REPUBLIC OF ZAMBIA

MINISTRY OF HEALTH

NATIONAL GUIDELINES FOR EARLY DIAGNOSIS OF BREAST CANCER IN ZAMBIA

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NATIONAL GUIDELINES FOR EARLY DIAGNOSIS OF BREAST CANCER IN ZAMBIA

First Edition

Foreword

The Government of the Republic of Zambia is resolved to ensure that its people are healthy and productive as this is a cornerstone to socio-economic development of our country. Zambia faces a double burden of disease emanating from Communicable and Non-Communicable diseases and has continued to invest in various high impact interventions to address the scourge. Zambia's goal is attaining universal health coverage by creating strong, resilient and people centred health systems using a community based primary health care approach. The Zambian Government recognizes the disease burden caused by noncommunicable diseases, such as breast cancer, and is implementing high impact evidence based interventions to improve the health and well-being of its people in line with the Universal Health Coverage agenda. This aspiration is aligned to the overarching Government's Vision 2030 and the National Development Plan 2017- 2021 to which the Ministry of Health has dovetailed its National Health Strategic Plan (2017-2021) and the National Cancer Control Strategic Plan (2016-2021).

The National Cancer Control Strategic Plan (2016-2021) prioritized four cancers as benchmarks in rolling out its program, with breast cancer being one of them. The key objective of the strategic plan is to expand access to breast cancer awareness, early detection, treatment and care in order to reduce the current mortality rate by 25% by the year 2025. To operationalise the National Cancer Control Strategy, one of the major documents produced is the National Guidelines for Breast Cancer Diagnosis in Zambia. These guidelines shall play a pivotal role in accelerating the reduction of breast cancer morbidity and mortality amongst the affected individuals, especially women who bear the greatest burden of breast cancer in our country. These guidelines will further catalyse the reduction of healthcare costs as treatment modalities for early diagnosis of breast cancer will be less costly and complicated with better health outcomes, a key to socio-economic development of the country.

This document therefore contains useful guidance that will enhance the successful implementation of the national program on early diagnosis of breast cancer in Zambia.

I urge all health care workers, partners and stakeholders to fully utilise these guidelines for us to improve the health and wellbeing of our people particularly our women who continue to get the biggest brunt of breast cancer in our country.

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Content

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Acronyms

AIDS	Acquired Immune Deficiency Syndrome
AJCC	American Joint Commission on Cancer
ANC	Antenatal Clinics
BI-RADS	Breast Imaging Reporting and Data System
BHA	Breast Health Awareness
BMI	Body Mass Index
BOADICCEA	Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm
BRCA	Breast Cancer gene
CBE	Clinical Breast Examination
CBO	Community Based Organizations
CBV	Community Based Volunteers
CCPPC	Cervical Cancer Prevention Program in Zambia
CDH	Cancer Diseases Hospital
CHA	Community Health Assistants
CNB	Core Needle Biopsy
CSO	Civil Society Organizations
DCIS	Ductal Carcinoma In-Situ
DHD	District Health Directors
DHIS	District Health Information Systems
DMO	District Medical Officers
EHT	Environmental Health Technicians/Technologists
ER	Estrogen Receptor
FBO	Faith Based Organizations
FNA	Fine Needle Aspiration
FNAC	Fine Needle Aspiration Cytology
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information Systems
HPCZ	Health Professions Council of Zambia
HPR	Histopathology Report
IBCIS	International Breast Cancer Intervention Study
LCIS	Lobular Carcinoma In-Situ
MCH	Maternal and Child Health
MDT	Multidisciplinary Team
M & E	Monitoring and Evaluation
MMG	Mammography
MOH	Ministry of Health
MRI	Magnetic Resonance Imaging
NCD	Non-Communicable Diseases
NCCSP	National Cancer Control Strategic Plan
NCCTWG	National Cancer Control Technical Working Group
NGO	Non-Governmental Organizations
NHC	Neighborhood Health Committees

NHSP	National Health Strategic Plan
PATHAZ	Pathologists Association of Zambia
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary Health Care
PHD	Provincial Health Directors
PR	Progesterone Receptor
SBCU	Specialized Breast Cancer Units
SMAG	Safe Motherhood Action Groups
TAT	Turnaround Time
TBA	Traditional Birth Attendants
TNM	Tumor-Nodes-Metastases
TWG	Technical Working Groups
UICC	Union for International Cancer Control
US	United States of America
USG	Ultrasound-Guided
UHC	Universal Health Coverage
UTH	University Teaching Hospital
WLE	Wide Local Excision
WHO	World Health Organization
ZNCR	Zambia National Cancer Registry
ZNHSP	Zambia National Health Strategic Plan

Executive Summary

The primary goal of the national guidelines for early diagnosis of breast cancer in Zambia is to ensure that all women with a suspected breast mass are timely referred to the appropriate level of health care. The identification, diagnosis, treatment and management of breast cancer in its earliest stages are more effective, less costly, has fewer complications, and greatly improves the quality of life of patients. The Ministry of Health's vision of universal health coverage by the year 2030 includes utilization of integrated delivery platforms and a strong primary level of health care. To this effect, each health care level facility will be required to provide services toward the attainment of early breast cancer diagnosis through sustainable awareness and education programs, clinical breast examination, provision of breast radiological services, core needle biopsy, pathology services, and multidisciplinary team approach to breast cancer management and care.

It is apparent that outcomes and survival rates are improved or increased in patients who have been diagnosed at early stages of breast cancer disease. Early diagnosis requires effective and efficient referral systems, timely coordination of services that include imaging studies, biopsy of suspicious lesions, pathology reports, appropriate treatment and management plans. The program on early diagnosis of breast cancer focuses on making the initial connection between community members and health facilities so that individuals with signs and symptoms of breast cancer are evaluated quickly, at the entry-point to the health care delivery system.

Every health facility should be actively involved in early diagnosis of breast cancer to identify people who have signs and symptoms consistent with the disease. Both rural and urban communities should be aware of specific breast cancer signs and symptoms, understand the urgency of these symptoms, overcome misconceptions, fear, and social stigma associated with the disease. This requires an effective strategy to engage communities in the design, planning, implementation, monitoring and evaluation of health promotion interventions directed at early diagnosis of breast cancer at all levels of contact in the health care delivery system.

The national guidelines intend to contribute to the provision of quality and efficient breast cancer services, and to guide health providers at all levels within the health care delivery system on evidence-based, focused interventions that improve breast cancer outcomes, through integration of the program within the existing platforms, such as maternal and child health, and cervical cancer prevention program. This will facilitate identification of breast cancer at the earliest possible opportunity and link the patient to an appropriate level of health care without delay. Women should be encouraged to reduce their risk of breast cancer by undertaking appropriate measures to curb the modifiable risk factors. Primary health care providers should recognize the signs and symptoms of breast cancer and facilitate prompt referral for early diagnosis, treatment and management.

1.0 Introduction

Breast cancer is the most common malignancy among women in Zambia, followed by cervical cancer (Ferlay et al., 2018). Most patients present with late stage disease either at stage III (locally advanced) or stage IV (metastatic), resulting in complicated and costly treatments and poor outcomes (Cancer Diseases Hospital. (2013). In order to mitigate this, the Ministry of Health (MOH) has developed, for implementation, the national guidelines for early diagnosis of breast cancer in Zambia. The national guidelines intend to contribute to the provision of quality and efficient breast cancer services, and to guide health providers at all levels within the health care delivery system on evidence-based, focused interventions that improve breast cancer outcomes through integration of the program with existing services.

The MOH has implemented most of its vertical programs based on a multisectoral approach with donor funding from government bilateral agreements, international donor organizations, and community participation. For instance, the Cervical Cancer Prevention Program in Zambia (CCPPZ) was initiated in 2006 with support from the US President's Emergency Plan for AIDS Relief (PEPFAR), to provide services to women accessing health care in over 90 government-operated clinics countrywide and has screened over 500,000 women to date (Mwanahamuntu et al., 2011). Another example is the Maternal and Child Health (MCH) service, a widespread platform that provides integrated services such as antenatal, postnatal, growth monitoring, vaccination and immunization against childhood diseases, nutrition care and family planning, whose clients are mainly women under the age of 50 years.

Most breast cancer patients in Zambia are under 50 years, and it is this age group that normally access the MCH and CCPPZ platforms (Cancer Diseases Hospital. (2013). These platforms are ideal avenues for reaching out to women of appropriate age groups and providing early breast cancer diagnostic services. One of the most appropriate wide-scale interventions in resource limited settings to reduce the proportion of breast cancer diagnosed at advanced stages is implementing Breast Health Awareness (BHA) and Clinical Breast Examination (CBE). The MCH and CCPPZ platforms would be used as entry points to the program, since BHA and CBE could be delivered by the same nurses providing cervical cancer screening and MCH services at Primary Health Care (PHC) level clinics, without new infrastructure or additional personnel costs.

2.0 Situational Analysis

According to GLOBOCAN (Ferlay et al., 2018), breast cancer is the number one cause of morbidity at 11.6%, at par with lung cancer, and ranks 5th as the cause of premature mortality in both women and men worldwide. Women are the most affected by breast cancer disease in most countries, although the incidence in Africa is much lower than other large mass continents but with the highest mortality in comparative terms. Among the causes of this disparity in breast cancer care and outcomes is the availability of breast health care services for the affected women population in high-income countries in comparison to the low- and middle-income countries that lack such services. Examples of such services are: existence of robust breast health awareness programs, population-based screening programs, locally designed diagnostic and treatment guidelines, human resources for health with sound knowledge in breast health care service delivery, finances for health, and availability of diagnostic equipment and infrastructure.

2.1 Breast cancer in Zambia

Cancers, like other Non-Communicable Diseases (NCD), are on the increase in Zambia. This is significantly adding to the management and care burden of chronic diseases at the country level. According to GLOBOCAN (Ferlay et al., 2018), breast cancer is ranked 1st as the most prevalent cancer amongst women, the 1st cause of cancer morbidity and the 2nd cause of cancer mortality in both female and male patients (Ferlay et al., 2018). A majority of breast cancer cases are diagnosed at late stage disease (Stages III and IV), at which survival rate is poor and treatment options are limited and costly. The Zambia National Cancer Registry (ZNCR) report also shows that the distribution of cancer cases across the country is variable, with Lusaka, Eastern, Central and Western provinces recording the highest numbers (Kalubula et al., 2018).

Studies show that outcomes and survival rates are improved or increased in patients who have been diagnosed at early stages of the disease (Cao & Lu, 2016, McKenzie, 2018, Foerster, 2019). This is because at this stage, treatment modalities—such as appropriate surgical intervention with or without radiotherapy—are less costly, more effective and less toxic; and could, therefore, be offered even in low- and middle-income countries where resources are limited. Early-stage breast cancer is confined to the breast with or without regional lymph node involvement, and there is an absence of distant metastatic disease. Early-stage breast cancer is potentially treatable, whereas advanced disease with distant metastasis is not.

2.2 Health service delivery

The MOH vision of UHC includes use of integrated health delivery platforms and primary health care systems to provide early diagnosis of breast cancer care services in Zambia. This will be achieved through the key principles of **primary health care; equity of access; affordability; cost-effectiveness; accountability; partnerships and linkages; decentralization and leadership; and a clean, caring and competent health care environment.**

As such, each health care level facility will be required to provide services toward the attainment of early breast cancer diagnosis through awareness and education programs, clinical breast examination (including patient initiated clinical breast examination), provision of breast radiological services (breast ultrasound and mammography), Ultrasound guided (USG) core biopsy, pathology (specimen preparation and reporting), and multidisciplinary team (MDT) approach to breast cancer management and care.

The health care provision in Zambia starts from the lowest level of community health posts where there are ideally providers such as nurses. In certain rural areas, where nurses are not available, Community Health Assistants (CHA) can often fill this role. This level feeds into health centers located in both rural and urban areas. The health centers are usually managed by nurses or clinical officers and supported by other auxiliary staff. Patients requiring further attention are usually referred to first level hospitals at the district level.

At district hospital level, medical doctors manage these facilities with support from clinical officers, nurses,

midwives, and other health care providers. The district hospitals (level I) refer complicated cases to level two (II) hospitals, also known as general hospitals at the provincial level. In Lusaka, the first level hospitals have specialists and they refer their patients directly to level three hospitals, such as the University Teaching Hospital (UTH), and the only referral cancer center at the Cancer Diseases Hospital (CDH).

The CCCPZ utilizes the already existing primary health care service platform and the number of cervical cancer screening providers has since risen significantly. Maternal and child health services exist in all the health facilities countrywide, including some health posts. It would be cost effective to implement the breast health care service through these already existing platforms. However, training of key personnel in breast health care at these health services is of critical importance in order to ensure integration and efficient delivery of services at all levels of contact.

2.3 Major constraints

A review of the breast cancer situation in Zambia shows that the most notable constraints to improve breast cancer outcomes include:

- financial, logistical and sociocultural barriers;
- lack of technologically cost-effective facilities and infrastructures for the diagnosis and treatment of breast cancer;
- inadequate knowledge and breast health awareness;
- low access and utilization of breast cancer screening opportunities;
- inadequate trained personnel to improve service delivery;
- low effective community involvement and participation in demand creation for breast cancer services;
- lapses in the referral systems; and
- lack of policy guidelines on integration of programmatic interventions.

  The lapses in referral systems and policy guidelines encompass inherent challenges, such as long waiting period between diagnosis and treatment, patient attrition, and limited number of experts and their attendance days in clinics. This results in patients waiting for long periods with a possibility of not being attended to at the most critical opportune time, thereby contributing to poor patient outcomes, prolonged suffering and eventual death.

3.0 Policy Guidelines

The identification, diagnosis, treatment and management of breast cancer in the earliest stages is more effective, less costly, has fewer complications, and greatly improves the quality of life of patients. It also provides consistency in patient care and outcomes.

3.1 Vision

All women with breast cancer are diagnosed at early stages of the disease.

3.2 Goals

The overarching goal of the national guidelines for early diagnosis of breast cancer in Zambia is that all women with a suspected breast mass are timely referred to the appropriate level of health care, reducing unnecessary visits to health providers. The specific aims are:

- Provide a framework for health facilities on the provision of high quality and effective breast cancer care services at the national level.
- Provide guidance to policymakers, managers, departmental heads, and other stakeholders on how to implement a breast cancer control program focused on early diagnosis of the disease.
- Increase survival and quality of life of patients with breast cancer.

3.3 Guideline Components

3.3.1 Early diagnosis of breast cancer

According to WHO, early diagnosis is defined as the early identification of cancer in patients who have symptoms of the disease. The objective is to identify the disease at the earliest possible opportunity and link to diagnosis and treatment in a timely manner, to improve survival, reduce suffering and lessen the cost of prolonged care. Table 1 depicts early diagnosis methods, target populations and limitations (World Health Organization, 2017).

Table 1: Early diagnosis methods, target populations and limitations

Method	Description/Purpose	Population	Limitations
Breast Health Awareness (BHA)	Train in signs and symptoms, risk factors and risk reduction strategies.	Health providers, community health assistants, traditional healers, traditional and religious leaders, women over 20 years of age (linked with reproductive health)	Only effective if women have access to timely diagnosis and treatment

Clinical Breast Examination (CBE)	CBE performed by a trained health provider, involves a physical examination of the breasts and underarms with proper positioning of patient for breast palpation (upright and lying flat) Diagnostic tool with educational benefits	Symptomatic women presenting with signs and symptoms Asymptomatic women over 30 years of age as a breast awareness education tool Women with family history of breast cancer at a young age, may have CBE performed before 30 years of age	Not proven effective as a screening method to decrease deaths Requires proper training, practice and quality assurance Health providers need feedback on patient diagnosis
Diagnostic Imaging Ultrasound/ Mammography	Ultrasound as a diagnostic tool can characterize a mass either as solid or cystic Ultrasound can be used to guide biopsy techniques, inform surgical management and potentially identify additional lesions in the same breast or opposite breast Diagnostic mammography can be used to evaluate the extent of disease in the affected breast and evaluate the opposite breast	Use as a diagnostic tool for suspicious findings on CBE	Requires specialized training Ultrasound is operator-dependent and can be less sensitive than mammography

- Early diagnosis of breast cancer is intended for people who have signs and symptoms of the disease (see Appendix A for details). This is different from cancer screening that seeks to identify unrecognized (pre-clinical) cancer or precancerous lesions in an apparently healthy target population.
- Early diagnosis increases the chance of successful treatment by detecting disease at an early stage when it is less extensive, but when effective treatments can be provided, with increased likelihood of achieving remission.
- Early diagnosis requires effective and efficient referral systems, timely coordination of services that include imaging studies, biopsy of suspicious lesions, pathology (histology/cytology) reports, appropriate treatment and management plans.
- The promotion of early breast cancer diagnosis programs in the absence of available proper treatment is not only ineffective, but also unethical and a breach of human rights to equitable health.
- Access to quality primary health care is critical for the early diagnosis of breast cancer. Diagnostic delays can occur if women do not present for evaluation, but also because health care providers fail to recognize the early signs and symptoms of breast cancer. However, early diagnosis can only be effective if it is promptly supported by effective cancer treatment, management and care.
- An effective early diagnosis program includes the following components:
    - Breast health awareness and education (health worker and community training)

- Health-seeking behavior target population
- Trained workforce starting with primary health care providers, including pathologists
- Clear patient pathways and efficient referral system
- Identification and reduction of barriers to timely diagnosis and care
- Clinical evaluation performed by primary health care providers
- Timely diagnosis for all women with abnormal findings
- Timely treatment for all women proven by tissue diagnosis to have breast cancer

These components should be integral to effective breast cancer care services at all levels of the health care delivery system, as illustrated in Tables 2-6, below:

Table 2: Breast health awareness (BHA)

Description	Breast health awareness is the education on the risk factors and symptoms of breast cancer as well as the importance of seeking timely medical evaluation for breast concerns.
Objective	Improve knowledge and awareness about breast cancer among target populations (both the public and health professionals), and the importance of early diagnosis with appropriate subsequent management.
Principles	• Definition of target population: primary care physician (first point of contact), midwives, nurses, advocates/volunteers, cancer survivors and caregivers, traditional and religious leaders, civic leaders and the community at large. • Education approach: This must be appropriate, culturally acceptable and tailored to the educational level of different groups of the target population. • Target population should participate in the design, development and implementation of educational activities. • Breast health awareness includes awareness on; ▪ Risk factors; sex, age, genetic factors, family history, personal history, hormonal and reproductive factors, behavioral factors e.g. unhealthy diet, alcohol consumption, tobacco use, ▪ Sedentary lifestyles signs and symptoms; breast masses, skin thickening, breast skin ulceration, breast pain, nipple discharge, nipple inversion and enlarged lymph nodes ▪ Men and women should know what is normal for their bodies and recognize any unusual or unexpected changes in their breasts ▪ Risk reduction/lifestyle modifications; breastfeeding, physical activity, diet, healthy weight (normal BMI), avoid tobacco use and excessive alcohol consumption.

Recommended Strategies	• Strengthen and support community awareness programs to educate women, men and health care providers on breast cancer risk factors, breast self-awareness, early detection, treatment and care. • Reach the target population with tailored, accurate, current, consistent, and evidence-based breast cancer awareness information and educational materials, using a variety of communication channels. The modes of reaching out may include: one-on-one communication, small group discussions, and health promotion talks in various setups such as clinics, markets, schools, churches, community meetings, women and men's groups, health campaigns, and social services. • Leverage internal Ministry of Health protocols and partners, such as community-based organizations (CBO) and faith-based organizations (FBO) to expand the breast cancer awareness training to a broader network of health facility and community outreach educators and volunteers. • Advocate for the inclusion of breast cancer awareness initiatives in existing health programs and all learning institutions. • Conduct social mobilization for breast cancer awareness, particularly in hard to reach communities and with underserved groups, such as prisons and refugee camps. • Display printed educational materials in health facilities, market places, mosques, churches and other public places. • Promote breast health interventions and information through mass media channels, such as electronic, print and social media, billboards or street adverts • Improve referral systems: this should be done for all levels of contact, such as the household, community, health post, health center and higher levels of the health care delivery system.

Table 3: Clinical breast examination (CBE)

Description	Clinical breast examination performed by a trained health care provider involves a physical examination of the breasts and underarms with proper positioning of the client for breast palpation (upright and lying flat).
Objective	To evaluate breast complaints for appropriate triage and improved diagnosis.
Principles	• CBE should be offered to any woman with a breast finding that she identifies as abnormal for her or any woman who wants her breasts examined for abnormalities. • CBE for symptomatic women is the recommended approach to early diagnosis in settings where screening mammography is not available. • Incorporate CBE into standard medical and nursing school curricula and training programs, i.e. the cervical cancer screening training program. • Employ quality assurance measures to ensure that health professionals are proficient in CBE and know how women with abnormalities in their breasts can access diagnostic services. • CBE should be performed by health care providers.

Recommended Strategies	• CBE should be offered to all women with a breast health concern, regardless of their age. • CBE should be offered to all women presenting for cervical cancer screening and MCH service providers. • CBE for women without symptoms or concerns should be performed as part of breast health awareness. • CBE training should be offered to primary health care providers and specialists. Post information components of breast health care visits on facility walls.

Table 4: Diagnostic breast imaging

Description	Diagnostic breast imaging is the use of imaging tools (ultrasound, mammogram or magnetic resonance imaging) to assess breast concerns or symptomatic palpable masses, not as a screening method among asymptomatic women.
Objective	To distinguish benign from malignant masses, guide biopsy techniques, and inform surgical management.
Principles	• Diagnostic ultrasound can be used to distinguish cysts from solid masses and identify enlarged lymph nodes; and to guide biopsy techniques, inform surgical management, and potentially identify additional lesions in the same breast or opposite breast. • Diagnostic mammography is used to screen patients who present with concerns for breast cancer after CBE or screening mammography. • Magnetic resonance imaging (MRI) is best used only for patients with diagnostic challenges and breast implants. Evaluate the extent of disease in the affected breast and evaluate the opposite breast.
Recommended Strategies	• First level Hospital: Consider breast imaging using ultrasound. If ultrasound is present, use routinely and adapt to appropriate frequency (linear transducer >7.5 MHz) for breast tissue; provide training. Ultrasound core needle biopsy (CNB) at district level, when available. If CNB is not available, refer patient to the next level of care, if possible. • Second level Hospital: Adapt ultrasound units for breast imaging and introduce ultrasound-guided core needle biopsy. Use mammography, if available. • Third level Hospital: Diagnostic ultrasound and mammography using BI-RADS. Use MRI for diagnostic challenges and breast implants, if available.

Table 5: Pathology

Description	Accurate clinical and pathologic workup of a biopsy sample is required for a definitive diagnosis, to include staging and tumor receptor status (estrogen receptor, progesterone receptor, HER2 nue/erbB2 and Ki67) for informed prognosis and treatment decisions.
Objective	To enhance timely and accurate diagnosis to inform appropriate treatment.

Principles	• All women with a suspected breast mass require an accurate pathologic diagnosis before initiating treatment, even when the clinical findings are strongly suggestive of cancer. The success of an effective breast health care program is directly related to the availability and quality of breast pathology. • Proper handling of the tissue during the pre-analytic phase and timely processing are essential to the quality and validity of the results and subsequent treatment. • Breast cancer early diagnosis program should be implemented and integrated with accessible services like the cervical cancer screening program. • Benign breast conditions are four times more prevalent than breast cancer. Therefore, obtaining a diagnostic biopsy rather than performing open surgery for diagnosis of breast lumps will reduce cost and morbidity. • Timely reporting of breast diagnostic tests to the appropriate health provider is critical to improving patient outcomes. • The health system needs to ensure that patients referred for biopsy actually follow through and obtain the procedure. • Staging criteria are available online from the American Joint Commission on Cancer (AJCC, latest version)
Recommended Strategies	• First and Second Level Hospitals: Clinical assessment, tissue sampling (ultrasound guided core biopsy), tumor-nodes-metastases (TNM) staging and estrogen receptor (ER), progesterone receptor (PR), HER2 neu/erbB2 and Ki67 (IHCs) status. Results should be recorded and communicated to the referring doctor. • Third level Hospitals and Cancer Centers/ Super-specialized centers: Routine determination of TNM staging and IHC testing to determine potential benefit from endocrine therapy (i.e. oral tamoxifen/aromatase inhibitors) and targeted therapy. The centers should also provide diagnostic imaging and patient navigation.

Table 6: Tissue biopsy techniques

Technique	Description	Advantage	Disadvantage
Surgical Biopsy	A definitive diagnosis can be made, and biomarkers can be obtained on the biopsy specimen. This can either be excision biopsy (whole mass removed) or incisional biopsy (small part of mass removed)	Provides definitive diagnosis. Often performed with local anesthesia	It is expensive as it is done in theatre. Requires waiting for the next available theatre space

Fine Needle Aspiration Cytology (FANC)	A small, hollow needle and syringe are used to obtain cells from a palpable breast lump for examination under a microscope by a cytopathologist. FNAC is not currently suitable for the evaluation of asymptomatic women without a palpable lump	Rapid, safe and usually less painful than a surgical biopsy or a core needle biopsy in women with a palpable breast lesion. In some settings, a preliminary interpretation of whether or not the patient has cancer can be done at the time of FNAC, which may facilitate patient flow and assist in treatment planning.	The incidence of false negative results has been estimated to be 4–27%. Thus, the absence of cancer cells upon FNAC does not rule out invasive cancer, and a tissue-based biopsy (large core needle or surgical) may be needed if FNAC results are non-diagnostic or negative, must be read by a trained breast cytologist
Core Needle Biopsy (CNB)	Consists of the removal of a tissue specimen with a hollow cutting needle (usually size 14-gauge). Obtaining 4 specimens with a 14-gauge needle usually provides enough tissue for diagnosis. It can be done under mammographic (stereotactic) or ultrasound guidance	Lower sampling error and larger volume of tissue retrieved, compared to FNAC, allows pathologists to document invasive versus in situ disease, grade tumor accurately, and perform tumor biomarker tests. CNB does not require a trained cytopathogist. CNB is less costly than a surgical biopsy and can demonstrate benign findings that may spare women unnecessary surgical biopsies.	False negative results can occur with core needle biopsies, especially if insufficient tissue is obtained.
Recommended Strategy	• Ultrasound guided core needle biopsy is recommended for all sites with ultrasound and core biopsy equipment. • Incisional biopsy is recommended for facilities that do not have equipment for core needle biopsy. • Excisional biopsy is recommended for benign conditions and not for suspicious breast lesions in women above 25 years old.		

3.3.2 Disease staging

Breast cancer characterization and staging is a critical component of diagnosis and is required for treatment planning. There are standardized systems for describing a breast tumor:

- Non-invasive (pre-cancerous) or invasive
- Size
- Lymph node involvement
- Cancer cells spread to other parts of the body (metastasis)

A commonly used system is the Union for International Cancer Control–American Joint Commission on Cancer (UICC-AJCC) TNM system, which includes metrics of clinical stage (results of physical exam, biopsy and imaging tests) and pathologic stage (clinical staging information plus biopsy and laboratory findings). In the TNM system,

- T refers to the size and characteristics of the tumor,
- N refers to the extent of lymph node involvement, and
- M refers to the degree of distant metastasis.

The size and characteristics of a tumor can be assessed by CBE, biopsy and imaging. The extent of lymph node involvement can be assessed by CBE, biopsy and imaging. The degree of metastatic disease can be informed by physical examination, biopsy and imaging. The actual stage of disease (Stages I-IV) is determined by a combination of different TNM characteristics, as outlined in Appendix B. The progressive staging of breast cancer disease is reflected in Table 7, below.

Table 7: Progressive stages of breast cancer

Stage 0	Ductal carcinoma in situ (DCIS)
Stage I	Invasive breast cancer with tumor up to 2cm and no axillary lymph nodes involved
Stage II	Invasive breast cancer with one of the following: Tumor <2cm with spread to axillary lymph nodes; No tumor in the breast but cancer cells in axillary lymph nodes; Tumor 2 to 5 cm with spread to axillary lymph nodes; or Tumor >5cm without spread to axillary lymph nodes
Stage III	Tumor has spread to axillary lymph nodes which are clumped together, has spread locally to the chest wall or the skin of the breast or to infra and supra-clavicular nodes
Stage IV	Distant metastasis
Note: Histological staging or classification is used as prognostic factor	

3.3.3 Triple assessment

The triple assessment procedure refers to clinical assessment, diagnostic imaging, and pathology assessment. A clinical assessment of breast complaints is a crucial first step in breast cancer diagnosis. Diagnosis requires a timely coordination of services that include:

- Initial presentation for evaluation of a breast complaint, to include a medical history and a clinical breast examination
- Imaging studies and biopsy of suspicious lesions

- Pathology (histology/cytology) studies.

A lack of coordination and poor patient access to care can cause delays in definitive diagnosis and initiation of treatment, with the potential to negatively influence outcomes and survival rates.

3.3.4 Risk factors for developing breast cancer

Various risk factors for developing breast cancer have been highlighted in the medical literature; and these can be classified in two folds, as below.

- Modifiable risk factors
  - Age at first child birth
  - Number of term pregnancies breastfed
  - Obesity or high body mass index (BMI)
  - Lack of physical exercise
  - Increased alcohol intake
  - Smoking tobacco
  - High fatty meat diet
  - Hormone replacement therapy
  - Dense breasts
- Non-modifiable risk factors
  - Being female
  - Early menarche, before the age of 12 years
  - Late menopause
  - Family history of breast cancer or prostate cancer
  - Inheritance of some genetic mutations, e.g. BRCA I/II.
  - Previous treatment to the chest wall with radiotherapy
  - Personal history of breast cancer

It must be noted that genetic mutations cause only about 15% of breast cancer. The majority of cases are due to sporadic changes, i.e. occurring in those with no family history or inherited genetic mutations.

In a resource limited setting like Zambia, women should be encouraged to reduce their risk of breast cancer by undertaking appropriate measures to curb the modifiable risk factors. This reduction will also contribute to their chances of developing other non-communicable disease (NCD) such as diabetes mellitus and hypertension.

A. **Relative Risk in People without Family History**

The relative risk for developing breast cancer in people without family history is usually determined by a Gail model. The Gail model (Gail et al., 1989) is one of the several risk assessment models that can help determine

the absolute 5-year risk and lifetime risk for developing breast cancer. The Gail model for breast cancer risk, can easily be used in resource limited settings like Zambia, to stratify risk of the patients seeking breast health care services and to improve early breast cancer diagnosis. The breast cancer risk can be calculated by using the online calculator link: https://bcrisktool.cancer.gov/. The model is not recommended for use in women with strong family history of breast cancer hereditary syndromes.

B. **Risks of Developing Breast Cancer based on Pathological Findings.**

If a person is symptomatic for breast disease, e.g. a lump or nipple discharge, risk assessment and evaluation of such a pathology needs to be discussed with the patient by the health care provider. This will reduce chances of the individual being lost to follow up and presenting later with advanced breast cancer that has complex treatment modalities and poor outcomes. To establish the risk in a patient, a breast core needle biopsy or cytology specimen should be collected and reported by a trained pathologist, to ascertain the histological or cytological type of disease the patient has, in case it is not invasive carcinoma. These pathologies are generally divided into proliferative and non-proliferative, with or without atypia.

Some common pathologies with their risk of developing breast cancer based on pathological or cytological reports are reflected in Table 8, below.

Table 8: Common pathologies and risk outcomes

Histological category of lesion	Pathology	Relative risk of developing breast cancer	Management, Approach and Recommendation
Non-Proliferative Lesions	Simple cyst Mild hyperplasia	1	Discuss with patient and initiate follow-up
Proliferative lesions – without Atypia	Sclerosing adenosis Radial scar Fibroadenoma Intraductal papilloma	1.3 – 1.9	• Discussion with patient • Appropriate Wide Local Excision (WLE) • Review of Histopathology report (HPR)
Proliferative lesions – with Atypia	Atypical hyperplasia Atypical ductal hyperplasia Atypical lobular hyperplasia	3.9 – 13.0	MDT/Tumor board
	LCIS		MDT/Tumor board
Pre-invasive malignancyDCIS			MDT/Tumor board

3.4. Service Provision and Program Coordination

3.4.1 Health facilities

Every health facility should be actively involved in the early diagnosis of breast cancer to identify people who have symptoms and signs consistent with the disease. The objective is to identify the disease at the earliest possible opportunity and link the patient to diagnosis and treatment without delay. The various levels of contact in health care provision, coordination and referral systems is summarized in Table 9.

Table 9: Levels of health service provision

Level	Location	Services	Referral
Health Post	Rural/ Urban	Basic	Health Centre
Health Center	Rural/Urban	Primary	Zonal/District
Hospital I	District/Urban	Secondary	General
Hospital II	Provincial	Advanced	Central
Hospital III	Central	Specialist	Teaching hospitals
Hospital III	CDH	Super-specialist	Internal/External

A. **Health Posts and Health Centers**

Health posts and health centers should be able to provide breast health awareness and refer clients to the next level of care for further evaluation. The local health providers should be trained in practical skills relevant to early breast cancer diagnosis and should be able to recognize the early signs and symptoms of the disease.

Symptomatic clients should receive a full clinical health assessment, including breast-specific history and detailed clinical breast examination. These clients should then be referred to the nearest designated Specialized Breast Cancer Units (SBCU) according to triage. Asymptomatic clients with high risk for developing breast cancer, as defined by the risk assessment tool, may be referred directly to a SBCU at the higher level of health care. While waiting for their turn in the various clinics, all patients should be educated on breast health care and awareness.

Requirements for this provision:

- Primary health care nurses trained in breast health care.
- Protocols facilitating seamless transfer to the designated open access breast cancer unit at the district hospital level.
- Breast cancer referral forms with all relevant data (checklists and boxes) for audit and appraisal.
- Seamless clients' navigation to the next level of health care.

B. **Level I: District Hospitals**

The resources and level of care at level 1 district hospitals, including expertise, can be variable between different health facilities.

Requirements at this level are:

- Standardize the management of patients with breast complaints. It is advisable that no unnecessary delay is incurred with investigations. Currently these centers will have a resident surgeon, and as such, an appropriate breast core needle biopsy could be offered, if the personnel have been trained. In addition, properly placed incision biopsy may be offered.
- Asymptomatic patients presenting to primary health care clinics for non-breast related problems should ideally be targeted for opportunistic breast health awareness. While waiting for their turn in the various district level facilities, patients should be educated on breast health awareness.
- Breast cancer diagnostic clinic using high resolution ultrasound guided (>7.5 MHz) core needle biopsy should be considered at this level of care.

- Seamless clients' navigation to the next level of health care.

C. Level II: General Hospitals

The requirements at this level of care are:

- Primary health care nurses and doctors trained in breast health care should be available.
- It is desirable that all doctors at these facilities are trained in breast health care and systematic clinical breast examination.
- Protocols facilitating seamless transfer to the next level of care should be in place.
- Breast cancer referral forms with all relevant data (checklists and boxes) for audit and appraisal are completed.
- Mammography services using digital imaging modality should be considered at this level of care.
- Breast cancer diagnostic clinic using high resolution ultrasound/image guided core needle biopsy should be considered at this level of care.
- Seamless clients' navigation to the next level of health care.

D. Level III: Central and Teaching Hospitals

These centers should be available to receive patients from primary health care facilities and general hospitals. The hospitals should be equipped with the necessary resources such as breast health care infrastructure, surgical facilities, and staffed with appropriately trained clinical expertise, operating through their established SBCU. These designated centers should be equipped to make a definitive diagnosis, provide staging investigations for biopsy-proven cancers, offer breast surgical services (benign and malignant), chemotherapy and radiotherapy services. These centers should be fully functional, with multidisciplinary teams, to offer comprehensive early breast cancer diagnosis, treatment and management.

Requirements for this provision are:

- Standardized breast cancer medical records.
- Breast imaging:
    - Mammography: film or digital, depending on the resources available (highly recommend digital mammography units so that images can be transmitted via telemedicine in view of limited radiologists to read the films.)
    - Stereotactic biopsy attachment (optional)
    - High resolution ultrasound
    - Breast mammographers and radiologists
- Meetings at which surgeons and radiologists discuss client findings (benign and malignant) and management
- Tissue sampling equipment; core needle biopsy, which may be image-guided.
    - Access to a regional histopathology laboratory

- Swift transport of specimens
- Timely standardized reporting with two weeks turnaround time for computerized access.
- Specific timelines should be adhered to and work-up routinely completed within two weeks from histological cancer diagnosis.
- Protocols facilitating seamless navigation of clients to the cancer center that have multidisciplinary team meetings.

E. Level III: Specialist Hospitals and Cancer centers

Prior to consultation at a cancer center, a definitive diagnosis of cancer must be made, and the patient should be counseled about the diagnosis, prognosis and management options. The patients should be presented at the multidisciplinary team meeting, where their overall management and care plan will be agreed upon.

Requirements for this provision:

- Specialized budget to allow for cost of chemotherapy and biological therapies.
- Standardized breast medical records.
- Breast imaging such as digital mammography and tomosynthesis units with available services of breast MRI, for selected cases in case of diagnostic challenges.
- Specific timelines for consultation after referral should be adhered to and work-up routinely completed within two weeks from presentation.
- Seamless navigation of clients at the cancer center.
- Presence of multidisciplinary team.

3.4.2 Breast health awareness and education

This activity intends to strengthen the capacity of communities to promote early diagnosis and treatment of breast cancer. Building community awareness involves sharing information with different segments of the community to enhance knowledge and understanding, promote behavior and attitude change, and create demand for community-based services. It is an essential component of improving access to breast cancer care services and patient outcomes.

Both rural and urban communities should be aware of specific breast cancer signs and symptoms, understand the urgency of these symptoms, overcome misconceptions, fear, and social stigma associated with the disease. They should be able to access informed primary health care services and be evaluated and referred appropriately for diagnosis and treatment. Awareness and education for breast cancer control must be based on scientific evidence and translate into appropriate health seeking behavior. Breast health services must be accessible, affordable and offered in a respectful manner.

The MOH has developed a community health strategy (Zambia Ministry of Health, 2017) that ensures effective and active community engagement in the design, planning, implementation, monitoring and evaluation of health promotion interventions. It is anticipated that program planners, policy makers and supervisors oversee the development of a pathway for continuous capacity building, skills training, and delivery of health promotion strategies at the community level.

Awareness and educational interventions can be instrumental in providing information about breast health and early signs of breast cancer, dispel myths and misconceptions, and help individuals understand what actions to take. Sustainable awareness and educational interventions will depend on the support

and ownership by the community, as well as an inclusive social and policy environment for community involvement and participation at national, provincial, district and community levels.

3.4.2.1 Community engagement

Community engagement refers to the process of getting community members involved in decisions that affect them. This includes planning, development, management and evaluation of health services that are aimed to improve health or reduce health inequalities. Addressing breast cancer control in Zambia requires that the community is informed, educated and empowered to make decisions and take affirmative action about their breast health challenges.

The community health strategy must engage the community in dialogue and decision-making, to improve the relevance and efficiency of breast cancer control interventions at all levels of contact. The effectiveness is likely to depend upon identification of explicit methods for involving individuals and communities, clearly defined roles and responsibilities, training for policymakers and clients, adequate funding, and psychosocial counseling.

Educational interventions should be promoted to implement the community-based component of early diagnosis of breast cancer that is linked to accessible treatment and care services. Raising awareness about breast cancer where there is no effective diagnosis or treatment program is not ethical; and it is likely to reinforce beliefs that the disease is not treatable or curable. The multidisciplinary participants and their level of involvement in BHA are reflected in Tables 10 and 11 below.

Table 10: Multidisciplinary participants in BHA

Health Service Delivery Level	Who is Responsible for BHA?	Responsibility
Community	CHA, CBV, SMAG, NHC, influential community leaders	• CHA/CBV can raise awareness at village meetings, in small groups or one-on-one • Nurses can raise awareness at ANC, or other specialized clinics • Breast cancer survivors, in collaboration with clinicians, can also help raise awareness • NGO, FBO and CBO can help support the CBV
Health Post	CHA, CBV, SMAG, FBO, CBO, nurses	
Health Centre	Clinicians, nurses, psychosocial counsellors, EHT, CBV, FBO, CBO, NGO	
District Hospital	Clinicians, nurses, psychosocial counsellors, EHT, NGO	
Provincial Hospital	Clinicians, nurses, psychosocial counsellors, NGO	
Referral Specialized Hospital	Surgeons, medical specialists, trained health providers (multidisciplinary team), NGO	
All Levels	CBO, FBO, CSO, NGO, professional associations, partners (local/international), media, policy makers, program planners, supervisors	• Multidisciplinary approach with appropriate partnerships and collaboration

Table 11: Activity coordination in BHA

Administrative Level	Who is Responsible for BHA?	Responsibility
Village	Involve village headman/woman, ward chairperson, religious leaders, traditional healers.	• Advocacy • Community sensitization
Ward	Ward chairperson NHC chairperson	
District	Involve DHD, TWG, Clinical Care Officer, Cancer focal point person	• Community mobilization to promote early detection and treatment services • Organization of community breast awareness activities • Organization of campaigns to promote breast cancer early detection through mass media channels • Fundraising
Provincial	Involve PHD, TWG, Clinical care specialist, Cancer focal point person	
National	Involve National Coordinator Cancer Control, Assistant Director Cancer, Assistant Director Reproductive Health, Director Clinical Care and Diagnostics Dept., NCCTWG,	

3.4.2.2 Key interventions in BHA and education

- Engage local government authorities and influential community leaders and partner with both community-based organizations (CBO), faith-based organizations (FBO), traditional community leaders and chiefs, and non-governmental organizations (NGO). Sensitize community leaders to provide positive responses, create an enabling environment and mobilize women and men to seek breast health services.

- Use behavior change messages to increase awareness, ability and motivation to use breast health services.

- Develop, adapt and print training and educational materials, including job aids and referral pathways, for distribution to service providers and community members.

- Execute breast cancer awareness outreaches: service providers (e.g. nurses) should visit communities and offer free information about the importance of early detection, as well as ways to reduce the risk of developing breast cancer.

- Train community leaders, health providers, supervisors, managers, community health workers/ volunteers and psychosocial counselors in techniques that will help them engage with the communities, such as participatory discussions, life skills techniques, consensus building and adherence counseling.

3.4.2.3 Facility and community links

The program on early diagnosis of breast cancer focuses on making the initial connection between community members and health facilities so that individuals with signs and symptoms of breast cancer are evaluated quickly, at the entry-point to the health care system, to establish if cancer may be present. Patients with suspicious findings should be connected to an appropriate health facility for diagnostic tests, pathological confirmation, and staging studies before being linked to care and follow up, as appropriate.

Equally, strengthening community and health facility links through existing structures to improve referrals, increase follow up for patients diagnosed with breast cancer and enhance the quality of care, should be given priority. Strengthening partnerships and linkages between health facilities and communities can significantly improve equitable access to care without duplication of services. Sustainable improvement of

service delivery is essential to quality breast cancer patient outcomes.

3.4.3 Referral systems

The referral system in all environments of primary health care ensures equitable possibility of access to secondary and tertiary health care by all members of the community. The way a referral system is implemented has influence on the quality of the health care process in both urban and rural areas, but more especially in rural areas.

The process of referral and patient follow-up is usually disturbed by lack of feedback on the referral system. The lack of feedback from higher to lower levels has been one of the hindering factors in the referral system and adversely affects the quality of health care provision. Feedback is very important to the treatment and management of patients. All referred cases should receive prompt feedback. The apparent disconnect between different levels of the referral system acts as a barrier to the efficiency and quality of patient care.

Non-compliance with the hierarchy of the referral system and referring directly to the physicians and more specialized levels as self-referral is another problem in health care provision. This is more prevalent to those that can pay their way through the system, or in case of emergency, and some people are not prepared to go through the referral process. Admission without referral forms is common; and there is no reference among patients with or without referral forms. Equally, the referral system between the private medical service and specialized cancer services is weak and needs to be strengthened.

The current Zambian referral system requires sufficient coordination and interrelationships between its different levels and elements. In such a system, reference to the higher level will only be possible through the lower level; and referred cases can then be tracked by receiving feedback from the higher levels.

3.4.3.1 Levels of competency in referral chain

The detection of breast cancer in a patient should be as early as possible in the referral chain, starting from the lowest level at the health post up to the highest-level specialist contact at CDH. Although the services are varied depending on the levels of competences available at each health facility, the early diagnosis of breast cancer should not be delayed, but rather enhanced through the existing channel of referral systems. This will help overcome myths and misconceptions amongst the patients and health providers that may find difficulties along the hierarchy of health care provision. This will improve competency amongst health providers and influence their efficient performance.

Competencies can be delineated according to the level of application. The different levels of application are: (a) knowledgeable (work activities are often carried out under guidance); (b) proficient (can perform work without guidance), work activities are performed effectively within quality standards; and (c) advanced (work activities consistently conform to high-quality standards), can also perform the role of advisor and trainer.

3.4.4 Pathology Service

Histopathological and cytopathological services are key in cancer diagnosis. Breast biopsy and surgical specimens should be processed according to acceptable standards and reported in the breast standardized reporting system (see Appendix C for details). Breast markers on DCIS and invasive carcinoma should be done on the core biopsy specimen, where relevant. Only if the results appear discrepant or incongruous with the histology, should the markers be repeated on the excision specimen.

3.4.4.1 Turnaround Time

Turnaround Time (TAT) is broadly defined as the time between specimen receipt by the laboratory and the issuing of the final pathology report. TAT for large or complex surgical pathology specimens is an indicator of efficiency in anatomic pathology and may affect coordination of patient care. Assessment of TAT should account for variable fixation and processing duration.

The following are minimum accepted TAT for breast specimens:

a)	FNAC	5 days
b)	CNB	7 days
c)	Incisional biopsy	7 days
d)	Excisional biopsy	7 days
e)	Mastectomy	14 weeks

3.4.4.2 Specimen collection, fixation, preservation and transportation

Types of specimens taken at surgery of breast include small biopsies (such as core needle biopsies) and larger samples including part of or entire breast (mastectomy). Collection and transportation of these specimens for histopathological examination involves a series of essential steps from the time it is taken at surgery to its reception in the laboratory. These include:

- Putting the specimen in an appropriate container
- Immersed in an appropriate type and amount of fixative
- Accurate identification and labelling of the specimen container with corresponding patient details on the request form
- Completeness of information in the request form including relevant clinical details

3.4.4.3 Guidelines for handling and transporting histopathology specimens

These include instructions for collection and transportation of histopathology specimens of different sizes to ensure optimal tissue fixation as well as accurate documentation, and inclusion of clinical information in the request form that may be needed to aid histopathological diagnosis.

Pathology request form

The use of a standardized request form for all breast tissue specimens is strongly recommended. The information on the request form should be precise and provided by the surgeon, or other clinician, as relevant to the specimen type. It is strongly recommended that the surgeon who performs the procedure must fill the pathology request form (see Appendix D for details).

Small biopsy specimens (CNB, incisional and excisional biopsies)

The specimen should be collected into a wide-mouthed container with a well-fitting lid containing an adequate amount of 10% neutral buffered formalin to completely submerge the specimen. The container should be accurately labelled, including patient name, age, sex, ward, and hospital number.

If multiple biopsies are sent from the same patient, each specimen should be sent in a separate container indicating the sites of biopsy. Core needle biopsies should be placed on a filter paper and then submerged in fixative.

Large specimen samples (partial or total mastectomies)

The specimen should be placed in a wide-mouthed container with a well-fitting lid, containing an adequate amount of 10% neutral buffered formalin. The container should be larger than the specimen, preferably a bucket. Do not squeeze the specimen into the container.

The container should be accurately labelled, including patient name, age, sex, ward, and hospital number.

Orientation sutures should be placed and clearly identified in the request form. Slicing the specimen is not recommended in general. This is because the sliced specimen distorts on fixation and affects accurate measurement of distance of the lesion to excision margins.

Transportation of specimens

Specimens should be transported to the laboratory as soon as possible for proper fixation procedures to be carried out. For transport of all pathology specimens and associated materials by air or surface transport methods, the packaging must consist of three components:

- Primary receptacle
- Secondary packaging
- Outer packaging.

This is also known as ***triple packaging.***

Steps to better specimen collection and transportation

Step 1 - Avoid Mechanical Trauma

Ensure that tissue is removed gently to avoid trauma to the specimen caused by crushing or tearing. This applies both during surgery and any further dissection that may be required of a fresh specimen. Do not allow the specimen to be damaged before fixation by crushing or tearing during removal.

Step 2 - Prevent Specimen Drying

Ensure that the specimen is not allowed to dry prior to fixation. If immediate fixation is not practicable, gauze moistened with saline can be used to prevent this. Do not allow the specimen to be left on absorbent surface for some time prior to fixation.

Step 3 - Avoid Heat Damage

Ensure that you avoid local heat damage to specimens (some damage by cautery may be unavoidable). Do not allow any unnecessary local heat applied to tissue to cause damage. Fresh tissue is particularly susceptible.

Step 4 - Avoid Chemical Damage

Ensure that you avoid contaminating fresh specimens with foreign chemicals or substances such as disinfectants. Do not allow the surface of unfixed tissue to be penetrated and damaged by foreign reagents or substances.

Step 5 - Label Specimens Properly

Ensure that each specimen is properly identified, and all details recorded as soon as possible after collection. Do not allow delays in recording of specimen details.

Step 6 - Ensure Prompt Fixation

Ensure that fixation is always carried out promptly. If it is necessary that a specimen remains unfixed for a short period of time, it should be refrigerated at 4 °C. Do not allow delays in fixation (degeneration of tissue elements commences as soon as the specimen is deprived of blood supply).

Step 7 - Use Sufficient Fixative and Suitable Container

Ensure that an adequate volume of fixative (ratio of at least 20:1) is used in a container of an appropriate size. This avoids distortion of the fresh specimen and ensures good quality fixation. Do not allow specimens to be squashed into a small container with insufficient fixative to cover the specimen surface.

Step 8 - Check Fixative pH

Ensure that the fixative is of high quality and at the optimal pH. Do not allow a fixative of poor quality and unknown pH. If formalin is used at acid pH, it rapidly produces "formalin pigment" by reaction with hemoglobin. Near neutral solutions will still produce the pigment, but much more slowly. In good histological preparations, formalin pigment should be removed prior to staining.

Role of second opinion: Second opinions are an integral part of pathology services. In most instances, a second opinion will confirm the original diagnosis, with only minor changes of no substantial impact for that person.

In about 1 to 10% of the cases, a second opinion can translate into a substantial change in treatment. For example, a diagnosis of non-invasive breast cancer, i.e. ductal carcinoma in situ (DCIS), on second opinion may reveal microscopic evidence of a small invasive cancer. This finding may require a more aggressive approach to treatment.

If someone receives a diagnosis of breast cancer and wants to ask for a second opinion, the sooner it is done, the better. Certainly, a second opinion should be obtained before any definitive surgery, like a mastectomy, or a treatment with substantial side effects, such as radiation therapy or chemotherapy. Anyone requesting a second opinion needs to provide information of the first report, the name and contact information of the doctor to be notified.

A second opinion will only be accepted if it was reported by a qualified medical doctor who is specialized in histopathology, surgical pathology, anatomic pathology or equivalent;

AND: is recognized and registered on the histopathology specialist register of the Health Professions Council of Zambia (HPCZ);

AND: is recognized and registered as a histopathology specialist by the Pathologists Association of Zambia (PATHAZ).

3.4.5 Monitoring and Evaluation

Monitoring and evaluation (M&E) is a process that helps improve performance and achieve the planned results. Its goal is to improve current and future management of inputs, outputs, outcomes and impact. Monitoring and evaluation of the breast cancer early diagnosis program will aim to:

- Monitor and evaluate the implementation of the national guidelines for early diagnosis of breast cancer through appropriate existing and new mechanisms.
- Design of the monitoring tools in collaboration with clinicians. The national breast cancer sub-committee (NCCTWG), will be responsible for periodic review of the tools. This will ensure timely provision of information on how the interventions are performing and whether the intended objectives and targets are being achieved.

Further, it will show the extent to which the Ministry of Health is achieving desired outcomes and impact as outlined in the National Health Strategic Plan [NHSP 2017-2021] (Zambia Ministry of Health, 2016a) and National Cancer Control Strategic Plan [NCCSP 2016-2021] (Zambia Ministry of Health, 2016b). This enables informed decisions regarding program management, service delivery, and appraisal of outputs.

This program will be guided by the following:

- The NHSP M&E framework (2017-2021) and NCCSP 2016-2021
- Clearly defined and measurable indicators
- Standard data collection tools to be used at established SBCU
- Data from the Cancer Diseases Hospital (CDH)
- The Zambia National Cancer Registry (ZNCR) database
- Clear guidelines for data management
- Effective scheduled collection of essential information
- Generation of regular (weekly and monthly) monitoring reports at health facility level

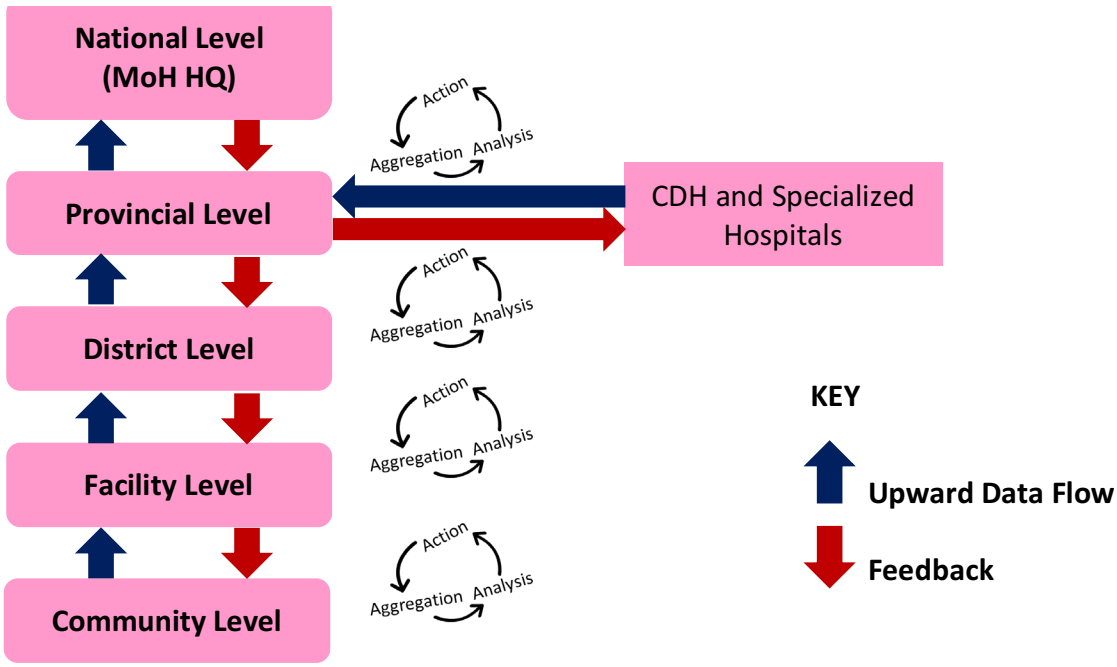
The M&E system will detail the approaches to monitor, evaluate and report the activities based on specific objectives linked with the existing Health Management and Information System (HMIS). The program will use the existing system protocol which is operational from the facility to central level for data collection and reporting. The DHIS2, HMIS and Zambia National Cancer Registry's CANREG5 systems will be used to monitor the national program. Analysis of the available information will be coordinated by the Directorate of Monitoring & Evaluation at the Ministry of Health.

3.4.5.1 Reciprocal data flow

Provision of breast cancer early diagnosis will be instituted at all levels of health care service delivery. It is imperative that primary health care providers recognize the signs and symptoms of breast cancer and then initiate a referral mechanism for diagnosis. The location of the patient will determine whether the referral is to a district, general, central or teaching hospital. Existing referral forms in the health facility should be used as appropriate.

Figure 1 below outlines recommendations for data flow from the health facility to central level and vice versa. This should be integrated in the existing monitoring and evaluation systems.

Figure 1: Reciprocal data flow



3.4.5.2 Program indicators

The program will track key performance indicators through the HMIS, using the indicators outlined in Table 12, below:

Table 12: Key program indicators

Level	Location	Suggested Indicators
Health Post	Rural/Urban	• Number of health posts offering BHA activities and CBE • Number of BHA activities by health post • Number of clients accessing CBE monthly • Number of clients with abnormal findings/total number of clients seen • Number of staff trained in CBE • Number of clients with breast cancer symptoms referred to the next level
Health Center	Rural/Urban	• Number of health centers offering BHA activities and CBE • Number of BHA activities carried out by health center • Number of clients accessing CBE monthly • Number of clients with abnormal findings/total • Number of clients seen • Number of staff trained in CBE • Number of clients with breast cancer symptoms referred to the next level
Hospital I	District/Urban	• Number of level I hospitals offering breast health awareness activities and CBE • Number of BHA activities carried out • Number of clients accessing CBE monthly • Number of clients with abnormal findings/total • Number of clients seen • Number of staff trained in CBE • Number of breast USG done • Number of breast USG core biopsies • Number of clients with breast cancer symptoms referred to the next level • Number of breast pathology reports received • TAT for pathology reports

Hospital II	Provincial	• Number of level II hospitals offering breast health awareness activities and CBE • Number of BHA activities carried out • Number of clients accessing CBE monthly • Number of clients with abnormal findings/total • Number of clients seen • Number of staff trained in CBE • Number of breast USG done • Number of MMG done • Number of breast USG core biopsies • Number of clients with breast cancer symptoms referred to the next level • Number of breast pathology reports received • TAT for pathology reports • Number of malignant biopsy reports/total number of biopsies • Number of clients receiving chemotherapy • Number of clients receiving radiotherapy • Number of breast surgeries done according to protocol • Number of clients with early stage breast cancer (I & II)/ total number of clients with breast cancer • Number of clients with late stage breast cancer (III & IV)/ total number of clients with breast cancer
Hospital III	Central	• Number of level III hospitals offering breast health awareness activities and CBE • Number of BHA activities carried out • Number of clients accessing CBE monthly • Number of clients with abnormal findings/total • Number of clients seen • Number of staff trained in CBE • Number of MMG done • Number of breast USG done • Number of breast USG core biopsies • Number of clients with breast cancer symptoms referred to the next level • Number of breast pathology reports received • Number of malignant biopsy reports/total number of biopsies • TAT for pathology reports • Number of clients receiving chemotherapy • Number of clients receiving radiotherapy • Number of breast surgeries done according to protocol • Number of clients with early stage breast cancer (I & II)/ total number of clients with breast cancer • Number of clients with late stage breast cancer (III & IV)/ total number of clients with breast cancer

CDH and Specialized Hospital	CDH	• Number of level III hospitals offering breast health awareness activities and CBE • Number of BHA activities carried out • Number of clients accessing CBE monthly • Number of clients with abnormal findings/total number of clients seen • Number of MMG done • Number of staff trained in CBE • Number of breast USG done • Number of breast USG core biopsies • Number of clients with breast cancer symptoms referred to the next level • Number of breast pathology reports received • Number of malignant biopsy reports/total number of biopsies TAT for pathology reports • Number of clients receiving chemotherapy • Number of breast surgeries done according to protocol • Number of clients receiving radiotherapy • Number of clients with early stage breast cancer (I & II)/ total number of clients with breast cancer • Number of clients with late stage breast cancer (III & IV)/ total number of clients with breast cancer • Disease free survival, overall survival

4.0 Conclusion

The national guidelines for early diagnosis of breast cancer increases the chance of successful treatment by detecting disease at an earlier point when it is less extensive, with increased likelihood of achieving remission. The identification, diagnosis, treatment and management of breast cancer in the earliest stages is more effective, has fewer complications, is less costly, and greatly improves the quality of patient care and outcomes. Women should be encouraged to reduce their risk of breast cancer by undertaking appropriate measures to curb the modifiable risk factors. However, it is also imperative that primary health care providers recognize the signs and symptoms of breast cancer and facilitate prompt referral for early diagnosis, treatment and management.

Every health facility should be proactively involved in breast health awareness activities and the early diagnosis of breast cancer to identify people who might be affected with the disease. The purpose of these national guidelines is to facilitate identification of breast cancer at the earliest possible opportunity and link the patient to an appropriate level of health care without delay.

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Appendix A

Breast Cancer Signs and Symptoms

- The warning signs of breast cancer are not the same for all women.
- The most common symptom of breast cancer is a new lump or mass.
- Other possible symptoms of breast cancer include:
  - Swelling of whole or part of a breast even if no distinct lump is felt
  - Skin irritation or dimpling
  - Breast or nipple pain
  - Nipple retraction (turning inward)
  - Redness, scariness, or thickening of the nipple or breast skin
  - Nipple discharge (other than breast milk)
- Sometimes a breast cancer can spread to lymph nodes under the arm or around the collar bone and cause a lump or swelling there, even before the original tumor in the breast tissue is large enough to be felt. Swollen lymph nodes should also be checked by a healthcare provider.
- In late stages, common presentations include:
  - Ulceration
  - Enlarged lymph nodes in the armpit and neck
- Signs and symptoms of distant metastasis such as un-resolving cough, weight loss, shortness of breath, bone pain and pathological fractures may also be present. Pain is usually a late symptom.
- Breast cancer can also occur or be diagnosed during pregnancy.

Appendix B

ACR BI-RADS® Atlas Fifth Edition

QUICK REFERENCE

ULTRASOUND			MAMMOGRAPHY		
Tissue composition *(screening only)*	a. Homogeneous background echotexture – fat b. Homogeneous background echotexture – fibroglandular c. Heterogeneous background echotexture		Breast Composition	a. The breasts are almost entirely fatty b. There are scattered areas of fibroglandular density c. The breasts are heterogeneously dense, which may obscure small masses d. The breasts are extremely dense, which lowers the sensitivity of mammography	
Masses	Shape	Oval	Masses	Shape	Oval
		Round			Round
		Irregular			Irregular
	Orientation	Parallel		Margin	Circumscribed
		Not parallel			Obscured
	Margin	Circumscribed			Microlobulated
		Not circumscribed - Indistinct - Angular - Microlobulated - Spiculated			Indistinct
					Spiculated
				Density	High density
					Equal density
					Low density
					Fat-containing
	Echo pattern	Anechoic	Calcifications	Typically benign	Skin
		Hyperechoic			Vascular
		Complex cystic and solid			Coarse or "popcorn-like"
		Hypoechoic			Large rod-like
		Isoechoic			Round
		Heterogeneous			Rim
	Posterior features	No posterior features			Dystrophic
		Enhancement			Milk of calcium
		Shadowing			Suture
		Combined pattern		Suspicious morphology	Amorphous
Calcifications	Calcifications in a mass				Coarse heterogeneous
	Calcifications outside of a mass				Fine pleomorphic
	Intraductal calcifications				Fine linear or fine-linear branching
Associated features	Architectural distortion			Distribution	Diffuse
	Duct changes				Regional
	Skin changes	Skin thickening			Grouped
		Skin retraction			Linear
	Edema				Segmental
	Vascularity	Absent	Architectural distortion		
		Internal vascularity	Asymmetries	Asymmetry	
		Vessels in rim		Global asymmetry	
	Elasticity assessment	Soft		Focal asymmetry	
		Intermediate		Developing asymmetry	
		Hard	Intramammary lymph node		
Special cases	Simple cyst		Skin lesion		
	Clustered microcysts		Solitary dilated duct		
	Complicated cyst		Associated features	Skin retraction	
	Mass in or on skin			Nipple retraction	
	Foreign body including implants			Skin thickening	
	Lymph nodes – intramammary			Trabecular thickening	
	Lymph nodes – axillary			Axillary adenopathy	
	Vascular abnormalities	AVMs (arteriovenous malformations/ pseudoaneurysms)		Architectural distortion	
		Mondor disease		Calcifications	
	Postsurgical fluid collection		Location of lesion	Laterality	
	Fat necrosis			Quadrant and clock face	
			Depth		
			Distance from nipple		

MAGNETIC RESONANCE IMAGING					
Amount of fibroglandular tissue (FGT)	a. Almost entirely fat b. Scattered fibroglandular tissue c. Heterogeneous fibroglandular tissue d. Extreme fibroglandular tissue		Associated features	Nipple retraction	
			Nipple invasion		
			Skin retraction		
			Skin thickening		
Background parenchymal enhancement (BPE)	Level	Minimal		Skin invasion	Direct invasion
		Mild			Inflammatory cancer
		Moderate		Axillary adenopathy	
		Marked		Pectoralis muscle invasion	
	Symmetric or asymmetric	Symmetric		Chest wall invasion	
		Asymmetric		Architectural distortion	
Focus			Fact containing lesions	Lymph nodes	Normal
Masses	Shape	Oval			Abnormal
		Round		Fat necrosis	
		Irregular		Hamartoma	
	Margin	Circumscribed		Postoperative seroma/hematoma with fat	
		Not circumscribed - Irregular - Spiculated	Location of lesion	Location	
				Depth	
			Kinetic curve assessment Signal intensity (SI)/ time curve description	Initial phase	Slow
					Medium
					Fast
				Delayed phase	Persistent
					Plateau
					Washout
	Internal enhancement characteristics	Homogeneous	Implants	Implant material and lumen type	Saline
		Heterogeneous			Silicone - Intact - Ruptured
		Rim enhancement			
		Dark internal septations			Other implant material
Non-mass enhancement (NME)	Distribution	Focal			Lumen type
		Linear			- Single
		Segmental			- Double
		Regional			- Other
		Multiple regions		Implant location	Retroglandular
		Diffuse			Retropectoral
	Internal enhancement patterns	Homogeneous		Abnormal implant contour	Focal bulge
		Heterogeneous			
		Clumped		Intracapsular silicone findings	Radial folds
		Clustered ring			Subcapsular line
Intramammary lymph node					Keyhole sign (teardrop, noose)
Skin lesion					
Non-enhancing findings	Ductal precontrast high signal on T1W				Linguine sign
	Cyst			Extracapsular silicone	Breast
	Postoperative collections (hematoma/ seroma)				Lymph nodes
			Water droplets		
	Post-therapy skin thickening and trabecular thickening			Peri-implant fluids	
	Non-enhancing mass				
	Architectural distortion				
	Signal void from foreign bodies, clips, etc.				

BI-RADS® ASSESSMENT CATEGORIES			
Category 0:	**Mammography: Incomplete** – Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison **Ultrasound & MRI: Incomplete** – Need Additional Imaging Evaluation		
Category 1:	Negative		
Category 2:	Benign		
Category 3:	Probably Benign		
Category 4:	Suspicious	Mammography & Ultrasound:	Category 4A: Low suspicion for malignancy
			Category 4B: Moderate suspicion for malignancy
			Category 4C: High suspicion for malignancy
Category 5:	Highly Suggestive of Malignancy		
Category 6:	Known Biopsy-Proven Malignancy		

For the complete Atlas, visit acr.org/birads

Source: D'Orsi, Sickles, Mendelson, Morris, et al., 2013

Appendix C

Standardized Breast Histology Report System

<table>
<tr><th>Microscopic examination</th><th>Basic immunohistochemistry</th></tr>
<tr><td rowspan="3">

Histological diagnosis: State any specific type of carcinoma. (WHO classification of breast cancer)
Size of lesion: Check if greater than gross estimate: use a micrometer, if possible, greatest dimension.
Histologic grade of tumor: Use the Nottingham histologic score
Lymphovascular invasion outside the tumor: Indicate if present or absent
Relation with margins: Distance to closest margin and state which margin, if possible
Skeletal muscle involvement: State if invaded
Skin involvement: Ulceration/dermal invasion/ dermal lymphatic invasion
Nipple involvement: State the presence of Paget's disease or stromal invasion
Intraductal component: State if present or absent, pattern and grade of DCIS, margin status
Intralobular component: State the presence or absence of LCIS
Calcification in the tumor (or DCIS): State if present or absent
Lymph Nodes: Number of sentinel nodes removed, and number of sentinel nodes positive for metastases
Extra nodal extension: Measure distance from capsule
Pathological TNM stage: Based on information available to the pathologist

</td><td>
Estrogen Receptor
Results and interpretation:

State if positive or negative
State the percentage of tumor cells with nuclear positivity
Sate the average intensity of tumor cell nuclei staining: weak/moderate/strong

</td></tr>
<tr><td>
Progesterone Receptor
Results and interpretation:

State if positive or negative
State the percentage of tumor cells with nuclear positivity
Sate the average intensity of tumor cell nuclei staining: weak/moderate/strong

</td></tr>
<tr><td>
HER2 neu/ erbB2
Results and interpretation:

State if positive or negative or equivocal
MiBB/ Ki67 index
E- Cadherin

</td></tr>
</table>

Appendix D

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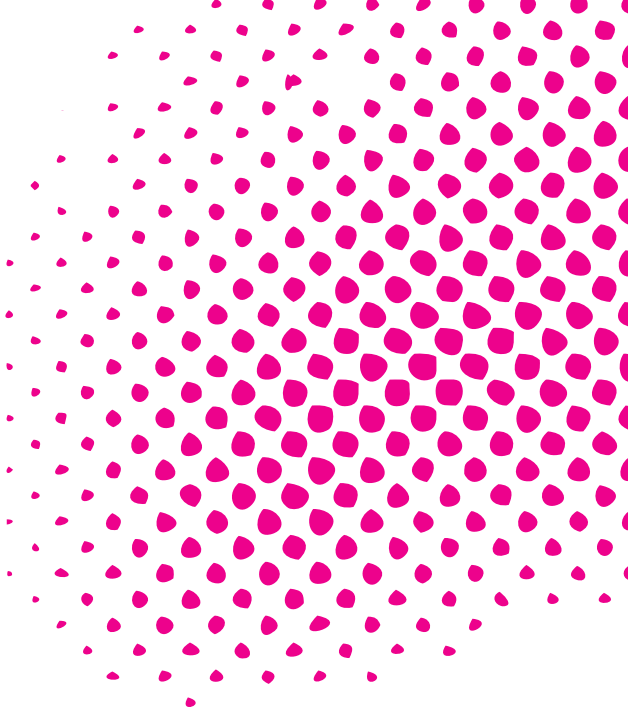

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