National Guideline on

Early Detection & Referral Pathways of Common Cancers in Sri Lanka

For Primary care Physicians

NATIONAL CANCER CONTROL PROGRAMME
MINISTRY OF HEALTH &
INDIGENOUS MEDICAL SERVICES
SRI LANKA

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Early Detection & Referral Pathways

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For primary care physicians

National Cancer Control Programme
Ministry of Health & Indigenous Medical Services
Sri Lanka

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CONTENTS

PREFACE

Noncommunicable Diseases (NCD) have been recognized as a serious public health concern worldwide as well as in Sri Lanka. Cancer is an important component of NCD burden globally and it is the second leading cause of death in Sri Lanka. Annually about 23500 new cancer patients are detected in the country .

National Caner Control programme (NCCP) was established in 1980 and it is the national focal point for prevention and control of cancer. NCCP plays a key role in planning, coordinating, implementing, monitoring and evaluating the cancer control activities in Sri Lanka.

Guidelines and manuals are considered as fundamental requirement to implement an effective, uniform and evidence based programme throughout the country. Primary care doctors and family physicians are the first contact person for many individuals with risk factors and/or early signs and symptoms. NCCP has taken steps to develop guidelines and referral pathways for most common cancers in order to facilitate primary care physicians to detect suspicious cancers among symptomatic patients, refer them appropriately and to promote preventive measures for high risk individuals.

New guidelines and referral pathways were prepared for Thyroid, Prostate, Colo-rectal and esophageal cancers and already circulated breast, common gynecological and OPMD guidelines were reviewed and updated in order to prepare a single book with all guidelines.

In this manual, guidelines related to each cancer has been described in a separate chapter. Each of these guidelines has been developed by an expert panel which represented nominees from all relevant professional colleges. Most updated internationally and locally available evidences were reviewed during this process. A special emphasis was taken to generate user-friendly and tailor-made guidelines which are compatible with existing healthcare system in Sri Lanka while maintaining international standards.

This manual contains guidance for screening, early detection and referral systems of selected cancers. The diagrams, images, flow charts and sample formats were used to minimize the complexity of the subject and to improve the practical usage of this manual.

Our thanks are due to World Bank and Ministry of Health Sri Lanka for providing the funds for the preparation and printing of this manual and to all authors, experts and professional colleges for their contribution.

August 2020
National Cancer Control Programme

ABBRIVIATION AND ACRONYMS

AJCC	American Joint Committee on Cancer
AUCUS	Atypical Squamous Cells of Undetermined Significance
BMI	Body Mass Index
BPH	Benign Prostatic Hyperplasia
BSE	Breast Self-Examination
CBE	Clinical Breast Examination
CEA	Carcinoembryonic Antigen
CEDC	Cancer Early Detection Center
CPG	Cancer Predisposition Genes
CRC	Colorectal Cancer
DCIS	Ductal Carcinoma In Situ
DRE	Digital Rectal Examination (DRE)
ER	Estrogen Receptor
FAP	Familial Adenomatous Polyposis
FMTC	Familial Medullary Thyroid Carcinoma
FNAC	Fine Needle Aspiration Cytology
GP	General Practitioners
GORD	Gastro-Oesophageal Reflux Disease
HER	Human Epidermal Receptor
HIV	Human Immunodeficiency Virus
HLC	Healthy Lifestyle Center
HNPCC	Heriditory Non-polyposis Colorectal Cancer
HPV	Human Papilloma Virus
HRT	Hormone Replacement Therapy
HSIL	High Grade Squamous Intra Epithelial Lesions
IARC	International Agency for Research on Cancer
IBD	Inflammatory Bowel Diseases
IBS	Irritable Bowel Syndrome
IUAC	International Union Against Cancer
LCIS	Lobular Carcinoma In Situ

LLETZ	Large Loop Excision of the Transformation Zone
LOA	Loss Of Appetite
LOW	Loss Of Weight
LSIL	Low grade Squamous Intra epithelial Lesions
LUTS	Lower Urinary Tract Symptoms.
MALT	Mucosa-Associated Lymphoid Tissue
MEN	Multiple Endocrine Neoplasia Type 2
MOH	Medical Officer of Health
MNG	Multinodular Goiter
MRI	Magnetic Resonance Imaging
MTC	Medullary Thyroid Carcinoma
NCCP	National Cancer Control Programme
NCD	Noncommunicable Diseases
NGS	Next-Generation Sequencing
NILM	Negative for Intraepithelial Lesion or Malignancy
OCP	Oral Contraceptive Pills
OE	Oral Erythroplakia
OLP	Oral Lichen Planus
OPMD	Oral Potentially Malignant Disorders
OSF	Oral Submucous Fibrosis
PR	Progesterone Receptor
PSA	Prostate Specific Antigen
PSSP	Primary Health Care System Strengthening Project
SCC	Squamous Cell Carcinoma
SCJ	Squmo-Columnar Junction
SLE	Systemic Lupus Erythematosus
TNM	Tumour, Nodes, Metastases
VIA	Visual Inspection with Acetic Acid (VIA)
WHO	World Health Organization

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Chapter 1

Introduction to the guideline

National Guideline on Early Detection and Referral Pathways of Common Cancers in Sri Lanka

1. Introduction to the Guideline

1.1 Cancer burden

Cancer has become a leading cause of death worldwide, accounting for an estimated 9.6 million deaths in 2018[1]. The total annual economic cost of cancer in 2010 globally, was estimated at approximately US$ 1.16 trillion[2]. Physical, emotional, and financial wellbeing of individuals, families, communities and health systems has been seriously disturbed by the increasing trend of cancer. Lung and breast cancers are the most common cancers world wide which account for 22% of global cancer burden[3]. However, the incidence of cancers may vary from region to region in the world, Prostate cancer has become the most common cancer among males in some western and African countries while oral cancer is the most common cancer among males in many South Asian countries.

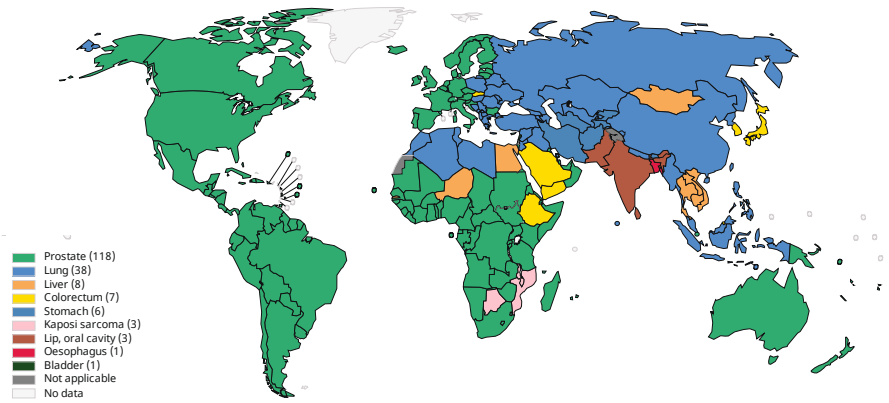


Figure 1.1 Top cancer per country, estimated age-standardized incidence rates (World) in 2018, males (all ages)

Source: *GLOBOCAN 2018,Graph production: IARC (http://gco.iarc.fr/today) World Health Organization*

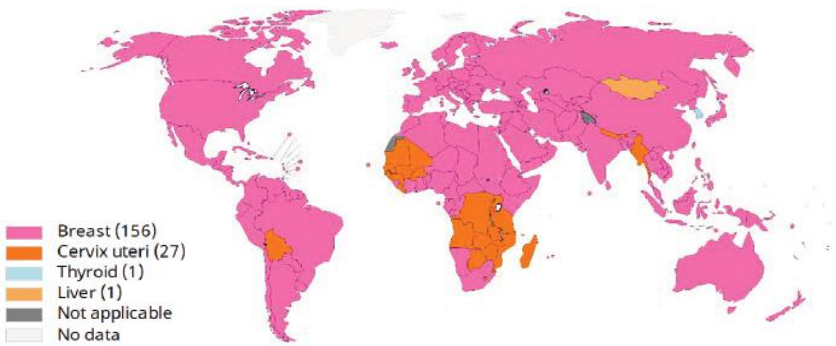


Figure 1.2 Top cancer per country, estimated age-standardized incidence rates (World) in 2018, females (all ages)

Source: *GLOBOCAN 2018,Graph production: IARC (http://gco.iarc.fr/today) World Health Organization*

World Health Oraganization (WHO) reveled that approximately 70% of deaths due to cancer occur in low and middle income countries.[4] According to the GLOBOCAN estimates for Sri Lanka 23530 incident cases and 14013 deaths should have been occurred in 2018.

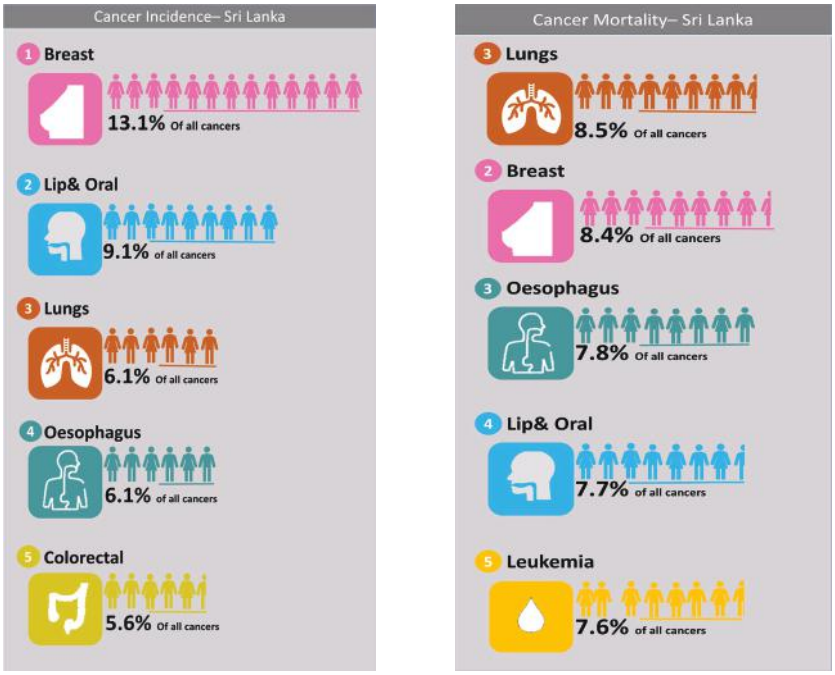
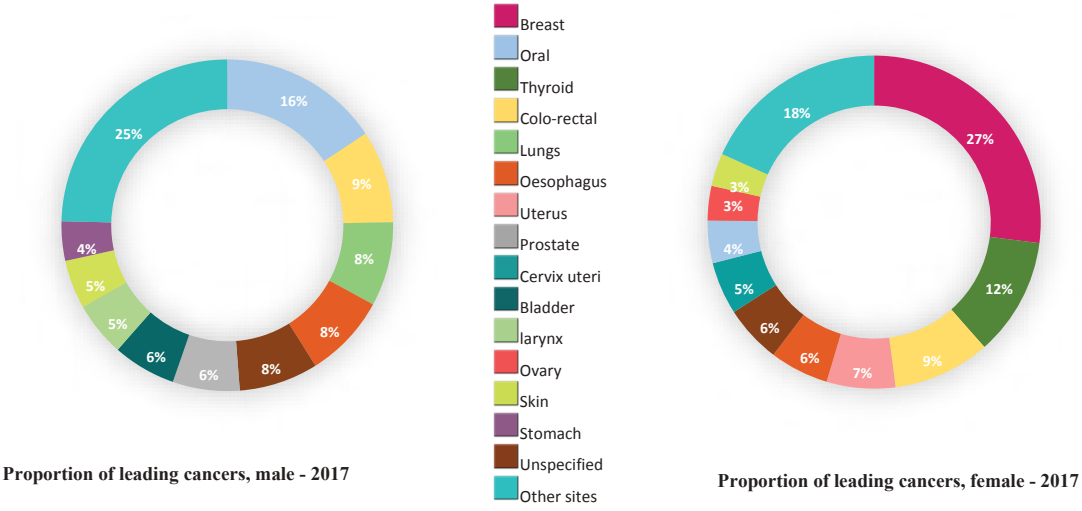


Figure1.3 : Cancer incidence and mortality of most common cancers in Sri Lanka.
(GLOBOCAN estimates)

Cancer incidence is on upward trend according to the national cancer incidence data. Breast cancer is the commonest cancer overall in Sri Lanka where as in males oral cancer is the commonest cancer.



Proportion of leading cancers, male - 2017

Proportion of leading cancers, female - 2017

Figure 1.4 Cancer incidence in Sri Lanka according to sex
(pathology-based cancer frequency data-2017)

1.2 Scope and purpose of the guideline

The aim of this guideline is to build capacities of the primary care physicians on early detection of common malignancies and minimize delays in referring them for further care. This will reduce the burden of cancers in the country. Table 1.1 Illustrates the WHO recommended evidence-based intervention to improve the capacity of early diagnosis at primary care level.

Table 1.1: Sample interventions to improve early diagnosis capacity at the primary care level

Building capacity in primary care	Impact
Develop protocols for clinical assessment (e.g. WHO PEN) Sensitize providers to cancer signs/symptoms	Improve diagnostic accuracy
Ensure sufficient time to evaluate patient Train practitioners in how to diagnose cancer including use of medical devices	Facilitate enabling factors for accurate diagnosis and appropriate referral to specialized cancer care Reduce risk of loss to follow-up
Promote clear communication between provider and patient	Reduce risk of loss to follow-up
Establish clear referral mechanisms	Reduce delays in care

Source: Guide to cancer early detection : WHO – 2017 [6]

This guideline is in par with the above recommendations. Primary care physicians will be trained on these guidelines at regional level. Sri Lanka is in the process of reorienting the primary health care system (Primary Health Care System Strengthening Project (PSSP)), improving service utilization and repositioning. Introduction of proper referral pathways and streamlining the patient management and care are major purposes of this activity. It is expected that this book will play a key role in improving the cancer early detection in the country.

***Technical details about concepts of National Cancer Control Programme, cancer screening, early detection and currently available facilities in Sri Lanka have been discussed as a separate attachment at the end of this book.*

1.3 The target audience & expected outcome

This guideline is intended to be used by the primary care physicians in Sri Lanka including Medical Officers (MO) of out-patient departments of hospitals, Medical Officers of Health (MOH) and General Practitioners (GPs).

Adherence to the guideline will improve early detection and down staging of cancers at the time of diagnosis. It will minimize diagnosis delays as well, due to the proper referral of symptomatic patients. Ultimate goal of preparing these guidelines is to reduce the cancer related morbidity and mortality in the country.

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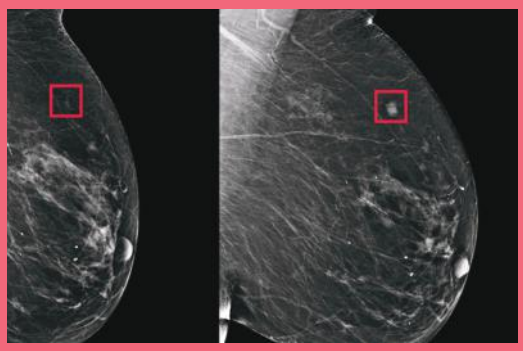

Chapter 2

Breast cancer

National Guideline on Early Detection and Referral Pathways of Common Cancers in Sri Lanka

We would like to acknowledge the authors of previous version of guidelines on Breast cancer (ISBN: 978-955-0505-21-0 published in 2014) which was reviewed and updated for preparation of this common book.

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2. Breast Cancer

2.1 Introduction

Breast cancer is the most common cancer among women in Sri Lanka. According to estimates, 24% of all newly diagnosed cancers among women are breast cancers[1]. Around 3000 – 3500 women are diagnosed with breast cancer annually and there is an increasing incidence of breast cancer over the last 25 years. Breast cancer incidence is increasing with the age and comes to a peak at ages between 45 to 65 years.[2]

Even though, it is rare to find breast cancers among males, attention should be paid if male patients presenting with signs and symptoms. As the cause of breast cancer is multi factorial, primary prevention may be difficult. Therefore, early detection is the main recognized control strategy for breast cancer globally.

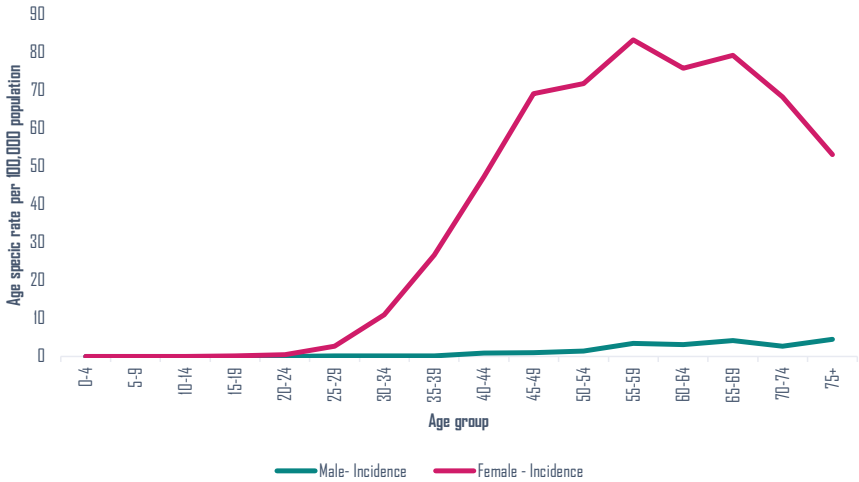


Figure 2.1: Age specific incidence rates-Breast-2012
Source: National cancer registry, Sri Lanka- 2012

2.2 Pathophysiology

Breast cancer which originates within the terminal duct lobular system is initially confined to this duct lobular system. This is the 'in situ carcinoma' stage and could be either ductal (Ductal Carcinoma In Situ-DCIS) or lobular (Lobular Carcinoma In Situ-LCIS) in type. Invasive disease occurs when the cancer cells penetrate through the defining basement membranes of the duct lobular system in to the adjacent breast stroma. Following this, the breast cancer cells have the ability to invade the adjacent breast and extra mammary tissue (local invasion), as well as stromal lymphovascular spaces.

Lymphatic and vascular space invasion leads to local and distant metastasis of breast cancer in to the lymph nodes and the visceral organs. Sentinel lymph node in the axilla which is commonly checked at surgery for metastatic breast cancer, is the first lymph node to which the cancer cell is likely to spread via draining lymphatics. Cancer confined to the breast with or without regional lymph node involvement, with absent distant metastasis is considered early stage breast cancer.

For the pathogenesis of breast cancer, multiple linear models where a normal breast epithelial cell undergoes initiation, transformation and progression to being a cancer cell have been described. Molecular data suggests that breast cancers develop along two pathways related to hormone receptors and have demonstrated that Oestrogen Receptor (ER)-positive and (ER)-negative breast cancers are two distinct diseases. Supported by molecular data these two linear pathways, based on the hormone receptor status and the morphology of the cancer have been further described. The ER-positive pathway recognizes low grade lesions (flat epithelial atypia, atypical ductal hyperplasia and ER-positive DCIS) as non obligate precursors of ER-positive breast cancer. The ER-negative model recognizes micro-glandular adenosis and ER-negative DCIS as precursor lesions for ER-negative cancers. Traditionally breast cancer has been sub-typed based on the histological appearance. Based on the most recent 5th series WHO classification of breast tumours[3], commonest morphological pattern of breast carcinoma is the 'Invasive breast carcinoma, no special type'.

Several other morphological subtypes are also described, including invasive lobular, mucinous, tubular cribriform and metaplastic carcinomas among others. Grading to assess the degree of differentiation of the breast cancer is performed based on the histological appearance of the surgically removed cancer and is scored on a three point scale (Modified Bloom and Richardson grades 1-3). Well differentiated cancers are grade 1 and poorly differentiated cancers fall in to the grade 3 category.

Breast cancer is also divided into biomarker-defined subtypes based on the hormone receptor (ER and Progesterone receptor-PR) and Human Epidermal Receptor 2 (HER2) gene expressions in surgically removed cancer tissue, assessed by immunohistochemical methodology also available in the local setting. These immunohistochemically defined subtypes of breast cancers include;

- Luminal (hormone receptor positive)
- HER2 enriched (HER2 positive, hormone receptor negative) and the
- Triple negative (hormone receptor and HER2 negative) subtypes.

Identification of these immunohistochemically defined subtypes is clinically relevant and important for the management and prognostication of patients. Luminal type breast cancers have a better prognosis. Triple negative cancers occur at a younger

age in a familial setting and are linked to Germline BRCA1 mutations. Germline BRCA2 mutations are associated with hormone receptor positive breast cancers.

These immunohistochemical markers (ER, PR, HER2) are also predictive of cancer response to specific target therapy (endocrine therapy and anti HER2 therapy). For target treatment options breast cancer is viewed as 4 subtypes;

- Hormone receptor (ER)-positive/HER2-negative
- ER-positive/HER2-positive
- ER-negative/HER2-positive and
- ER-negative/HER2-negative.

Endocrine therapy is beneficial and is provided for patients with ER-positive cancers and HER2 targeted therapies are helpful for women with HER2-positive cancers. Standard clinicopathological factors routinely considered to assess the prognosis of a breast cancer include the patient's age, disease stage (the degree of tumour spread known as tumour stage), tumour grade, tumour type, surgical margin status of the excised cancer and the lymphovascular status in addition to the hormone receptor and HER2 status. Tumour infiltrating lymphocytes have recently been shown to have prognostic value in certain subtypes of breast cancers. Several prognostic scoring systems are also available for assessing the prognosis of an individual breast cancer patient following standard care.

2.3 Risk factors and protective factors

The specific cause of breast cancer is unknown and there are known risk factors. Most of the risk factors (approximately 90%) are environmental and life-style related; while the rest (5% to 10%) are genetic.

Personal factors

- Sex: Females have a 100 times higher risk of getting breast cancer than males (Female: male = 100:1)
- Age: although breast cancer can occur at any age, it is more common in older women. 70% of breast cancer patients diagnosed are within 40 – 69 years of age. Peak age range is 45 – 65 years[2].
- Breast density: Dense breast means presence of more glandular tissue compared to the fat in the breast. (Breast density is a mammographic finding and cannot be reliably defined by a physical examination). Women with extremely dense breasts have a two-fold increased risk compared to women with breasts of average density[4]. Usually younger women are more likely to have dense breasts than older women. However, there are outliers at both ends of the age spectrum.

Genetic factors

- **Family history of breast or ovarian cancer –** Strong family history indicates a risk of gene mutation in the family. Having one first degree relative with breast cancer is associated with excess incidence of breast cancer of 5.5% and if two first-degree relatives affected, the risk is increased up to 13.3%. The increase in risk greater when the relative was affected at a younger age. Maternal and paternal sides of the family equally important[5].

- **Known mutations –** Women who are born with specific abnormal genes are at higher risk of developing breast cancer. (In a population-based series of breast cancer cases it has shown that approximately 1 -2% of women with breast cancer have BRCA 1 or BRCA 2 mutations[6])

  Men and women can pass these abnormal genes to their children and transmission is autosomal dominant, so each child has a 50/50 chance of inheriting these gene mutations. It is important to assess history of cancer in maternal and paternal sides of the family.

Medical history and medications

- Previous breast cancer, Ductal carcinoma in situ, Lobular carcinoma in situ or proliferative breast disease can increase the chance of developing breast cancer during the life time. Risk of breast cancer will increase by at least four-fold in women with biopsy proven atypical hyperplasia or Lobular carcinoma in situ. This risk will persist for at least 25 years[7].

- **Chest wall radiation:** Women with a history of chest wall radiation for treatment of another disease condition have up to 10-fold-increased risk of breast cancer. The risk varies with the age of the woman when she had radiation therapy. Risk is highest if the woman had radiation before menarche[8].

- **Hormone Replacement Therapy:** Women who are using combine estrogen -progesterone Hormone Replacement Therapy (HRT), are at higher risk of developing breast cancer. Risk increases with the length of HRT use. After five years of using combined HRT, the risk of breast cancer increases by about 15% and the risk return to baseline within about two years of stopping HRT. Estrogen therapy alone increases breast cancer risk but the increased risk is lower than for combined therapy [9,10]

- **Oral Contraceptive Pills (OCP):** Slight increased risk is observed in current users especially long term use. Rapidly decreases the risk after stopping OCP.

Factors related to reproductive system

- **Hormonal influences:**
  Menarche and Menopause: Women with earlier age of menarche (before

the age of 11 years) and/or later age of menopause (after the age of 55 years) have an increased risk of breast cancer, mediated in part by the increased number of menstrual cycles and the longer lifetime exposure to estrogen and progesterone.

Reproductive History: Nulliparity increases a woman's risk of breast cancer and every live birth reduces the relative risk by about 7%. Women 30 years or older at the time of their first child birth have a higher risk of breast cancer than women having their first child birth at a younger age.[11]

Breastfeeding: The relative risk of breast cancer decreases by about 4% for every month of breastfeeding[12]. Reduced lifetime exposure to estrogen and progesterone may explain the protective effect conferred by breastfeeding.

Factors related to Lifestyle

- **Overweight /Obesity –** High BMI is associated with higher risk of post – menopausal breast cancer[13]. It also negatively affects the prognosis of early stage breast cancer[14] .

  Weight gain – Increased risk in post - menopausal breast cancer.
  Increased weight → increased circulating estrogen

- **Physical activity:** Compared to the least active women breast cancer risk is reduced by 25% among women who are physically active[15] .
- **Alcohol consumption:** Regular consumption of alcohol as little as one drink per day increases the risk of breast cancer by 4%[16]
- **Smoking:** Association between active smoking and breast cancer is consistent with causality. In addition, the association between secondhand smoke and breast cancer among younger, primarily premenopausal women who have never smoked is consistent with causality[17].

Negligible radiation risk – the risk of mammogram induced cancer is generally considered to be negligible because of the very low dose of radiation and the relative insensitivity[18,19].

Modifiable lifestyle factors such as body weight, physical activity, alcohol consumption and smoking should be addressed in the context of an overall wellness strategy.

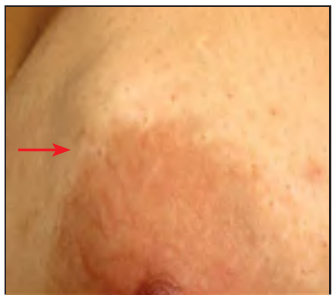
2.4 Clinical features

Clinical features of breast cancer can be varied at the time of presentation. Clinicians should be vigilant enough to detect them early to minimize the complications of breast cancer.

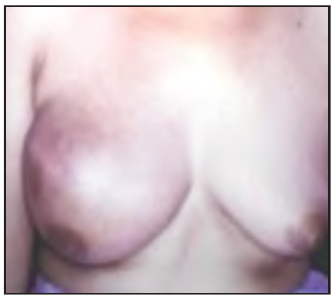
Clinical presentation - A lump, lumpiness, thickening and asymmetry

A palpable mass is a discrete lesion that can be readily identified during a physical examination and is the commonest form of presentation.
Thickening – usually this finding is ill defined and often vague.

Asymmetry – need to find out whether it is a recent onset or normal asymmetry



Breast lump



Asymmetry

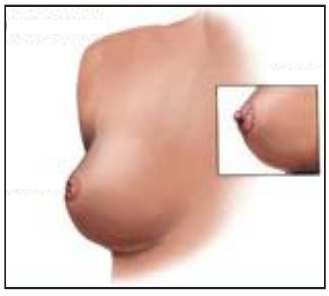
All women with breast lumps should be referred to a surgical clinic or Breast clinic

If a woman complains of a lump do not ignore it even if you cannot detect it by physical examination

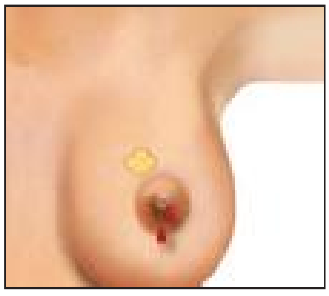
Clinical presentation - Changes to nipple

A change in shape
Crusting, a sore or an ulcer, redness, unusual discharge, nipple that turns in (inverted) recently

Nipple discharge without a palpable mass – In benign breast disease, nipple discharge is a common symptom that may occur unrelated to breast pathology. However, it can rarely be seen in cancer. Non-spontaneous discharge from multiple breast ducts in a non-lactating woman can occur during pregnancy, following breast stimulation, women with certain thyroid conditions and in those taking certain medications (e.g. estrogen, oral contraceptives, opiates, and particular anti-hypertensive agents)



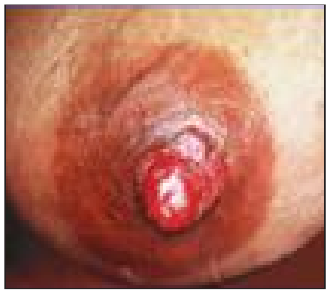
Recent onset inverted nipple should be referred to a surgical clinic / Breast clinic

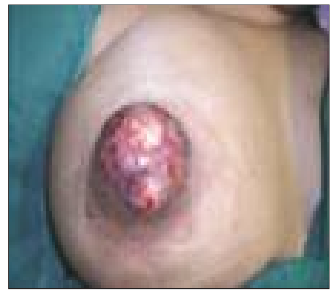


Single duct discharge, unilateral of any colour should be referred to a surgical clinic / Breast clinic

Clinical presentation - Paget's disease

Nipple excoriation, scaling and eczema should increase clinical suspicion of Paget's disease. Paget's disease of the breast is a rare manifestation of breast cancer characterized by neoplastic cells in the epidermis of the nipple areolar complex. Paget's disease most commonly presents with eczema of the areolar, bleeding, ulceration and itching of the nipple

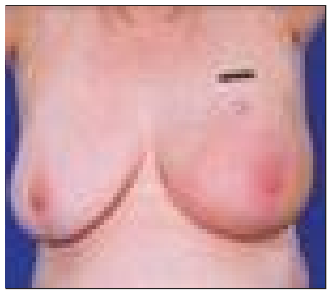




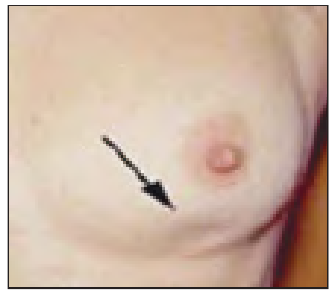
Any women with nipple excoriation, ulcer, eczema should be referred to a surgical clinic/ Breast clinic

Clinical presentation - Changes to the skin of the breasts

Dimpling, unusual redness or other colour changes



Unusual Redness

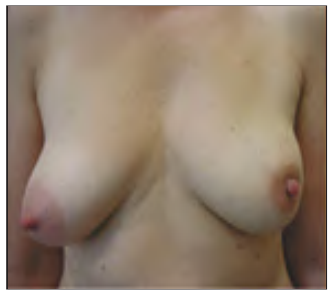


Dimpling

Any of the above changes should be referred to a surgical clinic/ Breast clinic

Clinical presentation - A change to shape or size of the breast

A change to the shape of the breast, increase or decrease the size of one breast (asymmetry which is recent onset)

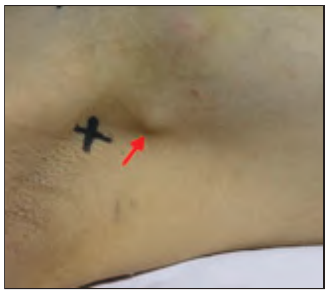


Asymmetry

Any of the above changes in size and/ or shape of the breast should be referred to a surgical clinic/ Breast clinic

Clinical presentation - Changes in axilla

A swelling, lump or the discomfort of the axilla



An axillary mass should be referred to a surgical clinic/ Breast clinic

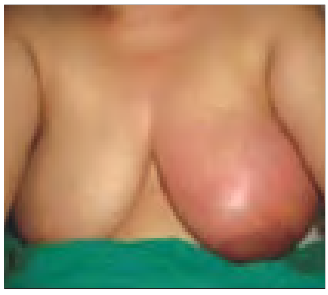
Clinical presentation - Mastalgia

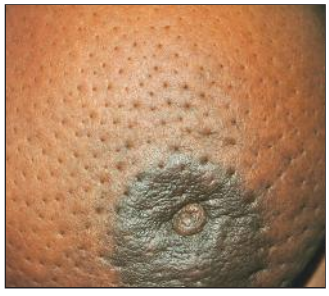
Persistent, unusual pain that is not related to normal monthly menstrual cycles, remains after the period and occurs in one breast only. (Cardiac pain and chest wall pain should be clearly differentiated from the history)

Mastalgia (especially unilateral non-cyclical) should be referred to a surgical clinic/ Breast clinic

Clinical presentation - Inflammatory breast cancer

Inflammatory Breast Cancer (IBC) should be considered when dermal oedema (Peau d'orange) and breast erythema are present. IBC is a rare form of aggressive breast cancer





Breast erythema and peau d'orange appearance

Inflammatory breast cancer should be referred immediately to a surgical or breast clinic

Presence of any of the above clinical features do not always indicate the presence of a breast cancer. However, all complaints including change of the contour of the breast, nipple inversion, mastitis, sinuses etc. should be referred to a surgical clinic / Breast clinic

Referral pathway women with or without breast symptoms

Well Women Clinic (WWC)
Healthy Lifestyle Centers (HLC)
Outpatient Departments (OPD) of smaller hospitals
Cancer Early Detection Center

Normal clinical breast examination findings and/or normal mammography findings in asymptomatic women

Women with breast symptoms, Abnormal findings on clinical breast examination or abnormal mammography findings.

Surgical clinics/ Breast clinics in TH, PGH,DGH,BH, Private hospitals

Triple assessment
History & clinical Examination
Mammography/ Ultra sound scan
Fine Needle Aspiration Cytology (FNAC)/ biopsy

If Triple assessment findings are negative

Abnormal findings in tripe assessment

Further management based on triple assessment findings

Advice to conduct Breast Self-Examination (breast awareness) monthly. If 20-40 years-advice to come in 3 years for Clinical breast examination
If more than 40 years - advice to come for yearly clinical breast Examination

Diagnosis at the secondary/tertiary care level

- Diagnosis of a breast cancer is made at secondary/ tertiary care level
- It is diagnosed by the Triple assessment
- Triple Assessment refers to three diagnostic components (Figure 2.2)

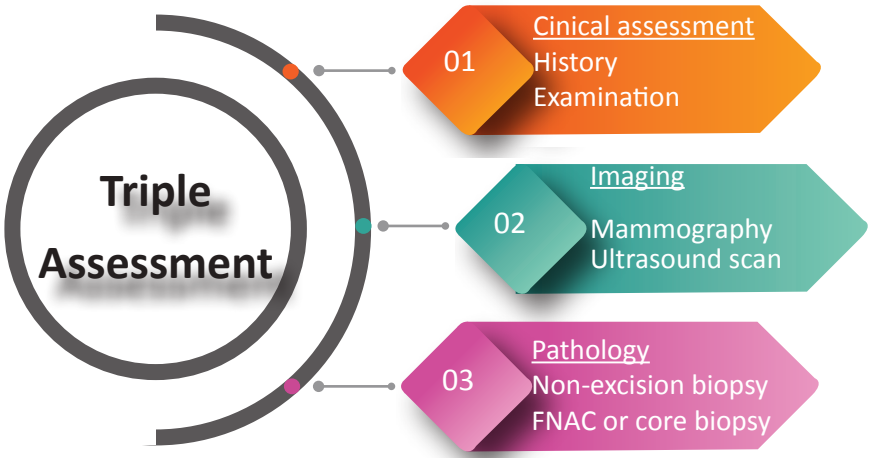


Figure 2.2 Components of triple assessment

The triple test is more accurate at detecting breast cancer than any of the individual component alone. Any abnormal results (Intermediate, suspicious or malignant) in any component of the triple test requires specialist referral and further investigations. If more than one component of the triple test is positive the likelihood of cancer is high. On the other hand, if all components of the triple test is negative, it provides good evidence that the cancer is unlikely.

Recommendations to be followed at primary care level

- Presenting complaint and risk factors (if present) should be documented
- Any breast lump should be considered as a cancer until proven otherwise. Special attention should be paid for pregnant women and lactating women when they complain/or if you detect any abnormality
- Attention should be paid to benign conditions such as nipple discharge and mastalgia as they could precede the symptoms of cancer
- If a dedicated breast clinic is available in the area, women with breast symptoms can be referred directly to those clinics. (The breast clinic is a dedicated clinic for breast problems. Breast clinic is conducted by a team led by a consultant surgeon or a consultant onco-surgeon. Medical and nursing staffs are specially trained in providing services for breast problems. Patients attending breast clinics have the opportunity for timely access to radiological and pathological laboratory services for triple assessment). If there is no

breast clinic closer to patient's residence, she should be referred to a surgical clinic.

- No surgery should be done on the breast unless supervised or authorized by a consultant surgeon/ consultant onco- surgeon.
- Women over the age of 50 years should be discouraged to be on Hormone Replacement Therapy (HRT) unless for severe postmenopausal symptoms (WHO recommendation).
- Women who are on long term HRT and having family history of breast cancer should be referred for surgical or oncological opinion at least once in two years. If HRT has to be started for severe postmenopausal symptoms, it should not be continued for more than two years without the opinion of an oncologist. These women should be given special attention for early detection of breast cancer. Preferably they should undergo a screening mammography.
- Any male patient presenting with breast symptoms should be referred to a surgical clinic.

If any abnormality is detected during clinical breast examination, suggesting breast pathology it does not indicate that she is having a cancer. Diagnosis should be confirmed by triple assessment at the next level of care. So, need to communicate in a proper way without unnecessarily frightening the client, at the same time persuading her to attend for further evaluation.

2.5 Early detection of Breast Cancer

Importance of early detection of breast cancer

Methods of early detection of breast cancer (Breast Screening and early diagnosis)

Breast screening is performed in women without any signs or symptoms of breast cancer in oder to detect breast cancer as early as possible. The components and timing of breast screening evaluation depend on the woman's risk level.
Components of breast cancer screening include:

1. Breast awareness / Be Breast aware
2. Self Breast Examination

3. Clinical breast examination and risk assessment

4. Screening mammography, ultrasonography and in selected cases screening breast MRI

Breast awareness (Familiarity with the breasts "Be Breast Aware")

- Annex I

Women should be familiar with their breasts (appearance & usual texture) and encouraged to report changes; Woman checks her own breasts at intervals of her choosing.

Breast self- examination- Annex II

Monthly examination of breast by women themselves is referred to as self breast examination

Clinical breast examination

Clinical breast examination serves two purposes. It can be used as a screening method for women without any signs and symptoms of breast cancer and as a component of triple assessment in women with signs and symptoms when diagnosing breast cancer. A detailed history and thorough clinical examination provide important information on which, further investigations would be based.

Clinical history

History should be taken from women presenting to the clinic either with signs and symptoms or without signs and symptoms before doing clinical breast examination. Following are the possible signs and symptoms and information need to be collected.

Table 2.1 Possible signs and symptoms and information to be collected

Breast Lump	• Site – Constant or changing
	• Duration – when and how it was noticed
	• Any new changes since first notice (eg: getting bigger)
	• Relationship to menstrual cycles or exogenous hormones
	• Associated symptoms
Breast Pain	• Site – Constant or changing/ unilateral or bilateral
	• Cyclical or noncyclical
	• Duration – how long and characteristics of pain
	• Any recent change such as intensity, frequency, site of pain
	• Relationship to menstrual cycles or exogenous hormones
	• Associated symptoms
Nipple discharge or any other nipple changes	• Duration – when and how first noted (Spontaneous or not)
	• Any changes since first notice
	• Bilateral or unilateral
	• From single duct or multi duct

Following information also need to be gathered in addition to signs and symptoms.

- Previous history of pathological condition (either breast)
- Previous breast investigations:
  Most recent imaging if available (Screening or diagnostic) date and results
  Biopsy results – FNAC/Histology/Lumpectomy
- Risk factors – Try to identify risk factors (please refer section 2.3)

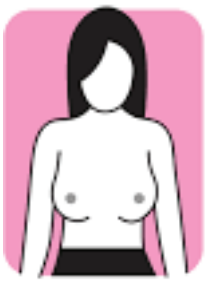
Steps of Clinical Breast Examination (CBE)

CBE should be done in a covered room with good light. A female chaperon should be there if the examiner is a male.

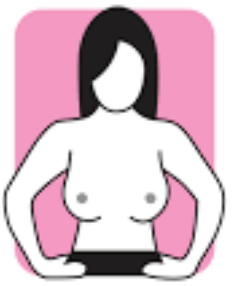
Before starting the examination, it is necessary to explain the procedure to the client.

Inspection
Breasts should be inspected in each of the following positions

1. Arms relaxed at her sides
2. Hands placed on the hips and pushing inward (contraction of the Pectoralis Major muscle)
3. Arms raised over her head



Arms by the side



Hands placed on the hips

Arms raised over the head

Figure 2.3 Inspection of breasts

The breasts should be inspected from the front and from each side.

Pay particular attention to:

- Breast size, contour, shape, symmetry
- Skin changes such as erythema, dimpling, tethering or puckering, Peau d' orange, eczematous skin changes, visible lumps
- Nipple – position, height, inversion, retraction, erythema, eczema, nodules ulceration and discharge

Palpation

The ability to identify breast lumps by palpation is influenced by the characteristics of the tumour, the surrounding breast tissue, the position of the lesion in the breast, proper positioning of the client and thoroughness of the search, the area covered and use of a consistent pattern of search.

During the process of palpation, the client should feel comfortable and need to ask about it.

- Positioning the woman for palpation

For the palpation of the breasts, the woman should be placed in the supine position, placing both arms under her head, which will facilitate palpation of the outer quadrant of a large breast.

Use both hands to stabilize breast in position.

Perimeter of the breast should be noted during clinical breast examination. Anatomically, breast tissue extends superiorly from the second rib or clavicle, medially to the lateral border of the sternum, inferiorly to the sixth rib and laterally to the Latissimus Dorsi muscle.

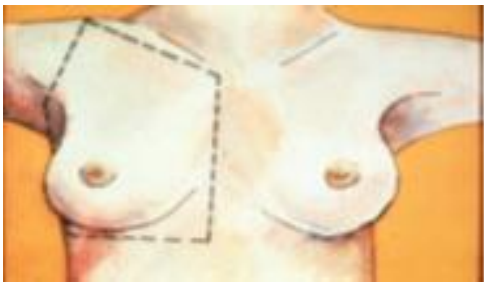


Figure 2.4 Perimeter of the breast

Palpation technique

The examiner should use the distal phalanges of the middle three fingers to palpate the breast. The entire breast should be palpated using overlapping dime–sized circles. Use three different levels of pressure (superficial, intermediate and deep) at each point to palpate different layers of the breast

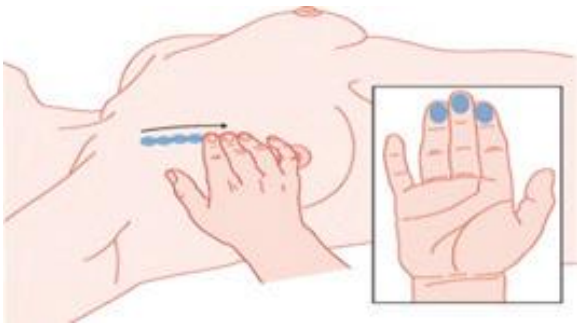


Figure 2.5 Palpation technique

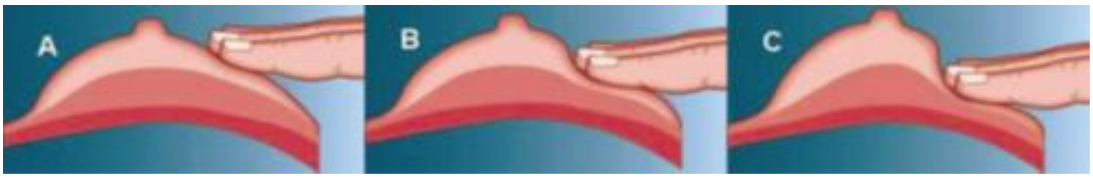


Figure 2.6 Palpation of the breast using three pressure levels (Superficial, intermediate and deep)

There are three typical patterns used to palpate the breast:

- Circular technique
- Radial spoke technique (wedges)
- Vertical strip technique (lines)

Figure 2.7 Three patterns of palpation

Note that the circular method does not always cover the entire perimeter of the breast, unless a conscious effort is made to do so.

The woman should be asked to squeeze areolar region of the nipple to see whether there is any nipple discharge. (Nipple discharge that occurs only with nipple or breast stimulation is a normal physiological function.)

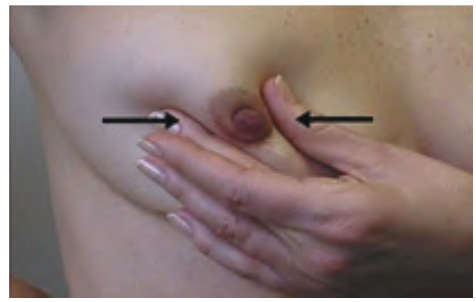


Figure 2.8 Look for nipple discharge

Palpation of Regional Lymph Nodes

The regional lymph nodes (Supra-clavicular, Infra-clavicular and axillary nodes) should be palpated while woman is in the sitting position.

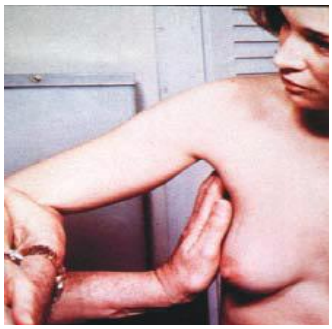


Figure 2.9

Palpation of axillary lymph nodes

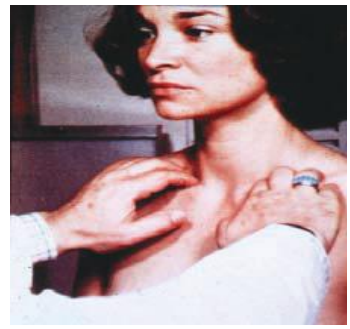


Figure 2.10

Palpation of supra and infra clavicular lymph nodes

Mammography / Ultra sound scan/ MRI scan

These investigations are components of the triple assessment in diagnosing breast cancer in a symptomatic patient. However, these investigations can be used in breast screening as well.

Mammography

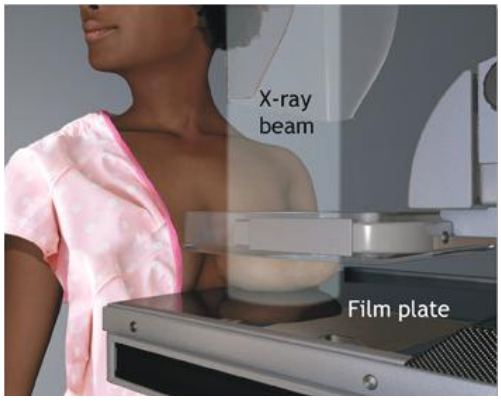


Figure 2.11: Procedure of mammography

A mammography is a low-dose x-ray of the breast tissue. This X ray can find changes that are too small to be felt during a physical examination. It is used for screening and diagnosis of breast cancer. Mammography is the investigation of choice for screening of early breast cancer when the lumps are not palpable by the patient or the doctor. Although relatively fast and accurate, it is a highly technological test that requires highly trained personnel and elaborate equipment. Sensitivity of mammography increases with age. Before the age of 40 years, mammography is not usually recommended for screening. This is because younger women tend to have denser breasts which reduce the sensitivity of mammography. Therefore, the risk of radiation tends to over-weigh the benefit of screening mammography for women less than 40 years of age.

Ultrasound Scan

There is insufficient evidence to support the use of ultrasound for routine screening. Ultrasound scan should not be used as a stand-alone screening test. It is generally used for further evaluating a mammographically detected anomaly in breast screening. Ultrasound scan may also have a role as an adjunct to mammography in screening women with dense breasts, as determined by a radiologist.

Magnetic Resonance Imaging (MRI)

MRI is a non-radiation incurring imaging modality with high sensitivity for detecting breast cancer. However, it is relatively less specific, costlier and not readily available.

MRI is recognized as a screening tool, either as stand-alone or as an adjunct to mammography for screening of women at high risk of breast cancer as determined by a radiologist.

Recommended screening protocol

- Breast self-examination should be conducted once a month by all women starting from 20 years of age.
- Clinical Breast Examination (CBE) is recommended every 3 years for all women from the age of 20 to 40 years. Women aged 40 or over, CBE is recommended annually.
- In women whose relatives had breast or ovarian cancer under the age of 40 years, annual clinical breast examination should be started 5 years before the index case.
- Breast self-examination should be taught and reinforced at every consultation.
- Screening mammography is offered once in 2-3 years for women aged 50 – 69 years. (Can be adopted only when adequate mammography facilities are available throughout the country)

Women who need more intensive screening

- Women with one or two first degree relatives with invasive breast cancer.
- Women with a breast biopsy showing atypical hyperplasia or lobular carcinoma in situ.
- Women with a history of chest wall radiation (e.g. mantle radiation for treatment of Hodgkin's lymphoma) at age 30 or younger.
- Women with known mutations (e.g. BRCA 1 BRCA 2).

Chapter 02

ANNEXES

I.Be Breast Aware
II. Breast Self-Examination
III. Hereditary Breast Cancer

BE BREAST AWARE

(Take care of your own well-being)

What is Breast Awareness?

Breast awareness is a part of general body awareness. It is a process of getting to know about your own breasts and becoming familiar with their appearance. Learning how your breasts feel at different times will help you to know what is normal for you. You can become familiar with your breast by looking and feeling – at a convenient time for you (e.g. while having a bath, shower, when dressing). Being breast aware and knowing what is normal for you will help you to be aware of any changes from normal.

The Normal Breast

(Know what is normal for you)

Before Menopause

Before the menopause normal breasts feel different at different times of the menstrual cycle. Milk-producing tissue in the breast becomes active in the days before menstrual period starts. In some women, the breasts at this time feel tender and lumpy, especially near the armpits.

After Menopause

After the menopause, activities of milk-producing tissues stops. Normal breasts feel soft, less firm and not lumpy.

Changes to look for

Appearance

Any change in the outline or shape of the breast, especially those caused by arm movements or by lifting the breasts, any puckering or dimpling of the skin.

Feelings

Discomfort or pain in one breast that is different from normal, particularly if new and persistent.

Lumps

Any lumps, thickening or bumpy areas in one breast or armpit which seem to be different from the same part of the other breast and armpit. This is very important if new.

Nipple change

- Nipple discharge, which is new for you and not milky.
- Bleeding or moist reddish areas which don't heal easily.
- Any changes in nipple position – pulled in or pointing differently.
- A nipple rash on or around the nipple.

Report any changes without delay

What to do if you find a change

There can be many reasons for changes in the breast. Most of them are harmless but all of them need to be checked as there is a small chance that they could be the first sign of cancer. If you are aware of any change in your breasts from what is normal for you, tell your doctor without delay.

Remember, you are not wasting anyone's time. If there is a cancer present, the sooner it is reported, the more simple treatment is likely to be. This offers greater prospects of benefit in terms of quality of life.

Likelihood of developing breast cancer increases with age.

4 POINT CODE

- Know what is normal for you
- Look and feel
- Know what changes to look for
- Report any changes without delay

Breast Self-Examination (BSE)

Health education on breast self-examination

Breast self-examination is the inspection and palpation of the breast by the woman herself. The role of the primary health care physician/ staff is to provide necessary information to women and to make them competent in breast self-examination.

Information that should be provided to the woman

- **Why it is important**

If breast cancer is detected early, it gives the better outcome. A practice of breast self-examination on monthly basis is very important for early detection of breast cancers.

- **When to carry out BSE**

It is better to conduct BSE one week after the start of menstruation (During menstruation, some women feel their breasts painful and lumpy). If she is not menstruating, a conveniene fixed date should be selected.

- **Frequency**

This should be carried out once a month by all women over the age of 20.

- **Place and postures to conduct Breast Self-Examination**

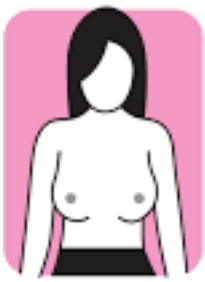
Instructions to be given to the woman on steps of Breast Self-Examination

Breast self-examination has two components:

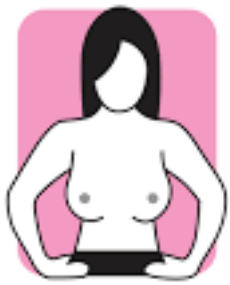
1. Inspection (Preferably in standing position)

2. Palpation (Either lying down, sitting, standing or while bathing)

Inspection



Arms by the side



Hands placed on the hips

Arms raised over the head

Figure II.I inspection

Stand in front of the mirror exposing the chest up to the waist, look at the breasts through the mirror, while keeping the arms in positions shown in figure (II.I) (1. arms hanging by the side, 2. hands pressed on the hips, 3. arms raised over the head)

Note changes mentioned below

- Skin changes of the breasts
- Color changes of the breasts
- Change in shape of the breasts
- Orange peel / Peau d'orange appearance of the breast
- Ulceration on the breast
- Late occurrence of breast asymmetry (most women may have asymmetry in normal circumstances. Therefore, a long- standing breast asymmetry is not a sign of a cancer)
- Nipple changes, discharges other than breast milk/ inverted nipple (having inverted nipples from birth is not a sign of a cancer)
- Breast lump, change in the texture, thickening of the breast skin
- Lumps in the arm pit or around the neck

Palpation (while standing)

Palpate the breast using middle three fingers to identify thickened areas and/ or lumps. Use the palmer surfaces of the fingers (flat surface of the three middle fingers). Palpation of breast can be done in sitting/ lying down positions or while bathing.

On examining right breast, raise the right arm over the head and palpate the right breast using the left hand. While examining the left breast raise the left arm and palpate the left breast using the right hand

Figure II.II Palpation of the breast

Continue palpating the breast in a clockwise direction (Figure II.II) from outer circle of the breast towards the nipple using three pressure levels as shown in figure II.III (Superficial, intermediate and deep)

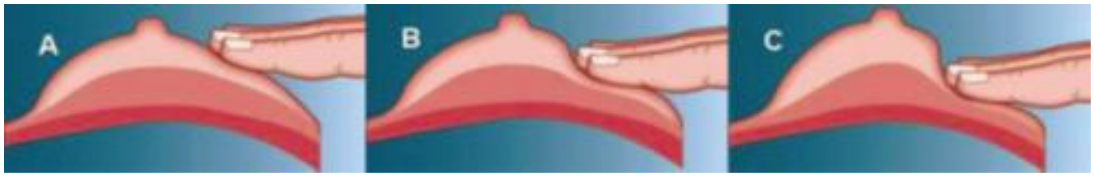


Figure II.III Palpation of the breast using three pressure levels (Superficial, intermediate and deep)

Start with applying 'minimal' pressure as indicted (to feel the area just beneath the skin) and then gradually increase the pressure (to feel the tissue deeper within)

Then examine the arm pit and look for lumps

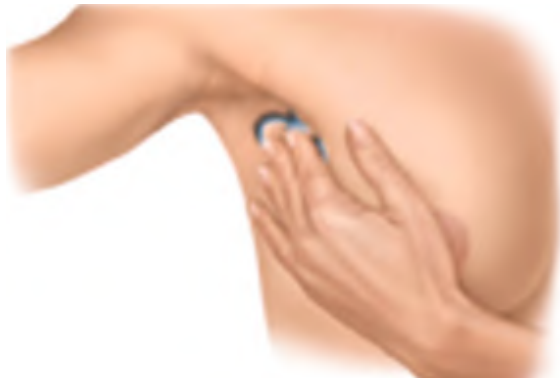


Figure II.IV Examination of arm pit

Find out whether there is a nipple discharge by squeezing the areola using thumb and middle finger.

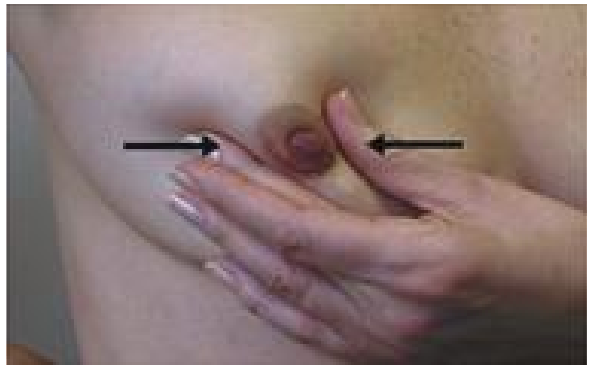


Figure II.V Look for nipple discharge

Use the same technique to examine the other breast.

Palpation of breast in lying down position.

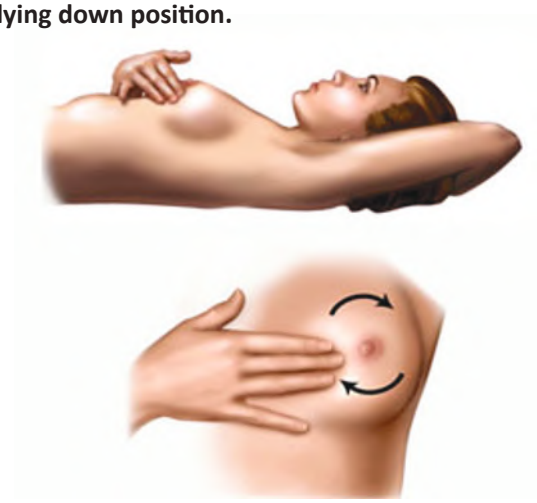


Figure II.VI Palpation of breast in lying down position

To palpate the right breast, keep the right palm beneath the head and palpate the breast using the left hand.

For the palpation of left breast, keep the left palm under the head and palpate with the right hand.

What to do after breast self-examination?

If any abnormality is detected during breast self-examination, it is necessary to consult a doctor even though all the changes may not be due to breast cancer.

National recommendation for breast self-examination:

All women should practice breast self-examination once a month from 20 years of age.

Hereditary Breast Cancer

Although all cancers are genetic, only some are hereditary. Five to ten percent of breast cancers have a strong hereditary component due to highly penetrant germ-line mutations in autosomal dominant Cancer Predisposition Genes (CPGs), while 15–25% are familial due to a combination of multiple moderate-low penetrant genes and shared environmental/lifestyle risk factors.
Hereditary breast cancers occur in individuals with germ line variants in various CPGs such as

- High-penetrance genes: BRCA1, BRCA2, TP53, PTEN, STK11, CDH1, APC, MLH1, MSH2
- Moderate-penetrance genes: ATM, CHEK2, PALB2, BRIP1
- Low-penetrance genes: BARD1, CDKN2A, RAD51, RAD51C, RAD51D, XRCC2, NBN, FANCA, FANCC, FANCCM

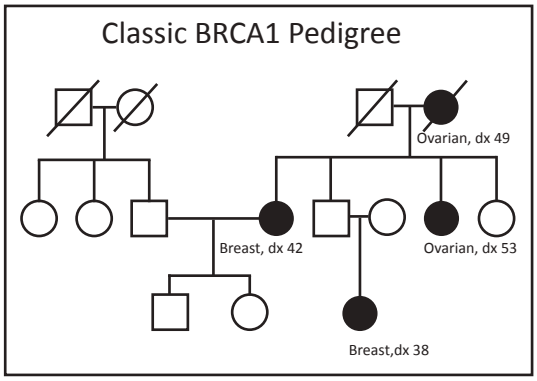
Genetically determined breast cancer syndromes

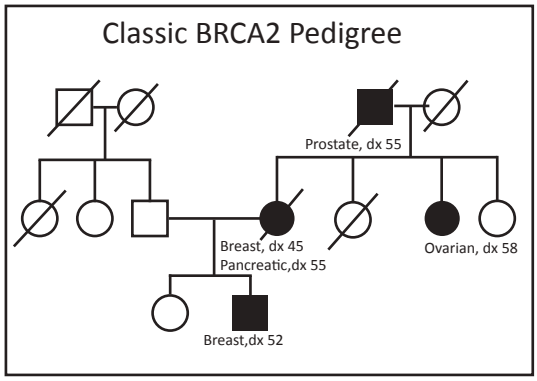
- Hereditary breast and ovarian cancer syndrome (HBOC) - BRCA1 and BRCA2 genes [OMIM 604370, 612555]
- Cowden syndrome (Multiple Hamartoma syndrome) - PTEN gene [OMIM 158350]
- Li-Fraumeni syndrome - TP53 gene [OMIM 151623]
- Peutz-Jeghers syndrome - STK11 gene [OMIM 175200]
- Lobular breast cancer and hereditary diffuse gastric cancer - CDH1 gene [OMIM 137215]

Identifying hereditary breast cancer

The key to identifying individuals who are at risk for a hereditary predisposition to breast cancer lies in obtaining and analyzing a complete and accurate three- generation family history (pedigree). Pedigrees should include detailed medical history of the person seeking consultation (who may or may not be a person affected with breast cancer at the time of consultation), as well as their first, second- and third-degree maternal and paternal relatives (i.e. children, parents, siblings, grandparents, aunts, uncles, nephews, nieces and first cousins).

The pedigree should document the type and primary site of cancer, laterality, age at diagnosis and the current age or, if deceased, the age at death for each affected individual as well as information about other family members. Confirmation of cancer diagnosis through review of medical records, pathology reports or death certificates of family members will be useful in families where the verbal history appears to be unreliable.





When to refer patients for a genetic consultation?

Referral for genetic counseling and testing for individualized cancer risk assessment should be offered to patients who meet any of the following "hereditary breast cancer" criteria[20]:

- Multiple cases of breast and/or ovarian cancer in the family occurring in two or more close relatives:
  - Two 1st degree, or one 1st and one 2nd degree relative with breast cancer <60 yrs and/or ovarian cancer at any age on the same side of the family.
  - Three or more family members (1st or 2nd degree) with breast or ovarian cancer on the same side of the family, any age.
- Patient or 1st degree relative with breast cancer <40 yrs, with or without family history.
- A family member with bilateral breast cancer.
- A family member with both breast and ovarian cancers.
- A family member with primary cancer in both breasts if one or both cancers was diagnosed before age 50 years.
- A family member with male breast cancer.
- A family member with ovarian cancer.
- Diagnosis of a hereditary breast cancer syndrome in a family member.
- A family member with an identified BRCA1 or BRCA2 mutation.

(First degree relatives - parents, children, siblings; Second degree relatives - grand-parents, grandchildren, aunts/uncles, nephews, nieces, half-siblings; Third-degree relatives - first-cousins, great grandparents, great grandchildren).

Genetic counseling for hereditary breast cancer

Genetic counseling allows individuals an opportunity to learn how heredity contributes to cancer risk, understand their personal risk of developing cancer, understand their options for managing their cancer risk and encourages adoption of risk-reducing behaviors that are appropriate for them. All those undergoing genetic testing should be offered comprehensive pre-test and post-test counseling.

Pre-test counseling is a process that includes discussion of personal risks of cancer based on the family history, the possible outcomes of genetic testing, including benefits, risks, limitations of testing and obtaining informed consent prior to testing.

Post-test counseling is a process in which the genetic test results and their significance are discussed, and medical management is reviewed, including screening and treatment options.

Other matters to be discussed during counseling include: privacy and confidentiality of genetic information; potential insurance, employment and social discrimination; adverse psychological reactions; and sharing test results with relatives.

Although BRCA1 and BRCA2 mutations are inherited in an autosomal dominant manner, their expression depends on acquiring a second mutation in the normal BRCA1 or BRCA2 gene in somatic cells. Although children of mutation carriers are at 50% risk of inheriting the mutation, the age of onset of their cancer is difficult to predict. It is important therefore to explain the difference between inheriting the mutation and development of the cancer to those seeking genetic counseling to help them understand the meaning of a positive test result and discuss with them the estimated lifetime risk of cancer for BRCA1 and BRCA2 mutation carriers given below:

Table III.I: Estimated lifetime risk for developing cancer in BRCA1 and BRCA2 mutation carriers[21]

Type of Cancer	Lifetime risk of developing cancer	
	BRCA 1	BRCA 2
Breast cancer before the age of 50 years	50%	28%
Breast cancer up to the age of 70 years	50 - 85%	50 - 85%
Ovarian cancer up to the age of 70 years	40 - 60%	10 - 20%
Male breast cancer Prostate cancer	1.2%	Up to 8.9%
Male breast cancer	8.6% by age 65	15% by age 65 20% lifetime
Pancreatic cancer	1 - 3%	2 - 7%
Melanoma (cutaneous & ocular)	No increase	Increased Risk

Genetic testing

Advances in molecular genetics have led to the identification of numerous genes associated with inherited susceptibility to cancer. Inherited genetic alterations (germ line mutations) can be identified by testing DNA extracted from blood of any person using Next-Generation Sequencing (NGS) cancer gene panels. Identifying the underlying germ line variants using multi-gene cancer panel testing is valuable in guiding treatment decisions and genetic counseling/screening of at-risk family members.

Cancer panel testing for germ line mutations in CPGs is now available in Sri Lanka. Testing is done on DNA extracted from a 5ml sample of venous blood collected to a green top EDTA tube from the patient. The cancer gene panel test that we offer tests 94 genes associated with inherited predisposition to cancer, including genes associated with both common (e.g. breast, ovarian, uterine, colorectal, prostate, thyroid) and rare cancers. It is performed using the Illumina TruSight Cancer® sequencing kit produced by Illumina, Inc., USA. This kit has been developed by Illumina in collaboration with Professor Nazneen Rahman and team at The Institute of Cancer Research (ICR), London, UK (http://www.illumina.com/products/trusight_cancer.html). It provides a rapid and economical solution to single-gene tests as it can analyse multiple genes simultaneously at a lower cost.

The steps involved in genetic testing:

- Test an affected family member FIRST after providing pre-test counseling and obtaining written informed consent to identify the mutation and confirm it.
- If a mutation is found, then other family members, including those who are not affected, can be tested for that mutation.
- Always provide post-test counseling.

Benefits of cancer gene panel testing:

- Clarify risks of hereditary breast cancer.
- Identify individuals who are at increased risk who could benefit from in creased cancer surveillance or measures to decrease risk.
- Identify individuals who may not be at increased risk.
- Simultaneous analysis of multiple CPGs allows rapid diagnosis of specific he reditary breast cancer syndromes.
- Saves money and time than single gene testing for patients suspected of having multiple hereditary cancer syndromes.
- A greater likelihood of identifying a hereditary cause for the cancer(s) in patients and/or their families.
- Reduces false negative results.
- Offers treatment guidance once the mutation is identified.
- Identification of the mutation in the family allows other at-risk healthy family members to be screened with targeted genetic testing to determine their individual risk status.
- Allows for earlier intervention through targeted individualized cancer screening and prevention programs in individuals who are mutation carriers.
- Assists couples in reproductive decision making.

What are the limitations of cancer gene panel testing?

- The test may miss large structural genetic variations. These are usually very rare.

Who should undergo genetic testing?

Breast cancer, with at least one of the following[22]

01. Diagnosed at age < 45 years
02. Diagnosed at age < 50 years with
    - two breast primaries; or
    - > 1 close relative with breast, pancreatic or prostate cancer
03. Diagnosed at age < 60 years with triple negative breast cancer

04. Family history of cancer:
    - > 1 close relative with breast cancer diagnosed at age < 50 years
    - > 1 close relative with ovarian cancer
    - > 2 close relatives with breast, pancreatic or prostate cancer; or male breast cancer relative
05. Male breast cancer
06. Ovarian cancer
07. Pancreatic cancer or prostate cancer with:
    - > 1 close relative with ovarian cancer (any age) or breast cancer (age < 50 years); or
    - > 2 close relatives with breast, pancreatic or prostate cancer
08. Unaffected individual (family history only):
    - 1st-, 2nd-degree relative meeting any of the above criteria;
    - 3rd-degree relative with breast/ovarian cancer and has > 2 relatives with breast/ovarian cancer

Implications of a positive test result:

- Clinical intervention can improve outcomes e.g. risk reduction mastectomy reduces risk of breast cancer and salpingo-oophorectomy reduces risk of ovarian and breast cancer (in premenopausal women).
- Family members at risk can be offered testing and identified.
- Healthy life styles can be reinforced.

Implications of a negative test result:

Reassures the individual and their family members.

Management Guidelines

The options described below are available for managing the increased cancer risk in BRCA1 and BRCA2 mutation carriers[22]:

For women:

- Breast awareness starting at age 18 years
- Clinical breast exam, every 6-12 months, starting at age 25 years

- Breast screening:
  - Age 25-29 years, annual breast MRI screening with contrast or mammogram
  - Age 30-75 years, annual mammogram and MRI with contrast
  - Age >75 years, individual basis
- Consider options of risk-reducing mastectomy and/or salpingo-oophorectomy.
- Consider trans-vaginal ultrasound starting at age 30-35 years or CA-125 screening, every 6 months.
- Consider risk reduction agents.

For men:

- Breast self-exam, starting at age 35 years
- Clinical breast exam, every 12 months, starting at age 35 years
- Prostate cancer screening, starting at age 45 years

For men/women:

- Pancreatic cancer and melanoma screening, based on family history
- Advise about options for prenatal diagnosis and assisted reproduction

WHERE TO REFER PATIENTS FOR GENETIC CONSULTATIONS:

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25, Kynsey Road,
Colombo 08.

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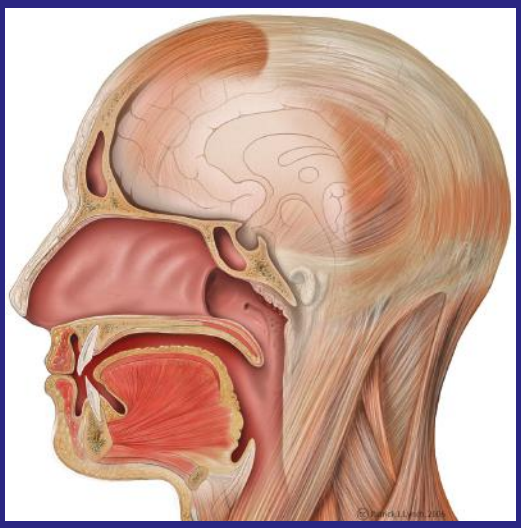

Chapter 3

Oral cancer

National Guideline on
Early Detection and Referral Pathways of
Common Cancers in
Sri Lanka

We would like to acknowledge the authors of the guideline for management of Oral Potentially Malignant Disorders (ISBN: 978-955-3666-27-7 published in 2019) from which necessary contents were extracted for this book.

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3. Oral cancer

3.1 Introduction

Oral cancer is the commonest malignancy among males in Sri Lanka and the seventh most common cancer among females. Malignancies of the lip, tongue & mouth are estimated to account for 9.1% of all reported cancers among the Sri Lankan population. It is estimated (GLOBOCAN), that there are 2152 cases of cancer Lip, tongue & mouth in 2018. Out of them 1576 were male patients while 576 were females[1]. Cancer incidence is increasing with the age and comes a peak at the age of 70 years (figure 3.1)

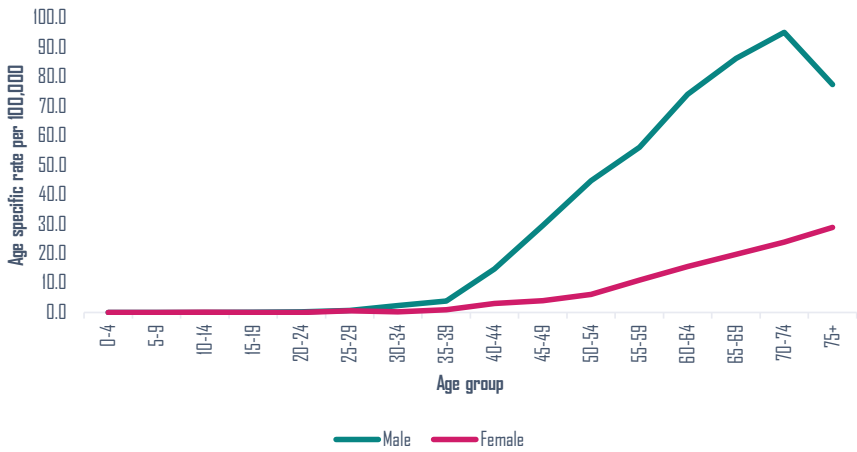


Figure 3.1 Age specific incidence rate - lip, tongue and mouth- 2012
Source: national cancer registry, Sri Lanka - 2012

More than 90% of oral cancers are Squamous Cell Carcinoma (SCC)[2] . In most instances in South Asia oral SCC is preceded by clinically recognizable disorders appearing on the oral mucosa such as leukoplakia, erythroplakia, oral sub mucous fibrosis and oral lichen planus.

These diseases that precede the appearance of oral cancer are collectively referred to as Oral Potentially Malignant Disorders (OPMDs)[3] . Summary of the genetic alterations that are observed at the different stages of oral carcinogenesis is depicted in Fig 3.2. The molecular changes that are associated with dysplasia grade and transformation to oral cancer are shown in this figure.

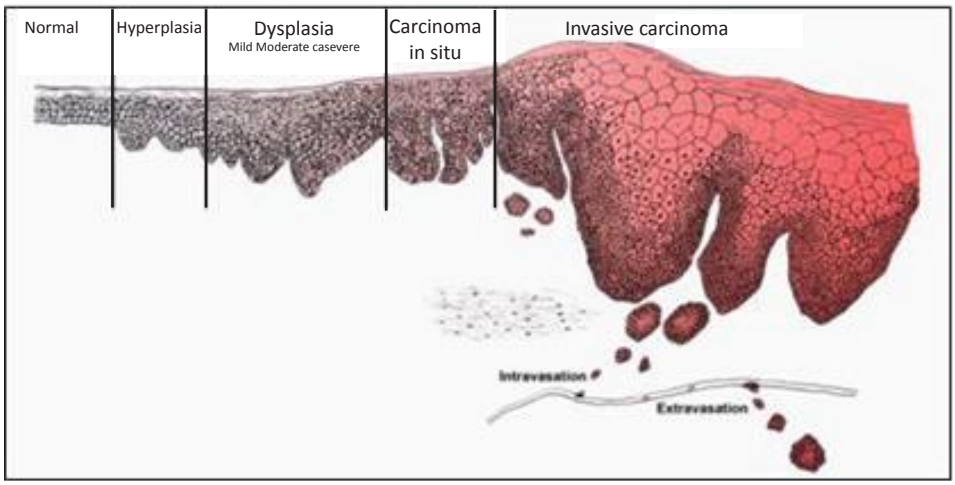


Figure 3.2: Summary of the genetic alterations that are observed at the different stages of oral carcinogenesis.

3.2 Risk factors

Oral Potentially malignant disorders and oral cancer are usually associated with the habits such as betel quid chewing, chewing tobacco, smoking, snuff dipping, areca nut chewing and alcohol intake[4,5]. Smokeless tobacco in the form of betel quid, oral snuff and betel quid substitutes (locally called guktha, nass, naswar, khaini, mawa, mishri and gudakhu) increases the risk of oral precancerous lesions and oral cancer between 2-fold and 15-fold[6].

Tobacco chewing, smoking and consumption of alcohol have been shown to act synergistically with the combined risk being considerably increased in comparison to individual risk factors[7]. Combination of risk factors also can act as a promoter in the malignant transformation from OPMD to oral cancer.

Smokeless tobacco use among young people is increasing in South Asia, with the marketing of conveniently packaged products made from areca-nut and tobacco; as a consequence, oral precancerous conditions in young adults have increased significantly[8]. Only a portion of OPMDs necessarily undergo malignant transformation.

Apart from the variables considered smokeless tobacco and areca-nut products (Babul beeda, Pan Parag, Mawa etc.) could be considered as emerging risk factors for OPMDs / oral cancer among Sri Lankans[9].

3.3 Clinical features and Diagnosis

3.3.1 Oral Potentially Malignant Disorders

Table 3.1 shows the disorders that are considered as OPMDs[3,10]. However, only four most important disorders (leukoplakia, erythroplakia, oral sub-mucous fibrosis and oral lichen planus) are described in this book as those are the most common types observed in Sri Lanka.

Table 3.1: List of oral potentially Malignant Disorders

Oral Potentially Malignant Disorders	
Leukoplakia Erythroplakia Oral Submucous fibrosis Oral lichen planus	Palatal changes due to reverse smoking Discoid lupus erythematosus Actinic keratosis Inherited disorders Dyskeratosis congenita Epidermolysis Bullosa Xeroderma pigmentosum Fanconi's anaemia

1. Leukoplakia

Leukoplakia is generally defined as a predominantly white lesion of the oral mucosa that cannot be clinically or histopathologically characterized as any other definable lesion[3,11,12,13,14]. Leukoplakia is the most common potentially malignant lesion of the oral mucosa[14]. The term leukoplakia is a clinical descriptor only[15]. The terms keratosis and dyskeratosis are histological features and should not be used as clinical terms.

On the basis of the following clinical features a provisional diagnosis of leukoplakia is made when the lesion cannot be clearly diagnosed as any other disease of the oral mucosa with a white appearance.

Clinical features

Leukoplakia is usually a solitary white patch with a clear boarder/margin. It may appear on any site of the oral cavity. But the most common sites for leukoplakia are buccal mucosa, alveolar mucosa, floor of the mouth, tongue, lips and palate[16].

Generally, two clinical types of leukoplakia are recognized: homogeneous and non- homogeneous, which can be co- exist[3].

Homogeneous leukoplakia

Homogeneous leukoplakia is defined as a predominantly white lesion of uniform flat and thin appearance that may exhibit shallow cracks and that has a smooth, wrinkled surface with a consistent texture throughout[3]. This type is usually asymptomatic (Fig 3.3).

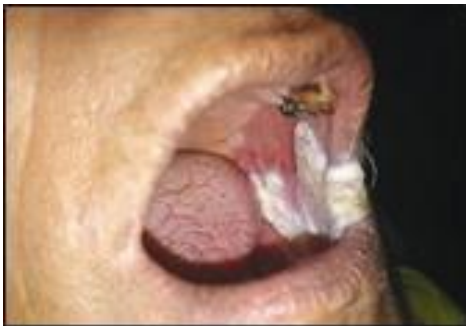


Fig. 3.3 : Homogeneous leukoplakia on the left buccal mucosa

Non - homogeneous leukoplakia

Non-homogeneous leukoplakia is defined as a predominantly white and red lesion (Erythroleukoplakia) that may be either irregularly flat (speckled) or nodular[17].

Types of non- homogeneous leukoplakia

- Verrucous leukoplakia (Fig.3.4)
- Nodular leukoplakia (Fig.3.5)
- Ulcerated leukoplakia (Fig.3.6)

Figure 3.4 Proliferative verrucous leukoplakia. Note the extensive thick white plaques

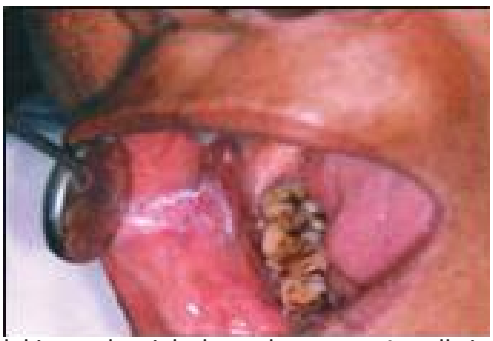


Figure 3.5 Nodular leukoplakia on the right buccal mucosa. A well circumscribed lesion with pin head sized nodules scattered on an erythematous base

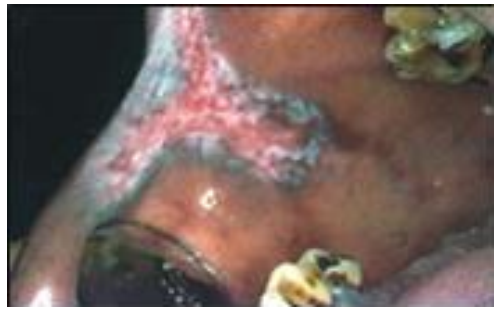


Figure 3.6 Ulcerated leukoplakia on right commissure and buccal mucosa

Diagnosis

Clinical diagnosis of Leukoplakia is based on approaches mentioned in Fig 3.13 Clinical differential diagnosis includes the disorders mentioned in Table 3.1

Provisional clinical diagnosis: It is based on clinical features stated above using examination and palpation as the only diagnostic measures[17].

Definitive clinical diagnosis: It is based on clinical evidence obtained by lack of changes after identifying and eliminating suspected aetiologic factors during a follow-up period of 2-6 weeks (In some cases the time may be longer)[17].

Histopathologically proven diagnosis: Definitive clinical diagnosis complemented by biopsy in which, histopathologically, no other definable lesion is observed.

2. Erythroplakia

Oral Erythroplakia (OE) is considered a rare potentially malignant disorder of the oral mucosa and is classically defined as ‘‘fiery red patch of the oral mucosa that cannot be characterized clinically or pathologically as any other definable disease”[12]. It must be noted that in case of a mixture of red and white changes, such lesion is usually categorized as non-homogeneous leukoplakia (Erythroleukoplakia) A new approach to perceive the lesion is proposed based on the clinical features of a fiery red, sharply demarcated lesion situated at a slightly lower level than the surrounding mucosa. Such a definition would help clinicians distinguish erythroplakia from other red lesions of the oral mucosa. Although the course of such lesions varies, a significant proportion will develop into malignant condition, which is why they should be followed up at short intervals[18,19]

Clinical features:

Lesions of OE are typically less than 1.5 cm in diameter but lesions larger than 4 cm in diameter have been reported[20]. The clinical appearance may be flat or with a smooth or granular surface[19]. The surface of OE is often depressed below the level of the surrounding mucosa[21]. Any site of the oral cavity and oropharynx may become

involved, usually in a solitary fashion. This solitary presentation is often helpful in clinically distinguishing erythroplakia from several other erythematous lesions affecting the oral mucosa, since these other lesions occur almost always in a bilateral, more or less symmetrical pattern[22]. OE is soft to palpation and does not become indurated or hard until an invasive carcinoma develops in it. The soft palate, the floor of the mouth and the buccal mucosa are most commonly affected by OE[19]. The tongue is rarely affected[12].

Oral erythroplakia is diagnosed by exclusion. The term OE does not carry a histopathological connotation. As for oral leukoplakia the principle of provisional diagnosis and definitive diagnosis is also suggested for OE.

Provisional clinical diagnosis:

''A provisional diagnosis of OE is made when a lesion at clinical examination cannot be clearly diagnosed as any other disease of the oral mucosa with red appearance''.

Definitive clinical diagnosis:

''A definitive diagnosis of OE is made as based on identification, and if possible elimination, of suspected aetiological factors and, in the case of persistent lesions, histopathological examination''. OE is seldom multicentric and rarely covers extensive areas of the mouth[22].

Histopathologically proven diagnosis:

The term erythroplakia is regarded as a clinical term with no specific histopathological connotations. However, most cases of erythroplakia appear to harbor some degree of epithelial dysplasia/ carcinoma-in-situ or frank carcinoma[18]

Since the malignant transformation rates are very high (vary from 14% to 50%) it needs to be treated expeditiously. Malignant transformation of OE rates are considered to be the highest among all OPMDs[23]. Surgical excision is the treatment of choice[19].

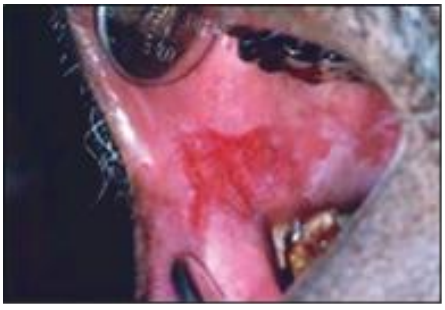


Fig 3.7: Erythroplakia
(Red patch on the right buccal mucosa with white areas posteriorly).

3. Oral Submucous Fibrosis (OSF)

Unlike other potentially malignant disorders, Oral Submucous Fibrosis (OSF) is insidious in origin and is not amenable to reverse at any stage of the disease either spontaneously or with cessation of habit. The condition may remain either stationary or become severe, leaving an individual challenged both physically and psychologically[24]

This condition is associated with burning sensation in the oral mucosa from the early stages and with a significant risk for malignancy. It is a chronic disease with progressive fibrosis in the sub-mucosa tissues leading to restriction in opening the mouth with the advancement of the disease[5,25]. Fibrosis initially affects the lamina propria of the oral mucosa and as the condition worsens, extends to the sub mucosa and the deeper tissues including oral musculature. Consequently the elasticity of the oral mucosa is progressively lost. Malignant transformation varies from 4.5% to 30 % [26].

It has been shown that either an increased collagen synthesis or reduced degradation of collagen may be responsible for the development of OSF. Based on the evaluation by the International Agency for Research on Cancer (IARC) conclusive evidence now exists that the disease is caused by the consumption of areca nut[9]. Alkaloids in areca-nut, importantly, arecoline, have been implicated in stimulation of fibroblast proliferation while tannins in the nut appear to stabilize collagen structure that resists degradation by collagenases resulting altered collagen metabolism leading to fibrosis. The disease is associated with certain genetic groups[5].

Clinical features

Clinical features that are useful in the diagnosis include:

Table 3.2 :Clinical features of OSF

Early disease	Late disease
• Burning sensation of the oral mucosa	• Palpable fibrous bands in cheeks, along the faucial pillars, soft palate and lips
• Blanching and stiffening of the oral mucosa leading to limitation in mouth opening	• Tightening of the lips with resultant lack of their elasticity
• Widespread pallor of the oral mucosa. Depigmentation of the mucosa particularly noticeable on the vermilion border of the lips in a significant proportion of patients	• Depapillation of the dorsum of the tongue with restricted mobility of the tongue including protrusion
• Vesiculation of the oral mucosa is sometimes described but not often seen	

Other OPMDs such as leukoplakia may be seen in long standing OSF.

Diagnosis of OSF

Diagnosis can be made easily in established OSF based on the above clinical features. In early stages, however, the diagnosis may be difficult to establish purely on clinical grounds and a biopsy may be necessary for the diagnosis. Biopsy is also necessary in advanced stages to determine the presence of epithelial dysplasia, if there are clinically suspicious features. The condition may need to be distinguished from other diseases that may exhibit fibrosis and may cause limitation in mouth opening such as epidermolysis bullosa, post-irradiation fibrosis, cicatricial pemphigoid, progressive systemic sclerosis etc. (Fig 3.8).

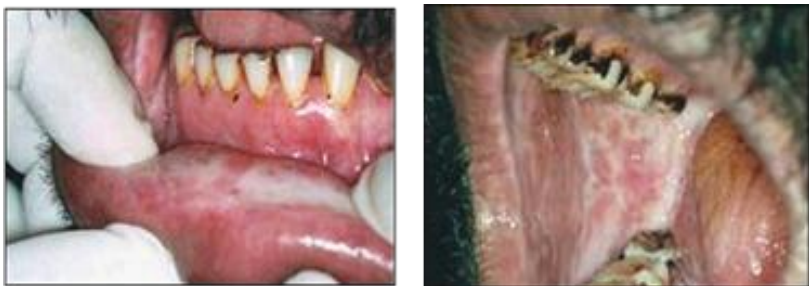


Fig 3.8: Oral Sub-mucous Fibrosis

Grading of OSF

Unlike other OPMDs, OSF is a disorder that is associated with a functional disability. Attempts have been made to grade OSF using mainly clinical / functional criteria[27,25]. A grading scheme proposed by Kerr et al, in 2011, is a useful one and is shown in Table3.3.

Table 3.3 Disease Grading of Oral Sub-mucous Fibrosis

Grade	Clinical and functional features
Grade 1 – Mild	Any feature of the disease triad for OSF ((burning sensation, depapillation, blanching or leathery mucosa) present + inter-incisal opening >35 mm
Grade 2 – Moderate	Above features of OSF + inter-incisal limitation of opening 20–35 mm
Grade 3 – Severe	Above features of OSF + inter-incisal opening <20 mm
Grade 4A	OSF + other potentially malignant disorder on clinical examination
Grade 4B	OSF with any grade of oral epithelial dysplasia on biopsy
Grade 5	OSF + oral squamous cell carcinoma (SCC)

4. Oral Lichen Planus

Oral lichen planus is a common chronic inflammatory mucocutaneous disorder that typically affects the skin and/or mouth[3,28] Lichen planus can also affect other extra oral sites such as the genitals[26].

Clinical features

Oral lichen planus has a bilateral distribution[29] that typically affects the buccal mucosa, dorsum and ventral surfaces of the tongue and/or gingiva. Other mucosal surfaces can be affected but palatal involvement is particularly rare. Oral lichen planus is often asymptomati[28,29] although when there are areas of erosion or ulceration, the patient may have variable amounts of discomfort, being particularly troublesome when eating spicy or acidic type of food. The variable clinical presentations of oral lichen planus comprise white patches, erosions, ulcers and very rarely, blisters[28,29].

Patients with disease involving the gingiva may have areas of white patches or striae superimposed upon redness of the gums. These lesions are often painless, although patients may complain of a slight roughness or dryness to the affected mucosal surfaces. Around 30% of patients with oral lichen planus will have lesions in other parts of the body.

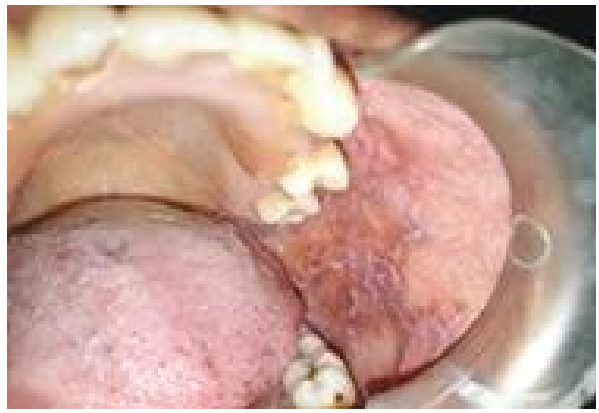


Figure 3.9: Oral Lichen planus

Diagnosis

The diagnosis of oral lichen planus is initially based on the clinical presentation of bilateral white patches with or without erosions, ulcers or blisters, typically affecting the buccal mucosa, dorsum of tongue and gingiva[30].

Biopsy with subsequent histopathological examination of affected tissue is essential to exclude other disease that may mimic oral lichen planus – such as lupus erythematosus[30].

In addition, it is advantageous to undertake a biopsy to identify possible areas of cellular atypia (dysplasia) within the involved tissue[31].

Worldwide it is accepted that oral lichen planus has a malignant transformation rate of 0.4% to 5% over a period of observation from 6 months to 20 years and seems to be independent of the clinical types of OLP or the treatment used[23].

Oral cancer

Oral cancer may take various clinical forms. It may resemble a leukoplakia, a verrucous leukoplakia, an erythro- leukoplakia, or an erythroplakia, any of which may even totally develop into a necrotic looking ulcer with irregular, raised indurated borders, or into a broad based exophytic mass with a surface texture which may be verrucous, pebbled or relatively smooth. (Figure 3.10&3.11) When traumatized, oral cancer bleeds readily and often becomes superficially secondarily infected. Oral cancer is usually painless unless it is secondarily infected. Large lesions may interfere with normal speech, mastication or swallowing[32,33,34].

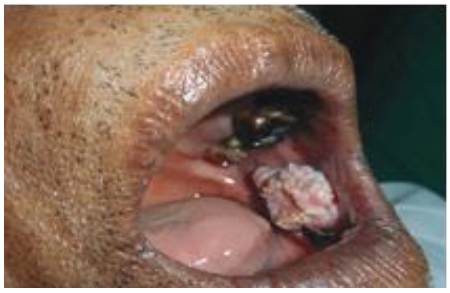


Fig: 3.10 Oral cancer presented as an exophytic mass

Fig: 3.11 Oral cancer presented as an ulcer

3.4 Management of Oral Potentially Malignant Disorders and Oral Cancer

Diagnosis and treatment in the asymptomatic stage will lead to better outcomes than diagnosis and treatment following the presentation of symptoms. Oral cancer is a disease which fulfils most of the criteria for screening. It is considered to be one of the most cost-effective approaches for control of oral cancer in a high risk country. The screening test for oral cancer might be affordable, acceptable, easy to use, accurate and effective in controlling oral cancer. Employing such a screening test will increase treatment demand. However, the level of health service development and available resources should be considered before the decision to introduce population based screening. The target population for oral cancer screening which includes of those age 30 years and older who use tobacco and/ or alcohol could be considered as a better approach.[35]

Visual screening of the oral cavity has been widely evaluated for its feasibility, safety, acceptability, accuracy to detect OPMDs and cancer, and efficacy and cost- effectiveness in reducing oral cancer mortality[36,37,38].Visual screening involves systematic visual and physical examination of the intraoral mucosa under bright light for signs of OPMDs, as well as early oral cancer, followed by careful inspection and digital palpation of the neck for any enlarged lymph nodes. Since the performance of oral visual screening in detecting lesions varies among providers, the providers should have comprehensive knowledge of the oral anatomy, the natural history of oral carcinogenesis, and clinico-pathological features of OPMDs and preclinical cancer[35]

Screening strategies adapted in Sri Lanka for OPMD and Oral cancer

There are two main strategies used of screening of OPMDs / oral cancer

1. Risk strategy

There are two screening types using risk strategy

I. Targeted screening for high risk individuals

II. Targeted screening for population sub-groups who are at risk

This risk strategy used for screening for OPMDs/oral cancer could be performed even by primary health care workers. Feasibility of this approach was demonstrated in a study conducted in Sri Lanka in early 80s[39].

2. Opportunistic screening at dental / medical clinics

This could be done when patients who are attending a health care provider for another purpose are examined for clinical signs of OPMDs/ oral cancer.

To facilitate opportunistic and population-based screening, a criterion is introduced based on habits of betel chewing, smoking, alcohol use and the use of areca-nut packets. This was developed by the reviewing Risk Factor Model developed by Amarasinghe et.al 2010 and the emerging trend of commercially available areca-nut packets[40]. (Table 3.3) All health staff is requested to adhere to this criterion to select high risk individuals for OC/OPMD and are requested to refer them to dental clinic for further care.

Table 3.4: Criteria to identify individuals at higher risk for OPMDs and oral cancer

Criteria	Description
1	Those who chew betel quid three or more times a day
2	Those who chew betel quid less than three times a day and additionally smoke and / or consume alcohol habitually
3	Those who habitually consume smokeless tobacco and areca-nut products (Babul Beeda, Pan parag, Mawa etc.)

Role of Medical Officers (especially at HLCs / OPD)

- Identify high-risk individuals according to the developed criteria and refer them to the nearest dental clinic to carry out a proper clinical oral examination.
- Assist individuals having higher risk for OPMD/Oral cancers for cessation of risk habits.

Role of Medical Officer of Health (MOH)

- Implement the oral cancer prevention and early detection programme in the MOH area.
- Coordinate with Regional Dental Surgeon and Dental Surgeons of the area to ensure that the Dental Surgeons screens high risk individuals referred by the PHC staff.
- Coordinate training programmes for Dental Surgeons, Medical Officers, Registered Medical Officers and PHC staff with the Regional Dental Surgeon.

For detailed information, refer 'Guideline for Management of Oral Potentially Malignant Disorders' published by National Cancer Control Programme. WWW.nccp.health.gov.lk

Screening and referral pathway

Individuals are referred to dental clinics for clinical oral examinations and the referral pathway is mentioned in figure 3.12.

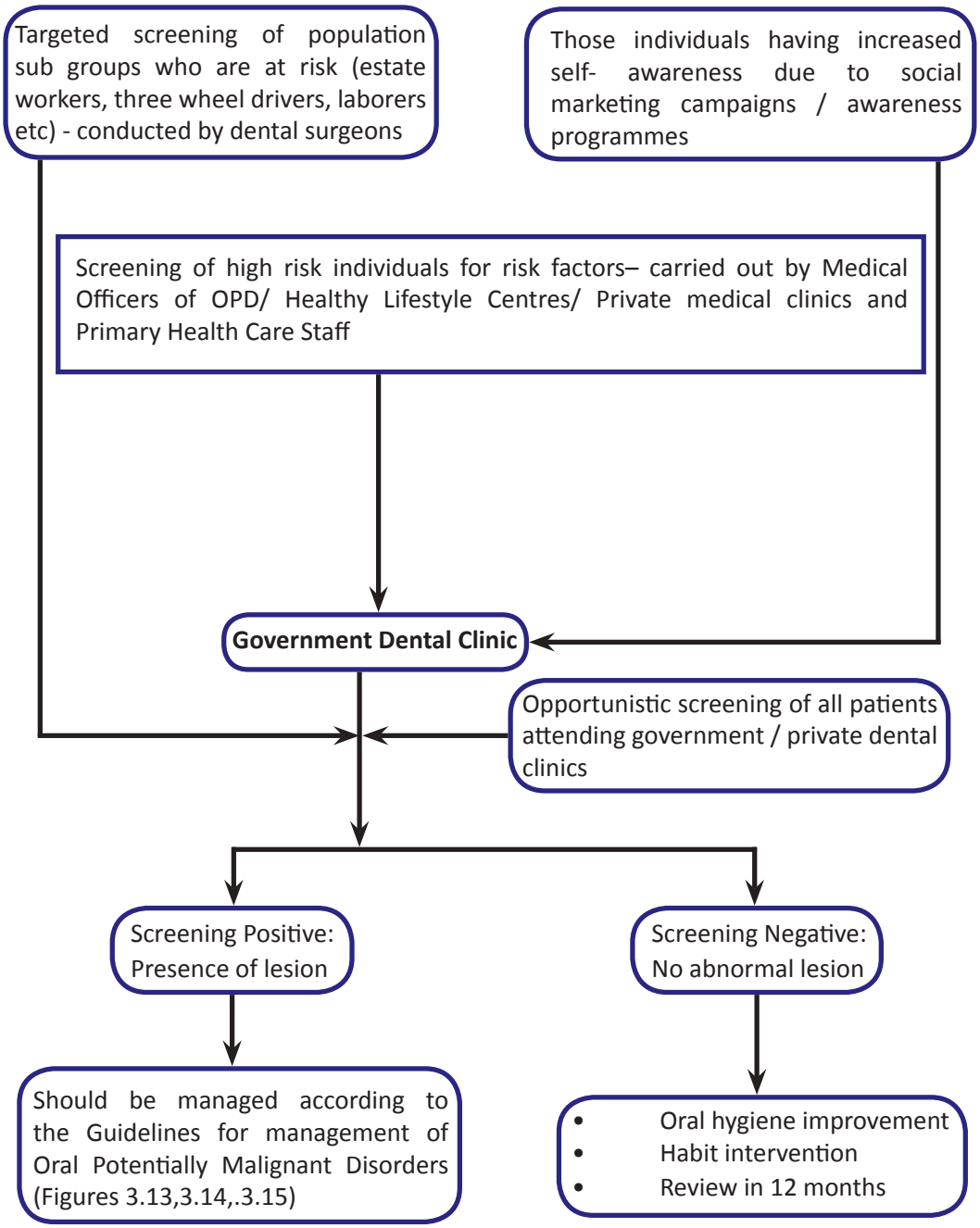
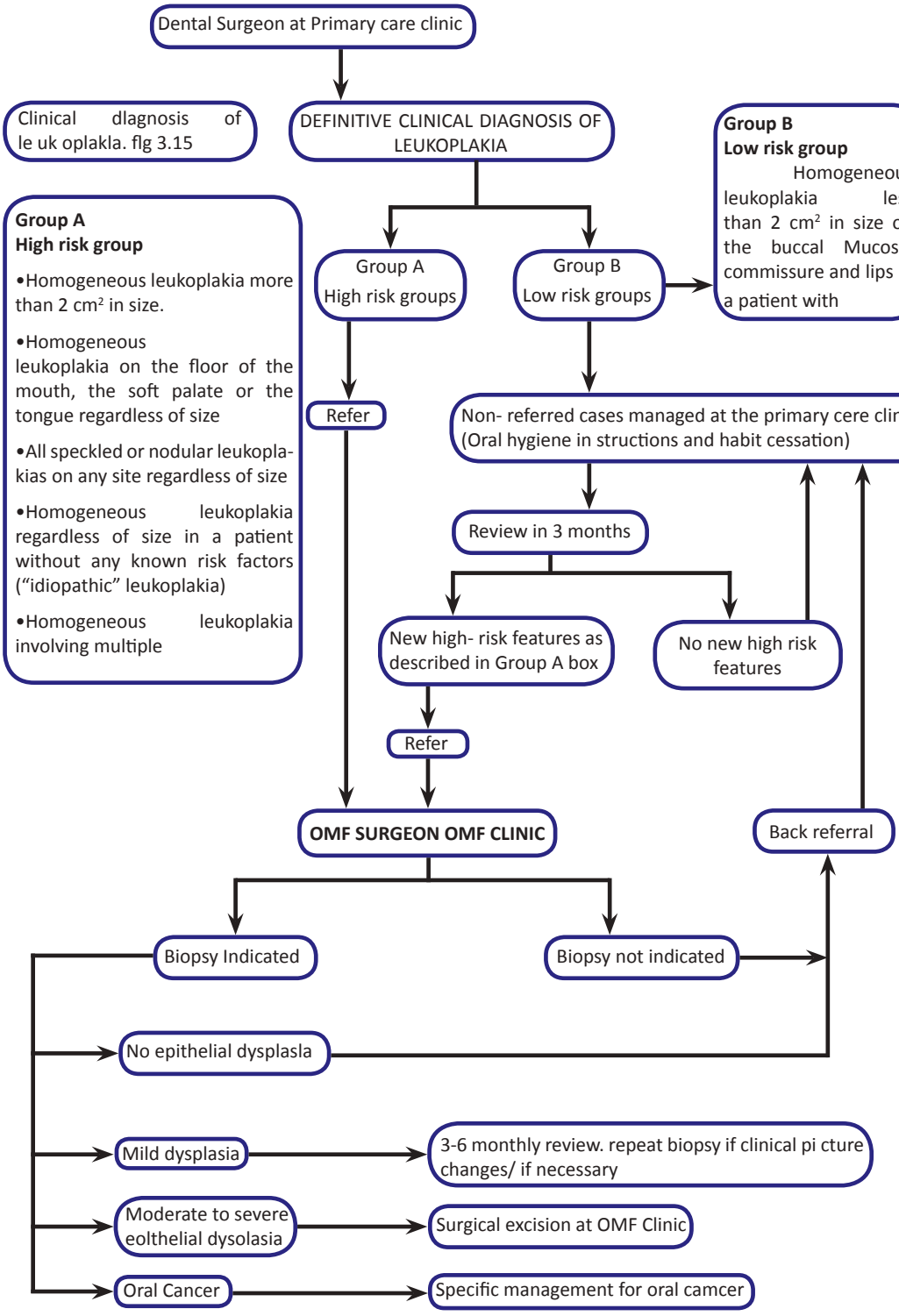


Figure 3.12: OPMD and oral cancer refferal pathway

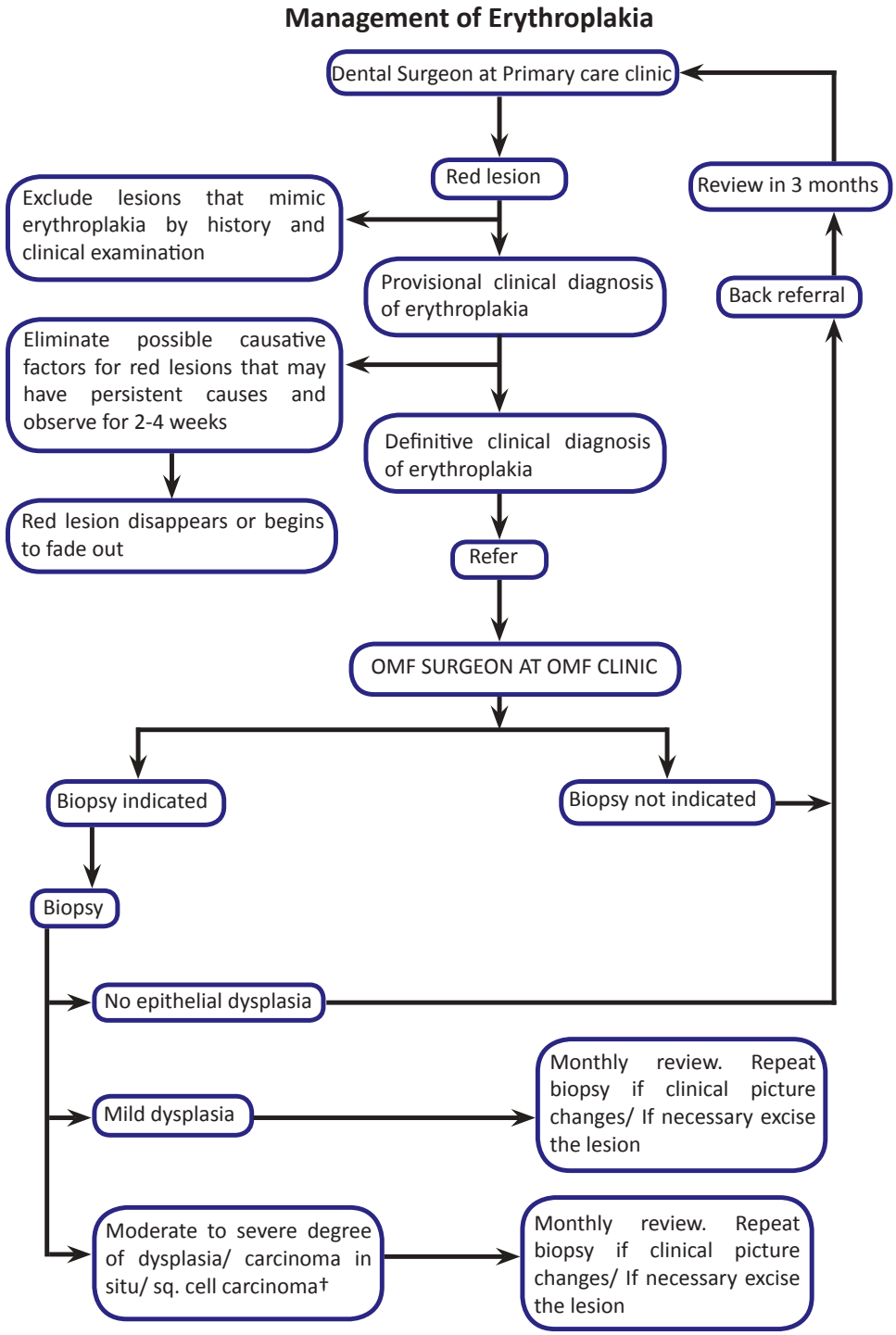
Management of Leukoplakia



†-Taking into consideration patient factors such as medical/social status etc

**-No treatment method including surgical excision is shown to prevent development of SCC (Holmstrup et al., 2006)*[41]

Figure 3.13: Flow chart for the management of leukoplakia



Follow separate guidelines – National Guidelines for Management of Oral Cancer;
** No treatment method including surgical excision is shown to prevent development of SCC[41]*
Constructed on model advocated by Isaac van der Wall 2010 and modification of model suggested by Warnakulasooriya et al., 2007, Hashibe et al., 2000 [3,42]

Fig 3.14: Flow chart for the management of erythroplakia

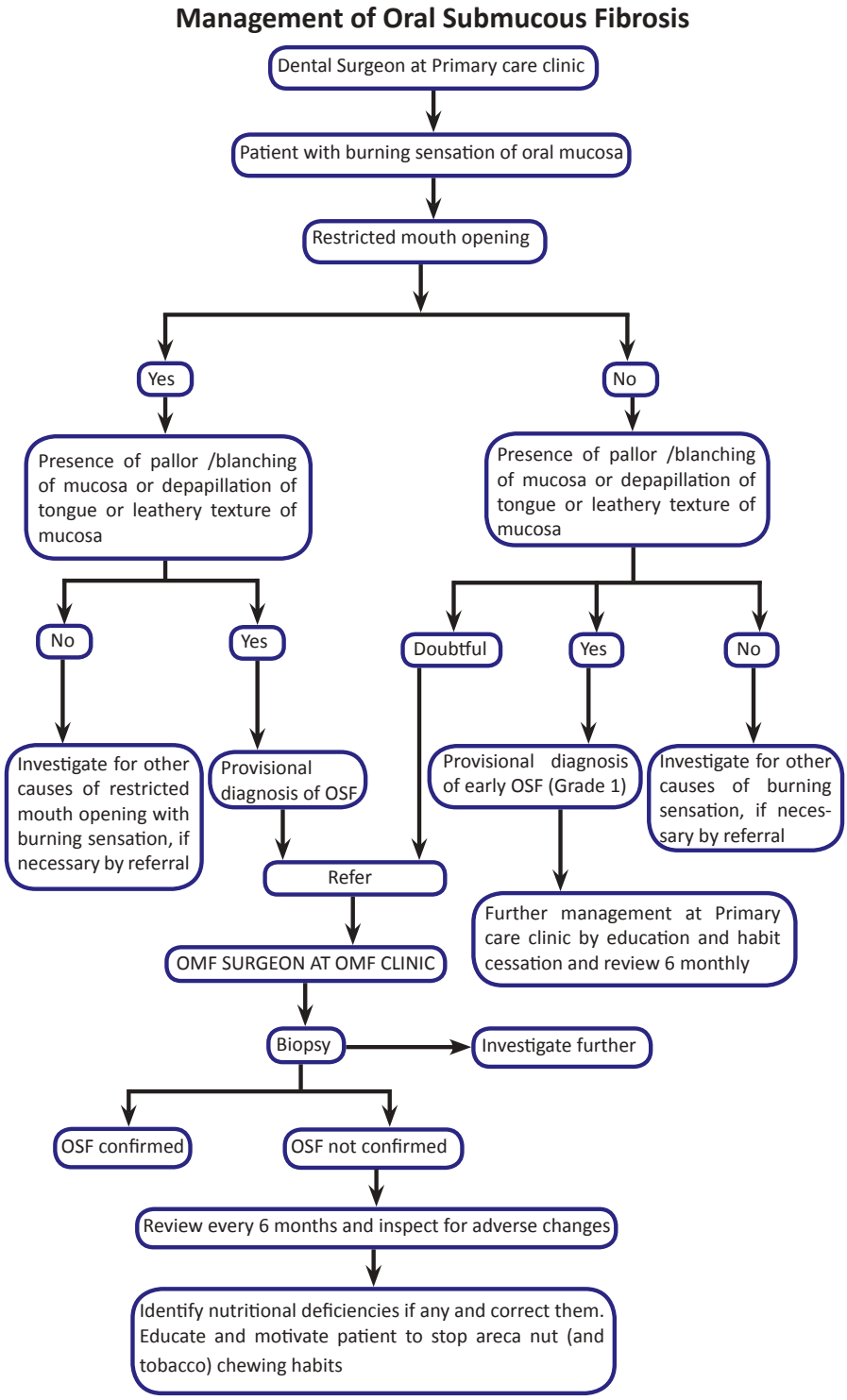


Figure 3.15: Flow chart for management of oral submucous fibrosis

Treatment of OSF

There is no single satisfactory and evidence-based treatment method for the OSF. Cessation of areca-nut consumption by regular users remains the most vital step in the management of OSF. Physical, medical, nutritional and surgical treatments have all been tried with claims of varying rates of success[25].

Physical methods such as stretching exercises aimed at increasing mouth opening and medical treatments such as nutrients, antioxidants, tropical and intra- lesional corticosteroids, intra-lesional enzymes and peripheral vasodilators have been reported [25]. Intra lesional steroid (for example methyl prednisolone) injection is the widely practiced treatment[25,43] in most centers, especially for symptomatic cases with developing limitation in mouth opening associated with burning sensation. As nutritional supplements, patients are advised to have a diet rich in fresh fruits and vegetables.

Initial stage of OSF should be included counselling of patients along with anti-oxidants (lycopene, spirulina, curcumin), multivitamins and minerals. Moderate stages of OSF should be treated with intra-lesional steroids and peripheral vasodilator (pentoxifylline), whereas advanced stages should be treated surgically [44]. A full blood count is recommended for every patient when the diagnosis of OSF is made. When deficiencies are detected, treatment must be instituted to correct them.

Management of Oral Cancer

The clinical behaviour of oral cancer and prognosis will depend on the site of origin and aetiological factors. Staging of the disease is very essential for treatment planning and outcome evaluation. It is based on clinical examination under anaesthesia, supported with radiological assessment using X-ray/CT scan/MRI scan. The staging usually follows Tumour, Nodes Metastases (TNM) classification established by International Union against Cancer (UICC) and American Joint Committee on Cancer (AJCC).

The management of patients with oral cancer should be a multi-disciplinary approach where surgeons, oncologists, speech therapists and nutritionists play a very important role[10]. Factors that influence the choice of treatment are primary site, grade of tumour, TNM staging, patients' age, and co-morbid conditions. Goals in the management of oral cancer are; high loco-regional control with preserved organ functions and survival rates and reduced probability of distant metastases. According to evidence, single modality treatment with surgery or radiotherapy is recommended for patients who are with early stage disease. Combined modality of treatment for advanced stage disease will benefit with local control and survival improvement. Especially concurrent chemo-radiotherapy has shown 8% survival benefit compared to radiotherapy

alone. Targeted therapy with EGFR blockers have shown absolute improvement in local control and also survival benefit. Which selected group is going to benefit is yet to be discovered in oral cancers[13,46].

Oral cancer management guideline for In Sri Lanka is under development. The expert has agreed to follow the NCCN clinical practice guidelines in Oncology (Head and Neck version) for management of Oral cancer with few modifications.

Chapter 03

ANNEXES

I. circulars

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சுகாதாரம், போசணை மற்றும் சுதேச வைத்திய அமைச்சு
Ministry of Health, Nutrition & Indigenous Medicine

General Circular No: 01-14/2018

To: All Provincial Directors of Health Services,
All Regional Directors of Health Services,
All Heads of Institutions including Medical Officers of Health

Banning of betel quid chewing and selling of betel quid, tobacco and areca nut products in hospital premises and all other healthcare facilities

Betel chewing is considered as a socially and culturally accepted habit among Sri Lankans from the historical times and is continuing in the same manner. However, there is sufficient scientific evidence that chewing betel quid with or without tobacco, and chewing tobacco and areca nut mixed products, are to be major risk factors for oral cancer.

In Sri Lanka, betel chewing is more prevalent in the rural communities when compared to urban communities. This was more prevalent among older age groups. However, there is an emerging trend of increased usage of commercially as well as self-prepared smokeless tobacco and areca cut products among younger age groups. Unhealthy habits acquired younger age are more likely to last longer and more difficult to reverse. Non Communicable Risk Factor Survey (STEPS Survey) Sri Lanka 2015, reported that among the adults aged 18-69 years - more than one fourth of males (26.0%) and nearly 5% of females are currently using smokeless tobacco. The National Oral Health Survey 2003, showed a betel-chewing prevalence of 34% among 34 - 44 year olds and 47.7% among 65 -74 year olds.

Oral cancer is traditionally defined as squamous cell carcinoma of the lip, oral cavity and oropharynx. According to cancer incidence data in year 2010, lip, oral cavity and oropharyngeal cancers accounted for 14.3% of all reported cancers in Sri Lanka and it is the commonest cancer among males. Out of new cancer cases reported among males in 2010, 24% were cancers of the lip, oral cavity and pharynx. Apart from being a major risk factor for oral cancer, there are other health and cosmetic effects of betel chewing such as cracked lips and tongue, attrition of teeth, discoloration of mouth and teeth. Such effects may contribute towards personality problems of these betel chewers. The betel spit can make the environment unpleasant and could be considered as a major threat to the cleanliness of the institutional environment.

385, පූජ්‍ය බද්දේගම විමලවංශ හිමි මාවත, කොළඹ 10, 385, வணக்கத்துக்குரிய பத்தேகம விமலவங்ச தேரோ மாவத்தை, கொழும்பு 10.
385, Rev. Baddegama Wimalawansa Thero Mawatha, Colombo 10, Sri Lanka.

Therefore, a decision has been made at the National Advisory Committee on Prevention and Control of Cancers, which was held on 24 November 2017, to ban betel quid chewing within hospital premises and all other healthcare facilities with immediate effect. Furthermore, selling of betel quid and any form of tobacco and areca nut products within hospital premises and all other healthcare facilities will be banned.

All the heads of institutions should take responsibility to ensure that their institutions are free of betel quid chewing and selling. Appropriate disciplinary actions should be taken against if any employee continue to not to adhere to above instructions. If any person wants to quit the habit but in difficulty due to addiction, they should be referred for a dental surgeon.

All the Provincial and Regional authorities are advised to take necessary measures to facilitate and coordinate this initiative in order to reduce the burden of oral cancer and other related health problems in Sri Lanka.

If you need any further clarifications please contact the Director or Consultant in Community Dentistry of National Cancer Control Programme (Tel: 0112368627).

Janaka Sugathadasa
Secretary
Ministry of Health, Nutrition & Indigenous Medicine
"Suwasiripaya"
385, Rev. Baddegama Wimalawansa Thero Mawatha,
Colombo 10, Sri Lanka.

Janaka Sugathadasa
Secretary
Ministry of Health, Nutrition & Indigenous Medicine

cc: Hon. Minister of Health, Nutrition & Indigenous Medicine - for your information please
Deputy Minister of Health, Nutrition & Indigenous Medicine - for your information please
All Provincial Health Ministers
All Provincial Health Secretaries
Director General of Health Services
All Deputy Director Generals
Director - National Cancer Control Programme
Director - NCD
Director - Dental Services
Director - Mental Health
Director - Primary Care
Director – Family Health Bureau
Provincial Consultant Community Physicians/ Consultants in Community Dentistry
Chief Medical Officer (School Health)
All Regional Dental Surgeons
All Medical Officers (Non Communicable Diseases)
All Medical Officers (Maternal and Child Health)

My No : EST-3/DICIP/06/0275
Ministry of Public Administration &
Disaster Management
Independence Square
Colombo 07.

06.05.2019

Secretaries to Ministries
Chief Secretaries of Provinces
Heads of Departments
Heads of Public Corporations and Statutory Boards

Prohibition of using and selling of Betel, Tobacco and Areca nut related Products in the Premises of State Institutions

Further to the Public Administration Circular 08/99 dated 18.03.1999 on Prohibition of Smoking in State Institutions.

02. Since it has been prohibited by the Gazette Extraordinary of Democratic Socialist Republic of Sri Lanka No 1982/33, to produce, import, sale and presenting to sell smokeless tobacco products, it has been decided by the Cabinet of Ministers at the meeting held on 12.03.2019 to take actions as follows as a measure of reducing the risk of mouth cancer which is high among males in Sri Lanka.

03. Accordingly,

I. Using and selling of betel, tobacco and areca nut related products in the premises of State Institutions is prohibited.

II. Sale of betel, tobacco and areca nut related products in canteens of these institutions should be prohibited.

04. Heads of the State Institutions should ensure the adherence to these provisions.

Sgd/J.J. Rathnasiri
Secretary
Ministry of Public Administration &
Disaster Management

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Chapter 4

Common Gynecological Cancers

National Guideline on Early Detection and Referral Pathways of Common Cancers in Sri Lanka

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4. Common Gynecological Cancers

4.1 Cervical cancer

4.1.1 Introduction

Cervical cancer is a preventable disease, yet it is the third commonest malignancy among females in Sri Lanka. According to GLOBOCAN estimates, there were 1136 newly diagnosed cervical cancer patients in 2018[1] which accounts for almost 9% of famale cancers. Cancer incidence increases with the age and comes to a peak at the age group of 60 to 65 years[2] (Figure 4.1). In 2010, cervical cancer cost on global economy was estimated as USD 2.7 billon[3]. Cervical cancer will continue to devastate the lives of many women, families and their societies if action is not taken. World Health Organization (WHO) has set following targets called "90-70-90 targets" that need to be met by 2030 for countries to be on the path towards cervical cancer elimination[3] as a public health problem.

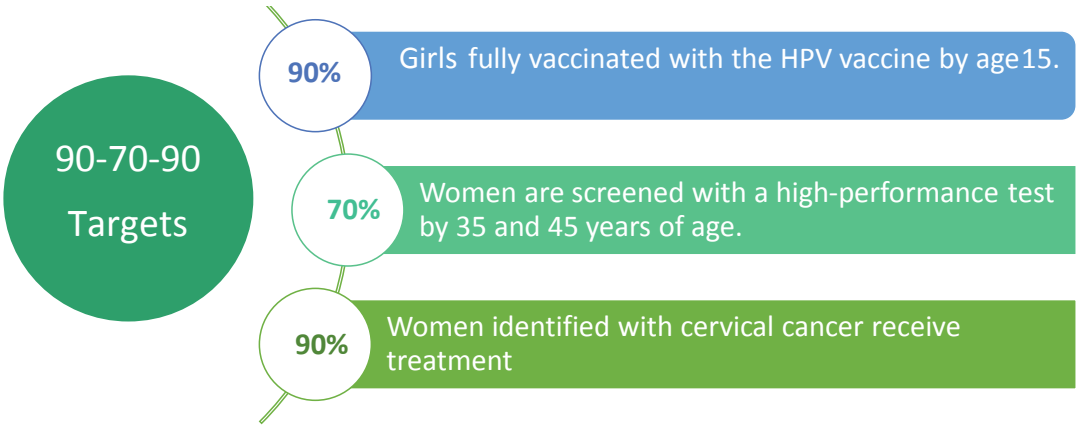


Figure 4.1.1: 90-70-90 targets of cervical cancer control

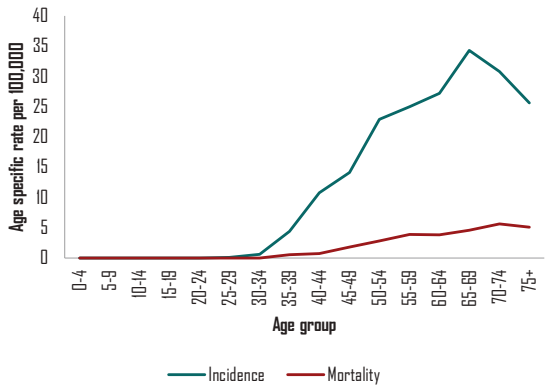


Figure 4.1.2: Age specific incidence & mortality rates - Cervix - 2012

4.1.2 Pathophysiology of cervical cancer

Ninety percent of cervical cancers are squamous cell carcinoma and the other 10% are adeno-carcinomas. Squamous cell carcinoma arises from the metaplastic squamous epithelium of the transformation zone and adeno-carcinoma arises from the columnar epithelium of the endo-cervix.

The squamo – columnar junction of the cervix

The cervix is lined by both stratified non- keratinizing squamous and columnar epithelium. These two types of epithelia meet at the Squmo-Columnar Junction (SCJ) (Figure 4.1.3)

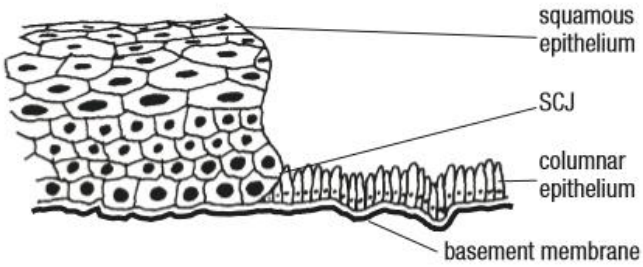


Figure 4.1.3: squamo-columnar junction (SCJ) of the cervix[5]

Adapted from : Sellors JW, Sankaranarayanan R, Colposcopy and treatment of cervical intraepithelial neoplasia: a beginnerss' manual, Lyon: International Agency for Research on Cancer; 2002.

Position of the SCJ in relation to the external os tends to vary over a woman's lifetime. It depends upon factors such as age, hormonal status, birth trauma, use of Oral Contraceptive Pills (OCP) and physiological conditions such as pregnancy.

Squamous metaplasia and the transformation zone

The columnar epithelium of the cervix is gradually replaced by stratified squamous epithelium as a result of exposure to the acidic environment of the vagina. This normal replacement process is termed squamous metaplasia and it gives rise to a new SCJ. The mature new squamous epithelium closely resembles the original squamous epithelium. The newly formed SCJ and the original SCJ are distinct on examination. The area between the original and the new SCJ is called the transformation zone.

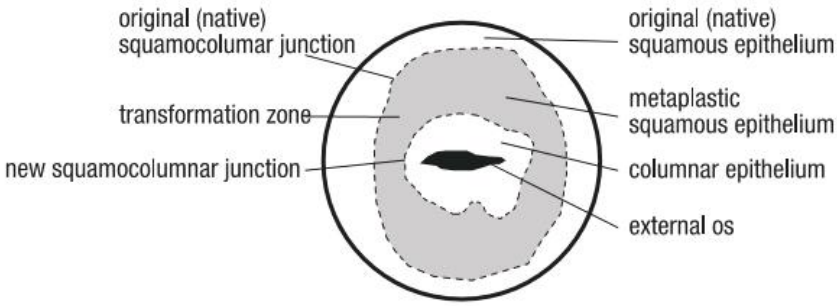


Figure 4.1.4 – Transformation zone of a parous women of reproductive age[5]

Source: Sellors JW, Sankaranarayanan R, Colposcopy and treatment of cervicalintraepithelial neoplasia: a beginnerss' manual, Lyon: International Agency for Research on Cancer; 2002.

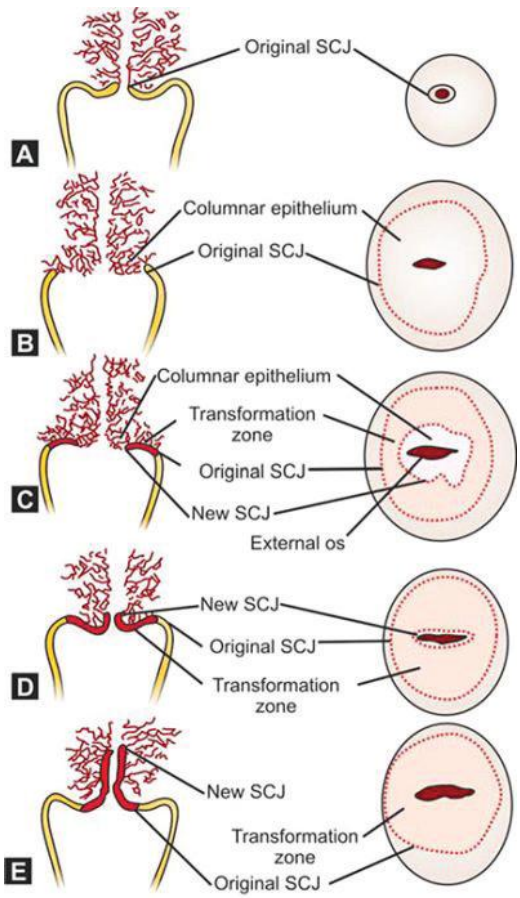


Figure 4.1.5 -Location of the squamocolumnar junction (SCJ) and transformation zone: (a) before menarche; (b) after puberty and at early reproductive age; (c) in a woman in her 30s; (d) in a peri-menopausal woman; and (e) in a post- menopausal woman[5]

Source: Sellor JW & Sankaranarayanan, Celospy and treatment of Ceovicol intra – epithlat neoplasia a biginers manual, Lyon, France, IARC Press, 2002

Development of cervical carcinoma

Primary cause of carcinoma of cervix is the persistent infection with one or more of the oncogenic types of Human Papillomavirus (HPV). It is reported that HPV serotypes 16 and 18 are found in 70% of all cervical cancers[6].

However, most HPV infections are transient, regardless of the serotype, with only a few of them persisting and even fewer progressing to precancerous lesions or invasive carcinoma.

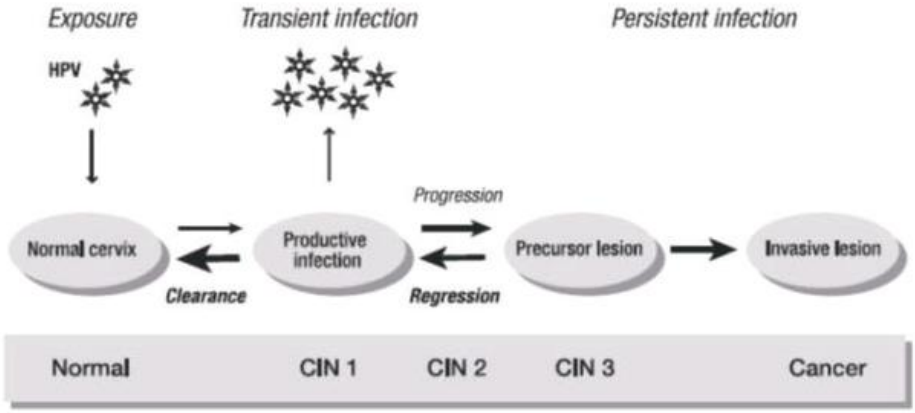


Figure 4.1.6 – Natural history of Cervical Cancer CIN: Cervical Intra epithelial lesion[7]
Adapted from: Cervix cancer Screening Lyon, IARC Press, 2005 (IARC Handbooks of Cancer Prevention Vol. 10)

It may take 10 – 20 years for the precursor lesions caused by HPV to develop into invasive carcinoma. Therefore, most cervical cancers can be prevented by early detection and treatment at the level of pre-cancerous lesions.

4.1.3 Risk factors for cervical carcinoma

- The primary cause of cervical cancer is persistent or chronic infection with one or more of the high risk (or oncogenic) types of Human papilloma virus (HPV).
- HPV is the most common infection acquired during sexual relations, usually early in sexual life.
- Most women and men who become infected with HPV will resolve spontaneously.
- A minority of HPV infections persist, in women this may lead to cervical pre- cancer, which may progress to cancer 10 – 20 years later if not treated[8] .

Other risk factors classified as:

1. Co – factors favouring acquisition of HPV infection

- Commencement of sexual activity at an early stage.
- Multiple sexual partners.
- Partner having multiple sexual partners.
- Poor socio – economic status – poor hygiene.
- Immunosuppression – acquired or primary.

  (Immunosuppressive drugs taken after organ transplant and HIV infection)
- High parity.
- Young age at first childbirth.

2. Co-factors favouring persistence of HPV infection

- HPV type – its oncogenicity.
- Immune status – women who are immunocompromised, such as those living with HIV, are more likely to have persistent HPV infection and more rapid progression to pre-cancer and cancer[9].
- Co – infection with other sexually transmitted agents such as those that cause herpes simplex, chlamydia and gonorrhoea.
- High parity (number of babies born) and young age at first birth.
- Tobacco smoking (both active and passive)
- Poor socio –economic status.
- Poor nutritional status.
- Prolong usage of oral contraceptive pills (slight increase in risk is observed with usage for >10 years)

4.1.4 Clinical features of cervical cancer

Women with pre–cancerous lesions are usually asymptomatic. Symptoms begin when a pre-cancer becomes a true invasive cancer.

Symptoms of invasive cervical cancer

Relatively early symptoms

- Vaginal discharge, sometimes foul smelling.
- Irregular bleeding (of any pattern) in women of reproductive age.
- Post –coital spotting or bleeding in women of any age, even young women.

- Post-menopausal spotting or bleeding.
- In case of abnormal peri menopausal bleeding cervical cancer should always be considered, particularly if the bleeding fails to respond to appropriate treatments.

Advanced (Late) symptoms

- Urinary frequency and urgency.
- Lower abdominal pain.
- Severe back pain.
- Weight loss.
- Decreased urine output (from obstruction of the uterus or renal failure)
- Leaking of urine or faeces through the vagina (due to fistula)
- Swelling of the lower limbs.
- Breathlessness (due to anaemia or rarely lung metastasis or effusion)

If symptoms are present, it is essential to do a speculum examination, pap smear is mandatory even if the cervix looks normal

4.1.5. Prevention and early detection of cervical carcinoma

Cervical cancer is a highly preventable cancer because

- The definitive cause of cervical cancer is known and infection with high risk HPV types, itself can be prevented.
- Very slow progression of the disease from the time of initial infection with oncogenic HPV virus to pre-cancer and to potentially fatal invasive cancer, which offers ample time to screen, detect and treat pre- cancer.
- However, majority (70%) of cervical cancers are diagnosed at a late stage (Stage III and IV) in Sri Lanka.

Primary Prevention

Reduce the risk of HPV infection and persistence

- HPV vaccination
- Health information and warning about tobacco use
- Sexuality education tailored to age and culture

HPV vaccination

Vaccination prevents infection with two high risk HPV strains 16 and 18 which are responsible for nearly 70% of cervical cancers. Vaccine only work to prevent HPV infection; they will not treat an infection that is already there. Thus, effective if used in HPV naïve females.

National Immunization programme in Sri Lanka started HPV vaccination in 2017 with the quadrivalent vaccine as a school-based vaccination programme[10].

The quadrivalent vaccine was developed to avert the risk attributed by genotype 16 and 18 (for cervical cancer prevention, also protective for other ano-genital and oropharyngeal cancers) which includes protection for non-oncogenic components of genotype 6 and 11; for the prevention of genital warts and recurrent respiratory papillomatosis (RRP) / Laryngeal papillomas.

- Two doses of vaccine given to 10 – 11 years old girls (in grade 6) with a minimum interval of 6 months through school-based vaccination programme.
- The HPV vaccine is recombinant quadrivalent vaccine (major capsid (L1) protein of HPV types 6,11, 16 and 18).
- HPV vaccine is currently available as a single dose vial (WHO – prequalified in May 2009), liquid suspension hence does not require reconstitution. 0.5 ml given through intramuscular route.
- For girls and boys aged 9 – 13 years, this vaccine can be administered according to a 2-dose schedule (0.5 ml at 0 and 6 months).
- For girls and boys 14 years of age and older, 3 doses of vaccine (0.5 ml at 0, 2 & 6 months) should be given.

Secondary Prevention

Secondary prevention aims at detection and treatment of precursor lesions and thus prevents these lesions evolving into cancerous lesions. Screening for cervical cancer is one of the most effective strategies in controlling cervical cancer. Screening is done for asymptomatic population. It takes about 10 – 20 years for pre – cancerous lesions to become an invasive cancer. If pre-cancerous lesions are identified and treated early, development of cervical cancer can be prevented. Detection of invasive cancer at an early stage leads to 5-year survival rate of approximately 92% and dramatically reduces cervical cancer mortality.

Available Screening Methods	Cervical cytology (Pap smear)
	HPV DNA testing
	Visual Inspection with acetic acid or Lugol's iodine

Cervical cytology:

It could be conventional pap smear or liquid based cytology. This test is done to identify pre-cancerous lesions which are usually asymptomatic (Treatment of identified pre – cancerous lesions before they progress to invasive cancer).

HPV testing

Molecular HPV testing methods are based on the detection of DNA from high risk HPV types in vagina and / or cervical sample. Testing women younger than 30 years old for these viruses is not advised because many young women are infected with them, but most HPV infections will be spontaneously eliminated before they reach the age of 30. Therefore, HPV testing should be reserved for women over 30 years of age.

Visual Inspection with acetic acid

Visual inspection with acetic acid (VIA) is a method for detecting early cell changes that are visible when using a speculum to inspect the cervix with the naked eye after applying dilute (3 – 5%) acetic acid.

VIA is appropriate to use in women whose squamocolumnar junction (SCJ) is visible, typically in those younger than 50 years. This is because the SCJ gradually recedes into the endocervical canal when menopause occurs, making it possible to oversight lesions when relying on visual inspection.

Tertiary prevention

- Proper referral to health care facilities that offer cancer diagnosis and treatments
- Accurate and timely cancer diagnosis by exploring the extent of invasion
- Treatment appropriate to each stage, based on diagnosis, following are the treatment modalities available,
    - Ablative surgery
    - Chemotherapy
    - Radiotherapy
    - Palliative care

Screening guidelines in Sri Lanka

The primary target age for cervical cancer screening is the cohort of women who are 35 years of age. From 1st of July 2016 the 45 years age cohort was also included as a target age group for cervical cancer screening.

While actively campaigning for the cohort of women aged 35 and 45 years for cervical cancer screening, those who are voluntarily request should also be screened depending on service availability.

Informed consent is a must before a woman is screened for cervical cancer

History

Taking a history to assess whether the woman has specific risk factors or suggestive symptoms

Ask the client about:

- Age, education, number of pregnancies, births and living children, last menstrual period, menstrual pattern, previous and present contraception
- Previous cervical cancer screening tests, their dates and results
- Medical history: including factors that may increase her risk of cervical cancer
- Social history: including factors that may increase her risk of cervical cancer
- Sexual history: including age of sexual initiation and of first pregnancy, number of partners, previous sexually transmitted infections (STIs) and any behaviours that may suggest an increased risk of cervical carcinoma
- Symptoms and signs of cervical malignancies and other illnesses

* Pelvic examination : see annex 1

Pap smear screening should be continued in the following women.

- **Women who have undergone hysterectomy for pre-cancerous conditions of the cervix (vault smear)**
- **Women who have undergone a subtotal hysterectomy**
- **Women who received HPV vaccination earlier**

Technique for obtaining Pap smear

- Explain the client that the Pap smear is not a diagnostic test, but a screening test to detect precancerous lesions. Development of cervical cancer can be prevented by treating pre-cancerous lesions.
- The technique of obtaining pap smear is mentioned in Annex II

However, if there is a lesion, ideal test is biopsy even though the smear is negative

Places where pap tests are performed:

- Well Women clinics conducted by MOH and staff
- Well Woman clinics/Gynaecological clinics in government hospitals
- National Cancer Control Programme, Cancer early detection center, Narahenpita
- General Practice
- Private hospitals

Well Women Clinic (WWC)

The well women Clinic programme was established in 1996, at the time when the Reproductive Health concept was introduced into primary health care services with the objective of improving the health of women in the country. By the end of 2016, approximately 850 WWCs were functioning island wide. According to the revised guideline for implementation of Well Women Clinic Services following decisions were taken.

- All Medical Officer of Health (MOOH), Heads of health institutions, and MOOH of Municipal Councils should have functioning WWCs in their respective institutions/ Hospitals.
- Any woman between 35 to 60 years of age (including those in the peri-menopausal age or in menopause) should be encouraged to attend WWC services.
- There should be at least one WWC per 15,000 population and clinics should be held at least once a month.

Screening for women living with HIV

- Screening for cervical pre-cancer and cancer should be done in women and girls who has initiated sexual activity as soon as the woman or girl has tested positive for HIV, regardless of age.
- Women living with HIV whose screening results are negative (i.e. no evidence of pre-cancer) should be re screened within 3 years.

Women living with HIV who have been treated for cervical pre-cancer should receive post treatment follow up after 12 months.

4.1.6. Classification of cervical lesions

Sri Lankan guideline of classification for cervical cytology was adapted from the Bethasda system (Family Health Bureau, 2010)[11].

Categories included in Modified Bethesda Classification adapted for Sri Lanka:

1. Negative for Intraepithelial Lesion or Malignancy (NILM)
2. Low Grade Squamous Intra Epithelial Lesions (LSIL)
3. High Grade Squamous Intra Epithelial Lesions (HSIL)
4. Atypical Squamous Cells of Undetermined Significance (ASCUS)
    - Atypical Squamous Cells of Undetermined Significance – low grade (ASCUS low grade)
    - Atypical Squamous Cells of Undetermined Significance – high grade (ASCUS high grade)
5. Glandular cell atypia
6. Benign endometrial cells in a woman >40 years
7. Squamous or glandular malignancy

Table: 4.1: Management of Cervical lesions based on Cytological and Histological Classifications

Cytological classification (Modified Bethesda System adapted to Sri Lanka)	Histological classification (used for diagnosis)	Recommendation
Normal	Normal	Routine re-screening (5 yearly) If inflammatory – treat and follow up
ASCUS – Low grade	Atypia	Medical officer at primary health care level to follow up and repeat smear in 6 months
ASCUS – High grade		Refer for Colposcopy If Colposcopy biopsy is positive, treat as for HSIL.
LSIL	CIN 1 (including flat condylomata)	If HPV DNA is not available Repeat smear in 6 months If repeat smear LSIL or above –Refer to a gynaecologist for Colposcopy. If HPV DNA is available, triage – If HPV DNA positive + LSIL – refer to Colposcopy
HSIL	CIN 2 / CIN 3	Refer for Colposcopy
Glandular cell atypia		Refer for Colposcopy
Invasive carcinoma	Invasive carcinoma (Squamous or Glandular malignancy)	Urgent referral (For gynaeoncologist / VOG opinion)

Recommendation for management and follow up

(Source: Family Health Bureau 2010)

- For women with normal pap smear test – repeat pap test after five years.
- For women with abnormal pap smear test – adhere to the following guideline.

Guideline on clinical management of those screened based on cytology report

Satisfactory: In the presence of satisfactory smear when endo–cervical and metaplastic cells are lacking, the woman should be further evaluated to see whether she is pregnant, postmenopausal or on oral contraceptive pills.

Unsatisfactory: Repeat the smear as soon as possible.

Cytological types

1. Negative for intraepithelial lesion or malignancy (NILM)

- Repeat the smear in 5 years.
- Inflammation – Treat only if a specific organism is identified or if the client is symptomatic. Clients with non – specific inflammatory smears without symptoms should not be treated.
- All other reactive changes – As medical officers at primary health care level, offer treatment if possible. Refer if further management is necessary.

2. Low grade squamous intra epithelial lesions (LSIL)

- If HPV DNA available : HPV DNA positive + LSIL refer for colposopy.
- If HPV DNA not available : Repeat smear in 6 months. If smear positive refer to a gynaecologist for colposcopy.

3. High grade squamous intra epithelial lesions (HSIL)

- Refer to a gynaecologist for histological diagnosis. Colposcopy and large loop excision of the transformation zone (LLETZ) or cold knife conisation are recommended. If colposcopy biopsy is positive and if the lesion is excised al ready, medical officer at primary health care level should obtain a follow up smear after 6 months. If the follow up smear is positive, refer the patient back to the gynaecologist. If the smear is negative, it should be repeated at 6 months intervals.
- If biopsy is negative, medical officer at primary health care level should obtain a follow up smear and act accordingly.

4. Atypical squamous cells of undetermined significance (ASCUS)

- ASCUS high grade – refer for colposcopy.

If colposcopy biopsy is positive treat as for HSIL. In case of a negative biopsy, follow up with 3 smears, 3 months apart.

- ASCUS low grade- Medical officer at primary health care level to follow up and repeat smear in 6 months.

5. Glandular cell atypia

- Refer to a gynaecologist to investigate for cervical or endometrial lesions based on clinical details.

6. Benign endometrial cells in a woman aged >40 years

- Refer to a gynaecologist to investigate based on clinical details.

7. Squamous or glandular malignancy

- Urgent gynaecological referral for appropriate management is needed.

Follow up of high-risk women need more frequent (once a year) screening even if the pap smear results are negative.

Women under the following categories should be considered as high risk

- Those on immunosuppressive drug treatments (Including patients who had organ transplant).
- Those infected with HIV.
- Those having Systemic Lupus Erythematosus (SLE)[12].
- Those on chronic corticosteroid treatments.
- Those with other HPV related malignancies such as cancers of the anus, vulva and cervix.

4.1.7. Counselling women after positive screening test results

Counselling women after positive test results that are NOT suspicious for cancer

When explaining to a woman that her screening test is positive, but NOT suspicious of cancer, the following information should be provided in clear and simple language.

1. Tell that her test is positive and explain what this means, while reassuring her it does not mean that she has cervical cancer.

In the case of positive cytology or VIA test

- Explain to her that the test looks for early changes, called pre-cancer, which could become cancer if left untreated.

- Explain that there is simple and safe treatments available to remove the area with early changes, which is very effective in curing these pre – cancers.

In the case of a positive HPV test

- Explain to her that a positive HPV test means that there is an infection with the virus present in her cervix. Reassure her that very few HPV positive women will develop cervical cancer.
- If she has a positive HPV test and a negative Pap/VIA test, explain to her that this means she has a persistent infection with HPV, but it has not yet caused cell changes.

2. Explain her what further testing and treatments (if any) she should undergo, how long it will take and what she can expect.

3. Emphasize the fact that if she does not receive treatment or close follow up, in the case of a positive HPV test combined with a positive VIA or cytology screening test, she could develop cervical cancer.

4. A positive HPV test results does not mean that the woman will develop cervical cancer or have any problems in the future or that she has pre – cancer. It might still be upsetting for her to hear that she is HPV positive, therefore, answer any questions that the woman has about HPV infection and provide her with the following information.

- HPV is transmitted during sexual activity, but it is impossible to know when or from whom she got it (unless she has had sexual contact with only one partner in her life).
- HPV is not a sign of promiscuity or infidelity.
- HPV is very difficult to prevent, though use of condoms can protect against HIV and unwanted pregnancy, they do not provide complete protection from HPV.

Chapter 04

ANNEXES

I. Pelvic examination (WHO guideline)
II. Pap smear-cervical cytology
III. Referral pathway for colposcopy
IV. Algorithm for HPV DNA Test
V. Referral form for pap smear cytology

Pelvic examination (WHO guideline)

The following equipment and supplies should be available:

- Papers and pencil.
- Soap and water for washing hands.
- Source of light to examine the cervix.
- Examination table or couch covered by clean paper or cloth.
- Disposable or high-level disinfected examination gloves.
- Cusco's specula of different sizes (high-level disinfected)
- High stool.
- Dustbin for clinical waste .

Before the examination

- Have all necessary equipment and supplies ready.
- Ensure the speculum is at a comfortable temperature.
- If planning to do a Pap Smear test, inform the woman what it is, what it is for and when you expect to have the results.
- Allow the woman to ask questions and answer them truthfully.
- Explain what the pelvic examination consists of and show the woman a speculum.
- Ask the woman to empty her bladder (urinate) and remove her underwear (waist down). Be particularly sensitive to her sense of modesty about uncovering normally clothed areas or if the examination is perceived to be invasive.
- Position the woman on the examination table.

PERFORMING A PELVIC EXAMINATION

There are three components:

- An external genital examination;
- A speculum examination;
- A bimanual examination;

Examination using Cusco's speculum

- Before putting the speculum examine external genitalia - using a gloved hand to gently touch the woman, look for redness, lumps, swelling, unusual

discharges, sores, tears and scars around the genitals and in between the skin folds of the vulva. These can be signs of a sexually transmitted infection (STI).

- Hold the Cusco's speculum blades together and insert speculum directly as the vagina is a structure which is flat antero – posteriorly.
- Gently open the blades and look for the cervix.
- Move the speculum slowly and gently until you can see the entire cervix. Tighten the screw so it will stay in place.
- Check the cervix, which should look pink, round and smooth. There may be small yellowish cysts, areas of redness around cervical os or a clear mucoid discharge; these are normal findings.
- Look for any abnormalities, such as;
    - Vaginal discharges and redness of the vaginal walls, which are common signs of vaginitis. If the discharge is white and curd like, there is a possibility of yeast infection.
    - Ulcers, sores or blisters-genital ulcers may be caused by syphilis, chancroid, herpes virus or in some cases due to a cancer. Sores and blisters are usually caused by herpes virus.
    - Easy bleeding when the cervix is touched with a swab or a muco – purulent discharge are signs of a cervical infection.
    - An abnormal growth or tumour, might be due to cervical carcinoma.

- In order to remove the speculum loosen the screw of the speculum, gently pull the speculum towards you until the blades are clear of the cervix, close the blades and remove the speculum.

Bimanual vaginal examination

Bimanual vaginal examination including test for cervical motion tenderness should be performed only after the cervical smear has been taken.

Test for cervical motion tenderness:

- Put the pointing finger and the middle finger of your gloved hand in the woman's vagina. Turn the palm of your hand up. Feel the cervix to see whether it is firm and round.
- Then put one finger on either side of the cervix and move the cervix gently while watching the woman's facial expression.

- If this cause pain (you may see the woman grimace) will indicates cervical motion tenderness, and she may have an infection of the uterus, tubes or ovaries (pelvic inflammatory disease – PID). If her cervix feels soft, she may be pregnant.

Bimanual vaginal examination

- Feel the uterus by gently pushing on her lower abdomen with your other hand. This moves the uterus, tubes and ovaries closer to the fingers inside the vagina. The uterus may be tipped forwards or backwards.
- When you find the uterus, feel for its size and shape. It should feel firm, smooth and smaller than a lemon.
    - If the uterus feels soft and large, the woman is probably pregnant
    - If it feels lumpy and hard, she may be having a fibroid or another growth
    - If it hurts her when you touch it, she may have an infection
- If it does not move freely, she may have scars from an old infection / endometriosis.
- Feel the tubes and ovaries.
    - If these are normal, they will be hard to feel.
    - If you feel any lumps that are bigger than an almond or that cause severe pain, she may have an infection or other condition needing urgent treatment.
    - If she has a painful lump and her period is late, she may have an ectopic pregnancy; in this case, she needs medical help right away.
- Move your finger to feel the inside of the vagina. Make sure that there are no unusual lumps, tears or sores.
- Ask the woman to cough or push down as if she were passing stool. Look to see if something bulges out of the vagina (uterine prolapse).

After the examination

- Place used equipment in disinfectant solution and discard the gloves in to the clinical waste bin.
- Wash your hands with soap and water.
- Record all findings on the woman's chart.
- Tell the woman whether her examination was normal or abnormal. Explain what kind of abnormality you noted and what does it mean.

- If you noted any signs that might indicate a sexually transmitted infection (STI), refer her to STI clinic of the closest hospital. In case of non- compliance, treat the woman and her partner immediately (Follow national guidelines). Provide condoms and teach how to use them.
- If you find something that needs urgent treatment or that cannot be handled at your centre, refer the woman to a higher level of care.
- Give her a date to return for follow-up if necessary.

Pap smear-Cervical cytology

(Source: Family Health Bureau, 2010)[13]

Cytological testing involves collection of exfoliated cells from the cervix and microscopic examination of those cells after staining.

Labelling & Obtaining a Cervical smear

- Cervical screening should be done after clearly explaining the importance of the procedure and the steps to the client.
- Clients should be instructed not to douche on the day of the examination. She should not be using any intra vaginal medication at the time of testing. A cervical smear should not be performed if she has bleeding or obvious infection is present, cervical smear should be performed only after appropriate treatment.
- Before starting the procedure, all necessary equipment and supplies should be available at hand. The glass slides should be correctly labelled. The Coplin jar filled with 95% ethanol / isopropyl alcohol should be kept ready.

Labelling of Slides

This is a very important aspect as incorrect labelling of slides will result in erroneous reports or even a mix up of results among several patients.

Please ensure that the following precautions are taken:

1. An identification mark should be made on each slide using a diamond pencil before the smear is made.
2. Before the smear is made, ensure that the slide is labelled according to the instructions given. Same identification number must be written on the accompanying referral form (Annex V)

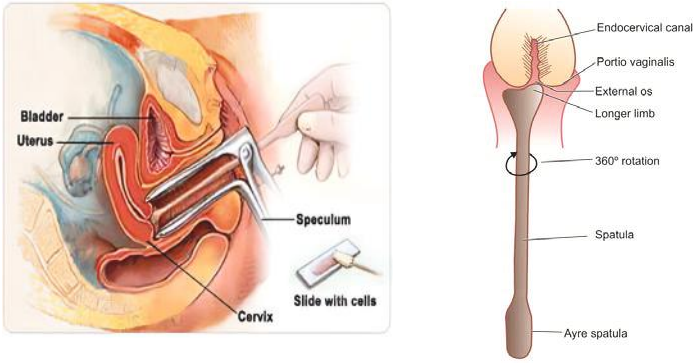


Figure 4.1.7- Visualization of cervix and Pap Smear taking

- The dorsal position is suitable for smear taking and a source of good illumination must be available at the foot end of the bed.
- A speculum of suitable size should be chosen for examination. It may be slightly moistened with water before insertion. Use of other lubricants or antiseptics should be avoided.
- Once the speculum is inserted the ecto-cervix should be clearly visualized.
- The thinner extended prong (narrow end) of the spatula should be inserted into the cervical os and rotated 360 degrees clockwise while keeping it opposed to the cervix (Figure 4.1.6). Since there is a tendency to slip over certain areas, a reverse (anticlockwise) rotation towards the opposite direction should also be performed immediately.
- In the case of a large patulous or multi-parous cervix, the broader end of the spatula is most suitable to take the smear. This requires thorough scraping of the ecto-cervix over the whole area, using the broad, flat end of the spatula in backwards and forwards movement.
- Postmenopausal or postconisation os, with no visible squamo-columnar junction demands careful sampling of the canal. In this situation, an additional sample may be taken with an endo-cervical brush.

Bimanual vaginal examination should be performed only after the cervical smear has been taken.

Spreading the smear

The material collected on the spatula should be quickly and evenly spread on to the relevant slide.

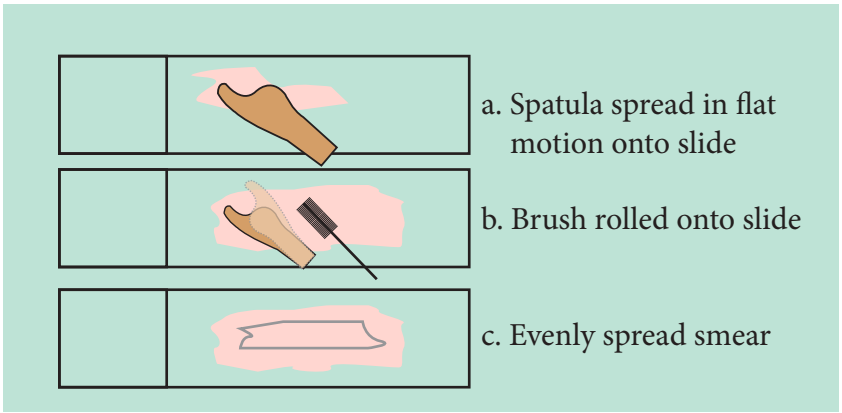
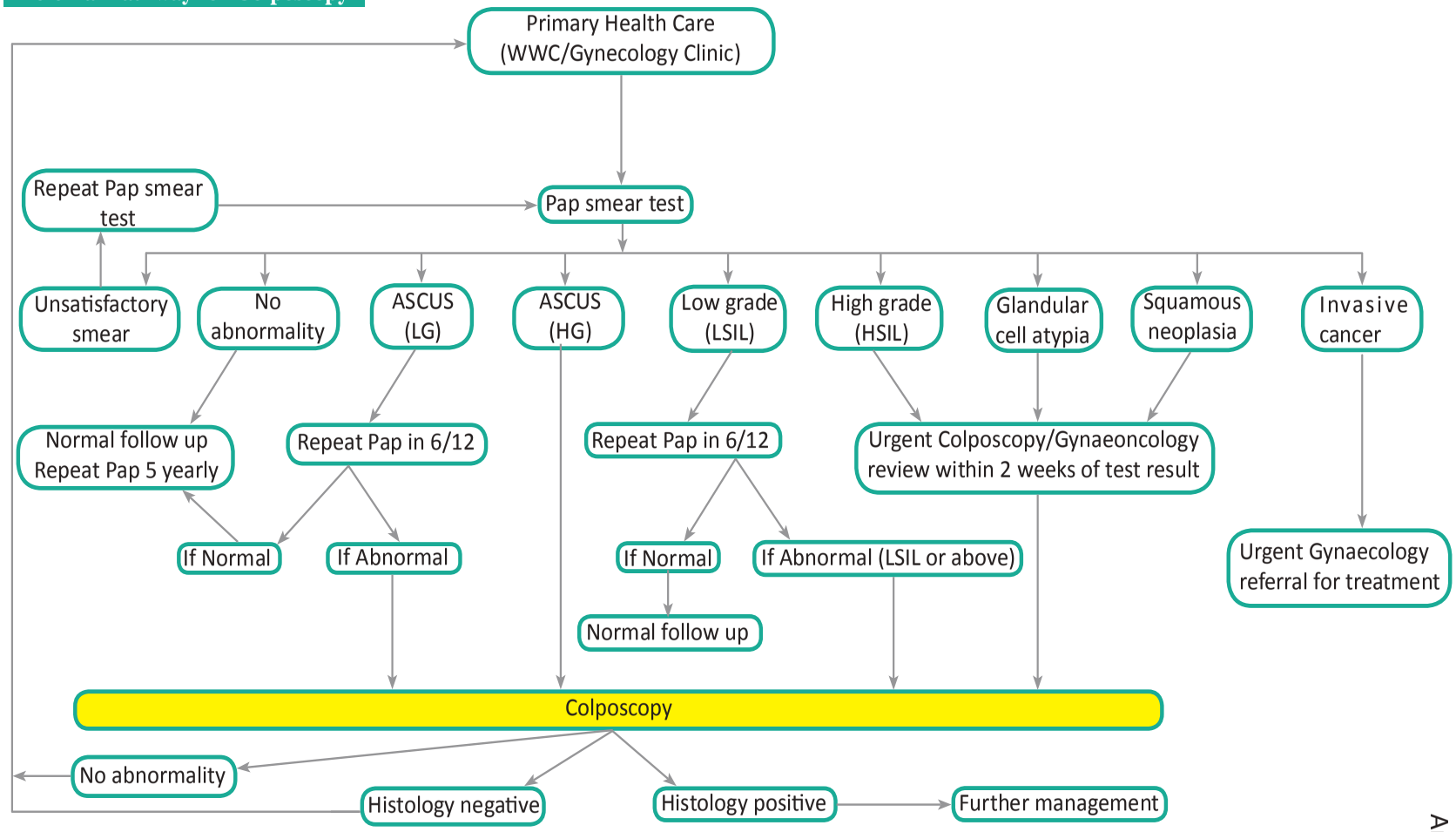


Figure 4.1.8- Slide preparation in Pap Smear test

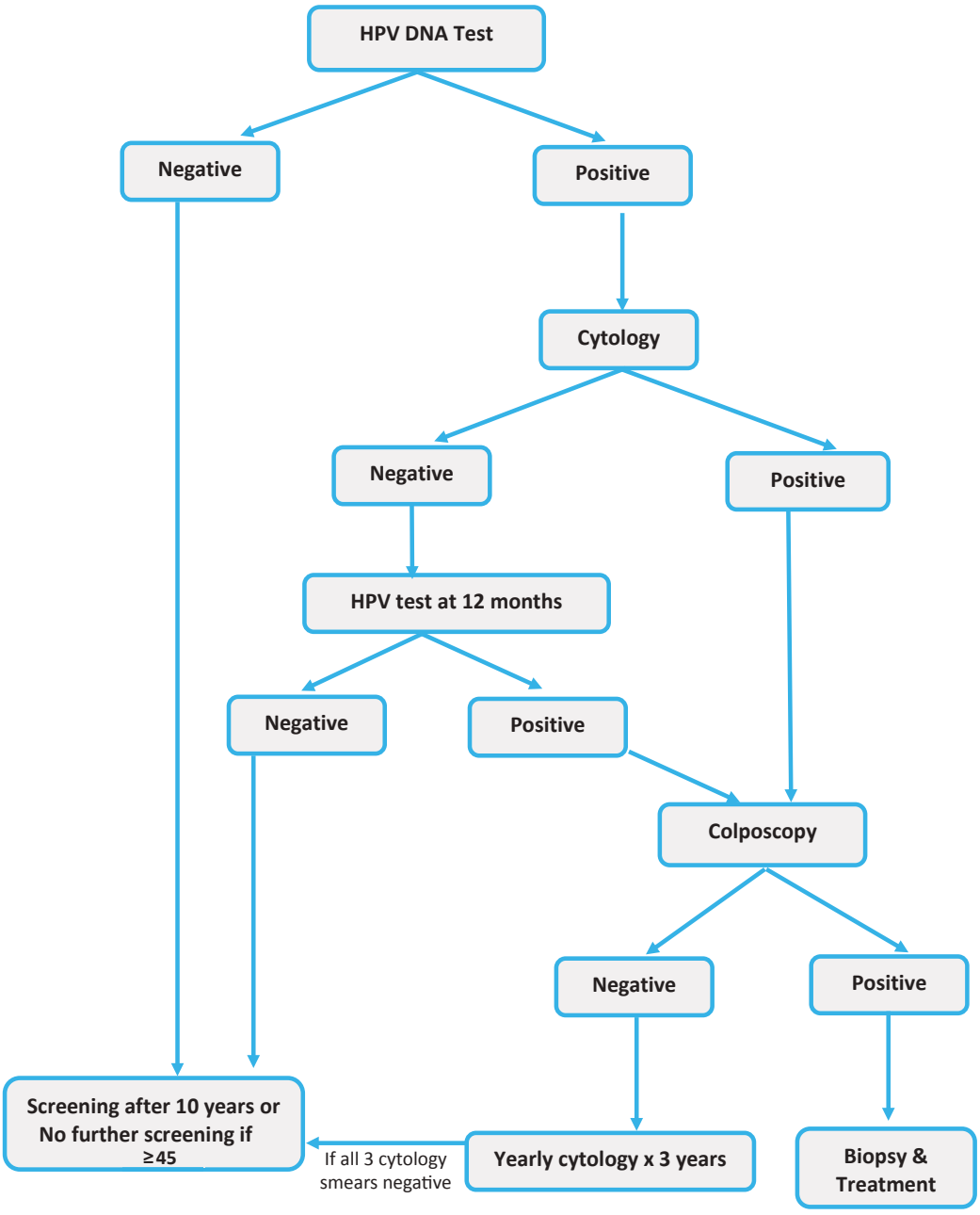
Fixation and transportation of cervical smears

- The smear should be wet fixed without air –drying. The slide should be fixed immediately to prevent drying by immersing it in a jar of 95% alcohol. Handle the slide only by the labelled end of the slide.
- The fixation can be carried out in a Coplin's jar filled with alcohol. Do not put more than 5 smears into the same coplin jar.
- The slides should be wet fixed in alcohol for 30 minutes, taken out, air dried for 30 minutes and then transporting to the laboratory within next 7 days.
- If alcohol sprays are used, ensure that the whole smear is covered with the spray. Ideally the alcohol in the coplin jar used for fixation should be discarded after each fixation, but due to practical problems, alcohol in the jar can be used to fix about 20 slides and changed.
- Transporting the slides "dry" can be carried out in readymade wooden boxes. Adequate measures should be taken to ensure that the slides do not break during transport.
- It is very important that each slide is accompanied by a duly completed referral form (Annex II). A common form indicating the number of slides sent, and the place from where it is being sent should accompany a set of slides, which is sent to the laboratory for screening.
- A blue colour referral form should be filled & sent with all repeat smears of positive cases. This will enable the cyto screener to prioritize the screening and screen these slides first.

Referral Pathway for Colposcopy



Screening for cervical cancer – Algorithm for HPV DNA Test



Referral form

MOH area ☐

1. Full name :

2. Age :

3. Address /Contact No :

4. NID No :

5. Identification No (Same as the slide) :

6. Name of the clinic :

7. LRMP:

D D M M Y Y

8. specimen type

Present first smear ☐

Follow up ☐ Date ☐

Previous Date ☐ Slide No ☐

Normal ☐ Abnormal ☐

Diagnosis of previous smear ☐

Treatment ☐

9. Symptoms

- Discharge ☐
- Post coital bleeding ☐
- Inter- menstrual bleeding ☐
- Post- menstrual bleeding ☐
- Other (Specify) ☐

10. Appearance of Cervix

- Normal ☐
- Abnormal ☐
  - Malignant ☐
  - Cervicitis ☐
  - Polyps ☐

11. Condition

- Pregnant
- Post – natal (12/52)
- IUCD inserted
- Oral contraceptive
- Menopause
- Other hormones (specify)

Comments …….....

.....

Date Signature …….....

Designation…….....

4.2 Ovarian cancer

The ovarian cancer incidence is gradually increasing over the years in Sri Lanka and according to the GLOBOCAN estimates for 2018 there were 856 incident cases of ovarian cancers[1]. The incidence is increasing with the age and peak between 60 to 65 years (Figure 4.2.1).

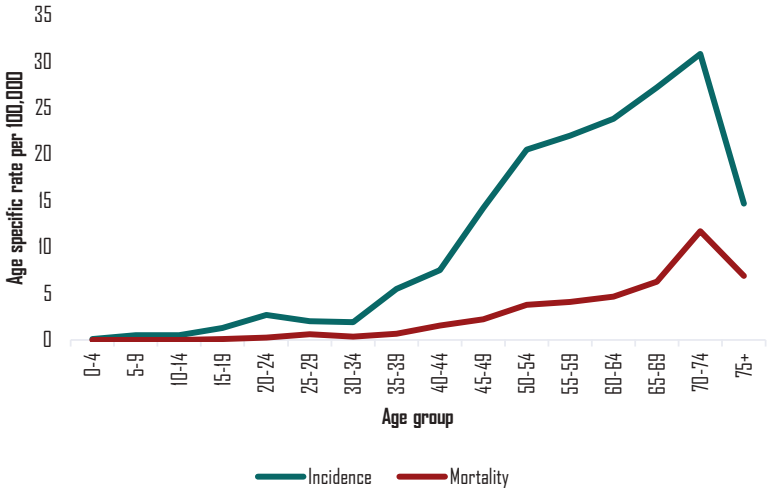


Figure 4.2.1 Age specific incidence and mortality rate of ovarian cancer

Types of Ovarian tumours

The ovaries each about a size of an almond. Most ovarian tumours are benign. Ovarian cancer often goes undetected until it has spread within the pelvis and abdomen.

There are three main types of ovarian tumours

- Epithelial tumours
- Germ cell tumours – occurs in relatively young age, Symptoms such as abdominal mass should be referred to a gynaecologist without delay.
- Sex cord stromal tumours

About 90% of ovarian cancers are epithelial in origin.

Rick factors for ovarian cancer[14]

- Increasing age (women who are menopausal)
- Family history of ovarian carcinoma
- Personal history of breast cancer
- Nulliparity
- Sub – fertility
- Use of hormone replacement therapy (HRT) for menopause related symptoms especially prolonged use (over 5 years) of oestrogen unopposed by progesterone
- Family history of breast cancer – mutations in the genes BRCA 1 increase the risk of breast and ovarian cancer while mutations in BRCA 2 genes increase the risk of breast, ovarian, endometrial and colonic cancers[15].

Factors reducing the risk

- Increasing parity
- Breast feeding
- OCP use (reduce the risk by about 60%)
- Hysterectomy or tubal ligation

Clinical features

- It has very nonspecific symptoms.
- Majority may have gastric symptoms (heart burn, dyspeptic symptoms).
- If a post-menopausal woman complains of sudden onset of these symptoms more attention should be given to exclude an ovarian malignancy.
- Other symptoms include abdominal distension or pain, loss of appetite, urinary symptoms (urgency, frequency).

Most of these symptoms are common to other less serious conditions as well. Majority of ovarian cancers are diagnosed at an advanced stage as symptoms are being non-specific. Prompt attention to symptoms may improve the chance of early diagnosis and successful treatment.

Early detection

- Routine trans-vaginal ultrasound scan (TVS) and serum Cancer Antigen 125 (CA 125) are not useful for early detection of ovarian cancers.

- Any woman having above mentioned symptoms persistently should be referred to a gynaecologist to exclude an ovarian malignancy.

Once a year screening is indicated with pelvic examination, TVS and CA 125 in the following categories of women who are at high risk of developing ovarian cancer.

- Three or more relatives with Lynch syndrome related malignancy. (Colorectal, Endometrial, ovarian and breast cancers).
- First degree relative suffering from ovarian cancer.

CA 125 could be elevated in following benign conditions

- Fibroids
- Endometriosis
- Pelvic Inflammatory Disease (PID)

4.3 Endometrial Cancer

Similar to other cancers, endometrial cancer incidence is also increasing in Sri Lanka. It accounts for 4% of all cancers among women. The incidence is increasing with the age and peak between 60 to 70 years (Figure 4.3.1).

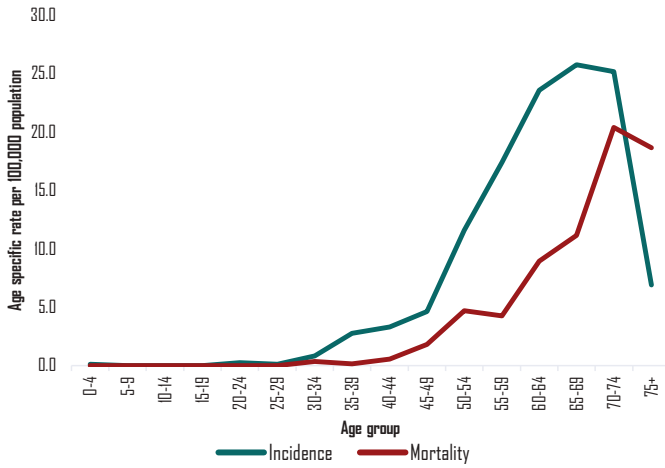


Figure 4.3.1 Age specific incidence and mortality rate endometrial cancer

Types of Endometrial Carcinomas

The most common endometrial carcinoma is endometrial adenocarcinoma.

Histological classification is as follows

- Endometrioid (75% - 80%)
    - Ciliated adenocarcinoma
    - Secretory adenocarcinoma
    - Papillary or villoglandular
    - Adenocarcinoma with squamous differentiation
        - Adenocarcinoma
        - Adenosquamous
- Uterine papillary serous (<10%)
- Mucinous (1%)
- Clear cell (4%)
- Squamous cell (<1%)
- Mixed (10%)
- Undifferentiated

There are several risk factors for endometrial cancer

- Increasing age
- Early menarche and late menopause
- Use of HRT containing exogenous estrogen unopposed by progesterone
- Nulliparity
- Subfertility
- Polycystic ovarian disease/s
- Endometrial hyperplasia with cellular atypia

Risk factors

- A certain type of ovarian tumours, the granulosa –theca cell tumour secreting estrogen
- Family history of uterine, colon and breast cancer
- Personal history of breast cancer
- Obesity
- Pre – existing diabetes
- Tamoxifen used in treatment of breast cancer

Protective factors (Factors reducing the risk)

- Increasing parity

Clinical features

- Abnormal vaginal bleeding
- Peri or post-menopausal vaginal bleeding

All women with abnormal vaginal bleeding should be referred to a gynecologist.

Even a single episode of post-menopausal vaginal bleeding after one year of menopause should be investigated[17].

Prevention and early detection

There is no screening test recommended for endometrial carcinoma.

The best way to identify endometrial cancer is to recognize symptoms early. Majority of the uterine cancers present due to early onset of symptoms like heavy irregular vaginal bleeding before menopause

If a woman complains of symptoms, she should be referred to a gynecologist. About 70% of endometrial cancers are diagnosed at an early stage.

Increased endometrial thickness in transvaginal ultrasound scan warrants further investigation in women who are having abnormal vaginal bleeding. Transvaginal ultrasound scan, hysteroscopy and endometrial biopsy can be used to detect endometrial cancer. Occasionally pap smear done for screening of cervical cancer may reveal endometrial cells. They should be referred for further assessment.

Uterus

- Tumours of trophoblast including chorio-carcinoma
- Leiomyosarcoma
- Endometrial stromal tumours in cluding stromal sarcoma
- Carcinosarcoma

Vulvar cancers

- Squamous cell carcinoma
- Melanoma
- Verrucous carcinoma
- Basal cell carcinoma
- Other - adenocarcinoma, sarcoma

Other malignancies of Female Genital Tract (Less common)

No recommened methods of early detection

Vaginal cancers

- Adenocarcinoma
- Squamous cell carcinoma
- Sarcoma – eg: sarcomabotryoides
- Melanoma

Fallopian tubes :

- Adenocarcinoma of the fallopian tubes

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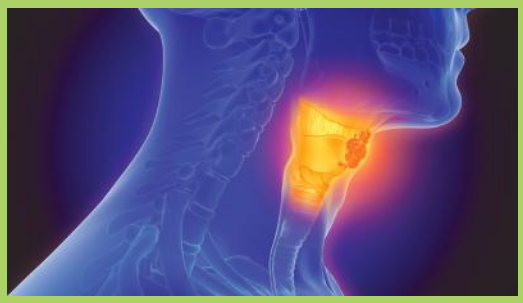

Chapter 5

Oesophageal cancer

National Guideline on Early Detection and Referral Pathways of Common Cancers in Sri Lanka

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5. Oesophageal cancer

5.1 Introduction

Oesophageal cancer is the eighth commonest cancer worldwide. GLOBOCAN estimated 532,034 new cases (3.2% of the total 2018), while developing countries accounting for 81% of these cases[1]. Oesophageal carcinoma is rare in young people and incidence is icreasing with age and peak is observed around 70 years. It is associated with a poor prognosis. Despite advances in diagnosis and treatment, the overall five-year survival rate for persons with oesophageal cancer is 15% to 20% worldwide. The two main subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. These subtypes account for more than 95% of malignant esophageal tumors. Squamous cell carcinoma is more common in non-industrialized countries. Adenocarcinoma is the predominant oesophageal cancer among developed nations.

Oesophageal cancer is estimated to be the fifth commonest cancer in Sri Lanka in 2018[2]. It is the third commonest among males and the sixth commonest among females, accounting for 1441 new oesophageal cancer patients. Early detection of oesophageal cancer has a better prognosis[3]. Population screening for oesophageal cancer is not possible in our set-up due to the high cost involved. Therefore, we need to identify the high- riskgroups in the future. Endoscopy is the gold standard for screening. Symptomatic patients should be promptly referred for further management to the surgical/Gastro-Intestinal (GI) clinic at the secondary/tertiary care hospital.

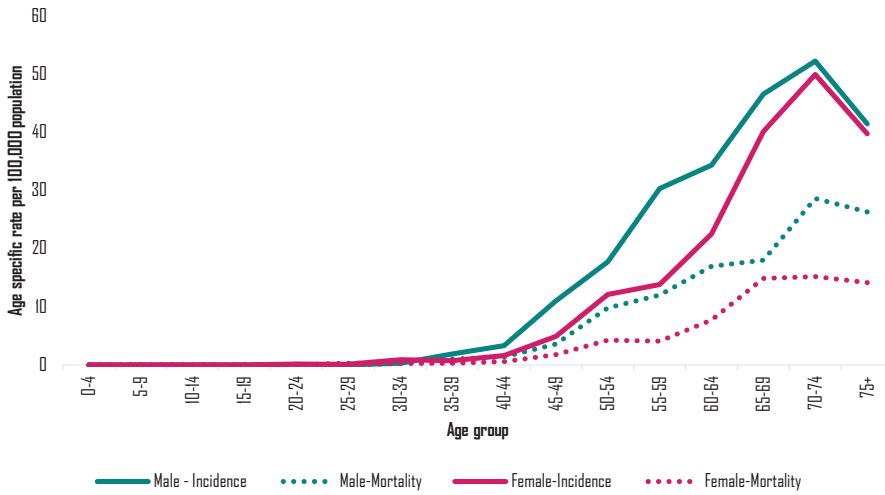

Figure 5.1: Age specific incidence and mortality rates - Oesophagus- 2012

5.2 Risk Factors

Major risk factors for oesophageal squamous cell carcinoma are:

- Smoking
- Alcohol abuse
- Betel chewing
- Long standing oesophageal strictures
- Long standing achalasia

Major risk factors for adenocarcinoma are:

- Overweight and Obesity
- GORD/Barrett Oesophagus

5.3 Clinical features

Oesophageal cancer is often asymptomatic in the early stages. Dysphagia is the presenting symptom in most of the patients. Presence of alarming symptoms favoring gastrointestinal malignancy should be referred for further investigations even in the absence of dysphagia.

Alarming symptoms and signs (RED FLAG SIGNS)

- Dysphagia
- Vomiting after meals
- Unintentional loss of weight (loss of more than 2 kg within one month)
- Recent loss of appetite
- Unexplained anaemia
- Lump in the abdomen (Epigastric mass)
- Recent onset *dyspeptic symptoms in patients over the age of 50 years

***Dyspepsia**

Dyspepsia is usually a combination of several symptoms such as epigastric pain related to meals, post prandial discomfort and early satiety.

Any individual over 50 years with *dyspeptic symptoms presenting with any of the alarming symptoms and signs, prompt referral is mandatory for further investigations even in the absence of dysphagia.

They should be referred to a surgical/GI clinic at the Secondary/ Tertiary Care Hospital for Upper Gastro Intestinal Endoscopy (UGIE) and further management.

Increased risk of oesophageal cancer is associated with:

- Age > 40 years
- Family history of oesophageal carcinoma
- Smoking
- Alcohol consumption
- Betel chewing
- Patients having long standing symptoms suggestive of Gastro-Oesophageal Reflux Disease (GORD) and/or Barrett's oesophagus
- Past history of oesophageal strictures/ Achalasia

DIAGNOSIS

Endoscopy with biopsy is the primary method for the diagnosis of oesophageal carcinoma. Early cancers of the oesophagus generally are asymptomatic, although ulcerated lesions may sometimes present with evidence of gastrointestinal bleeding, such as malaena or be found during workup for occult gastrointestinal bleeding or iron deficiency anemia.

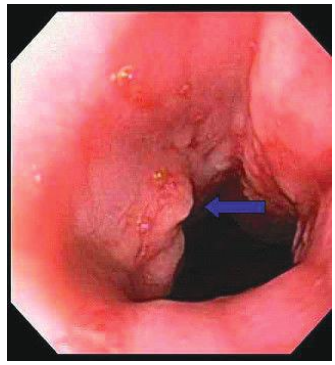

Figure 5.2: Oesophageal cancer

Differential diagnosis

- Oesophageal stricture from any cause
- Achalasia (& other motility disorders)
- Gastric (Cardia) cancer
- Rare causes (External compression, benign tumors)

5.4 Early detection

Squamous cell carcinoma of the oesophagus and adenocarcinoma of the oesophagus have different risk factors and thus require different approaches for prevention. Attempts to reduce the risk factors such as obesity and smoking have not been rigorously evaluated in the setting of esophageal cancer prevention. Nonetheless, primary care physicians should make lifestyle recommendations on the basis of promoting overall health. There are no recommendations for screening oesophageal cancer in the general population. But patients attending the OPD, Healthy Life style Clinics, Well Women Clinics and GP s can be screened for related signs and symptoms to identify their risk of developing oesophageal cancer and refer for further investigation.

Clinical history

- Dysphagia score *
- LOA (Loss of appetite)
- LOW (Loss of weight)
- Change of voice
- Back pain (thoracic region)
- Cough on swallowing
- Risk factors
- Co morbidities

Dysphagia score*	Description
0	No dysphagia, able to eat normal diet
1	Moderate passage, able to eat some solid foods
2	Poor passage, able to eat semisolid foods
3	Very poor passage, able to swallow liquids only
4	No passage, unable to swallow anything

General examination:

The physical examination is usually unremarkable unless it is advanced disease.

Indications for referral to a specialist care hospital

- Any patient presenting with dysphagia / alarming features to a primary care physician should be referred to a secondary/ tertiary care hospital (General surgeon/GI Physician/ GI Surgeon/ENT surgeon/ Oncosurgeon) without any delay for further investigations.

**Please use the sample referral form when referring patients to a specialist

Oesophageal cancer can be present only with dyspeptic symptoms

Sample referral form

Name of the patient: .....

Age (in years completed at the last birthday): .....

Male/ Female

Occupation: .....

Address: .....
.....
.....

Contact No: Home: .....

Mobile:.....

Presenting compliant:

Progressive Dysphagia ☐ Other----------

Duration (M) ----------

Referred by:

Name: .....

Designation: .....

Institution: .....

Signature: ..... Date: .....

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Chapter 6

Colorectal cancer

National Guideline on Early Detection and Referral Pathways of Common Cancers in Sri Lanka

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6. Colorectal Cancer

6.1 Introduction

Cancers, which origin from the caecum, ascending colon, transverse colon, descending colon, sigmoid colon, recto-sigmoid junction and rectum are included as colorectal cancers and has been recognized as a major cause of mortality and morbidity throughout the world[1]. These cancers are grouped together because they have many features in common. Survival rates of colorectal cancer are based on the stage of the disease at the time of diagnosis. An early stage colorectal cancer which has not extended beyond the bowel wall is associated with a five-year survival of more than 90% of the patients. However, the five-year survival decreases up to 60% for patients having tumours with lymph node involvement and to less than 10%, if metastases are present. This shows that colorectal cancer has good survival rate with early detection and prompt treatment[2]. The aetiology of Colorectal Cancer (CRC) is complex and appears to involve interactions between inherited susceptibility and environmental factors[3,4,5].

Colorectal cancer is the third most common cancer in the world and it is the second leading cause of death due to cancers globally.

A gradual increase in incidence of colon and rectal cancers (Age standardized rate) was observed in Sri Lanka over the last few years. In 2018, the total estimated number of colorectal cancers reported was 1441 with 734 cases among males and 707 among females[6]. The lifetime risk of developing colorectal cancers is 1 in 147 males and 1 in 143 females[6].

Incidence of the colorectal cancer is increasing with the age and comes to a peak at the age group of 65 to 75 years[7] (Figure 6.1)

Figure 6.1: Age Specific incidence rate - Colon and rectum- 2012
Source: Cancer registry- Sri Lanka (2012)

6.2 Risk factors for colorectal cancer

Several non-modifiable and modifiable risk factors for colorectal cancer have been identified in the literature. While the knowledge on modifiable risk factors is used to prevent occurrence of colorectal cancer, knowledge on non-modifiable risk factors is specifically important to identify high risk persons and to direct them for screening of colorectal cancer enabling early diagnosis and treatment for better outcome.

Modifiable risk factors

Evidence obtained from epidemiological studies consistently showed positive association of many modifiable risk factors with the risk of colorectal cancer.

- **Over-weight /obesity**

Overweight and obesity are risk factors for developing and dying from colorectal cancer. Being overweight raises the risk of colon cancer in both men and women, but the link seems to be stronger in men[8].

- **Physical Inactivity**

Physical inactivity is a risk factor for many cancers including colorectal cancers. Being more active might lower the risk. There is consistent evidence from epidemiological studies that high level of physical activity (occupational or recreational) reduces the risk of developing colorectal cancer.

A meta-analysis in 2002, found that physical activity among males to be a protective factor for colorectal cancer[9].

- **Certain types of Diet**

A diet rich in red meat (ex: beef, pork, lamb or liver) and processed meat (ex: sausages, luncheon meat) can increase the risk of colorectal cancers. Among the dietary factors, diets high in fat[10] and high red meat consumption have been identified as risk factors for colorectal cancer[11]. An inverse relationship between occurrence of colorectal cancer and consumption of fruits and vegetables has also been observed[12]. It has been proposed that differences in consumption of dietary fibers accounts for the differences in colorectal cancer rates among African populations and people living in westernized countries. High intake of dietary fiber increasing the faecal bulk and consequently reducing the transit time has been postulated as the mechanism of high fiber diet decreasing the risk of colorectal cancer[13].

- **Smoking**

Smoking is a well-known cause of lung cancer, but it is also linked to other cancers like colorectal cancers. People who have smoked for a long time are more likely to develop and die from colorectal cancers than non-smokers.

- **Heavy alcohol use**

Colorectal cancer has been linked to heavy alcohol use. Regular consumption of alcohol and tobacco smoking have been found to be associated with increased risk of developing colorectal cancer[13].

Non- modifiable risk factors

- **Older age**

Risk of developing colorectal cancer is more in people older than 50 years of age. However, younger adults also can develop colorectal cancer. It has been portrayed that the risk of colorectal cancer increases after the age of 40, with more than 90% of colorectal cancer cases being 50 years or older[15,16]. However, colorectal cancer appears to be increasing among individuals who are younger.

- **Personal history of colorectal polyps or colorectal cancer**

People with history of adenomatous polyps (adenomas) in the colon or rectum have a higher risk of developing colorectal cancers, especially if the polyps are very big or multiple in numbers. People with a history of colorectal cancer have a higher risk of developing another new cancer in other areas of the colon and rectum. If someone had a colorectal cancer in younger age, the chance of developing another cancer is greater.

Having a past history of adenomatous polyps, in particular plays a crucial role as a risk factor for developing colorectal cancer regardless of the size, histology and the site of the polyp[17]. It has been also shown that large adenomatous polyps act as the 'precursor lesion' for the colorectal cancer[18], with approximately 80% to 90% of the colorectal cancers developing from these large adenomas[19].

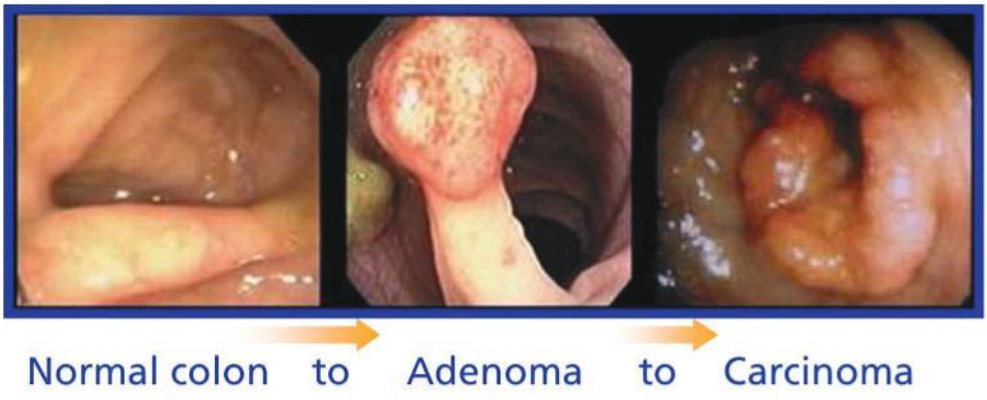


Figure 6.2: Process of differentiating normal colon to adenoma

- **Personal history of inflammatory bowel disease**

People with Inflammatory Bowel Diseases (IBD) either Ulcerative colitis or Crohn's disease has a higher risk of developing colorectal cancer than a normal person.

However, Irritable Bowel Syndrome (IBS) is not linked to an increased risk of colorectal cancer.

Having a personal history of inflammatory bowel disease[20] is also an established risk factor for developing colorectal cancer.

- **Family history of colorectal cancer or adenomatous polyps**

Majority of colorectal cancer patients do not have a family history of colorectal cancers. However, people with a history of colorectal cancer in a first-degree relative (parent, sibling, or child) are at increased risk. The risk is even higher if the first-degree relative was diagnosed when they were younger than 45 or if more than one first-degree relative is affected.

Cancers can "run in the family" because of inherited genes, shared environmental factors or some combination of these. Having family members who have had adenomatous polyps is also linked to a higher risk of colon cancer. (Adenomatous polyps are the kind of polyps that can become a cancer.)

A history of colorectal cancer among first degree relatives diagnosed at or before 45 years of age[21] is identified as non-modifiable risk factors for developing colorectal cancer.

- **Inherited cancer syndrome**

About 5% to 10% of people who develop colorectal cancer have inherited gene defects (mutations) that can cause family cancer syndromes. The most common inherited syndromes linked with colorectal cancers are as follows,

1. Familial Adenomatous Polyposis (FAP)
2. Lynch syndrome (Hereditary Non-Polyposis Colorectal Cancer -HNPCC)

However, other rarer syndromes can also increase colorectal cancer risk.

- **Type 2 diabetes**

People with type 2 (usually non-insulin dependent) diabetes have an increased risk of colorectal cancer. Both type 2 diabetes and colorectal cancer share some of the same risk factors (such as being overweight or obese). But even after taking these factors into account, people with type 2 diabetes still have an increased risk. They also tend to have a less favorable prognosis (outcome) after diagnosis.

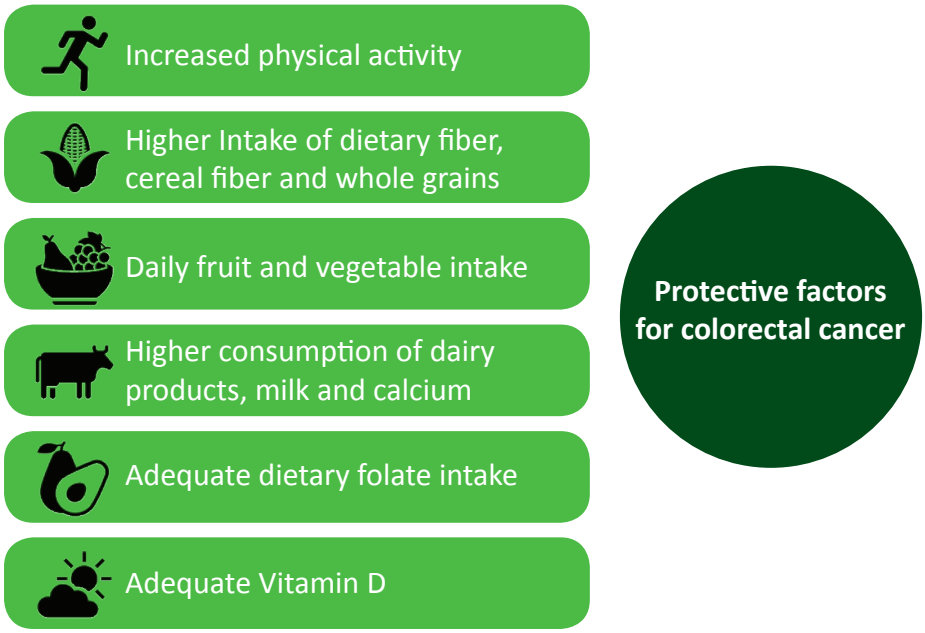
Risk factors

Non- modifiable risk factors

- Older age
- Personal history of colorectal polyps or colorectal cancer
- Personal history of inflammatory bowel disease
- Family history (colorectal cancer /adenomatous polyps)
- Inherited cancer syndrome
- Type 2 diabetes

Modifiable risk factors

- Over-weight /obesity
- Physical Inactivity
- Certain types of diet rich in red meat
- Smoking
- Alcohol



6.3 Clinical Features

History

Relevant history should include symptoms related to digestive system and general body symptoms. In early stages, the general symptoms may not be prominent. If the metastasis has occurred, symptoms related to the metastasized organs may also be present.

General Symptoms

- Loss of appetite
- Weakness and lethargy
- Fatigue
- Unexplained weight loss

Digestive system symptoms

- Rectal bleeding (mixed with stools or not) – should ask the amount and duration.
- A change in bowel habits, such as diarrhoea, constipation or narrowing of the stool that lasts for more than four weeks.
- A feeling that bowel doesn't empty completely.
- Persistent abdominal pain or discomfort (cramps, gas or pain).
- Mucus in the stools.
- Feeling bloated or full.

Should ask for family history of colorectal cancer and other cancers.

Clinical examination

This includes general examination as well as abdominal examination with attention to rectal examination.

Digital examination of the rectum (see the annex 1 for the procedure)

This is compulsory for all patients presenting with suspected colorectal cancer. With this procedure, it will be possible to palpate the distal 5-8 cm of the rectum.

Investigations

- Full Blood Count (mainly Hb)
- Faecal occult blood test (if there is no obvious bleeding PR) Guaiac based Faecal Occult Blood Tests (FOBT) or Fecal Immunochemical tests (FIT).

  Guaiac tests are based on the pseudo peroxidase activity of Haem, Immunochemical tests utilize antibodies against human hemoglobin.

Individual with a positive FOBT is 12 – 40 times more likely to have a colorectal cancer than some body with a negative test. It is mandatory that any positive FOBT be appropriately investigated.

6.4 Early detection

If diagnosed at an early stage, 90% of patients survive at least five years, compared to less than 8% of those diagnosed at an advanced stage. Currently within the country, there is no established screening programme to detect colorectal cancers. However, presence of risk factors warrants screening for colorectal cancer.

Early detection of colorectal cancers

Patients attending the OPD with related signs and symptoms should be screened according to the risk level. People attending Healthy Life Style Clinics, Well Women Clinics and GP s can be assessed to identify their risk level and refer for further investigation.

Diagnosis of colorectal cancer in symptomatic patients

- Symptomatic patients should be categorized into "High" or "Low" risk after history and examination (a Digital Rectal Examination (DRE) is mandatory).
- "High risk" patients should be investigated urgently.

High Risk

- Rectal bleeding with changes in bowel habits persisting for 6 weeks (all ages).
- Change in bowel habits without rectal bleeding (>60 years).
- Persistent rectal bleeding without anal symptoms (Itching, lumps, prolapse) (> 60 years).
- Palpable Right Iliac Fossa (RIF) mass (all ages).
- Palpable rectal mass (all ages).
- Unexplained iron deficiency anemia (all ages).
- Symptomatic patient (all ages) with:
    - a personal history of colorectal cancer or adenomatous polyps.
    - a personal history of longstanding inflammatory bowel disease (ulcerative colitis or Crohn's disease).
    - a strong family history of colorectal cancer or polyps.
    - a family history of a hereditary colorectal cancer syndrome such as familial adenomatous polyposis (FAP) or Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC).

Low Risk

- Rectal bleeding with anal symptoms and no persistent change in bowel habits (all ages).
- Rectal bleeding with an obvious anal cause eg: anal fissure (all ages).
- Change in bowel habits without rectal bleeding (<60years).
- Transient change in bowel habits particularly decreased frequency (all ages).

Diagnosis of colorectal cancer in asymptomatic patients by screening

- Colorectal cancer is a suitable condition for screening asymptomatic high - risk population because of its good prognosis after treating early lesions.
- Asymptomatic patients can be categorized into three groups for screening. Average risk, Increased risk and High- risk groups.

Average risk

- Age >= 50 yrs.
- No history of adenoma, sessile serrated polyp or colorectal carcinoma.
- No history of inflammatory bowel disease.
- Negative family history for colorectal cancer.

  These patients can be screened using Feacal occult blood test (Guaiac based Feacal Occult Blood Tests (FOBT) or Feacal Immunochemical Tests (FIT)) or Flexible Sigmoidoscopy or Colonoscopy.

Recommended age for screening in the west is between 50-75 years age group. Sri Lanka currently doesn't have a colorectal cancer screening programme. Screening should be individualized and include a discussion of risk and benefit of each modality.

Increased Risk

- Personal history of adenomatous or sessile serrated polyps.
- Personal history of colorectal cancer.
- Personal history of long standing IBD.
- Strong family history.

Patients with history of adenoma or serrated polyp:

- Should undergo colonoscopies 3-5 yearly depending on the size, number and histological characteristics of the polyp. Patients with history of colorectal cancer should undergo surveillance colonoscopies in 1, 3 and then every 5 years apart from CEA, USS and CT scans which are done in the first 5 years.

Patents with Ulcerative colitis and Crohn's disease:

- Should initiate surveillance colonoscopies form 8 years of onset of symptoms and continue.

Patients with a family history of CRC or advanced adenoma:

- One or more first degree relatives with CRC - Screening colonoscopy should be started at 40 years or 10 years before the age of the relative at the time of diagnosis (Relative who had CRC at the youngest age) and repeated 5-10 yearly.

- One or more second degree relative with CRC aged less than 50 years- screening should be started at 50 years and repeated 5-10 yearly.

- First degree relative with an advanced adenoma (high grade histology, size of the adenoma >1cm) colonoscopy at 40 years or at the age of onset of adenoma in relative whichever is first and repeated every 5-10 yearly.

High Risk

Inherited cancer syndromes falling into this category include.

- Lynch syndrome (hereditary non- polyposis colorectal cancer (HNPCC).
- Polyposis syndromes (Classic Familial Adenomatous Polyposis (FAP), Attenuated FAP, Peuts Jeghers syndrome, Juvenile polyposis syndrome, Serrated polyposis syndrome).
- Cowden syndrome.
- Li Fraumeni syndrome.

Patients who are at high risk need to undergo surveillance colonoscopies starting at different ages and repeated at different time intervals depending on the clinical condition.

Patients with Lynch syndrome should start colonoscopic screening at 20-25 years or 5-10 years prior to the age of first diagnosis in the family (which ever first) and repeated 1-2 yearly.

Patients with family history of FAP should start colonoscopic screening at 10-15 years and every year till 24 years, 2 yearly till 34 years, 3 yearly till 44 years and then 3-5 yearly.

Indications for referral to a specialist care hospital

- Any high- risk patient presenting to a primary care physician with or without suspected symptoms should refer to a secondary/tertiary care hospital (Surgical/GI clinic) without delay for further workup.
- Any average risk patient coming with suspected symptoms should be referred to a Surgical/ GI clinic.
- Patient at any age coming with suspected symptoms and signs (including investigation findings) without any other probable diagnosis should refer to a Surgical/GI clinic.

Please use the sample referral form when referring patients to a specialist Annex II.

KEY MESSAGES

01 Overall incidence of colorectal cancer is increasing over the last few decades in Sri Lanka.

02. Significant increase in the incidence can be seen in the 60-65 years age group.

03. Early detection of colorectal cancer has a good prognosis with >90% survival rate.

04. Diagnosis of colorectal cancer could be made in an asymptomatic high-risk patient by screening for colorectal cancer.

05. Symptomatic patents should be promptly evaluated and referred early for further investigations.

06. Colorectal cancer can be present without bleeding PR.
Attention should be paid to benign conditions such as hemorrhoids as they could mimic the symptoms of a cancer.

07. Current investigative techniques include sigmoidoscopy, colonoscopy, barium enema, computed tomography colonography (CT colonography).

Chapter 06

ANNEXES

I. Digital Rectal examination
II. Sample referral form

Digital Rectal Examination

Procedure

Inform and get the consent from the patient. Patient should lie in a left lateral position with both the knees drawn up to the chest and the buttock at the edge of the examination table.

Inspection

Inspect the anus after separating the buttocks.

Apply gel to the perianal area and to the tip of your examining index finger. Ask the patient to breath comfortably and bear down while you gently introduce the finger into the anal canal. This will help to reduce the internal anal sphincter tone and facilitate anal canal opening. If the patient is in severe pain, the internal sphincter is likely to be in spasm probably due a fissure.

Once the finger is within the anal canal, try to palpate for a mass, polyp, wall thickening or ulcers and palpate anterior, posterior and lateral walls as well. In males, palpate for prostate gland. In females, palpate for pouch of Douglas. After withdrawing the finger, observe for any blood stain. On completion of the examination, wipe the perineum dry.

Proctoscopy examination

Through this procedure, you can clearly visualize the distal 5-8 cm of the rectum. A proctoscope, disposable gloves and a lubricating gel are needed to perform the procedure.

Procedure –

Inform and get the consent from the patient. Ask the patient to lie in a left lateral position with both the knees drawn up to the chest and the buttock at the edge of the examination table. After applying gel, gently introduce the instrument in to the anal canal. Once fully inside the canal, remove the obturator, attach the light source and gradually withdraw the instrument keeping the mucosa in full view. Observe for,

- Mucosal changes – colour, bleeding, fissures, thickenings
- Haemorrhoids
- Polyps
- Ulcers

Sample referral form

Name: ..... Age .....

Address: .....

Presenting complain

1. Rectal bleeding yes ☐ no ☐ duration ☐

   Mixed with stools ☐ Not mixed with stools ☐

2. Change in bowel habits yes ☐ No ☐ duration ☐

   Increased frequency ☐ consistency loose ☐ solid ☐ both ☐

3. Feeling of incomplete emptying yes ☐ No ☐ Duration ☐

4. Mucus in the stools yes ☐ No ☐ Duration ☐

5. Abdominal pain/ discomfort yes ☐ No ☐ Duration ☐

6. Any other relevant symptoms: .....

7. Past medical history: .....

8. Family history:

Cancer: ..... relationship: .....

Polyps: ..... relationship: .....

9. Any relevant social/ dietary or drug history: .....

10. Clinical examination Findings: .....

11. Investigation findings: (if available) Hb%: .....

12 FOB: .....

Referred by

Name:..... Designation:..... Date:..... .

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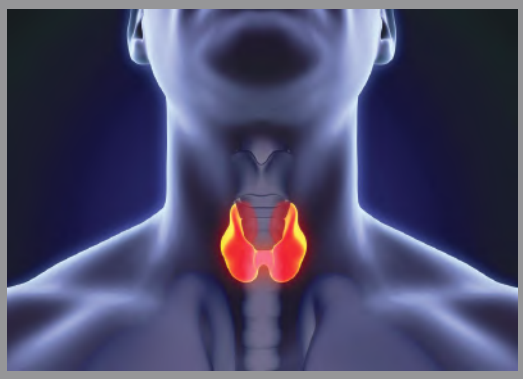

Chapter 7

Thyroid cancer

National Guideline on
Early Detection and Referral Pathways of
Common Cancers in
Sri Lanka

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7. Thyroid cancer

7.1 Introduction

Thyroid cancer is the commonest malignant endocrine tumour but represents only about 3.1% of all malignancies[1]. In spite of advances in diagnostic methods, surgical techniques & clinical care, the incidence of thyroid cancer is increasing globally, including among the paediatric population.

Thyroid nodules, particularly when solitary and clinically obvious, should be investigated as they carry a small but significant malignant potential (about 10% or less). The overall 10-year survival rate for differentiated thyroid cancer is 80–90%[2,3]. Five to twenty percent of patients develop local or regional recurrences and 10–15% develops distant metastases.

During 2018, there were 567,233 new cases of thyroid cancer in the world population and 41,071 people died from thyroid cancer. (77% of cases and 62% of deaths occurr in women)

According to the "Pathology based cancer registry 2017-Sri Lanka" thyroid cancers are the second commonest cancer (11.5%) among females[4]. It is the 4th commonest cancer when both male and female cancers taken together. In 2018, GLOBOCAN has estimated that there were 1272 new thyroid cancer cases in Sri Lanka[5]. It was the commonest cancer among females of 15 – 34 years age group in 2012 (37.2%)[6].

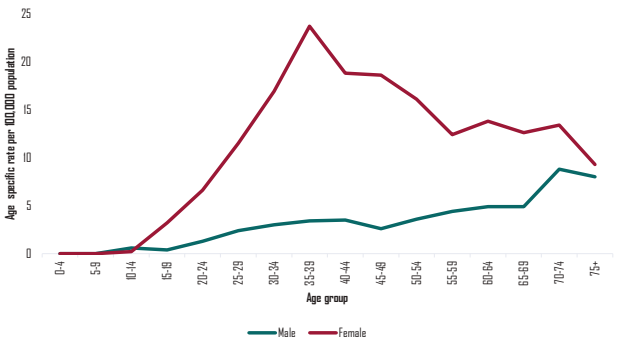


Figure 7.1: Age specific incidence rate- thyroid cancer- 2012

7.2 Risk Factors

The following are considered as risk factors for thyroid cancer

01. Sex: For unclear reasons thyroid cancers (like almost all diseases of the thyroid) occur about 3 - 4 times more often in women than in men.

02. Hereditary conditions : Several inherited conditions have been linked to different types of thyroid cancers. Still, most people who develop thyroid cancer do not have an inherited condition or a family history of the disease.

- **Medullary thyroid cancer:** About 8 out of 10 medullary thyroid carcinomas result from inheriting an abnormal gene. These cases are known as familial medullary thyroid carcinoma.
- **Familial Adenomatous polyposis (FAP):** People with this syndrome develop many colon polyps and have a very high risk of colon cancer. They also have an increased risk of some other cancers, including papillary thyroid cancer.
- **Multiple Endocrine Neoplasia Type 2 (MEN 2)**
- **Cowden disease:** People with this syndrome have an increased risk of thyroid problems and certain benign growths (including hamartomas). They also have an increased risk of cancers of the thyroid.
- **Carney Complex, type 1:** People with this syndrome may develop a number of benign tumors and hormone problems. They also have an increased risk of papillary and follicular thyroid cancers.
- **Familial non-medullary thyroid carcinoma:** Thyroid cancer occurs more often in families, and often seen at an earlier age. The papillary type of thyroid cancer most often runs in families.
- **Having a first-degree relative (parent, brother, sister or child) with thyroid cancer:** Thyroid cancer risk increases even without a known inherited syndrome in the family.

03. Long term Multinodular Goiter

04. Thyroiditis

05. Radiation: Radiation exposure is a proven risk factor for thyroid cancer[8]. Having had head or neck radiation treatments in childhood is a risk factor for thyroid cancer. Risk depends on how much radiation is given and the age of the child. In general, the risk increases with larger doses and with younger age at treatment. Cancer may not occur until 20 years or more after the radiation exposure. However, most people with such exposures do not get thyroid cancers and most people with thyroid cancers did not have such exposures. Nuclear fallout is a well-recognized cause of an increase risk of thyroid cancer in children

**A diet low in iodine is a known cause for childhood thyroid nodule.

Risk factors

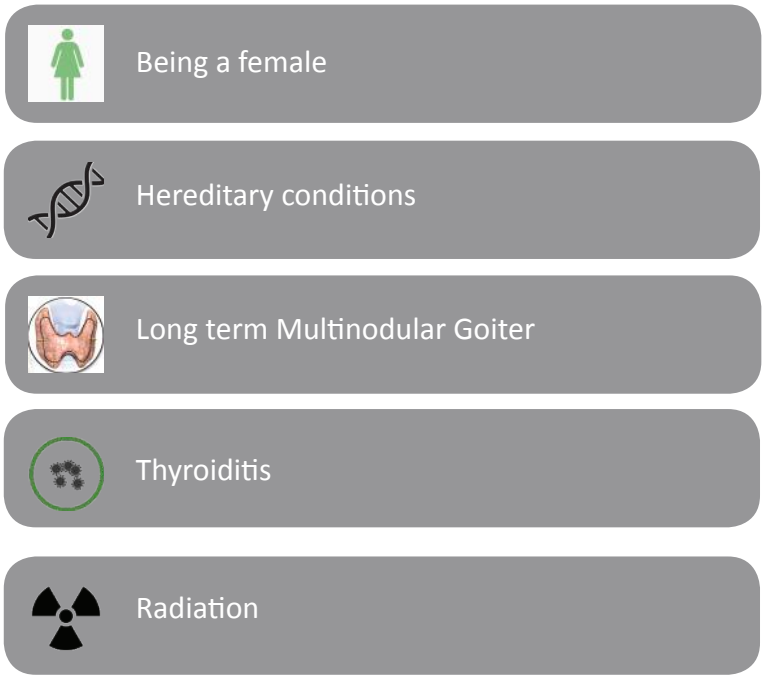


Figure 7. 2 Risk factors of thyroid cancer

7.3 Clinical features

A solitary nodule is the commonest presenting feature of a thyroid malignancy. (Refer: Annex I)

Following features in a nodule needs special attention and early referral.

- Thyroid nodule in <15 and > 45 years of age.
- Thyroid nodule in males.
- Recent onset progressively enlarging nodule.
- Other local symptoms, with thyroid nodule,
    - Hoarseness of voice
    - Dyspnea
    - Dysphagia
- Other neck lumps.
- Evidence of metastasis.
    - Dyspnea
    - Bone pain
    - Bony lumps
- Exposure to ionizing radiation.

- History of/ Family history of,
    - Multiple Endocrine Neoplasia- 2 (MEN-2)
    - Familial Papillary thyroid carcinoma
    - Familial Adenomatous Polyposis (FAP)
    - Cowden syndrome
    - Carney complex
    - Family history of Medullary or Papillary carcinoma
    - Chronic autoimmune thyroiditis
- New or enlarging nodule in a long- standing multinodular goiter (MNG).

Physical Examination (Favours malignancy)

- Solitary thyroid nodule
- Firm or hard in consistency
- Fixed to surrounding structures
- Berry's sign (Absence of ipsilateral carotid pulse)
- Skin infiltration/ ulceration (Suspect Anaplastic carcinoma)
- Cervical lymphadenopathy
- Distal metastasis
    - Lung signs
    - Bony tenderness
    - Pulsatile bony lumps

Majority of patients with thyroid malignancies are euthyroid.

Patients with one or more of the above features should be referred to a surgical or ENT unit immediately for further investigation and management. If there is a delay in referring, please obtain the following investigations if feasible.

Serum T4, TSH, US Scan of thyroid & neck, FNAC of the nodule

7.4 Early detection

Preventing thyroid cancer is not possible in most cases, but complications can be minimized if presented and detected early. Commonest presentations, their assessment and basic management steps of thyroid caner are described below.

Management of a patient with solitary thyroid nodule at secondary/tertiary care level

Management plan should be based on the clinical, biochemical, radiological and histopathological findings of the patient with solitary thyroid nodule. The assessment of a thyroid nodule serves several purposes. The patient may experience symptoms from a functional or sizable lesion or may be at risk of cancer.

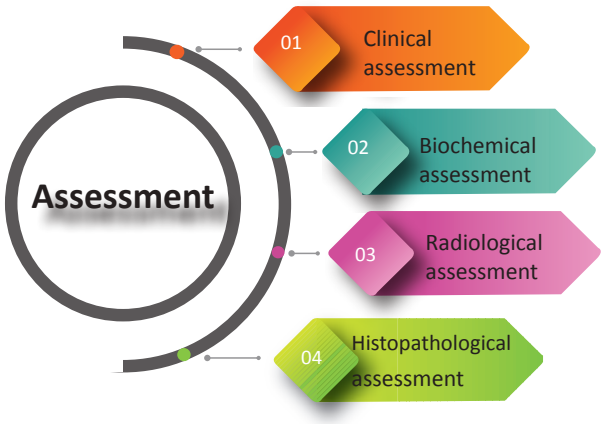


Figure: 7.3 Components of assessment of patient with suspected thyroid cancer

Clinical Assessment

Clinical assessment comprises of detailed history taking and proper physical examination.

History

Detailed history and thorough physical examination are required in patients who present with thyroid nodules. Most nodules are asymptomatic and are often discovered accidentally by the patient or a medical practitioner.

The possible presence of neoplasia, especially malignancy should be suspected if patient present with evidence of direct spread e.g. hoarseness, lymphatic spread or of distant metastatic spread. (E.g. bone pain, bone swelling)

However, patient should be evaluated for symptoms of hypothyroidism or hyperthyroidism and for local compressive symptoms such as dysphonia, dysphagia and dyspnoea.

Factors that increase the likelihood of malignancy are the following:

- Age at presentation <20 years or >60 years
- History of rapid growth - Rapid growth of a solid thyroid mass within days or weeks almost always corresponds to Anaplaspic thyroid carcinoma or lymphoma. In both conditions the diagnostic work-up needs to be performed with urgency.

- History of head and neck irradiation
- Dysphonia/hoarseness
- Family history of medullary thyroid carcinoma, other thyroid carcinomas, multiple endocrine neoplasia or Cowden's syndrome.
- Associated with palpable tumour elsewhere

Symptoms of Hyperthyroidism	Symptoms of Hypothyroidism
Irritability	Cold intolerance
Increased perspiration	Constipation
Heat intolerance	Weight gain
Palpitations	Fatigue
Tremors	Dry and itchy skin
Insomnia	Menorrhagia
Fine brittle hair	
Frequent bowel movements	
Weight Loss	

Physical examination

Physical examination includes inspection and palpation of the anterior and lateral aspects of the neck to assess for thyroid enlargement, the presence of nodules and lymphadenopathy. Asking the patient to swallow during palpation can improve the detection of nodules.

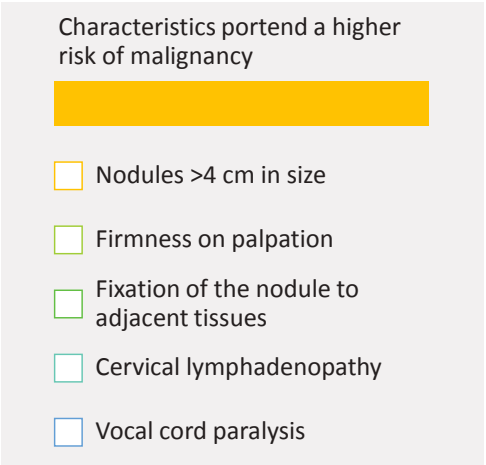
Signs of Hyperthyroidism	Signs of Hypothyroidism
Tachycardia	Bradycardia
Arrhythmias	Myxoedema (Thickened and puffy appearance of skin)
Muscle wasting	Delayed reflexes (relaxation phase)
Fine tremor	
Brisk reflexes	
Friable hair	

Visualization of vocal cord movement is very important if the patient presents with dysphonia. This can be done with a dental mirror and a headlight, an ultrasound examination or with a flexible nasopharyngoscope. A paralyzed vocal cord ipsilateral to the thyroid mass is always present in invasive thyroid cancer.

Radiological assessment

Ultrasonography

- Initial imaging modality of choice
- Most sensitive diagnostic modality to assess the thyroid nodules.
- Should be performed in all suspected and patients known to have a nodule to confirm the presence of a nodule, evaluate for additional nodules, cervical lymph nodes and assess for suspicious sonographic features.



- Gives very important and clinically useful clues whether the nodule is benign or malignant
- FNAC decision making is guided by size of the nodule and ultrasound characteristics.

Radionuclide scanning

- Performed in patients with thyroid nodule and a low serum TSH, suggesting overt or subclinical hyperthyroidism to assess the function of the nodule.
- In patients with normal or high serum TSH, isotope scan is not performed as the initial imaging evaluation.

Other imaging techniques (CT and MRI)

- Limited role in the initial evaluation of solitary thyroid nodule.
- Indications for these imaging techniques include suspected tracheal involvement, either by invasion or compression, extension into the mediastinum or recurrent disease.

Biochemical assessment

All patients with solitary nodules should be evaluated to assess the level of functioning of the thyroid gland. Therefore, they should undergo thyroid function tests.

Cytological Assessment

Fine-Needle Aspiration Cytology (FNAC) - Fine needle aspiration cytology has sensitivity and specificity > 95%, provided the sample taking and interpretation done by an experienced person. Palpation FNAC should be used only for palpable thyroid nodules. US guided FNAC is mandatory for impalpable lesions, as well as multinodular goiters.

Management of Thyroid Cancer (at a specialized center)

Patients with thyroid cancer commonly undergo thyroidectomy, followed in some cases by an ablative dose of radioiodine$^{I\ 131}$. Thereafter patients will generally require levothyroxine to suppress TSH to <0.1 mu/l and some will need treatment to correct hypocalcaemia. Measurement of serum thyroglobulin (Tg) will be performed at regular intervals to detect possible recurrence.

Levothyroxine treatment

The dose of levothyroxine is usually higher than a normal replacement dose as it is intended to suppress the level of serum TSH to <0.1 m u/l. For example, if the TSH is in the normal range, the dose of levothyroxine should be increased. Suppressive levothyroxine therapy is best supervised by a member of the thyroid cancer Multi-Disciplinary Team, preferably an endocrinologist. The primary care physician will be advised of the target levels of TSH.

Treatment of hypocalcaemia

Patients taking calcitriol/alfa calcidol and/or calcium supplements must be monitored closely (eg: every 3 months until stable, annually thereafter) to ensure that hyper-calcaemia does not occur. The dose is kept to the minimum required to maintain serum calcium in the (low) normal range.

Medullary Thyroid Carcinoma (MTC)

Following investigations are also conducted for FNAC suspicious MTC in developed countries:

- Serum calcitonin assay
- Serum Carcinoembryonic Antigen (CEA) measurement
- DNA analysis for RET germline mutation

Special situations

Nodule presenting in pregnancy

- Thyroid nodules will enlarge slightly throughout gestation, though this does not imply malignant transformation.

- The recommended evaluation of a clinically significant nodule in a pregnant patient is same as for a non-pregnant patient, with the exception that a radionuclide scan is contraindicated.
- Pregnancy does not modify microscopic cellular appearance; therefore, standard diagnostic criteria should be applied for cytological evaluation.
- FNA of clinically relevant thyroid nodules should be performed in euthyroid and hypothyroid pregnant women.
- For women with suppressed serum TSH levels that persist beyond 16 weeks of gestation, FNA may be deferred until after pregnancy and cessation of lactation. At that time, a radionuclide scan can be performed to evaluate nodule function if the serum TSH remains suppressed.
- Patients with nodules diagnosed as diffreantiated thyroid carcinoma by FNA during pregnancy, surgery delayed until after delivery does not affect outcome of cancer.
- Surgery performed during pregnancy is associated with greater risk of complications, longer hospital stays and higher costs.
- Radioiodine is contraindicated in pregnant patients.
- Pregnancy must be avoided for 6 months after Radioiodine Remnant Ablation (RRA) or therapy in women and 4 months for men[10].
- Breastfeeding needs to be stopped at least 4 weeks and preferably 8 weeks before radioiodine ablation or therapy and not be resumed until after a subsequent pregnancy

Thyroid nodule presenting during childhood and adolescence

Thyroid nodules are less common among children than adults but are more likely to be malignant.

Papillary Thyroid Cancer is the commonest cancer type.

The differential diagnosis comprises benign thyroid conditions such as Congenital hypothyroidism, Thyroid hemiagenesis, Thyroglossal duct cyst, Simple goiter, Cystic lesion, Nodular hyperplasia, Follicular adenoma, Nodular Graves' disease and Hashimoto thyroiditis which predisposes to the development of thyroid nodule.

Evaluation and treatment of thyroid nodules in children should be the same as in adults with the exceptions that ultra sound characteristics and clinical context should be used rather than size alone to identify nodules that warrant FNA. An annual physical examination is recommended for children at high risk for thyroid neoplasia Eg: Prior radiation exposure, a history of antecedent thyroid disease and several genetic syndromes.

Additional imaging should be arranged if palpable nodules, thyroid asymmetry and/or abnormal cervical lymphadenopathy are found on examination.

FNA is not warranted for a nodule <1 cm in size unless the patient is considered high-risk, most commonly with a history of exposure to ionizing radiation or the nodule is associated with pathological regional lymph nodes.

All FNA in children should be performed under ultra sound guidance.

In all children with a suspicious nodule, ultra sound evaluation of the cervical lymph nodes should also be performed.

Surgery (lobectomy plus isthmusectomy) is favoured over repeat FNA for most nodules with indeterminate cytology.

The following algorithm (figure 7.4) was extracted from the American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer – 2015.

Please refer the document for relevant recommendations and for further reading.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4739132/

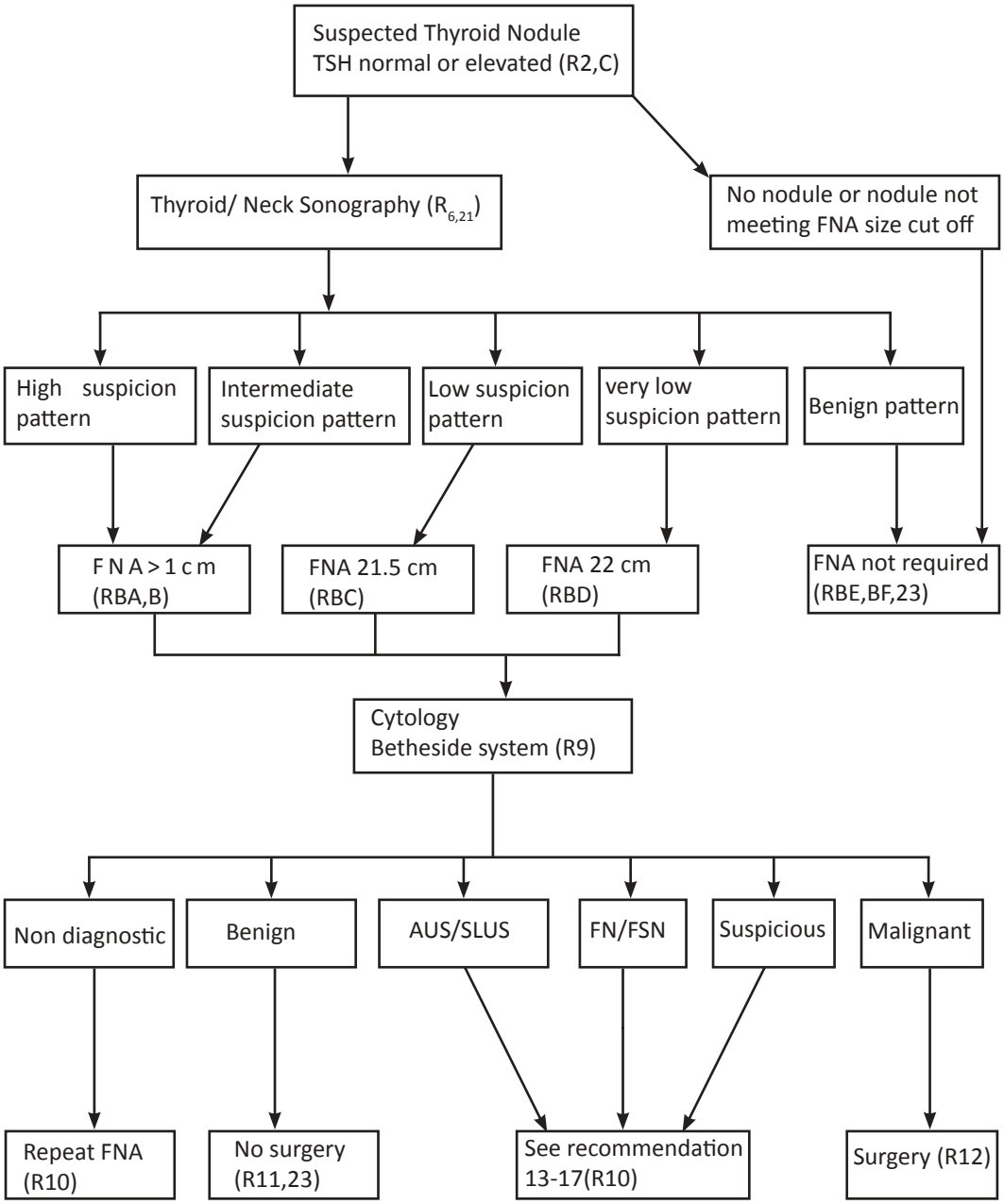


Figure 7.4 : Algorithm for evaluation and management of patients with thyroid nodules.
Source: American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules

Chapter 07

ANNEXES

I. Thyroid Nodules

Thyroid Nodules

A thyroid nodule is a discrete lesion within the thyroid gland radiologically distinct from surrounding thyroid parenchyma. Non-palpable nodules detected on ultrasound or other imaging studies are termed incidentally discovered nodules "incidentalomas".

Conditions presenting as Solitary Thyroid Nodule

Many thyroid diseases can manifest clinically as solitary thyroid nodules. A solitary thyroid nodule could be non-neoplastic or neoplastic. Neoplastic nodules could be either benign or malignant. Some solitary thyroid nodules represent a palpable nodule in an early stage multi nodular goiter.

Benign Thyroid Nodules

- Colloid cyst
- Hyperplastic nodule/toxic nodule
- Thyroid adenoma (Adenomas are benign neoplasms arising from the follicular epithelial lining of the thyroid follicles)
- Hashimoto's thyroiditis

Malignant Thyroid Nodules

Thyroid malignancies can be categorized into the following key subtypes:

Primary thyroid cancers

- Papillary Carcinoma: 60-80% of thyroid carcinomas.
- Follicular carcinoma: 10-20%
- Medullary carcinoma: 5%
- Anaplastic carcinoma: 1-2%

Thyroid lymphoma: 2.5%

- Primary thyroid lymphoma
- Secondary thyroid involvement with lymphoma

Metastases to the thyroid: 1%

Squamous cell carcinoma (rare)

- Primary squamous cell carcinoma
- Secondary - Direct invasion from head and neck squamous cell carcinoma (Metastatic disease)

Thyroid Malignancy

Well differentiated Thyroid Carcinoma

Differentiated thyroid cancers arise from thyroid follicular epithelial cells and constitute 90% of all thyroid cancers. Papillary carcinoma and follicular carcinoma make up the well-differentiated thyroid carcinomas.

- **Papillary carcinoma**

Papillary carcinoma is the most common thyroid malignancy, representing approximately 80%. It is a slow-growing tumor that arises from the thyroxine (T4) and thyroglobulin-producing follicular cells of the thyroid. The cells are TSH sensitive and take up iodine. They produce thyroglobulin in response to TSH stimulation. This feature has both diagnostic and therapeutic value for managing thyroid cancer.

Papillary carcinoma has a classic histological appearance with many variants. The papillary carcinoma variants other than the classical type as recognized by the WHO classification include,

Follicular, Encapsulated, Papillary micro carcinoma, Columnar cell and Oncocytic variants.

Columnar cell variant has a worse prognosis

Follicular variant of papillary carcinoma is further subtyped as[8],

a) **Non-encapsulated or infiltrative –** The clinical behaviour is similar to classical papillary thyroid cancer

b) **Encapsulated, non-invasive –** 'Encapsulated, non-invasive, follicular variant of papillary thyroid carcinoma' has been identified as an indolent tumour and renamed as **'Non-invasive follicular thyroid tumours with papillary like nuclear features'** (NIFTP). The diagnosis is based on histological criteria and its surgical management has been downgraded from total thyroidectomy to hemithyroidectomy with no additional therapy. Its molecular profile is similar to follicular thyroid cancer.

c) **Diffuse/ aggressive/ Mutinodular –** This type is rare and usually occur in young patients. It has a worse prognosis than above two types.

Local invasion

Tumors can grow directly through the thyroid capsule to invade surrounding structures.

Regional and metastatic disease

Another common feature of papillary carcinoma is it's propensity to spread to the cervical lymph nodes. Clinically evident lymph node metastases are present in approximately one-third of patients at presentation. Microscopic metastases are present in one-half. Distant spread of papillary carcinoma typically affects the lungs and bones.

Follicular carcinoma

Follicular carcinoma is the second most common thyroid malignancy and represents about 10% of thyroid cancers. Similar to papillary carcinoma, follicular carcinoma occurs 3 times more frequently in women than in men. Patients with follicular carcinoma are typically older than those with papillary carcinoma at presentation. The mean age at diagnosis is in the fourth to sixth decades.

Like papillary carcinomas, follicular carcinomas arise from the follicular cells of the thyroid. The neoplastic cells are TSH sensitive as well, taking up iodine and producing thyroglobulin—a feature that is exploited diagnostically and therapeutically.

There are 3 main types of follicular carcinoma according to the WHO classification[9]

1) **Follicular thyroid carcinoma, minimally invasive -** This is a single encapsulated nodule in which focal early capsular invasion can be found histologically. These tumours have an excellent prognosis.

2) **Follicular thyroid carcinoma, encapsulated with angio-invasion –** There is a risk of blood borne metastatic disease.

3) **Follicular thyroid carcinoma, widely invasive -** Gross invasion or extensive microscopic infiltration can occur. Prognosis is worse than in the minimally invasive tumours.

Cervical lymph node and distant metastases

Unlike papillary carcinoma, cervical lymph node metastases from follicular carcinomas are uncommon. Blood borne metastasis to the lungs and bones are common.

Oncocytic (Hürthle Cell) Carcinomas

Hürthle cell carcinoma is a rare thyroid malignancy (2-3%) considered a variant of follicular carcinoma. About 75-100% of the tumour is composed of Hürthle cells. These are large, polygonal follicular cells that contain abundant granular acidophilic cytoplasm. Hürthle cells are found in a variety of benign thyroid conditions as well, such as Hashimoto thyroiditis, Graves' disease and multinodular goiter. They are

more common in women than in men and typically manifest in the fifth decade of life. The clinical presentation is similar to that of other thyroid malignancies. Hürthle cell carcinomas behave aggressively. Patients with these lesions are at higher risk of recurrent and metastatic disease.

Poorly Differentiated Thyroid Carcinoma

These are follicular cell neoplasms that show only limited amount of structural follicular cell differentiation. Both morphologically and behaviorally, they occupy an intermediate position between differentiated and undifferentiated carcinomas.

Undifferentiated Thyroid Carcinoma

Anaplastic Thyroid Carcinoma

Anaplastic thyroid carcinoma is the least common thyroid carcinoma, accounting for 1.6% of all thyroid cancers. However, it has the most aggressive biologic behaviour of all thyroid malignancies and one of the worst survival rates of all malignancies in general. Like papillary and follicular carcinomas, anaplastic thyroid carcinomas affect more women than men. Patients with anaplastic thyroid carcinomas present later typically in the sixth or seventh decade of life.

Anaplastic thyroid carcinoma manifests as a rapidly growing thyroid mass and patients commonly present with associated symptoms due to local invasion.

Most of the patients already have distant metastases at the time of diagnosis. The most common sites of involvement are the lungs, bones and brain.

Medullary Thyroid Carcinoma (MTC)

MTCs represent approximately 5% of all thyroid malignancies. A slight female preponderance is observed and tumours arise from the para-follicular C cells of the thyroid gland. C cells are neural-crest derivatives and produce calcitonin. About 75% of MTCs occur sporadically and 25% occur familiarly. They are inherited in an autosomal dominant manner.

When MTC arises as part of a familial syndrome, assessment and management of the other endocrine tumours are required. Patients may survive for many years even with a significant tumour burden although prognosis is poorer than differentiated cancer.

Presentation – MTC may present with a neck mass, symptoms related to pressure effects (Dysphagia, dysphonia) or with distant metastasis. In addition, patients with extensive MTC may present with frequent loose stools and vaso motor flushing that result from coincident secretion of peptide.

In all cases, a comprehensive family history must be taken to include first and second-degree relatives to search for features of MTC or other endocrinopathies.

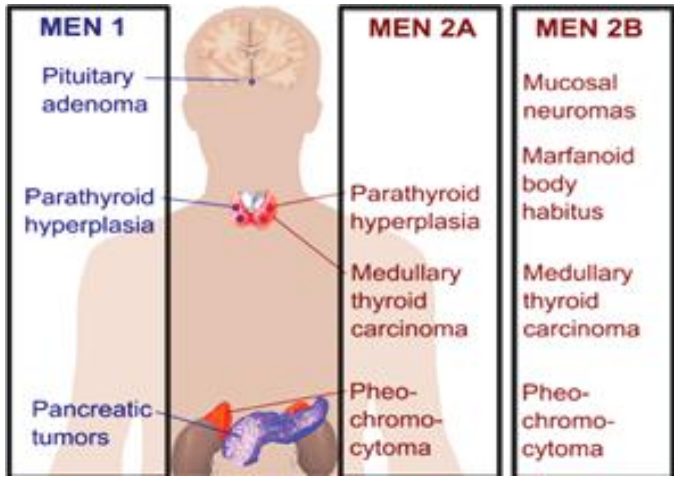


Figure : I.I Types of Multiple Endocrine Neoplasia (MEN)

Genetic testing for MEN and FMTC

Genetic testing is now the mainstay in the diagnosis of the FMTC syndromes in developed countries.

Biochemical testing for MTC

Because MTC cells produce calcitonin, elevated serum calcitonin levels are diagnostic of MTC. Plasma calcitonin levels are commonly increased before clinical evidence of MTC appears. Plasma calcitonin testing is now used for the early detection of MTC in patients already known to be at risk for MTC because of their family history and genetic results. This level is most commonly used as a tumour marker to identify residual and metastatic disease after thyroidectomy to treat MTC.

Primary Thyroid Lymphoma

Primary lymphomas of the thyroid gland represent approximately 2-5% of all thyroid malignancies. Most thyroid lymphomas are Non-Hodgkin B-cell tumours. The next most common histologic type is low-grade Malignant Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT). This tumour is highly associated with chronic lymphocytic thyroiditis (Hashimoto thyroiditis).

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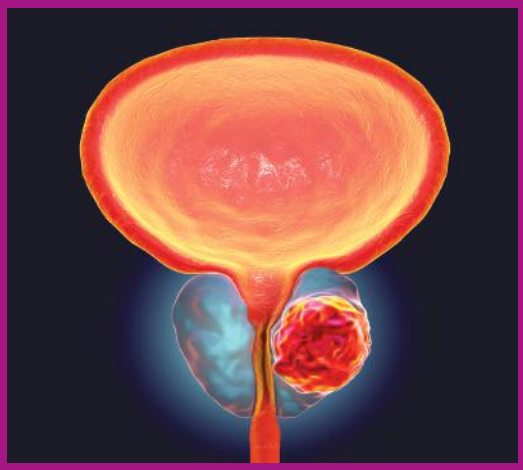

Chapter 8

Prostate cancer

National Guideline on Early Detection and Referral Pathways of Common Cancers in Sri Lanka

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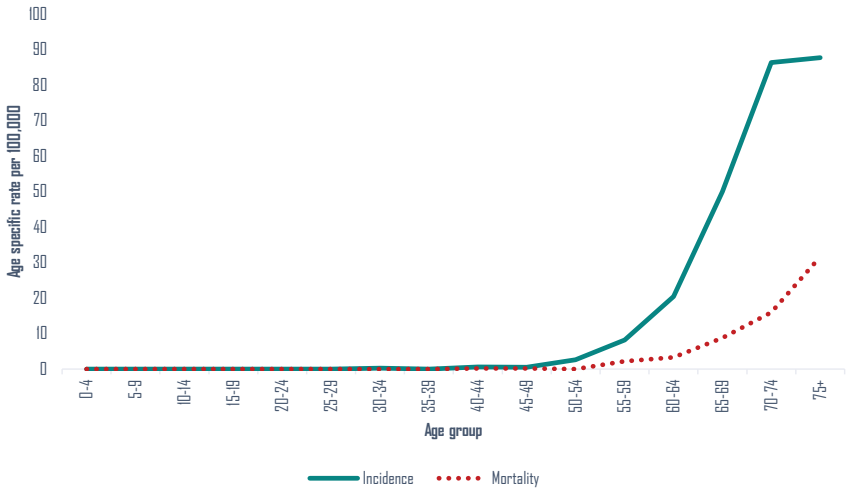
8. prostate cancer

8. 1 Introduction

The incidence of prostate cancer in Sri Lanka is 6.4 per 100 000 population[1] and is much lower than that in United States of America and Europe. Though the epidemiological data in Sri Lanka is not comprehensive, numbers are in par with the rest of the Southeast Asian region[2].

Prostate cancer incidence starts to rise around the age of 50 years and the upward trend persists with the increasing age (Figure 8.1)[1].



Fugure 8.1: Age specific incidence & mortality rates - Prostate- 2012
Source: National cancer registry Sri Lanka- 2012[1]

Average age (70.5 years) at diagnosis of prostate carcinoma among men in Sri Lanka is higher than that in the developed world where the median age is approximately 67 years [5]. According to a study from a urology unit in Sri Lanka, 79% of the patients had either locally advanced (19%) or metastatic disease (60%) at the time of diagnosis[5,6]. Therefore, in contrast to the developed countries, prostate cancers are diagnosed at a late stage [6]. In countries where serum Prostate Specific Antigen (PSA) testing is freely available as a screening tool, the detection rate of prostate cancer is high [7]. Although the observed low incidence of prostate cancer in Sri Lanka could be partly due to low detection rates, with the increasing availability of PSA together with a rapidly ageing population and change in dietary habits[8], the incidence of prostate cancer in Sri Lanka may be increased in future. Therefore, greater vigilance should be exercised on the population of elderly patients presenting with Lower Urinary Tract Symptoms (LUTS).

8.2 PSA and prostate cancer screening

Routine population-based screening is not recommended even in Europe and North America where the incidence is equal or above 100 per 100000 population[3,4]. While the population-based PSA screening (initiated by authorities for community) is not recommended worldwide, opportunistic PSA screening (initiated by the patient, mainly presenting with lower urinary tract symptoms (Box 1) and self-requested screening in selected individuals is recommended after careful explanation of why it is being performed and its implications[9].

Box 1: Common Lower Urinary Tract Symptoms (LUTS)

- Hesitancy – longer than usual wait for the stream of urine to begin
- Weak stream
- Straining to urinate
- Dribbling after urination has finished or an irregular stream
- Urgency – feeling an urgent need to urinate
- Frequency – a short time between needing to urinate
- Nocturia – waking from sleep to pass urine two or more times during the night
- Urge incontinence – a sudden, intense urge to urinate followed by an uncontrolled loss of urine

Before discussing with the patient, the clinician should be thoroughly familiar with the evidence-based facts on the serum PSA testing (Box 2).

Box 2: Evidence-Based Facts on the Serum PSA

A. PSA is not an ideal screening tool due to its low specificity and issues with sensitivity; which subjects many patients with elevated serum PSA to repeat tests including invasive Trans-rectal Ultrasound (TRUS) guided biopsies without actually having a prostate cancer.

B. Current evidence shows no significant reduction of prostate cancer related mortality in population-based screening compared with non-screened controlled group [10,11]. This is mainly due to low absolute risk reduction observed in population-based screening which results in unacceptably higher number needed to be screened, biopsied and treated in order to prevent a single cancer death. (NNS=129)[12]. Both the biopsy and the treatment have serious unwanted side effects.

C. Since a significant number of prostate cancers are latent (heterogeneity in aggressiveness) detected early and treated aggressively includes large number of clinically non-significant tumours hence subjecting patients to unnecessary overtreatment with added morbidity including sexual dysfunction, incontinence and affected psychological wellbeing with no advantage in survival.

D. Proceeding with PSA screening demands many additional diagnostic services along the management pathway. This includes template and targeted prostate biopsies, MP-MRI and MRI fusion biopsies which are currently not available in many state sector Sri Lankan settings. This may affect optimal active surveillance approach and evidence-based selection of patients for appropriate radical forms of therapy.

E. However, evidence shows a small mortality benefit of screening in some individuals which increases the detection of more organ confined (potentially curable) disease and reduction of incidence of higher stage (metastatic) diseases[13]. This does not justify the blind recommendation of PSA based screening in men since the harms of it will outweigh the benefits but could be considered as a benefit in opportunistic screening in selected[14.]

F. Clinicians should discuss and explain the above evidence and the fact of low prostate cancer incidence in Sri Lanka with the patients before offering opportunistic screening when presented with LUTS or any patient self-requesting PSA with a view of screening for prostate cancer.

G. Clinicians should be able to guide the patient in an individual basis considering his age, co-morbidities, risk factors including family history and patient values about the benefits and harms of the screening.

8.3 Referral Pathways

Prostate cancer referral pathways could be broadly categorized as:

1. Opportunistic screening

These are the patients presenting to primary health care provider with LUTS. Mostly their symptoms are attributable to underlying Benign Prostatic Hyperplasia (BPH).

2. Clinically advanced disease

Patients presenting with clinical features of metastatic or locally advanced prostate cancer.

3. Self-requested screening

Asymptomatic men requesting self-screening for prostate cancer.

Referral Pathways

Those who plan to request serum PSA to detect prostate cancer should be aware of the following facts.

(a) Serum PSA can be elevated in the presence of urinary tract infection and after acute urinary retention. Therefore, avoid requesting PSA until the infection is effectively treated and few weeks have elapsed after urinary retention.

(b) Serum PSA elevation following Digital Rectal Examination (DRE) is negligible (0.26ng/ml).

(c) According to WHO statistics the average life expectancy of a Sri Lankan man is 72 years

1. Opportunistic screening

A man over 50 years with LUTS

Digital Rectal Examination (DRE) is essential.

1. If DRE shows a clinically malignant/ suspicious prostate gland

Request a serum PSA and refer to a urological surgeon.

2. If DRE is clinically benign

(a) If the age is less than 70 years and no clinical evidence of a UTI, do a serum PSA after explaining the patient about pros and cons of the test (see Box 3). If the serum PSA is elevated than the normal range refer to a urological surgeon. If it is normal review in one year.

(b) If age is above 70 years, serum PSA is unlikely to be useful in prolonging the life span.

2. Clinically advanced disease

A man over 50 years presenting with LUTS and Red flag symptoms or signs of metastatic or advanced prostate cancer such as significant lower back pain, bone pain, lower limb neurology, bilateral lower limb swelling etc.

Do DRE and request a serum PSA as early as possible.

1. **If DRE is abnormal and neurology is positive** (Impending cord compression) ⟶ patient need urgent hospital admission.

   Do **DRE** and request a **serum PSA** as early as possible for those with normal neurology.
2. **If DRE is abnormal with normal neurology** ⟶ Urgent referral to Urological surgeon.
3. **If DRE is normal** ⟶ Consider other diagnosis and wait for PSA before referring to Urological surgeon.

3 Self-requested screening

Asymptomatic man who requests a serum PSA after knowing about it from elsewhere.

DRE is essential.

1. If DRE shows a **clinically malignant/ suspicious** prostate gland request a serum PSA and refer to a urological surgeon.
2. **If DRE is clinically benign and age is less than 70** years do a serum PSA test after discussing pros and cons **(Box 3)**. If it is above the normal range refer to a urological surgeon. If not review in one year.
3. **If DRE is clinically benign and age is over 70** years explain the patient that serum PSA may not be advantageous but if patient still wants do a serum PSA. If it is above the normal range refer to a urological surgeon. If the clinician is uncertain of the DRE findings, refer to a urological surgeon.

Box 3: Patient information leaflet

Blood PSA test

Doing the PSA test, in the absence of suspicious symptoms or examination findings (clinical features) has both advantages and disadvantages and some of them may be serious. Therefore, please study and understand the benefits and risks before you decide to have the test.

Benefits

1. It may provide reassurance if the test result is negative.
2. It may find cancer before symptoms develop.
3. It may detect cancer at an early stage when treatment could be beneficial.
4. If treatment is successful, the consequences of more advanced cancer (eg bone fractures, paralysis of lower limbs) are avoided.
5. It may reduce your chances of dying of prostate cancer.

Downsides

1. It can miss cancer and provides false reassurance (even with normal PSA result cancer may be present).
2. It may lead to unnecessary anxiety and medical tests when no cancer is present. Those tests can be costly and may cause serious complications like severe infections, bleeding and urine block.
3. It might detect slow growing cancer that may never cause any symptoms or shorten your lifespan.
4. The main treatments of early prostate cancer may have significant side effects (continuous urine leakage, erectile dysfunction, bleeding from urinary passage and bowel) and there is no certainty that the treatment will be successful and prolong your life span.
5. Cost of the test

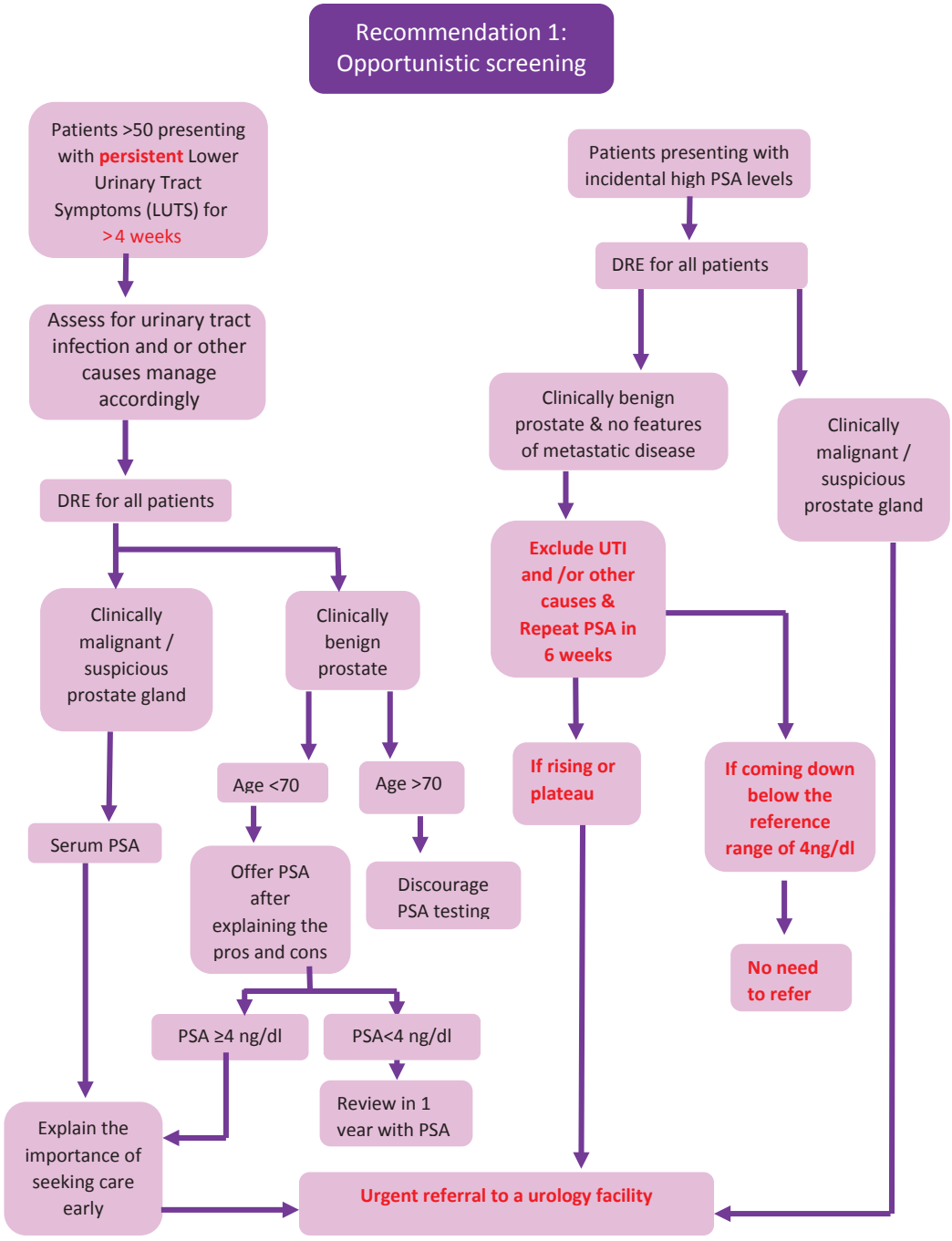


Figure 8.2: Referral pathways- Opportunistic screening

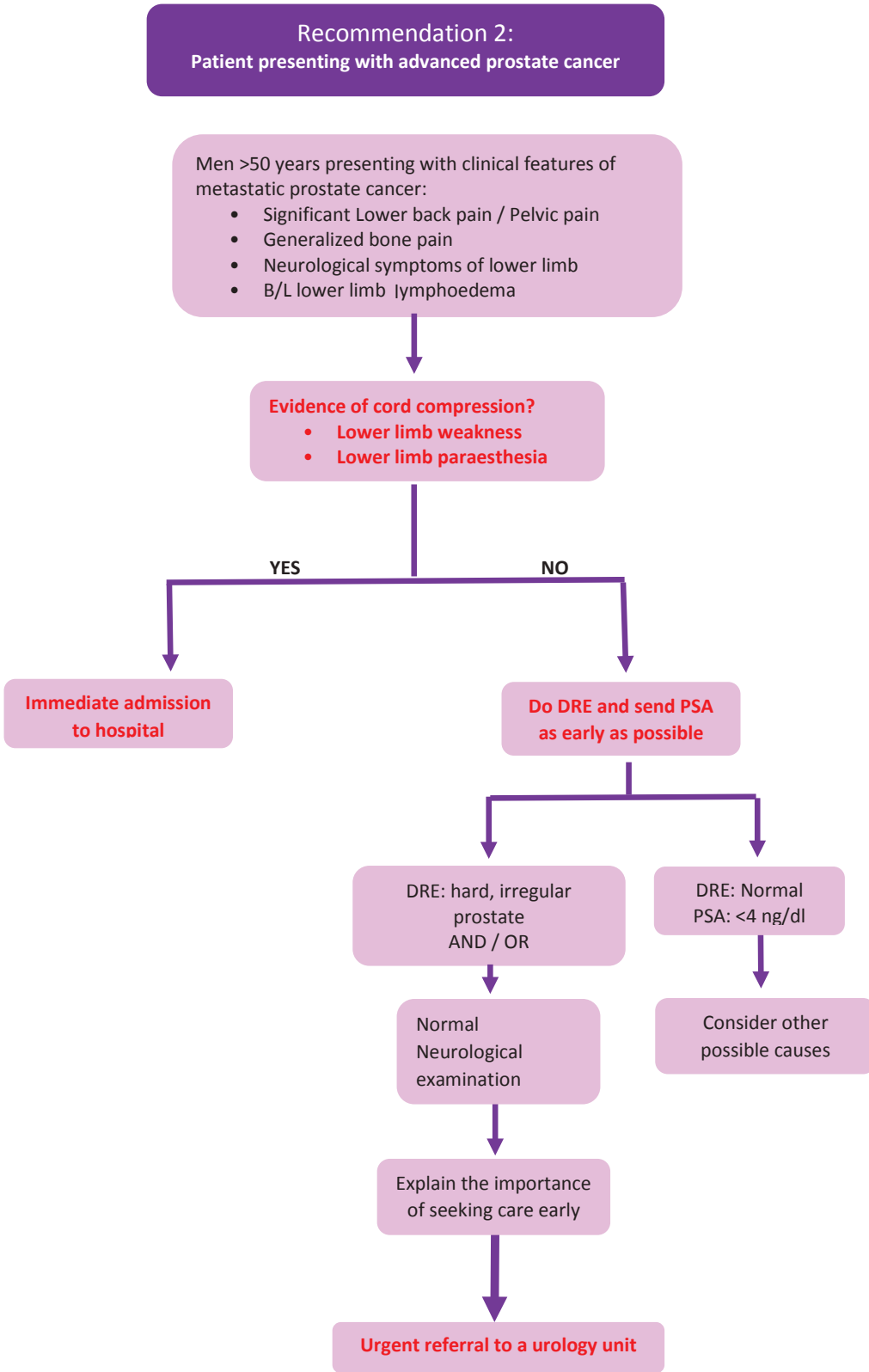


Figure 8.3: Referral pathways- Patient presenting with advanced prostate cancer

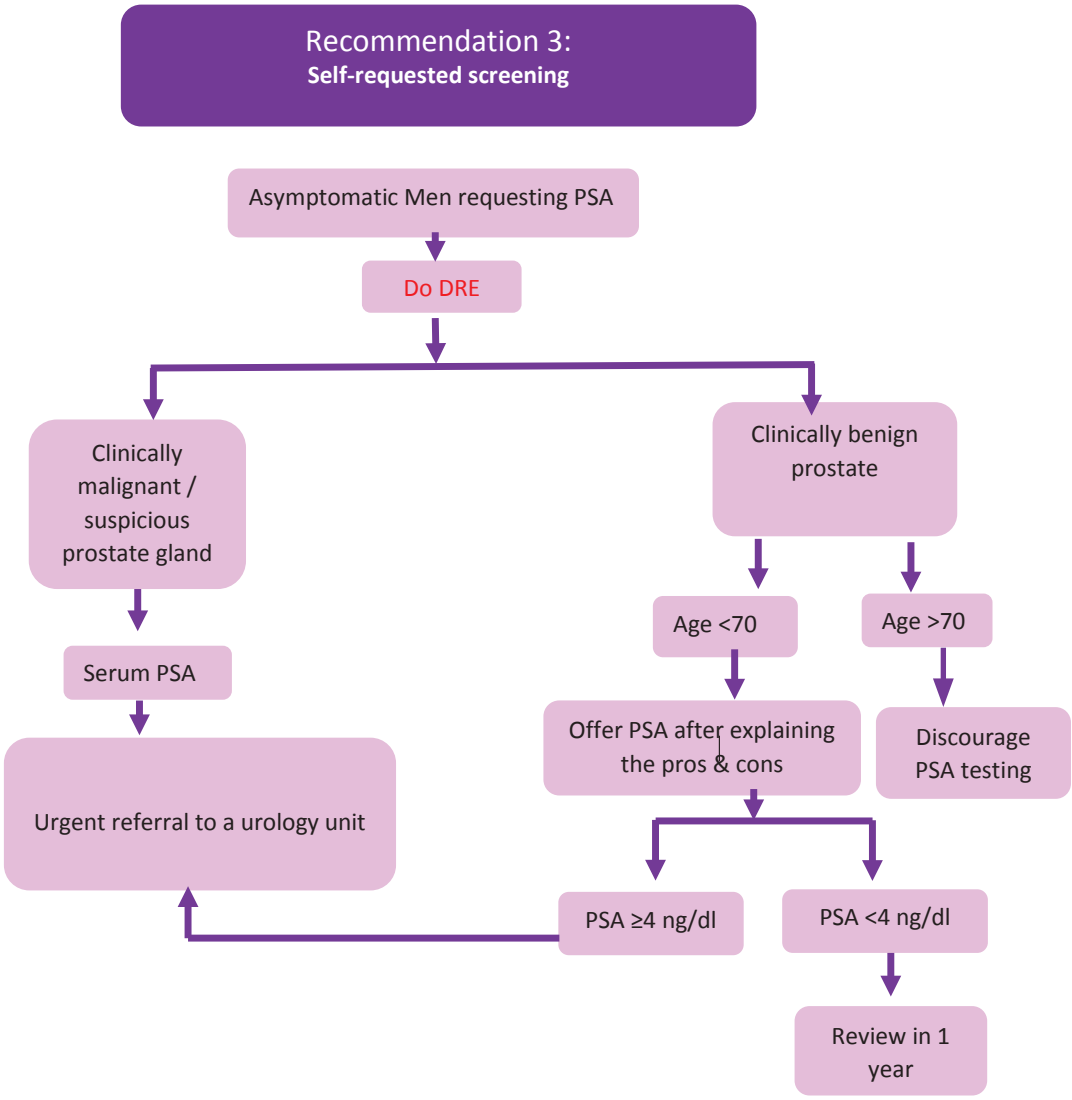


Figure 8.3: Referral pathways- Self-requested screening

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Attachment 1

We would like to acknowledge WHO as the author of "Guide to cancer early diagnosis"(ISBN 978-92-4-151194-0) which was used to prepare the content of "Attachment 1"

Concept of Cancer screening and early detection

Increasing trend in cancer incidence emphasizes the importance of a well-planned and evidence-based interventions to alleviate the cancer risk in the island. WHO recommends to its member countries to have key essential components of their National Cancer Control Programmes. Figure 1 illustrates the recommended framework for national cancer control programme in a country.

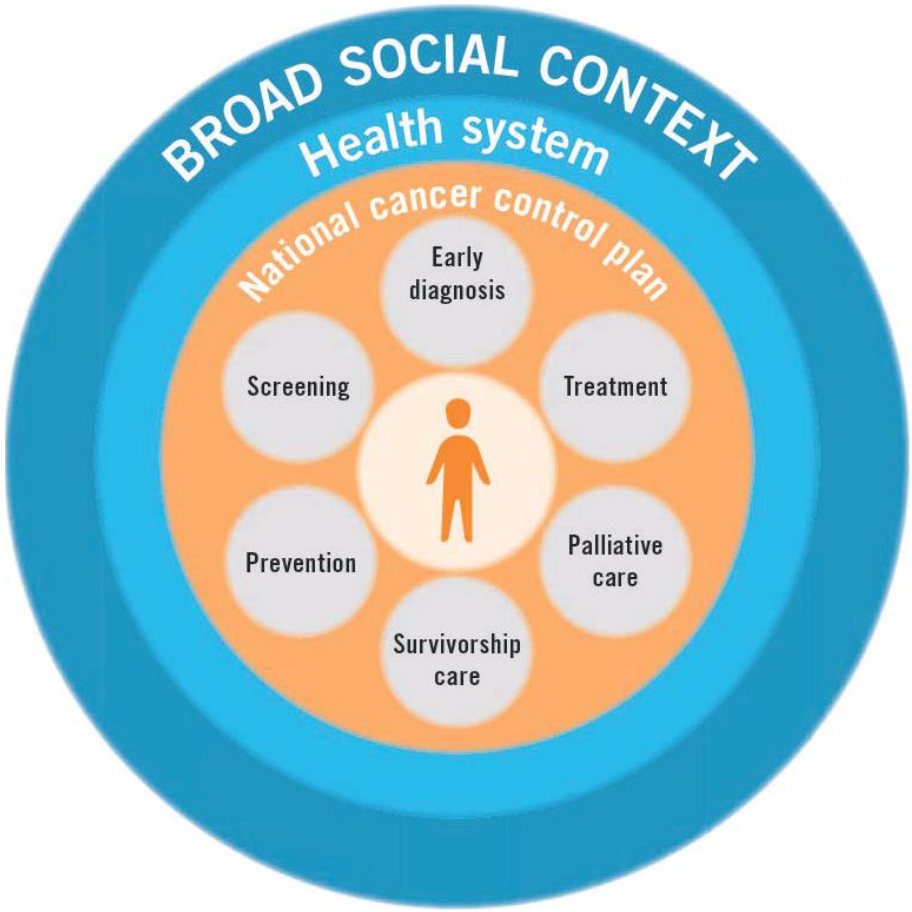


Figure : 1 Framework of a National Cancer Control Programme.

Source: Adapted from WHO 2002

Scientific evidence highlights the most cost-effective strategy to control cancer is primary prevention. Almost one third of deaths due to cancers occurring globally are due to five main modifiable risk factors[1] (Figure 2).

Figure 2: Most common risk factors leading to deaths due to cancer

The control strategies may be varied from one cancer to the other. Evidence says that about 30% to 50% cancers are preventable[1]. For cancers of the lung, liver, oral cavity, uterine cervix and many cancers of the oesophagus, primary prevention is the main strategy. There are some cancers which are not preventable, but have opportunities to detect them early and have better health outcomes. If detected early cervical cancer and oral cancer can be preventable as well due to the presence of pre-cancerous stages. Breast cancer which is hardly preventable can be detected early and have a better survival outcome with timely treatments. Another one third of cancers which are not preventable, as well as there is no proven benefit by early detection can be treated to prevent complications and give a better-quality life for patients until they die. It is necessary to pay attention to provide palliative care and survivorship care services when planning and implementing cancer control activities in a country. Therefore, Cancer Control Programme in the country should be customized according cancer profile.

Cancer early detection

Importance of early detection

It is well known that at least one third of cancers in the world can be detected and treated early and have better health outcomes.

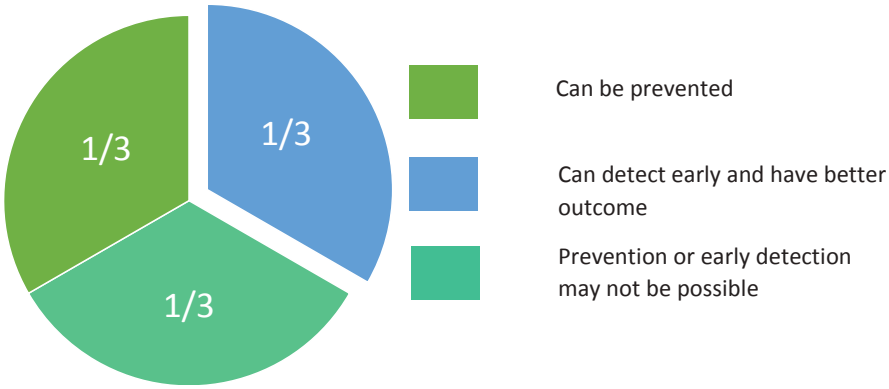


Figure 3: Proportions of cancers can be prevented and early detected

Cancer early detection has two components

1. Screening - to detect pre-cancer lesions or early cancer among asymptomatic population
2. Early diagnosis – to detect early stage cancer among symptomatic individuals

Cancer screening

Cancer screening is a process which invites apparently healthy population to participate and undergo the screening test. With a screening programme people with precancerous or early asymptomatic cancers will be detected. In cancer screening, comparatively large number of actually healthy individuals have to go through the process. In order to carry out a screening programme there should be a system of informing and inviting the target population to participate, administration of the screening test, follow up with test positive patients and refer them for further testing. This process needs to be backed up with timely pathological diagnosis, staging and effective treatment.

Decision to introduce cancer screening programmes should be based on a careful assessment of

- disease burden
- current health system capacity
- available infrastructure
- competing health priorities and resource requirement.

The health care system must be able to cope with patients who produce positive results and thus require further investigations

An evidence-informed assessment of current capacity and potential harms versus benefits must be performed before introducing or scaling a programme for cancer screening.

Early Diagnosis

In early diagnosis, attention will be given to symptomatic patients and aim is to detect cancers in early and treatable stages to have better survival outcome and quality of life. Out of these two strategies which strategy to be selected will be depend on the type of the cancer, available resources, infrastructure requirements, cost estimates, potential harms and benefits and the final impact.

WHO recommendation

An evidence-informed assessment of current capacity and potential harms versus benefits must be performed before introducing or scaling a programme for cancer screening.

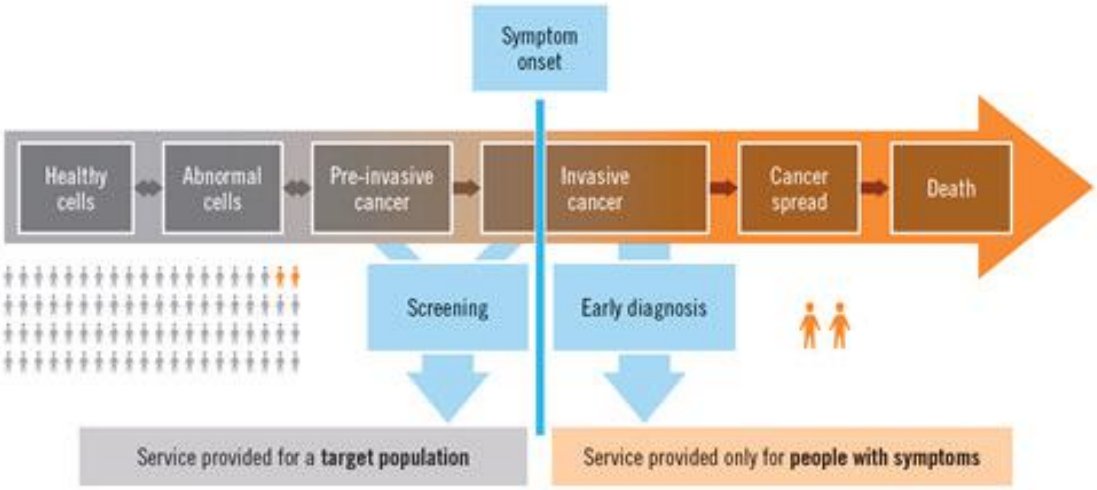


Figure 4: Distinguishing screening for early diagnosis according to onset
Source: Guide to cancer early detection ;WHO – 2017[2]

Cancer early detection has three main components (Figure 4)

1. Awareness of cancer symptoms and accessing care
2. Clinical evaluation, diagnosis and staging
3. Access to treatment, including pain relief

Cancer early detection programme should always be supported by improved community awareness, accurate clinical diagnosis, accepted diagnostic testing and staging, clear and quick referral systems and high-quality treatment options for it to become effective.

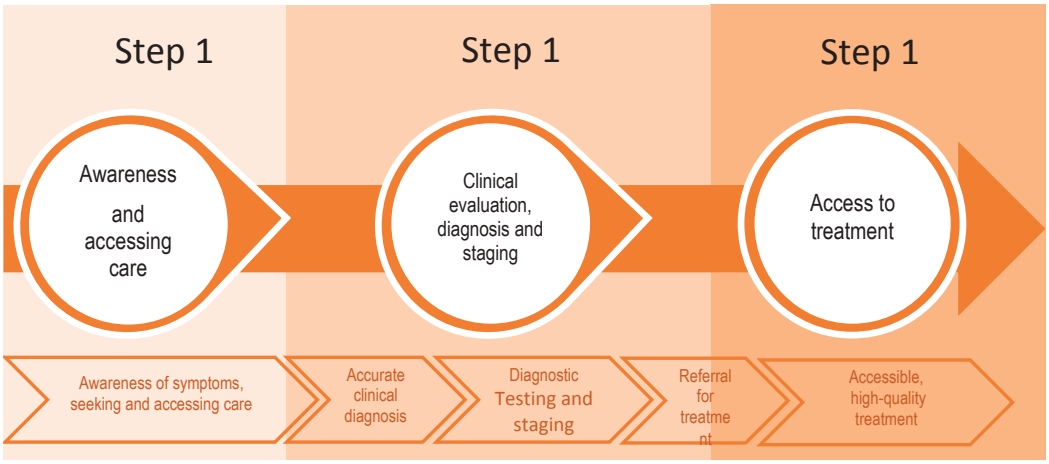
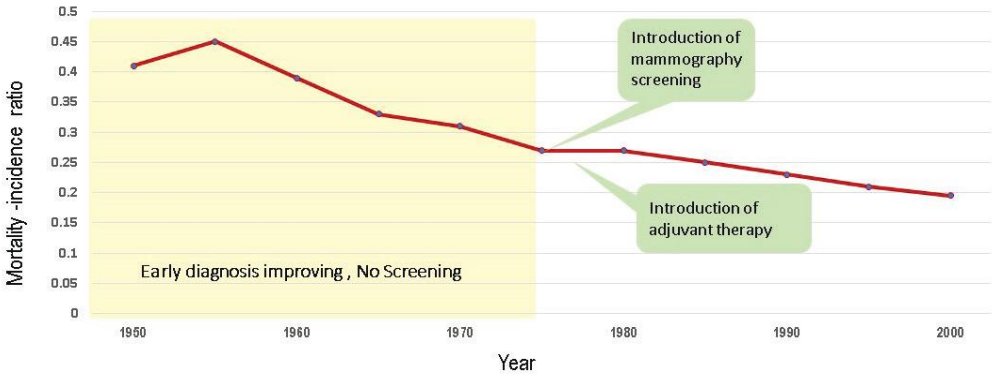


Figure 5: Essential elements of cancer early detection

Source: Guide to cancer early detection; WHO – 2017[2]

There is enough evidence to prove that the early detection has improve the survival and quality of life of the patients[3,4,5]. Figure 6 Illustrates the impact of improving early detection facilities on reduction of mortality due to breast cancer in USA.



Notes: Impact of improved awareness on reduction in breast cancer mortality in the United States as measured by the mortality-to-incidence ratio. A high mortality-to-incidence ratio is a general estimate that a high proportion of people diagnosed with cancer are dying from it. Before the introduction of mammography and adjuvant therapy, there was a significant improvement in breast cancer survival due to early diagnosis.

Figure 6: Example of early diagnosis impact from united states

Source: Guide to cancer early detection ;WHO – 2017& Shulman et al. 2010.

Table 1.1 Key features of cancer early detection and Screening

Parameter	Early diagnosis	Screening programme
Volume of participant	Limited to those with symptoms suspicious for cancer	Entire target population (can be 50–100 times higher number of participants than early diagnosis)
Test	Diagnostic tests only for those with symptoms	Screening test for an entire target population & diagnostic test for those who screen positive
Health system requirements	Facilities and human resources for timely clinical diagnosis, pathology, radiology, staging, access to prompt treatment	Health system requirements for early diagnosis & significant additional resources for inviting and testing an entire target population & additional diagnostic tests for all people who screen positive with recall mechanism & systematic evaluation
Training and human resource needs	Health-care providers to identify symptoms and signs of early cancer, and diagnose, stage and treat cancer	Providers needed for early diagnosis & additional providers, pathologists and/or biomedical laboratory scientists to perform test and interpret results
Public awareness	Attention to signs and symptoms to obtain prompt medical evaluation	Attention to signs and symptoms of cancer & participation in screening programme
Follow-up care	Referral mechanisms to ensure treatment is accessible and affordable	Complex process that includes call–recall mechanism and counselling. Increased responsibility for screening programme to ensure follow-up care of screen positive participants Increased risk of loss to follow-up
Potential benefits	Reduction in stage of disease at diagnosis When linked to treatment reduction in mortality generally evident in three to five years	Potential reduction in incidence in target population if precursor detected and treated by screening (e.g. cervical and colorectal cancers) Reduction in stage of disease at diagnosis in target population (generally earlier stage than early diagnosis) Reduction in mortality when screening delivered effectively and linked to treatment, but not for many years (often >10 years)
Potential for harm	Low: testing limited to only those who have signs and symptoms	Potentially high as test applied to an entire target population. Generally, most who screen positive will not have cancer or precancerous abnormalities, but require additional tests and procedures that can potentially lead to complications, psychological distress & utilization of resources Some may be over diagnosed and overtreated.
Applicability and current scientific evidence	Accepted core component of health services to improve timely diagnosis of cancer. Relevant for all settings, especially those with weaker health systems	Benefits documented in high-resource settings for limited number of cancers (e.g. cervical, breast) Evidence of harms and significant costs in high income countries. Benefits and harms in LMICs not well established except for cervical cancer screening

Adapted from Guide to cancer early detection ;WHO – 2017[2]

The benefit of early detection will depend on the type of the cancer. Cancers with high incidence rates, that have detectable early stages from signs and symptoms and for which early treatment is known to improve the outcome are generally those that benefit most from early diagnosis. Notably, the most common cancers in Sri Lanka including breast, oral , cervical, colorectal cancers have these features. But 2011 cancer incidence data illustrates that 33% of breast cancers, 53% of cervical cancers and 77% of oral cancers were diagnosed at the late stages (Stage III or IV)[6]. These figures highlighted the importance of strengthening the cancer early detection strategies. Primary care service providers in the county have a key role to play in improving the detection of cancers at early stages.

Implementation of cancer early detection programme

As discussed earlier, the early detection programme should be constantly consider all the key elements of the concept of cancer early detection from the planning stage. Most importantly respective community should have a better understanding about the early symptoms of cancers and their health seeking behavior must be improved. The fear and stigma associated with cancer should be addressed. However, this improved awareness must be transformed in to practice by providing accessible, affordable, culturally and gender appropriate health care services.

When the community awareness is improving more and more people will seek medical care. Accurate clinical evaluation , tests for diagnosis , proper staging and prompt referral for the treatment should be improved to match the demand. This is where standard guidelines and protocols are required.

Those who diagnosed with cancer should have access to affordable treatment facilities without any delay. As a general rule WHO recommends the duration from symptom onset to initiation of treatment should be less than 90 days to reduce delays in care[2]. However, it can be varied depending on the type of the cancer and health care setting. Aim is to give the best possible care as early as possible to the patients. There are several identified delays in this process. Table 1.2 summarizes the possible delays in the process of cancer early diagnosis.

Table 1.2 Possible delays in the process of cancer early detection

Step of early diagnosis	Component	Potential delays
Awareness and accessing care (patient interval)	Population aware about symptoms (appraisal interval) Patients with symptoms seek and access health care (health-seeking interval)	Access delay
Evaluation, diagnosis and staging (diagnostic interval)	Accurate clinical diagnosis (doctor interval) Diagnostic testing and staging Referral for treatment	Diagnostic delay
Access to treatment (treatment interval)	Treatment timely, accessible, affordable, acceptable and high quality	Treatment delay

Source: Guide to cancer early detection ;WHO – 2017[2]

It is very important to identify the potential barriers of the system which give rise to above delays. Figure 7 demonstrates the barriers at each steps of the process of cancer early detection.

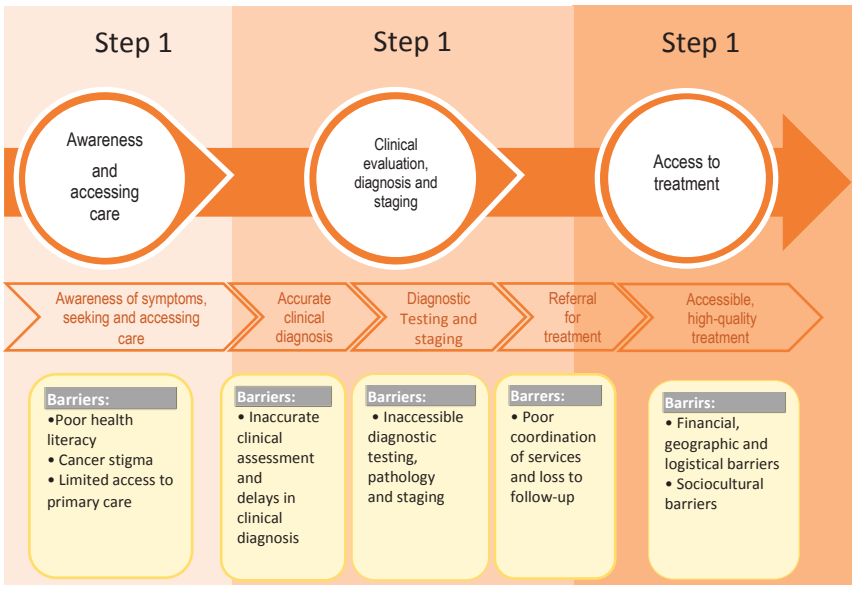


Figure 7: Common barriers to early detection
Guide to cancer early detection ;WHO – 2017[2]

After identifying the possible barriers, it is necessary to take actions to overcome these issues. Figure 8 illustrates the possible interventions that can be adopted to improve the cancer early detection process.

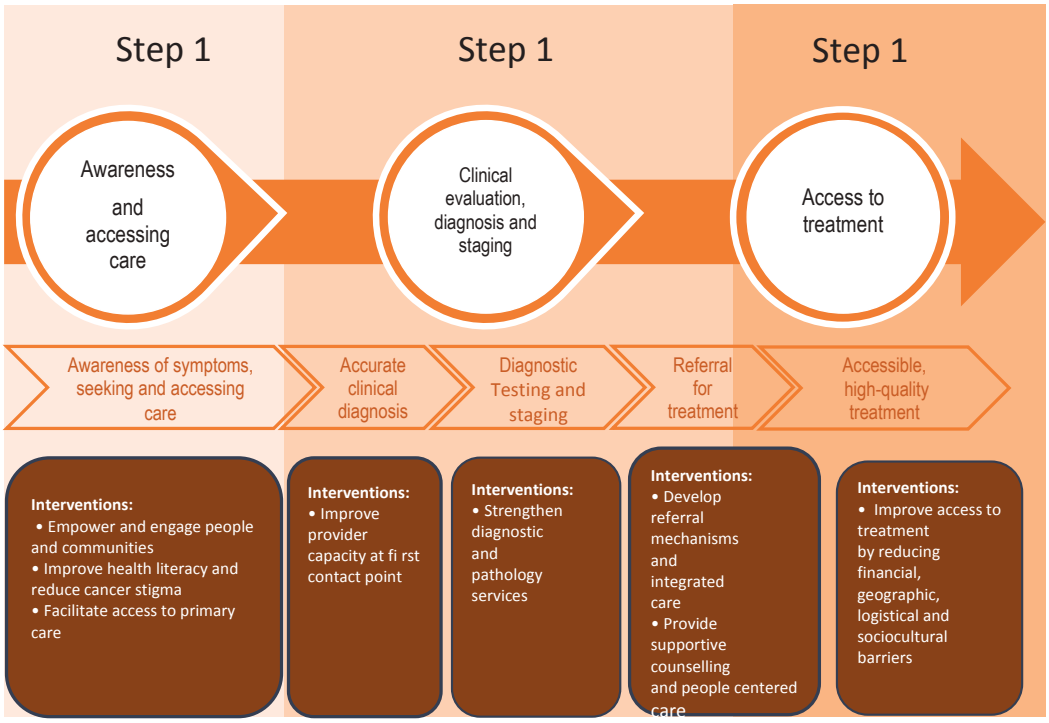


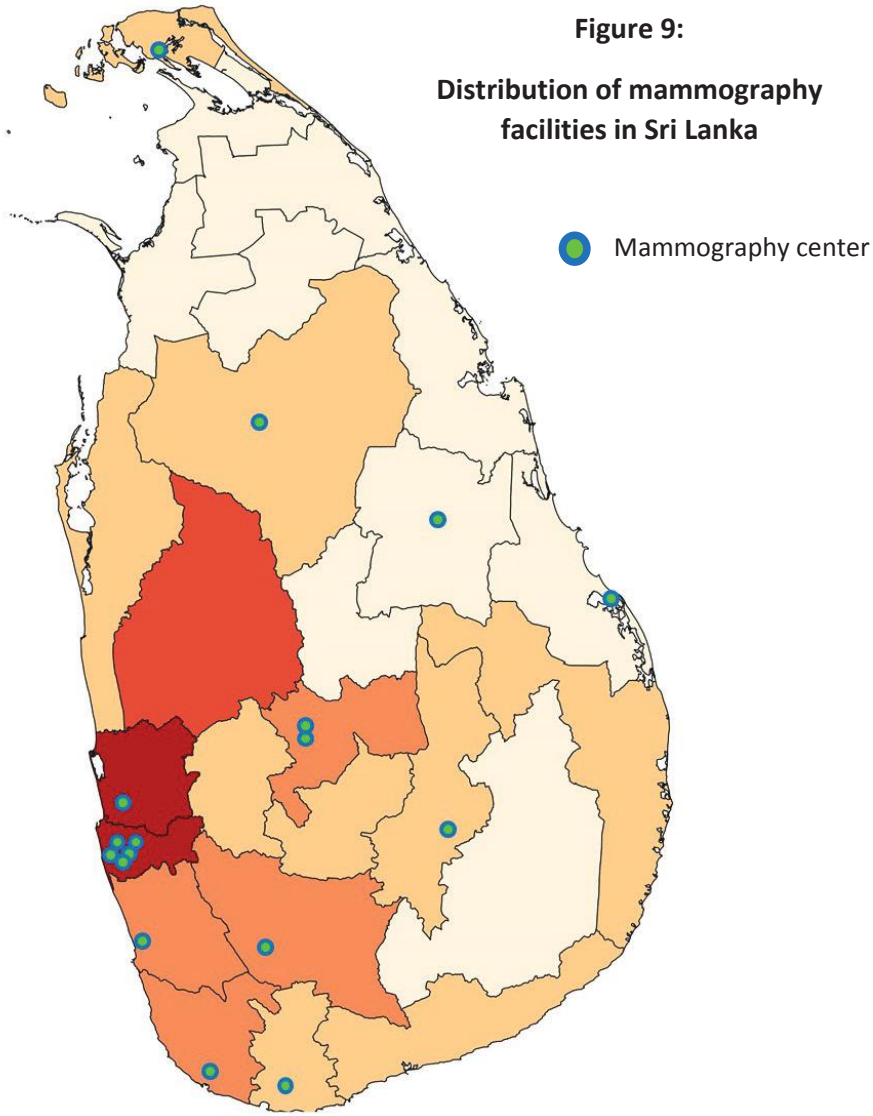
Figure 8: Potential interventions to improve the cancer early detection
Guide to cancer early detection ;WHO – 2017

Cancer care facilities in Sri Lanka

As the national focal point, National Cancer Control Programme (NCCP) is responsible for planning implementing and monitoring the ongoing cancer control activities in the country. Based on the cancer control policy and strategic plan NCCP is in the process of expanding the cancer care facilities in Sri Lanka. Figures 9,10,11 and 12 illustrate the distribution of key cancer care facilities in the country.

Figure 9:

Distribution of mammography facilities in Sri Lanka



Western Province
- National Hospital, Colombo (D-2)
- Apeksha Hospital, Maharagama (D)
- Colombo South Teaching Hospital (A)
- Sri Jayewardenepura General Hospital (D)
- District General Hospital, Kalutara (D)
- Colombo North Teaching Hospital (D)
- Cancer Early Detection Center: (A) Narahenpita

Southern Province
- Teaching Hospital Karapitiya(A,D)
- Base Hospital -Kamburupitiya (A)

Eastern Province
- Teaching Hospital Batticaloa(D)

Northern Province
- Teaching Hospital Jaffna (D,A)

North Central Province
- Teaching Hospital Anuradhapura (D)
- Teaching Hospital Polonnaruwa (A)

North western province
- Teaching Hospital Kurunegala (A,D)

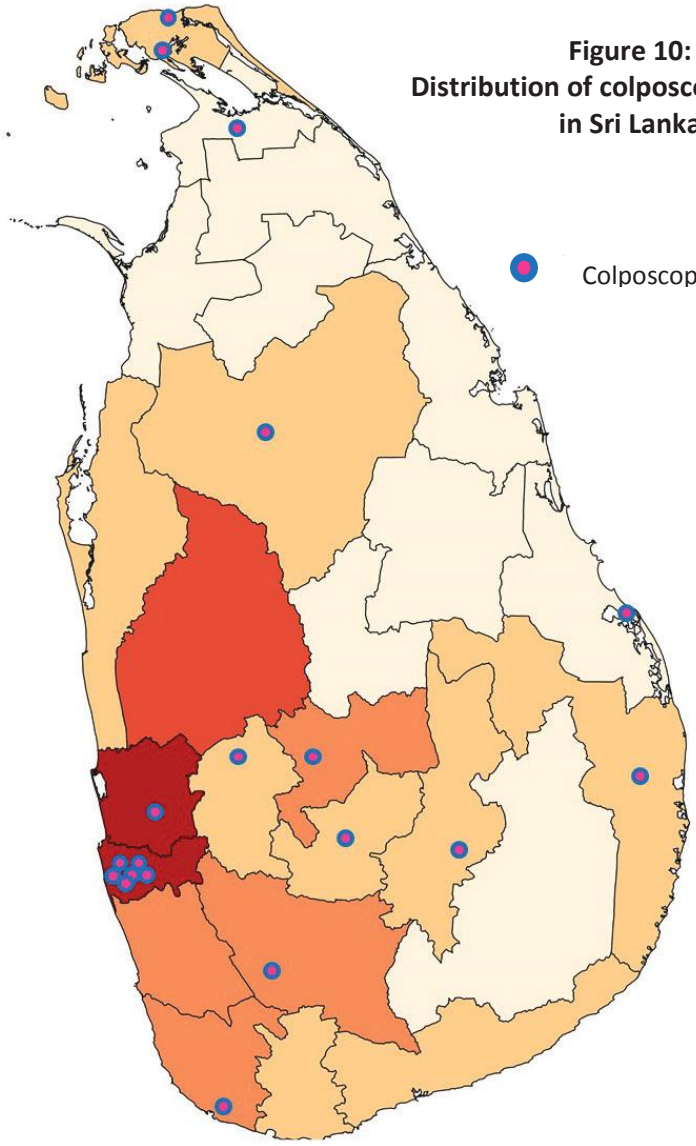
Central Province
- National Hospital Kandy (D)
- Teaching Hospital Peradeniya (D)

Sabaragamuwa Province
- Teaching Hospital Ratnapura (D)

Uva Province
- Provincial General Hospital Badulla (D)

A- Analog D- Digital

Figure 10:
Distribution of colposcopy facilities in Sri Lanka



Western Province

- Castle street Hospital for Women
- De Soysa Hospital for Women
- Family Health Bureau
- Apeksha Hospital, Maharagama
- Colombo South Teaching Hospital
- Sri Jayewardenepura General Hospital
- District General Hospital, Kalutara

Southern Province

- Teaching Hospital Mahamodara

Eastern Province

- Teaching Hospital Batticaloa
- District General Hospital Amapara

Northern Province

- Teaching Hospital Jaffna
- Base Hospital Thellippalai
- District General Hospital Kilinochchi

North Central Province

- Teaching Hospital Anuradhapura

Central Province

- District General Hospital Nuwaraeliya
- Teaching Hospital Peradeniya

Sabaragamuwa Province

- Teaching Hospital Ratnapura
- District General Hospital Kegalle

Uva Province

- Provincial General Hospital Badulla

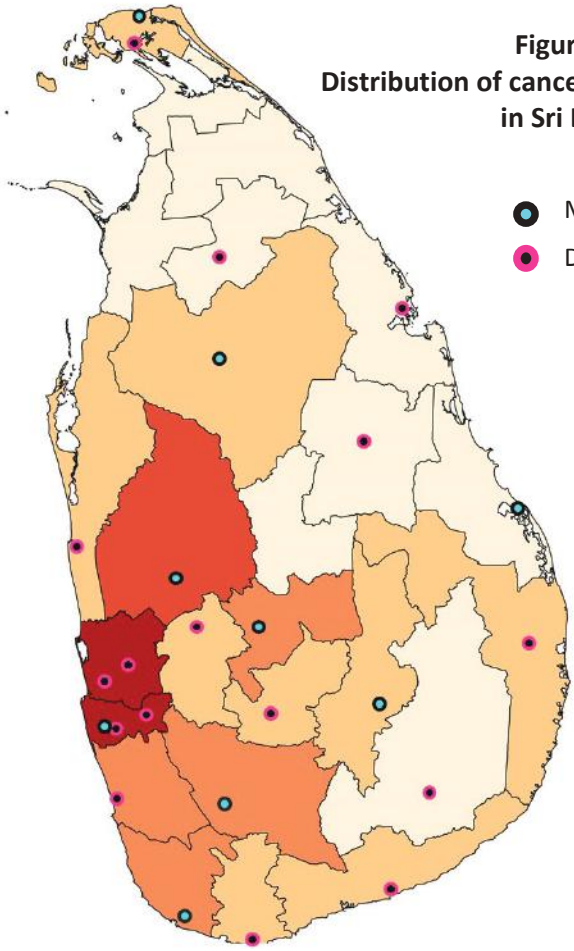


Figure 11
Distribution of cancer treatment centers in Sri Lanka

Main treatment center

District treatment center

Western Province

1. **Apeksha Hospital Maharagama**
2. *Teaching Hospital North Colombo (Ragama)*
3. *District General Hospital Gampaha*
4. *District General Hospital Kaluthara*
5. *District General Hospital Awisswella*
6. *Sir John Kotalawala Defense University Hospital*

Southern Province

7. **Teaching Hospital Karapitiya**
8. *District General Hospital Hambanthota*
9. *District General Hospital Matara*

Eastern Province

10. **Teaching Hospital Batticaloa**
11. *District General Hospital Trincomalee*
12. *District General Hospital Ampara*

Northern Province

13. **Teaching Hospital Jaffna/B.H Thellippalai**
14. *District General Hospital Vavuniya*

North Central Province

15. ***Teaching Hospital Anuradhapura***
16. *District General Hospital Polonnaruwa*

North western province

17. **Teaching Hospital Kurunegala**
18. *District General Hospital Chilaw*

Central Province

19. **National Hospital Kandy**
20. *District General Hospital Nuwaraeliya*

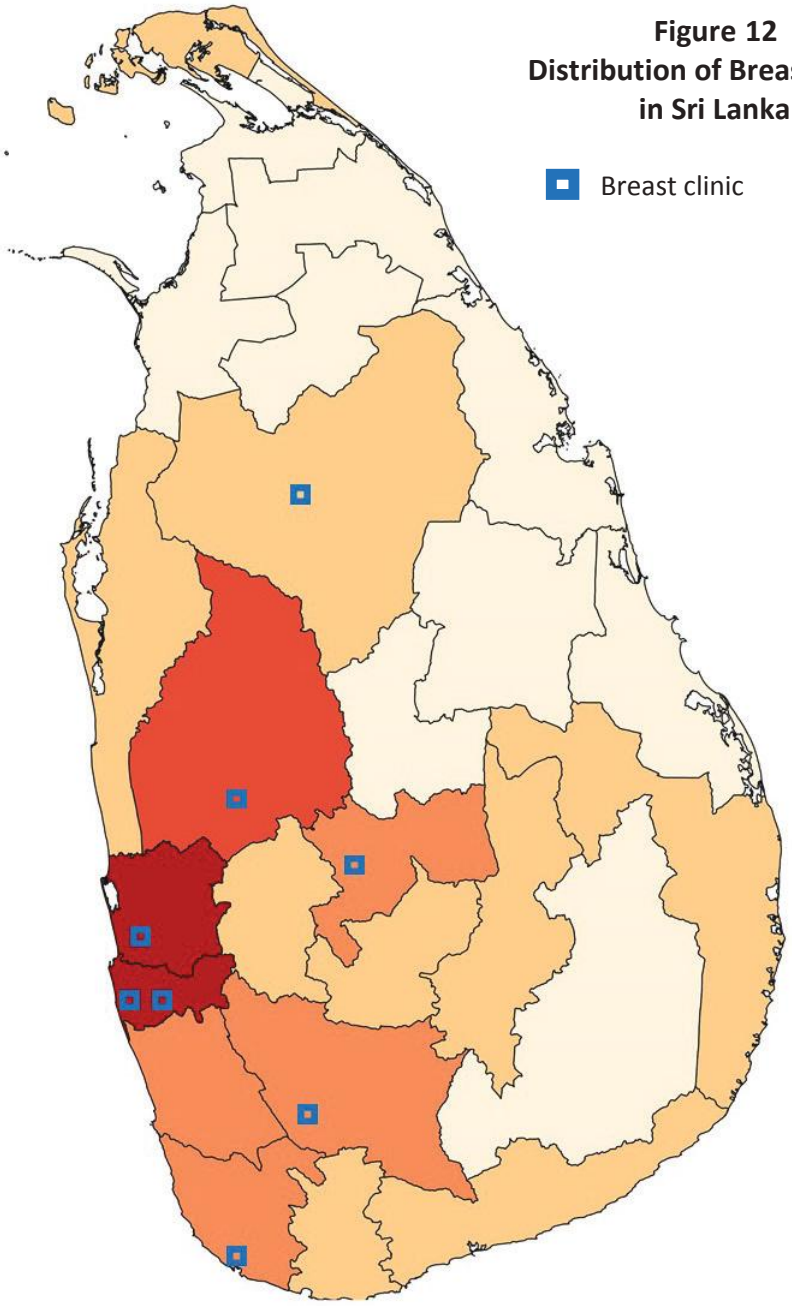
Sabaragamuwa Province

21. **Provincial General Hospital Rathnapura**
22. *District General Hospital Kegalle*

Uva Province

23. **Provincial General Hospital Badulla**
24. *District General Hospital Monaragala*

Figure 12
Distribution of Breast clinics in Sri Lanka



- **National Hospital, Colombo**
- **National Hospital, Kandy**
- **Apeksha Hospital Maharagama**
- **Teaching Hospital North Colombo**
- **Teaching Hospital Karapitiya**
- **Teaching Hospital, Anuradhapura**
- **Teaching Hospital Kurunagala**
- **Teaching Hospital Rathnapura**

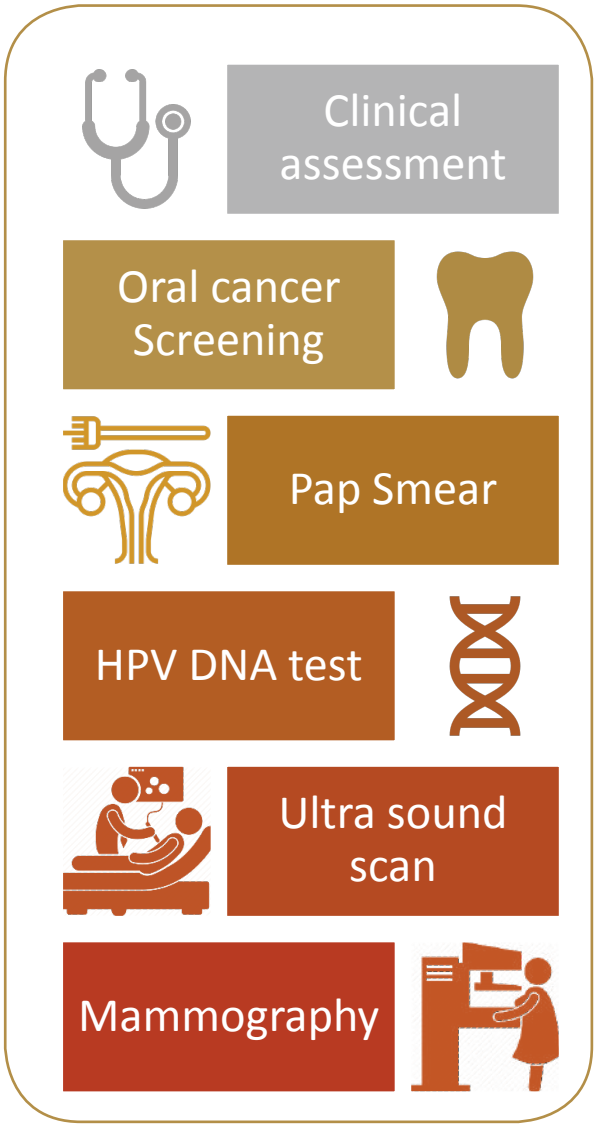


Figure 13 : Facilities available CEDC

Cancer Early Detection Center (CEDC) is the first dedicated center established in Sri Lanka for cancer screening and early detection. This was established in 2004 with the financial support of Colombo branch of international rotary club. This center is functioning as a walk in clinic. Any person with or without a referral note can come to the clinic and obtains the available services. CEDC is functioning during weekdays form 8.00 am to 4.00 pm. Figure 13 illustrates the services available in CEDC for cancer screening and early detection.

Depending on the initial clinical evaluation and test results patients are directly referred to the specialized units by passing the routine patient pathways to minimize the delays.

NCCP is co-ordination with relevant authorities to establish similar type of cancer early detection centers throughout the country (one per province).

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