical depression and anxiety was too low to be meaningfully considered in the analysis, we identified women who reported at least one symptom on the PHQ9 scale for depression and on the GAD7 scale for anxiety, and used this variable for analysis. To assess mental health status, women who reported experiencing any one of the symptoms of anxiety or depression were compared to women who scored nil on the test.

4.3.4 Clinic visit characteristics

Distance travelled by women to reach the health center might have an impact on the decision to accept or refuse screening. [50] The extra time commitment involved in undergoing opportunistic VIA screening during a scheduled PPC visit might influence the woman's choice to accept or refuse the test.

4.4 Analysis plan

First, we described the sample of women who accessed postpartum care at QECH, Blantyre and among those, women who were offered VIA screening as part of routine clinical care. Next, we explored the relationship between each of our independent variables and the outcome—woman accepting VIA screening –

among women who were offered VIA using t-tests and chi-square for significance testing. Following this, we conducted bivariate and multivariate logistic regression analysis assessing the odds of accepting VIA in relation to women's characteristics. All analyses were conducted using STATA ver14.1.

4.5 Results

4.5.1 Characteristics of the study population

Table 5 describes the background characteristics of the full sample of 242 women who were surveyed while accessing postnatal care, and the subset of 194 women who were offered VIA screening (analytical sample) during the physical exam (Table 5). Of the 229 women who had a physical exam, 35 were not offered VIA, and the clinician's reasons for not offering are described in Table 6. Overall the characteristics of the women in the analytic sample were similar to the full sample enrolled in the study.

4.5.2 Sociodemographic, relationship and self-reported health

The mean age of the sample of 194 women offered VIA was 26.4 years, (range 15-50 years). Over two-thirds of the women were educated up to secondary school or higher, and 37.6% were currently employed at the time of the study (Table 5). More than a third of the women were attending postpartum clinic following their first delivery, and about 10% had had five or more pregnancies carried to term. Almost 90% of women were either married or currently cohabiting, and almost a

similar proportion (88.7%) reported currently enjoying good or very good health. Less than 10% of our sample (6.7%) reported being afraid of their partner either some or all of the time, and a vast majority (80.4%) reported being currently satisfied with their sex life. An overwhelming majority of women reported no symptoms suggestive of anxiety or depression.

4.5.3 Visit characteristics

About one-third of the women travelled less than 30 minutes to reach the clinic, and two-thirds took longer (Table 5). The women were all residents of different administrative wards in Blantyre city, but their commute times may have been influenced both by proximity to the hospital as well as availability of transportation. Almost two-thirds of the women attended the postnatal clinic to access contraceptive services.

***Table 5**: Sociodemographic, Relationship, Self-Reported Health, and Visit Characteristics of Women attending the Post-Partum Clinic (PPC)*

Category	**Total sample % (n) (N=242)**	**Analytic sample of women offered VIA % (n) (N=194)**
Sociodemographic characteristics		
Age years		
Mean	26.4	26.4
Range	15-50	15-50
Literacy, % (n)		
Illiterate/ partially literate	12.4 (30)	13.4 (64)
Literate	87.6 (212)	86.6 (130)

Education		
Primary school or less	28.9 (70)	33.0 (97)
Secondary school and higher	71.1 (172)	67.0 (33)
Employment Status, % (n)		
Unemployed	60.3 (146)	62.4(121)
Currently employed	39.7 (96)	37.6(73)
Number of pregnancies carried to term, % (n)		
1	38.8 (94)	36.1 (70)
2-4	52.1 (126)	54.6 (106)
5 or more	9.1 (22)	9.3 (18)
Relationship characteristics		
Marital status, % (n)		
Married/ cohabiting	89.3 (216)	89.2 (173)
Single/ separated /divorced	10.7 (26)	10.8 (21)
Fear of partner, % (n)		
Never	93.0 (225)	93.3 (181)
At least some of the time	7.0 (17)	6.7 (13)
Satisfied with sex life since delivery, % (n)		
No	19.4 (47)	19.6 (38)
Yes	80.6 (195)	80.4 (156)
Self-reported health		
Self-reported health, % (n)		
Good/ very good	88.4 (214)	88.7 (172)
Neutral, poor, very poor	11.6 (28)	11.3 (22)
Self-reported depressive symptoms PHQ9		
No symptoms reported	84.3 (204)	87.6 (170)
At least one symptom reported	15.7 (38)	12.4 (24)
Self-reported anxiety symptoms GAD7		
No symptoms reported	73.1 (177)	75.3 (146)
At least one symptom reported	26.9 (65)	24.7 (48)
Visit Characteristics		
Time taken to reach health center, % (n)		
<30 mins	36.4 (88)	33.5 (65)
>/= 30 mins	63.6 (154)	66.5 (129)
Cesarean section delivery, % (n)		
No	78.1 (189)	79.9 (155)
Yes	21.9 (53)	20.1 (39)
Family Planning Visit		
No	35.5 (86)	33.5 (65)
Yes	64.5 (156)	66.5 (129)

Table 6: Stated reasons for not offering VIA screening to women who attended Post-Partum clinic

Reason for not offering VIA	Frequency (%, n)
Menstruating	28.6 (10)
Done recently / scheduled for gyn clinic	14.3 (5)
Recent episiotomy	14.3 (5)
No supplies	14.3 (3)
Hysterectomy	8.6 (3)
VIA not done	0.3 (1)
Cervicitis	0.3 (1)
Missing/ reason not recorded	20.0 (7)
Total	**35**

4.5.4 Factors related to women's acceptance or refusal of VIA screening during the postpartum visit

Table 7 shows the characteristics of the women who were offered screening, by their acceptance or refusal of VIA testing status. A total of 194 women were offered VIA screening, of which 40 women (20.6%) refused screening. There were no significant differences in terms of mean age, literacy status or education. On analyzing factors that might be related to the women's decision to accept or refuse VIA, we found a significant association with relationship factors, especially marital status and reported satisfaction with sex life. Women who refused screening were less likely to be married (80% vs. 92%, p=0.04) and less likely to be satisfied with their sex lives (68% vs. 84% p=0.02). They tended to be more likely to report fear of partner (13% vs. 5% p=0.10). None of the other factors were significantly associated with the woman's acceptance or refusal of screening.

Table 7: Women Accepting or Refusing Visual Inspection with Acetic Acid (VIA) screening by Sociodemographic, Relationship, Self-Reported Health, and Visit Characteristics

Category	VIA Accepted % (n) (n=154)	VIA refused % (n) (n=40)	Total % (n) (N=194)	p-value
Sociodemographic				
Age, years				**p=0.15**
Mean	26.8	25.1	26.4	
Range	15-50	16-46	15-50	
Literacy, % (n)				**p=0.39**
Illiterate/ partially literate	12.3 (19)	17.5 (7)	13.4 (26)	
Literate	87.7 (135)	82.5 (33)	86.6 (168)	
Education, % (n)				**p=0.65**
Primary school or less	33.8 (52)	30.0 (12)	33.0 (64)	
Secondary school or more	66.2 (102)	70.0 (28)	67.0 (130)	
Relationship				
Marital status, % (n)				**p=0.04**
Married/ cohabiting	91.6 (141)	80.0 (32)	89.2 (173)	
Single/ separated/ divorced	8.4 (13)	20.0 (8)	10.8 (21)	
Fear of partner[a] , % (n)				**p=0.10**
Never	94.8 (146)	87.5 (35)	93.3 (181)	
At least some of the time	5.2 (8)	12.5 (5)	6.7 (13)	
Satisfied with sex life since delivery, % (n)				**p=0.02**
No	16.2 (25)	32.5 (13)	19.6 (38)	
Yes	83.8 (129)	67.5 (27)	80.4 (156)	
Self-reported health, % (n)				
Self-reported health				**p=0.17**
Good/ very good	90.3 (139)	82.5 (33)	88.7 (172)	
Neutral/Poor/Very Poor	9.7 (15)	17.5(7)	11.3 (22)	
Self-reported depressive symptoms PHQ9				**p=0.98**
No symptoms reported	87.7 (135)	87.5 (35)	87.6 (170)	
At least one symptom	12.3 (19)	12.5 (5)	12.4 (24)	
Self-reported anxiety symptoms GAD7				**P=0.20**
No symptoms reported	77.3 (119)	67.5 (27)	75.3 (146)	
At least one symptom	22.7 (35)	32.5 (13)	24.7 (48)	
Visit Characteristics				
Time taken to reach health center, % (n)				**p=0.33**

<30 mins	31.8 (49)	40.0 (16)	33.5 (65)	
>/= 30 mins	68.2 (105)	60.0 (24)	66.5 (129)	
Family Planning Visit, % (n)				**p=0.88**
No	33.8 (52)	32.5 (13)	33.5 (65)	
Yes	66.2 (102)	67.5 (27)	66.5 (129)	

[a] Fischer's test used due to small cell size

Table 8 displays the results of bivariate and multivariate logistic regression analysis of the factors influencing women's decision to refuse VIA screening during the postpartum visit. We selected those variables that were theoretically important and/or significantly associated with the outcome (based on Table 7).

Following trends observed in Table 7, marital status and reported satisfaction with sex life were significantly associated with the decision to refuse VIA screening. In the multivariate model, we found some shifts in statistical significance but no shift in the direction of the associations. Older women were significantly less likely to refuse VIA as (AOR=0.93, p=0.05). Women who reported satisfaction with their sex lives were also significantly less likely to refuse screening (AOR=0.34, p=0.02).

Table 8: Unadjusted and adjusted odds ratio for women's decision to refuse VIA screening during postpartum visit

	Unadjusted Odds Ratios (n=194)	**95% CI (p-value)**	**Adjusted Odds Ratios[1] (n=194)**	**95% CI (p-value)**
Sociodemographic				

Age	0.96	0.91-1.01 (p=0.15)	0.95	0.90-1.02 (p=0.14)
Education (Secondary or more v/s Primary or less)	1.14	0.56-2.53 (p=0.65)	1.19	0.55-2.72 (p=0.62)
Relationship Characteristics				
Married/Cohabiting	0.37	0.14 – 0.96 (p=0.04)	0.46	0.16-1.27 (p=0.13)
Fear of Partner reported	2.61	0.80 – 8.46 (p=0.11)	1.67	0.47-5.85 (p=0.43)
Satisfied with sex life	0.40	0.18 – 0.89 (p=0.02)	0.37	0.15-0.86 (p=0.02)
Self-Reported Health				
Overall health is good/very good (vs neutral/poor)	0.51	0.19 – 1.35 (p=0.22)	0.50	0.20-1.55 (p=0.27)

[1] Adjusted for all variables in the unadjusted column

4.6 Discussion

This paper analyzes the choices made by 194 women accessing postpartum clinic at Queen Elizabeth Central Hospital in Blantyre to accept or refuse VIA screening offered as part of routine care. Overall, more than two-thirds of the women had had two or more deliveries, and almost 90% reported currently enjoying good health, with extremely low levels of anxiety and depressive symptoms. A significant majority of women had traveled more than 30 minutes to attend clinic, and an equally large majority reported an intention to access family planning services as their motivation to attend PPC clinic.

Contrary to what might be expected from the literature, neither lower education attainment nor the time taken by the woman to reach the clinic were associated

with refusing VIA. In addition, we hypothesized that factors like overall health, depressive and anxiety symptoms, and the intention to access family planning during the postpartum visit may be associated with refusal, but these were seen to be statistically unrelated. Relationship factors were significantly related to screening uptake. Married women were significantly more likely to accept screening, although this association attenuated in the multivariable model. The relationship between women's sexual satisfaction and rates of acceptance remained significant even after adjusting for other variables. Women's sexual satisfaction was unrelated to whether they had resumed sexual activity following their most recent delivery (76.9% who had resumed sex since delivery reported sexual satisfaction compared to 80.7% among women who had not, p=0.74), which might indicate a greater degree of autonomy within relationships. Additionally, it is possible that women reporting lower levels of satisfaction might wield relatively less autonomy, leading to lower rates of uptake of opportunistic screening offered during routine postpartum care.

Screening for syphilis and HIV/AIDS are the most common diagnostic interventions offered to women during antenatal visits in LMICs. [5,66] Like HIV and syphilis, HPV transmission is linked to unprotected heterosexual contact and a positive VIA result elicited through screening during routine maternal care provides an opportunity for further evaluation and management. Co-location of VIA testing services with postpartum services, thus, follows an established scientific and logistic rationale. By virtue of its etiological link to HPV infection,

cervical cancer screening is a logical candidate for integration with postpartum care. In our study, we saw that women attending postpartum clinic were significantly more likely to accept VIA screening (79.4% v/s 20.6%) than refuse, which has positive implications for integrating screening into routine postpartum care. Rates of refusal were not associated with time taken to reach clinic, employment status, parity, or the intention to access family planning services during the PPC visit. This indicates that women's motivation to accept opportunistic VIA screening integrated with PPC might be unrelated to factors that are typically thought to influence their decision to access PPC.

This study has some limitations that must be considered. The sample described in the study is restricted to women who accessed PPC at QECH in Blantyre. Thus, it is likely that the study sample is more health-compliant than the general population of women in Malawi, and that acceptance rates might be higher than what they would be in a community-based sample. A second limitation of the study is related to the sample sizes for some variables and the relatively smaller number of women who refused screening. Effective evaluation of a program designed to integrate VIA with PPC services would ideally capture a larger, more representative sample. Thirdly, as we do not have access to key information, including women's financial status, reasons to accept or refuse screening, and other factors that may impact cervical cancer screening uptake, additional research is necessary to ensure that these findings hold for different settings. Further research would include qualitative data collection and evaluation of

process indicators (time from onset of symptoms to screening, screening to confirmation, accessibility of healthcare facilities and quality of care) within the context of affordability of services. Finally, given the importance of relationship variables in determining acceptance of screening, future studies should investigate the role of these factors, including those of partners, in strategies designed to increase screening uptake.

In spite of these limitations, we find strong evidence that it is feasible to integrate VIA screening with routine PPC visits in this setting in Malawi. Integration efforts would ideally institute staff training to make screening a routine component of PPC, as well as ensure appropriate referral and follow-up of positive cases (which was the prescribed protocol in this study as well). These results are particularly notable as Malawi has among the highest age-standardized rates of cervical cancer in the world along with low rates of screening coverage. [45] The total fertility rate continues to be high in Malawi, and nearly 75% of all postpartum women report accessing PPC either at home (health visit) or at a facility in 2015. [67] Aggressive efforts to include VIA testing as a universal diagnostic option during PPC would contribute significantly to Malawi's efforts to increase rates of early diagnosis and treatment of HPV infection More broadly, efforts to integrate VIA screening for early detection of cervical cancer into routine clinical settings is urgently needed in LMICs like Malawi that rely on overstretched health systems and inadequate funds to tackle high incidence rates of cervical cancer among their populations.

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Chapter 5: Impact of Labia Minora Elongation (LME) on obstetric management and screening interventions among women attending antenatal or postpartum services in Queen Elizabeth Central Hospital, Blantyre

5.1 Introduction and significance

5.1.1 Background

Labia minora elongation (LME) is a form of female genital modification practiced by multiple communities in Africa, including Malawi, Zimbabwe, Uganda, South Africa Mozambique and the DRC. [1-6] First described in western scientific literature as a morphological characteristic specific to the *Khoi-San* in South Africa, [7,8] LME has subsequently been established as a long-standing cultural practice in multiple communities across South Eastern Africa, either alone or part of a series of puberty initiation rites for pre-pubescent and adolescent girls. [9] Manual stretching of the labia minora begins among girls aged 7-11 years within gender-segregated groups and may be accompanied with the use of special oils and powders prescribed by traditional healers. [10,11] LME is practiced among different ethnic communities in Malawi, including the *Chewa,* the country's largest ethnic group, and communities like *Nyanja* and *Mang'anja* in the South.

[12,13] Specific rates of adherence to the ritual may vary in different geographical locations (for eg. *Nyanja* in Mozambique v/s Malawi), and might be influenced by factors like education and rural/ urban status. [14]

The WHO/ UNFPA/ UNICEF joint statement in 1997 classified "all procedures involving partial or total removal of the external female genitalia or other injury to the female genital organs for non-medical reasons" as female genital mutilation (FGM), categorized from 1-4 based on severity and type of practice. Categories 1-3 referred to clitoridectomy, labial excision and infibulation respectively, while category 4 was all unclassified practices including pricking, piercing, incising, cauterizing or pulling of the clitoris/ labia minora. [15,16] The revised statement in 2008, while acknowledging that LME had no long-term health consequences, justified it's inclusion under FGM category 4, because it was "a social convention, and hence there is social pressure on young girls to modify their genitalia, and because it creates permanent genital changes". [17] The 2006 Malawi Human Rights Commission report, while simultaneously expressing concern about girls' absence from families during initiation rituals and the potential for sexual abuse therein, nevertheless recognized the centrality of LME to marriage and fertility in Malawian society. [18] More recently, noting the vast difference in practice, implication and cultural significance between 'restrictive' FGM procedures (cats. 1-3) and 'expansive' methods like LME as well as the ubiquity of the practice among communities where it is prevalent,

researchers have questioned the utility of including LME within FGM category 4. [19-21]

5.1.2 Sociodemographic and cultural implications of LME

The practice of LME among different communities in Africa is almost always related to fertility and marriage, with some communities describing it as an essential pre-requisite for matrimony, and absence as grounds for abandonment or infidelity. [22-24] With a few reonal exceptions like in Lesotho, LME is linked to its role in enhancing sexual pleasure for men and women, as a signifier of fecundity in women, and for enlarging the introitus to promote easier childbearing. [4,10,25-27] In Malawi, labia minora elongation is seen as the first step in a series of puberty initiation rituals, often referred to as *chinamwali*, that follow a specific structure and are overseen by an older female instructor called the *anamkungwi*. Participation in the rites and fulfilment of the rituals is seen as integral to the process of transition from childhood to adulthood, and LME is central to beliefs surrounding sexual expression and fecundity. Puberty initiation rituals for girls may also include a period following the ceremonies characterized by social acceptance of sexually risky or promiscuous behavior, often with older men. Meanwhile, initiation rituals for boys often involve circumcision and a period of instruction and confinement culminating in a central event, which may be followed by a period of apparent social tolerance for sexually promiscuous behavior. [1,3,18,28] Although regular labial stretching is encouraged only up to the initiation ceremony, continuation of elongation practices in adulthood may be

accompanied by the use of specific herbal oils, unguents, powders or poultices. [2,9,11,29]

Labial elongation is currently practiced by multiple tribes in Malawi with different degrees of adherence, and it is widely recognized that the introduction of Christianity over the last two centuries has irrevocably changed traditional practices and imperatives among various groups, for eg the introduction of *chilangizo*, a Christianized alternative to traditional *chinamwali* ceremonies in the Baptist Synod of Malawi. [30,31]

The scientific literature surrounding labia minora elongation is fairly recent and almost exclusively qualitative. [32-35] Data from the Gender, Sexuality and Vaginal Practices (GSVP) study, a 2007 World Health Organization (WHO) - led multi-country cross-sectional population-based survey study conducted in Mozambique and South Africa provides the few quantitative insights about the practice. [14,36] Although there is considerable heterogeneity among specific practices, LME is often observed in matrilineal societies, and involves early initiation of girls in gender-segregated groups, often guided and supervised by older female relatives. [28,32] Themes of enhanced confidence and social capital that accrue to girls who undertake LME and its associated rituals are almost ubiquitous in the literature. Furthermore, ritual instruction by the *anamkungwi* is also seen as an opportunity for education about social customs and cultural expectations. [4,28,32,35,37] Results from the 2007 WHO study in Central Mozambique suggests

that LME is associated with being younger than 25 years; being a resident in rural areas; not having completed primary level education; and belonging to the *Nyungwe* ethno-linguistic group. Women who had LME were more likely to currently be in a relationship, have more than one partner, and have had history of recent sexual activity. [14]

In cases where LME is either universal or very rare among the local population, women who do not conform to the established norm may potentially face isolation and ostracism. [38] Interviews with immigrant women who had LME suggest that healthcare providers are often uninformed about the practice and mistakenly diagnose labial hypertrophy as a physiological artefact during clinical consultations. Women report a sense of enhanced scrutiny and judgement, especially when consulting clinicians unfamiliar with the practice or its cultural ramifications. This experience has been reported by immigrants in both European and African country contexts. [34,38] Within Malawi, discussions of LME have often been couched in the language of human rights violation of participating girls, and on the possible adverse consequences that may occur in situations where unsupervised sexual contact is encouraged among adolescents, especially after the initiation ceremony is complete, at 15 years of age. [18]

5.1.3 Health impact of LME

The health risks associated with LME that have been explored in the literature are mostly confined to local trauma and irritation due to the act of stretching or

application of herbal remedies, and the possibility of increased transmission of sexually transmitted infections (STIs) like HIV, especially in the context of superficial abrasions or trauma to the skin.[39] Another area of research focuses on the implied consequences of puberty initiation rituals, of which LME might be a part. Specifically, the possibility of increased levels of promiscuity and risky sexual practices among adolescents who had undergone initiation rituals is hypothesized to be linked with increased STI transmission. [6,40] In spite of these different hypotheses, the review of literature provides little evidence of increased STI incidence among women practicing LME. [40-42] Psychological consequences arising from shame or ostracism are among the more serious health consequences of LME reported in the literature, although these seem to primarily be reported within the immigrant context. [34,38]

Our study represents the first attempt to describe sociodemographic background and healthcare access of women with LME in a large facility-based sample. Based on the research surrounding LME in Malawi, we anticipated that women who had LME who were attending maternal healthcare in Malawi might be largely similar to urban women in terms of health outcomes and care-seeking behavior, with possibility of difference in sociodemographic background, specifically education levels, marital status and fear of IPV. Noting the cultural explanations for LME as a means to enhancement of pleasure for both partners during sex, we expected some association with women's reported sexual satisfaction. Again, considering the proposed role of LME and other initiation rituals in strengthening marital

partnerships, we expected an association with women's reported fear of violence from their partners. Also considering the role of LME as a marker for female participation in larger social networks built on shared experiences and instruction, we hypothesized that it may influence rates of depression and anxiety. We also hypothesized that LME's association with puberty initiation rituals and its prevalence among rural women with low levels of educational attainment may lead healthcare providers to assume different levels of health risk for these women. Specifically, clinicians might view women with LME as more promiscuous, or less informed about good clinical practices. They may be more likely to offer STI-related tests to women who have LME, or might be less likely to offer diagnostic and management interventions during antenatal and intrapartum care.

5.2 Methods

This study analyzes data from a pilot study on maternal morbidity in Malawi. Data were collected from women seeking antenatal and postpartum care in in Jamaica, Kenya and Malawi in 2015-16, to assess and quantify morbidities. The study consisted of a questionnaire administered by trained investigators, a physical exam conducted by a clinician and a medical record review. The questionnaire recorded women's reports of clinical symptomatology as well as maternal history and current health status, including functional assessment and mental health screening. [43-45] The questions were designed to assess female respondents' health status and healthcare utilization during the current or most

recent pregnancy. The questionnaire was administered by trained investigators who were newly graduated physicians from the College of Medicine, Blantyre. The physical exam, conducted either by a physician or nurse, consisted of a general obstetric exam followed by a pelvic inspection and internal exam. During the physical exam, attending clinicians recorded FGM status and specified the category (1-4). Additional details of the study protocol are described elsewhere. [43] Ethics approval was provided by WHO's Research Ethics Review Committee (ERC) as well as the College of Medicine Research Support Center (COMREC), the ethics review and support board at the College of Medicine, Blantyre.

5.2.1 Study site

In Malawi, the Queen Elizabeth Central Hospital, Blantyre (QECH) was the study site. QECH is a 1120-bed public hospital serving the healthcare needs of Blantyre, Malawi's second-biggest city, and of Southern Malawi. It is a tertiary care center, one of four 'Central Hospitals' as well as the only teaching hospital in Malawi [46]. Due to the often-unreliable public healthcare services in rural areas of Southern Malawi, QECH caters to the primary care needs of the surrounding areas in addition to provision of tertiary care in all specialties. The Department of Obstetrics and Gynecology at the hospital has had between three and six specialist physicians, two to three registrars and three to five intern medical doctors at different times over the past decade. There are between two and four nurse-midwives for each shift. [47,48]

5.2.2 Study protocol

Women attending either ANC clinic and more than 28 weeks pregnant, or attending PPC clinic at six weeks postpartum were invited to be part of the study. On agreeing to participate, women were screened to determine eligibility and were asked about their demographic background by the investigators. Eligible women who further consented to participating in the survey were administered the questionnaire, physical exam and record review. All data were collected on site by study investigators using hand-held devices, collated and transmitted to a central data repository where it was entered and cleaned. The physical exam was conducted following the interview by a clinician (physician or nurse) in a separate location at QECH, and the medical records were accessed from a review of National Health Passports in the possession of women participating in the study. Examining clinicians were not privy to the results of the questionnaire or the women's responses. [49]

5.2.3 Study sample

A total of 529 women (ANC=252, PPC=277) were approached to participate in the study and of these, 481 (ANC=239, PPC=242) consented to enroll in the study. 230 women from the ANC sample and 189 from the PPC sample (total N= 419) were examined by the clinician during the pelvic exam and the LME status recorded.

5.2.4 Study variables

The outcome of interest is the LME status of the woman, as reported by the clinician during the physical exam. We attempted to understand how LME status was related to woman's sociodemographic characteristics, their health and wellbeing, and to access to healthcare services. To assess women's sociodemographic background and access to healthcare service, we considered the woman's age, education, marital status, parity (first pregnancy or delivery v/s all others) and time taken to reach the clinic. Education was assessed using both literacy and actual years of schooling, and the variable that was significantly associated was retained in the final model. The time taken to reach clinic is influenced by both distance and mode of transport, and may suggest levels of wealth - longer journey times may indicate the woman walked to QECH for her appointment or had access only to slower modes of public transportation. It may also be an indication of the distance from the Hospital, especially in the case of rural patients.

We then analyzed the woman's health and wellness, including reported fear of intimate partner violence (IPV), sexual satisfaction since onset of most recent pregnancy, self-reported health, and symptoms of depression or anxiety as recorded in the Generalized Anxiety Disorder (GAD7) or Personality Health Questionnaire (PHQ9) screening protocol. [50,51] As the incidence of clinical depression and anxiety was too low to be meaningfully considered in the analysis, we identified women who reported at least one symptom on the PHQ9 scale for

depression and on the GAD7 scale for anxiety, and used this variable for analysis. In an attempt to determine signs of high risk pregnancy and postpartum morbidity recognizable to the clinician, we also explored the rates of anemia and pre-eclampsia as determined by clinical diagnosis, and abnormal signs on vaginal or vulvar exam during the physical exam. To assess whether health providers treated women with LME differently, we explored services women received after it was evident that the provider knew the woman's LME status. Specifically, we considered the utilization of ultrasound services by currently pregnant women, cesarean section or use of instrumentation during most recent delivery and the offer of Visual Inspection with Acetic Acid (VIA) test for cervical cancer screening during the physical exam. In all three cases, the interventions would be offered to the patient by a clinician who was aware of their LME status. We expected that clinicians might be more likely to offer VIA screening to women with LME, probably influenced by notions about increased sexual exposure risk. Meanwhile, we expected rates of cesarean section and other interventions during delivery to be unchanged, in contrast to FGM categories 1-3, which demonstrate a clear association with higher rates of cesarean deliveries across Africa. [52]

5.2.5 Analysis plan

We used t-tests and chi-square for significance testing to explore the bivariate associations between the sociodemographic characteristics of women who had (LME+) and had not undertaken LME (LME-). Next, using the same method, we analyzed the distribution of health and wellness characteristics, by LME status.

Next considering only the theoretically important or statistically significant variables from the bivariate analysis, we created a series of multivariable logistic regression models that considered health outcomes and screening and management decisions associated with the woman's LME status.

5.3 Results

Table 9 describes select sociodemographic, health and wellness and health access characteristics of women who have LME versus those who have not. Of the 481 women attending ANC/ PPC clinic at QECH, 419 had a complete physical exam in which their LME status was recorded and routine screening tests were offered.

54% of the sample had LME based on clinician examination. There were no significant differences between the women with and without LME in terms of age, marital status, parity or miscarriage rates. Women who had LME were significantly more likely to be illiterate or partially literate (12.4% v/s 6.2%, p=0.03), and were more likely to have taken more than half an hour to reach the clinic (74.3% v/s 62.2% p=0.007). In terms of their self-assessments, these women were neither more nor less likely to report satisfaction with their sex lives, report fear of IPV or report better or worse overall health (see Table 9). There was no difference in rates of anemia or pre-eclampsia diagnosed by the clinician, nor was there a difference in the rate of abnormal vaginal and vulvar signs on examination. Women who had undertaken LME were significantly less likely to report symptoms suggestive of anxiety (GAD7) (38.9% vs. 48.2%, p=0.06) or

depression (PHQ9) (23% vs. 33.7%, p=0.02). Women with LME attending postpartum clinic were also significantly less likely to report any depressive symptoms (23% vs. 33.7%, p=0.02) as compared to women without LME.

When considering healthcare service provision, women with LME were significantly more likely to be offered VIA testing (77% vs. 66.1%, p=0.001). ANC clinic attendees who had LME were significantly less likely to have had an ultrasound during the current pregnancy (24.4% vs. 42.3%, p=0.04), and PPC clinic attendees with LME were far less likely to have had a cesarean section or any other form of instrumentation used during the most recent delivery (9.4% vs. 22.0%, p=0.01). Of the 47 women who had had some form of intervention during the most recent delivery, 43 had had cesarean sections and the others had a forceps extraction during labor.

Table 9: Sociodemographic and health characteristics of women accessing maternal healthcare services (ANC/ PPC) at QECH, Blantyre by LME (Labia Minora Elongation) status

Category	No LME recorded n=193	LME recorded n=226	Total n=419	p-value
Sociodemographic Characteristics				
Age (years) Mean Range	 27.21 15-40	 27.06 15-50	 27.13 15-50	0.80
Literacy (%)				0.03
Partially literate/ illiterate	6.2 (12)	12.4 (28)	9.6 (40)	
Literate	93.8 (181)	87.6 (198)	90.5 (379)	
Education				0.24
Primary school or lower	25.4 (49)	30.5 (69)	28.2 (118)	

Secondary school and higher	74.6 (144)	69.5 (157)	71.8 (301)	
Marital status				0.51
Single/ divorced/ separated	8.8 (17)	7.1 (16)	7.9 (33)	
Married/cohabiting	91.2(176)	92.9 (210)	92.1 (386)	
Expresses fear of intimate partner violence[a]				0.17
No	95.3 (184)	91.6 (207)	93.3 (391)	
Yes	4.7 (9)	8.4 (19)	6.7 (28)	
Time to reach clinic				0.007
<30 mins	37.8 (73)	25.7 (58)	31.3 (131)	
>/= 30 mins	62.2 (120)	74.3 (168)	68.7 (288)	
Parity[a]				0.18
First pregnancy/ delivery	38.9 (75)	33.6 (76)	36.0 (151)	
2 – 4 prev pregnancies	56.5 (109)	57.5 (130)	57.0 (151)	
5+ prev pregnancies	4.7 (9)	8.9 (20)	6.9 (29)	
Woman's health and wellness				
Self-reported health good/ very good				0.93
No	20.7 (40)	20.4 (46)	20.5 (86)	
Yes	79.3 (153)	79.7 (180)	79.5 (333)	
Any anxiety symptoms (GAD-7)				0.06
No	51.8 (100)	61.1 (138)	56.8 (238)	
Yes	48.2 (93)	38.9 (88)	43.2 (181)	
Any depressive symptoms (PHQ-9)				0.02
No	66.3 (128)	77.0 (174)	72.1 (302)	
Yes	33.7 (65)	23.0 (52)	27.9 (117)	
Anemia (pallor + hemocue)				0.85
No	90.2 (174)	90.7 (205)	90.5 (379)	
Yes	9.8 (19)	9.3 (21)	9.6 (40)	
Abnormal signs on vaginal exam[a] (N=409)				0.20
No	94.6 (176)	97.3 (217)	96.1 (393)	
Yes	5.4 (10)	2.7 (6)	3.9 (16)	
Satisfied with sex life				0.78
No	29.5 (57)	28.3 (64)	28.9 (121)	
Yes	70.5 (136)	71.7 (162)	71.1 (298)	
Signs of pre-ecclampsia				0.30

noted (Only ANC)[a] (n=230)				
No	91.0 (101)	95.0 (113)	93.0 (214)	
Yes	9.0 (10)	5.0 (6)	7.0 (16)	
Diagnostic and screening tests offered during ANC/ PPC care				
VIA screening offered				0.001
No	39.9 (77)	23.0 (52)	30.8 (129)	
Yes	60.1 (116)	77.0 (174)	69.2 (290)	
Ultrasound during current pregnancy (Only ANC)	**No LME recorded n=111**	**LME recorded n=119**	**Total n=230**	**0.004**
No	57.7 (64)	75.6 (90)	67.0 (154)	
Yes	42.3 (47)	24.4 (29)	33.0 (76)	
Cesarean section/ instrumentation during most recent delivery (Only PPC)	**No LME recorded n=82**	**LME recorded n=107**	**Total n=189**	**0.01**
No	65.9 (54)	82.2 (88)	75.1 (142)	
Yes	34.2 (28)	17.8 (19)	24.9 (47)	

[a] : Fischer's exact test used due to small cell size

Table 10 describes results of the adjusted multivariable logistic regression analyses of associations between LME status and women's self-reported health as well as between LME status and treatment by the healthcare provider.

Overall the results of multivariable logistic regression mirror the results from Table 9. There was minimal attenuation after adjustment for important potential confounders. After adjustment, women with LME were statistically significantly less like to report symptoms of depression (AOR=0.62, 95% CI: 0.40-0.95) or anxiety, although this association was only significant at the $p<0.10$ level (AOR=0.71, 95% CI:0.48-1.05).

Women who had LME were significantly more likely to be offered VIA screening by clinicians during the physical exam (AOR=2.15, 95% CI:1.40-3.29, p=0.001). Among ANC clinic attendees, women with LME were significantly less likely to be given an ultrasound (AOR=0.41, 95% CI:0.23-0.72, p=0.002) while PPC clinic attendees were less likely to have had instrumentation (including cesarean section) during the most recent delivery (AOR=0.49, 95% CI:0.24-1.00, p=0.06), even after controlling for parity, age, literacy, marital status and distance traveled to the clinic.

Table 10: Health-related outcomes and provider treatment according to women's LME status, adjusting for women's sociodemographic characteristics among women attending ANC/ PPC care in QECH, Malawi (n=419)

	Unadjusted Odds Ratio (95% confidence interval)	**Adjusted Odds Ratioa (95% Confidence interval)[a]**
Any depressive symptoms	0.59 (0.38-0.90) p=0.02	0.65 (0.42-1.01) p=0.06
Any anxiety symptoms	0.69 (0.46-1.01) p=0.06	0.71 (0.50-1.11) p=0.15
VIA offered	2.22 (1.45-3.39) p=0.0001	2.06 (1.34-3.18) p=0.001
Ultrasound during current pregnancy[b]	0.44 (0.25-0.77) p=0.004	0.41 (0.23-0.74) p=0.002
Cesarean section/ instrumentation during delivery[c]	0.42 (0.21-0.82) p=0.01	0.50 (0.24-1.02) p=0.06

[a:] Adjusted for age, literacy, marital status, parity, time traveled to the clinic
b Only reported for women seeking antenatal care (n=230)
[c] Only reported for women seeking postnatal care (n=189)

5.4 Discussion

This paper analyzes sociodemographic, wellness, and healthcare intervention data from 419 women accessing ANC/PPC care at the Queen Elizabeth Central Hospital, Blantyre in 2015, to determine the associations between cultural practices like LME and women's wellness and reproductive healthcare access. LME is a clinical finding that is significant in and of itself, as well as through its association with a range of ethno-specific puberty initiation rituals that imply specific notions about personal behaviors or practices. Rural/urban differences and endogamous community practices might result in incomplete understanding of these customs across communities, extending sometimes to clinician attitudes.

Although the cultural significance of LME is deeply entwined with its professed role in enhancing sexual pleasure for both partners, LME positive women in our sample did not report enhanced sexual satisfaction or reduced fear of IPV compared to their peers who did not undertake the practice. In general, we found that women who had LME had similar backgrounds to women who did not have LME, and enjoyed somewhat similar health status. However, they were more likely to be illiterate and rural residents, which may indicate a diminished capacity to negotiate with caregivers regarding healthcare interventions. They did not seem to exhibit an increased risk of adverse obstetric or physical health outcomes, however they were significantly less likely to report symptoms of anxiety or depression. Noting the voluntary nature of maternal healthcare access, we can hypothesize that ANC/PPC clinic attendees are probably less likely to

suffer from anxiety and depression. This hypothesis is reflected in the low prevalence of mental health symptoms and generally high rates of good health reported by women in the study sample.

The impact of LME was seen most strongly on clinical decision-making during maternal health provision, specifically the rates at which interventions like VIA screening for cervical cancer or elective procedures like ultrasound during antenatal care are offered to women Our analysis suggests that women who were LME positive were significantly more likely to be offered VIA screening during their ANC/ PPC visit. It is possible that clinicians might see LME as a marker for risky sexual behavior, and noting the well-established connection between multiple sexual partners and the risk of developing cervical cancer, [53] might choose to selectively offer VIA screening to these women. Conversely, women who were LME positive were significantly less likely to receive other interventions like ultrasound or cesarean sections during the antenatal and intrapartum periods. This is contrary to what has been observed in studies from multiple African countries of women exhibiting FGM categories 1-3 for whom cesarean rates seem to be significantly higher. [54]

The comparable sociodemographic and health profiles of women with LME and those without lead to inevitable questions about the wisdom of classifying LME within FGM category 4, and indeed, of the utility of a category that represents a broad and unconnected range of genital modification practices. Preliminary

evidence from this paper seems to point to the potential impact of LME on healthcare provider behavior, leading to differential rates of service provision. While it is difficult to speculate on the full range of preventive, diagnostic and curative interventions offered to a woman accessing ANC/ PPC care from this limited sample, the interventions we have chosen for analysis represent ones that were ostensibly ordered by a clinician who was aware of the patient's LME status. The systematic differences between women who had LME and those who had not seems to indicate that healthcare providers may be treating these women differently, especially when assessing their eligibility for diagnostic, screening or management interventions. We do not know whether this translated into adverse health outcomes for women who had LME, but it is undeniable that differential rates of access to healthcare services to different populations impedes the goal of universal healthcare service provision.

This study has some important limitations that must be kept in mind when considering the results of the analysis. Firstly, the absence of variables describing interventions that may have been offered to women by clinicians unaware of their LME status makes it difficult for us to authoritatively comment on the relationship between LME on inspection and clinical decision-making. Secondly, since the study did not measure care providers' attitudes regarding their clinical practices, it is difficult to attribute the difference in rates of interventions offered to specific beliefs that may be held by the clinicians that are influencing their behavior. Thirdly, our analysis of sociodemographic background was limited by

the variables that were collected in the MMMT study, allowing for possible confounding of results. Finally, the data are cross-sectional and reflect a selected sample of women who chose to come in for ANC and PPC. Therefore, the data cannot be generalized to a non-facility sample and likely underrepresents women with adverse birth outcomes for the PPC sample. Again, since we do not know the full range of facilities and services accessed by the women for antenatal or postpartum care, it is difficult to draw conclusions about differential provision of healthcare. In spite of these limitations, this paper represents the first attempt to analyze the healthcare experiences of women who have LME from within a facility-based sample. Further studies would analyze the reasons for the observed gap in offering these women routine services during healthcare, while also assessing the impact on their long-term health and wellness.

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Chapter 6: Discussion and Conclusions

6.1 Discussion

Integration of reproductive, maternal, newborn, child and adolescent health (RMNCAH) services follows a simple rationale – that although intended beneficiaries may access care at different 'entry points', their visit to healthcare facilities offers an opportunity to provide them the full range of appropriate screening, evaluation and management. [1] Employing a life cycle approach, healthcare providers can offer care that addresses both the patient's current needs as well as anticipates their risk of future morbidity. [2] In low- and middle-income countries (LMICs), visual inspection with acetic acid (VIA) testing for women accessing antenatal (ANC) or postpartum care (PPC) fulfils both these criteria by offering screening to women who are at risk of having contracted HPV but if infected, are likely to present with precancerous lesions that may be managed by passive management or early surgical intervention. VIA screening offers an accessible screening option that can be scaled up in resource-constrained settings. Furthermore, LMICs tend to have high fertility and early childbearing along with a large proportion of screening-naïve women, making the logic of integrating VIA screening with maternal health services all the more persuasive.

Our study represents an attempt to understand the factors that might influence the provision and acceptability of VIA screening to women attending ANC and

PPC clinics at a tertiary center in Malawi. By analyzing clinician and patient behavior as two distinct decision points, we attempt to understand potential barriers to VIA screening for women accessing maternal healthcare services. Since the data represent the experiences of women in a research study that required VIA screening of eligible women, our sample likely approximates the behavior of clinicians who might be part of an integrated program that mandated universal cervical cancer screening of ANC and PPC clinic attendees.

Our results indicate that 4.4% of eligible women for VIA in ANC and 63.6% in PPC ultimately received VIA services. While this would imply that integration of VIA screening with PPC clinics at a tertiary center like Malawi's Queen Elizabeth Central Hospital (QECH) is more efficient, ANC integration remains important considering the asymmetry in coverage of care. According to the 2015-16 Demographic and Health Survey (DHS), only 42% of women who had given birth in the previous two years accessed PPC in Malawi, compared to 95% women who had at least one ANC visit with a skilled provider. In both cases, however, our assessment of VIA integration opportunities are likely over-estimated as a vast majority (72%) of pregnant women in Malawi access antenatal care from nurses or midwives who might not be currently capable of offering screening services. [3]

One of the primary advantages of healthcare integration is to reach out to a population with limited access to healthcare services. While the tertiary hospital setting of our study provides no opportunity to investigate VIA screening

provision among the most vulnerable group of women who do not seek services, our results suggest no evidence of social disparities in service provision of VIA once women enter the healthcare system, as women with less than secondary education were more likely to be offered services than higher educated women. We found differential provider practices for women with LME, a marker of ethnicity and cultural practice in Malawi. Noting the cultural behaviors associated with LME and puberty initiation rituals, the rural-urban divide, and the prevalence of endogamy within traditional communities likely to practice the ritual, [4-6] it is possible that clinicians might ascribe riskier sexual behaviors to these women, and offer them VIA screening at higher rates. Beyond these social determinants in VIA screening, our results suggest other forms of clinical barriers to VIA services, including pregnancy and abnormal vaginal discharge. Although VIA is not contraindicated in these circumstances, the exclusion of women with symptoms suggestive of sexually transmitted infections (STIs) from screening represents an added concern regarding those most at risk of harmful sequelae from HPV infection.

To explore the impact of distinct socio-cultural practices on women's access to obstetric screening, diagnostic and management options, we analyzed the effect of LME on VIA screening during the visit, ultrasound during current pregnancy and cesarean sections offered at most recent delivery. Women with LME were more likely to be illiterate and live in rural areas compared to women without LME. The health status of both groups was largely comparable, although women

with LME were less likely to report symptoms of depression compared to women without LME. Providers were significantly more likely to offer VIA screening to women with LME. Conversely, women with LME were significantly less likely to have been offered ultrasound services during their current pregnancy and less likely to have had a cesarean section during their most recent delivery. This may be a reflection of the differential access to tertiary services between rural and urban areas in Malawi, or may indicate a systematic exclusion of women with LME from diagnostic and management interventions during pregnancy and postpartum period. Although the reasons for this difference are not clear, it is possible that clinician attitudes about LME might impact appropriate offering of care.

While service provision of VIA screening seems to favor women from less advantageous social backgrounds, women's social status and personal attitudes still seem to be linked to the uptake of preventive care, as unmarried women and women reporting low sexual satisfaction were less likely to accept screening when VIA was integrated with PPC clinics. Women in less stable relationships may exercise lower autonomy over their healthcare decisions during routine primary care, prompting lower rates of screening uptake.

6.2 Public Health Significance

This study represents an exploration of the factors influencing uptake of cervical cancer screening when integrated with ANC and PPC services. While

opportunistic VIA screening during maternal health services makes intuitive sense, the success of such a program depends on shared understanding by care providers and patients regarding the importance of universal screening coverage. Recognizing that care providers might exclude some kinds of women from screening and that women may be reluctant to undergo screening when offered, health information efforts should focus on emphasizing the goal of universal coverage and the benefits of early diagnosis and treatment. The experiences of integrating HIV/AIDS screening with ANC care could provide direction for the expansion of VIA screening access in LMICs. Offering VIA as an 'opt out' intervention during ANC and PPC, similar to current protocols for HIV and syphilis testing would likely impact screening coverage and improve early detection rates. At the same time, policymakers must be aware of the possibility of inadvertent exclusion of other women at risk of developing cervical cancer in an integrated maternal health – VIA screening program. The rollout of such an initiative must be accompanied by other integration strategies such as provision of VIA in HIV/AIDS counselling and testing centers, STI and family planning clinics.

6.3 Conclusion

Integration of VIA screening with maternal healthcare provision must always be evaluated in the context of traditional community-based programs for cervical cancer screening. An evaluation of integrated program efficacy would ideally assess cost effectiveness compared to existing passive surveillance efforts. Our

study, while providing one of the first looks at programs that integrate VIA screening with ANC and PPC clinics, also suggests some clear direction for future research in this area. Analysis of provider-patient interactions during VIA provision must extend to more generalizable primary care settings with variable clinician competence and differential access to follow up. Focused qualitative studies to understand women's refusal of VIA screening in ANC clinics would help to identify barriers to care provision. Further investigation of healthcare providers' attitudes regarding disease risk and VIA eligibility would inform training and clinical protocols. Understanding the barriers to provision and acceptance of VIA screening within integrated healthcare settings would allow us to create targeted programs that improve screening access and early detection and management of cervical cancer in LMICs like Malawi.

6.4 References

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Curriculum Vitae

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PROFILE

Aravind Menon, born 2nd October 1979 in Kerala, India, is a medical doctor with strong clinical background and has a Master of Public Health with 10+ years public health experience in South Africa, USA and India. He is currently a PhD candidate at Johns Hopkins Bloomberg School of Public Health. His research experience includes primary data collection, development and oversight of randomized clinical trials, and analysis and presentation of qualitative and quantitative data. He has program management experience including curriculum development, training-of-trainers, and management of large-scale public health interventions. His interests include health systems research and evaluation, reproductive and child health, and global health with a focus on resource-poor settings. He has received multiple NIH training grants and helped develop a project which received grant funding from the National Science Foundation. He has strong research, writing and interpersonal skills and is fluent in several North and South Indian languages. He is an Indian citizen with US permanent residency.

ACADEMIC QUALIFICATIONS

Philosophiae Doctor (PhD – anticipated graduation May 2019) 2012 - 2019
Johns Hopkins Bloomberg School of Public Health Baltimore, USA

Master of Public Health (MPH) 2006
Sree Chitra Tirunal Institute of Medical Science and Technology Trivandrum, India

Bachelor of Medicine, Bachelor of Surgery (MBBS) 2003
Armed Forces Medical College Pune, India

AWARDS AND FELLOWSHIPS

Gordon Croft Fellowship in Environment, Energy, Sustainability and Health 2013-2014

- Member of qualitative research team looking at waste management issues at personal, household and societal level, and its impact on critical ecosystems in the Baltimore watershed area. Fellowship awarded by the Environment, Energy, Sustainability and Health Institute, Johns Hopkins University.

National Institutes of Health T32 Training Grant 2012-2014

- PhD candidate supported by the Inderdisciplinary Training grant on Preventing and Addressing Violence in Families. Participated in 2-year seminar addressing topics including interpersonal violence, gun safety and injury prevention. Special focus in climate change, migration and interpersonal violence.

National Institutes of Health Fogarty Fellowship 2009-2010

- Spent one year at the rural headquarters of the Centres for AIDS Programmes of Research in South Africa (CAPRISA), worked on RHIVA (Reducing HIV in Adolescents), a cluster-randomized controlled trial to assess the impact of a school-based intervention of incentivized behavior change on HIV incidence in grade 9 and 10 children in 14 rural South African schools.

RESEARCH AND CLINICAL EXPERIENCE

Lexington Regional Health Center Lexington, USA

Director, Population Health Oct 2015-present

- Member, transition team for implementing CMS-recognized Chronic Care Management Program. Updated clinical workup and management protocols, part of team creating service integration and long-term management guidelines.
- Member of hospital team for Quality Payment Program (QPP) operations – strategy, compilation, reporting and feedback
- Creation of referral and follow-up protocols for clinic-based Medically Managed Programs - combining chronic care with outpatient physiotherapy services
- Oversaw data collection for Behavior Risk Factor Surveillance System (BRFSS) survey among recent refugees in Dawson County
- Co-ordinated cervical cancer education project for Somali refugee women with College of Public Health, UNMC

World Health Organization Geneva, Switzerland

Consultant, Maternal Morbidity Measurement Tool Pilot Study Jun 2015—Jul 2016

- Trained clinical investigators in Blantyre, Malawi and St Ann's Bay, Jamaica
- Collaborated in creation of clinical codebook and reference guide for statistical analysis of morbidity conditions
- Oversaw analysis on Visual Inspection with Acetic Acid (VIA) provision and uptake among antenatal and postnatal women in Blantyre, Malawi

Johns Hopkins Bloomberg School of Public Health Baltimore, USA

PhD Candidate (Dept of Population, Reproductive and Family Health) Sept 2012—present

- Passed comprehensive exam January 2014, schoolwide preliminary oral defense Jun 2017
- Coursework included statistics, epidemiology, research methods, demographic methods, large scale program effectiveness evaluation
- Collaborated with inter-disciplinary team from Johns Hopkins School of Public Health, Whiting School of Engineering, and Carey Business School on project focused on promoting appropriate waste disposal practices in low-income neighborhoods. Assisted in development of grant which was funded by National Science Foundation (Interdisciplinary Behavioral and Social Science Research).

Energize the Chain Philadelphia, USA

Executive Director (Programs) April 2011-Oct 2014

- Led project conceptualization, background research, protocol development and grant writing for innovative vaccine cold chain strengthening initiative.
- Fostered partnerships with public and private partners in Kenya, India, Nigeria, Zimbabwe and USA.
- Presented components of EtC model at United Nations (UNICEF June 2013 and ECOSOC April 2014).
- Conducted feasibility study in 5 sites in Karnataka, India supported by Rockefeller Foundation.
- Conducted preliminary health impact study in 8 primary and secondary health centers across Zimbabwe in collaboration with EcoNet Zimbabwe and National Healthcare Trust.

Centre for AIDS Programmes of Research in South Africa KZN, South Africa

NIH Fogarty Post-Doctoral Fellow June 2009–June 2010

- Collaborated in baseline research and protocol development for CAPRISA 007 "Reducing HIV in Adolescents" RCT evaluating conditional cash transfers for HIV prevention in school-going adolescents
- Developed adolescent sexual and reproductive health curriculum for public schools in 14 districts
- Conducted chart review of adolescent HIV patients to facilitate development of a treatment cohort within a rural HIV/AIDS clinic.

Institute of Health Management, Pachod Pune, India

"Safe Adolescent Transition and Health Initiative" Program Director Mar 2007—Mar 2009

- Director of a community-based research project providing health surveillance, referral, treatment and behavior change communication for married adolescent girls in 400+ villages in Maharashtra – collaborated with State health department and National Rural Health Mission.
- Oversaw baseline study, supervised 30+ field staff; oversaw project implementation, prepared monitoring and evaluation tools.
- Developed sexual and reproductive health training manual for village-level community health workers. Prepared material and coordinated training for nurses across 30 health centers.

Institute of Health Management Research Jaipur, India

Public Health Intern Nov 2006—Dec 2006

- Helped develop Disaster Management Training module for paramedical staff

General Practice Physician Multiple sites, India

Sep 2003—Dec 2004

- Patient care with focus on obstetrics and gynecology, (management of labor, antenatal and postnatal care, routine gynecology), as well as primary care, (chronic disease management, acute conditions, infectious disease, vaccine clinics, pediatric well and sick visits).
- Worked in various settings, including Primary Health Centers, District Hospitals, rural and semi-rural clinics in public and private sectors in India

COMMITTEES AND MEMBERSHIPS

Minority Health Council, Nebraska Lincoln, Nebraska

Member Jan 2016 — Jan 2018

Chairperson Jan 2018 - present

- Council meets once every quarter to offer guidance to the Office of Health Disparities and Health Equity, Division of Public Health, and co-ordinates the annual minority health conference
- Members appointed by Nebraska Department of Health and Human Services

CERTIFICATIONS AND SKILLS

- Certifications: Collaborative Institutional Training Initiative (CITI) Training for Human Subjects Research (2017) / Good Clinical Practices (2009) / Sexuality Rights Institute (2007)
- Languages: English, Malayalam, Hindi, Urdu (fluent) / Tamil, Marathi (working)
- Programs: Microsoft Office, EndNote, STATA, EpiData

PUBLICATIONS AND PRESENTATIONS

- AR Menon. “Public-Private Partnerships in Health: View from the Developing World” presented at *An Integrated Future: Multisectoral partnerships and perspectives in global health*, UN symposium New York, 8 April 2014.
- H Rubin, AR Menon, A Conant, T Fu, A Raghavan. “Energize the Chain Impact Model” presented at UNICEF Forum “Energy and Connectivity for Health” New York, 12 June 2013.
- A Dyalchand, M Khale, AR Menon, P Gangodkar. “Sexual and Reproductive Health Supplementary Training Module for Accredited Social Health Activist (ASHA) in National Rural Health Mission” Institute of Health Management, Pachod, Pune, India (in print, 2010)
- AR Menon. "Role of NGOs in the Rural Health Sector" presented at Symbiosis Institute of Health Sciences, Pune, India. Jan 2008
- AR Menon. “Males who have Sex with Males in Kerala: Sexual Health and Health Care Access” Achutha Menon Centre for Health Science Studies, Thiruvananthapuram, Master of Public Health Thesis, October 2006

- AR Menon. “Media representation of religious NGO’s involved in rehabilitation of Tsunami victims” presented at National Bioethics Conference. Mumbai: India. Nov 2005