health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

Breast Cancer Prevention and Control Policy

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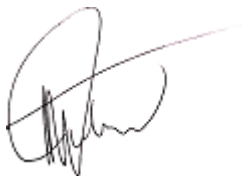
FOREWORD

The Breast Cancer Prevention and Control Policy is an important document aimed at prioritising breast cancer awareness, prevention, treatment and care in South Africa. It provides the clinical support for women, who are both at-risk of developing the disease later in life and are currently undergoing treatment, to survive and live healthy lives.

Breast cancer, along with cervical cancer, has been identified as a national priority in South Africa. Breast cancer is the most prevalent cancer and a leading cause of death among South African women. The increasing incidence of breast cancer is a major health concern with 19.4 million women aged 15 years and older at-risk of contracting the disease. Per the National Cancer Registry in 2012, 8 203 new cases of breast were observed. Given the recent advances in medicine and technology, however, we have a tremendous opportunity to attack breast cancer energetically and effectively with a revised national programme.

Against this background I am delighted to release the revised policy on breast cancer prevention and control. And it is being launched during an exciting period in the history of healthcare in South Africa –the introduction of the National Health Insurance. This updated policy entails the implementation of interdependent strategies: (i) increasing early recognition of breast cancer, (ii) treating breast cancer more effectively, and (iii) providing timely treatment and palliative care for invasive cancer. It also includes the administration of Herceptin for early stage cancer at designated sites nationally.

We envisage that this policy, along with the accompanying programme implementation strategy and clinical guidelines, will be applied in the public sector at all levels of the health system thereby positively contributing to reducing breast cancer's incidence and mortality rates as well as improving the quality of life for women in South Africa.



Dr PA Motsoaledi
Minister of Health
June 2017

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The national Department of Health would like to acknowledge the exceptional contribution of the writing group of breast cancer clinicians responsible for the KwaZulu-Natal breast cancer policy and Breast Interest Group of Southern Africa (BIGOSA). The majority of evidence for this policy is derived from their intellectual input and literature review. The authors of this document would like to make clear however, that any conclusions in this document and standards derived from this evidence are not necessarily the opinion of this writing group and should not be taken as such.

The contributors consisted of breast surgeons, plastic and reconstructive surgeons, oncologists, radiologists, nuclear physicians, pathologists, geneticists and obstetrics and gynaecology specialists. In addition, experts in the various fields, including civil society organisations and other interest groups, were also contacted when necessary for further opinions. It is also worth noting that although considerable reference was made to the Malaysian guidelines because both countries are classified as middle-resource countries and demonstrate many similarities, this Breast Cancer Prevention and Control Policy document is aligned to the healthcare situation in South Africa and the needs envisaged by the people of this country.

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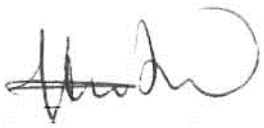


MP Matsoso
Director-General: Health
Date: June 2017

ABBREVIATIONS AND ACRONYMS

ACRA	American College of Radiologists
ADH	Atypical ductal hyperplasia
ALH	Atypical lobular hyperplasia
ALND	Axillary lymph node dissection
ASIR	Age specific incidence rate
ASR	Age standardised rate
AUS	Axillary ultrasonography
BCCCP	Breast Cancer Comprehensive Control Policy
BCN	Breast care nurse
BCS	Breast conserving surgery
BI-RADS	Breast imaging-reporting and data system
BMI	Body mass index
BPM	Bilateral prophylactic mastectomy
BPSO	Bilateral prophylactic salpingo-oophorectomy
BRCA	Breast cancer gene mutation
BRCA1	Breast cancer gene 1
BRCA2	Breast cancer gene 2
BSE	Breast self-examination
CBC	Contralateral breast cancer
CBE	Clinical breast examination
CI	Confidence interval
CISH	Chromogenic in-situ hybridization

CMF	Cyclophosphamide, methotrexate and fluorouracil
CNB	Core needle biopsy
CPM	Contralateral prophylactic mastectomy
CT	Computerised tomography
DCIS	Ductal carcinoma in situ
DFS	Disease free survival
DOH	Department of Health
ER/PR	Estrogen-receptor/progesterone receptor
ESMO	European Society for Medical Oncology
FDG-PET	Fluorodeoxyglucose-positron emission tomography
FEC	5-fluorouracil, Epirubicin, and cyclophosphamide
FISH	Fluorescent in-situ hybridization
FNAC	Fine needle aspiration cytology
H&E	Haematoxylin and eosin
HER-2	Human epidermal growth factor receptor 2
HERA	Herceptin Adjuvant
HR	Hazard ratio
IDC	Invasive ductal carcinoma
IHC	Immunohistochemistry
ILC	Invasive lobular carcinoma
LABC	Locally advanced breast cancer
LCIS	Lobular carcinoma in situ
LHRH	Luteinizing-hormone-releasing hormone
LN	Lobular neoplasia

LTR	Lifetime risk
MMG	Mammography
MRI	Magnetic resonance imaging
NCCN	National Comprehensive Cancer Network
NCR	National Cancer Registry
NICE	National Institute for Health and Care Excellence
OS	Overall survival
PCHCT	Palliative and hospice care team
Pcr	Pathological complete response
PCR	Polymerase Chain Reaction
PET/CT	Positron emission tomography/computerised tomography
PPV	Positive predictive value
QoL	Quality of life
RCT	Randomised control trial
RR	Relative Risk
RRSO	Risk reducing salpingo-oophorectomy
SISH	Silver-enhanced in-situ hybridisation
SLNB	Sentinel lymph node biopsy
SR	Systematic review
TRAM	Transverse rectus abdominismyocutaneous
WHO/IARC	World Health Organization / International Agency for Research on Cancer

SECTION A:BACKGROUND AND THE SOUTH AFRICAN CONTEXT

CHAPTER 1: INTRODUCTION AND BACKGROUND

Breast cancer is both the most common cancer and the leading cause of cancer deaths among women worldwide. According to the 2015 Global Burden of Disease (GBS) study, of the 17.5 million cancer cases globally, breast cancer accounted for 2.4 million new cases and 523 000 deaths in2015. Although breast cancer is more common in industrialised countries, the World Health Organization-International Agency for Research on Cancer (WHO/IARC) reports increasing breast cancer trends worldwide. This is further supported by the 2015 GBD study, which reports a 43 per cent increase in new cases. This increase in new cases is due to population growth and aging rates, which contribute an additional 13 and 15 per cent respectively. With regards to lower and middle-income countries (LMIC), studies suggest a higher burden of mortality in less developed countries with incidence ratios of 0.44 compared to 0.29 in more developed countries. See table below. Concern around the increase in cancer incident cases and rising trends in cancer risk factors has led to the recognition that cancer not only threatens development but also that many cancer cases and deaths can be prevented. To this end, as reflected in Sustainable Development Goal 3: *"to reduce, by one-third premature mortality from non-communicable diseases through prevention and treatment, by 2030"* the international health community has begun focusing on global oncology. In addition, the World Health Assembly together with the World Cancer Declaration and Global Action Plan for the Prevention and Control of Non-Communicable Diseases (NCDs) 2013 – 2020 have formalised strategies and targets to prevent and control cancer.

Table 1: Female breast cancer incidence rates, mortality rates, and mortality: incidence ratios for selected countries and the world, by World Bank income classification (Wadler et al, 2011)

Country name	Region	Incidence rate[cf]	Mortality rate[df]	Mortality to incidence ratio[e]
World	World	37.4	13.2	35.3
Middle incom-upper[b]				
Botswana	**Africa**	**33.4**	**25.0**	**74.9**
Brazil	Latin America	46.0	14.1	30.7
Colombia	Latin America	30.3	12.5	41.3
Gabon	**Africa**	**18.2**	**13.1**	**72.0**
Lebanon	Middle East	52.5	23.4	44.6
Malaysia	East Asia	30.8	13.5	43.8
Mexico	Latin America	26.4	10.5	39.8
Namibia	**Gabon**	**24.7**	**18.8**	**76.1**
Panama	Latin America	29.0	12.0	41.4
Peru	Latin America	35.1	14.0	39.9
Romania	Europe	44.3	16.7	37.7
South Africa	***Africa***	***35.0***	***16.4***	***46.9***
Turkey	Europe	22.0	9.7	44.1
Middle income lower[b]				
Bolivia	**Latin America**	**24.7**	**11.6**	**47.0**
Honduras	Latin America	25.9	12.1	46.7
Jordan	Middle East	33.0	14.6	44.2
Nigeria	**Africa**	**31.2**	**21.9**	**70.2**
Sudan	**Africa**	**22.5**	**16.6**	**73.8**
Low income[b]				
Mozambique	**Africa**	**3.9**	**2.8**	**71.8**
Tajikistan	**Europe**	**13.2**	**6.2**	**47.0**
Uganda	**Africa**	**18.3**	**13.4**	**73.2**
Vietnam	East Asia	16.2	7.1	43.8
Yemen	Middle East	35.1	15.6	44.4
Zimbabwe	**Africa**	**19.0**	**14.1**	**74.2**
High income[b]				
Australia		83.2	18.4	22.1
Italy	Europe	74.4	18.9	25.4
Japan	Asia	32.7	8.3	25.4
United States	North America	101.1	19.0	18.8

Notes: (a) bold type indicate higher mortality: incidence ratios than South Africa, (b) income classification based on World Bank list of economies (July 2009) [8], (c) incidence rate (IR): number of new cases of breast cancer per 100,000, age-standardized to the world population (ASR), (d) mortality rate (MR): Number of deaths due to breast cancer per 100,000 (ASR), (e) Mortality to Incidence Ratio = MR/IR, (f) IR and MR from GLOBOCAN 2002 [13].

CHAPTER 2: THE SOUTH AFRICAN CONTEXT

2.1 Epidemiology

Breast and cervical cancer are leading causes of cancer related deaths in South African women, together accounting for 38.5 per cent of all cancers diagnosed in women(1). In 2013, deaths from breast cancer and cancers of the female genital tract accounted for 0.7 and one per cent of all deaths in South Africa respectively (2). Breast cancer is the most common form of cancer to affect women in South Africa and in 2013 was responsible for 20.8 per cent of female cancers and more than 10 per cent of the entire cancer burden (1). Per the 2012 National Cancer Registry, 8 203 new cases of breast were observed and the age standardised incidence rate of 35.12 per 100 000 per year.

In South Africa cancer morbidity is collated by the National Cancer Registry (NCR), a specialised division of the National Health Laboratory Services (BIGOSA doc)**.** The cancer methodology and procedures follow those of the WHO-IARC.

The latest available South African breast cancer statistics were published in 2011. When compared with the statistics published in 2010, there appears to have been no significant increase in the number of breast cancer cases.

In 2011 breast cancer was the leading cause of cancer among South African women accounting for 21.46 per cent of all new cancers. An average of 6 849 new cases per annum was reported: 19.89 per cent occurred in white women, 20.87 per cent in black women, 26.63 per cent in coloured women and 35.44 per cent in Asian women. By comparison, an average of 6 125 new breast cancer cases per annum was reported in 2010, which accounted for 20.6 per cent of all new female cancer cases.

In accordance with WHO-IARC methodology the statistics were reported in terms of lifetime risk (LTR) from zero to 74 years of developing cancer as expressed as one in eight number of people; age standardised rate (ASR) per 100 000 (world standard population) and age specific incidence rates (ASIR).

In 2011 the overall lifetime risk was 1:29, but varied from 1:12 in white women to 1:50 in black women. The risk in coloured women was 1:18 and in Asian women was 1:25.

The overall ASR of breast cancer in 2011 was 31.43/ 100 000 compared to 25.86/ 100 000 in the previous report (2010). In terms of population groups, this translated to 74.55/ 100 000 in whites, 47.34/ 100 000 in coloureds, 31.43/ 100 000 in Asians and 18.63/ 100 000 in blacks. These figures were comparable to those of the 2010 report in black females: 18.33/ 100 000, had decreased in Asian females (46.04/ 100 000), but had increased in white: 49.02/ 100 000 and coloured females (37.35/ 100 000)

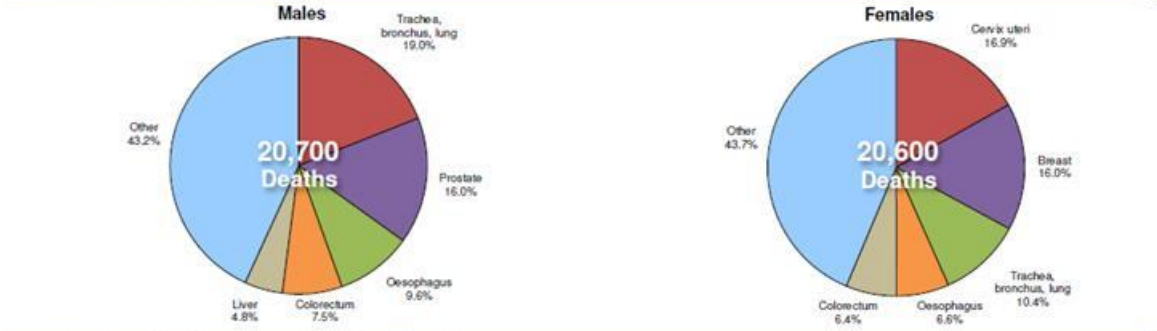
Several studies have investigated the lower incidence of breast cancer in black South African women compared with other population groups in the country. They concluded that certain factors, known to be important in the epidemiology of breast cancer, are unique in this racial group. These factors include late menarche, early age of first birth, multi-parity, universal and prolonged lactation, low use of hormone replacement therapy and a diet low in fat/ high in fibre. These data parallel reports in African-American, Hispanic and Native American women. However, a more recent study from Johannesburg revealed that increased urbanisation and ongoing changes in the lifestyle of urban African women have resulted in a decrease in the intensity of the above protective factors. Changes in these respects have been associated with rises in the incidence of the disease.

South Africa

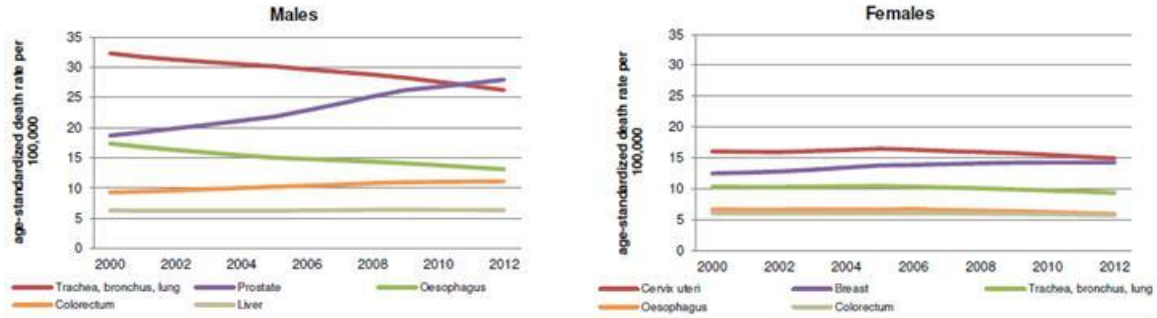
Total population: 52,386,000
Income group: Upper middle

Total deaths: 608,000
Life expectancy at birth: Total:59 Males:56 Females:62

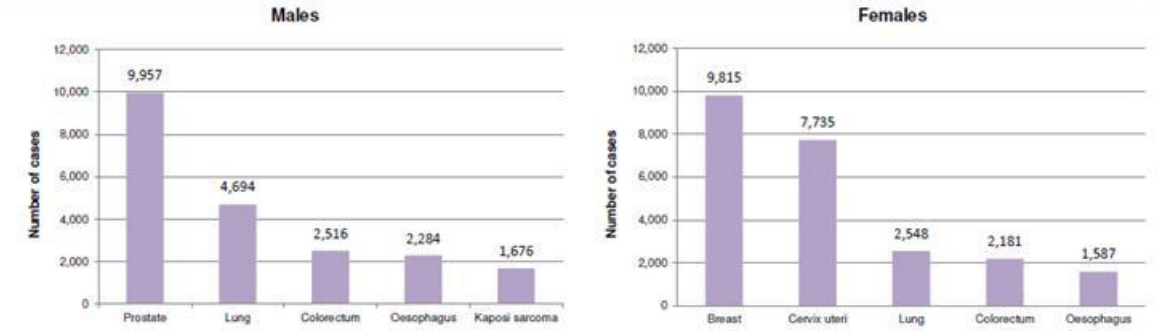
Cancer Mortality Profile



Age-Standardized Cancer Mortality Trends



Cancer Incidence



Adult Risk Factors

	Males	Females	Total
Current tobacco smoking (2011)	27.7%	7.7%	17.6%
Total alcohol per capita consumption, in litres of pure alcohol (2010)	18.4	4.2	11.0
Physical inactivity (2010)	40.5%	53.1%	47.1%
Obesity (2014)	14.6%	36.0%	25.6%
Household solid fuel use (2012)	-	-	13.0%

World Health Organization - Cancer Country Profiles, 2014.

Figure 1: World Health Organization Cancer Country Profile, 2014

2.2 Challenges facing South Africa

There are several factors that were taken into consideration when developing this policy document. These include the following:

The high HIV prevalence in the country

- **Place of residence (urban versus rural), socio-economic status and educational level:** The high rural population in South Africa. Women who live in rural area are disadvantaged regarding access to appropriate information and access to services.
- The default community messaging strategy is through written material. Furthermore, the medium of communication is written in English which excludes most of women living in rural areas.
- The limited level of understanding of the disease process, especially among the rural communities, due to mixed and often poorly understood messages communicated primarily in writing and in the English language, which tends to exclude the already marginalised
- **Barriers in accessing services**: Lack of infrastructure and equipment in many provinces as well as significant disparities and inequitable distribution of services, especially in terms of availability of specialised healthcare services in South Africa, render such services inaccessible to many.
- **Poor referral systems and problems with transport:** In some cases where a woman has access to a primary healthcare facility for screening, the referral to the next level of care is delayed due to poverty or financial challenges.
- **Healthcare workers skills:** Inadequately trained healthcare workers delay diagnosis and referral to the next level of care (KZN DOC).
- **Data accuracy:** Cancer incidence is largely under-reported due to a lack of population based data/registry. The National Cancer Registry is a pathology-based registry only, and is currently not up to date.

SECTION B: POLICY FRAMEWORK

CHAPTER 3: GENERAL POLICY DIRECTION

3.1 Vision

To introduce a system of breast cancer control that will:

(I) reduce breast cancer morbidity and mortality by promoting breast healthcare awareness and access to early breast cancer detection and, diagnosis, appropriate treatment and palliative care

(II) serve to streamline the overall breast care service

3.2 Overall aim

To ensure that South Africans have access to a network of breast units, which provide timely breast management. The desired outcomes of units should include early disease recognition, work-up and treatment and thus ensure expeditious movement through the healthcare system with shortening of waiting times, and effectively prevention or minimisation of morbidity and mortality due to disease progression.

3.3 Goals:

- improve survival
- decrease time to presentation and time to treatment
- decrease stage at presentation
- improve quality of life in survivorship and palliation
- effectively monitor and evaluate programme implementation and the impact of breast cancer interventions.

3.4 Strategic objectives

- to improve early detection rates by promoting community awareness, and educating communities and health care workers on breast healthcare and breast cancer management
- to facilitate referral pathways for patients with breast healthcare concerns
- to provide guidelines for establishing appropriate facilities for the management and care of breast conditions
- to set standards for optimal care and management of breast conditions
- to provide a framework for auditing standards and outcomes

CHAPTER 4: POLICY GUIDING PRINCIPLES AND FRAMEWORK FOR CANCER PREVENTION AND CONTROL

There are many challenges to breast cancer control in LMICs such as South Africa which finds itself facing demanding health concerns such as access to clean water and infectious disease control, some may question the priority of the time and expense needed to initiate a successful programme. The intention has been to develop a policy and guidelines that will suit both the current situation as it stands and the possibility of future developments in the country regarding breast healthcare**.**

4.1 The development of this policy document is guided by:

Global framework:

- South Africa recognises the United Nations' Resolution adopted by the General Assembly on September 25, 2015: Transforming our world: the 2030 agenda for sustainable development. The development of the policy is thus guided by sustainable development goal (SDG) 3: *"Ensure healthy lives and promote well-being for all at all ages"*. One critical SDG target states that governments must ensure universal access to sexual and reproductive healthcare services, including family planning, information and education, and the integration of reproductive health into national strategies and programmes by 2030.

National frameworks:

- In recognising that health and development of the country are integrally linked, health reform in South Africa is firmly embedded in the country's **National Development Plan 2030** ***Our Future – make it work*****.** The NDP aims for an inter-connectedness with the World Health Commission on the Social Determinants of Health which are considered key to any equitable health service delivery platform and includes the need to: improve the conditions of daily life, tackle inequitable distribution of power, money and resources and measure the problem, evaluate actions and expand the knowledge base (NCD DOC).

- South Africa is in the process of introducing the **National Health Insurance (NHI)**, in line with the National Development Plan. The NHI is a health financing system whose aim is to ensure that all South Africans have access to affordable, quality health services, based on health needs, rather than socio-economic status. Quite importantly, NHI also recognises that there is a need for massive reorganisation of the healthcare system to create a new platform for service provision which will also forms the basis for this policy development.

Policies, strategic plans and programmes

- Strategic Plan for Maternal, New-born, Child and Women's Health and Nutrition (MNCWH&N) in South Africa (2012-2016), and the National Contraception and Fertility Planning Policy and Service Delivery Guidelines (2012) cover other SRH priorities, and provide platforms for the implementation of the policy. All the above guidelines allow the full integration of this policy with other existing policies in the department to comprehensively address the non-communicable diseases. **Integration**: The policy is providing synergy with other existing policy guidelines that are aiming to ensure universal access to sexual and reproductive health services.

Outcome focus

- The main focus is on promoting early detection and treatment. This policy includes prevention, screening, diagnosis, treatment, care, and palliative care services. It includes the service delivery package in the community, primary healthcare, district, regional and tertiary hospitals and private institutions.

Special considerations:

As the policy is aligned with the WHO recommendations, in the South African context special considerations for other high risk groups are made such as women living with HIV, sex workers, adolescents and migrants.

Community engagement and involvement

Included in the policy is the role of civil society organisations and the various ways of raising community the awareness around breast cancer.

4.2 Framework for cancer prevention and control

Prevention of cancer should be integrated with prevention of chronic diseases and other related areas of healthcare (such as reproductive health, hepatitis B immunisation, HIV/AIDS, occupational health and environmental health). Around 40 per cent of all cancers are now preventable by modifying or reducing the vulnerability of persons exposed to the main risk factors (WHO, 2008).

Early detection, **diagnosis and treatment**: the aim should be to detect and treat breast cancer disease, by ensuring access to appropriate diagnostic and treatment procedures in designated breast units. The most effective and efficient treatment is linked to early detection programmes and follows evidence-based, gold standards of care.

Survivorship and palliative care: Ensuring that these services meet the needs of all patients requiring relief from symptoms or pain as well as the needs of patients and their families for psychological and supportive care. This is particularly true when patients are in advanced stages and have a very low chance of being cured, or when facing the final or terminal phase of the disease.

Multidisciplinary teams of healthcare professionals at the specialist units of care should evaluate the patient early in the management process and guide treatment and follow-up. All relevant healthcare professions should be represented in the team, including radiation oncologists, surgeons, medical oncologists, paediatric oncologists, haematologists, radiologists and oncology nurses, as well as psychosocial and rehabilitation staff. Teams should comprise of members from several stakeholders and partners as well as be situated at various levels of care, from primary to tertiary/quaternary levels.

The multilevel context perspective for cancer control considers nested levels of influence on care, from individual patients and their families to provider teams, organisations, communities, provinces and the nation (Taplin, 2012). Factors at each of the levels shown in figure 2 can affect the quality of care and improve health outcomes and should be considered during the creation of intervention strategies.

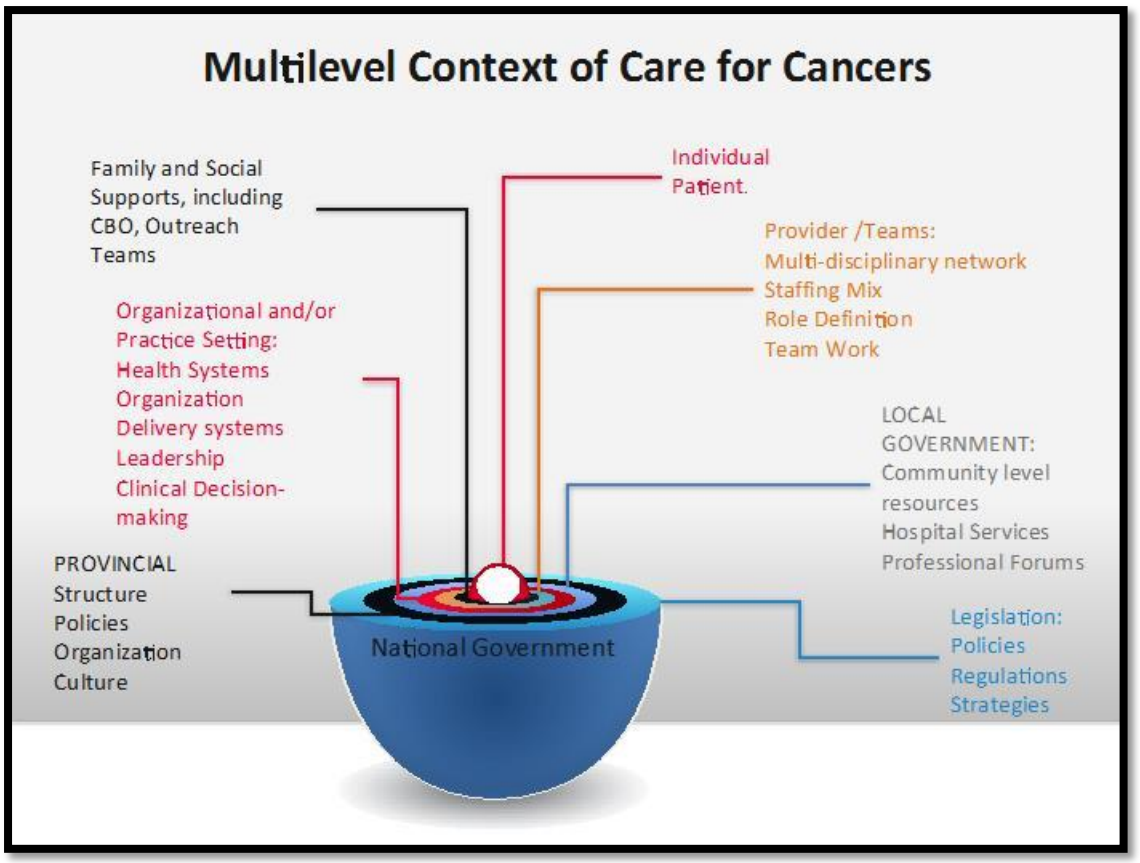


Figure 2: Multilevel context of care (Source: Adapted from Taplin, 2012)

SECTION C: STANDARDS OF CARE

The breast cancer policy has been developed as a series of standards of care. The aim of this process is to ensure high-quality and appropriate care is administered in the diagnosis and management of patients irrespective of their geographical location or social circumstances. Describing standards of care also allows continuous auditing in all facilities providing care, with coordination within and between provinces.

Within breast disease management, eight *key areas* for service delivery have been identified. Nested within these are a number of *objectives* each focusing on an important part of breast cancer care. The objectives focus on a number of standards, which are then explained in a rationale section.

Further to the *clinical rationale* for the standard of care are a number of notes for good *clinical practice*. These are areas which can direct good care but fall short of being measurable standards, yet help direct to the standards. These points are supported by literature or expert opinion, which is either referenced or addressed in the further discussion. These standards are designed to complement current good practice.

Monitoring and evaluation points describe key performance indicators derived from the standards of care.

These standards have been designed to be applicable to all situations in South Africa. Whilst individual provinces may vary in its model of how the standards are achieved, the clinical notes and standards should act as guidance for all breast services in the country.

The key areas are:

Key Area 1	***Prevention and early detection, screening and genetic assessment***
Objective 1	Screening and early diagnosis

Objective 2	Risk assessment
Objective 3	Genetic services
Objective 4	Management of women known or suspected to have a breast cancer susceptibility gene mutation
Key Area 2	***Timely access to care***
Objective 5	Specialist breast units for the diagnosis and management of breast disease
Objective 6	Clear referral pathways and access points to breast diagnosis
Objective 7	Clear referral pathways and access points in breast cancer care
Key Area 3	***Assessment, diagnosis and staging***
Objective 8	Triple assessment
Objective 9	Staging
Objective 10	Supportive care (including psychology)
Objective 11	Patient navigation
Key Area 4	***Treatment of breast cancer***
Objective 12	Surgery (early and advanced breast cancer)
Objective 13	Breast reconstruction (immediate versus delayed)
Objective 14	Systemic therapy in early stage breast cancer
Objective 15	Systemic therapy in locally- advanced stage breast cancer
Objective 16	Systemic and local therapy in metastatic breast cancer

Objective 17	Radiotherapy in breast cancer
Key Area 5	***Palliative care in breast cancer***
Objective 18	Palliative care management for patients
Key Area 6	***Follow-up and surveillance in breast cancer***
Objective 19	Appropriate cost-effective strategy for follow-up
Objective 20	Lymphedema care
Key Area 7	***Data, monitoring and research***
Objective 21	Monitoring and research
Key Area 8	***Community outreach and engagement***
Objective 22	Community engagement and CSOs

Key Area 1: Prevention and early detection, screening and genetic assessment

Objective 1: Screening and early diagnosis

Standard 1.1	Women over 40 years attending a Primary Health Clinic will have a clinical breast examination (Provider Initiated Screening Clinical Breast Exams (PISCBE)) biannually.
Standard 1.2	All women attending Primary Health Clinics will be given opportunistic breast education including printed education material and taught breast self-examination.
Standard 1.3	Awareness messages should be disseminated for communities and healthcare workers that any woman who notices a change in breast should report promptly to a health facility for further assessment.

Rationale

Early detection followed by appropriate treatment is currently the most effective strategy to reduce breast cancer mortality. The overall success works on the assumption that the smaller the cancer detected, the better the survival outcome. Early detection programme is the organised and systematic implementation of interventions that comprise early diagnosis, screening (if sufficient resources are available), diagnosis, treatment and follow-up.

Early diagnosis is the awareness (by the public or health professionals) of early signs and symptoms of breast cancer in order to facilitate diagnosis before the disease becomes advanced, thus enabling more effective and simpler therapy. This concept is also referred to as “down-staging” by some researchers. Screening is the systematic mass application of a simple screening test in a presumably asymptomatic population at regular intervals in order to identify individuals with an abnormality suggestive of specific cancers, who then receive further investigation

Ideally a screening tool for breast cancer would reduce mortality from breast cancer while having a low false alarm rate and being relatively cheap. The ideal screening test would be simple, inexpensive and effective. Public awareness is augmented by

training primary healthcare staff to perform resource-appropriate and cost-effective screening. To be effective, national screening programmes have to target women who will benefit the most, together with being affordable and sustainable.

Screening modalities

Clinical breast examination (CBE) refers to a breast examination performed by a trained healthcare worker. CBE is relatively simple and inexpensive, but its efficacy in reducing mortality from breast cancer has not been directly tested in a randomised controlled trial. CBE is more likely to detect cancers that are potentially lethal.

The Canadian national breast screening study II (CNBSS-II), which randomised women aged 50 to 59 years to mammography and CBE or CBE alone, concluded that the mammographic detection of impalpable cancers does not contribute to reduced mortality from breast cancer. These results are encouraging and may result in CBE assuming particular importance in resource-strapped countries where mammography is unavailable or expensive, and disease is at an advanced stage at time of diagnosis. CBE has sensitivity of 40 to 69 per cent and specificity of 88 to 99 per cent.

Economic models suggest that clinical breast examination by ancillary health workers (PI-CBE) performed annually from the ages of 40 to 60 years can be nearly as effective as biennial mammographic screening for reducing breast cancer mortality in developing countries, but at substantially lower cost. Any screening programme, irrespective of modality, should encourage early diagnosis of breast cancer, especially in women between the ages of 40 to 69 years. Thus opportunistic CBE and awareness promotion should be pursued in women between those ages who attend primary healthcare centres or hospitals for other reasons.

Breast self-examination (BSE) fulfils the criteria of being simple and inexpensive. Systematic BSE has been recommended for over 70 years, despite lack of compelling evidence of its efficacy in reducing deaths from breast cancer. Numerous non-randomised trials have produced conflicting results. However, early results of two randomised trials conducted in Russia and China suggest that it would not be effective in reducing mortality from breast cancer.

A further contentious issue relates to what constitutes a competent BSE and how often it should be performed. Variations, inconsistency and complexity in suggested techniques of self-examination have been considerable and served to confuse women.

The Shanghai trial, published in 2002 has provided high quality evidence of the lack of effect of BSE in reducing breast cancer mortality. The results after 10 to 11 years showed that the proportion of deaths due to breast cancer and the cumulative mortality were almost identical in both the interventional and control groups; the number of breast cancers was similar in both groups, and the size and stage of the cancers did not differ appreciably.

The notion that BSE is not efficacious seems unwarranted when many studies have demonstrated that breast cancers detected by BSE are diagnosed at an earlier stage and are smaller than in women who do not practice BSE. An Egyptian study demonstrated a higher rate of early stage tumours (Stage I and II) at diagnosis in women reporting BSE compared to those who never self-examined (84% versus 51%).

Although neither CBE nor BSE has yet to be established as screening tools, the utility of these interventions in limited resource areas lies in promoting breast health awareness. BSE as part of breast health awareness has been advocated for early detection in low resource settings. Thus, the main message for communities and healthcare workers is that any woman who notices a breast lump, abnormal nipple discharge, breast ulcer, unexpected breast skin changes, or axillary lump should report promptly to a health facility for further assessment.

Clinical notes

1.1 Encouraging women to return six-monthly for PI-CBE

1.2 Risk assessment and modality-triage of women should accompany PI-CBE to ensure referral of high-patients who would benefit from imaged based screening. (Standard 1.3)

1.3 Ensure women have discussion around other beneficial screening available such as HIV-testing and cervical cancer screening.

1.4 There is little utility in screening patients if treatment cannot be offered at diagnosis. Treatment must be available and accessible when cancers are discovered.

Further discussion

Mammography (MMG) is the most commonly used screening test in developed countries. It is expensive and complex, requiring substantial financial and manpower resources. The goal of breast screening is to prevent death and not simply to detect cancers by mammography.

Screening MMG results in early diagnosis and more conservative therapies, but the exact benefit of screening mammography in decreasing breast cancer mortality is unknown due to the inconsistency of results across studies. These range from no reduction in breast cancer mortality to a 30 per cent reduction among women aged 50 and above. It bears noting that improvements in breast cancer treatment have had a greater effect on breast cancer mortality than mammographic screening. **Screening mammography should not be introduced unless resources are available to ensure effective and reliable screening of at least 70 per cent of the target group i.e. women aged 50 and older.**

Lack of resources and infrastructure in the South Africa public healthcare system render this strategy untenable. Presently MMG should be performed on symptomatic and identifiable high risk patients at specialist breast units.

Monitoring and evaluation point

ME1	Biannual clinic figures of uptake in eligible women in health facilities.
ME2	Audit and comment forms to allow healthcare workers to report barriers to uptake at patients and facility level.

Objective 2: Risk assessment

Standard 1.4	All eligible women should have their risk of breast cancer determined and be managed according to local protocol.

Rationale

There are a number and variety of risk factors that cause the complex multifaceted nature of breast cancer. The prevention strategies for the development of breast cancer includes knowledge of high risk factors including gender, age, family history, endogenous and exogenous hormone exposure, previous benign and malignant breast disease, breast density and lifestyle factors.

A tool by Cancer Australia places patients into one of three broad risk categories according to family history:

- **At or slightly above average/population risk:** This includes women with no family history, and women with one first degree relative or one or two second degree relatives diagnosed at age 50 or older. Lifetime risk of breast cancer (LTR) is between one in eight and one in 11 (9–12%). Covers more than 95 per cent of the female population.
- **Moderately increased risk:** This includes women who have a first degree relative diagnosed before age 50, or two or more first degree relatives on the same side of the family diagnosed at any age. LTR is between one in four and one in eight (12–25%). Covers less than four per cent of the female population.
- **High risk:** Potential high risk and known high risk includes women who are known to carry a breast cancer susceptibility gene mutation (e.g. BRCA1 or BRCA2) and women who have a strong family history with at least two first degree relatives affected, plus other features. LTR is between one in two and one in four (>25%). Covers less than one per cent of the female population.

These categories are primarily based on familial risk assessment. Individual breast cancer risk may include other factors such as biopsy showing benign breast disease or a previous history of cancer. Detailed risk assessment can be carried out using a number of tools. These include a manual assessment of the family pedigree by the genetic counsellor and any one of a number of statistical models, which may be computer programmes or scoring models. Factors that are taken into account when deciding on a risk assessment tool include age of onset of cancer or age achieved cancer-free; number of affected relatives and the ratio to unaffected relatives; degree of biological relationships of affected individuals; presence / absence of associated cancers; and ethnic background.

Limitations to certain tools can include small family size; reduced penetrance and variable expressivity; a paucity of individuals of the susceptible gender for sex-influenced cancers; and inaccurate or incomplete family histories. The different methods all have advantages and disadvantages and it requires an experienced eye to determine which approach would work best in what setting. Genetic counsellors and clinical geneticists are trained to do this.

The American Cancer Society recommends yearly mammograms to women at high risk (greater than 20% LTR). Women at moderate risk (15-20% LTR) should discuss with their doctors regarding the benefits and limitations of adding MRI to yearly mammograms. Yearly MRI has not been recommended for women with less than 15 per cent LTR.

Clinical notes

1.5 Women with a family history of breast cancer may overestimate their own risk.

1.6 Due to the limited information regarding genetic and familial breast cancer in South Africa, local protocols regarding referral to genetic services should be utilised or developed.

1.7 In addition to family history, women with a history of neoplastic disease of the breast (see further discussion) should be considered in a moderately increased risk group.

1.8 Women with an increased risk of breast cancer may be modality-triaged to receive image-based screening after referral to a specialist breast unit. Women who should be considered for this include:

(a) personal history of invasive breast cancer
(b) lobular neoplasia
(c) proliferative breast disease with atypical ductal hyperplasia
(d) therapeutic ionising radiation for Breast cancer or Hodgkin's disease
(e) carrier of BRCA1 or 2 gene mutation
(f) significant family history i.e. first degree family with breast cancer
(g) receiving hormone replacement therapy (HRT)

1.9 Women at moderately increased risk or greater should be encouraged to undergo yearly mammography from 40 to 50 years and yearly or biennial from 50 years.

1.10 Women should be reminded that most breast cancer is unrelated to a positive family history and any breast changes should be reported and acted on.

1.11 Young women with a moderately increased risk of breast cancer or greater should have an annual clinical breast examination with a breast-trained healthcare provider from 10 years younger than the age of onset for the youngest affected family member.

Further discussion

Further information concerning high risk factors is elaborated below:

Gender: Females have a higher risk of developing breast cancer than males. The ratio of male to female breast cancers is 1:135

Age: The risk increases with age. From 35 to 65 years there is a six-fold increase in breast cancer.

History of neoplastic disease of the breast:

a. Prior history of breast cancer carries an elevated risk of developing new primary breast cancer. The risk is one and two per cent per year above the LTR at time of diagnosis, respectively for IDC and ILC.
b. Lobular neoplasia (LN): LN, which includes atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS) is associated with an increased risk of breast cancer: three to four times with ALH and eight to 10 times with LCIS.
c. A breast tissue biopsy showing proliferative disease with or without atypical cells results in an increased risk of developing breast cancer; the risk is higher with atypical ductal hyperplasia (ADH): RR four to five times.

Family history: Family history of breast cancer is an independent risk factor. The risk is higher in women with young first degree relatives who have a history breast cancer. A sister with breast cancer carries more risk than a mother. Carriers of BRCA1/ BRCA2 and other high penetrance genetic mutations are at high risk for developing breast cancer. (Refer to Standard 1.4 on genetic assessment)

Radiation exposure: Multiple exposures of therapeutic radiation to the chest/head and neck region at an early age (less than 20 years old). High dose radiotherapy for breast cancer may be a risk factor for developing subsequent contralateral breast

cancer (CBC). Patients with Hodgkin's disease who received radiotherapy at high doses are at high risk of developing breast cancer. Screening mammography (MMG) does not significantly increase breast cancer risk.

Hormone exposure:

a. nulliparity
b. first full-term pregnancy after the age of 35
c. oral contraception as a risk factor for breast cancer is controversial
d. hormone replacement therapy in post-menopausal is associated with an increased risk of breast cancer if used for more than five consecutive years
e. prolonged oestrogen window:
    a. menopause > 55 years of age
    b. menarche < 12 years of age
    c. not breastfeeding

Breast density: Mammographic dense breast. Relative risk (RR) is up to four times in an extremely dense breast (ACR 4)

Lifestyle: Including a body mass index (BMI) > 25, alcohol more than 10g per day especially among postmenopausal women and a sedentary lifestyle- more than seven hours a week of moderate exercise is protective.

LOW RISK (RR 1.0 – 1.4)	MODERATE RISK (RR1.5 – 2.0)	HIGH RISK (RR >2.0)
Alcohol consumption	Increasing age from 40 years	Personal history of invasive breast cancer
Reproductive factors First full term pregnancy > 35 years Hormone replacement therapy	Reproductive factors Early menarche (< 12 year: RR 1.02) Late menopause (> 55 year: OR 2.4) Nulliparity	Lobular neoplasia
Obesity	Proliferative breast disease without atypia	Proliferative breast disease with atypical ductal hyperplasia
	Dense breast tissue	Therapeutic ionizing radiation for Breast cancer or Hodgkin's disease
		Carrier of BRCA1 or 2 gene mutation
		Significant family history i.e. first degree family with breast cancer

Monitoring and evaluation point

ME3	Biannual clinic figures of uptake in eligible women in health facilities.
ME4	Recording of numbers of patients referred for genetic assessment.

Objective 3: Genetic services

Standard 1.5	Referral to genetic services is offered to women whose family history meets the criteria for referral.

Rationale

Cancer is a common disease, with one in three people being diagnosed with cancer at some point in their life. Approximately five to 10 per cent of the common cancers, including breast, ovarian and colorectal cancer, are due to inherited cancer predisposing genes. Individuals and families who are at risk for inherited breast cancer require genetic counselling, genetic testing and potentially further management, depending on the outcome of their testing.

Genetic counselling is a relatively new profession in South Africa but is available in all provinces. Genetic counselling is a process that involves "helping people understand and adapt to the medical, psychological, and familial implications of the genetic contributions to disease." The process includes:

- interpreting family and medical histories in order to assess the risk of occurrence or recurrence of disease
- educating individuals and families about the genetic aspects of disease, testing, management, resources and research
- as well as providing psychosocial support to assist individuals to adapt to their risks and to make informed decisions

Genetic counselling for familial breast cancer involves assessing family pedigree, discussion of inherited breast and or ovarian cancer, and an assessment of the chance that there is an inherited cancer syndrome in the family as well as an individual's personal chance of developing cancer. Depending on the risk

assessment, options regarding genetic testing, screening and management are discussed.

Clinical notes

1.12 Women whose family history is associated with an increased risk for deleterious mutations in BRCA1, BRCA2 or TP53 genes should be referred for genetic assessment.

1.13 Although there are no standardised criteria for selecting candidates for BRCA counselling, the National Cancer Institute, the National Comprehensive Cancer Network and the US Preventive Services Task Force outline family history red flags, which generally point to first-and second-degree relatives with breast and or ovarian cancers, especially at young ages:

(a) two first degree relatives (mother, daughter or sister) diagnosed with breast cancer, one of whom was younger than 50 years

(b) three or more first or second-degree relatives (aunt or grandmother) diagnosed regardless of age

(c) combination of first or second-degree relatives diagnosed with breast and ovarian cancer regardless of age

(d) first-degree relative with bilateral breast cancer

(e) breast cancer in a male relative

(f) combination of two or more first or second-degree relatives with ovarian cancer.

(g) multiple primary cancers in one individual, including bilateral and multifocal cancers

(h) family history of breast cancer in combination with other BRCA-related cancers such as pancreas, prostate and esophageal cancers on the same side of the family

(i) certain ethnic groups (Ashkenazi Jewish, Afrikaner) with any first or second-degree relatives on the same side of the family diagnosed with breast or ovarian cancer

(j) family history of early onset breast cancer in combination with other TP53-related cancers such as sarcomas and multiple cases of childhood cancers on the same side of the family.

1.14 The availability of genetic testing in South Africa is limited, but one of the NHLS laboratories in Bloemfontein offers fairly comprehensive screening.

1.15 Patients from population groups with specific mutations should be screened for those first. For all other patients and for patients who test negative for the population specific mutation, testing should then be extended in discussion with the laboratory.

1.16 Management of individuals with Hereditary Breast and or Ovarian Cancer Syndrome may include intensive screening, chemoprevention and prophylactic surgery.

Further discussion

Familial breast cancer can be associated with a number of inherited cancer predisposing syndromes.

Table 2: Berliner and Fay, 2007 observed cancer groupings in some hereditary cancer syndromes

Condition	Gene	Malignancy
Hereditary breast and ovarian cancer syndrome (HBOC)	BRCA1	Breast, Ovary
HBOC	BRCA2	Breast, Male Breast, Ovary, Pancreas, Melanoma, Stomach
Hereditary non-polyposis colon cancer	MLH1 MLH2	Bowel, Uterus, Ovary, Stomach, Upper urinary tract, Biliary tree, Brain
Li-Fraumeni	TP-53	Breast, Brain, Rhabdomyosarcoma, Leukaemia, Adrenocortical carcinomas, Lung adenocarcinomas
Peutz-Jeghers Syndrome		Breast, Ovarian, Gastrointestinal, Sex cord, Testicular
Cowdens Syndrome	PTEN	Breast, Thyroid, Endometrium

The majority of familial breast cancers fall within the Hereditary Breast and or Ovarian Cancer Syndrome (HBOC). The existence of an inherited predisposition for breast and or ovarian cancer has been recognised for years, but it was only in the early 1990s that evidence for the genetic cause of this predisposition was reported.

HBOC is caused by a mutation in one of two highly penetrant genes, which are both inherited in an autosomal dominant manner. The BRCA1gene is located on chromosome 17 and BRCA2 on chromosome 13. Mutations in either the BRCA1 or BRCA2 gene lead to an increased predisposition to the development of cancer. The most commonly associated cancers are breast and ovarian cancer, but other cancers including stomach, colon, prostate, pancreatic and melanoma are observed.

Women that carry a BRCA1 mutation have an approximately 60 to 80 per cent chance of developing breast cancer in their lifetime and a 40 to 60 per cent lifetime risk for ovarian cancer. There is also a one per cent risk of male carriers developing breast cancer. BRCA2 mutation carriers have a 50 to 80 per cent lifetime risk of developing breast cancer and a 20 to 30 per cent chance of developing ovarian cancer. The risk for male breast is higher (5–10 %) and males with BRCA2 mutations also have an increased risk for prostate cancer (14 %).

The specific mutation identified in the BRCA genes are often family specific, however, certain population groups have common mutations that account for a significant proportion of mutation in families from that population group. The Ashkenazi Jewish population has three founder mutations, two in BRCA1 and one in BRCA2 – these three mutations account for 90 per cent of HBOC in this population. The South African Afrikaner population also has three founder mutations (two in BRCA1 and one in BRCA2) – they account for approximately 60 per cent of HBOC in this group. A common Xhosa mutation has also been identified, which is also been seen in the coloured population.

Monitoring and evaluation point

ME5	Annual figures for genetic counselling.
ME6	Proportion of patients offered counselling or genetic testing.

Objective 4: Management of women known or suspected to have a breast cancer susceptibility gene mutation

Standard 1.6	Women who are known to carry a gene mutation should have annual image-based screening with MRI where available, otherwise mammography, from 10 years prior to the age of onset for the youngest

	affected member of the family.
Standard 1.7	Women at high risk of developing breast cancer should be considered for annual breast MRI in addition to mammography and CBE.

Rationale

MRI is the most sensitive and specific method of screening in breast cancer susceptibility mutation carriers. In a systematic review by Lord et al, there was strong evidence that the addition of breast MRI to conventional screening tests provides increased sensitivity for early detection of breast cancer in young high risk women. However, there was also evidence that additional MRI may increase patient recall rate due to its high false positive findings.

Clinical notes

1.17 Women with other gene mutations (see objective 3, further discussion) should be also be screened using MRI

1.18 Mammography should not be carried out under the age of 30 years due to its low sensitivity and increased risk of radiation-induced cancers. Patients with p53 mutations should be screened using MRI only (including whole body MRI) because of the risk of radiation induced malignancy. The low prevalence of this condition allows for these intensive measures.

1.19 Because patients have an increased risk for a variety of cancers, multidisciplinary care, including screening for those variety of cancers, is particularly important and will include GIT, gynaecology and medical specialists.

1.20 Women who are known or suspected of carrying a gene mutation should be managed in a specialist breast unit where options of management can be discussed. Options for management may include intensive screening, chemoprevention or prophylactic surgery.

1.21 Female carriers of the BRCA-1 or BRCA-2 mutations may consider risk-reducing salpingo-oophorectomy from 40 years. The risk of delaying surgery until after child-bearing is low. Patients should be managed in multi-disciplinary teams with gynaecological specialist experienced in the

management of these patients. The consequences of early menopause should be discussed and managed.

Monitoring and evaluation point

ME7	Annual figures for screening of eligible patients with genetic mutations.

Key area 2: Timely access to care

Objective 5: Specialist breast units for the diagnosis and management of breast disease

Standard 2.1	SBUs should have minimum staffing and equipment to provide accurate diagnosis of benign and malignant disease (see an appendix describing staffing and equipment at this level).
Standard 2.2	SBUs should either be open-access or appointment based that allows rapid referral and Specialist Breast Assessment (SBA) within 21-45 days according to referral triage (Standard 2.6-7).
Standard 2.3	SBUs have multidisciplinary capability for diagnosis and appropriate management of breast benign disease (Breast surgery, Radiology, Pathology).
Standard 2.4	SBUs have multidisciplinary capability for diagnosis and, in most cases, appropriately-timed [at least basic] surgical management of breast malignant disease (Breast surgery, Radiology, Pathology).
Standard 2.5	Multidisciplinary teams and meetings with provincial oncology units (POU) allowing rapid bidirectional referral of patient information, aiming to prevent inappropriate appointments or delays.

Rationale

Currently, resources and level of care, including expertise, are fairly variable between different regional facilities. In order to avoid delays in the assessment of symptomatic patients, and to utilise the available resources appropriately, the recommendation is that the most appropriate regional facilities in each province should be ear-marked as **Specialist Breast Units (SBUs**) receiving patients from primary healthcare facilities and district hospitals. ***See figure below and Appendix A.***

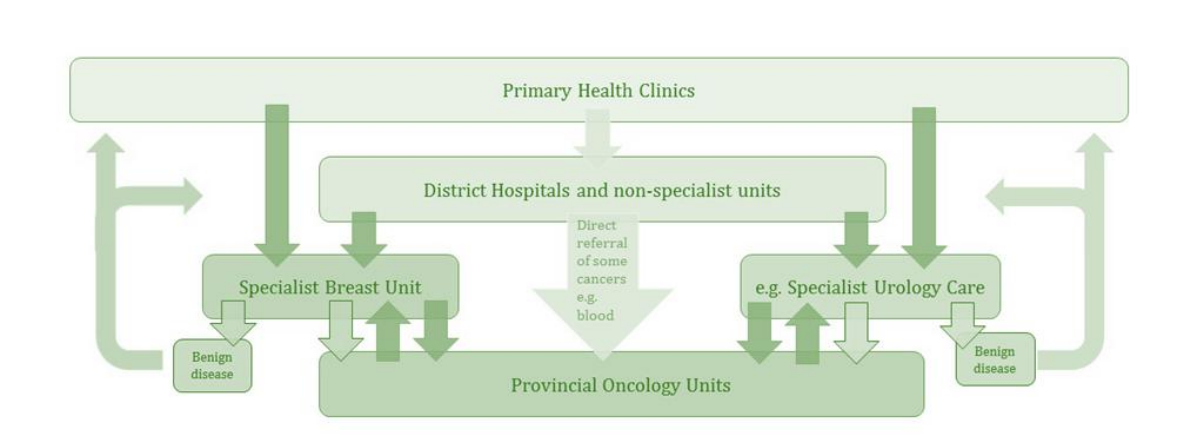


Figure 3: How SBUs and other specialist units would integrate together, in the co-ordinated health system

In provinces where SBU/POU care does not currently exist, patients are to be referred to the neighbouring province that has such offerings. Depending on population density in South Africa, and current models of care, there may be different provincial methods of separating SBU and POU services. This can be tailored to local needs. The main area of difference at present is the capability of SBUs to provide only diagnostic (and follow-up) or diagnostic and therapeutic care.

Provincial Oncology Units (POUs) should function as tertiary centres of excellence for clinical oncology provision. These are commonly found in one or two hospitals in each province due to the highly-specialised nature of the medical provision. However, they are required to serve all oncology for large populations and therefore should be focused on giving care in the specialist areas not reproducible at lower levels (such as chemotherapy, specialised radiology/nuclear medicine and radiation). Because of the centralised situation, these centres may be very far for patients to travel and separated from their support structures, so they should complement but not replace or duplicate SBUs or PHC/DHs. SBUs become centres of excellence in management and training in breast disease to allow rapid accurate diagnosis and management. POUs will provide definitive clinical oncology (medical and radiation oncology) services.

Clinical notes

2 Multidisciplinary teams and meetings with provincial oncology units (POU) allowing rapid bidirectional referral of patient information, aiming to prevent inappropriate appointments or delays.

2.1 Due to the specialist nature of breast disease and economy of clustering specialist staff, progression through the tiers of the traditional levels of healthcare may be avoided with immediate transfer from PHC, district or non-specialist regional centres to SBUs.

2.2 SBUs will act as the focus of breast care management to include: up skilling of PHC and district hospitals within the cluster; outreach to PHC; survivorship support for patients; co-ordination or provision of palliative care; audit and documentation of individual patient care pathways.

2.3 Although levels of care may be artificially separated in function in this document, they may well exist within the same hospital or geographical location (e.g. SBU and POU in the same hospital but providing different functions).

Further discussion

Breast healthcare is a paradigm for healthcare inequality in South Africa, leading to delays in the diagnosis of, and appropriate referral for breast cancer. This disparity can largely be avoided by defining the scope of care at each healthcare level, requirements to provide this level of care, and the appropriate pathway to definitive care.

Designated SBUs and POU will be identified and up skilled according to local capacity and needs. An appendix to this document should describe the staffing and functions for the sub-units of an SBU including radiology, pathology, surgery but also physiotherapy, psychology, counselling, genetics, etc. There should also be engagement with NGOs and government budget to provide navigators to help patients through the referral system and assist staff in transfer of information (addressed in objectives 10 and 21). Locally and nationally coordinated computerised breast software will allow recording of treatments for access by the

complete multi-disciplinary teams and allow for audit of standards implemented (objective 21).

Monitoring and evaluation point

ME8	Compliance of designated SBU and POU with minimum staffing and functional requirements.
ME9	Audit of cases via coordinated national computerised network.

Objective 6: Clear referral pathways and access points to breast diagnosis

Standard 2.6	Any women with a breast symptom will have a clinical breast examination, and immediate referral to a designated SBU as per protocol (Standard 2.2-2.4).
Standard 2.7	Women with high or medium suspicion should have SBA within 21 days.
Standard 2.8	Women with a low suspicion of breast cancer should have SBA within 60 days.
Standard 2.9	SBU should move toward an open-access model to facilitate rapid transfer and review.
Standard 2.11	Written and verbal communication should be provided at each consultation to patient.

Rationale

Inequitable access to appropriate services perpetuates disparity in diagnosis and breast cancer care. Ultimately this impacts on delay to treatment and patient outcomes. The scope of breast cancer care of each level of healthcare can be defined, with rapid bidirectional referral between appropriate facilities at different levels.

Clinical notes

2 Due to the specialist nature of breast disease and economy of clustering specialist staff, progression through the tiers of the traditional levels of healthcare may be avoided with immediate transfer from PHC, district or non-specialist regional centres to SBUs.

2.1 The role of mobile image-based screening is not defined in this model with little value in the screening model. Mobile breast-exam based services by NGOs may have value as feeders in the PHC category.

2.2 The written and verbal communication that is provided at each consultation should be kept as an integrated patient record accessible to each member of the MDT, and given to the patient or family after each consultation. It should include information about their breast diagnosis and current treatment options and plan.

2.3 Designated SBU will be identified and up skilled according to local capacity and needs to accomplish:

(a) training of medical and nursing staff

(b) time allocated to open-access clinics

(c) appropriate diagnostic pathways (see section on radiology and pathology)

(d) local protocols facilitating seamless transfer to the closest designated SBU (commonly an open access breast unit at the Regional Hospital)

(e) breast referral forms with all relevant data (check lists and boxes) for two-way information, and audit capability

2.4 Patient transport should be designed or co-ordinated at appropriate times for patients in need to the designated referral facility to ensure ease of access and to minimise delays.

Further discussion

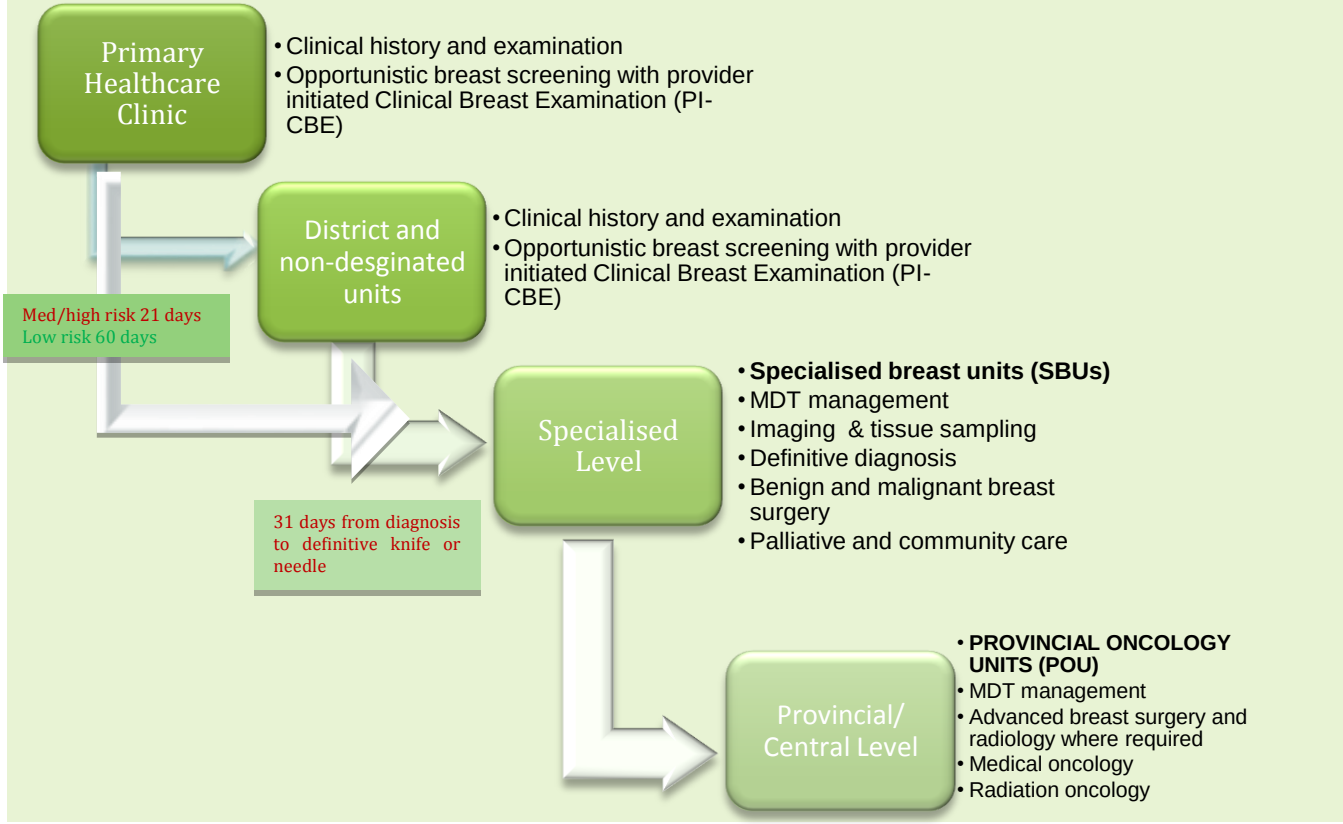


Figure 4: **Sample of referral care pathway with timelines**

Services at these proposed levels of care are detailed below:

A. Primary health clinics and NGO-based services

Asymptomatic patients presenting to primary care clinics for non-breast related problems should be targeted for opportunistic breast screening in the form of a clinical breast examination (PI-CBE). While waiting for their turn in the various clinics, they should be educated on breast healthcare and taught breast self-examination.

Symptomatic patients should receive a full breast-specific history and detailed CBE. These patients should then be referred to the nearest designated SBU according to triage. Patients who are found to have any form of breast pathology should urgently be referred to the nearest designated SBU.

The role of mobile mammography units is unclear, and presently of no value in the public healthcare setting at present. However, offering clinical breast examinations (CBE) in a community setting for the convenience of users or health care users is a relevant contribution and area where the sector can add measurable value. The role of NGOs in facilitating access to care is also important.

Requirements for this provision:

1. primary healthcare nurses trained in breast healthcare.
2. protocols facilitating seamless transfer to the designated institution, namely an open access breast unit at the regional hospital
3. breast referral forms with all relevant data (check lists and boxes) for audit and M&E
4. patient transport to be made available for patients in need to the designated referral facility to ensure ease of access and to minimise delays.

B. District hospitals and non-specialist units

Resources and level of care, including expertise, can be variable between different district facilities. Thus, to standardise the management of patients with a breast complaint, it is advisable that no unnecessary delay is incurred with investigations.

Asymptomatic patients presenting to primary care clinics for non-breast related problems should ideally be targeted for opportunistic breast screening (PI-CBE). While waiting for their turn in the various district level facilities, patients should be educated on breast healthcare and taught breast self-examination.

Symptomatic patients should receive a full breast-specific history and detailed CBE. These patients should then be referred to the nearest designated SBU according to triage. Patients who are found to have any form of breast pathology should urgently be referred to the nearest designated SBU.

Requirements for this provision:

1. primary healthcare nurses and doctors trained in breast healthcare.
2. it is desirable that all doctors at these facilities are trained in breast healthcare and systematic breast examination.

3. protocols facilitating seamless transfer to the designated institution, namely an open access breast unit at the regional hospital.
4. breast referral forms with all relevant data (check lists and boxes) for audit and m&e.
5. patient transport to be made available for patients in need, to the designated referral facility to ensure ease of access and to minimise delays.

C. Specialist breast unit (regional and tertiary level)

These units should be available to receive patients from primary healthcare facilities and district and non-specialised units. These facilities should be should be equipped with the necessary resources and breast healthcare infrastructure, surgical facilities staffed with appropriate level of clinical expertise. Effectively, these designated SBUs should be equipped to make a definitive diagnosis, and offer a breast surgical service (benign and basic malignant).

Asymptomatic patients are usually patients who request screening because they are at high risk for developing breast cancer, as defined by risk assessment. These patients should be referred directly to the open access SBUs.

Symptomatic patients should receive a full breast-specific history and detailed CBE. These patients should then be referred for imaging and appropriate tissue sampling via image-guided core biopsy (or fine needle aspiration cytology where core biopsy is not possible). The SBUs have capacity to diagnose and fully characterise breast malignancies, and provide staging investigations for biopsy-proven cancers.

A definitive diagnosis can and must be made at the SBU and the patient should be counselled by breast specialists about the diagnosis, prognosis and management options in order that she/he can make an informed decision regarding treatment prior to presentation at a multi-disciplinary meeting in the case of malignant disease. These patients should be presented and discussed with the multi-disciplinary team where their overall management plan will be decided on.

Requirements for this provision:

1. Standardised breast proformas.

2. Breast imaging:
    a. Mammography: film or digital, depending on resources
    b. Stereotactic biopsy attachment (optional)
    c. High resolution ultrasound
    d. Dedicated breast mammographers and radiologists
    e. Meetings at which surgeons and radiologist discuss patient findings and management (benign and malignant)
3. Tissue sampling equipment; core needle biopsy, which can be image-guided.
4. Access to a regional histopathology laboratory:
    a. swift transport of specimens.
    b. timeous synoptic standardised reporting.
    c. computerised access.
5. Specific timelines should be adhered to and work-up routinely completed within two weeks from presentation.
6. Protocols facilitating seamless transfer to the POUs. This includes open access breast clinics, multidisciplinary team meetings or dedicated screening clinics run weekly at the SBUs
7. Patient transport to designated up- and down-referral.

D. Provincial oncology unit (tertiary or central level)

These units should be available to receive diagnosed patients from SBUs. These facilities should be should be equipped with the necessary resources and oncology facilities staffed with appropriate level of clinical expertise. Effectively, these designated POUs should be equipped to giving oncological care of chemotherapy and radiation in the specialist areas not reproducible at lower levels. Because of the highly-specialised nature of the medical provision and intense workload, care in these centres should be optimised to augment but not duplicate care available at lower-tiers. These units may be stand-alone provide diverse oncological care to all specialities, or situated together within a SBU.

To reiterate: Designated POUs should be equipped to give specialist oncological care of chemotherapy and radiation not reproducible at lower levels of care.

Asymptomatic patients should not be seen at a POU. Patients post-treatment for surveillance can be managed at a unit level according to local protocols. The management and surveillance should follow all protocols to prevent multiple duplicate visits to different units, and potentiate cost-effective surveillance and follow-up.

Symptomatic patients should receive a full breast-specific history and detailed CBE. These patients should have a confirmed diagnosis of malignancy, with appropriate investigations carried out by the referring SBU. The POUs have capacity to treat and support patients with breast malignancies, and provide additional specialised staging investigations as required.

Prior to consultation at the POU a definitive diagnosis can and must be made at the SBU and the patient should be counselled about the diagnosis, prognosis and management options. These patients should be presented and discussed with the multi-disciplinary team where their overall management plan will be decided on, therefore ensuring fewer delays to care, and expense at central level over-subscribed services.

Requirements for this provision:

1. Specialised budget to allow for cost of chemotherapy and biological therapies
2. Standardised breast proformas.
3. Breast imaging and pathology available
4. Specific timelines for consultation after referral should be adhered to and work-up routinely completed within two weeks from presentation.
5. Protocols facilitating seamless transfer to the POUs. This includes weekly multidisciplinary team meetings and patient navigation.
6. Patient transport to and from designated POU

In provinces where SBU/POU care does not currently exist, patients are to be referred to the neighbouring province that has such offerings. Depending on population density in South Africa, and current models of care, there may be different provincial methods of separating SBU and POU services. This can be tailored to local needs. The main area of difference at present is the capability of SBUs to provide only diagnostic (and follow-up) or diagnostic and therapeutic care.

Monitoring and evaluation point

ME10	Ensure that at least 90 percent of patients are referred within appropriate timelines for diagnosis.
ME11	Audit and comment forms to allow healthcare workers to report barriers to uptake at patients and facility level.

Objective 7: Clear referral pathways and access points in breast cancer care

Standard 2.11	Women referred to SBU with high risk of breast cancer, if diagnosis positive, should receive treatment within 60 days of first (PHC/DH) consultation.
Standard 2.12	Women with a confirmed diagnosis of breast cancer should receive their first definitive treatment within 31 days of the decision to treat.
Standard 2.13	Following surgery for breast cancer, the first adjuvant therapy (chemotherapy or radiation) should occur within 60 days of surgery, and no more than 90 days.

Rationale

One of the factors that has been assessed in terms of patient outcome is delay in presentation, diagnosis and primary treatment of breast cancer. Delay has been defined in terms of patient delay and provider delay. Provider delay is defined as the time taken from first presentation to a health care practitioner to receiving the primary treatment, be that surgical or non-surgical (primary chemotherapy, radiation therapy or hormonal treatment). Some studies have assessed whether a delay of one week, one month or even two months from confirmation of disease via tissue biopsy to primary treatment has any effect on mortality.

A recent meta-analysis found that there was no correlation between provider delay of up to two months and mortality, however in those patients presenting with advanced disease, a delay of more than 60 days from tissue diagnosis to primary treatment has been shown to result in a statistically significant adverse impact on mortality.

There is marked heterogeneity in the country regarding provider delay. When considering a standard for treatment, it would be ideal to aim for the same delay intervals as other middle or high income countries within a system of designated units. An acceptable standard in our setting would be two months (60 days) from first presentation to treatment initiation for 90 per cent of our patients and between surgery and first adjuvant therapy.

Clinical notes

2.5 Standards are set for the majority of women, however, some women will have more complex paths to diagnosis or in treatment decision -making. The longer routes should be documented.

2.6 Women may have delays to diagnosis and treatment related to access and barriers to care. It is important these are audited to allow for local changes in practice or additional navigation to allow patients to reach appropriate care in timeous fashion.

2.7 Date of surgery or medical treatment should be set at the consultation where decision to treat is made. Anxiety around waiting times is often related to the anxiety of not knowing or fear of breakdown in care pathway rather than to the length of wait.

2.8 Comprehensive information including treatment decision, types, locations and dates of treatments should be given verbal and in writing for patients and family at the consultation where decision to treat is made. Information may have to be passed between family members, or forgotten after the consultation.

Monitoring and evaluation point

ME10	Ensure that at least 90 per cent of patients are referred within appropriate timelines for surgical and non-surgical treatment
ME9	Audit and comment forms to allow healthcare workers to report barriers to uptake at patients and facility level

Key Area 3: Assessment, diagnosis and staging

Objective 8: Triple assessment

Standard 3.1	All eligible patients should be diagnosed using triple assessment (clinical examination, imaging and histological confirmation)
Standard 3.2	All patients completing triple assessment should have their findings discussed in a combined clinical/radiology meeting.
Standard 3.3	Routine histology should be achieved with image-guided core needle biopsy
Standard 3.4	Histological assessment should be synoptic and include Bloom-Richardson grading, ER, PR and HER2. Ki67 should be used where available according to local protocol

Rationale

Radiology is an integral part of breast cancer assessment and management. It is essential to provide high quality and accessible radiological services at the appropriate centres, regional or tertiary. This has been discussing in the screening area of this document (Key Area 2)

In order to appropriately diagnose and treat breast cancer it is important to fully ascertain the biological and clinical characteristics of the disease. This includes clinical staging, and the pathological assessment with immunohistochemistry to determine receptor status. Receptor status may help guide treatment options in breast cancer.

An American audit demonstrated that the majority of the pathology reports did not fulfil the criteria set by College of American Pathologists. Another audit, from Australia, looking at completeness of randomly selected histopathology reports of newly diagnosed breast cancers noted that 88 per cent of synoptic (checklist) reports had all seven criteria whereas only 27 per cent of non-synoptic (free text format) reports had the same. Similarly, an audit done in the United Kingdom showed that the introduction of a standard proforma, that included 18 criteria outlined in the Royal College of Pathologists Minimum Dataset for breast cancer reports, led to a significant improvement ($p < 0.001$) in the completeness of breast cancer histopathology report (74% in the proforma versus34% in the free text group).

Clinical notes

3 Patients with symptomatic disease should undergo imaging as part of triple assessment. This includes:

(a) mammogram (if not already done) with 3-D Digital tomosynthesis where available

(b) ultrasound scan for patients with dense breasts

(c) additional mammography views as necessary (repeat views, compression, extended views, skin marks, magnification, etc.)

(d) breast ultrasound (*where appropriate*)

(e) image-guided biopsy (core biopsy; fine needle aspiration biopsy; vacuum-assisted)

(f) radiological interventional procedures, e.g. cyst aspiration

3.1 Ultrasound is the appropriate first modality of imaging in women under 35 years, due to the increased breast density and absence of radiation in the modality.

3.2 In a woman with early or locally advanced breast cancer, MRI may be considered if there is a likelihood that it can lead to a change in surgical management. MRI may be considered in:

(a) invasive lobular cancers

(b) suspicion of multi-centricity

(c) genetic high risk: BRCA1or BRCA 2

(d) patients with breast implants

(e) diagnosis of recurrence post-BCS

(f) assessment after neo-adjuvant treatment

(g) extent of DCIS

(h) occult primary breast cancer

3.3 All patients should be referred back to the surgical team within the SBU for after completion of radiology investigations for discussion of results.

3.4 FNAC is useful if adequately trained staff is available, and should be used in conjunction with ancillary investigations.

3.5 Core biopsies are the gold standard for diagnosis of breast cancer and are essential to provide material for assessment of prognostic and predictive markers

3.6 Excisional or incisional biopsies should not be performed unless two image-guided core biopsies are inconclusive or discordant with radiological findings

3.7 In the presence of biopsy for calcifications, radiology of paraffin-embedded formalin fixed specimens is used to confirm or exclude the presence of calcifications within a sample.

3.8 Synoptic reporting is recommended to improve consistency, decrease turn-around-time and ensure that all available macroscopic and microscopic information is conveyed to clinicians. An adequate pathology report for breast cancer should be synoptic must have the following minimum parameters:

(a) location (side and quadrant), maximum diameter, multifocality
(b) tumour type (histology)
(c) histological grade
(d) lymph node involvement and total number of nodes examined
(e) resection margins
(f) lymphovascular invasion
(g) non-neoplastic breast changes
(h) hormone receptor status [oestrogen-receptor/progesterone receptor (ER/PR)]
(i) HER-2 assessment

3.9 HER2 stains which are 2+ (equivocal) should be subjected to further molecular techniques e.g. FISH/ CISH. In about 20 per cent of cases these will be positive; i.e. HER2+.

3.10 Internal and external quality control, assessment and assurance systems should be integrated into laboratory practice to ensure that results are accurate and reproducible.

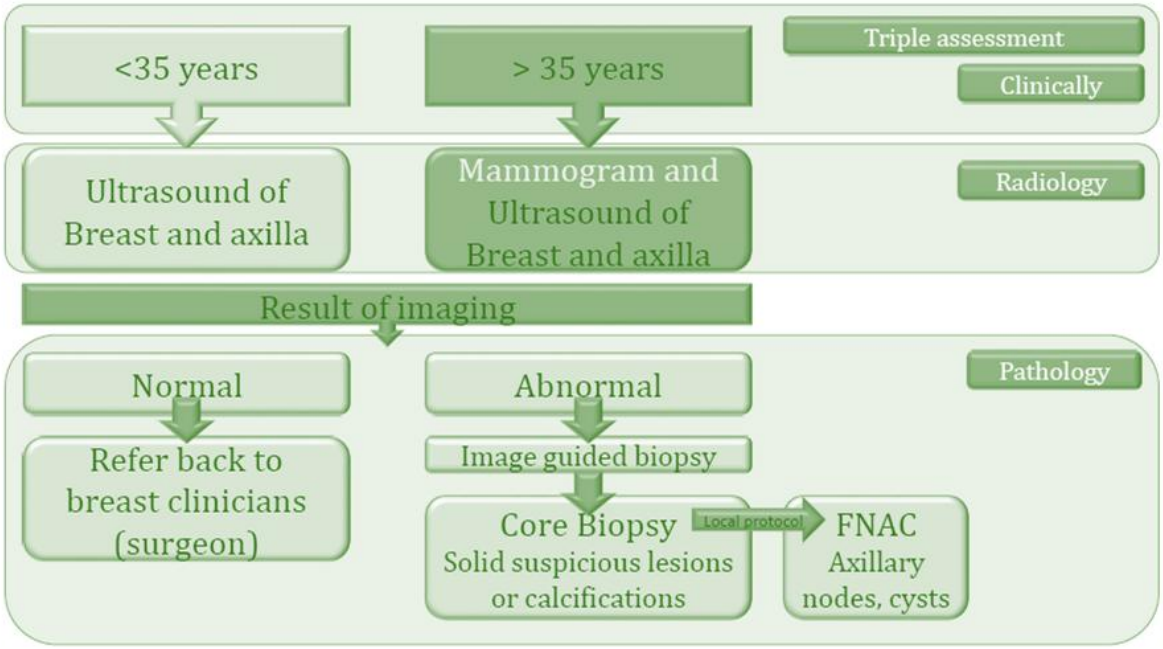


Figure 5: Flowchart of triple assessment

Further discussion

Fine needle aspiration cytology (FNAC) is of value in the initial assessment of palpable breast lumps and should be regarded as a screening test which may provide a definite diagnosis in certain situations and may also be therapeutic e.g. in the assessment of cystic lesions. Fine needle aspirates are useful in the context of "triple assessment" of lesions and may support the benign clinical and radiologic appearances of a lesion. Difficulties encountered in FNAC include sampling errors which may depend on the skill of the clinician, available real-time imaging modalities (e.g. ultrasound versus free-hand guidance) and access to rapid on-site screening.

Fine needle aspiration cytology cannot reliably distinguish between ductal and lobular carcinomas, as well as in-situ and invasive malignant lesions. Important exceptions are the finding of malignant cells within an axillary node sample or the presence of a non-epithelial breast neoplasm, e.g. malignant lymphoid or melanocytic cells. Grading of invasive lesions is not possible using routine histologic criteria, although grading systems which rely on nuclear morphology alone may be utilised.

Immunocytochemistry can be performed on FNAC specimens, although this is limited by the availability of representative slides. Immunocytochemical stains affect

the morphologic preservation of the sample; however, hormone receptor and HER2 assessment can be performed on cytology specimens, particularly if a cell-block is prepared. Cell-block preparations can be subjected to immunohistochemical, histochemical and molecular analyses.

The **core needle biopsy** specimen is the gold standard in the initial histopathologic/ "tissue" diagnosis of breast carcinoma. Ideally this should be a 14-16 G biopsy. Core, incision or excisional biopsies should be placed in 10 per cent buffered formalin as soon as possible to facilitate rapid formalin penetration and fixation of the specimen. Delayed fixation adversely affects the morphologic preservation of the specimen and may render a diagnosis of malignancy difficult or impossible. In addition, accurate grading of neoplasms depends on preservation of neoplastic tubular structures and on arrest of mitotically active cells to perform accurate mitotic counts. The volume of 10 per cent formalin should be at least 10 times the volume of the specimen.

Reporting of core biopsy specimens should be standardised to allow clinicians to plan management with all available information. Use of a proforma system of reporting core biopsy specimens also ensures that registrars and consultants include all relevant diagnostic and prognostic information in the report. In the case of registrars, use of a free-text description of the tumour is also encouraged for training purposes. The use of a categorical coding system ("action codes") is not widely practiced in the South African context; the action codes are included at the end of reports and give a simple indication of actions which the biopsy should trigger. The categorisation system also allows trend analysis and research. See attached proforma and synoptic reports.

Assessment of **hormone receptors** and HER2 status is performed on core biopsy specimens with an adequate volume of well-preserved tumour tissue. Oestrogen, progesterone and HER2 stains are performed according to standard immunohistochemical staining procedures. Laboratories should ensure that antigen retrieval processes are optimised to ensure appropriate positive staining and to minimize background artefact. The exact antibody clone used should be recorded in the laboratory notes but is not usually specified in reports. Laboratories are encouraged to perform daily immunohistochemistry quality checks coupled with

ongoing quality assurance processes. In addition, laboratories should subscribe to external quality assurance (EQA) programmes, which include immunohistochemistry, breast receptor and HER2 modules. The results of these EQA assessments should be readily available to pathologists and clinicians on request.

Scoring of immunohistochemical stains is performed at low power (X10 objective; 100X magnification) and both intensity and proportion are recorded using the Quick score (Allred score) system. Scoring is performed on the invasive tumour present; however, if a significant volume of in-situ tumour is present, receptor status in the in-situ lesion may also be reported. A common error in the reporting of hormone receptor scores occurs when pathologists misinterpret the proportion scores and assume that a proportion score of five must mean that 100 per cent of tumour cells are positive; however, a score of five can mean anything from above two thirds to 100 per cent of cells. Pathologists should also ensure that only nuclear staining is regarded as positive.

HER2 assessment by immunohistochemistry is performed on core biopsy specimens. Invasive tumour cells are assessed for the presence and intensity of membrane staining, which may be complete or incomplete. Control sections should be utilised and pathologists must first assess external control staining. Benign breast tissue present in specimens serves as an additional positive internal control specimen, while non-epithelial elements function as negative controls. HER2 slides should include controls which indicate 1+, 2+ and 3+ stains, which have been validated with ancillary molecular techniques. HER2 stains which are 2+ (equivocal) should be subjected to further molecular techniques e.g. FISH/ CISH. In about 20 per cent of cases these will be positive; i.e. HER2+.

Specimen radiology is important in ensuring adequacy and relevance of the specimen for diagnosis. Radiology of paraffin-embedded formalin fixed specimens is used to confirm or exclude the presence of calcifications within a sample. This is utilised for screen-detected lesions as initial histologic sections may not show calcifications and further levels (cutting deeper into the tissue) may be necessary to assess the nature of calcifications present in a biopsy sample.

Wide-local excision and mastectomy specimens should be submitted in an adequate volume of 10 per cent buffered formalin. Specimens should be orientated using clips or sutures and the specimen request form should indicate which margins are marked. The standard orientation is short tie for superior margin; long tie for lateral margin; double tie for deep margin, or clips applied to local protocol. Cavity shaving specimens should also have an orientation suture or clip on the cavity side.

Gross examination of the resected specimen is of critical importance and should be performed by a specialist pathologist or registrar. Extensive guidelines for breast specimen dissection are available and laminated copies should be placed in the dissection room for easy reference.

Other methods of breast imaging are possible and in development worldwide. There applicability and cost-effectiveness is yet to be determined. This includes (not exclusively) automated breast ultrasound, breast contrast mammography, scintimammography, thermography and elastography.

Monitoring and evaluation point

ME11	Percentage of patients who complete appropriate triple assessment (audit)
ME12	More than 80% of patients should complete triple assessment within 21d

Objective 9: Staging

Standard 3.5	All breast cancer patients should be adequately assessed for metastatic disease at diagnosis

Rationale

Staging investigations may be done pre-or post-operatively depending on clinical staging and symptomatology. In early breast cancer, distant metastatic disease is uncommon.

Clinical notes

3.11 Baseline staging is warranted in the following groups:

(a) node-positive disease,

(b) patients <35 years old,

(c) unfavourable cancer histology is diagnosed (such as triple negative disease) patients considered for neo-adjuvant treatment

(d) patients present with advanced disease

3.12 Investigations should include:

(a) CXR and liver ultrasound if locally advanced disease (above stage 1)

(b) CT chest and abdomen is preferable if available

(c) Bone scan for initial staging and follow-up monitoring

(d) CT chest and abdomen

(e) Plain X-ray correlation in patients with equivocal abnormalities on bone scan

(f) PET – CT selective cases for metastatic disease or response to treatment

(g) MRI whole spine if bone pain and non-contributory imaging

3.13 To aid in prompt staging, local protocol can encourage liver sonar at the time of imaging and biopsy of suspicious lesions.

3.14 2-D cardiac echography should be performed to assess ejection fraction prior to anthracycline-based chemotherapy regimens and Herceptin therapy for cardiac assessment. The ejection fraction should ideally be > 50 - 53 per cent prior to commencing these therapies.

3.15 PET/CT may be useful in the monitoring of therapy and therapy response in metastatic disease, and restaging

3.16 PET/CT should not be used for initial diagnosis of breast cancer or axillary lymph node staging and surgical planning

3.17 The place for tumour markers in breast cancer is not yet fully known, and should be used only in individual clinical contexts at the POU.

3.18 Multigated Acquisition Scan (MUGA scan) may be used for the assessment and monitoring of ejection fraction pre andor- post chemotherapy regimens.

Further discussion

The stages for breast cancer are described clinically and pathologically by the AJCC (American Joint Committee on Cancer). The current criteria are from the 8th edition.

ANATOMIC STAGE/PROGNOSTIC GROUPS			
Stage 0	Tis	N0	M0
Stage IA	T1*	N0	M0
Stage IB	T0	N1mi	M0
	T1*	N1mi	M0
Stage IIA	T0	N1**	M0
	T1*	N1**	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Figure 6: https://cancerstaging.org/references-tools/quickreferences/Documents/BreastMedium.pdf

Monitoring and evaluation point

ME	
ME	

Objective 10: Supportive care (including psychology)

Standard 3.6	Women diagnosed with breast cancer should be screened for emotional distress and referred to psychology as appropriate.

Rationale

The diagnosis of breast cancer is understandably distressing to patients and elevated levels of distress may continue throughout the treatment and follow-up of the disease process. Up to 45 per cent of women with breast cancer continue to experience clinical anxiety and depression many months into their illness. Their distress, in turn, affects various realms of their illness experience including their

physical, psychological and social functioning. The treating team must be cognisant of this, as anxiety and depression may go undetected. Individual therapy, such as Cognitive Behaviour Therapy, has been found to be useful in helping women to utilise effective coping strategies in dealing with their breast cancer.

The involvement of breast care nurses (BCN) and psychologists who are aware of the distress associated with breast cancer and who have cultural and religious insight into patient's background are essential to ensure the overall well-being of the breast cancer patient.

Clinical notes

3.19 Women diagnosed with breast cancer should be screened for emotional distress.

3.20 Cognitive behaviour therapy should be offered by trained personnel to patients with breast cancers in an individual context, across all stages of disease, particularly for the emotionally vulnerable groups identified by the prior assessment of distress.

3.21 Cognitive behaviour therapy should be offered preferably right after diagnosis/surgery or months after diagnosis but not during medical treatment.

3.22 Psychosocial support should be provided by trained personnel for women with breast cancer, particularly to those with high initial emotional distress who will support them throughout the diagnosis, treatment and follow up.

Further discussion

Social support, whether tangible, informational or emotional, is necessary for women to adjust to life with breast cancer. Research has indicated that women who receive quality support have improved physical and emotional outcomes. This may be done via breast care nurses or groups such as hospice or local NGOs. The role of a BCN is to provide treatment and management, information and psychosocial support from the time of diagnosis and throughout women's treatment journey.

NICE guidelines suggested that adding the services of an advanced practice care nurse to standard care significantly reduced uncertainty, complexity, inconsistency and unpredictability without influencing quality of life or mood. Support from a BCN

following cancer surgery alleviated depression over time and receiving support from the BCN before and after receiving a pre-surgical diagnosis significantly lowered clinically-relevant anxiety. The addition of BCNs to the MDT should decrease the substantial number of geographically or socially vulnerable patients who fail to complete treatment, do not come for surgery, or do not attend follow-up.

Objective 11: Patient navigation

Standard 3.7	A named breast care nurse or counsellor should be allocated to each breast cancer patient to ensure a point of contact to the MDT.

Rationale

Social support, whether tangible, informational or emotional, is necessary for women to adjust to life with breast cancer. Research has indicated that women who receive quality support have improved physical and emotional outcomes. This may be done via breast care nurses, NPOs or groups such as hospice or local NGOs.

The role of a BCN or patient navigator is to provide treatment and management information and psychosocial support from the time of diagnosis and throughout women's treatment journey.

The addition of BCNs or patient navigators to the MDT should decrease the substantial number of geographically or socially vulnerable patients who fail to complete treatment, do not come for surgery, or do not attend follow-up.

Clinical notes

3.23 Patients should be provided with named BCNs or patient navigator within the SBU who will be point of contact to the MDT and co-ordinate their care.

3.24 Due to the paucity of trained and specialist BCNs the function of navigation may be performed by trained NPO lay counsellors, co-ordinated by a MDT (ideally a BCN or otherwise a clinician).

3.25 BCN/navigators will also form the link with the ward-based PHC outreach teams to provide an umbrella of support, particularly for vulnerable patients.

Further discussion

NICE guidelines suggested that adding the services of an advanced practice care nurse to standard care significantly reduced uncertainty, complexity, inconsistency and unpredictability without influencing quality of life or mood. Support from a BCN following cancer surgery alleviated depression over time and receiving support from the BCN before and after receiving a pre-surgical diagnosis significantly lowered clinically-relevant anxiety.

Key Area 4: Treatment of breast cancer

Objective 12: Surgery (early and advanced breast cancer)

Standard 4.1	All women with early breast cancer should undergo BCS or mastectomy (with or without reconstruction) to obtain cancer clearance from the breast.
Standard 4.2	All patients eligible for breast conserving surgery should be offered the procedure in a centre capable of performing this, with appropriate reconstruction.
Standard 4.3	All patients with eligible axillary finding for a Sentinel Lymph Node Biopsy should be offered this procedure above a ALND in a centre capable of providing it (SBU).

Rationale

Early breast cancer is breast cancer that has not spread beyond the breast or the axillary lymph nodes. This includes ductal carcinoma in situ (DCIS) and stage I, stage IIA (T0N1, T1N1, T2N0) and stage IIB (T2N1, T3N0) (See Figure 1). Surgery is the mainstay of treatment for early breast cancer and consists of either breast conserving surgery (BCS) or mastectomy (with or without reconstruction), and assessment of axillary lymph nodes.

A systematic review which included six randomised controlled trials (RCTs) with a 20 year follow up concluded that BCS and radiotherapy offers the same survival benefit (overall and disease free survival) as modified radical mastectomy in women with early breast cancer. Other outcome measures showed no substantial difference in post-operative psychological health between women who have had either modality.

Tumour size, axillary node involvement, histological grade and type are no longer considered valid reasons for not performing breast-conserving surgery. These, and other poor prognostic factors, predict the risk of distant failure, not local recurrence, and may indicate the need for systemic therapy, but are not indications for mastectomy.

BCS is accepted as the surgical technique for treatment of early breast cancer, provided the dual goals of complete extirpation of tumour and good cosmesis can be achieved in the same procedure. However, mastectomy is required if there are absolute contraindications to BCS. A retrospective study (n=1485) found that there was no difference in overall survival and disease free survival between BCS and mastectomy in centrally located tumours. In the same study, no difference was seen in BCS between centrally located and peripheral tumours.

Clinical notes

4 BCS is accepted as the surgical technique for treatment of early breast cancer. However, mastectomy is required if there are absolute contraindications to BCS. Contra-indications to BCS are:

(a) poor ratio of tumour size to the size of the breast
(b) location of the tumour would result in unacceptable cosmesis
(c) collagen vascular disease (scleroderma and systemic lupus erythematosis)
(d) conditions where local radiotherapy is contraindicated (such as previous radiotherapy at the site or connective tissue disease)
(e) multi-centric disease clinically or radiologically
(f) persistent positive margins post-breast conserving surgery
(g) radiotherapy not available or acceptable to patient
(h) pregnancy, although such surgery may be done during the third trimester with irradiation following delivery

4.1 In breast conserving surgery is an option for a woman with a centrally located tumour, although it may require excision of the nipple and areola, which may compromise cosmesis.

4.2 Access to radiation is an important contra-indication in South Africa where access to timely radiation can be difficult for geographically or socially vulnerable patients. BCS should not be performed if there is any doubt to the ability for the patient to undergo timely radiation, and should be confirmed with the patient pre-operatively.

4.3 Complete excision of the cancer with clear margins (between “no tumour on ink” for primary surgery or greater than or equal to 2 mm according to local protocol) is advised in breast conserving surgery.

4.4 For DCIS, margins should be no less than 1mm.

4.5 Sentinel node biopsy should not be carried out in women with clinically involved nodes.

4.6 Sentinel lymph node biopsy may be offered to the following:

(a) unifocal tumour of ≤ 3cm

(b) clinically non-palpable or equivocal axillary nodes (i.e. node negative)

(c) extensive DCIS or DCIS necessitating a mastectomy

4.7 Sentinel lymph node biopsy should only be performed by surgeons who are trained and experienced in the technique.

4.8 Dual technique (most commonly with isotope and blue dye) in performing the sentinel lymph node biopsy is preferred.

4.9 The patient should be informed of the potential for an unsuccessful SLNB or a false negative result.

4.10 Surgery of the primary tumour may be considered in Stage IV breast cancer as part of an individualised MDT team decision.

4.11 A CPM should be considered in patients where there is:

(a) a high risk for CBC, i.e. BRCA mutation carriers, family history of breast or ovarian cancer in multiple first degree relatives

(b) difficult surveillance- mammographic dense breasts /diffuse indeterminate micro-calcifications

(c) improved symmetry or desire for bilateral reconstruction

Further discussion

Cancer free margin in breast conserving surgery (BCS):

Surgical margins are the strongest predictor of local recurrence following BCS. Complete excision reduces the risk of local recurrence. Consequently, the primary aim of surgery is to obtain adequate negative margins of excision. The NSABP-06 study was the first to define the margin as negative if no tumour cells were found at the ink of the surgical specimen on pathology. This has now become the universally accepted definition of a negative margin for invasive breast cancer, irrespective of

age, tumour pathology or anticipated adjuvant therapy, after the SSO/ASTRO consensus guidelines in 2014 decreed that “No ink on tumour is the standard for an adequate margin in invasive cancer in the era of multimodality therapy”.

Taking cavity shaves around the BCS specimen at the time of initial surgery has been shown to reduce re-excision. A recent single centre RCT of cavity shave margins by Chagpar *et. al* demonstrated that patients in the shave group had a significantly lower rate of positive margins than did those in the no-shave group (19% vs. 34%, P = 0.01) as well as a lower rate of second surgery for margin clearance (10% vs. 21%, P = 0.02). There was no significant difference in complications between the two groups.

The recommended margin for DCIS is still controversial. Current NCCN guidelines for DCIS state, “margins less than 1 mm are considered inadequate.” However, close surgical margins (<1 mm) at the fibroglandular boundary of the breast (chest or skin) do not mandate surgical re-excision but can be an indication for higher boost dose radiation to the involved lumpectomy site.

Axillary surgery in early breast cancer:

Axillary lymph node dissection (ALND) comprises removal of one, two or three levels of nodes relative to the pectoral is minor muscle. Typically, 10 - 15 lymph nodes are retrieved and at least one section from each assessed by standard haematoxylin and eosin (H&E). The New Zealand guidelines highlighted the importance of accurate assessment and management of the axillary nodes in women with early breast cancer. The assessment should be undertaken for most early invasive breast cancers in order to stage the disease, minimise the risk of loco-regional recurrence and assist in planning of adjuvant therapy.

Several adverse events are associated with the management of the axilla and women should be advised of the benefits and potential harms associated with each procedure. Axillary node dissection is more effective at lowering the risk of local recurrence than axillary node sampling, which in turn is more effective than no axillary surgery. No evidence was identified on the effectiveness of excision of the supra-clavicular and internal mammary chain nodes compared with no excision.

Indications for sentinel lymph node biopsy (SLNB) in breast cancer:

SLNB is the new gold standard for staging the clinically node negative axilla. This was confirmed in five RCTs: Milan, NSABP-32, RACS SNAC, ALMANAC, and the ACOSOG trials (see references). NZGG reviewed NBOCC guidelines and one systematic review, and concluded that SLNB should be performed by surgeons who are trained and experienced in SLNB. Another trial noted that the accuracy increased and false negative decreased when the surgeon performed 30 or more procedures. Four RCTs and one systematic review evaluating technical aspects of SLNB, reported that combination radioisotope and blue dye has a higher rate of sentinel lymph node detection than blue dye method *alone*.

SLNB is evolving in selected clinical settings such as older women, men and in locally advanced or multicentre disease:

In **older women**, a positive SLNB followed by a completion axillary lymph node dissection (ALND) did not improve all-cause or breast-cancer-specific survival in women over 65 years of age. In a retrospective review of the Surveillance, Epidemiology, and End Results (SEER) database, the five-year all-cause survival for patients with a positive sentinel node who underwent a completion ALND (n = 4586) did not statistically differ from similar women who did not undergo an ALND (n = 629), (84 versus 83 percent) [85]. In addition, there was no significant difference in five-year breast-cancer-specific survival (94.6 versus 91.6 percent). An analysis of prospective data is needed to confirm these retrospective findings.

Data are limited in **male breast cancer** (MBC), because it is uncommon. The vast majority of published studies of SLNB for breast cancer are in women. A retrospective study of 30 men with breast cancer reported a 100 percent SLNB identification rate and a false-negative rate of zero per cent. Prospective studies establishing the sensitivity and specificity of SLNB in MBC have not been carried out. However, the principles guiding SLNB in women appear to apply to men. Due to the limited amount of data, the 2005 American Society of Clinical Oncology (ASCO) guidelines on SLNB did not make a specific recommendation about the use of SLNB in MBC, although it was deemed "acceptable".

The 2005 ASCO guidelines on SLNB did not recommend the routine use of SLNB in patients with **locally advanced or inflammatory breast cancer** for whom ALND was recommended to ensure loco-regional control. Consensus recommendations

from an International Expert Panel published in 2010 considered inflammatory breast cancer to be the one of the few absolute contraindications to SLNB.

Most studies have restricted SLNB to T1 or T2 breast cancers <5 cm in size, since larger tumours have a higher likelihood of positive axillary nodes. However, some studies have shown that SLNB is accurate in patients with T3 tumours and clinically negative axillae. Many clinicians do not recognize large breast tumours as a contraindication to SLNB, as long as the axilla is clinically negative. However, patients with T4 tumours (locally advanced) or inflammatory breast cancer are not considered candidates for SLNB. The false-negative rate is high in patients with inflammatory breast cancer, presumably because of the presence of partially obstructed, functionally abnormal subdermal lymphatics.

Many women with large primary breast tumours are offered **neoadjuvant chemotherapy** prior to definitive loco-regional therapy. The optimal timing for SLNB in patients receiving neoadjuvant therapy remains controversial and is discussed separately.

ASCO guidelines indicate that a SLNB is appropriate for patients with **multicentric disease**. Studies that evaluated the functional anatomy of lymphatic drainage support the theory that all quadrants of the breast drain into the same lymph node(s). Thus, subareolar and intradermal (rather than peritumoral) injection of radiolabeled colloid or blue dye render SLNB feasible for patients with multicentric disease. The success of SLNB for multicentric disease has been demonstrated in several studies. In a study of 142 women with multicentric breast cancer, SLNB was successful in 91 per cent, with a false-negative rate of four per cent. However, the number of patients requiring completion ALND because of a positive SLN is higher in multicentric compared with unicentric disease. The likelihood of finding additional disease at the time of completion ALND is also higher with multicentric disease.

Most women with **ductal carcinoma in situ (DCIS)** do not require assessment of the axillary nodes, particularly if they are undergoing breast-conserving therapy. However, women with DCIS may be candidates for SLN mapping if they are undergoing mastectomy, because the performance of SLNB will be impossible at a later time if invasive disease is found. An intact breast with its lymphatic plexus is necessary for injection of both the blue dye and the radioisotope tracers.

SLNB can be considered in patients who are undergoing breast-conserving therapy or mastectomy for DCIS only if the risk of node metastases is increased, as with extensive high-grade DCIS, a strong suspicion of invasive disease based upon ancillary imaging, or documented microinvasive disease in the core biopsy. If BCS is performed and invasive disease is identified, a SLNB can be done as a separate operation. This approach can minimize unnecessary morbidity, since SLNB can be associated with complications.

Other important considerations for Sentinel Lymph Node Biopsy (SLNB) in breast cancer:

Pregnancy — According to the 2014 ASCO guidelines, a SLNB should not be performed in women who are pregnant or lactating. Concern for teratogenic effects with the use of isosulfan blue dye has limited the use of SLNB during pregnancy, despite the lack of studies testing the foetal safety of the dyes. There are limited data that suggest it might be safe. As an example, a retrospective study that included 25 clinically node-negative pregnant patients who were administered methylene blue (n = 7), 99-Tc (n = 16), and another type of injection material not otherwise specified (n = 2) found no adverse foetal outcomes that could be attributed to the injection at 2.5 years of follow-up.

Previous breast or axillary surgery for non-malignant conditions: The feasibility of SLNB in women who have undergone other non-oncologic types of breast surgery such as reduction mammoplasty or augmentation with breast implants is unclear. The expert panel convened by ASCO did not make a recommendation for or against SLNB in women who have had breast reduction or augmentation because of insufficient data. They suggested that if SLNB was considered in this setting that it might best be performed with preoperative lymphoscintigraphy.

Recurrent breast cancer and previous axillary procedures: SLNB after previous axillary surgery has not been widely studied. Guidelines from ASCO recommend against SLNB in women who have undergone prior axillary surgery. However, this practice is becoming more frequently employed and further study is indicated, including the optimal interval before repeat sentinel node biopsy should be attempted. There are accumulating reports of successful second SLNB in patients with local breast cancer recurrence following a previous SLNB and/or ALND. A

retrospective review of 150 patients with a previous SLNB or ALND, revealed that lymphatic mapping (lymphoscintigraphy) using 99 m Tc-colloidal albumin identified a sentinel node in 63 per cent, and the sentinel node was successfully removed in 52 per cent of patients. Aberrant drainage patterns were identified in 59 per cent; patients with a previous ALND were more likely to have an aberrant pattern compared with patients who had a previous SLNB (79% versus 25%, p <0.001). A micrometastasis was identified in 18 patients (23%), and a confirmation ALND in all 18 patients identified no additional positive axillary lymph nodes.

Contralateral Prophylactic Mastectomy (CPM):

The risk of contralateral breast cancer (CBC) is low. The annual incidence is reported as 0.13 per cent (Quan et al) and 0.6 per cent (Swedish cancer institute BC data base). A CBC is usually a lower stage than the initial unilateral breast cancer. If the initial breast cancer was stage II or III, overall survival with CBC is the same as the unilateral breast cancer. (SEER1998-2003). However, CBC adversely impacted survival for low stage initial breast cancer patients who developed CBC within three years.

Some subgroups of breast cancer patients are more likely to get CBC including:

- there is a significant family history of breast cancer
- the patient is a BRCA mutation carrier
- the first breast cancer was diagnosed at a younger age
- the initial cancer was multi-centric
- the Gail risk was >1.67

The 15-year risk of CBC in BRCA carriers was 35.4 per cent compared with 10.4 per cent in non-carriers, and was as high as 52.4 per cent in carriers <40 years at initial breast cancer diagnosis. A case control study (n=2000) reviewing the effect of BRCA status on risk for CBC revealed a 4.5 per cent increase of CBC in BRCA I mutation carriers and a 3.4 per cent increase of CBC in BRCA II mutation carriers. The MD Anderson reviewed the histology of 542 contralateral prophylactic mastectomies (CPM) in patients with unilateral breast cancer and revealed cancer in 4.6 per cent and atypical cells with a moderate to high risk of cancer in 15 patients. The majority of studies of CPM in high risk women indicate an 85-100 per cent reduction of developing contralateral breast cancer and increased overall survival.

Monitoring and evaluation point

ME 13	Percentage of eligible patients undergoing breast conserving surgery
ME 14	Percentage of node-negative patients receiving ALND

Objective 13: Breast reconstruction (immediate versus delayed)

Standard 4.4	All patients should have reconstruction options discussed with them in their pre-operative consultation
Standard 4.5	The choice of immediate or delayed reconstruction should be discussed with the MDT and made with the patient for best oncological and cosmetic outcome

Rationale

The aim of immediate breast reconstruction is to improve well-being and quality of life (QoL) for women undergoing mastectomy for breast cancer. Although many factors may influence QoL, patients with immediate reconstruction after breast cancer surgery reported the same emotional well- being and physical role functioning as that of the normal population at one year.

Evaluation to determine psychosocial differences between patients who underwent immediate (n = 25) versus delayed (n=38) breast reconstruction revealed that only 25% of the women who underwent immediate reconstruction reported “high distress” in recalling their mastectomy surgery compared with 60 per cent of the delayed reconstruction group (p = 0.02). However patient recorded outcomes (PROM) in some studies suggest delayed reconstruction may have more durable long-term satisfaction.

There is very limited high quality evidence as to whether the timing of breast reconstructive surgery alters the local recurrence rate and overall survival. However, based on the NICE guideline, there is no difference in recurrence and survival following mastectomy with immediate reconstruction compared to mastectomy with no reconstruction. Based on observational studies, breast reconstruction does not

appear to be associated with an increase in the rate of local cancer recurrence, or to impede the ability to detect recurrence if it develops.

Clinical notes

4.12 Caution is required before offering immediate breast reconstruction to women who are active smokers or obese.

4.13 Discuss immediate breast reconstruction with all patients who are advised to have a mastectomy for early breast cancer, and offer it, except where significant co-morbidity or (the need for) adjuvant therapy may preclude this option.

4.14 In patients who are candidates for breast reconstruction and need adjuvant radiotherapy, commonly reconstruction should be delayed until radiation therapy is completed.

4.15 However, when immediate breast reconstruction is undertaken in patients who need post-mastectomy radiotherapy, autologous reconstruction should be the preferred method of reconstruction.

Further discussion

Expert opinion from NZGG Development Group noted that radiotherapy to the reconstructed breast may result in significantly worse cosmetic outcome, especially when an implant had been used.

A retrospective study carried out in the MD Anderson Cancer Centre showed that 87.5 per cent of patients who had radiation therapy after immediate free transverse rectus abdominis myocutaneous (TRAM) flap reconstruction had late complications compared to 8.6 per cent of patients who had delayed free TRAM flap reconstruction after radiotherapy. Distorted contour due to flap contraction from radiation therapy required re-operation in 28 per cent of these patients. These findings indicate that, in patients who are candidates for free TRAM flap breast reconstruction and need post-mastectomy radiation therapy, reconstruction should be delayed until radiation therapy is complete.

A meta-analysis reviewing the optimal sequencing of breast reconstruction in patients receiving post-mastectomy radiation therapy included 1 105 patients from 11 selected studies found that those undergoing post-mastectomy radiation therapy are 4.2 times more likely to suffer adverse events as patients not undergoing post-mastectomy radiation therapy. When post-mastectomy radiation therapy was delivered after immediate breast reconstruction, patients who had autologous tissue–based reconstruction had one-fifth the risk of adverse events compared with patients who had implant-based reconstruction. Delay of breast reconstruction until after post-mastectomy radiation therapy had no significant effect on outcome.

A retrospective review of 224 pedicled TRAM flap reconstructions in 200 patients over a 10-year period found that active or former smoking and obesity contribute to a significant complication rate. Similarly, the Michigan Breast Reconstruction Outcome Study, a prospective cohort study of 326 patients, found that the most significant factors associated with higher complication rates were timing of reconstruction and body mass index. Both immediate breast reconstruction and obesity were associated with higher and major complication rates. The type of reconstruction, whether implant, pedicled TRAM or free TRAM, had no effect on complication rate.

Monitoring and evaluation point

ME 15	Number of patients undergoing reconstruction
ME 16	Documentation of reconstruction discussion in medical notes.

Objective 14: Systemic therapy in early stage breast cancer

Standard 4.6	All patients with breast cancer should have access to adjuvant systemic therapies including chemotherapy, biological therapies and hormonal blockade
Standard 4.7	Adjuvant systemic therapy, given after definitive surgery, should be offered to all eligible patients for presumed micro-metastatic disease.

Rationale

In early stage breast cancer, long term survival is governed by the control of micro-metastatic disease; which may occur very early in the evolution of the malignancy.

Multiple randomised controlled trials have demonstrated both a local control and overall survival benefit from the use of systemic therapy (given either before, or shortly after, definitive surgery for breast cancer).

The indications for, and type of, adjuvant systemic therapy is based on the biological subtype of the primary tumour; the risk of recurrence; patient co-morbidities and patient preferences. Adjuvant systemic therapy may involve one, or a combination of, the following options: endocrine therapy, chemotherapy and biological therapies

Clinical notes

Adjuvant endocrine therapy

4.16 Almost all patients with endocrine sensitive tumours should be considered for adjuvant endocrine therapy.

4.17 In patients with node negative, ER (endocrine receptor) positive, tumours of <0.5cm (with no adverse biological features) however, the risk of recurrence is so small that this may be omitted.

4.18 Adjuvant Endocrine options for post-menopausal women include:

(a) Selective Estrogen-Receptor Modulators (SERMs), e.g. Tamoxifen

(b) Aromatase Inhibitors (steroidal and non-steroidal) for Tamoxifen-intolerance

(c) Tamoxifen followed by an Aromatase Inhibitor or Aromatase Inhibitor followed by Tamoxifen (so called “switching” strategy)

4.19 Adjuvant Endocrine options for premenopausal women include:

(a) SERMs – Tamoxifen

4.20 Current recommendations on the duration of hormonal therapy depend on the type of blockade used and the risk of recurrence. Extended adjuvant therapy (i.e. beyond five years) is generally restricted to those patients with high risk disease.Acceptable options include:

(a) AI for 5yrs (ATAC and BIG-19-8 studies)

(b) Tamoxifen for two to three years followed by AI for two to three years or *vice versa* (TEAM and IES study)

(c) Tamoxifen for 10 years (ATLAS study)

Adjuvant chemotherapy:

4.21 If adjuvant chemotherapy is given, a multidrug regimen should be used. Anthracycline and Taxane based regimens have shown superiority to older chemotherapy regimens especially in high-risk patients, but may not be appropriate for low-risk patients and patients with cardiac and other co-morbidities.

4.22 In BRCA1 mutated patients, the inclusion of a platinum agent may be considered, but this is not currently recommended for all “triple negative” breast cancers.

4.23 In platinum should only be used in patients with creatinine clearance above 6ml/min while carboplatin used in patients with creatinine clearance above 30ml/min. It is more myelo-suppressive especially on platelets.

4.24 Level 1 evidence supports the use of the following adjuvant chemotherapy regimens. Refer to Appendix for flow diagram of treatment regimen.

Adjuvant biological therapy:

4.25 Due to the high risk of micro-metastatic disease associated with HER2+ tumours (even small, node negative tumours), adjuvant trastuzumab based therapy should be considered in all HER2+ tumours.

4.26 Adjuvant trastuzumab is not recommended in either low-risk, negative patients or patients who have not received adjuvant chemotherapy.

4.27 Trastuzumab (given every three weeks) for one year in the adjuvant setting is the current, international, standard of care.

4.28 Due to overlapping cardiotoxicities of anthracyclines and trastuzumab, the benefit of trastuzumab is greater if given concurrently with adjuvant chemotherapy (as opposed to sequentially).

Neoadjuvant systemic therapy:

4.29 All chemotherapy regimens used in the adjuvant setting can be used in the neo-adjuvant setting.

4.30 In HER2+ breast cancer, trastuzumab should be included in the neoadjuvant regimen.

Further discussion

Adjuvant endocrine therapy

The EBCTCG meta-analysis (updated in 2015) showed a significant reduction in the risk of recurrence; breast cancer mortality and overall mortality with use of adjuvant aromatase inhibitors, compared with Tamoxifen. A switching strategy (incorporating sequential use of Tamoxifen and an Aromatase Inhibitor) was also shown to be better than Tamoxifen alone (and to havesimilar effect breast cancer mortality, although associated with a slightly higher recurrence rate, than five years of an Aromatase Inhibitor).

The results of the SOFT and TEXT trials have shown that there is no difference between Tamoxifen alone and Tamoxifen + Ovarian Suppression. A DFS advantage was, however, shown in the Ovarian Suppression + exemestane group vs. Ovarian Suppression + Tamoxifen group. This was particularly pronounced in those women who remained premenopausal after exposure to chemotherapy. Therefore, ovarian suppression + exemestane should be considered for high risk premenopausal patients but Tamoxifen alone is appropriate treatment for low risk patients.

Adjuvant chemotherapy

Data from the EBCTCG meta-analysis of numerous randomised trials have demonstrated that adjuvant chemotherapy results in a 36 per cent reduction in the 10-year risk of breast cancer mortality. This holds across all subgroups, however, the absolute benefit for an individual patient is governed by the risk of recurrence.

The probability of recurrence can be determined from risk factors related to the pathological features of the tumour (such as nodal status; size of tumour; grade; hormone receptor expression; HER2 expression and Ki67 index). Mathematical calculations such as Adjuvant Online; Lifemath.net and Predict use these features to calculate the risk of recurrence and probable benefit of adjuvant chemotherapy.

Adjuvant biological therapy:

In patients with HER2+ disease, the addition of trastuzumab (a recombinant monoclonal antibody directed at the extracellular domain of HER2) to adjuvant chemotherapy confers a 48% reduction in risk of local recurrence and a 39%

reduction in the risk of death. Due to the high risk of micro-metastatic disease associated with HER2+ tumours (even small, node negative tumours), adjuvant trastuzumab based therapy should be considered in all HER2+ tumours > 0.5cm.

Whilst evidence shows that the addition of trastuzumab confers substantial risk reduction in recurrence and death, discussion regarding cost of treatment is beyond the scope of this document. It is recommended subject to negotiations with the pharmaceutical providers for a cost that will not compromise care-provision in other sectors of the healthcare system.

Neoadjuvant systemic therapy

Clinical trials have shown no difference in overall survival when adjuvant systemic therapy is given either before or after surgery. Potential advantages of neo-adjuvant systemic therapy include:

- down-staging of locally advanced tumours, thereby rendering them amenable to surgical resection
- down-staging tumours to facilitate breast conserving surgery
- evaluation of “in vivo” chemo-sensitivity of the tumour

In general, chemotherapy is preferred over hormonal therapy in the neoadjuvant setting (although hormonal blockade alone is a reasonable option in patients who are strongly ER positive and in which chemotherapy is contra-indicated). All chemotherapy regimens used in the adjuvant setting can be used in the neo-adjuvant setting.

There is more evidence to consider the incorporation of a platinum agent depending on the renal function in the neoadjuvant treatment of TNBC, as studies have shown improved PCR rates in this setting (although it is not yet known whether this will translate into overall survival advantage)

In HER2+ breast cancer, trastuzumab should be included in the neoadjuvant regimen.

Monitoring and evaluation point

ME 17	Documentation of all patients discussing in MDT with systemic therapy decision made
ME 18	Percentage of eligible patients seen and commenced on neo-adjuvant therapy within 30 days of diagnosis
ME 19	Percentage of eligible patients seen and commenced on adjuvant therapy within 90 days of surgery

Objective 15: Systemic therapy in locally- advanced stage breast cancer

Standard 4.8	Neo-adjuvant chemotherapy or primary systemic therapy is an established option for most patients with LABC

Rationale

Locally advanced breast cancer (LABC) is a heterogeneous group of invasive cancers, from slow growing to rapidly proliferating and aggressive tumours, characterised clinically by size, features suggesting infiltration of chest wall or skin by tumour, and/ or nodal status. This is a common stage of presentation in breast cancer patients in South Africa. LABC includes cancer with:

- large size (> 5 cm) TNM stage IIIA: T3 with any N
- fixed or matted axillary : TNM stage IIIA: N2 with any T1-3
- skin ulceration or satellite nodules, peaud'orange or chest wall involvement
- inflammatory breast cancer
- supra-clavicular nodes (N3)

These patients do not have distant metastatic disease.

The NICE guidelines stated that there was no significant difference in overall survival (OS) and disease free survival (DFS) between neo-adjuvant chemotherapy and postoperative chemotherapy. However, better tumour response to chemotherapy was associated with better outcomes. The NICE guidelines also elaborated that after neo-adjuvant chemotherapy for LABC, surgery and/or radiotherapy is still essential for adequate long term local control. This included patients with complete clinical

response. Many retrospective reviews suggest that radiotherapy reduces LRR and improves survival in patients following neo-adjuvant chemotherapy and mastectomy.

Clinical notes

4.31 Neo-adjuvant chemotherapy or pre-operative systemic therapy can be offered to downsize operable locally advanced breast cancer that is not amenable for BCS at presentation.

4.32 In locally advanced breast cancer that is inoperable, neo-adjuvant chemotherapy should be given to downsize the tumour to enable subsequent surgery.

4.33 Patients undergoing neo-adjuvant therapy with an expectation of BCS should have a V-marker inserted under sonar guidance prior to the commencement of therapy.

4.34 All patients with LABC should be adequately staged according to local protocol before commencing neo-adjuvant chemotherapy

Further discussion

Neo-adjuvant chemotherapy can be given to downsize the tumour in an attempt for BCS or enable subsequent surgery for initially inoperable breast cancer. The placement of metal clips into the tumour, prior to oncology treatment, aids the location of the cancer for BCS when there has been a significant response to neo-adjuvant chemotherapy.

In addition to improving both operability and rates of BCS, neo-adjuvant chemotherapy also provides a valuable window to assess disease response to treatment and perform correlative tissue analyses. A systematic review concluded that neo-adjuvant chemotherapy gives better clinical and pathological response in ER-negative tumours. Combinations of a taxane and anthracycline and the use of biological response modulators (e.g. Trastuzumab) gives high pathological complete responses (pCR) in HER-2 positive tumours.

Other characteristics of tumours which respond well to chemotherapy include the non-lobular type, high grade histology, high Ki67 and luminal type B. These tumour types have a greater chance of responding and should be considered for neo-

adjuvant chemotherapy. In contrast, tumours which show low response to chemotherapy (such as lobular type and low Ki67) should be considered for alternative approaches (such as neo-adjuvant endocrine therapy or mastectomy as initial treatment).

Monitoring and evaluation point

ME 20	Percentage of eligible patients seen and commenced on neo-adjuvant therapy within 30 days of diagnosis for LABC
ME 21	Percentage of patients eligible for surgery following neo-adjuvant therapy

Objective 16: Systemic and local therapy in metastatic breast cancer

Standard 4.9	Patients with metastatic breast cancer should be offered appropriate systemic therapy for symptom control
Standard 4. 10	All patients should be discussed by the MDT and those suitable for surgery or adjuvant radiation referred for treatment within 42 days of referral

Rationale

Metastatic breast cancer is generally regarded as an incurable condition and the aim of treatment is an improvement in quality of life and prolongation of survival. The tumour biology, patient comorbidities and potential impacts of treatment modality on quality of life have to be considered in decision making regarding the selection of systemic therapy in these patients. Median survival is around two years (but ranges between a few months and many years).

The true value of the removal of the primary tumour in patients with *de novo* stage IV breast cancer is currently unknown, but can be considered in selected patients. Some studies suggest that surgery is only valuable if carried out with the same attention to detail as in patients with non-metastatic breast cancer in terms of margin status and addressing disease in the axilla.

Clinical notes

4.35 Because the selection of treatment is dependent on tumour biology (and this may change from the primary to metastatic sites) biopsy of a metastatic lesion is recommended, wherever technically feasible.

Hormonal therapies

4.36 In the absence of a visceral crisis, or situation where a very rapid response to treatment is required, patients that have ER positive disease should be considered for hormonal therapy as the first line of treatment.

4.37 The type of hormonal blockade depends on the menopausal status of the patient and drug availability/ affordability.

Systemic therapies

4.38 In patients with hormone sensitive disease hormonal blockade should be used in sequence with the chemotherapy (not concurrently).

4.39 The choice of cytotoxic agent (and sequencing thereof) in the metastatic setting is dependent on patient preference; patient comorbidities and specific toxicity profiles of the various agents.

4.40 The duration of treatment is determined by the impact of the treatment on quality of life and tumour response.

4.41 Surgery for the primary tumour in metastatic breast cancer still requires more evidence. Until it is available surgery of the primary should not be offered as a routine practice but offered to selective patients.

Further discussion

As with adjuvant therapy, the systemic treatments in the metastatic setting can be divided into:

1) Cytotoxic Chemotherapy
2) Hormonal therapies
3) Biological therapies
4) Bone directed therapies

Cytotoxic chemotherapy

For those patients who have hormone receptor negative disease (or who have progressed on hormonal blockade) cytotoxic chemotherapy has the potential to improve survival; palliate symptoms and improve quality of life. In the absence of a visceral crisis (or need for rapid disease response to alleviate symptoms) sequential single agent chemotherapy is usually preferred. Combinations of chemotherapeutic agents have been shown to improve response rates, but have very little impact on overall survival and are associated with increased toxicity profiles.

Biological therapies

HER2 targeted therapy has been shown to significantly improve disease free and overall survival in patients with metastatic HER2+ disease. In most patients, this is initially given in conjunction with chemotherapy and then continued as (single agent) maintenance treatment (or in conjunction with hormonal blockade, in ER positive patients). In some instances, where there is limited disease burden or chemotherapy is contra-indicated, a combination of HER2 targeted therapy with hormonal therapy alone may be considered upfront. The costs of HER2 targeted treatments, however, limit accessibility worldwide and in the South Africa settings.

Based on the highly significant survival benefit demonstrated in the Cleopatra study, the combination of Pertuzumab, Trastuzumab and Docetaxel has become the preferred first line regimen for patients with metastatic HER2+ disease in countries where Pertuzumab is available and affordable. The combination of Trastuzumab and Chemotherapy remains the recommended first line option.

HER2 amplified tumours have been shown to remain “oncogene addicted” and the continuation of HER2 directed therapy post progression has been shown to impact on progression free survival and, in some instances, overall survival.

Bone Directed Therapies

For patients with bone metastases, the use of bisphosphonates and Rank Ligand Inhibitor has been shown to reduce bone pain; pathological fractures and hypercalcemia.

Surgery for the primary tumour in metastatic breast cancer:

In 2012 the British Columbia large retrospective series reinforced the importance of treating the primary; with the most favourable survival rates observed in subsets of patients with young age, good performance status, ER positive disease, distant disease limited to one site, bone-only involvement or fewer than five metastatic lesions. A 2012 meta-analysis of 15 publications reinforced the idea that surgery to the primary tumour appeared to be an independent factor for improved survival in the multivariate analyses from the individual trials, with a hazard ratio of 0.69 which was statistically significant ($p < 0.00001$).

There are presently six randomised trials comparing locoregional treatment of the primary versus no locoregional treatment in patients presenting with stage IV disease. In 2013 very early data from two of these prospective trials could not confirm the previous conclusions from the retrospective trials. These two trials suggested that only a limited sub-group of patients with solitary bone metastases seemed to profit from surgery, while patients with multiple visceral metastases showed a worse prognosis after initial surgery. However, there were limitations to these trials. More studies with better patient selection are necessary to resolve the question of surgery for the primary tumour in metastatic breast cancer. Until these results are available, surgery of the primary should not be offered as a routine practice, but offered to selective patients.

Resection of metastases in metastatic breast cancer:

The NICE guidelines concluded that there was no good evidence on the surgical treatment of metastatic brain disease from breast cancer. However, they suggested surgical therapy followed with whole brain radiotherapy may be considered in patients with a single or a small number of potentially respectable brain metastases who have good performance status and no or well-controlled other metastatic disease.

Retrospective studies have shown that there may be an OS benefit in resection of lung or liver metastases in selected cases. Yashimoto et al. retrospectively followed up 90 patients who had surgery for lung metastases and concluded that surgery may benefit those who had early breast cancer with a disease free interval of > three years and metastatic disease of <2 cm. Two small studies looking at liver metastasis

from breast cancer showed no benefit in overall survival in patients with synchronous tumours, a short disease free interval and an aggressive cancer.

Monitoring and evaluation point

ME	Documentation of all patients with metastatic disease discussed in MDT with systemic therapy decision made
ME	Metastatic patients referred for surgical or radiation managed within 42 days

Objective 17: Radiotherapy in breast cancer

Standard 4.1	Radiation should be offered to all patients after breast conserving surgery within 90 days
Standard 4.2	Post-mastectomy radiation should be offered in where there is a high-burden of disease in either the breast or axilla within 60 days
Standard 4.3	A written local protocol for radiation should be disseminated by the radiation oncology department of the POU to all referring MDT and SBUs

Rationale

Radiotherapy plays an important role in the management of breast cancer in both adjuvant and metastatic settings.

Post-operative radiation may be given after all breast-conserving surgery or in selective cases after mastectomy. The indications for radiation after mastectomy have been expanded over the last few years due to a number of studies which have indicated further benefit to be derived from treatment.

The 2011 EBCCTG meta-analysis of randomised trials comparing radiotherapy vs none following breast conserving surgery showed that the addition of adjuvant whole breast irradiation reduced the 10 year relative risk of local recurrence by almost 50 per cent (RR – 0.52; absolute benefit of 16%). In addition, a reduction in the risk of death of 18 per cent (absolute benefit of 4%) at 15 years, was observed. Based on

these (and other) results, the majority of breast cancer patients treated with breast conserving therapy should receive adjuvant irradiation to the breast.

Fractionation schedules vary, but the results of the START A and B trials make hypo-fractionated regimens (given over 3 weeks) a reasonable alternative to conventionally fractionated regimens (given over 5 weeks). Controversy exists as to whether hypo-fractionated regimens are appropriate for node positive patients (where regional nodal irradiation is required) and those treated with neo-adjuvant chemotherapy.

The EBCTCG meta-analysis (and other randomised studies) has shown significant improvements in both loco-regional control and overall survival with the inclusion of radiotherapy (post mastectomy) in node positive patients. Similar benefits were demonstrated in those patients with one to three positive nodes and > 4 positive nodes.

Clinical notes

4.42 It may be reasonable to consider omission of radiotherapy in women over the age of 70 with T1N0 ER positive tumours treated with hormonal therapy (based on the results of the CALGB 9394 study, which showed a reduction in the risk of local recurrence at 10 years, from 10 to two per cent, but no impact on overall survival or mastectomy rate).

4.43 Most node negative patients, treatment of the breast only is required (however, inclusion of regional nodes may be considered in those patients with high risk, node negative tumours).

4.44 In node positive patients, the radiation fields should be extended to include regional nodal groups.

4.45 Fractionation schedules may vary according to local protocols, but should be agreed and disseminated within the MDT.

4.46 A boost to the tumour bed has been shown to improve loco-regional control and is generally recommended in younger patients. As there is no evidence of improved survival benefit, with a boost, it is reasonable to omit this in older patients with low risk disease.

4.47 Post-mastectomy radiation is beneficial for all node positive patients. Patients with one to three positive nodes may have post-mastectomy radiation on an individualised basis or according to local protocol.

4.48 Post-mastectomy radiation should be considered in high risk node negative patients i.e. those with:

(a) tumours >5cm;

(b) positive margins and

(c) greater than T2 tumours with other risk factors (such as very young age; triple negative phenotype and lympho-vascular invasion)

4.49 In general, the radiation fields for post mastectomy irradiation include regional nodal basins. Inclusion of internal mammary nodes is individualised.

4.50 Palliative radiotherapy is an extremely useful modality for alleviating symptoms in patients with metastatic breast cancer (including those with soft tissue; bone and brain metastases).

Monitoring and evaluation point

ME	Patients simulated within 60 days
ME	Treatment completed within 120 days

Key Area 5: Palliative care in breast cancer

Objective 18: Palliative care management for patients

Standard 5.1	Palliative care services should be available to every eligible patient (Stage 4 disease) and involved early in their care.
Standard 5.2	In collaboration with palliative care services, nursing professionals specific to palliative breast cancer care in SBUs/POUs can provide basic palliative care and provide liaison for further care.

Rationale

Palliative care is necessary to alleviate pain and unnecessary morbidity. The WHO recommends a comprehensive national palliative care programme in every country. South Africa is developing a palliative care policy and the aim of these standards is to provide care to dovetail into that more holistic programme.

Palliative care has its genesis in the hospice tradition. Previously this type of care was delivered primarily at the end of life. It is now recognised that palliative care should be given at earlier stages of the disease, alongside standard medical treatment, to improve the quality of care.

Palliative care is of critical importance for patients present with advanced disease. Barriers to palliative care include the lack of knowledge by practitioners of the correct use of opioids, fear of punishment for inappropriate use and concern that patients may become addicted. These barriers can be addressed through education of healthcare workers and patients.

The role of palliative care is distinct from that of oncology, although the two are complementary. Palliative care specialists concern themselves with psychosocial issues and building relationships with patients and families; oncologists, on the other hand, focus on cancer treatment and the management of medical complications.

Clinical notes

5 WHO guidelines emphasise the following in order to improve palliative care provision:

(1) access to affordable opioids

(2) trained and available personnel for palliative care

(3) development of effective home care programmes

5.1 Home care is the preferential approach in LRCs. Home palliative care programmes, even in remote rural areas, have been shown to be feasible and cost-effective in a range of LRCs.

5.2 Palliative care is not restricted to pain management by opioids. It includes radiotherapy, management of treatment side-effects, and other breast cancer therapies. The focus of palliative care is not only on end-of-life care, but on supporting patients and families to navigate the diagnosis, and helping them cope with their illness and prognosis.

5.3 The roles of palliative care in cancer services may not be to duplicate the palliative care services available, but as a liaison service to allow the provision of basic palliative care and referral for more complex services.

Further discussion

The skill set for basic provision of palliative care for each doctor in the SBU and POU should include:

1) Basic Management of Pain and Symptoms
2) Basic Management of Depression and Anxiety
3) Basic Discussions Regarding Prognosis, Treatment Goals, Suffering and Code Status

Cases where more complex speciality services are required may be:

1) Management Refractory Pain and Other Symptoms
2) Management of More Complex Depression, Anxiety, Grief and Existential Distress
3) Assistance with Conflict Resolution Regarding Goals or Methods of Treatment within Family Units, Between Staff and Families and Among the Healthcare Teams

Key Area 6: Follow-up and surveillance in breast cancer

OBJECTIVE 19: APPROPRIATE COST-EFFECTIVE STRATEGY FOR FOLLOW-UP

Standard 6.1	Regular clinical follow-up for patients according to local protocol.
Standard 6.2	Annual MMG should be offered to all patients with early and locally advanced breast cancer following treatment.
Standard 6.3	Routine bloods and other imaging should be avoided in asymptomatic patients.

Rationale

All patients should be followed up in a hospital setting after treatment of breast cancer. Available studies are unable to indicate an ideal frequency of follow up. Minimal requirements for regular follow up of a primary breast cancer is a clinical review every three months for the first two years, then six-monthly for a further two years, then an annual review lifelong.

During follow-up a careful history is obtained and a thorough physical examination performed. Routine blood tests (including tumour markers) and diagnostic imaging have not been found to improve survival or quality of life more than physical examination for detecting distant metastases. Patients are also advised to perform monthly breast self-examination.

Annual MMG should be offered to all patients with early and locally advanced breast cancer following treatment. MMG has a high sensitivity and specificity to detect ipsilateral breast tumour recurrences and contralateral new primary breast cancers. However, systematic reviews of observational studies have shown that routine follow up MMG does not directly improve survival in patients treated with breast cancer (see section on contralateral breast cancer).

Clinical notes

6 Regular follow-up schedule should be defined and discussed with the patient at the end of treatment. The recommended intervals for clinical examinations are:

(1) three monthly for the first two years

(2) six monthly for the following two years

(3) annually thereafter

6.1 The clinical follow-up visits should include a full history and physical examination at each visit with blood tests and diagnostic imaging only if patient is symptomatic. An annual mammogram should be requested if there is any residual breast tissue bilaterally

Objective 20: Lymphedema care

Standard 6.	The quantified risk of lymphedema should be discussed with every patient undergoing lymph node surgery.
Standard 6.	Patients at risk of lymphedema or with lymphedema should be referred for specialist physiotherapy.

Rationale

Lymphedema is an accumulation of protein rich lymph fluid. It may occur with damage to any part of the lymphatic system. Damage can occur from infection, surgical removal of lymph nodes, or with radiation therapy.

Any patient with a mastectomy, lumpectomy in combination with lymph node removal and/or radiation to the underarm area, breast or chest wall are at risk to develop lymphedema. Lymphedema can occur immediately postoperatively, during radiation, within a few months, a few years or even decades or more after cancer treatment.

When left untreated, protein-rich fluid continues to accumulate, leading to an increase of swelling and hardening or fibrosis of the tissue. Untreated lymphedema can lead to a decrease or loss of function of the arm, skin breakdown, chronic infections and possible irreversible complications.

Clinical notes

6.2 Lymphedema management can be offered by trained physiotherapists

6.3 Symptoms that may indicate lymphedema include:

- feeling of fullness, puffiness or heaviness in your arm
- decreased flexibility of movement in your hand, wrist or arm

- jewellery (including watches) feeling tight even though your weight
- problems fitting your arm into your sleeves
- redness or increased warmth, which may mean that you have an infection

6.4 Although lymphedema is a chronic condition, with proper treatment, education and simple care, it can be greatly minimised and controlled therefore early referral is mandatory.

Key Area 7: Data, monitoring and research

Objective 21: Monitoring and research

Standard 7.1	Reliable monthly and annual figures should be available from each facility providing breast examination or care, in particular each PHC, SBU and POU.
Standard 7.2	It is recommended that SBU and POU have database information on patients for clinical management, further surveillance and research purposes.
Standard 7.3	Population based breast cancer incidence and mortality should be available using a national cancer registry, with compliance from diagnosing clinicians and pathologists.

Rationale

Breast Cancer Registry is important for reliable breast cancer statistics. These are required to formulate and re-evaluate local and national breast cancer plans or policies. Breast cancer incidence and mortality data should be obtained from population-based national cancer registries (PBCRs) and mortality registers, such as the National Cancer Registry currently in place. Data for stage, tumour size at diagnosis and survival by stage (to monitor quality of treatment) should be collected to assist policy-makers recognise the prevalence and public health burden of breast cancer, and attention paid to timelines to ensure adequacy of treatment and health system improvement.

All health facilities should collect breast cancer related data from diagnosis and throughout the course of disease. This should be entered electronically into a data-base. The information gathered will determine priorities and aid with the implementation of targeted initiatives.

Clinical notes

7 All health facilities should collect breast cancer related data from diagnosis.

7.1 Data should be entered electronically into a data-base. The information gathered will determine priorities and aid with the implementation of targeted initiatives.

7.2 A data manager should be allocated to for quality assurance, ethical use of data and to respond to audit requests.

Key Area 8: Community outreach and engagement

Objective 22: Community engagement and CSOS

Standard 8.1	User-friendly educational materials available in all PHC/DH areas.
Standard 8.2	Teaching programmes developed and made available for healthcare workers at all levels.

Rationale

Providing user-friendly and understandable information for eligible women is an essential part of screening to ensure that women understand the rationale for screening, and uptake the service. Important information and education strategies include providing information on breast cancer through one-on-one health education by trained healthcare workers and community dialogues and support groups using various participatory methods.

Civil Society Organisations and NPO single-issue advocacy groups for breast health and cancer can assist in developing appropriate information, educational and communication (IEC) materials and strategies that: facilitate dialogue between communities and health workers and peer counselling; engagement of the broader public (e.g. through mass media methods such as radio and TV broadcasts and edutainment programmes, and inclusion of important community leaders such as advocates for screening).

Clinical notes

8 Client recruitment through information, education and communication by civil society organisations in a coordinated manner will improve awareness of the community about the breast cancer. Coordinated strategies are needed to inform and educate women at risk about screening, breast cancer prevention and the benefits of early detection.

8.1 Counselling service by community healthcare workers in primary health care facilities is envisaged as the main drivers of the screening programme. Structured counselling will be provided free of charge at the primary care level – all clinics and community health centres, as well as designated SBUs and POUs.

8.2 Community healthcare workers should provide information on linkage to screening services with every household visit.

Further discussion

It is of fundamental importance that policy makers and the public are educated to counter the entrenched fatalistic myths and misconceptions that undermine any effort to mobilise forces against cancer, and deter people who suspect they may have cancer from seeking early medical advice.

Educational campaigns can be implemented at low or minimal cost. Public awareness of the early symptoms and signs of breast cancer, a focus that breast cancer is a treatable disease and that outcomes are improved through early detection, is a crucial initial step to improve participation in cancer control programmes, irrespective of the screening technique applied and setting (urban or rural). Where screening programmes are available, public awareness is necessary to encourage participation. It is important to educate both genders of the local population about breast cancer and the importance of early detection. Awareness can be promoted by education via videos, posters and pamphlets.

In some communities, there are misconceptions about the nature of breast cancer and the curability thereof. These misconceptions can be addressed through researching appropriate community information sources and beliefs.

Failure to appreciate the negative effects of social obstacles and cultural beliefs can adversely affect even the most well-designed research protocols, as demonstrated by a 2006 trial on screening clinical breast examination (CBE) in the Philippines which could not be completed as two-thirds of women with findings on clinical examination refused the follow-up diagnostic studies.

With appropriate qualitative research the community can be educated about the disease, curability thereof and that treatment does not always involve a mastectomy,

particularly with early diagnosis. The inclusion of key healthcare decision makers within communities (village elders, traditional healers, religious leaders) is vital to educational programmes. Endorsement by a programme champion (politician, celebrity, sports star) is also effective.

In religiously conservative communities peer education has been shown to be more effective and successful in increasing knowledge, belief and practice of women with respect to breast cancer. In general women identify more easily with their peers, and where there is a similar environment, social fabric and belief system, cancer education has been more effective.

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APPENDCES

Appendix A: What is a breast unit?

A specialised breast unit facilitates a dedicated clinic offering a team approach to breast health. Multidisciplinary care is provided by a team of clinicians and other professionals specialising in a single “anatomical area”, namely the breast. A number of reports published from groups concerned in the management of breast diseases all recommend that breast disease be cared for by specialists in breast disease working as teams in breast units.

These specialists combine their expertise and skills to formulate local and national protocol and procedure guidelines which govern individualised treatment for every patient irrespective of breast complaint. In benign and malignant breast disorders, all factors predicting the course of the disease, as well as patient preferences, are taken into account to ensure optimal treatment and outcome. A service provided by trained specialists is more efficient, more cost effective whilst delivering high quality breast are. The objectives of a breast unit are to ensure access to high quality specialist breast services to all patients with breast cancer; to define the standards of such services; and to be recognisable to patients, practitioners and health authorities as being of high quality, based on voluntary certification and audit. The recognised requirements for a breast unit are well described internationally and described below.

1. **Critical mass:** The unit must have at least 150 newly diagnosed cases of primary breast cancer under its care annually. Primary treatment (surgery and adjuvant therapies) must be carried out within the unit. The minimum number is to ensure a caseload sufficient for each team member to maintain expertise and to ensure the cost-effective functioning of the unit.
2. **Clinical director:** The UNIT should be co-ordinated by a Clinical Director of Breast Services, who must be a medical doctor, and can be from any specialty of the core team.
3. **Protocols:** Written protocols for the diagnosis and management of cancer at all stages must be available. These must be agreed upon by the core team members. Any protocol amendments/ new protocols must be discussed and formally recorded by the core team.

4. **Audit and breast cancer registry:** A database for audit purposes is an essential component of a breast unit. A data manager, whose responsibility is the collection (contemporaneously or retrospectively), recording and analysis of relevant data, must be appointed. The data recorded includes:
    i. Source of referral:
        - screening programme
        - spontaneous screening
        - symptomatic
    ii. Diagnosis
    iii. Pathology
    iv. Timelines from first presentation (irrespective of facility) to definitive diagnosis and first MDT visit. This should be no longer than four weeks
    v. Primary treatment
    vi. Treatment outcomes
    vii. If the unit offers screening programmes, then a record should be kept of whether cancer cases diagnosed are screen-detected or interval cases. SBU/POUs need to be independently audited to ensure they fulfil their service obligation and adhere to national guidelines.
5. **Breast Multidisciplinary Teams (MDTs):** It is widely accepted that breast care should be the ambit of breast specialists in each discipline and that Breast MDTs form the basis for best practice, particularly in cases of breast cancer, as they provide multidisciplinary care. All consultation for Breast disease must be done in dedicated clinics.
    i. New Patient Clinics
        i. At least one clinic per week for newly referred or self-referred, symptomatic women should be held.
        ii. Multidisciplinary working must allow for all standard investigations for triple assessment to be completed at one visit.
        iii. All referred patients who default their appointments to these clinics need to be traced via their primary referral centres, irrespective of level

iv. The members of the MDT can be sub-divided into two separate but inter-dependent groups with overlap by most members. In this policy, this can be divided into the functions of the SBU and POU.

ii. **Diagnostic Team (situated at SBU):** Most patients visiting a Breast Clinic do not have a breast malignancy. Thus, the role of the Breast Clinic is both to diagnose breast cancer and to treat and reassure patients with benign breast disorders. The key component members of this group are:

(a) Breast Specialist Clinician: this is normally a consultant surgeon with an interest in breast disease, who is usually assisted by a team which includes associate specialists, breast clinicians, staff grade surgeons and specialist trainees. The Breast Specialist is also the MDT co-ordinator
(b) Specialist radiologist
(c) Mammographers
(d) Pathologist (cyto- and/or histopathologist)
(e) Breast care nurse
(f) Clinic staff
(g) Administrative staff
(h) Oncology social worker/ psychologist

iii. Cancer treatment team (SBU/POU): This includes most of the diagnostic team members as well as:

(a) Clinical oncologist (POU only)
(b) Medical Oncologist (POU only)
(c) Reconstructive and/or Oncoplastic breast surgeon
(d) Medical geneticist
(e) Clinical psychologist/ Oncology Social Worker
(f) Lymphoedema therapist
(g) Research nurse
(h) Data management personnel
(i) Medical prosthetist
(j) Palliative care health-worker

In provinces where SBU/POU care does not currently exist, patients are to be referred to the neighbouring province that has such offerings. Depending on

population density in South Africa, and current models of care, there may be different provincial methods of separating SBU and POU services. This can be tailored to local needs. The main area of difference at present is the capability of SBUs to provide only diagnostic (and follow-up) or diagnostic and therapeutic care.

APPENDIX B: INTERNATIONAL BREAST CANCER STAGING

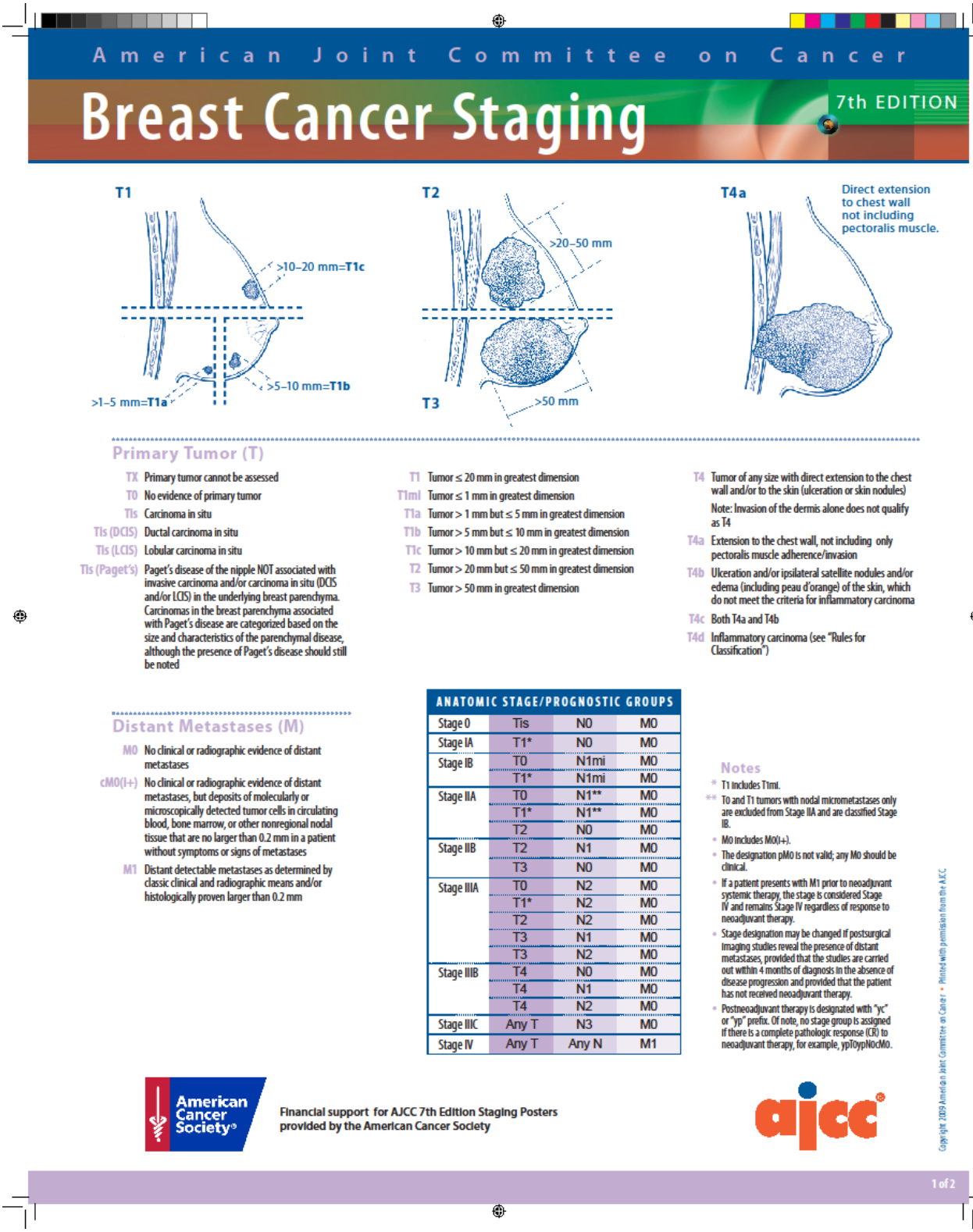


Figure 7: International staging for breast cancer

APPENDIX C: BREAST CANCER PATIENT PROTOCOL

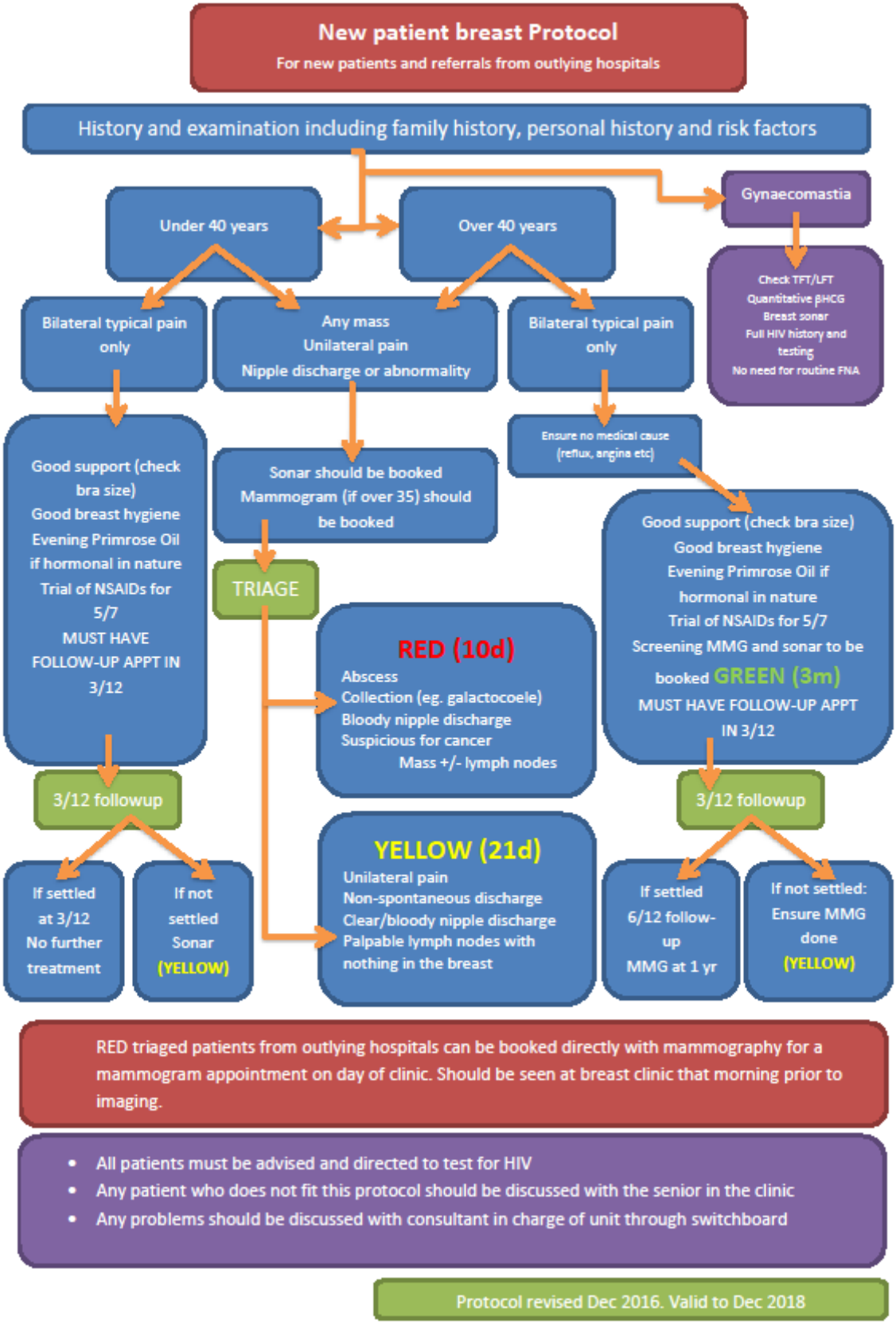


Figure 8: Example of new patient SBU protocol

APPENDIX D: BREAST PROFORMA

Welcome to the [hospital] Breast Care Clinic

To speed up your passage through the clinic but ensure that nothing is missed, please fill in the first sheet of this form yourself while you are waiting. The second sheet will be filled in by your doctor.

Name and Surname: _____ AGE: _____

Reason for visit today:

- ☐ Lump in the breast
- ☐ Pain in the breasts
- ☐ Discharge from the nipple
- ☐ Size of breasts
- ☐ Other breast problem: details.....
- ☐ General checkup and/or yearly tests

Past Gynaecological history

What age did you start your periods?:.....

How many times have you been pregnant?.....

How old were you when you had: your first child?..... your last child?.....

How long did you breastfeed for? (total years for all children)
☐ Never ☐ Less than 1 year
☐ 1-3 years ☐ More than 3 years

Have you used birth control pills? ☐ No ☐ Yes For how many years?.....

or birth control injections? ☐ No ☐ Yes For how many years?.....

Have you had a hysterectomy (womb removed)? ☐ No ☐ Yes How old were you?.....

Have you gone through the menopause (change of life, stopping of periods due to age) how old were you?.....

Have you used hormone replacement pills (HRT)? ☐ No ☐ Yes How many years?.....

Family History

Has anyone related to you by blood had cancer?	☐ No	☐ Yes	If yes- who?
Relationship (mother, father, sister, brother, aunt, uncle, grandmother, grandfather)	Cancer type		Age at diagnosis

Medical History

Have you been tested or treated for HIV in the last year? ☐ No ☐ Yes-negative ☐ Yes-positive

Do you take any medicines regularly? ☐ No ☐ Yes

If yes- what medicines- please list the medicines and why you take them

Medicine name	What problem do you take it for?

Do you smoke tobacco? ☐ No ☐ Yes ☐ Ex-smoker How many years?.....

Do you drink alcohol ☐ No ☐ Sometimes ☐ Often ☐ Everyday

Thank you for filling in this page The doctor will see you as soon as possible

Figure 9: Sample breast proforma (1/2)

Welcome to the [hospital] Breast Care Clinic

Name and Surname: _____ Hospital Number:_____

- ☐ Lump in the breast
- ☐ Pain in the breasts
- ☐ Discharge from the nipple
- ☐ Size of breasts
- ☐ Other breast problem: details.....
- ☐ General checkup and/or yearly tests

Details- how long, side, size

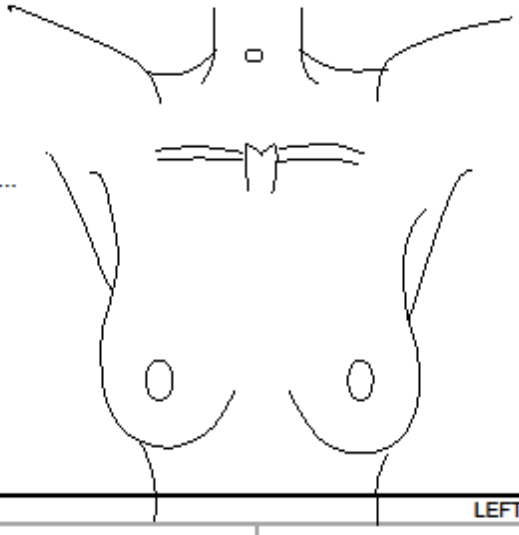
Please draw all findings

RIGHT LEFT

Axilla
- ☐ No nodes
- ☐ Soft nodes
- ☐ Hard nodes
- ☐ Other .....

Axilla
- ☐ No nodes
- ☐ Soft nodes
- ☐ Hard nodes
- ☐ Other .....

Draw size and shape or characteristic of any breast finding



Describe breast findings

RIGHT	LEFT

Clinical staging if cancer suspected T ☐ N ☐

DIAGNOSIS	NOTES
☐ Probably benign ☐ Susp. For Ca	

PLAN

Ultrasound +/- Mammogram ☐ No ☐ Yes

Triage level
- ☐ Red
- ☐ Yellow
- ☐ Green

Blood tests .....

Other .....

FUTURE PLAN

Date of next appointment

- ☐ To come back with results
- ☐ Discharge SOS
- ☐ Referral to oncology
- ☐ Other.....

Signed:

Date:

Figure 10: Sample of breast proform (2/2)