GUIDELINE FOR

SCREENING GASTRIC CANCER, CERVICAL CANCER & BREAST CANCER

Health Flagship Project
Ministry of health
Royal Government of Bhutan

Table of Contents

Executive Summary

The current health system with its focus on primary health care has remained the backbone of health services in the country and contributed immensely to health outcomes in the past 5 decades, with Bhutan achieving most of the Health MDG goals. The rapid socio-economic development, the national goal of Universal Health Coverage and the epidemiologic transition of diseases to more NCDs and Cancers has resulted in more demand for tertiary healthcare services, expansion of health facilities and increasing patient referrals, leading to escalating costs for healthcare provision. The budget allocation for health services has not seen a corresponding increase; in fact, the Health Ministry's annual budget allocation has been decreasing over the years as a proportion of the annual government budget. Recognizing that Gastric and Cervical cancers contribute to most of the cancer burden and mortality, this Flagship project specifically targets prevention of Gastric, Cervical and Breast cancers, by introducing early screening programs for Gastric and Breast cancers and improving on the existing cervical cancer screening program. The strategies involve the introduction of new screening tests with the goal of reaching all the target populations and providing treatment, sustained health advocacy, and having adequate human resources in place. The health flagship project is one of the many flagship-projects the government has committed. The health flagship project has allocated funds of Nu. 1109.572 million and the project has to be completed by 2023.

For a successful implementation of the project, a separate Project Management Unit (PMU) for the health flagship project is established in MoH. The overall target of the project and implementation strategy will be based on the project blueprint approved by Gross National Happiness Commission (GNHC). However, in order to have a robust and evidence-based screening program in the field, it is imperative to have a technical

good guideline in place. So, the Technical Working Group (TWG) for the program has developed the guideline for screening gastric and breast cancer before the actual implementation of the screening program. The TWG is a group expert from various medical fields formed to give technical guidance to the PMU during the implementation of the project. The guideline is developed in reference to available scientific evidence, international screening documents and at the same time considering our own context in terms of availability and capacity of infrastructure and human resources.

Background

As per the population-based cancer registry of Bhutan 2014-2018, the age-adjusted incidence rate per 100,000 populations is 64 and 89.8 for male and female, respectively. The cumulative risk of getting cancer among females is 1 in 9 (11%) and among male is 1 in 11 (9%). The top five cancers in male are Stomach, Oesophagus, Liver lung and Rectum cancer whereas Cervix Uteri, Stomach, Breast, Thyroid and Ovary cancers are five leading cancers in females. Around 62% of cancer cases were referred out of the country for treatment and confirmation of diagnosis. By district wise, the highest number of stomach cancer case was from Paro, followed by Wangdue Phodrang, Punakha, Trashigang and Haa, whereas the highest number cervical cancer case was from Trashigang, followed by Mongar, Wangdue Phodrang, Chukha and Samtse. The age-adjusted cancer mortality rate in Bhutan per 100,000 populations is 30.7 and 31.5 for male and female, respectively. The leading cancer death in males is due to stomach cancer, followed by Oesophagus, Liver, Lung and Gallbladder cancer and in females is due to cervix uteri, followed by Stomach, Lung, Ovary and Liver cancer. The First Report on the Prevalence and Epidemiology of Helicobacter pylori in Bhutan has shown almost all Bhutanese carry H. *pylori* bacteria, with the prevalence rate of 66% to 82%. Through genotyping, H. *pylori* strains in Bhutan are found to be very virulent which are responsible for causing gastric cancer.

Objectives:

The health flagship will contribute towards the above goals through the following objectives:

- Reduce Gastric cancer incidence and mortality through early screening and prevention
- Reduce Cervical cancer incidence and mortality through early screening and prevention
- Reduce Breast cancer incidence and mortality through early screening and prevention

Target:

The health flagship will aim to achieve the following measurable targets by 2023

A. Gastric cancer
   - All target population are screened for H. *pylori*
   - All screened population (H. *pylori* positive) receive triple therapy treatment
   - All high-risk target population are screened for gastric cancer and managed

B. Breast cancer
   - All target population are screened for breast cancer and managed

C. Cervical cancer
   - All eligible women are screened for cervical cancer
   - All screen positive women receive treatment/management

GASTRIC CANCER

I. Introduction:

Gastric cancer is one of the common malignancies worldwide and it is still the 3rd leading cause of cancer-related deaths globally. In Bhutan gastric cancer is the commonest malignancy in male with an incidence rate of 16.6 per 100000 population and the second commonest malignancy in females after cervical cancer with an incidence rate of 11.7 per 100000 population. At the same time, gastric cancer is also the leading cause of cancer mortality rate of 8.3 and 5.2 per 100000 population in male and females, respectively. (source: Population based cancer registry 2014-2018).

II. Risk factors for Gastric cancer

The cause of gastric cancer is multifactorial.

- H. pylori infection
- High salt intake and salt preserved food
- Smoking, alcohol and tobacco consumption
- Low dietary fibre intake
- Family history of gastric cancer

III. Prevention of Gastric cancer

a) Primary prevention-
   - Lifestyle changes
   - Cessation of smoking
   - Reducing salt intake
   - More fruits and vegetables
   - Eradicating H. *pylori*

b) Secondary prevention-
   - Detection of precancerous lesion, atrophy, intestinal metaplasia, dysplasia and early gastric cancer through the screening program.

IV. Gastric Cancer Screening Program

1. MASS H. PYLORI ERADICATION PROGRAM

Globally, following methods can be used for diagnosis of H. *pylori* infection:

- Stool antigen test
- Urea breath test
- Rapid Urease Test in UGIE biopsy specimen
- Histopathology
- Culture

a) Target Population: All population between 18 years- 75 years

b) Method: Rapid Stool Antigen Test

Steps for screening and treatment for H. *pylori* is given in the flow chart (figure 1)

» Test for H. *pylori* by Rapid Stool Antigen Test kit
» Treat all positives by CAP regimen
» Retest for eradication using Rapid Stool Antigen Test kit
» Put on second line treatment if still positive after treatment
» Refer for UGIE if still positive after a second line treatment

c) Definitive treatment

Initiate triple therapy (CAP) for 14 days for H. *pylori* infected patients as the 1st line drug. And put on quadruple therapy for 14 days as the 2nd line drug, if the patient tests positive on repeat H. *pylori* test. Do UGIE with biopsy and culture for H. *pylori*, if still resistant to 2nd line drugs.

1st line therapy (Triple Therapy)	2nd line therapy (Quadruple Therapy)
▪ Clarithromycin 500mg BD ▪ Amoxicillin 1g BD ▪ Pantoprazole 40 mg BD	▪ Tetracycline 500mg QID ▪ Bismuth Subsalicylate 520mg qid/Bismuth Subcitrate 120mg -one tablet QID ▪ Pantoprazole 40mg BD ▪ Tinidazole 500mg BD

***Note**: Before initiating CAP therapy, exclude penicillin allergy. If allergic to penicillin, replace it with Tinidazole 500 mg BD for 2 weeks. Advise patients to call 112 for help in case of drug allergy.*

2. ENDOSCOPY SERVICES

a) **Target Population**: Age 40- 75 years with following risk factors;

1. People with history of atrophic gastritis
2. History of H. *pylori* infection
3. People with history of gastric cancer in the family
4. Any patient with history of dyspepsia with alarm features
5. Smoking, tobacco and alcohol consumption

**Note: Endoscopy service to be given to any patient irrespective of age and sex if there are clinical indications, and for patients resistant to quadruple therapy.*

b) **Method:**

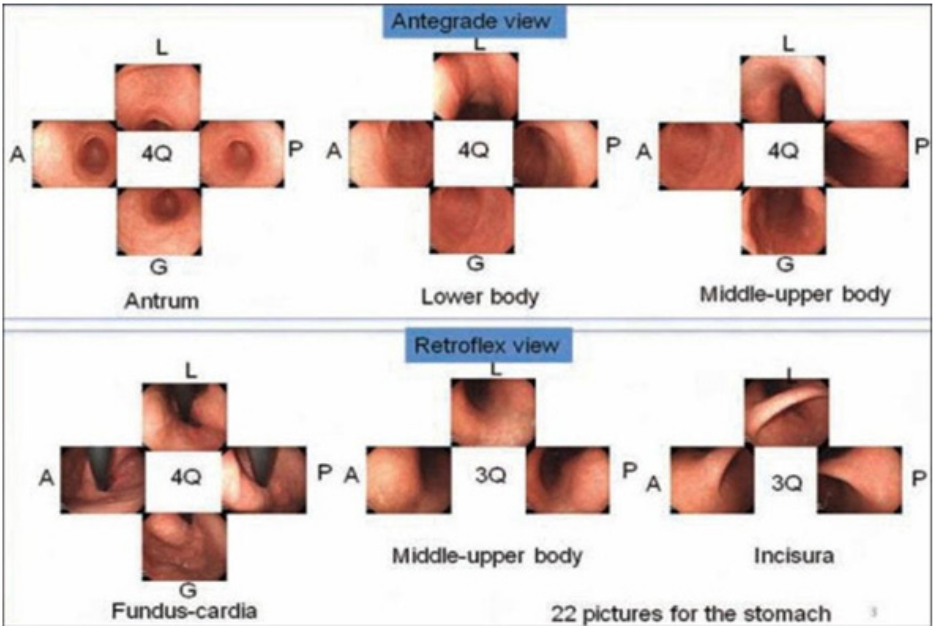
- Steps for screening for gastric cancer is given in the flow chart (figure 1)

» Do viral markers (HIV,HCV,HBsAg) before subjecting to endoscopy procedure
» Do Upper Gastrointestinal Endoscopy (UGIE)
» Take tissue biopsy from suspicious lesions
» If the biopsy report is malignant, refer to Oncosurgeon
» For mild/moderate atrophic gastritis, repeat UGIE after five 5 years
» For intestinal metaplasia and severe atrophic gastritis with family history of gastric cancer, repeat UGIE after 12 months
» For intestinal metaplasia and severe atrophic gastritis with family history of gastric cancer, repeat UGIE in 1 year and without family history, repeat UGIE after 3 years
» Forow-grade dysplasia, repeat UGIE after 1 year
» For high-grade dysplasia, repeat UGIE after 6 months
» High grade dysplasia with clinical suspicion for malignancy, refer for surgical procedure.

- **Procedure for Endoscopy:**

The systematic screening of the stomach must be used for endoscopy procedures and all endoscopists must follow this protocol while doing endoscopy for screening in a uniform manner.

» Map the stomach into 22 sites
» Take picture of suspicious sites
» Examine carefully to search for early gastric carcinoma
» Take tissue biopsy (minimum of 3) from suspicious lesions
» Tissue biopsy (minimum 3) for all suspicious lesion to be taken
» If biopsy result is positive, do further evaluation for staging by CT abdomen and follow with onco-surgeon/ gastroenterologist/ surgeon



A-Anterior wall of stomach; P-Posterior wall of stomach; L-Lesser Curvature of stomach; G-Greater Curvature of stomach; Q-Quadrant

Figure 1: Systematic Screening of Stomach (SSS) during endoscopy (22 pictures to be taken to map the entire stomach) (picture courtesy; Prof Kenshi Yao, Japan)

- **Standard Reporting format for Endoscopy:**

For uniform reporting, all endoscopists must use the standard reporting format given in the table below;

Esophagus	Stomach	Duodenum (D1)	Duodenum (D2)
▪ Normal ▪ Growth in Esophagus ▪ Polyp ▪ Barrett's Esophagus	▪ Normal ▪ Gastritis ▪ Erosion ▪ Ulcer ▪ Atrophy ▪ Suspicious lesion ▪ Polyp ▪ Growth in stomach	▪ Normal ▪ Deformed ▪ Duodenitis ▪ Ulcer	▪ Normal ▪ Polyps ▪ Growth in duodenum

- **Standard Reporting format for Histopathology (biopsy):**

For uniform reporting, all pathologists must use the following standard reporting format given below;

Stomach	
▪ Normal ▪ Erosion (present/Absent) ▪ Ulcer (present/Absent) ▪ Inflammation (Active/Chronic) ▪ H. *pylori* infection (present/absent) ▪ Gastritis (Active/chronic/chronic active)	▪ Atrophy (present/Absent), If present (mild/moderate/severe) ▪ Intestinal metaplasia (complete/incomplete) ▪ Dysplasia (low grade/high grade) ▪ Malignancy (Intramucosal carcinoma(carcinoma insitu)/Invasive carcinoma(adenocarcinoma))

Treatment of gastric cancer: refer to onco-surgeon for necessary treatment

Note:

- Get the consent from the patient before performing the procedure
- Detailed patient data must be maintained in the register and must be reported in the reporting system for gastric cancer screening program (DHIS-2)
- A unique sample identifier generated for a patient by the DHIS-2 system must be written on the biopsy sample and shipped to the nearest histopathology lab.
- Follow the screening algorithm given in Figure 1
- Refer SOP for early gastric cancer screening

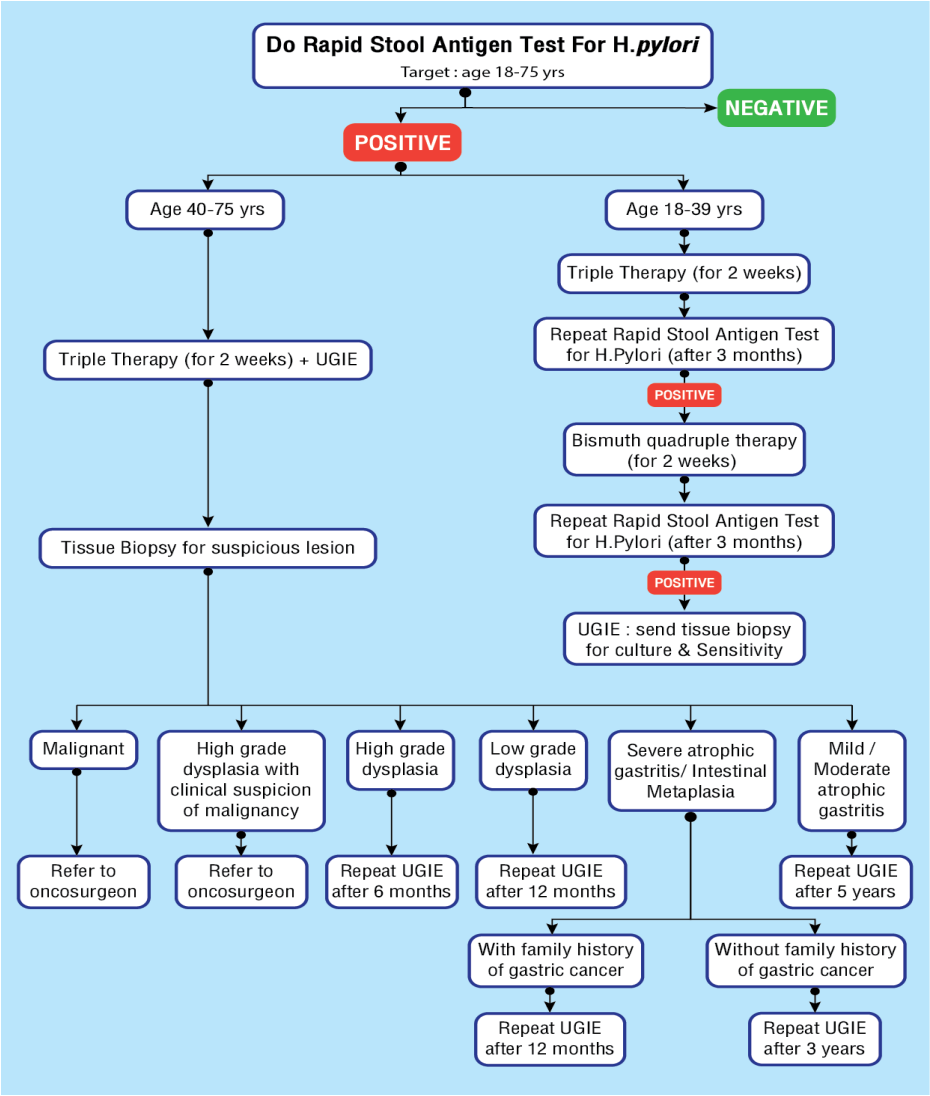


Figure 1: Flowchart for gastric cancer screening

3. ADVOCACY PROGRAMS ON GASTRIC CANCER

Health advocacies and education must be given to both health workers and the public

a. Training and educating health worker on prevention, early detection and treatment

b. Public awareness on gastric cancer through National TV programs, National events etc.

c. Public education by local health workers and CSOs

4. RESOURCE REQUIREMENT FOR GASTRIC CANCER SCREENING PROGRAM

Human Resource	Medical infrastructure
▪ Endoscopists ▪ Endoscopy nurse ▪ Pathologist ▪ Histotechnician ▪ Medical Technologists/Medical Lab Technicians	▪ Endoscopy set ▪ Rapid Stool Antigen test kit for H. *pylori* ▪ Pathology Equipment ▪ Other necessary accessories/consumables

BREAST CANCER

I. Introduction

Breast cancer is one of the top cancers in women both in the developed and the developing world. There are approximately over 2.08 million new cases of breast cancer worldwide and 627000 women died in 2018 due to breast cancer (source: GLOBOCAN 2018). The low survival rate in less developed countries can be explained mainly by the lack of early detection programmes, resulting in a high proportion of women presenting with late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities. Currently, breast cancer is the 3rd most common cancer in Bhutanese females with an incidence rate of 6.8 per 100000 population. Breast cancer can affect males also but it is very rare. Amongst the different screening methods available for breast cancer, mammography has been proven to be the most effective. However, it is very costly and is feasible in countries with good health infrastructure that can afford long-term organized population-based screening programmes. Low-cost screening approaches, such as clinical breast examination, could be implemented in limited resource settings. Breast cancer, if detected early and adequately treated, is curable.

II. Risk Factors for Breast Cancer

Several risk factors for breast cancer have been well documented. However, for the majority of women presenting with breast cancer it is not possible to identify specific risk factors (IARC, 2008; Lacey et al., 2009)

- Family history of breast cancer, uterine and ovarian cancer
- Genetic predisposition (BRCA1, BRCA2 and p53)
- Nulliparity (age above 40 years), Early menarche, late menopause, advanced age at first childbirth
- Prolonged (>10 years) use of oral contraceptive and hormone replacement therapy. (IARC, 2008, Lacey et al., 2009).

- History of chest radiation
- Modifiable risk factors including alcohol use, obesity, sedentary lifestyle and smoking

III. Prevention and control

Advocacy

» Control of specific modifiable breast cancer risk factors
» Early detection
» Timely diagnosis and treatment
» Rehabilitation and palliative care
» Breastfeeding and pregnancy before 30 years has a protective effect (Source: Helewa M et al.)

IV. Early detection and diagnosis.

a) **Screening:** Many women with breast cancer have no symptoms. Therefore, a systematic application of screening test in a presumably asymptomatic population is recommended; which aims to identify individuals with an abnormality suggestive of cancer.

b) **Early diagnosis:** Advocate awareness of early signs and symptoms in symptomatic populations in order to facilitate early diagnosis and treatment.

Following are some of the signs and symptoms of breast cancer;

- Lump/swelling in breast or arm pits
- Pain in the breast or nipple
- Nipple discharge and or retraction
- Change in skin color and texture of the breast
- Eczema of nipple and or areola
- Breast shrinking or enlargement

V. Screening Program

1. BREAST SELF EXAMINATION (BSE)

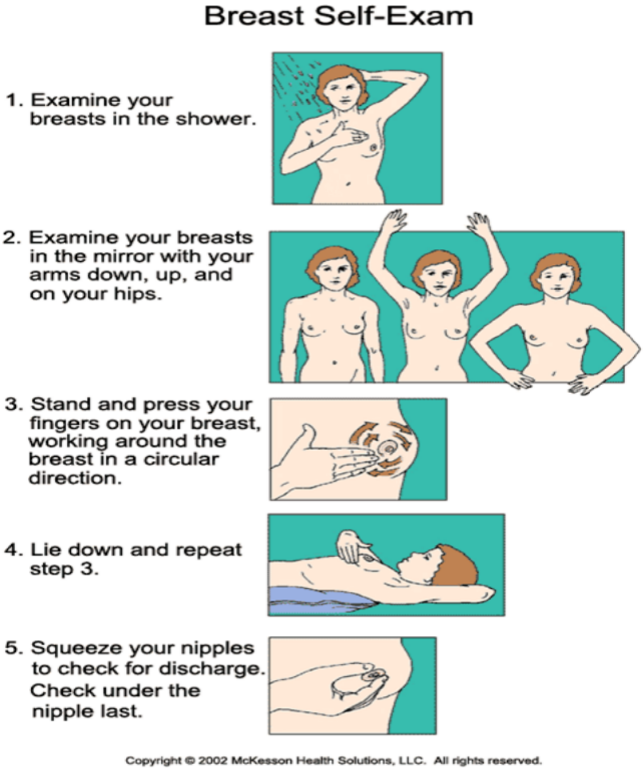


Image 1: Breast Self Examination

Note: BSE is recommended for raising awareness among women rather than as a screening method.

2. CLINICAL BREAST EXAMINATION (CBE)

Once the woman has signs and symptoms in the breast, this examination is conducted by a physician.

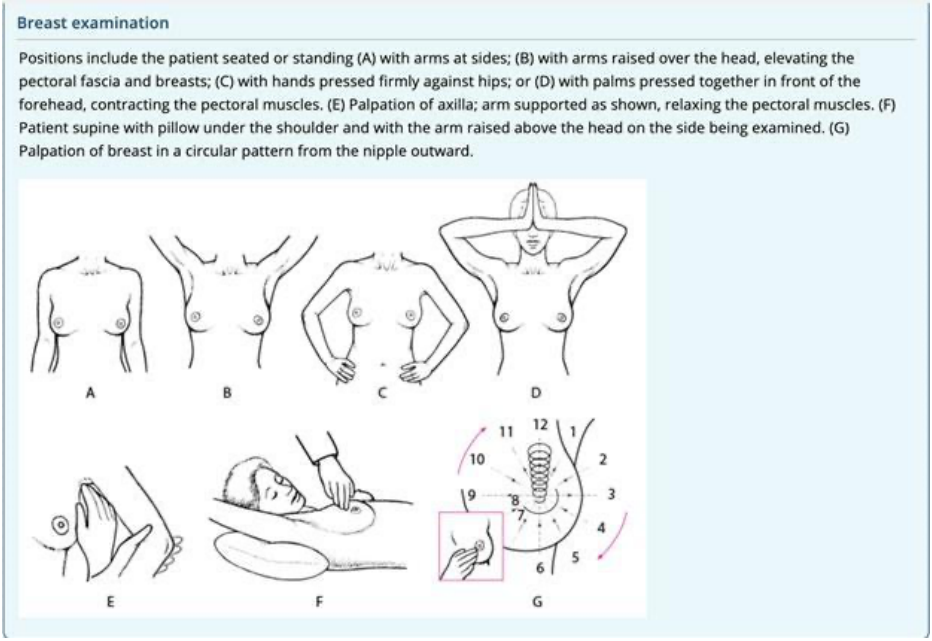


Image 2: Method of Breast Clinical examination

(Picture courtesy: Kosir MA (2018) Evaluation of breast disorders. Merck Manual Professional Version.)

Note: Clinical breast exams are not recommended for breast cancer screening among average-risk women at any age

3. BREAST CANCER IMAGING

i. Mammography

Mammography screening is the only screening method that has proven to be effective in reducing mortality. Mammography utilizes low-dose X-rays for breast imaging. Regular mammograms can help detect breast cancer at an early stage, when treatment is most successful. A small possibility of being over diagnosed (false positive) exists. It is important that women getting mammograms know what to expect and understand the benefits and limitations of the screening.

a) **Target group** (for mammography):
   1) Females aged 40-65 years with risk factors
   2) Females aged > 40 years with clinical indications
   3) Voluntary screening >45 years

b) **Method to check for microcalcification(s)**
   1) For benign microcalcification, follow up mammograms as per the clinicians advise.
   2) BIRADS-3: Repeat mammography after 12 months. If same findings, review with clinicians for the advice.
   3) BIRADS-4 and 5, do biopsy (stereotactic biopsy, wire localization and axillary nodal assessment).
   4) BIRADS 6 or Frank suspicious mass, refer to surgeon
   5) For suspicious microcalcification, perform core needle biopsy.
   6) If core needle biopsy is malignant, perform wire localization or radio-isotope insertion and refer back to the surgeon for necessary intervention.
   7) If suspicious mass, refer to onco-surgeon.
   8) After the surgical excision and post surgical treatment, necessary follow up mammography advised as per the surgeon's instructions.

***Note:**Mammography must always be correlated with sonomammography.

- **Reporting format (mammography):** To follow BIRADS reporting system
  1. BIRADS-0: Incomplete assessment needs additional evaluation
  2. BIRADS-1: Normal
  3. BIRADS-2: Benign
  4. BIRADS-3: Probably benign (2% of less chances of malignancy)
  5. BIRADS-4: Suspicious (2-95% chances of malignancy)
  6. BIRADS-5: Malignant (>95% chances of malignancy)
  7. BIRADS-6: Biopsy-proven malignancy

- **Reporting format (biopsy):** As per the standard/ protocol of the country.

- **Note:**
  - Develop separate requisition and consent forms for breast cancer screening
  - Get written consent signed by the patient before performing any invasive procedure
  - Detailed patient data must be maintained in the Register and must be reported in the reporting system for Breast cancer Screening program (DHIS-2)
  - A unique sample identifier generated for a patient by the DHIS-2 system must be written on the sample and shipped to the nearest histopathology lab.
  - Follow the screening algorithm given in figure 2
  - Core needle biopsy and wire localization or radio-isotope insertion to be performed by a Radiologist/Surgeon/Interventionist.
  - Breast biopsy is the confirmatory test for breast cancer. Types of Breast biopsies: Fine needle aspiration biopsy/cytology (FNAB/C), core needle biopsy (CNB) and surgical (open) biopsy.
  - Axillary lymph node (ALN) and Sentinel lymph node (SLN) biopsy can be performed with CNB or surgical (open) biopsy to rule out spread of disease.

ii. Ultrasonography

Ultrasound is used as an adjunct imaging modality for any breast abnormality. It is useful for looking at some breast changes, such as lumps (especially those that can be felt but not seen on a mammogram) or changes in women with dense breast tissue. It also can be used to re-look at a suspicious area that was seen on a mammogram. Ultrasound can differentiate between fluid-filled cysts and solid masses which mammography can not. Ultrasound can also be used to help guide a biopsy needle into the specific area so that tissue can be taken out and tested for cancer.

iii. MRI

MRI is used in instances where mammography is inconclusive such as in young females with dense breasts and females with difficult breast morphology. Breast MRI may sometimes be used in women already diagnosed with breast cancer, for more detailed assessment of the malignant breast lesion, look for other tumors in the breast, and to check for tumors in the contra-lateral breast.

iv. CT

Once breast cancer is confirmed by biopsy, CT is done for staging of the disease.

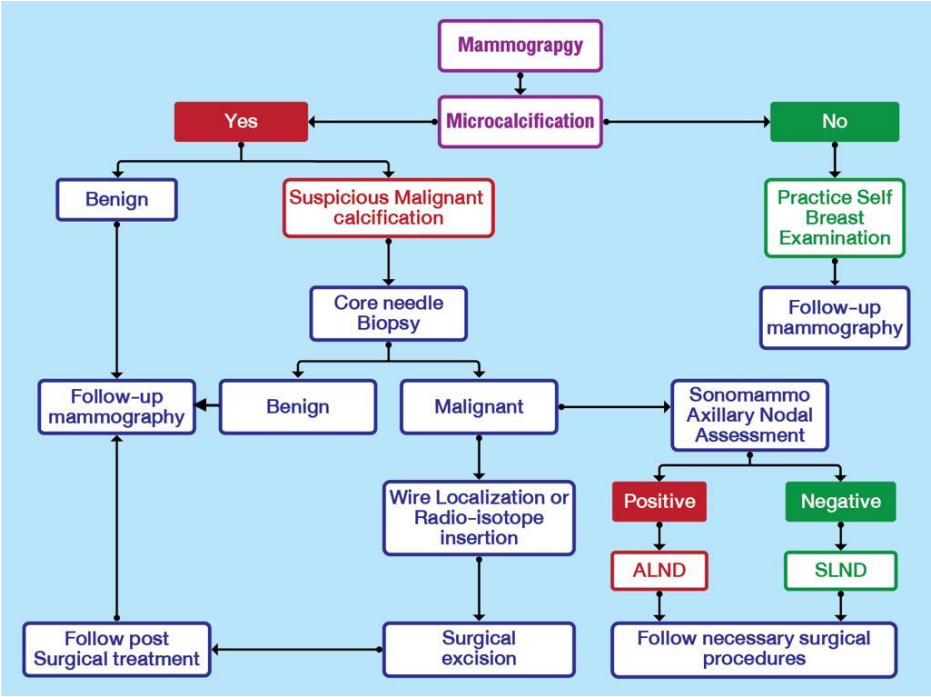


Figure 2: Flowchart for mammo sonography (Breast cancer Screening)

VI. Treatment

Early breast cancer detected on screening needs a less radical surgical approach to treatment. Surgical excisional biopsy is often adequate to treat the early condition while conserving most of the affected breast. Following are the treatment for early breast cancer:

1) Wide local excision/Lumpectomy
2) Sentinel lymph node biopsy (SLNB)
3) Mastectomy
4) Radiotherapy
5) Hormonal Therapy

VII. Resource requirement:

Human Resources	Medical Infrastructure
• Digital mammography machine with stereotactic biopsy facility • USG machine • Digital printer for films • Sentinel lymph node detection hand-held gamma probes (eg. truenode) • Intraoperative specimen X-ray (eg. Faxitron)	• Radiologist • Surgeon • Pathologist • Radio-technologist/Radio-technician • Histotechnologist/ Histotechnicians • Mammography nurse • OT scrub Nurse • Receptionist

VIII. Advocacy Programs on Breast Cancer

Health advocacies and education must be given to both health workers and the public

(a) Training and educating health worker on prevention, early detection and treatment
(b) Public awareness on breast cancer through National TV programs, National events, other media etc.
(c) Public education on self-breast examination by local health workers and CSOs

CERVICAL CANCER SCREENING

I. Introduction

Worldwide, cervical cancer ranks as the fourth most frequently diagnosed cancer and also the fourth leading cause of cancer deaths in women. In the year 2018 there were 5,69,847 new cases (source: Globocan 2018). It is the most frequent cancer diagnosed among Bhutanese women with peak incidence in women at 40-49 years of age. PBCR 2014-18 shows an age adjusted incidence rate of 20.5/100,000 and mortality rate of 5.3 per 1000,000 women in Bhutan.

Bhutan has had a cytology-based screening program with conventional Pap smear since 2006, but the STEPS survey in 2019 showed 60% coverage only. Besides, sensitivity to detect CIN III with conventional Pap smear is only 50%. According to WHO, to eliminate cervical cancer, 90% girls must be vaccinated, 70% of women must be screened with a high precision test like HPV testing and 90% of women with pre-cancers and cancers must be treated. More than 90% of our young women are covered by the HPV vaccine. For vaccinated women, HPV testing should be the primary screening method with cytology either as triage for HPV positive women or as co-test. When these 2 methods are used, screening intervals can be increased to 5 years.

II. Risk Factors

- Early age at sexual debut
- Early age at first child birth
- Multiple sexual partners.
- Multiparity
- Smoking
- Immuno-suppression
- Prolonged OCP use

Symptoms of cervical cancer

- Cervical cancer is frequently asymptomatic in the very early stage of the disease.
- Abnormal vaginal bleeding – It can be inter-menstrual, postcoital, postmenopausal or a woman may have just heavier and more prolonged menstrual flow than usual.
- Excessive or foul-smelling vaginal discharge may be there due to superadded infection of necrotic tissue.
- There may be urinary frequency, urgency and backache.
- In advanced cases, there may be:
- Pain in the pelvic region and/or lower limbs
- Swelling of lower limbs
- Renal failure in late stages
- Passage of urine and faeces per vagina (fistula formation)

III. Prevention

1. Primary prevention with HPV vaccination
2. Secondary prevention with the visual tests, cytology and HPV DNA tests

IV. Cervical Cancer Screening Program

A. **Target Population:** Women aged 30-65 years

B. **Methods for Screening:** HPV DNA test with reflex cytology

HPV-DNA Testing

Cervical cancer is a rare complication of HPV infection. HPV is a common STI in young sexually active women, but in most, it is cleared in the next 2-3 years by host immunity. While HPV infection is considered a necessary precursor of both cervical cancer and associated precancerous lesions, it is not a sufficient cause, as the majority of women with the infection will not progress to cancer. In 10-20% of women, HPV persists and leads to development of precancerous lesions. Screening helps to detect these pre-cancers. HPV diagnostics rely on molecular technologies that detect HPV DNA in cervical/vaginal samples. HPV-DNA testing has higher sensitivity in detecting CIN II/III lesions compared to cytology. It detects more than 90% of CIN II/III and invasive cancers. It is less specific in young women and should not be used as a screening method in women younger than 30 years. It has higher negative predictive value with longer protection against cancer which translates to increased screening interval (5-7 years compared to 3 years in cytology).
HPV samples can be self collected by women if they are unwilling to undergo collection by clinicians.

Liquid Based Cytology (LBC)

LBC is a new method of preparing cervical samples for cytological examination. Unlike the conventional 'smear' preparation, it involves making a suspension of cells from the sample and this is used to produce a thin layer of cells on a slide. Conventional Pap smears can have false-negative and false-positive results because of inadequate sampling and slide preparation, and errors in laboratory detection and interpretation. However, LBC rinses cervical cells in preservatives so that blood and other potentially obscuring material can be separated. The same LBC sample can be used for HPV-DNA testingand vice-versa.

V. Procedure of screening : Follow the screening algorithm flow chart (Figure 3)

- Collect vaginal/cervical sample and transfer to the nearest HPV testing Laboratory
- Do HPV DNA testing. If negative for HR- HPV, repeat HPV DNA test after five years. If positive for High-risk HPV (HR-HPV), do genotyping and genotyping and reflex cytology for HPV types other than HPV 16/18for HPV types other than 16/18.
- For abnormal cytology or positive for HPV 16/18 genotype, refer for colposcopy and manage manage accordingly.
- For normal cytology, repeat HPV DNA test and cytology in 12 months, and if positive for either HR-HPV or abnormal cytology , refer for colposcopy and manage accordingly.
- If negative for both HR-HPV and normal cytology, repeat HPV DNA test after five year.
- Colposcopy and treatment services/camps must be carried out in the nearest hospital.

Note:

- HPV testing or LBC should not be done in menstruating women.
- In pregnant women, do HPV testing/LBC 6 weeks after delivery/ miscarriage
- Women who had hysterectomy for reasons other than CIN or cervical cancer need not do HPV testing. Her histopathology hysterectomy report should not have CIN.
- Management of women with abnormal cytology results will be done as per the National Cervical Cancer Screening Manual.
- For women below 30 years of age, do HPV testing if they are already undergoing PAP smear screening or undergone treatment for precancers.

- Women who are HIV positive and those undergoing any immunosuppressive treatment should start HPV testing from the age of 25 years, at an interval of 3 years.
- Self sampling may be done for women unwilling to undergo clinical examination.

- **Reporting format (LBC):** Follow the Bethesda system of reporting

VI. Treatment

Method of treatment of pre-cancers are:

a) **Ablative methods**

1. Cryotherapy
2. Thermocoagulation

b) **Excisional method**

1. Loop electrosurgical excision procedure (LEEP)
2. Cold knife conization (CKC)
3. Hysterectomy is reserved only for those women not eligible for above procedures
4. Hysterectomy is reserved only for those women not eligible for above procedures

- **Reporting format (Colposcopy and LEEP):** As per Swede score

- **Reporting format (biopsy):** As per College of American Pathologist (CAP) protocol.

VII. Resource Requirement

a) Medical Infrastructure/Supplies

» For HPV testing

1. HPV DNA testing platform/machine
2. HPV Reagent
3. Sample collection medium and cyto-brush
4. Gloves and mask
5. Hand sanitizer
6. Chlorine solution
7. Waste disposal bags
8. Screening cards, registers and requisition/record forms

» For Liquid based cytology (LBC)

1. LBC processor/machine
2. LBC Reagent
3. Sample collection medium and cyto-brush
4. Registers /report form
5. Different Stains
6. Ethanol
7. Clearing agents
8. Mountant
9. Slides and cover slip

» For Colposcopy

1. Colposcope
2. Mini-bite biopsy forceps
3. Bivalve speculum
4. Sponge holding forceps
5. Instrument tray
6. Gloves
7. Swab sticks
8. Normal saline
9. Acetic acid
10. Lugol's iodine
11. Monsel's solution
12. Formalin
13. Chlorine
14. Biopsy vials

» For Cryotherapy

1. Cryo gun
2. Cryo-probe of different sizes
3. Carbon Dioxide or Nitrous oxide cylinders and wrench
4. Bi-valve speculum of different sizes
5. 5% Acetic acid/Lugol's iodine to demarcate lesions
6. Water soluble lubricant gel
7. Stopwatch/wall clock

» For Thermocoagulation

1. Thermocoagulator
2. Thermo-sounds of different sizes

» For Loop electrosurgical excision procedure (LEEP)

1. Cautery machine
2. Smoke evacuating speculum
3. Sponge holding forceps
4. Long tissue forceps (non toothed)
5. Dental syringe
6. Loop electrodes of different size
7. Ball cautery
8. Monsel's solution
9. 5% acetic acid or Monsel's solution
10. Local anaesthetic drugs
11. Spinal needles (23/24G sizes)

» For Cold knife conization (CKC)

1. Sim's speculum
2. Sponge forceps
3. Long suture cutting forceps
4. Long needle holder
5. Endocervical curette
6. Uterine sound
7. Knife handle
8. Syringe (5/10 ml)
9. Spinal needle (23/24G)
10. Adrenaline/Epinephrine
11. Suture

12. No. 11 blades
13. Monsel Solutions

b) Human Resource

i. Gynecologist
ii. Pathologist
iii. Nurse
iv. Cyto-technologist/technician
v. Histo-technologist/technician

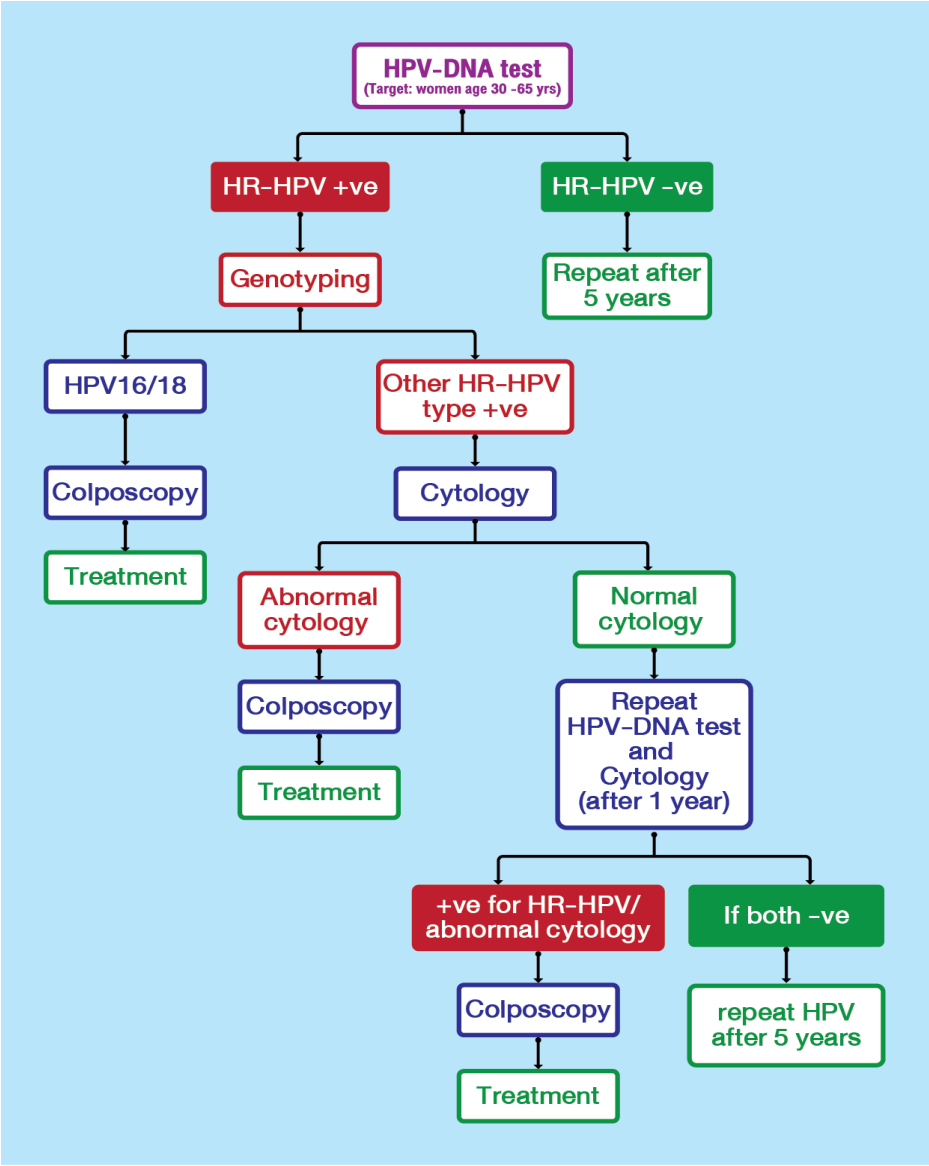


Figure 3: Flowchart for cervical cancer screening (with HPV testing system)

Note:

- Get the consent from the patient before performing the procedure Detailed patient data must be maintained in the register and reported in the reporting system for cervical cancer screening program (DHIS-2).
- A unique sample identifier generated for a patient by the DHIS-2 system must be written on the HPV sample and shipped to the nearest HPV testing lab.
- A unique sample identifier generated for a patient by the DHIS-2 system must be written on the biopsy sample and shipped to the nearest histopathology lab.

HISTOPATHOLOGY REPORTS (BIOPSY REPORTS)

» Biopsy to be processed and reported by two weeks.
» Modality to be worked out by MOH and hospital to meet the turn-around time (TAT).
» Follow up for biopsy reports: Follow up for biopsy reports to be done by the focal persons in the respective health facilities

REFERENCES

1. Anderson BO et al. (2008). Guideline implementation for breast healthcare in low-income and middle-income countries: overview of the Breast Health Global Initiative Global Summit 2007. Cancer, 113, 2221–43.

2. Coleman MP et al. (2008). Cancer survival in five continents: a worldwide population-based study (CONCORD). Lancet Oncol, 9, 730–56.

3. Danaei G et al. (2005). Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. Lancet, 366, 1784–93.

4. Sankaranarayanan R, Ramadas K, Thara S et al. (2011). Clinical breast examination: preliminary results from a randomized controlled trial in India. Journal of the National Cancer Institute, 103:1476-1480

5. IARC (2002). Breast cancer screening, IARC handbooks for cancer prevention, volume 7, Lyon, International Agency for Research on Cancer, IARCpress.

6. IARC (2008). World cancer report 2008. Lyon, International Agency for Research on Cancer.

7. Lacey JV Jr. et al. (2009). Breast cancer epidemiology according to recognized breast cancer risk factors in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial Cohort. BMC Cancer, 9, 84.

8. Peto J. (2001). Cancer epidemiology in the last century and the next decade. Nature, 411, 390–5.

9. Yip CH et al. (2008). Guideline implementation for breast healthcare in low- and middle-income countries: early detection resource allocation. Cancer, 113, 2244–56.

10. WHO (2007). Cancer control: knowledge into action: WHO guide for effective programmes: early detection.

11. WHO (2018). The global burden of disease: 2018 update.

12. American cancer society (2020), website.

13. NCCN Guidelines

14. New England Journal of Medicines

15. European Society of Gastroenterolog

16. Helewa M et al. Lévesque P, Provencher D, Lea RH, Rosolowich V, Shapiro HM; Breast Disease Committee and Executive Committeee and Council, Society of Obstetricians and Gynaecologists of Canada. Breast cancer, pregnancy, and breastfeeding. J Obstet Gynaecol Can. 2002 Feb;24(2):164-80; quiz 181-4. English, French. PMID: 12196882.)

17. ASCCP guideline

18. PBCR report