Review of cervical cancer screening program in Zambia

Sharon Katai Kapambwe

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Review of cervical Cancer screening program in Zambia

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<thead>
<tr>
<th>Acronym</th>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
<td></td>
</tr>
<tr>
<td>ACCP</td>
<td>Alliance for Cervical Cancer Prevention</td>
<td></td>
</tr>
<tr>
<td>ARVs</td>
<td>antiretroviral (drugs)</td>
<td></td>
</tr>
<tr>
<td>CBoH</td>
<td>Central Board of Health</td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>Cervical Cancer</td>
<td></td>
</tr>
<tr>
<td>CDC</td>
<td>Centre for Disease Control</td>
<td></td>
</tr>
<tr>
<td>CHAZ</td>
<td>Churches Association of Zambia</td>
<td></td>
</tr>
<tr>
<td>CIDRZ</td>
<td>Centre of Infectious Disease Research in Zambia</td>
<td></td>
</tr>
<tr>
<td>CSO</td>
<td>Central Statistical Office</td>
<td></td>
</tr>
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<td>FDA</td>
<td>Food and Drug Agency</td>
<td></td>
</tr>
<tr>
<td>FNDP</td>
<td>Fifth National Development Plan</td>
<td></td>
</tr>
<tr>
<td>GRZ</td>
<td>Government of the Republic of Zambia</td>
<td></td>
</tr>
<tr>
<td>HAART</td>
<td>Highly Active Antiretroviral Therapy</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papillomavirus</td>
<td></td>
</tr>
<tr>
<td>HRH</td>
<td>Human Resources for Health</td>
<td></td>
</tr>
<tr>
<td>HSV-2</td>
<td>Herpes Simplex Virus type 2</td>
<td></td>
</tr>
<tr>
<td>IARC</td>
<td>International Agency for Research in Cancer</td>
<td></td>
</tr>
<tr>
<td>LEEP</td>
<td>loop Excision Electrosurgical procedure</td>
<td></td>
</tr>
<tr>
<td>MDGs</td>
<td>Millennium Development Goals</td>
<td></td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry of Health</td>
<td></td>
</tr>
<tr>
<td>NAC</td>
<td>National Aids Council of Zambia</td>
<td></td>
</tr>
<tr>
<td>NGO</td>
<td>Non-governmental Organisation</td>
<td></td>
</tr>
<tr>
<td>NHSP</td>
<td>National Health Strategic Plan</td>
<td></td>
</tr>
<tr>
<td>PHC</td>
<td>Primary Health Care</td>
<td></td>
</tr>
<tr>
<td>PEPFAR</td>
<td>United States President’s Emergency relief Fund for AIDS Relief.</td>
<td></td>
</tr>
<tr>
<td>VIA</td>
<td>Visual Inspection with Acetic Acid</td>
<td></td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
<td></td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations programme on HIV/AIDS</td>
<td></td>
</tr>
<tr>
<td>UNGASS</td>
<td>United Nations General Assembly Special Session.</td>
<td></td>
</tr>
<tr>
<td>UNDP</td>
<td>United Nations Development Program</td>
<td></td>
</tr>
<tr>
<td>UTH</td>
<td>University Teaching Hospital</td>
<td></td>
</tr>
<tr>
<td>ZCCSP</td>
<td>Zambia Cervical Cancer Screening Program</td>
<td></td>
</tr>
<tr>
<td>ZDHS</td>
<td>Zambia Demographic Health Survey</td>
<td></td>
</tr>
</tbody>
</table>
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Working Definitions

Acetowhit e: area on cervical epithelium that turns white when acetic acid is applied.

Biopsy: Tissue specimen taken for morphological or immunohistochemical diagnosis

Carcinoma in situ (CIS): preinvasive stage of cancer involving the entire thickness of the covering layer, or epithelium, of an organ (e.g. cervix) but not penetrating the basement membrane.

Cervical intraepithelial neoplasia (CIN): a precancerous condition involving the covering layer (epithelium) of the cervix. It can be diagnosed using a microscope. The condition is graded as CIN 1, 2 or 3, according to the thickness of the abnormal epithelium (1/3, 2/3 or the entire thickness).

Coverage: Number of women invited as a proportion of target population. Also number of women who have a screening test within the recommended interval as a proportion of all women who are eligible to attend for screening.

Cytology: the study of the structure of cells under the microscope. Abnormal findings are usually confirmed by biopsy.

Cytopathologist/cytotechnician/cytologist: persons trained in the microscopic examination of smears for the presence or absence of abnormal cells.

Gold standard: a diagnostic method that is considered to have the best sensitivity and specificity among all methods available.

High-grade lesion: a term used in the Bethesda classification to denote cervical abnormalities that have a high likelihood of progressing to cancer if not treated. Includes CIN 2 and CIN 3.

High Risk HPV Type: Most likely to lead to the development of CC.

Low Risk HPV type: Rarely lead to development of CC

Informed choice: decision about whether or not to participate, based on the provision of information the benefits and limitations of screening.

Screen and Treat: A procedure where testing, confirmation and treatment take place during the same episode.

Screening policy: Specific policy of a screening programme which dictates the targeted age group, the geographical area, the screening interval, etc.

Screening test: Test applied to all women in a programme that’s results in discrimination between those who test positive from those who test negative (e.g. Pap smear).

Referral: Physical referral of women to a clinical facility as a consequence of the screening test for diagnostic confirmation, e.g., by histology.

Target population: the population eligible for screening i.e., all women recommended to undergo screening according to policy adopted.

Source: IARC, 2005
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Abstract

Cervical cancer is the second commonest cancer among women in the world and commonest cause of cancer related deaths in women in the developing world. Globally, over 80% of all new cases of cervical cancer occur in the developing world annually, where only less than 5% of the world health resources are found. Global estimates in 2000 showed that over 470,000 new cases were diagnosed and over 200,000 deaths occurred from cervical cancer. The highest incidence rates of cervical cancer are found in Latin America, sub-Saharan Africa, south and South East Asia accounting for 15% of cancers globally. Zambia has the second highest incidence (53.7/100,000 women) in the sub Saharan Africa and the 6th highest incidence rate in the world.

Screening has been known to reduce the incidence and mortality rates of cervical cancer in developed countries.

In developing countries, Zambia included, screening has been difficult to carry out due to many reasons. The country has urgent competing health needs like HIV and maternal mortality, limited financial and human resources and a poorly developed health system. In Zambia the economy has been on the decline with slight increase in the last few years.

Pap smear has been the screening test for many years in Zambia. With the limited human resource and poor laboratory infrastructure CC screening using Pap smear has failed to succeed. Alternative methods of screening for CC like VIA have been suitable for LIC countries like Zambia have been recommended. The Zambia Cervical Cancer Control Program started in 2006 with support of PEPFAR funds. VIA is used as the screening test.

Certain aspects of the screening process must be looked into. The follow up care of patients with abnormal results, sustainability of the program and whether the program meets the screening standards set by WHO.

KEYWORDS: Cervical cancer, screening, developing countries, resource limited countries, low income countries Zambia, VIA, Africa, Eastern Africa, HPV used in combination.
Introduction

Cervical cancer claims over a quarter of a million lives of women annually worldwide. 80% of these deaths occur in the developing world (Parkin et al, 2005). Over 470,000 women worldwide are diagnosed with cervical cancer annually, 80% of these new cases occur in the developing world. Cervical cancer is the leading cause for female cancer related deaths in developing countries.

Zambia has the second highest rate in sub Saharan Africa (53.7/100,000 women) second only to Tanzania and the 6th highest rate in the whole world (Parkin et al, 2002). Cervical cancer is the commonest cause of death from female related cancers.

The reason for these high rates is not because HPV infection is limited to a particular area but because preventive strategies and treatment are not well carried out in developing countries. In resource limited countries, like Zambia, shortage of skilled health workers, lack of political will and insufficient funds towards women’s health activities contribute to these high rates. One of the risk factors for cervical cancer is HIV. Zambia has one of the highest rates in sub Sahara Africa of 15.6% The HIV prevalence in Zambia stands at 17%.( UNAIDS 2007). Over 56% of HIV infections in Zambia are occurring in women.

As can be seen from the global distribution of cervical cancer, it is primarily a disease of poor and disadvantaged women. Cervical cancer is preventable yet, Zambia women will continue suffering and dying from cervical cancer as long as there is no screening. Traditional cytological based screening is difficult to implement because of the lack of financial and human resources in Zambia. The poorly organised health system also contributes to failure in using Pap smear as a screening test. New methods which are adapted to limited resource countries have been investigated are been used. Working in as medical doctor in Zambia made me see the cost of disability and mortality of women with cervical cancer to their family, community and nation at large. These costs are usually forgotten when analysing disease burden.

Centre for infectious Disease Research in Zambia started screening for cervical cancer using VIA which is adaptable to Zambia.

Findings in this thesis will go a long way in helping policy makers to put priority on cervical cancer control. Most of all, it will help save the Zambian from preventable deaths.
Chapter 1

1.1 Background Information

Zambia is found in the southern part of Africa. It is a landlocked country sharing its borders with eight countries (Zimbabwe, Malawi, Mozambique, Angola, Botswana, Tanzania, Democratic Republic of Congo and Namibia). Zambia is administratively divided into nine provinces and 72 districts. At the last census in 2000, the population of was estimated at 9.9million (CSO, 2000). The population is estimated to be above 12.2 million in 2007 (CSO, 2007). The annual growth rate currently is about 1.8% (WHO, 2006). About 47% of the Zambian population is below 15 years of age. This makes Zambia one of the countries with a high dependence ratio\(^1\) in the world. It however has an equal sex distribution of 50% males and 50% females. Life expectancy at birth among females in 2005 was 40 years. (WHO, 2006).

Zambia is one of the most urbanized countries in Sub-Saharan Africa with close 40% of the population living in urban areas. The urban area mainly consists of two provinces Lusaka and Copperbelt provinces. Over 60% of the population lives on less than one dollar (UNDP, 2007). These are people earning less than an equivalent of $30 per month. In 2004, 53% of the people were living in extreme poverty, earning less than $22 per month (FNDP, 2006).

In the rural areas 65% were living in extreme poverty during the same period.

Unemployment in Zambia is still very high. Out of an estimated labour force of slightly over 4 million, 14.7% were employed in the formal sector and the rest were in the informal sector. With such high unemployment and high dependence ratio providing quality health care is a great challenge for MOH. The GDP per capita in 2005 was 1,023 power purchasing parity (PPP). Human development index value was 0.434 in 2005(UNDP, 2008). The total expenditure on health as percentage of the gross domestic product in 2003 was 5.4% (WHO, 2006). The goal of the government is reach 15% allocation to health by 2015 according to the Abuja Declaration (NHSP, 2006). This has not been achieved. The figure below shows the government allocation to health as a total of the national budget.

The maternal mortality ratio between 1990 and 2004 was estimated at 730 per 100,000 live births (UNDP, 2008). See appendix for key health indicators.

\(^1\) The ratio of those of non-active age to those of active age in a given population. Shows the number of dependants (0-14 years and those above 65years old) to the total population. (OECD, 2005).
Graph 1: Health allocations in Total National Budget


In the 2001/2002 ZDHS, the average literacy level was estimated at 65.1%. The literacy level of men been higher than in women in all age groups. The average literacy levels for men were about 82% and that of women 61%. The literacy level among women in urban areas was 79% compared to those in rural areas of 59% (ZDHS, 2002).

Zambia is one of the countries with critical shortage of health workers as defined by WHO (WHO, 2006). This has made the provision of basic health services a daunting task. The health sector in Zambia is currently operating at 50% of the establishment. 45 of the rural health facilities are managed by unqualified health workers (FNDP, 2006). Zambia currently has 646 doctors instead of the needed 2300. This gives a deficit of 71.9%. There is a shortage of 63.6% for nurses and 59.4% for midwives. See tables below for details. In certain provinces the doctor to population ratio is so low. For instance in Northern Province, the doctor to population ratio is 1:69,000 compared to 1:5,000 recommended by WHO (FNDP, 2006). See tables below on staffing and distribution.
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Table 1: Current staffing, Approved establishment and deficit by HRH cadre in Zambia

<table>
<thead>
<tr>
<th>Staff category</th>
<th>Current staff levels</th>
<th>Recommended establishment</th>
<th>Deficit</th>
<th>Deficit (% of Recommended establishment)</th>
</tr>
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<tbody>
<tr>
<td>Doctor</td>
<td>646</td>
<td>2300</td>
<td>1654</td>
<td>71.9</td>
</tr>
<tr>
<td>Nurses</td>
<td>6098</td>
<td>16732</td>
<td>10636</td>
<td>63.6</td>
</tr>
<tr>
<td>Mid wives</td>
<td>2273</td>
<td>5600</td>
<td>3327</td>
<td>59.4</td>
</tr>
<tr>
<td>Clinical officers</td>
<td>1161</td>
<td>4000</td>
<td>22837</td>
<td>71.0</td>
</tr>
<tr>
<td>Pharmacists</td>
<td>24</td>
<td>42</td>
<td>18</td>
<td>42.9</td>
</tr>
<tr>
<td>Pharmacy technicians</td>
<td>84</td>
<td>120</td>
<td>36</td>
<td>30.0</td>
</tr>
<tr>
<td>Laboratory scientists</td>
<td>25</td>
<td>50</td>
<td>25</td>
<td>50.0</td>
</tr>
<tr>
<td>Lab technologists</td>
<td>100</td>
<td>210</td>
<td>110</td>
<td>52.4</td>
</tr>
<tr>
<td>Lab technicians</td>
<td>292</td>
<td>1300</td>
<td>1006</td>
<td>77.5</td>
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</tbody>
</table>

Adapted from: Ministry of Health. Human resources for Health Strategic Plan 2006-2010.

Table 2: Distribution of health human resource in Zambia in 2005.

<table>
<thead>
<tr>
<th>Province</th>
<th>Drs</th>
<th>CO</th>
<th>RM</th>
<th>RN</th>
<th>ZEM</th>
<th>ZEN</th>
<th>Pharm</th>
<th>Lab</th>
<th>Paramedic</th>
<th>EHT</th>
<th>TOTAL</th>
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<tr>
<td>Central</td>
<td>35</td>
<td>132</td>
<td>60</td>
<td>84</td>
<td>242</td>
<td>388</td>
<td>9</td>
<td>37</td>
<td>46</td>
<td>93</td>
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<td>Copperbelt</td>
<td>202</td>
<td>187</td>
<td>126</td>
<td>357</td>
<td>505</td>
<td>1160</td>
<td>33</td>
<td>110</td>
<td>140</td>
<td>79</td>
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<td>Eastern</td>
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<td>15</td>
<td>103</td>
<td>159</td>
<td>506</td>
<td>8</td>
<td>28</td>
<td>38</td>
<td>95</td>
<td>1119</td>
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<tr>
<td>Luapula</td>
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<td>65</td>
<td>10</td>
<td>36</td>
<td>39</td>
<td>274</td>
<td>5</td>
<td>25</td>
<td>21</td>
<td>55</td>
<td>545</td>
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<tr>
<td>Lusaka</td>
<td>256</td>
<td>212</td>
<td>129</td>
<td>421</td>
<td>305</td>
<td>1014</td>
<td>5</td>
<td>103</td>
<td>162</td>
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<td>2665</td>
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<td>North-West</td>
<td>21</td>
<td>55</td>
<td>5</td>
<td>38</td>
<td>41</td>
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<td>Northern</td>
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<td>5</td>
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<td>90</td>
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<td>Southern</td>
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<td>174</td>
<td>31</td>
<td>117</td>
<td>359</td>
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<td>4</td>
<td>18</td>
<td>36</td>
<td>81</td>
<td>720</td>
</tr>
<tr>
<td>TOTAL</td>
<td>646</td>
<td>1161</td>
<td>410</td>
<td>1288</td>
<td>1863</td>
<td>4956</td>
<td>92</td>
<td>417</td>
<td>545</td>
<td>750</td>
<td>12128</td>
</tr>
</tbody>
</table>

Co = clinical officer; rm = registered midwives; m = registered nurses; zem = zambia enrolled midwives; zen = Zambian enrolled nurse; eht = environmental health technician


The health care services in Zambia are essentially provided by public health facilities under MOH, Ministry of Define health facilities which includes one hospital, mine hospitals and clinics, clinics under ministry of Home Affairs, Mission hospitals and clinics under CHAZ, private hospitals and clinics, NGOs, and traditional healers. The health facilities are divided into hospitals (first
level hospitals, second level hospitals, general hospitals and tertiary hospitals), health centres and health posts (NHSP, 2005).
By the early 1990s, the Zambian economy had declined and the population was growing at a fast rate. This led to the deterioration of the quality of health services. The situation was further compounded by the HIV pandemic. The Zambian government was unable to meet the health care needs of the nation. This led to the introduction of health reforms in 1992 whose core purpose was decentralization of health services, planning and provision to the district level and finally, a focus on preventive rather than curative care. CBOH was created as a unit for delegation service delivery but failed and was dissolved in March 2006 (Deliver, 2007). Following the dissolution of CBOH, the health sector is currently undergoing a restructuring process. The functions of MOH and those functions which were under CBOH will eventually be joined. The running and control of all public health facilities and services will again fall under the MOH through Provincial Health Offices. The current hospital and district management boards will be replaced by advisory councils to ensure public participation in the running of these health facilities (NHSP, 2005).

1.2 Statement of the Problem
Zambia has the second highest prevalence rates of cervical cancer in sub-Saharan Africa second to Tanzania at 53.7/100,000 females (Globocan, 2002). Mortality due to cervical cancer stands 35/100,000 women. Cervical cancer is the commonest cause of death from cancer among females. It is also the commonest cancer among females.
The table below shows the projections of new cases and deaths due to CC. These are merely projections cases and deaths from CC in the rural areas go unreported. Therefore there is possible underestimation of the cases and deaths projected.

**Table 3: Projections of new cases of cancer among Zambian women in 2002**

<table>
<thead>
<tr>
<th>New Cases of Cancer in Women in Zambia Projections for 2002</th>
<th>Cancer Type</th>
<th>Age Standardized Incidence per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix uteri cancer</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>
Review of cervical Cancer screening program in Zambia

<table>
<thead>
<tr>
<th>NEW CASES OF PROJECTIONS FOR 2002</th>
<th>CANCER IN WOMEN ZAMBIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver cancer</td>
<td>11</td>
</tr>
<tr>
<td>Melanoma and other skin cancers</td>
<td>6</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>6</td>
</tr>
<tr>
<td>Ovary cancer</td>
<td>5</td>
</tr>
<tr>
<td>Oesophagus cancer</td>
<td>5</td>
</tr>
<tr>
<td>Lymphomas, multiple myeloma</td>
<td>3</td>
</tr>
<tr>
<td>Colon and rectum cancers</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: WHO Global InfoBase available at


Table 4: 10 leading causes of cancer deaths among Zambian women

| 10 LEADING CAUSES OF CANCER DEATHS IN WOMEN IN ZAMBIA PROJECTIONS FOR 2005 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| CANCER TYPE                 | AGE STANDARDIZED DEATH RATE per 100,000 |
| Cervix uteri cancer         | 35   |
| Bladder cancer              | 15   |
| Breast cancer               | 11   |
| Liver cancer                | 10   |
| Melanoma and other skin cancers | 5   |
| Stomach cancer              | 5    |
| Oesophagus cancer           | 4    |
| Ovary cancer                | 3    |
| Lymphomas, multiple myeloma | 2    |
| Colon and rectum cancers    | 1    |

Source: WHO Global InfoBase available at
Review of cervical Cancer screening program in Zambia


There are many reasons for the high prevalence rates of cancer in Zambia. As stated in the background information, the health care services in Zambia face a lot of challenges. The urgent competing health needs and critical shortage of qualified and skilled health workers make provision of quality health care almost impossible task. With the high prevalence rate of HIV Zambia has seen an increase in the cases of cervical cancer. Of the over one million people living with HIV in Zambia, 56% are women. A cross-sectional study done in Zambia showed that over 50% of HIV infected women with average CD4+ count of 165.0/μL had severe cervical abnormalities on cytology( Parham GP et al, 2006). The increase of oncogenic HPV strains in HIV infected women is due to the inability for the body to control the HPV which happens in immunocompetent women. In HIV negative women 12-32% of these abnormal cervical abnormalities were able to regress. HIV infected women are more prone to recurrences than HIV infected women.

In the last ten years Zambia has also had massive resources coming in for the fight against HIV/AIDS. Women now have access to the much needed ART (Stringer et al, 2006). Access to antiretroviral treatment has made possible for women to live longer. The impact of HAART on cervical neoplasia is still a grey area. Some studies show that HAART increases the rate of regression and progression is reduced (Howard et al, 2001). This means women who were dying early due to AIDS will now live longer due to HAART. The women will unfortunately live longer to have the cervical abnormalities progressing into invasive cervical cancer. This means the women whose lives have been prolonged by HAART will unfortunately die from cervical cancer. These deaths are preventable with regular screening targeting these HIV infected women.

For many years, there has been no organised cervical cancer screening services are not available for women. Screening services are available at a fee in the private health facilities which is out of reach for most Zambian women. Conventional cytology has been the main screening method. Cytology needs a well organised health system. Currently, physicians are the only smear collectors. With the high shortage of physicians in the country, screening has not been feasible. There is only one cytopathologist in the public sector in the country (Mulindi, 2008). Quality control in the laboratory is key in conventional cytology screening. Zambia also has a shortage of laboratory technicians. This has led to cervical screening been difficult to do (WHO, 2006).

Zambia has no national guidelines on cervical cancer control. It does not have National Cancer Control Programme (kanyimba, 2006). There is no
cervical cancer screening policy. With such high infection rates in HIV, there are still no clear guidelines for screening of HIV infected women for cervical cancer in the country. Zambia is a poor resource country with over 65% living below the poverty line. The country is faced with many competing health needs e.g. HIV, malaria, tuberculosis, maternal mortality, infant mortality with limited resources. Prioritising is very difficult in the current scenario. Every year thousands of women die from cervical cancer in Zambia. Cervical cancer is a disease which has a long preclinical stage thereby preventable. Women’s health is important in achieving MDGs. The loss of a woman is not only to her family but to the nation as whole for she is the cornerstone of every home. The centre for Infectious Disease Research in Zambia (CIDRZ) in colloraboration with MOH in Zambia is currently running a large cervical cancer screening program in Zambia. Over 10,000 women have been screened so far. The program is using Visual Inspection with Acetic Acid as screening method. Non-physicians are carrying out the test at the primary health facilities. Treatment is available on the same day and those requiring evaluation by gynaecologist are referred. It is currently available in 14 clinics around the country with plans to replicate around the whole country. The program targets HIV infected women though HIV uninfected women can also screen.

1.3 General Objective:
To review CC screening program in Zambia from January 2006 to October 2007, in order to make to make recommendations to policy makers on improved cervical cancer screening services in the country.

1.4 Specific Objectives:
1. To assess whether the program meets the standards for a successful screening program according to WHO standards.
2. To assess the follow up care of patients with abnormal results.
3. To analyse the sustainability of the program as a routine service in primary health care facilities.
4. To make recommendations to the policy makers on policy guidelines cervical cancer control and on possible integration on cervical cancer screening into all existing public primary health care services throughout the whole country.

1.5 Methodology:
This thesis is based on literature review of policy documents, scientific articles and secondary data from the cervical cancer control program in Zambia. Peer-reviewed journals and systematic reviews on cervical
Review of cervical Cancer screening program in Zambia

cancer were reviewed. Review also focused on literature on visual inspection with acetic acid as alternative screening method in resource limited countries.
Literature review will done using the search engine of Google, Google Scholar, Pubmed and Cochrane library The websites world health organization (WHO), International Agency for Research in cancer (IARC), Program for Appropriate Technology in Health ( PATH), Alliance for Cervical Cancer Prevention (ACCP), United Nations Development Fund for Women (UNIFEM), Ministry of health Zambia (MOH), National Aids Council Zambia (NAC), United Nations Development Program (UNDP), Central Statistical Office (CSO).

The limitations in the review of literature were the following:
- Only articles in English were reviewed
- Data on cervical cancer in Zambia is very limited.
- Limited data on cervical cancer screening programmes using Visual inspection with acetic acid as a screening test in low income countries.
Chapter 2

2.1 Natural History of HPV

For effective and efficient application of cancer control strategies the natural history of cervical cancer must be known. HPV is a necessary cause of cervical cancer but not a sufficient cause. There other factors necessary for progression from HPV infection to cancer (Walboomers, 1999). The prevalence of HPV infection among women in the population is estimated to be between 2% and 44%. Globally, HPV infection with various strains is common among sexually active women. In a study done by Baseland et al, involving sexually active female college students 60% of them acquired the HPV infection in a five year period. In 18 months over 80% of women the Baseland study cleared the infection. In other women the HPV infection persists. Most studies define persistent infection as HPV infection detected at two consecutive visits of 4-6 months interval (Baseland, 2005). In 90% of those with persistent infection, the changes which occur on the cervix reverse on their own. Infection with oncogenic HPV types is a necessary cause for cervical cancer. It is not a sufficient cause. Host immune factors are linked to the persistence of HPV infection. HIV infected women tend to have a longer time of shedding the infection than HIV non-infected women (Baseland, 2005). If the infection with oncogenic HPV types, persists it progresses to the precancerous stage. This progression usually takes decades though it can occasionally been short in young women. The precancerous stage has two types the low grade intraepithelial lesion and high grade intraepithelial lesions.

A study by Ng’andwe et al in Zambia involving seventy women showed HPV-16 and 18 as the most prevalent HPV genotypes in Zambia at 21.6% each respectively. This is very high compared to countries like USA with 7.5% of HPV-16 and 2.3% of HPV-18. This high rate in a way is in line with the high prevalence of cervical cancer in Sub-Saharan Africa. The incidence of HPV was 55% among those who were HIV negative compared to 80% among HIV infected women. The High Risk to Low Risk ratio in HIV infected women was 78% to 22 % (Ng’andwe, 2007).

Sarasbuddhe et al did a study on prevalence and distribution of HPV of among HIV infected women in Zambia around the same period as Ng’andwe and found that HPV-16 and 18 were not the prevalent types among the HIV infected women studied. The prevalence of any type of HPV in the study was 97.2% and 90% for any HR-HPV. 87.3% of the women had multiple types of HPV. The number of multiple HPV types increased with a reduction in immunity. In this study the most prevalent types of HR-HPV were 51, 52, 53, 58, 35, 31 and 45 (Sarasbuddhe, 2007). The information from the two
Review of cervical Cancer screening program in Zambia

studies is essential in view of upcoming primary prevention using HPV vaccines.

The study by Ng’andwe et al involved HIV positive and negative women while sarasbuddhe’s study was among HIV positive women. This might explain the conflicting findings on the most prevalent HPV genotype in Zambia. More studies are needed among HIV negative and HIV positive women to determine the distribution of HPV genotypes in Zambia. This information is useful in advocacy and implementation of vaccines should HPV vaccines become available in Zambia.

**Table 5: Classification of HPV types by cervical oncogenicity**

<table>
<thead>
<tr>
<th>Risk classification</th>
<th>HPV types</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-risk</strong></td>
<td>16, 18, 31, 33, 35</td>
</tr>
<tr>
<td></td>
<td>39, 45, 51, 52, 56</td>
</tr>
<tr>
<td></td>
<td>58, 59, 68, 73, 82</td>
</tr>
<tr>
<td><strong>Probable high-risk</strong></td>
<td>26, 53, 66</td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td>6, 11, 40, 42, 43, 44</td>
</tr>
<tr>
<td></td>
<td>54, 61, 70, 72, 81, CP6108</td>
</tr>
<tr>
<td><strong>Undetermined risk</strong></td>
<td>34, 57, 83</td>
</tr>
</tbody>
</table>

Data from Munoz et al. (2003).

**2.2 Risk Factors of Cervical Cancer.**

**2.2.1 HPV**

HPV is a necessary cause for cervical cancer but not a sufficient cause. There are other co-factors necessary for progression from HPV infection to cervical cancer. The established co-factors are high parity, long term hormonal contraceptive use, co-infection with HIV and smoking. Co-infection with Chlamydia and herpes simplex virus type-2, certain dietary deficiencies and
immunosuppression are probable factors (Munoz, 2006). Genetic and immunological factors together with viral factors are likely to be important not yet clearly understood.

2.2.2 Smoking
Based on the study by Winkelstein in 1977, there have been correlations seen between cervical cancer and the incidence of other tobacco related cancers. The hypothesis of synergistic action between cigarette smoking and HPV for the development of HSIL and cervical cancer is further strengthened detection of nicotine and tobacco-specific carcinogens in the cervical mucous of smokers (Prokopczyk et al, 1997). In a prospective study, smokers were found to have the HPV infection longer and lower probability of clearing it (Guilian et al, 2002).
The prevalence of smoking among female adults in Zambia is 1% compared with 16% among Zambian males (HPV centre, 2007). Smoking is therefore a very low risk factor among Zambian women.

2.2.3 High Parity
The fertility rate is used a proxy for measuring parity. The total fertility rate per woman in 2000 was 5.9. High parity increases the risk of cervical cancer because it maintains the transformation zone on the exocervix thereby increasing direct exposure to HPV. Hormonal changes that occur during pregnancy may also modulate the response to HPV and influence the risk of HPV infection persisting or even progressing to cancer (Munoz, 2002). Women with seven full term pregnancies or more were four times more likely to have cancer than nulliparous women. A study in Costa Rica showed the risk of HSIL or cancer increase significantly with increased number of live births (Hildesheim et al, 2001).

2.2.4 Hormonal Contraception
The mechanism by which hormonal contraception modulates the progression from HPV infection to advanced cervical cancer is well documented. Progression from pre-malignant to malignant cervical lesions through promotion of integration of HPV-DNA into the host genome this is most likely due to the influence of hormonal related mechanisms. The integration of HPV-DNA into the host genome results into the deregulation of HPV E6 and E7 expression (Castellsague et al, 2002).
With this in mind the key public health question is finding out to what extent the effects hormonal contraception persists after a woman ceases using the method. Women on hormonal contraception are less likely to use barrier methods or abstain from sexual intercourse hence an increase in their exposure to HPV. This is another argument for the increase of CC among women using hormonal contraception. In sub-Saharan the increased lifetime
risk of a woman with seven children on hormonal contraception for 10 years is about 40/10,000 women. Whole a woman in her 20s who uses for 10 years has a lifetime risk of 7-10/10,000 women (Sasieni, 2007). The protection from reduced parity definitely outweighs the effect of use of hormonal contraception. Therefore women should not abstain from use of hormonal contraception because of fear of CC.

2.2.5 HIV

HIV prevalence rate among adults is 15.6% (NAC, 2008). Over one million people are living with HIV/AIDS in Zambia. 56% of the infection is among women. A study by Ellerbrock et al showed that HIV-positive women were 4.5 fold more likely to have or develop CIN over a four and half year of follow-up period(Ellerbrock,2000). A cross-sectional study done in Zambia showed that over 50% of HIV infected women with average CD4+ count of 165 CD4 cells/mm³ had severe cervical abnormalities on cytology (Parham, 2006). The increase in oncogenic HPV strains is due to the inability of the body to control the HPV. In the study by Parham et al, 12-32% of these abnormal cervical abnormalities were able to regress in HIV negative women. The HIV seroprevalence among adults in Zambia is 15.6 % (NAC, 2008). About one million people in Zambia are living with HIV/AIDS, 56% of this infection is among women. There is high prevalence of HPV among HIV infected women. HIV is a known risk factor for cervical cancer development. It leads to faster progression rates of cervical cancer. Study by Parham et al among HIV infected women showed high rates of HSIL (33%) and invasive cervical cancer (20%). These rates are among the highest in the world (Parham et al, 2006)

The effect of HAART on the natural history of CC is remains unclear. A study by Sirera et al showed that there was no specific difference on the incidence of SIL among women on HAART and those not HAART who similar immunological status. The women in this study had an immunological status of above 350 CD4 cells/mm³ (Sirera et al, 2008).Unfortunately women in Zambia present late for HAART when the immunological status is below 350 CD4 cells/mm³. A study by Parham et al showed the average immunological status as 165 CD4 cells/mm³ among women seeking HAART who took part in the study (Parham et al). In a large cohort study by Minkoff et al, there appears to be a link between the immune status and viral load with progression and regression of CC. women on HAART seemed to have an increased regression and reduced progression of cervical cytology.

2.2.6 Diet

The possible role of diet is not well known. Though not conclusive most studies show that a higher intake of fruits and vegetables are associated with reduced risk of cervical cancer and HPV persistence. The evidence on this is too limited.
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It is probable that folate, retinol and vitamin E have a protective effect against cervical cancer neoplasia yet this is possible for vitamin B₁₂ and C and carotenoids. From the systematic reviews by Giuliano & Gapstur, 1998 and Castle and Giuliano, 2003 no clear patterns were observed for nutritional factors between low- and high- grade cervical lesions or between retrospective and prospective study designs (IARC, 2005). The evidence on the influence of nutrition on cancer is still not conclusive.

2.2.6 Sexually transmitted Infections

HPV infection with other sexually transmitted infections like HSV-2 and Chlamydia infection have been associated with CC though inconsistently. HSV-2 seropositivity was associated with an increased risk of CC. The hypothesis by the authors is that HSV-2 may act in conjunction with HPV infection to increase the risk of invasive CC. This action is likely to be mediated by the induction of inflammatory responses (Smith, 1999). A study, in which HPV was assessed serologically, showed that the presence of serum IG antibodies to C. trachomatis serotype G was associated with 6.6 fold increase in the risk of developing CC as compared with seronegative women (Astttila, 2001).
Chapter 3: Primary Prevention

This chapter will discuss the cervical cancer control strategies in terms of primary and secondary Prevention.

3.1 Primary Prevention definition

Primary prevention means elimination of exposure of known risk factors. From the risk factors mentioned above, primary prevention can be achieved through change of lifestyle, counseling and chemoprophylaxis (vaccination).

3.1.1 HPV Vaccination

Based on the natural history of cervical cancer HPV been the necessary cause of cervical provides great potential for cancer prevention through vaccination. Prevention of HPV infection should therefore eliminate cervical cancer. There are currently two HPV vaccines available on the market. Cervarix which protects against HPV-18 and HPV-16. HPV 16 and 18 are responsible for about 70% of cervical cancer globally (Goldie SJ, 2001). The other vaccine is Gardasil which protects against HPV-16 and 18, as well as HPV-6 and 11. The vaccines will stop the infection before it has begun. The vaccine is therefore suited to be administered prior to first sexual intercourse. In Zambia, the age of sexual debut for girls is currently 18.6 years (FNDP, 2006). This means girls have to be vaccinated pre-teens. However these girls will still need screening as adults in case they acquired an HPV oncogenic strain not covered by any of the two vaccines. Older women already sexually active will still need to be screened. Gardasil has been approved in more than 80 countries. It costs more $360 per three-dose series over a six month period (Milliez, 2008). Cervarix is available in Australia awaiting approval by European Agency for Evaluation of Medicinal Products (EMEA), FDA and other regulatory bodies. The cost of Cervarix is similar to Gardasil. Poor women in the developing world will not be able to afford these vaccines at present price neither will their governments. The prices will need tiering in low-income countries. Developing countries need to come up with strategies which will ensure that young and girls get access to the vaccines. According to UNIFEM the following steps must be taken for the vaccines to be accessible:

- Vaccine prequalification by the WHO
- In-country licensure
- Funding commitment from donor agencies
- Support and commitment of in-country health officials
- Developing country pricing
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- Platform chosen or developed for vaccine delivery.
- Personnel chosen to provide vaccinations
- Vaccines made available on the ground
- Public education campaigns on HPV vaccines
- Outreach to target population, including parental permission and comfort with vaccination for sexually transmitted infection of your girls.
- Follow up to ensure second and third doses are delivered (Balkin, 2007).

3.1.2 Lifestyle Changes
HPV is predominantly transmitted through sexual intercourse. Implications of routes of transmission such as mother to child, autoinoculation, are very minimal. The sexual behaviour of both men and women are key determinants in acquiring HPV infection. The risk factors for this sexual behaviour lifetime number of sexual partners, age of first sexual encounter and likelihood of one of the male sexual partners having HPV infection. Interventions aimed at promoting safer sexual behaviour through condom use, reduction in number of sexual partners and delay of first sexual encounter is critical.

Condom use and reduction in HPV transmission has been an issue of controversy. A longitudinal prospective study showed that condoms reduce transmission up to over 70% when used correctly and consistently. The incidence of genital HPV infection was 37.8% per 100 patient-years at risk who used the condoms 100%. In those who used condoms 5% of the time, the incidence of genital HPV was 89.3% per 100 patient-years at risk (Winer R, 2006). This study showed that condoms offer protection even when there is skin contact. Most studies have shown that condoms offer partial protection. The virus is able to live on body surfaces not covered by condoms. There has even been hearing addresses in the USA on condom use and prevention of HPV infection. Some sectors believe condoms should not be promoted for prevention against HPV (Christopher et al, 2004). Even though condoms offer partial protection condom use must still be encouraged as it prevents one from HIV infection which leads to fast acceleration of cervical cancer. Sexually transmitted infections like Chlamydia are also prevented, which are co-factors of cervical cancer. Condoms use among 15-24 year olds in Zambia is only 38% (NAC, 2007).

Program promoting safer sex is one of the objectives in the FNDP (FNDP, 2006) in reduce HIV prevalence in Zambia. Condom use should therefore be promoted to reduce the transmission of HPV and other sexually transmitted infections. A study on the influence of religion on sexual behaviour showed that helped in delaying the age of initiation of sex but
Review of cervical Cancer screening program in Zambia

condom use at first sexual encounter was very low. This cancels out the benefits of delaying age of first sexual encounter (Agha et al, 2006). Data has shown that those who have sexual their first sexual encounter before the age of 20 years are at a higher risk of having cervical cancer than those start less than 20 years old.

3.1.3 Male circumcision

Castellague et al, in a multi centre study by IARC found that circumcised were three times less likely to keep HPV DNA in their penis than uncircumcised men. The glans penis of a circumcised man is more resistant to cuts and therefore less liable to entry of HPV. Penile HPV infection increases the risk of cervical HPV a fourfold. Cervical HPV infection has an association of 77fold increased risk of cervical cancer. Therefore male circumcision reduces penile HPV which in turn reduces cervical HPV (Castellsague et al, 2002). However a study by Weaver et al showed no difference in HPV in the penis of circumcised men and uncircumcised men. The samples were collected from different genital sites (Weaver et al, 2004). There is enough evidence of circumcision been protective against HIV and other STIs. These findings are relevant in the fight against cancer.

3.3.2 HIV care and Treatment

From the studies discussed under risk factors it is prudent that women who are HIV positive need to be on ART to help improve the immune status. These studies suggest that progression may be related to the immune status of a woman. In Zambia women must be encouraged to know their status and seek HAART early. There many factors influencing seeking treatment early like stigma, socioeconomic status which are beyond the scope of this thesis.
Chapter 4: Secondary Prevention Cervical Cancer.

The United States Commission in 1957 defined screening as “the presumptive identification of unrecognized disease or defect by the application of tests, examination or other procedures that can be applied rapidly” (IARC, 2005). Screening is therefore the use of methods to detect unrecognized health risks or diseases in order to permit timely intervention. The main aim of screening is to detect and treat women with high-grade cervical intraepithelial neoplasia (CIN 2 and CIN 3 lesions) early in order to reduce cervical cancer incidence and mortality. Therefore the effectiveness of screening is evaluated by the extent of reduction in cervical cancer incidence and mortality following screening (Sankaranarayanan et al, 2005). Secondary prevention gives many benefits. The patient who has the disease detected early and preventive treatment given if required spends less time with the health provider and at the health facility, the health care provider has more time to spend with other patients and it is also cost saving for the patient, institution and nation at large. Junger and Wilson developed the ten principles of screening for a disease and WHO has developed its screening of diseases and research based on these principles (Junger et al, 1968). One of the objectives of this review is to see whether the cervical cancer screening programme in Zambia meets the standard of the WHO screening principles. The ten principles listed in the annex will be discussed in detail in chapter 5. See annex for principles of screening.

4.1 Screening Tests

A screening test is not meant to be diagnostic. A screening procedure is generally cheaper and easier to perform than diagnostic procedures (IARC, 2005). The results from a screening test require confirmation by a definitive diagnostic test. The screening test must have adequate sensitivity and specificity for detection of pre-cancerous lesions and yield results that can be reproduced. The screening tests used in cervical cancer screening are:

4.2.1 Conventional cervical cytology

This remains the gold standard for cervical cancer screening recommended by WHO. Cytology involves sample collection, slide preparation, staining, reading and reporting. Smear collection is of utmost importance. The way it is collected and the patient’s condition at time of collection determine the outcome. Conventional cytology requires three types of health workers. Health workers to collect the sample and prepare the slide. This could be doctors or nurses who have adequate training in slide preparation and smear
collection (IARC, 2005). Cytotechnicians are responsible for processing, staining and reading of slides. The cytopathologist is responsible for supervision and final reporting. Cytology requires a well organised health system. Doctors and nurses are required, good laboratory infrastructure with excellent quality control and a good network for communication of results to the women. The quality of training for the health workers must be of high quality and continued education is vital to ensure reliable and efficient testing.

Two factors need to be assessed when determining the accuracy of a screening test, the specificity and sensitivity. The sensitivity of cervical cytology in detecting CIN 2-3 in three recent reviews ranged from 47% to 62% and specificity from 60% to 95% (Sankarayarayan, 2005). Most of the studies reviewed however suffered from many deficiencies which included and verification bias and unblended non-independent assessments. Many of the women included in the follow-up data already had abnormal test results. The low to moderate sensitivity could also have been due to sampling and reading errors.

To improve the sensitivity of cytology attempts have been made by combining it with second test.

4.2.2 Liquid –based cytology

Liquid-based cytology was introduced in the mid-1990s to improve the performance of the test. The test depends on fluid medium to preserve collected cervical cells. Rather than the health worker preparing the cytological specimen, the cells are transferred to a liquid preservative solution that is transported to the laboratory where the slide is prepared. LBC apparently has a number of advantages over cervical cytology;

• More representative transfer of cells from collection device to the glass slide
• Elimination of problems such as poor fixation, air-drying artefact, uneven thickness of the cellular spread, debris from blood and inflammatory cells and overlapping of cells thus improving microscopic readability.
• Cell suspension remaining after the preparation of the smear is suitable for additional testing procedures for example HPV testing.

A study done in the Netherlands showed that LBC improves sample sufficiency and is likely more sensitive but less specific than conventional cervical cytology in detecting cervical neoplasia (Klinkhamer, 2003). The cost-effectiveness, impact on incidence and mortality due to cancer is yet to be established. LBC is not feasible for implementation in low-income countries. It is more costly than conventional cytology and needs extra instrumentation for slide preparation (Sankarayarayan, 2003).
4.2.3 HPV Testing
HPV is a necessary cause for cancer but not a sufficient cause. Persistence infection with HPV leads to cervical neoplasia. This knowledge is the basis of HPV testing as a screening test. Hybrid Capture systems is the only HPV test currently approved by FDA. The second generation HC system targets 13 high-risk HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 58, 59 and 68. However it does not determine the HPV genotype present. Polymerase Chain Reaction (PCR) assays has also been assessed. HPV is an approved test has also been approved technique for screening in western countries. The sensitivity of HPV testing with HC II in detecting CIN 2-3 lesions and invasive cancer varied between 66% and 100% (Sankarayarayan, 2003). Cross-sectional studies by Sankarayarayan et al in India, a developing country showed among women aged between 25-65 years showed sensitivity of 68.2%, specificity of 93.8%, negative predictive value (NPV) of 12.8% and positive predictive value of 99.5% of detection of CIN 2-3 lesions and invasive cancer( Sankarayarayan, 2004). The adequacy of specimen collection is a vital component of HPV testing.

4.2.4 Visual Inspection
Usage of visual inspection methods began in the 1930s with Schiller’s test screening for cervical neoplasia. Stjernward et al promoted the idea of down-staging, i.e. looking at the cervix with the naked eye for early detection of disease. This was promoted in low-income countries. From the last decade till now the application of dilute (3-5%) acetic acid before inspection has been investigated (VIA). Recently the application of Lugol’s is also been investigated. The test is known as visual Inspection with Lugol’s iodine (VILI). The main challenge of visual tests is that they are largely subjective. There are different tests under visual inspection. These include;

a) Unaided Visual inspection
This is also known as down-staging or unaided visual inspection. This involves clinical examination of the cervix using a speculum and a light source. VI lacks credible sensitivity to be used as a primary screening test. All studies done showed rather low sensitivity of between 30%-60% (IARC, 2005).

b) Visual Inspection with Acetic acid (VIA).
This method involves naked-y inspection of the cervix after application of 3%-5% solution of acetic acid. The test is considered positive when there is appearance of acetowhite areas in the transformation zone, close to the os or squamocolumnar junction.
The first study to give results with direct estimates of sensitivity and specificity was done in Zimbabwe. The procedure was performed by nurses at primary health care facilities. The primary endpoint of this study was to see the specificity and sensitivity of the test when performed by non-physicians. This study unlike other studies avoided verification bias because
all women with negative or positive results were offered the reference standard, which was colposcopy with biopsy. The sensitivity for VIA (HSIL) in this study was 76.7% compared with cytology 44.3%. The specificity however was lower than cytology by 1.4 times. The specificity for VIA was 64.1% compared with cytology 90.6% (University of Zimbabwe, 1999). The table below summarises the findings from different studies on sensitivity and specificity of VIA.

### Table 6: Accuracy of VIA in detecting CIN 2–3 lesions and invasive cancer in selected cross-sectional studies

<table>
<thead>
<tr>
<th>Author, year of publication, country of study</th>
<th>No. of participants</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Zimbabwe/JHPIEGO 1999, Zimbabwe</td>
<td>2148</td>
<td>77 (70–82)</td>
<td>64 (61–66)</td>
</tr>
<tr>
<td>Denny et al. 2000, South Africa</td>
<td>2885</td>
<td>67 (56–77)</td>
<td>84 (82–85)</td>
</tr>
<tr>
<td>Belinson et al. 2001, China</td>
<td>1997</td>
<td>71 (60–80)</td>
<td>74 (71–76)</td>
</tr>
<tr>
<td>Denny et al. 2002, South Africa</td>
<td>2754</td>
<td>70 (59–79)</td>
<td>79 (77–81)</td>
</tr>
<tr>
<td>Cronjé et al. 2003, South Africa</td>
<td>1093</td>
<td>79 (69–87)</td>
<td>49 (45–52)</td>
</tr>
<tr>
<td>Sankaranarayanan et al. 2004 India and Africa</td>
<td>54,981</td>
<td>79 (77–81)</td>
<td>86 (85–86)</td>
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</tbody>
</table>

Adapted from Sankaranarayanan et al, 2005.

Note. CI: confidence interval.

- Estimates for CIN 2–3 lesions only.
- Pooled results of 11 studies from Jaipur, Kolkata, Mumbai, and Trivandrum in India and Burkina Faso, Congo, Guinea, Mali, and Niger in Africa.
- Alliance for Cervical Cancer Prevention study.

**Advantages of VIA**

- VIA is as sensitive in detecting high grade disease as cytology.
Review of cervical Cancer screening program in Zambia

- Training health workers to perform VIA is much shorter than training cytotechnologists.
- Simple, safe and well accepted and cheaper compared to other screening tests.
- Can be performed by a wide range of health workers with low level infrastructure. Results are available immediately after the test. Referral can there be made for diagnostic tests.
- No need to recall women with positive results. This potentially reduces default rates as cryotherapy (in Zambia) is done after VIA if indicated.

**Disadvantages of VIA**

- Low specificity compared to cytology
- High rate of false positives (10-35%).
- Low positive predictive value (10-30%).
- Quality control not standardized.
- Essentially examines the ectocervix. Women above 50 years with migration of ectocervix into endocervix may not benefit.
- Over-investigation and over-treatment of patients with positive test (IARC, 2005).

**c) Visual Inspection with acetic acid with Low magnification (VIAM).**

VIAM was introduced with the hypothesis that low-level magnification could remove the proportion of false positive identifications which were due to metaplasia and inflammatory conditions without reducing sensitivity. A study done in South Africa under the ACCP portfolio screened 2574 women using both VIA and VIAM. The sensitivity of VIA for CIN 2-3 lesions was 69.8% and the sensitivity for VIAM was 74.0%. In three other studies involving multiple sites, under ACCP in 16,900 women participated the results for accuracy were not different. The results showed that magnification does not improve the test performance in comparison to naked eye visualization (Sankaranarayanan, 2005).

**d) Visual Inspection using Lugol’s iodine (VILI)**

Inspection of the cervix using Lugol’s was first described by Schiller as early as 1933. With the coming of cervical cytology, the test went into disuse. A test is positive when there is appearance of definite yellow area in the transformation zone close to the squamocolumnar junction or the os or on a growth.

Ten cross-sectional studies were done by ACCP involving 49,080 women in Burkina Faso, Congo, Guinea, India, Mali and Niger to evaluate the accuracy of VILI. From these studies the pooled sensitivity was 92.2%, specificity 85.4%, PPV 13.3% and NPV 99.8% at 95% CI. The above values were for detecting CIN2-3 lesions and invasive cancer. Specificity and sensitivity ranged from 73.0-91.3% and 77.8% and 98.0% respectively. From these findings VILI is a more sensitive test than VIA. More studies in other sites are however needed to substantiate this (sankaranarayanan, 2005).
4.2.5 Emerging Cervical Screening Techniques

There are three new developments in the screening methods;

- **Computer-assisted reading of cervical smears.**

  The main objective of this method is to increase sensitivity by finding things which are known to be very difficult to detect in conventional screening, for example, small abnormal squamous cells. Most importantly it should increase productivity through excluding normal slides from manual screening by selecting only the most atypical slides to be checked by the cytotologist. This makes it possible to analyse more slides without increasing of staff. The ThinPreP system which has FDA approval for primary screen for LBC specimens in the USA is an example. Image analysis and algorithmic processing to identify a fixed number of the worst microscopic fields on a given slide is utilised. The cytotechnician is then directly taken to these specific worst fields by a motorized computer-controlled microscope. Certain studies show that this method generally has a better sensitivity and same specificity as conventional cytology (IARC, 2005). This method seems to perform well in an organised screening program. It is not feasible in low income countries.

- **Use of physical real-time devices**

  The epithelia of the normal and neoplastic cervix have varied physical and biochemical properties. These properties make them give distinct patterns in conductance of electrical pulses and reflectance of light. The fluorescent spectroscopic devices utilize these differences in capturing electro-physical signals from the cervix and analysing the patterns using algorithms to discriminate between normal and neoplastic tissue. The findings in small trials by mostly by manufacturers on a selected group of women show promise but large multicentre trials are vital to confirm these findings (IARC, 2005).

- **Detection of molecular surrogate markers of cancer progression.**

  The current methods of screening for cervical cancer (HPV DNA testing, cytology, VILI and VIA), gives a considerable number for women referred for diagnostic tests who are later found not to have high grade disease. This causes anxiety for the women and ‘misuse’ of limited services like colposcopy and biopsy. It is therefore prudent look for markers that might identify women susceptible to progression with high predictive value. This is the basis of molecular surrogate markers test. Potential markers include;

  - Messenger RNA for the E6 or E7 proteins.
  - HPV DNA sequences integrated into the human genome
  - Over-expression of cell cycle regulator proteins or proliferation protein markers

  Determination of certain genetic or immunological profiles. (IARC, 2005). The emerging techniques are not feasible in low income countries. Both the financial and human resource for this type of screening is not available in low income countries.
4.3 Behaviour to consider in screening

For screening to be successful it is important to understand the behavioural factors involved in screening. These factors include psychological consequences of taking part in screening, communication about cervical cancer and the screening process and issues affecting participation. Screening is targeted at the asymptomatic populations potentiating the significance of negative consequences. Potential participants in a screening program must therefore make an informed decision on taking part or not taking part. These women must receive accurate information on the benefits and risks of screening prior to participating. They must have knowledge about cervical cancer and their perception of the risk of getting it. Women must have accurate knowledge on cervical cancer in general. A survey by Pitts and Clarke in England in 2002 among university female staff showed 70% of the respondent had never heard of HPV infection. The mean age for the respondents was 40 years old (Pitts et al, 2002). Different studies have reported similar limited levels of knowledge on cervical cancer and its risk factors (Adanu, 2002, (Gichangi et al, 2003). The study by Pitts et al however showed that respondents had a good understanding of screening process. Knowledge on the implication of an abnormal result is very important. Anxiety has been found as one of the reasons women do not screen. This stems out of patients having poor knowledge of the disease (Agurto et al, 2004). Adherence to follow-up appointment after an abnormal result varied between 53% and 75% (Bankhead et al, 2003). While it important to have good numbers screening, follow-up of patients with abnormal results is also extremely important. A study in the Amazon part of Peru showed that only 25% of the women received appropriate follow-up care after referral (Gage et al, 2003).

The main determinants of women taking part in screening must be well investigated into. These will vary from one setting to the next. Socio-demographic factors like age, socioeconomic status, and marital status, place of residence, ethnicity, health status and health care system organization are some of the determinants of taking part in screening. Younger women are more likely to screen than older women (sankaranarayanan et al, 2003). Women of low income status are very unlikely to seek screening services. One of the reasons for not going for follow-up visits in Zambia is a like of transport money (Mwanahamuntu et al, 2008). A study by Calle et al showed that 19% women below the poverty line had never screened compared with 5.8% of women who were above the poverty line (as cited by IARC, 2005). Single women were less likely to attend screening services compared to married, divorced and widowed women. Research has shown that women from urban areas are more likely to screen than women from rural areas though the picture is different in some European countries. The evidence on influence of ethnicity is not
conclusive. Women who have contact with the health care facilities are more likely to screen regardless of the service they are seeking (IARC, 2005).

Chapter 5: Diagnosis and Treatment

To make a definitive diagnosis after an abnormal or positive result further investigations are needed. Histopathological diagnosis is the standard for diagnosing somebody with cervical cancer. This is done through biopsy, with aid of colposcopy.

In the VIA method, after an abnormal result which is deemed precancerous by the nurse and meets criteria for cryotherapy, treatment is done within the same visit. Those with lesions ineligible for cryotherapy are referred for further evaluation by the gynaecologist (Pfaendler, 2008). It is not clear whether lesions with CIN1 should be treated or not. A study by Saw et al, showed that women with CIN1 who were followed up for 5 years, 34% had disease regression to normal, 11% had progression to CIN2 and 3 and about 55% had persistence disease (Saw, 2008). CIN2 has an average progression to carcinoma in situ of 22% and CIN3 about 12% (Ostor, 1993).

Women with HIV have an elevated rate of persistent HPV infection. They also have a higher rate of high grade lesions (Parham, 2006). There also seems to be a high recurrent and persistence of CIN2 and 3 after treatment (Holcomb, 1999). The whole purpose of treating histologically confirmed preinvasive CIN disease to effectively remove the lesion. This is done either by destruction (cryotherapy) or excision (LEEP). The choice of treatment depends on the extent and location of the lesion, the qualification and experience of provider and the cost mostly with CIN2 and 3 must be reviewed up every six months until regression to normal or progression of the abnormal findings. After LEEP women should be reviewed in 2-6 weeks. Women are asked to abstain from sexual intercourse while the healing of the cervix is taking place.

Microinvasive carcinoma is may be asymptomatic but invasive cervical carcinoma is usually symptomatic. Women present to the health providers because of symptoms.

Staging of cervical cancer is based on clinical evaluation. The evaluation assesses the extent of the cancer beyond the cervix. Extra routine investigations like renal function tests, X-ray, cystoscopy, etc supplement the staging.

Treatment of invasive cancer in Zambia is by surgery and radiation depending on the staging.

Both surgery and radiation are available in Zambia. Women with invasive cancer ≤ stage IIA are referred to UTH for surgical management. Patients found to have invasive cancer ≤ stage IIB are referred for radiotherapy. The first Cancer Hospital was open in Zambia in 2006 for radiotherapy services. It is based at the main referral hospital, UTH, in Zambia. The highest numbers of patients needing radiotherapy are cervical cancer patients
Review of cervical Cancer screening program in Zambia

accounting for 32% of patients referred. The radiotherapy department operates on a cost-sharing basis. Patients have to contribute $600 towards their treatment (IEAC, 2007). This is still out of reach for most Zambians. See Appendix1 for FIGO staging of cancer.

Palliative Care Services

Palliative services are an integral part of cervical control programmes. Palliation is meant to alleviate suffering and improve the quality of life for the patients and their families. The services include spiritual, physical and psychosocial support. At least one in 200 individuals needs palliation every year in Africa (WHO, 2007). At least 80% of patients with cancer will suffer from pain in the course of the ending phase of their disease (Singer, 2000). A needs assessment done in Uganda showed that 22% of the study sample was terminally ill cancer patients. The core needs identified in this study for terminal phase of disease were counseling, relief from pain and other symptoms like vomiting and diarrhoea, and financial aid for basic needs like food, shelter, children’s school fees, etc. The participants in this study preferred to be cared for at home. The reasons for this were it was cheaper, want to be surrounded by family, had privacy and care at home was adequate (Kikule, 2003). In Zambia, there is a palliative care unit at the UTH were patients needing palliation are referred. Those who wish to be cared for at home are supplied analgesics (opiates) on outpatient basis. Surgical interventions are also done like intestinal diversion if they are deemed to improve the quality of life (Mwanahamuntu, 2008). Management of advanced cervical cancer is multidisciplinary effort. It involves the departments of surgery, obstetrics and gynaecology, social welfare, community, religious groups and the families involved. Very little data is available on palliative care in Zambia.
Chapter 6: Cervical Cancer Screening Program in Zambia

6.1 Background

Screening is a difficult task to achieve in low income countries. There are urgent competing health needs of great significance particularly HIV, malaria and tuberculosis. The poor health system is another hurdle which makes screening a great challenge. This decade has seen enormous resources been committed to the fight against HIV. The resources have been towards treatment and care, and prevention of HIV/AIDS (kamwi, 2006). Zambia is one of the beneficiaries of these resources. This means that thousands of women who were unable to access ART in Zambia now have access. The ARVs will prolong the life of the expectancy of these women saving them from premature death. A considerable number of HIV infected seeking ART have high risk HPV infection as was seen by study by Sahasrabuddhe et al (Sahasrabuddhe, 2007). A study done by Parham et al showed that over 50% of HIV positive women have severe cervical abnormalities (Parham et al, 2006). It is with this background the Zambia cervical cancer program was launched.

As early as 2001, a collaborative team was formed comprising of members from Ministry of health working under Lusaka Urban Health district Management Team, University Teaching Hospital and the Centre for Infectious Disease research in Zambia(CIDRZ), a local non-governmental organization affiliated to University of Alabama. The main responsibilities of this team was to advocate for funding and support of the program, facilitate its acceptance in the community and by the government and offer technical support (Mwanahamuntu, 2008).

One of the main tasks of the team was to choose a screening test. The screening test had to be economical with optimal sensitivity and specificity and appropriate for other health workers to do not just doctors. Visual inspection with 3%-5% acetic acid was settled on as the screening test (mwanahamuntu, 2008). This test was chosen after looking at screening from various angles. Cryotherapy was to be used for treatment of precancerous lesions. A randomized trial done in India using VIA showed a reduction of 35% in incidence of invasive cervical cancer in intervention villages (sankaranarayanan, 2004). VIA and cryotherapy service in a single visit has been endorsed by WHO and Alliance for Cervical Cancer Prevention (ACCP) as prevention strategy for resource limited countries, where testing is based on cytology is not feasible.

Pap smear which has been used for many years as a screening test was not favorable for the Zambian setting. It requires a well structured health system. In Zambia pap smears are collected by physicians. As stated in the background, Zambia has a severe shortage of doctors. The laboratory services are not well developed in Zambia.
Apart from choosing the test, the team also came up with a screening policy. The screening policy consisted of the following;

**6.2.1 Age to start Screening**
Any woman who is sexually active is eligible for screening (Parham, 2008).

**6.2.2 Age to stop screening**
Screening continues as long as a woman is sexually active.

**6.2.3 Target population.**
With the high prevalence rate of HIV in the country, HIV infected women are the main target population. However any woman is eligible for screening regardless of status.

**6.2.4 Frequency of re-screening**
Women with negative VIA test results are followed-up annually *Algorithm of care in annex*. The program is funded by CDC through PEPFAR funds. It is directed by two directors who are qualified and experienced gynaecologists. One is a fulltime Zambian gynaecologist and the other is a U.S gynecologic oncologist, also an honorary professor in department of obstetrics and gynaecology UTH.

**6.3 Training**
After choosing the screening test, training was implemented for various cadres of the program. Nurses were trained to do VIA and cryotherapy. The nurses were all licensed under the Nursing Council of Zambia. The didactic training was for three days. This training consisted of basic knowledge on cervical cancer and the requirements for establishing a cervical cancer prevention program. After the class room training the nurses do an eight week practical training. The practical training consisted of VIA, digital cervicography and cryotherapy performance, management of cryotherapy complications and indications for referral. Each nurse was required to perform a minimum of 100 VIA examinations, take 100 digital cervicograms, and perform 35 cryotherapies and 10 distance consultations. After this training the nurses were qualified to run screening centres in PHC facilities. The initial training was facilitated by the gynaecologists in charge of the program. Sixteen nurses have so far been trained in the period under review. These nurses have in turn become trainers of other nurses.
Apart from training nurses, physicians were also trained in LEEP a service which was previously not available in Zambia. The training consisted of lectures and practical work. The physicians were required to observe 10 LEEP procedures done by experienced gynaecologists. After observation they performed 25 LEEP procedures under direct supervision, then 25 extra procedures with gynaecologists within close proximity. On completion of
Review of cervical Cancer screening program in Zambia

these 50 LEEP procedures the training was considered complete. A certificate in LEEP provision and management of its complications was awarded (Mwanahamuntu, 2008).

6.4 Community Sensitisation
Prior to opening a new clinic at the primary health facility the senior project staff meet the community members and key stakeholders to explain the problem of cervical cancer in their clinic catchment area. These discussions are unroused and in depth with use of visual aids. Presentations question and answer sessions and distribution of educational materials in preferred language is done in these meetings.
Apart from the meetings with community members, electronic media is also used. Educational programs on cervical cancer in general are conducted on radio and television. Any member of cervical cancer screening program can appear on the program. It has been noted that nurses and women who have screened before seem to make the most impact.
Continuous education in the community is done by peer-educators. The first group peer educators for program were trained by experienced peer educators from the HIV treatment and care program in the respective clinics. The peer educators came from within the community. The roles of the peer educators include:

- Talking to people in the community and potential clients at the ART clinic and other medical clinic at the local clinic on the cervical cancer screening service.
- Distribution of educational materials on cervical cancer and the program within the clinic and the clinic catchment area.
- Administer questionnaires to clients who are unable to read and/or write when the nurses are busy.
- Be in attendance during community- based drama presentations to answer any questions that may arise.

Drama groups from within the community were also used to announce the availability of screening services at the respective clinic. This was done through songs, street plays and skits.
Staff at the clinic is equally sensitised prior to setting up the screening service. Meetings are planned through the sister in charge who is the administrative head of the clinic with huge clinic and community influence. This is to generate support for the cervical cancer screening service. Cervical cancer prevention is discussed in these meetings. The critical role of staff is emphasized and importance inviting women for screening from their different departments (Mwanahamuntu, 2008).

6.5 First patient visit.
At the first visit, the nurse and the peer educator explain to the patient the procedure and the follow-up care in the patient’s language of preference.
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There is a short pamphlet written at a Zambian sixth grade level availed to the patient in their language of preference. The pamphlet has multiple photographs to ease patient’s understanding. After the procedure the nurse shows the patient the digital photograph (cervigram) of her cervix to explain the results and treatment decisions. These photographs and follow-up ones are shown to patient at later visits to help her understand (Mwanahamuntu, 2008).

CHAPTER 7: RESULTS

In January 2006, the VIA-based cervical cancer prevention program was established to function as a routine health care service. This thesis will review the program between January 2006 and October 2007. 14 cervical cancer prevention clinics were established in this period. Ten clinics have been established in the capital city Lusaka, 4 clinics in the rural areas and referral clinic at university teaching hospital. The clinics have been established on the existing HIV care and treatment infrastructure, targeting HIV-infected women accessing ARVs (Mwanahamuntu, 2008).

A total of 8823 patients have been screened in the initial 22 months of the service. 3661(41.5%) were HIV infected, 2534 (28.7%) were HIV uninfected and 2628 (29.8%) of unknown HIV serostatus. A total of 3855 women had positive test when VIA was done. 26.9% of all the women screened were eligible for cryotherapy and it was done by the nurses in the primary health facilities. 1477(16.7%) women were referred to the gynaecologists for further evaluation at the referral clinic at UTH. 769 women had cervical biopsy or LEEP done by the gynaecologist. 149(1.7%) of the women the women screened had histologically determined and/or clinically determined cancers. 86 women had microinvasive cancers (Pfaendler, 2008).

<table>
<thead>
<tr>
<th>Women screened using VIA</th>
<th>HIV Infected</th>
<th>HIV Uninfected</th>
<th>Unknown serostatus</th>
</tr>
</thead>
<tbody>
<tr>
<td>8823</td>
<td>3661</td>
<td>2534</td>
<td>2628</td>
</tr>
<tr>
<td>100%</td>
<td>41.5%</td>
<td>28.7%</td>
<td>29.8%</td>
</tr>
</tbody>
</table>
### Table 8: Outcome of VIA at PHC

<table>
<thead>
<tr>
<th>Women screened</th>
<th>VIA positive</th>
<th>VIA Negative</th>
<th>Eligible for Cryotherapy At PHC</th>
<th>Referred for Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>8823</td>
<td>3855</td>
<td>4968</td>
<td>2378</td>
<td>1477</td>
</tr>
<tr>
<td></td>
<td>43.7%</td>
<td>56.3%</td>
<td>61.7% (of VIA positive), 27% (women screened).</td>
<td>38.3% (VIA positive), 16.7% (women screened).</td>
</tr>
</tbody>
</table>

### Table 9: Follow up care

<table>
<thead>
<tr>
<th>Women Referred</th>
<th>Kept appointment</th>
<th>Didn’t keep appointment</th>
<th>Other Gynaecological Conditions (No histological evaluation)</th>
<th>LEEP done</th>
</tr>
</thead>
<tbody>
<tr>
<td>1477</td>
<td>875</td>
<td>602</td>
<td>106</td>
<td>748</td>
</tr>
<tr>
<td></td>
<td>59.2%</td>
<td>40.8%</td>
<td>12.1%</td>
<td>8.4% (women screened)</td>
</tr>
</tbody>
</table>

### Table 10: Outcome of LEEP

<table>
<thead>
<tr>
<th>LEEP Done</th>
<th>Abnormal Histological</th>
<th>Normal Histological</th>
</tr>
</thead>
<tbody>
<tr>
<td>748</td>
<td>448</td>
<td>300</td>
</tr>
<tr>
<td>100%</td>
<td>59.9%</td>
<td>40.1</td>
</tr>
</tbody>
</table>
Review of cervical Cancer screening program in Zambia

Table 11: Disease prevalence according to HIV serostatus

<table>
<thead>
<tr>
<th>Pathologic diagnosis</th>
<th>Overall</th>
<th>Proportion of pathologic diagnoses by HIV serostatus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HIV seropositive</td>
</tr>
<tr>
<td>CIN I</td>
<td>155</td>
<td>63%</td>
</tr>
<tr>
<td>CIN II/III</td>
<td>144</td>
<td>74%</td>
</tr>
<tr>
<td>Invasive cancer</td>
<td>149</td>
<td>60%</td>
</tr>
</tbody>
</table>

Source: Pfaendler et al, 2008

One of the determinants of the success of a cervical screening program is the follow up of women with abnormal/positive results. Once a woman has positive test she has cryotherapy done if she is eligible. If she is ineligible for cryotherapy but has positive test she is referred to UTH for further evaluation by gynaecologists. Women referred to UTH are given an appointment within one to two weeks. The referral is done by the nurses. The women go directly to the cervical cancer unit after opening a UTH medical record. 1477 patients were referred to UTH for further evaluation, 875(59.2%) kept their appointments meaning slightly above 40% missed their appointments. The patient tracking system is underway. This will help to track patients who miss their appointments. Out of these 875 women, 106 did not need histological evaluation. Twenty one women had clinically evident invasive cervical cancer. LEEP was done on 748 women. Out of 748 women, 465 (62.2%) were HIV positive, 116 (15.5%) and 167(22.3%) of unknown HIV status at time of screening (mwanahamuntu, 2008).

7.2 Referral System

Patients with a positive test and judged ineligible for cryotherapy by the health provider who did the VIA are referred to the gynaecologist at the Gynaecological cancer prevention unit at UTH. UTH is the main referral center. Patients are seen within 1-2 weeks after referral.

The gynaecologist at UTH repeat the VIA when patient goes for appointment. LEEP is done as per indication and cervical biopsy is done dependant on findings by gynaecologist. The specimens collected from the LEEP and biopsy are then sent to the pathology unit for histopathologic diagnoses which are reported based on WHO classification. The results are ready within a month. Clients found with stage≤stage 2A invasive cervical cancer are referred to
Review of cervical Cancer screening program in Zambia

the Gynaecology department of UTH for appropriate surgical management. Women with >2B are referred to the radiotherapy hospital. Women with cancers that do not respond to surgery or radiotherapy are referred to the Palliative Care Unit as needed. Those who opt not to be admitted to the palliative care unit are opiates as outpatients. Occasionally urinary and intestinal diversions are done to improve the quality of life.

See appendix 2 for algorithm of care in Zambia

7.3 Quality Assurance

The biggest challenge of VIA is the subjective nature of the test. It is dependent on the provider. Cervigrams of all patients screened are obtained daily. Those the nurse is not sure about or an indeterminate result are immediately uploaded onto a laptop and emailed to consultant gynaecologist for review. This is followed by a text message or a phone call informing the consultant of a pending consultation. This is done while the patient is still in clinic. If there is no telecommunication possible that day, the images are stored on a USB and sent to the consultant gynaecologist the following day. The program has weekly clinical cervigram review in which all the nurses from the clinics are required to participate. In these meetings the nurses make display cervigrams of all the patients seen in the previous week and give basis for their management decisions. Any differences in management decision between the nurse’s and the expert consultant in attendance ruled upon by the consultant. Included in these meetings is cervigram-histology correlation review. This is meant to assist the nurses understand the different ways of visual manifestation of varied types of underlying histology for example normal (Nabothian cyst, cervicitis, endocervical polyps, inflammation, etc.) and abnormal (CIN 1, CIN 2, CIN 3, microinvasive and invasive cancer).

Biannually, a seminar is held for the project staff to discuss latest findings in cervical cancer prevention.

An electronic database has been created to track enrollment, follow-up and referral for women in the program. Paper records are used as back-ups to the electronic medical records. This is aimed at improving the quality of follow-up of patients.
7.2 Discussion
This chapter will discuss the screening services based on the results presented in the previous chapter.

7.2.1 Principles of Screening
The first objective of this review was to assess whether the program meets the screening principles as outlined by WHO. See annex 7 for principles of screening.
Cervical cancer is a major public health problem globally. It accounts for 12% of all cancers in women. It is the second commonest cancer in women worldwide and the most common cancer among women in the developing world. 80% of all new cases occur in the developing world. Zambia has the second highest incidence in the Sub-Saharan Africa and the sixth highest in the world (Parkin, 2005). Annually, over a thousand women die from cervical cancer in Zambia (WHO, 2007).
The natural history of cervical cancer is well understood as described above in the background information. HPV is the necessary cause of cervical cancer but not a sufficient cause. There are other co-factors which are necessary for the progression from HPV infection to cervical cancer (Walboomers, 1999). Invasive cancer develops from pre-existing to intraepithelial dysplasia at slow progression as precursors. HSIL are the direct precursor of invasive squamous carcinoma, over one third to a half of the HSIL may progress to cervical cancer in 10-15 years. Most of the LSIL regress spontaneously (Sankaranarayan, 2005).
It was difficult from this review to determine the acceptability of the test by the population. The screening service is free at all points of delivery. This reduces the economic burden and improves the acceptability of the test. However there are many other determinants to screening as been outlined in section discussing behaviour consideration during screening. Research will need to be done to assess the other aspects of acceptability, like sociocultural factors, of the test.
Cryotherapy is done at the local clinic depending on the findings. Those with abnormal results but do not meet the criteria for cryotherapy are referred for further evaluation at UTH. LEEP can be done for all suspected pre-cancerous lesions. Those with invasive CC are referred for surgical or radiotherapy management as outlined in chapter on treatment and diagnosis.
The screening policy states that any woman who is sexually active or has had sex before is eligible for screening. HIV infected women are the main
Review of cervical Cancer screening program in Zambia

targets for the programme. They have a higher risk of developing cervical abnormalities though screening is open to all women regardless of status. The program is intended to be ongoing though this dependant on the availability of funds from external donors. Screening is supposed to be an ongoing procedure or it should not be started. Hence the need for internal funding.
Based on research done in other LIC in other countries VIA was found to be the most suitable test for screening in Zambia. VIA procedure has less demand on the health care system. The procedure can also be done by non physicians. No advanced laboratory infrastructure needed.

7.2.1 Follow- up care
The other objective of this review was to assess the follow up care of patients with abnormal results. High attendance for screening is important because a screening program must have a high coverage. However, follow up of patients with abnormal results is equally important. Failure can occur at different levels in the process of care. See annex 9 for the continuum of care. Out of 1477 patients referred for further management in this period only 875 went for further evaluation meaning about 40% were lost to follow up. This is huge number to be lost to follow up though some studies have shown figures up to 49% as failing to receive follow up care (Yabroff, 2000). Some of the reasons given for missing appointment according to Pfaendler et al were:
• Transport costs, $5 for those within the capital and more than $50 for those in the rural areas. For a country were 68% are living below the national poverty line this beyond reach of most Zambians.
• Sexual partners were not willing to abstain for up to six weeks after LEEP should the procedure be done.
• Fear of the procedure (LEEP) (Pfaendler, 2008).

A study by Yabroff et al shows that between 7% and 49% of women referred for further evaluation fail to receive the follow up care (Yabroff, 2000). Studies concentrate so much on attendance rather compliance to follow up. For most women in developing countries the involvement of the husband in the process of screening and treatment helps improve adherence to appointment. Study in Peru showed that women who social support was most likely to attend screening and compliant to follow up. Husband’s support was a determining factor in attendance of cancer screening services Women are also mostly to screen if they have friends who have screened before (Winkler J, 2008). Therefore the programme must start looking at programmes which can integrate men.
Kaplan et al in their study found that computerized follow up, transportation and financial incentives only had limited increase in compliance to follow up

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visits (Kaplan, 2000). The issue of transport money might not be a major contributor for adherence to follow up care since India and Zambia are both LIC countries with high cervical cancer burden. In other studies women seem to have “fear of cancer” rather than fear of the procedure (Agurto, 2004). Mandeblaat et al showed in their study that patient who were hopeful and not living in denial were more likely to screen (Mandeblaat, 1991) This fear is probably due to lack of understanding of cervical cancer in general. A study in India showed compliance for diagnostic investigations of 79% among women referred to cervical cancer unit screened at primary health facility. Increasing age, illiteracy, women working as manual labourers, screening for the first time, having dual morbidity (cervical cancer and breast cancer) and speaking another language other local language were predictors of poor compliance for diagnostic investigation follow up. Among non-compliant screen-positive patients husband’s opinion was found to be of great importance. The patients in this study were accessing all follow up care up to treatment if required free (Dinshaw K, 2008). One of the reasons for non-compliance is lack of support from the husband.

From the various studies including Zambia partner support is a predictor of poor compliance. Interventions into improving adherence to follow up must include partners.

7.2.3 Sustainability of programme

Financial sustainability
The program is funded by CDC through PEPFAR funds. The Zambian government provides space in the primary health facilities were screening is carried out. The program is therefore entirely dependant on external funding. The government has many urgent health needs prioritizing becomes a challenge. The sustainability of the project is a challenge. Government needs to slowly start funding the program. This will however only be possible if CC is identified as a priority health need by government.

Technical sustainability
Zambia physicians and nurses are continuously being trained in VIA, cryotherapy and LEEP. These doctors and nurses in turn train others. The approval by the University of Zambia senate of the application for cervical cancer prevention program to be an official rotation for Zambia medical students and postgraduates in Department of Obstetrics and Gynaecology. The government must also ensure that medical students rotating through this unit are assessed on both the practical and theory aspect. This will ensure that these students will perform the procedure in the district hospital. MOH has also agreed to the development of a curriculum that will lead to certificate in cervical cancer prevention for nurses. This will be at par with certificates like nutrition and midwifery. The above measures will help with technical sustainability of the program.

Organisational sustainability
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The ZCCSP is run vertically and has its own staff. The nurses running the various screening centres in the PHC are fully employed by CIDRZ and not GRZ. The program is modeled after the HIV care and treatment services offered by CIDRZ in over 53 PHC facilities by operating in the PHC facilities. The HIV program has managed to enroll over 100,000 people (Mwanahamuntu, 2008). Working through the PHC will ensure that many women are reached who come in contact with health facilities. The doctors seeing patients who are referred to UTH for further evaluation are GRZ employed. To make the program sustainable would mean the government having to pay the nurses employed by CIDRZ and integrating them into the government health delivery system. The program having its own staff may also be seen as a foreign project by local clinic staff thereby not have their support. Though they are informed about it they are not involved in the day to day running of the screening services. It is prudent to allow the nurses from the government to train in VIA and cryotherapy and rotate through the screening department on certain days of the week. This needs to be tabled with the PHC staff. Interest in screening for CC must be generated and the program must viewed like any other routine service offered, for example, youth friendly services, family planning, etc. These are preventive programs so is CC screening. The fact that the program was developed by Zambian doctors in collaboration with American counterparts gives some form of local ownership.

Sociocultural sustainability.
Behavioural aspects of screening are very important. One of the reasons for non compliant to follow up care is lack of support from partner. This shows that there is a social aspect to the screening process that is not acceptable. This could be due to lack of knowledge among the partners or the patients giving the message to partners. It goes to show that women cannot make an independent choice without social support. Therefore the decision to screen and obtain follow up care has sociocultural factors which must be addressed. Though the HIV positive women are the target of the program HIV negative women have screened meaning stigma is not an issue. The screening services are located in the public health centres with a referral at the UTH. To avoid stigma of the patients coming for screening, the screening clinic is a distance from the ART clinic but within same health facility.

From the close to 60% of women who screened in the period under review were either HIV negative women or those who did not know their status. Showing that the program is accessible to other women other HIV infected women.

Political Sustainability.
Stakeholders’ meeting was held in the community before the beginning of the program. The approval by MOH for a certificate in cervical cancer prevention shows a certain level of political will. The program operating in the PHC with the full approval of MOH is a sign of political approval. However
there has been little involvement by local politicians in the fight against CC, later support of the program. The uneven distribution of health workers in the country is a concern. North Western province only has 5 registered midwives even as the program expands these are issues to be looked into. See table 2. To integrate these nurses into the screening program when they also need to attend to urgent curative services is a challenge. Political will is needed to solve the human resource crisis for health.

7.2.3 Over treatment and Over diagnosis

Over treatment is a concern in VIA. The method is very subjective. Quality control is not standardized. This can lead to unnecessary medical intervention. Out of the 748 people who had LEEP only 448 had abnormal histology. This meant 300 were over treated by LEEP. This has both human and financial cost implications for the patient and the program to have 40% unnecessary referrals. The psychological impact of an abnormal result must also be considered. Excision can also lead to cervical incompetence if large parts of the cervical are removed. This may lead to complications like preterm deliveries. The procedure can also lead to bleeding during and after the procedure and vaginal infections (Pfaendler et al, 2008). Cervical stenosis is possible though not frequently reported is a complication of LEEP. This can in turn lead to infertility or menstrual problems (IARC, 2005). Screening is done among healthy people therefore diverting the much needed human and financial resources from urgent competing needs. The costs must therefore be evaluated against the benefits to the nation. CIN1 lesions were treated even though 60% CIN1 can regress in immunocompetent individuals. The high rate of false positives (40%) can occur at time of evaluation by gynaecologist or in the laboratory during histopathology evaluation. Therefore more quality control measures are needed. The country has a shortage of laboratory personnel. See annex 9 on cancer care continuum. Zambia has one cytopathologist in the public sector for the whole country. One of the reasons of choosing VIA is because it is not so dependant on laboratory facilities. Yet if a high percentage of biopsies will be false positives then the work of the laboratory will be increased unnecessary. This will defeat the very purpose of using VIA. The limited laboratory personnel will not cope with high number of specimens and backlog of results will start.

CHAPTER 8

8.1 CONCLUSION

The use of alternative method of screening (VIA) for a low income country like Zambia has availed Zambian women a chance to screen.
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However cervical cancer screening to succeed in Zambia the multiple factors involved must be carefully considered. The position of a woman in the Zambia society puts her at a disadvantage to make an informed decision concerning her health. Therefore the decision to screen and go follow up care is not entirely hers alone. The fact that 40% of the women cannot attend follow up care means there are sociocultural factors influencing screening must be looked into.

The very omission of any cancer control strategies in the policy documents like FNDP under health shows that still government needs to identify cervical cancer and prioritise it in their agenda. Women’s health need to be recognized and given due attention. The reproductive health policy must be finalized and implementation started.

The screening policy should be revisited. Annual follow up of women in a country with limited resources is not sustainable. Though the program is currently wholly funded by the CDC, the recommendations by WHO is that every woman in low income countries should at least be screened once in her lifetime to screen.

The financial sustainability of the programme is wholly dependant on funding from outside. This is a big challenge to the program. The government needs to gradually start funding the program.

The high rate of false positive results may defeat the very essence of screening using VIA. Quality control at every step of the screening process will lead to improved quality of service.

8.2 RECOMMENDATIONS
Following this review the following recommendations are made in line with policy, practice and research.

8.2.1

In terms of policy making the following recommendations are made:

The Zambian government needs to identify and prioritise CC issues in the country.

a) A national symposium on CC involving researchers, scientists, policy makers, health care service providers, community based organizations(CBOs), civil society, Faith Based organizations(FBOs) must be convened to help look at were we are with cervical cancer control in the nation and were we want to go. This will help identify priority areas in cancer control. It will also help to set a multisectoral approach to cervical cancer control since all stakeholders will be included.

b) Advocacy is needed for CC. In the FNDP for Zambia cancer is not even mentioned under health. The members of parliament sitting on the population and development committee which looks into reproductive health issues must play a key role in legislation issues concerning cancer. The ministry of Gender and development must particularly look into cervical cancer control in collaboration with the ministry of Health. The ministry of
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Gender and development should look into the sociocultural aspects of cervical cancer control. The gender disparities in Zambia make it difficult for women to make informed decisions.

d) Implementation of the national reproductive health policy is needed. Cervical cancer prevention and treatment are outlined in the policy. The policy still remains in first draft form. The policy needs revisiting since the draft was done over 8 years ago. The burden of diseases has changed a lot over the last years. HPV must be included in the STI policy for Zambia. The government must start lobbying for subsidized cost of HPV vaccines together with other resource limited countries. The Expanded Program of Immunization(EPI) is well spread in the country with good population coverage. This program could be used for HPV vaccination when available. The steps outlined under primary prevention by UNIFEM will help to make HPV vaccines accessible.

8.2.2 To promote adherence to follow up care after abnormal screening results among women:

a) The ZCCSP needs to integrate partner oriented programs. Partner support groups which will meet under the direction of community department should be established. These will ensure males are sensitised about cervical cancer and screening services available. Men who have had wives screened would be of encouragement to other. Experiences can be shared in these meetings. Male involvement is key in the screening process. Attendance for screening is important but adherence to follow up treatment is key in reducing morbidity and mortality.

b) The computer tracking system will be of great help for monitoring and evaluation of patient’s adherence to follow up care. The program must also define the time for a patient to be classified non-adherent. Priority should also be given to patients referred from outlying areas and with urgent medical needs. This will help reduce opportunity costs for patients from outlying areas.

c) Community participation needs to be more than informative. Finding stakeholders in the community is important not just outreach workers. These include religious leaders, traditional healers, teachers, nurses, traditional instructors, political leaders. These need to be involved in purposeful meetings and continuous meetings. They need to be updated on the findings. Successes and challenges of the programmes shared. Their input in brainstorming the way forward is highly needed. This will make sure information filters into the community through a mouthpiece they know and respect.

d) while operating within the primary care health care facilities is highly commendable. This brings the services to the grass root. However having staff from CIDRZ running the project reduces ownership by the public health facilities workers. The project will regarded as foreign program. Having staff from the clinic rotating a few hours in the cervical screening clinic will help
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further integration. The future should be finally have the workers from the
government running the services just like family planning services, youth
friendly services are integrated. The model ART programme uses mostly the
staff from the clinic to attend to patients. The ART clinic is part of other
routine services offered at the clinic.

8.2.3
a) Qualitative research needed on the sociocultural influences on screening
and follow up care after a positive VIA result. The non-attendance for
screening services and follow up care needs more evaluation.
Community sensitizations have been done but adherence is still low. This
means there are other factors at play which needs further research.
Interventions can then be targeted towards the influences found in the
research. It is important to study the health-seeking behaviour of women in
the community towards preventive medicine rather than curative.

b) A quantitative research on the women who seek screening services and
those who do not would give insight on possible barriers to screening in
terms factors such as sociodemographic.

c) Research on HPV genotypes among HIV positive and negative women
must be carried in readiness for HPV vaccination implementation.

d) With the high rate of false positives seen the studies need to be done on
sensitivity and specificity of the VIA as a screening test.
References:


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Howard M, Linda Ahdieh, Stewart L, Massad K, Watts H and Melnick S. The effect of highly active antiretroviral therapy on cervical cytological
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ANNEXES

Annex1: Summary of Key Health Indicators

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<tr>
<td>Life expectancy at birth</td>
<td>45</td>
<td>46.8</td>
<td>51.9</td>
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<tr>
<td>Infant Mortality rate per 1,000 births</td>
<td>107</td>
<td>109</td>
<td>95</td>
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<tr>
<td>Under five mortality per 1,000 births</td>
<td>191</td>
<td>197</td>
<td>168</td>
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<tr>
<td>Maternal Mortality per 100,000 live births</td>
<td>N/A</td>
<td>649</td>
<td>729</td>
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<td>HIV seroprevalence rate⁷</td>
<td>23</td>
<td>20</td>
<td>15.6</td>
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Source: Zambia Demographic Health Survey 1992; 1996; and 2001/2002

¹ For 1992 and 1996 Antenatal surveillance data was used to estimate the national seroprevalence of HIV/AIDS among the adult population whereas for 2001/2002 the HIV prevalence was estimated from population-based surveys.
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Annex 2: Political Map of Zambia

Annex 3: Annual incidence and death from cervical cancer in women from developed and developing countries.

Adopted from Globocan, 2002. Ferlay et al.
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Annex 4: Criteria for Cryotherapy:
Acetowhite lesion originating in the transformation zone that does not meet LEEP criteria

Annex 5: Criteria for Ineligibility for Cryotherapy

1. Incomplete visualization of acetowhite lesion
2. Acetowhite lesion occupying >3 quadrants or >75% of the transformation zone
3. Acetowhite lesion unable to be entirely covered by the tip of the cryoprobe.
4. Presence of a cervical lesion (e.g. polyp) or anatomic defect (e.g. fibrosis) that prevents distinct contact between acetowhite lesion/transformation zone and cryoprobe.
5. Lesion suspicious of cancer.

Annex 6: Criteria for LEEP:
Acetowhite lesion with one or more of the following characteristics:
- In 3 or more quadrants (≥75%) of the transformation zone
- Disappearing into the os (internal margin unable to be visualized)
- Opaque and/or thick
- Mosaicism
- Punctations
- Atypical vessels

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1. The disease must be an important public health problem.
2. The natural history of the disease must be understood.
3. There must be an identifiable or early symptomatic stage of the disease.
4. There should acceptable treatment for patients found with disease.
5. The tests should be acceptable to the population.
6. Facilities for diagnosis and treatment must be available.
7. The cost of screening must be acceptable.
8. There must be a policy on whom to treat and whom not to treat.
9. Screening must be an on-going process and not a one off project.
10. There should a suitable test or examination.

Source: Junger and Wilson, 1968.
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Annex 8: FIGO Staging of Cervical Cancer.

**Stage I**
Stage I is carcinoma strictly confined to the cervix; extension to the uterine corpus should be disregarded. The diagnosis of both Stages IA1 and IA2 should be based on microscopic examination of removed tissue, preferably a cone, which must include the entire lesion.

**Stage IA:** Invasive cancer identified only microscopically. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm.

**Stage IA1:** Measured invasion of the stroma no greater than 3 mm in depth and no wider than 7 mm diameter.

**Stage IA2:** Measured invasion of stroma greater than 3 mm but no greater than 5 mm in depth and no wider than 7 mm in diameter.

**Stage IB:** Clinical lesions confined to the cervix or preclinical lesions greater than Stage IA. All gross lesions even with superficial invasion are Stage IB cancers.

**Stage IB1:** Clinical lesions no greater than 4 cm in size.

**Stage IB2:** Clinical lesions greater than 4 cm in size.

**Stage II**
Stage II is carcinoma that extends beyond the cervix, but does not extend into the pelvic wall. The carcinoma involves the vagina, but not as far as the lower third.

**Stage IIA:** No obvious parametrial involvement. Involvement of up to the upper two thirds of the vagina.

**Stage IIB:** Obvious parametrial involvement, but not into the pelvic sidewall.

**Stage III**
Stage III is carcinoma that has extended into the pelvic sidewall. On rectal examination, there is no cancer-free space between the tumour and the pelvic sidewall. The tumour involves the lower third of the vagina. All cases with hydronephrosis or a non-functioning kidneys are Stage III cancers.

**Stage IIIA:** No extension into the pelvic sidewall but involvement of the lower third of the vagina.

**Stage IIIB:** Extension into the pelvic sidewall or hydronephrosis or non-functioning kidney.

**Stage IV**
Stage IV is carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.

**Stage IVA:** Spread of the tumour into adjacent pelvic organs.

**Stage IVB:** Spread to distant organs.

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Types of Care

- Risk Assessment
  - Age
  - Family Hx
  - Exposure Hx
  - Genetics
  - Lifestyle
  - Screening Hx

- Primary Prevention
  - Lifestyle counseling
  - Chemoprevention

- Detection
  - Screening
  - Asymptomatic
  - Symptomatic

- Diagnosis
  - Imaging
  - Biopsy
  - Repeat Exams
  - Laboratory Tests
  - Other Appropriate Procedures

- Cancer or Precursor Treatment
  - Excision
  - Surgery
  - Radiation
  - Adjunct Chemoh
  - Palliation

- Recurrence Surveillance
  - Testing
  - Follow-up Care
  - Palliation
  - Survivorship Care

- End-of-Life Care
  - Palliative Care
  - Advanced Care
  - Planning
  - Bereavement Support

Potential Failures During the Processes of Care

- Failure to Identify Need to Screen or Counsel
- Failure to Prevent Failure
- Failure in Detection
- Failure During Diagnostic Evaluation
- Failure During Treatment
- Failure in Surveillance
- Failure in Care

Annex9: The cancer care continuum
Zapka et al. (2003).
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Annex10: Algorithm for patient care in Zambia cervical cancer screening program