PREVALENCE OF THE KNOWN RISK FACTORS IN WOMEN DIAGNOSED WITH BREAST CANCER AT QUEEN II HOSPITAL, MASERU

by

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DECLARATION OF INDEPENDENT WORK

I declare that this dissertation which is hereby submitted by me for the qualification Magister in Nutrition, at the University of the Free State, is my own independent work and has not been previously submitted for a qualification at another university or faculty. I further cede copyright of this thesis to the University of the Free State.

Signed: _____

Ms MR Lehlasoa

30 November 2011

DEDICATION

This dissertation is dedicated to my family, friends, and prayer partners.

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He will never leave you nor forsake you.

Do not be afraid; do not be discouraged.

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ά	alpha
β	beta
AA	Arachidonic acid
ACS	American Cancer Society
AI	Adequate intake
AICR	American Institute of Cancer Research
AIDS	Acquired Immunodeficiency Syndrome
AMDR	Acceptable macronutrient distribution range
ARVs	Antiretrovirals
BMI	Body mass index
BRCA1	Breast cancer type 1
BRCA2	Breast cancer type 2
BSE	Breast-self examination
CBE	Clinical breast examination
CHO	Carbohydrates
CLA	Conjugated linoleic acid
cm	centimetre
CVDs	Cardio-vascular diseases
CHW	Community health worker
DASH	Dietary Approach to Stop Hypertension
dd/mm/yy	Day day/month month/year year
DCIS	Ductal carcinoma in situ
DGA	Dietary Guidelines for Americans
DGAC	Dietary Guidelines for Americans Committee

DHA	Docosahexaenoic acid
DHEA	Dehydroepiandrostenedione
DHHS	United States Department of Health and Human Services
DMA	Disasters Management Authority
DNA	Deoxyribonucleic acid
DRIs	Dietary Reference Intakes
EAR	Estimated average requirements
EER	Estimated energy requirements
EGCG	Epigallocatechin-3-gallate
EPA	Eicosapantaenoic acid
ER	Estrogen receptor
ER-ά	Estrogen receptor alpha
FAO	Food and Agriculture Organization
FGP	Food Guide Pyramid
FFQ	Food frequency questionnaire
g	Gram
GLA	Gamma-linolenic acid
HC	Hip circumference
HER *2+*	Human epidermal growth factor receptor 2 positive
HIV	Human Immunodeficiency Virus
HRT	Hormone replacement therapy
IDF	International Diabetes Federation
IGF	Insulin-like growth factor
IGFP	Insulin-like growth factor binding protein
ISI	Insulin sensitivity index

kcal	kilocalorie
Kg	kilogram
Kg/m^2	kilogram per meter square
kJ	kilojoule
kJ/ml	kiloJoule per millitre
km	kilometres
LCIS	Lobular carcinoma in situ
LDL	Low density lipoprotein
METs	Metabolic equivalents
ml	millitre
mph	miles per hour
mRNA	messenger ribonucleic acid
n	frequency of number
n-3/ *w*-3	omega-3
n-6/ *w*-6	omega-6
NGO	Non-government Organisation
OC	Oral contraceptive
PAL	Physical activity level
PEM	Protein-energy malnutrition
PPAR	Peroxisome proliferate-activated receptor gamma
PR	Progesterone receptor
PUFA	Polyunsaturated fatty acids
Queen II	Queen Elizabeth II hospital
RDA	Recommended dietary allowance
RNA	Ribonucleic acid

SeDs	Sedentary death syndrome
SHBG	Sex hormone binding globulin
TE	Total energy
TEE	Total energy expenditure
TNF-ά	Tumour necrosis factor alpha
tpd	times per day
tpm	times per month
tps	times per season
tpw	times per week
UFS	University of the Free State
UL	Tolerable upper intake level
USA	United States of America
USDA	United States Department of Agriculture
WC	Waist circumference
WCRF	World Cancer Research Fund
WFP	World Food Programme
WHO	World Health Organisation
WHR	Waist hip ratio
%	percentage
%TE	percentage of total energy
<	less than
>	greater than
≥	equal to or greater than
≤	equal to or less than
&	and

: Ratio

CHAPTER 1

INTRODUCTION AND MOTIVATION OF THE STUDY

1.1 Prevalence of breast cancer

Breast cancer is the leading cancer in the world among women (Saweer *et al*., 2003:1) both in the industrialised and the developing countries (Porter, 2009:142; Sasco, 2001:321). According to the World Cancer Report submitted by the World Health Organization (WHO) (2008), the prevalence of breast cancer could go up by 50% by 2020, from the current prevalence of 1.2 million worldwide to 1.5 million (World Cancer Report, 2008:421). Breast cancer is the most frequently diagnosed cancer among women in the United States of America (USA) representing an estimated amount of 203 500 of new cases among women (Daniel *et al*., 2003:28).

The prevalence rates of breast cancer differ from one country to another with the USA leading in deaths from the disease. Although the prevalence rates are high in the USA, indications are that mortality rates are decreasing (Sasco, 2001:321; Mettlin, 1999:138). The Eastern European prevalence rates are in the middle ranges, while Africa and Asia have low rates (Porter, 2009:141; Sasco, 2001:321).

African-Americans have the lowest prevalence rates among the American groups (Fregene & Newman, 2005:1540; Brawley, 2002:322), but are diagnosed with the disease at a younger age. More African-American women have the hormone receptor-negative disease thus accounting for mortality rates higher than the general prevalence rates (Kruger & Apffelstaedt, 2007:18; Fregene & Newman, 2005:1540).

In general, the prevalence of breast cancer in African women in Africa is lower than in Europe and the USA. Cancer of the breast is uncommon in Central Africa with Harare having prevalence rates of 0.02%, Kampala 0.016% and Gambia 0.003% (Vorobiof *et al.* 2001:126). Although there are low prevalence rates, women from Nigeria, Senegal and of African origin are likely to have a more aggressive form of breast cancer than women from the European origin (Fregene & Newman, 2005:1544; Easton, 2005:1) because breast cancers in African women produce a different pattern of gene expression (Easton, 2005:1).

African women are diagnosed with the disease in between the ages 35 to 45 years, which is 10 to 15 years earlier than women in the North America and Europe (Kruger & Apffelstaedt, 2007:19; Fregene & Newman, 2005:1542). African women also die from the disease around the ages of 40 years (Easton, 2005:2). In Sub-Saharan Africa mortality rates are high when compared to the prevalence rates (Fregene & Newman, 2005:1542) following the same pattern as among African-American women in the USA (Fregene & Newman, 2005:1540; Brawley, 2002:52).

Breast cancer is the most common cancer diagnosed in South African women. The figures from 1999 which were published in 2005 by the South African National Cancer Registry indicate that

breast cancer accounted for 19.4% of all cancers in women, which compared to 10% worldwide. The overall prevalence rate was 1:26 for South African women when compared with 1:9 in developed countries. The risk varies with racial differences, with lifetime risk of 1:12 for whites, and 1:49 for blacks. The ratio was 1:6 in 1993 and has risen to 1:4 in 1999, implying that breast cancer is becoming more common in the Black population (Loubser, 2008:497). Prevalence rates for white South African women are comparable with rates in the industrialised countries and are among the highest rates in the world. Prevalence rates in black South African women are comparable with those reported in the developing countries. Prevalence rates in Asian South African women of the Indian race are almost double of those reported in Bombay, India (Mqoqi *et al.,* 2004:31).

1.2 Risk factors

Various risk factors accounting for differences in prevalence rates are identified, including non-modifiable and modifiable risk factors.

1.2.1 Non-modifiable risk factors

Non-modifiable risk factors include gender, age, genetic susceptibility, history of breast cancer, ethnicity, and menstrual history.

Being a woman is the main risk factor for developing breast cancer. The reason women develop more breast cancer is because their breast cells are constantly exposed to the growth-promoting effects of the female hormone oestrogen and progesterone. The risk of breast cancer increases with age in women (Fregene & Newman, 2005:1541; Hayes, & Schnitt, 1993:2.2; MacKay & Steel, 1989:45), but the risk of cancer development is highly dependant on the hormones associated with ovarian function (Ralph & Provan, 2000:423). As aging is one of the prominent risk factors, rates are expected to be high in countries with larger populations of older people (Loubser, 2008:Online; Mettlin, 1999:139).

Genetic risk factors that are associated with breast cancer development include breast cancer type 1 (BRCA 1) and breast cancer type 2 (BRCA 2) gene mutations. Many familial breast cancers are hereditary and might be associated with germline mutations in the BRCA1 or BRCA2 gene. Breast cancers in families with several affected members are likely to be hereditary (Narod *et al*., 2000:1896). In such families in women who carry deleterious BRCA1 or BRCA2 mutations the lifetime risk of breast cancer is estimated to be as high as 80% (Kauff *et al*., 2002:1609; Hendenfalk *et al*., 2001:541; Narod *et al*., 2000:1896).

History of breast cancer risk factors associated with development of breast cancer includes family history and personal history of breast cancer. Having a first-degree relative with breast cancer increases the risk of developing the disease compared to women with no family history of the disease (Chen *et al*., 1999:858; Lundy, 1994:271; Hayes & Schnitt, 1993:2.2). The number of first-degree relatives having the disease increases the chances of developing the disease (Lundy,

1994:271). However, having a second-degree relative is still a risk factor (Hayes & Schnitt, 1993:2.2; Powles & Jones, 1991:290). A personal history of breast cancer is associated with breast cancer development. Having cancer in one breast increases the risk for developing a new cancer on the other breast or having a recurrence (Houssami & Ciatto, 2010:440; Hayes & Schnitt, 1993:2.2).

Menstrual history risk factors associated with development of breast cancer include age at first menarche and age at menopause. Early menarche at around 12 years and late menopause at around later than 55 years (Key *et al*., 2003:413) increase the duration of exposure of the breast to the high levels of oestradiol and progesterone of premenopausal women (Key *et al.*, 2003:413; Sasco, 2001:322) which influences risk of cancer by the endogenous hormonal mileau (Grant, 2008:965; Sasco, 2001:322). Late menarche leads to lower endogenous oestrogens levels over time, thereby diminishing cumulative breast cancer risk (Fregene & Newman, 2005:1543; Wrensch *et al*., 2003:94).

1.2.2 Modifiable risk factors

Identified modifiable risk factors for the purpose of this study include: socio-demographic profiles, lifestyle behaviours, reproductive factors, anthropometric status, and usual dietary intake (Kluttig & Schmidt-Pokrzywiniak, 2009:84).

Socio-demographic factors associated with breast cancer risk in women include marital status, place of residence, education level, and income. Single and nulliporous (without children) married women have a similar risk for breast cancer as compared with women of the same age (Abbasis *et al.*, 2009:9), although married women with cancer have a reduced risk of 15% of mortality compared to unmarried women (Osborne *et al*., 2005:41). More affluent women typically reside in urban areas, and urban areas are frequently characterised by westernised behaviours and lifestyles which have an increased risk of breast cancer development (Fregene & Newman, 2005:1543). Women who attain higher education level have an increased risk of breast cancer (Webster *et al*., 2008:1127; Fregene & Newman, 2005:1543). The considerable period spent in obtaining an education followed by building a career contributes to a delay in marriage, and a probable conception and childbirth at older ages, leading to an increased risk of breast cancer (Celik & Aksoy, 2007:10). Breast cancer is generally associated with affluence (Mettlin, 1999:139) and is common in high socio-economic groups (Shah & Shrestha, 2004:3).

Lifestyle behaviours associated with breast cancer risk in women include alcohol intake and physical activity level. Alcohol abuse leads to breast cancer and promotes the development of cancer once the disease has started (Sizer & Whitney, 2003:95). Alcohol increases the risk with the amount of alcohol consumed including amounts as low as one drink per day (Grant, 2008:966; Willett & Giovannucci, 2006:1274). Regular physical activity helps to control body weight (Grant, 2008:963), thus lowering production of oestrogen, a major source of hormone in

postmenopausal women (Kruk, 2009:447). While being obese increases the amount of circulating hormones which are associated with tumour growth (Grant, 2008:963).

Reproductive factors associated with breast cancer risk in women include oral contraceptive use, parity, age at first pregnancy, and breast feeding. Oral contraceptive use may have an increased risk for breast cancer (Fox, 2006:694), but this is still a controversial issue. Some epidemiological studies have shown no association between breast cancer and oral contraceptive use, while other studies show a less than two-fold (<2) increase among young women with breast cancer in relation to long-term use, recent use, and use at an early age (Gammon *et al.*, 1999:414).

Having at least one child is associated with a decrease in risk in the long-term compared with risk among the nulliporous. This protective effect increases with the number of children a woman has (Travis & Key, 2003:240). The reduction in risk per birth is greater for births at young ages than older ages (Travis & Key, 2003:240; Ebrahim *et al.*, 2002:12). The risk for breast cancer increases with having the first child after the age of 30 years or not having children altogether (Hamilton-Fairley, 2004:252). The risk is increased by three percent (3%) for each year delayed while it decreases with having multiple pregnancies at a young age (Ursin *et al*., 2005:356; Chen *et al.*, 1999:860). Late age at first birth increases life-time exposure to oestrogen which influences risk by endogenous hormonal mileau (Sasco, 2001:322). Breast feeding is likely to decrease lifetime risk of breast cancer by decreasing the cumulative number of ovulatory menstrual cycles (Fregene & Newman, 2005:1543). The risk is slightly reduced when women breast feed for about one and a half years to two years (1.5-2 years) (Ursin *et al*., 2005: 356; Whitney *et al*., 2002:489).

Anthropometric status is associated with risk of breast cancer development. Body weight may influence the growth of cancer cells through the promotion of hormones in the body such as oestrogens in the promotion of breast cancer (Thomas & Bishop, 2008:770). Other hormones, such as progesterone, prolactin, and testosterone are also important in the etiology of breast cancer (Travis & Key, 2003:243). Hormones play a key role in breast cancer development probably through stimulating cell proliferation and thereby increasing the chance that a mutation will occur that will lead to cancer, and by promoting the growth of early tumours (Key *et al*., 2003:413).

Overweight women with body mass index (BMI) of 25 and more (≥25) have about a two to three-fold (Chen *et al*., 1999:861) increased risk for postmenopausal breast cancer due to the fact that adipose tissue is able to aromatise circulating androstenedione and so synthesise oestrogen. However, serum levels of oestrogen do fall in women who lose weight (Bingham, 2000:774). Women with waist circumferences (WC) of 80 cm and more (≥80) (Alberti *et al.*, 2009:1642) and waist-hip-ratio (WHR) of more than 0.85 (>0.85) (Ness-Abramof & Apovian, 2008:399; Alberti *et al.*, 2006:472) are at a risk of developing obesity-related diseases (Alberti *et al.*, 2009:1642; Hammond, 2008:383).

Height reflects the total number of ductal stem cells that develop in the breast in utero and thus the importance of prenatal exposures in breast cancer etiology (Friedenreich, 2001:15; Ziegler, 1997:925). Increasing height is associated with an increased risk of breast cancer (Chang *et al*., 2006:336; Fregene & Newman, 2005:1543; Wrensch *et al*., 2003:94) in both pre- and post-menopausal women (Friedenreich, 2001:20). Height is related to nutrition (Nemesure *et al*., 2009:391; Friedenreich, 2001:15), demonstrating differences in energy intake, dietary patterns in early life (Chang *et al*., 2006:337), and adiposity associated to adult energy intake (Chang *et al*., 2006:336; Friedenreich, 2001:15), however, height also relates to genetic growth potential (Friedenreich, 2001:15).

High energy intakes stimulate the release of hormones which cause inflammation stimulating growth of tumours (Sizer & Whitney, 2003:415). Diets high in fat are also high in energy and may contribute to obesity which in turn is linked to increased risk of breast cancer (Grant, 2008:963; Willett & Stampfer, 2006:1628). Reducing fat content of the diet encourages weight loss, reduction of oestrogen levels, and of the risk (Ralph & Provan, 2000:423). Though it is the type of fat that is associated with an increased risk, an individual's genetic factors must also be considered (Grant, 2008:963) as some populations have a high dietary fat intake without high breast cancer rates. This is explained by the use of monosaturated fat sources, such as olive oil which are protective against breast cancer whereas the high risk is most specifically associated with polyunsaturated fat (Mettlin, 1999:142).

The effect of protein on cancer development depends on the tissue of origin, the type of tumour, the type of protein, and energy balance of the diet. Tumour development is suppressed by diets containing protein levels below the requirement of optimal growth, while it is increased by levels two or three times above the required amounts (Grant, 2008:964), especially with high saturated fat intake (Mettlin, 1999:142).

High fibre intake interrupts the enterohepatic circulation of oestrogens and as a result reduces the risk of breast cancer (Willett & Giovannucci, 2006:1274). High fibre and low meat intakes in adolescents delay the onset of menarche (Grant, 2008:964; Bingham, 2000:774; Ralph & Provan, 2000:423), and reduce gonadotrophin and oestradial levels thereby reducing the risk for postmenopausal breast cancer development (Bingham, 2000:774; Ralph & Provan, 2000:423).

Variety of phytochemicals from a variety of foods appears to protect against DNA damage and defend the body against cancer (Rolfes *et al*., 2006:465), because cancers arise when cellular DNA is damaged (Rolfes *et al*., 2006:391). The protective effect of fruits and vegetables has been attributed to phytochemicals, which are the non-nutrient plant compounds such as the carotenoids, flavonoids, isoflavonoids, and phenolic acids (Boyer *et al*., 2004:1188).

1.3 Problem statement

There are no national prevalence and mortality rates of breast cancer in Lesotho since there is no cancer registry to collect the information about cancer from all the health institutions nationally.

According to the available literature there is no published information about risk factors for breast cancer in women from Lesotho. This lack of statistics leaves a gap of information about Lesotho situation in as far as breast cancer is concerned.

However the Cytology Laboratory at the Queen Elizabeth II (Queen II) hospital runs the tests for breast diseases presented at the hospital. Queen II hospital is a control centre for all government hospitals in Lesotho to which new cases of breast problems are referred to before patients can be referred to Bloemfontein hospitals for treatment. Queen II hospital is the only government hospital with the authority of transfer system across the border at government expense. Although there are no prevalence and mortality figures of breast cancer in Lesotho, the following information was obtained from the Cytology Laboratory records at the Queen II hospital. According to a personal communication (Phaaroe, 2009) since January 2006 to September 2008 there were 238 new cases of breast problems, included were carcinoma and two types of breast lumps, fibrocystic disease and fibroadenoma. The majority (97.1%) of patients were women while 2.9% were men. Of the 238 cases presented at the hospital only 25 cases per year were reported to be breast cancer (Table 1.1).

Although there is no information on the prevalence of risk factors available and no published information on national prevalence of breast cancer in Lesotho, available data from the Queen II hospital shows a considerable prevalence of 38% of carcinoma and 59.2% benign breast lumps in a period of three years (2006-2008). The study will therefore be undertaken in an attempt to determine the prevalence of risk factors for breast cancer in women diagnosed with breast cancer at the Queen II hospital in Maseru. Results of the study will be used to develop screening charts which can be used to create awareness on risk factors for breast cancer in women. Knowledge on risk factors for breast cancer in Basotho women will create awareness to the individuals, health care team, and government so that caution may be taken with regard to diagnosis and treatment procedures. Knowledge on risk factors will also help to identify and prevent late diagnosis, promote prevention and early treatment procedures.

Table 1.1 Prevalence rate of carcinoma and breast lumps at Queen II hospital according to age ranges as of January 2006 to September 2008 (Phaaroe, 2009)**:**

	Females			**Males**
Age distribution	**Carcinoma**	**Breast lumps**		**Breast diseases**
		Fibrocystic disease	**Fibroadenoma**	
19	-	1	42	-
20-24	2	9	27	-
25-29	1	4	11	-
30-34	6	5	6	Gynaecomastia at 31 years-1
35-39	6	6	1	-
40-44	8	4	6	Gynaecomastia at 42 years-1 Ductal ca insutu at 40 years-1
45-49	62	7	6	-
50-54	9	4	8	
55-59	7	1	12	Fibroadenoma-1
60-64	3	3	9	Lobular/ductal-1
65-69	7	1	7	Fibroadenoma-1
70-74	11	-	11	Mixed- infiltrating-1
75-79	7	1	7	-
80-84	7	1	7	-
Total: (n=238)	**90**	**47**	**94**	**7**
% of cases:	**37.8%**	**19.7%**	**39.5%**	**2.9%**

1.4 AIM AND OBJECTIVES

1.4.1 Aim

The aim of this study was to determine the prevalence of the known risk factors for breast cancer, as reported in the literature, among women who are 19 years and older and are diagnosed with breast cancer at the Queen II hospital in Maseru.

1.4.2 Objectives

In order to achieve the aim, the following objectives are formulated.

To determine the prevalence of the known non-modifiable and modifiable risk factors in women diagnosed with breast cancer at the Queen II hospital in Maseru (19 years and older):

1.4.2.1 Non-modifiable risk factors:

- **Age at diagnosis**;
- **history of breast cancer** (family and personal histories of breast cancer); and
- **menstrual history** (age at first menarche and age at menopause).

1.4.2.2 Modifiable risk factors:

- **Socio-demographic profiles** (marital status, place of residence, education level, and income);
- **lifestyle behaviours** (alcohol intake and physical activity level);
- **reproductive factors** (oral contraceptive use , parity, age at first pregnancy, and breast feeding);
- **anthropometric status** (weight, height, waist and hip circumferences); and
- **usual dietary intake** (food, energy, macronutrient, and frequency) will be determined.

1.5 LIMITATIONS OF THE STUDY

1.5.1 Biochemical assessment including endogenous and exogenous hormones, genetic susceptibility, and environmental pollutants was not determined due to insufficient funds.

1.5.2 Some patients might not be reached as they would not be at the cancer clinic nor at the Queen II hospital during the researcher's visits therefore would be missed.

1.5.3 The patients might be limited to a certain number when excluding those not seen at the Queen II and the Universitas hospitals. The sample size was small (52), partly due to the fact that only about 25 patients are diagnosed at the Queen II hospital per year (aka cytology laboratory), and partly also due to the poor filing system at the hospital which does not allow easy access to the patients. Thus the results of the study cannot be generalised to all Lesotho women but could be used to indicate the tendencies for this group. The small sample size was also partly due to lack of funding and a single researcher having to perform the study.

1.5.4 The selection criterion used in this study was biased because of the following reasons:

- It was assumed that the prevalence of risk factors detected among breast cancer patients is lower than in women of the same age and socio-economic group in the community. It means that there is no data for non-breast cancer group for comparison;
- it was considered to include breast cancer patients with HIV/AIDS for this study, but due to the ethical dilemma concerning the disease questions regarding HIV status were included but were only asked to breast cancer patients willing to disclose their status; and
- since the data was derived from the Queen II hospital it is weak to apply country wide because there are patients who are not seen at this hospital.

1.5.5 There is no data for morbidity and mortality for breast cancer at national level, so the burden of disease cannot be described and not logic to plan for prevention.

STRUCTURE OF DISSERTATION

The structure of the dissertation will include the following chapters; introduction and motivation of the study, literature review, methods (methodology), results, discussion of results, and conclusions and recommendations, followed by a summary in both English and Afrikaans at the end of the dissertation.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Cancer is "an abnormal division and reproduction of cells that can spread throughout the body crowding out the normal cells and tissues" (Grant, 2008:959). Breast cancer originates in breast epithelium and is associated with progressive molecular and morphologic changes (Dooley *et al*., 2001:1624). Invasive cancers arise through a series of molecular alterations at the cellular level, resulting in the out growth and spread of breast epithelial cells with immortal features and uncontrolled growth (Swart *et al*., 2009:Online).

Cancer is known as a highly complex multifactorial disease caused by endogenous metabolic or other imbalances associated with age, genetic makeup, variety of exogenous factors including lifestyle, exposure to ionizing radiation, chemicals of natural or synthetic origin (Mandeville, 2001:28), diet, body weight, and reproductive factors such as age at menarche, menstrual cycle length, parity, and lactation period (Chyz *et al*., 2001:3).

A risk factor is anything that alters the chances of an individual to develop the disease such as breast cancer. However, having a risk factor does not mean that one will necessarily acquire the disease because some individuals have risk factors but never develop the disease and some do not have the risk factors, yet acquire the disease (American Cancer Society, 2007:Online).

2.2 Pathogenesis of breast cancer

Breast cancers can start in any tissue of the breast but most start in the ducts, a smaller percentage in the lobules, and fewer in other tissues of the breast. Breast cancer is either invasive or noninvasive (often referred to as in situ). There are two types of noninvasive breast cancers, included are ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). Noninvasive breast cancers do not invade the basement membrane of the breast ductal carcinoma but are found in the lining of the duct whereas lobular carcinoma in situ cancer cells are found in the lobules. The two types of invasive breast cancer include infiltrating ductal carcinoma and infiltrating lobular carcinoma (Danziger & Simonsen, 2000:Online). Infiltrating ductal carcinoma penetrates the wall of the duct and travels to areas outside of it whereas infiltrating lobular carcinoma spreads through the wall of the lobule and travels to areas outside of it. Infiltrating ductal carcinoma is the most common type of breast cancer, accounting for between 70% to 80% of the cases of breast cancer (Bleiweiss, 2010:Online; Danziger & Simonsen, 2000:Online).

Infiltrating ductal carcinomas are divided into three grades based upon a combination of architectural and cytologic features, included are: well-differentiated (grade 1) tumours which

have cells that infiltrate the stroma as solid nests of glands having uniform nuclei with little or no evidence of mitotic activity; moderately differentiated (grade 2) tumours which have cells that infiltrate as solid nests with some glandular differentiation. Grade 2 tumours have some nuclear pleomorphism and a moderate mitotic rate; and poorly differentiated (grade 3) tumours which are composed of solid nests of neoplastic cells without evidence of gland formation. Poorly differentiated tumours have marked nuclear atypia and considerable mitotic activity (Bleiweiss, 2010:Online).

Breast cancers are clustered according to their intrinsic gene expression patterns, revealing at least five intrinsic subtypes including; luminal A and B which typically express hormone receptor-related genes (Irvin & Carey, 2008:2801), the human epidermal growth factor receptor 2 positive (HER2+) or oestrogen receptor negative (ER-negative) subtype, normal breast-like, basal-like, and potentially a 'claudin-low' subtype (Hawk & O'Regan, 2010:328; Irvin & Carey, 2008:2801). These breast cancer subtypes are highly reproducible, persist before and after therapy, are concordant between the primary tumour and the metastasis, and are found in the preneoplastic lesion ductal carcinoma in situ (Irvin & Carey, 2008:2801; Danziger & Simonsen, 2000:Online).

Triple negative is a term based upon clinical assays for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), while 'basal-like' is a molecular phenotype (Irvin & Carey, 2008:2800). Triple-negative include subtypes ER-negative, PR-negative, HER2/neu not over-expressed and has distinct clinical and pathologic features and are considered high grade tumours (Hawk & O'Regan, 2010:328; Irvin & Carey, 2008:2799). Usually triple-negative cancers have a poor prognosis, aggressive behaviour, and lack targeted therapies, leaving chemotherapy as the core treatment (Irvin & Carey, 2008:2799). Targeted therapy is a type of medication that blocks the growth of cancer cells by interfering with specific targeted molecules needed for carcinogenesis and tumour growth, rather than by simply interfering with rapidly dividing cells (e.g. with traditional chemotherapy) (National Cancer Institute, 2011:Online). Depending on the type of cancer from which the patient is suffering, the standard treatment which patients usually undergo, either used alone or in combination, include classical treatment such as surgery, chemotherapy, and/or radiotherapy (Van de Loo, 2006:8).

Cancer has different stages and these include: stage 0 which include noninvasive carcinomas (LCIS or DCIS) where the cancer cells have not invaded the surrounding breast tissue (Pathophysiology & types of breast cancer:Online); stage I is where the tumour is less than 2cm in size and cancer cells have not spread beyond the breast; in stage II either the tumour has spread to the lymph nodes under the arms but it is more than 2 cm in size, or the tumour has not spread to the lymph nodes under the arms but is greater than 5 cm in size, or the tumour is between 2 cm and 5 cm and may or may not have spread to the nodes; while in stage III the tumour is greater than 5 cm in size and has spread to the lymph nodes under the arms; and in

stage IV the cancer has spread to other parts of the body (metastatic cancer) (Bentley *et al*., 1998:2; Pathophysiology & types of breast cancer:Online).

Germ line polymorphism is associated with human cancer risk (Hunter & Crawford, 2006:1251). Genetic polymorphism is the difference in DNA sequence among individuals that may underlie differences in health (National Cancer Institute, 2011:Online). Genetic polymorphism plays a significant role in person-to-person variability in metastasis frequency, raising the intriguing possibility that some individuals could be predisposed to secondary tumour development (Hunter & Crawford, 2006:1251).

2.3 Etiology of breast cancer

For the purpose of this study the etiology and biological mechanisms of breast cancer development will be discussed. The known risk factors associated with breast cancer may be classified as non-modifiable and modifiable (Figure 2.1).

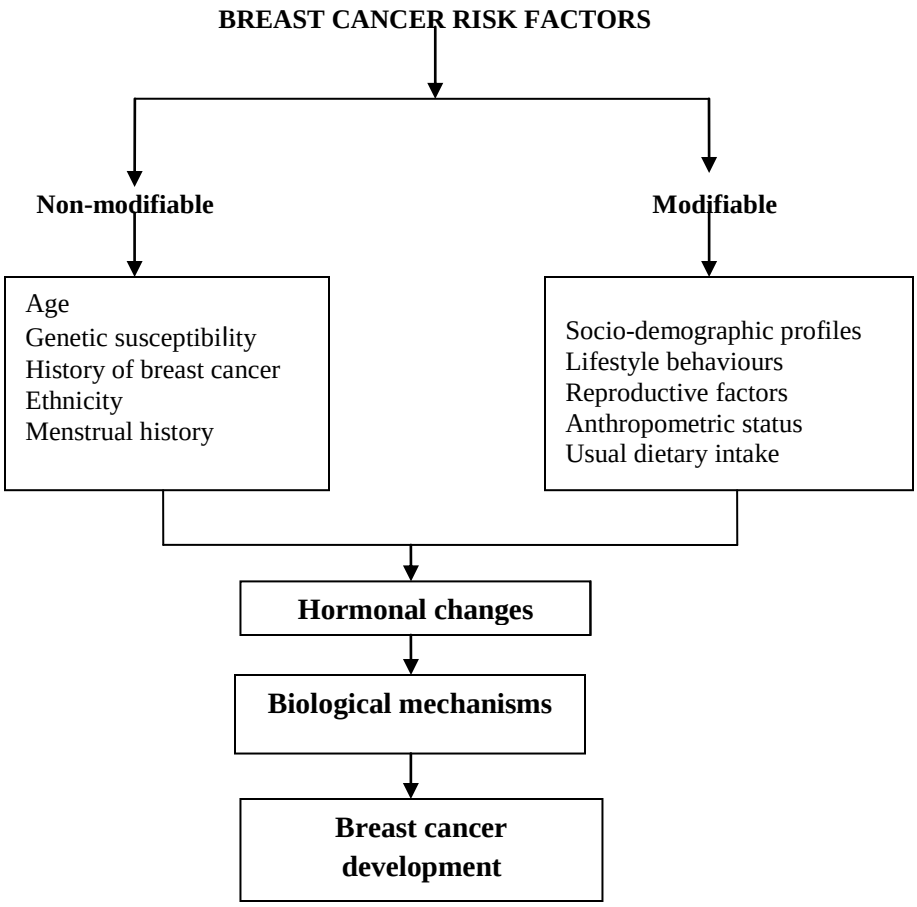

Figure 2.1 A diagram of the known risk factors for breast cancer (Kluttig & Schmidt-Pokrzywiniak, 2009:84-85**)**

2.3.1 Non-modifiable risk factors

Non-modifiable risk factors that are associated with breast cancer risk in women include age at diagnosis, genetic susceptibility, history of breast cancer, ethnicity, and menstrual history **(**Kluttig & Schmidt-Pokrzywiniak, 2009:84**)**.

2.3.1.1 Age at diagnosis

Although the risk of breast cancer increases with age in women (Fregene & Newman, 2005:1541), age at diagnosis differs among racial groups. In parts of the world older women are at a risk where approximately 77% of the breast cancer cases occur in women over 50 years. However, the trend is different in Africans where the disease is common at a young age (Rambau *et al*., 2011:214; Akarolo-Anthony *et al*., 2010:8), often between 35 and 45 years (Rambau *et al*., 2011:214; Kruger & Apffelstaedt, 2007:19) while in sub-Saharan Africa, the disease is common in women younger than 30 years (Rambau *et al*., 2011:214). Furthermore, age at diagnosis determines risk since the earlier a woman develops a first primary breast cancer, there is a greater risk of developing a secondary primary (Chen *et al*., 1999:857).

2.3.1.2 Genetic susceptibility

Genetic risk factors that might impose a risk in women for breast cancer development include Breast Cancer Type 1 (BRCA1) and Breast Cancer Type 2 (BRCA2) gene mutations. Only a small percentage (≤10%) of all breast cancers is associated with these gene mutations (American Institute for Cancer Research (AICR), 2007:2). If present, however, these mutations increase the chances of the individual to develop breast cancer with up to 50% to 85% (Hendenfalk *et al*., 2001:541) when compared to the general population (Begum *et al*., 2009:1; Kauff *et al*., 2002:1609; Hendenfalk *et al*., 2001:541; Armstrong & Weber, 2000:569).

i) Breast Cancer Type 1

BRCA1 is a human tumour suppressor gene which produces a protein called breast cancer type 1 susceptibility protein (BRCA1, 2010:Online; Park *et al*., 2000:5946). BRCA1 is expressed in the cells of breast and other tissue (BRCA1, 2010:Online) where it helps repair damaged DNA (BRCA1, 2010:Online; Park *et al*., 2000:5947), destroys the cell when DNA cannot be repaired (BRCA1, 2010:Online), and plays roles in both cell cycle control and transcriptional regulation (Park *et al*., 2000:563). When BRCA1 is damaged, the damaged DNA can allow the cell to duplicate without control and turn into cancer (BRCA1, 2010:Online).

BRCA1 mutations cause early onset breast cancer (Beeker *et al*., 2004:907; Hashizume *et al*., 2001:14538) but approximately 20% of women with this mutation never develop cancer (Beeker *et al*., 2004:907). Tumours with BRCA1 mutations, common among younger women and African-American women (Ziv *et al*., 2004:2093), are high grade cancers with a high mitotic

index, "pushing" tumour margins (non-infiltrating, smooth edges), and a lymphocytic infiltrate (Hendenfalk *et al*., 2001:543).

ii) Breast Cancer Type 2

BRCA2 is a protein that in human is encoded by BRCA2 gene and is involved in the repair of chromosomal damage with an important role in the error free repair of DNA double strand breaks (BRCA2, 2010:Online). Tumours with BRCA2 mutations are heterogeneous, are considered of high grade, display less tubule formation (Hendenfalk *et al*., 2001:543), and are positive for oestrogen and progesterone receptors (Ziv *et al*., 2004:2093; Hendenfalk *et al*., 2001:543).

iii) Gene mutations and breast cancer association

The BRCA1 and BRCA2 proteins take part in DNA repair, homologous recombination, and other cellular processes. A cell with BRCA1 or BRCA2 gene which lacks functional BRCA1 or BRCA2 proteins has a decreased ability to repair damaged DNA (Hendenfalk *et al*., 2001:543; Welcsh & King, 2001:706). Breast tumours in carriers of BRCA1 or BRCA2 genes mutations have a large number of chromosomal changes some which differ depending on the genotype (Hendenfalk *et al*., 2001:543). Germline mutations in the tumour suppressor genes BRCA1 and BRCA2 predispose individuals to breast and ovarian cancers (Afonso, 2009:44; Saslow *et al*., 2007:78; Welcsh & King, 2001:705).

Germ line polymorphism (difference in DNA sequence among individuals that may underlie differences in health) in metabolic genes encoding enzymes involved in the biosynthesis and metabolism of oestrogens may partly determine susceptibility to breast cancer (Travis & Key, 2003:241). Reproductive factors linked to oestrogen production, such as early onset of menarche and late menopause, are associated with breast cancer risk. During puberty and pregnancy when oestrogen levels are increased, BRCA1 and BRCA2 expression is developmentally regulated suggesting that oestrogen might stimulate expression of these gene mutations (Welcsh & King, 2001:706).

2.3.1.3 History of breast cancer

History of breast cancer risk factors in women include family history and personal history of breast cancer and will be discussed (Kluttig & Schmidt-Pokrzywiniak, 2009:84).

i) Family history

Family history may increase risk of breast cancer development in women (Abbasis *et al*., 2009:8; AICR, 2007:2) at a young age (Abbasis *et al*., 2009:8), though it does not guarantee that a woman will develop the disease (AICR, 2007:2). A woman is at an increased risk of breast

cancer if her blood relatives on either her mother or father's side have had breast cancer (Pakseresht *et al*., 2009:137). About 6% of breast cancers in women before the age of 55 years are linked to a family history of breast cancer in first-degree relatives. Having a sister with breast cancer poses a greater risk than having a mother with breast cancer. Women with a mother with bilateral breast cancer and with a sister or mother who developed breast cancer at a young age, have an increased risk (Chen *et al*., 1999:857).

Women with a family history of breast cancer have a number of risks including recurrence of first breast cancer and a new primary cancer (McDonnell *et al*., 2001:3938). Because age is an important risk factor for breast cancer, postmenopausal women with a family history of breast cancer are at a greater risk of developing breast cancer (Begum *et al*., 2009:1). A family history of other types of cancers such as endometrial and ovarian cancers may also increase the risk of developing a second primary breast cancer (Chen *et al*., 1999:857).

Features of the family history that suggest cancer risk include:

- Two or more first-degree (parent, sibling, or child) or second-degree (grandmother, granddaughter, aunt, niece, half-sibling) relatives with breast or ovarian cancer;
- premenopausal (before 50 years) breast cancer in a close relative;
- family history of both breast and ovarian cancers;
- one or more relatives with two cancers (breast & ovarian cancers or two independent breast cancers), (Afonso, 2009:44; Saslow *et al*., 2007:78); and
- two breast cancer susceptibility genes, BRCA1 and BRCA2 (Afonso, 2009:44).

ii) Personal history

Women with a personal history of breast cancer as well as a positive family history, are at risk of developing breast cancer recurrence, new primary cancer in the treated breast, and/or contralateral breast cancer (Houssami & Ciatto, 2010:440; McDonnell *et al*., 2001:3940). The risk among women with a personal history of breast cancer that a tumour will develop into a contralateral breast is twice the risk of an initial breast tumour among women without the history with a total incidence of approximately 0.5 to 1% per year (Hayes, 2007:2507).

2.3.1.4 Ethnicity or racial difference and breast cancer development

Breast cancer has some genetic bases which expression varying in different groups (Vona-Davis & Rose, 2009:883; Mettlin, 1999:139). Ethnicity relates to environmental influences of cancer causation, and influences are brought about by cultural differences in diet and other habits

(Brawley, 2002:233). The unique genetic features of racial groups, in combination with environmental factors, can influence carcinogenic mechanisms leading to biological differences in the molecular profile of a tumour (Taioli *et al*., 2010:516; Wiencke, 2004:81). Interactions between environmental and genetic factors should be considered when determining cancer susceptibility, regardless of intrinsic genetic differences between groups. The ethnic differences do not only determine cancer risk, but also potential responses to preventive measures and treatment (Wiencke, 2004:81).

Certain ancestral populations carry mutations or polymorphisms in genes that determine proteins thought to be directly involved in carcinogenesis (Wiencke, 2004:80). African-American women have more triple negative breast cancers, higher free oestradiol levels, and lower sex hormone binding globulin (SHBG) than white women. The characteristics of tumours in African women are similar to those of African-Americans, but are in contrast with those of non-Hispanic whites in the USA (Taioli *et al*., 2010:516; Adebamowo *et al*., 2003:19). Tumours from African women are likely to originate from a different group of cells within the breast and often do not present to the molecular targets that form basis of many standard therapies (Easton, 2005:1). The difference in breast cancer incidence in Africans compared with Western countries is related to environmental risk factors such as diet (Taioli *et al*., 2010:516; Adebamowo *et al*., 2003:19) and physical activity (both contributing to obesity), use of hormones or other medications, and gynaecological practices (Adebamowo *et al*., 2003:19).

Generally, African breast cancer patients are diagnosed at a young age (Vona-Davis & Rose, 2009:890; Adebamowo *et al*., 2003:19), and have cancer negative to oestrogen and progesterone receptors (Dona Davis & Rose, 2009:885; Marchbanks *et al*., 2002:2031). African patients also have more aggressive (Vona-Davis & Rose, 2009:883; Easton, 2005:1; Fregene & Newman, 2005:1544; Marchbanks *et al*., 2002:2031) large tumours (Taioli *et al*., 2010:515) and multiple nodal involvements (Taioli *et al*., 2010:515; Easton, 2005:2; Adebamowo *et al*., 2003:19). Relatively advanced stage (stage III or IV) of the disease (Fregene & Newman, 2005:1544), and poor clinical and pathological prognostic factors are also common in African than Caucasian patients (Adebamowo *et al*., 2003:19).

Large primary tumour size (Taioli *et al*., 2010:515; Vona-Davis & Rose, 2009:884) and the presence of wide regional lymph node metastasis and higher disease stage (Vona-Davis & Rose, 2009:884), are recognised indicators of a poor breast cancer prognosis (Akarolo-Anthony *et al*., 2010:8; Vona-Davis & Rose, 2009:884), and is often the consequence of delaying medical evaluation of self-detected breast abnormalities for too long (Fregene & Newman, 2005:1544). Occurrence of breast cancer at a young age is also associated with a worst prognosis of which will improve with age as prognosis is best in patients over 75 years (Rambau *et al*., 2011:214).

Women from Sub-Saharan Africa have low incidences of breast cancer due to the gynaecologic

and reproductive patterns in African populations which tend to result in fewer ovulatory cycles over a lifetime. Late menarche, multiparity, childbearing at young age, and long lactation periods lead to lower endogenous oestrogen levels over time, which reduce breast cancer risk (Fregene & Newman, 2005:1543). In South Africa the delayed presentation among black Africans results in significantly larger tumours and more advanced nodal pathology compared with white South Africans (Fregene & Newman, 2005:1544) and are diagnosed at a young age (Matatiele & Van den Heever, 2008:69).

2.3.1.5 Menstrual history

Menstrual history factors of women that are associated with breast cancer risk include age at menarche and age at menopause. Early menarche and late menopause are risk factors for breast cancer by increasing life time exposure to oestrogen (Friedenreich, 2001:21; Sasco, 2001:322).

i) Age at first menarche

Age at menarche is a strong indicator of breast cancer risk in the general population (Kotsopoulos *et al.*, 2005:667). There is 5% to 15% decrease in risk for developing breast cancer later in life (Travis & Key, 2003:240) for each year of menarcheal delay (Kotsopoulos *et al.*, 2005:670; Travis & Key, 2003:240).

Age at menarche vary and is dependent on the interaction between genetic and environmental factors (Karapanou & Papadimitriou, 2010:1477). Age at menarche is decreasing throughout the world probably due to anthropometric measures, nutritional influences (Karapanou & Papadimitriou, 2010:1480; Kotsopoulos *et al*, 2005:668), and decreasing physical activity during childhood (Kotsopoulos *et al*, 2005:668). African women experience menarche at older ages (Fregene & Newman, 2005:1543), with the median age of 14.7 years in rural black woman and 13.9 years in urban black woman, compared to 12.6 years in white women (Vorobiof *et al*., 2001:126). Generally tall and obese girls undergo earlier menarche, while physically active adolescents experience delayed menarche (Kotsopoulos *et al*., 2005:667).

ii) Age at menopause

Prevalence rates of breast cancer increase after menopause when ovarian oestrogen production stops. Circulating hormone levels may increase as a result of an overall increase in ovarian and adrenal secretion occurring or continuing after menopause (Friedenreich, 2001:21). After menopause, production of oestrogen in the ovaries stops and the major source of oestradiol is by conversion from oestrone produced through peripheral conversion of androgen precursors, predominantly androstenedione, in extraglandular tissue such as adipose tissue (Travis & Key, 2003:241). High serum concentrations of oestradiol are strongly associated with breast cancer risk after menopause (Key *et al*., 2003:413). Each year that the onset of menopause is delayed, is associated with a 3% increase in risk (Travis & Key, 2003:240).

2.3.2 Modifiable risk factors

Modifiable risk factors that are associated with breast cancer risk in women include socio-demographic information, lifestyle behaviours, reproductive factors, anthropometric status, and usual dietary intake (Kluttig & Schmidt-Pokrzywiniak, 2009:85-86).

2.3.2.1 Socio-demographic information

Socio-economic status is associated with a variety of lifestyles and dietary practices that will affect breast cancer risk (Fregene & Newman, 2005:1543). Socio-demographic profiles of women associated with breast cancer risk for the purpose of this study include marital status, place of residence, education level, and income.

i) Marital status

Marital status by itself is not a determining factor for increased or reduced breast cancer risk, but the main protective effect is from early full-term pregnancy (Abbasis *et al*., 2009:9; Ebrahim *et al*., 2002:11). This is explained by why single and nulliporous married women do have a similar increased risk for breast cancer when compared to women of the same age who have children (Abbasis *et al*., 2009:9).

ii) Place of residence

There is a doubling risk of breast cancer in women living in urban areas compared to those living in rural areas because urban areas are frequently characterised by westernised behaviours and lifestyles (Fregene & Newman, 2005:1543). Place of residence may also affect breast cancer patients with their decision to obtain early medical help and refrain from other proposed therapeutic methods, since people from the rural are areas may be prone to rather seek medical help from traditional healers (Vorobiof *et al*., 2001:127).

iii) Education level

Education is a major component of socioeconomic status. Many reproductive, lifestyle and behavioral factors associated with education may affect breast cancer risk including parity, age at first birth, physical activity, and diet (Hussain *et al*., 2008:166). Black women who obtain higher education levels and delay the time of their first pregnancy, have a similar increased risk of breast cancer to white women of the Western populations (Vona-Davis & Rose, 2009:890; Webster *et al*., 2008:1127; Hussain *et al*., 2008:166; Fregene & Newman, 2005:1543). Long periods of time spent in getting educated, followed by building a career contributes to marriage and motherhood being delayed (Celik & Aksoy, 2007:10). Possibly conceiving and having children at older ages increase the risk of breast cancer (Vona-Davis & Rose, 2009:890; Celik & Aksoy, 2007:10).

iv) Income

When people experience improved economic status, their dietary practices change and they grow taller and heavier, which may lead to obesity and early onset of menses, which in turn affect risk of breast cancer (Samaras, 2010:88).

2.3.2.2 Lifestyle behaviours

Lifestyle behaviours of women that are associated with breast cancer risk include alcohol use and physical activity level.

i) Alcohol intake

Alcohol is associated with both pre- and post-menopausal breast cancer (AICR, 2008:8; Wrensch *et al*., 2003:94) with recent alcohol intake increasing risk (Key *et al*., 2003:413; Wrensch *et al*., 2003:94). Breast cancer risk increases with alcohol intake, an intake of about 30 g (3 units) or more of alcohol per day (Tan *et al*., 2006:2; Key *et al*., 2003:413) is associated with about 20% increase in risk (Key *et al*., 2003:413). Moderate drinking (1 drink/day) (Tan *et al*., 2006:2) on a regular basis increases the risk of death from breast cancer (Grant, 2008:966; Tan *et al*., 2006:2; Sizer & Whitney, 2003:407) especially if there is a history of regular alcohol use, benign breast disease, and oestrogen or hormone replacement therapy (HRT) (Grant, 2008:966).

Association of alcohol consumption is dose-dependent increasing with an increase in alcohol intake (Tan *et al*., 2006:2). The intensity (number of drinks/day) of drinking determines the level of risk for breast cancer having more effect than recent alcohol use or duration of drinking. The association between alcohol intake and breast cancer risk is due to a causal effect (Tan *et al*., 2006:2; Key *et al*., 2003:413). However, the number of years in which alcohol was consumed does influence the risk of developing breast cancer (Tan *et al*., 2006:3; Parodi, 2005:557).

The mechanism for association of breast cancer risk and alcohol has not been established, but it is possible that alcohol increases endogenous oestrogen levels (Key *et al*., 2003:414; Travis & Key, 2003:240). Oestrogens play an important role in the cellular production of both normal and neoplastic breast epithelium. Alcohol interferes with oestrogen pathways in different ways, including alcohol drinking being associated with decreased menstrual cycle variability, long and frequent cycles, increased serum and urinary oestrogen metabolites, decreased SHBG, follicle-stimulating hormone, and luteinising hormone levels (Tan *et al*., 2006:7).

Chronic alcohol abuse moves nutrients from the diet by replacing food intake with alcohol. Alcohol also interferes with the body's metabolism of nutrients (Whitney & Rolfes, 2010:236). The decrease of nutrients may be associated with increased breast cancer risk because of negative impact of alcohol intake on the nature or biological value of dietary factors thought to

be cancer protective. Chronic alcohol abuse may modify folate status, and decrease concentrations of β-carotene, lutein or zeaxanthin, and vitamin C in the body (Tan *et al*., 2006:3).

ii) Physical activity level

Physical activity of all types protects against postmenopausal breast cancer (AICR, 2008:8), while sedentary behaviours increase cancer risk (Kruk, 2009:443; AICR, 2007:15). High levels of physical activity may reduce the risk of developing breast cancer by 10% to 70% (Begum *et al.*, 2009:4; Celik & Aksoy, 2007:10; Chang *et al*., 2006:335) and the effects may be more pronounced in woman doing regular exercise for 3 to 4 hours per week (Celik & Aksoy, 2007:10). The intensity and duration of physical activity also decrease the risk of breast cancer (Begum *et al.*, 2009:4; Smolin & Grosvenor, 2008:513; Celik & Aksoy, 2007:10; Chang *et al*., 2006:335).

Lifestyles leading to a positive energy balance are linked to risk for breast cancer (Begum *et al*., 2009:4; Key *et al*., 2003:415) in both pre- and post-menopausal women (Begum *et al.*, 2009:4; Travis & Key, 2003:240). Physical activity to balance energy intake may reduce the risk of developing cancer (Sizer & Whitney, 2003:415) by decreasing endogenous oestrogen exposure, decreasing obesity and abdominal fat mass, and by improving immune function (Friedenreich, 2001:15).

Among postmenopausal women, circulating levels of androstenedione and oestrone are low in women engaged in physical activity (Leitzmann *et al*., 2008:1190). Low risk in postmenopausal women may be due to physical activity preventing weight gain and obesity, while in premenopausal women the effects of high levels of physical exercise may be due to intense physical activity changing menstrual cycle characteristics, delaying menarche, and increasing the possibility of anovulatory cycles, amenorrhoea or oligomenorrhoea and so reducing exposure to ovarian hormones (Travis & Key, 2003:240).

2.3.2.3 Reproductive factors

Reproductive factors of women associated with breast cancer risk include oral contraceptive use, parity, age at first pregnancy, and breast feeding.

i) Oral contraceptive use

Controversy exists around oral contraception (OC) and risk for breast cancer. Hormonal effect of OC on the breast is complex. Hormones may have a protective anovulation effect on the breast, while on the other hand the mixture of oestrogen and progesterone may stimulate mitotic activity in the breast tissue (Clemons & Goss, 2001:277). In rodents, OC disturb the normal oestrogen or androgen balance and promote "unopposed" oestrogenic stimulation of breast epithelium and as a result breast cancer (Dimitrakakis *et al*., 2004:531).

However, while some epidemiological studies find no association between breast cancer and OC use, some studies indicate a moderate less than two-fold increase in relation to long-term use, recent use, or use at an early age (Clemons & Goss, 2001:277; Gammon *et al*., 1999:417). Recent use of OC may cause a small increase in risk of breast, but the effect of injectable progestogen contraceptive is less clear (Vorobiof *et al*., 2001:126). Long-term use of OC increases life-time exposure to oestrogen and thereby may influence the risk of cancer by changing the endogenous hormonal milieu (Sasco, 2001:322). There is also no evidence of increased risk after stopping use of OC for 10 years or more (Travis & Key, 2003:242; Marchbanks *et al*., 2002:2030; Clemons & Goss, 2001:277).

ii) Parity

The risk of breast cancer is lower in women with multiple pregnancies, especially if the first full term pregnancy occurs at a young age (Fregene & Newman, 2005:1546), however, early pregnancy may lead to young breast cancer age distribution. Multiparity is associated with an increased risk of breast cancer with late age at first full term pregnancy and absence of breast feeding (Lord *et al*., 2008:1723). The dual effect of parity on the risk of breast cancer may be due to differences in reproductive patterns explaining variations in primary tumour biology and tumour aggressiveness, however, in women of African origin the concept is still not well understood (Fregene & Newman, 2005:1546).

Breast cancer is related to increased number of regular cycles and lifetime exposure of ovarian hormones. The female breast development begins in embryonic life throughout a woman's lifetime (Kotsopoulos *et al*., 2005:671; Travis & Key, 2003:241). Multiparity causes endogenous oestrogen levels to be low over time decreasing cumulative risk of breast cancer (Fregene & Newman, 2005:1543). Nulliporous women have higher concentrations of prolactin than porous women, hence why nulliporous women have a higher risk for breast cancer (Travis & Key, 2003:243).

iii) Age at first pregnancy

Although many reproductive history factors are associated with increased risk of breast cancer development, however, an early first full term pregnancy is associated with a low risk. Protection of pregnancy is linked to the endocrine hormones responsible for stimulating breast gland development (Kleinberg *et al*., 2009:61).

In African women, childbearing begins at the young age with the median of 19 years. An early age (≤20 years) at first childbirth and multiparity may reduce the risk of developing breast cancer (Lord *et al*., 2008:1723; Kotsopoulos *et al*., 2007:3) by up to one-half (Kotsopoulos *et al*., 2007:3), whereas late age (≥30years) places a woman at an increased risk (Celik & Aksoy, 2007:10; Kotsopoulos *et al*., 2007:3). Women of mixed background in South Africa who had

their first child at the age of 30 years or older had the risk of twofold when compared with women who had their first child at the age of 16 years or younger (Fregene & Newman, 2005:1543).

Age at first childbirth reflects exposure to oestrogen and the effect of oestrogen on terminal duct epithelium not undergone the final separation induced by pregnancy and lactation (Clemons & Goss, 2001:276). High levels of oestrogens and progesterone during pregnancy stimulate growth of breast epithelium and promote separation of epithelium tissue reducing the number of epithelial structures vulnerable to malignant change. If a malignant change is present in the breast, the short term effect of pregnancy may promote growth of cancer but in the longer term the risk for breast cancer is reduced. Malignant changes are more likely to accumulate in the breast tissue of older women and they might be at a higher risk of cancer when breast cells are stimulated to divide during pregnancy (Travis & Key, 2003:240).

Breasts of nulliporous women are composed of unseparated (type 1) lobules having high growth index and concentrations of steroid hormone receptors. These breasts are more vulnerable to carcinogenic attack and are the sites of origin of breast carcinomas (Kotsopoulos *et al*., 2007:227). Parity induced protective effect is due to hormone induced transformation (Kotsopoulos *et al*., 2007:227; Fregene & Newman, 2005:1543; Jerry, 2007:103) occurring in the lobules of breast epithelial cells turning them into type 2 and type 3 lobules making them less vulnerable to carcinogens. An early age at first childbirth therefore results in a separated state and reduced risk of developing breast cancer (Kotsopoulos *et al*., 2007:227).

iv) Breast feeding

Breast feeding protects women against both pre- and post-menopausal breast cancer (AICR, 2008:5). Breast feeding is protective for the risk through hormonal changes in the body (Lord *et al*., 2008:1723; Travis & Key, 2003:240; Wrensch *et al*., 2003:93), delayed ovulation, increased breast separation, change in the hormonal environment of the breast, excretion of carcinogenic agents (Lord *et al*., 2008:1723), and other mechanisms. Inability to breast feed or suppressing breast feeding might have a damaging effect on the breast physiology (Wrensch *et al*., 2003:93).

Hormonal changes associated with breast feeding delay return of a new mother's menstrual periods thereby reducing a woman's lifetime exposure to hormones such as oestrogen (AICR, 2008:5; Clemons & Goss, 2001:276). During pregnancy and breast feeding, the breast tissue reaches the final stages of physical maturity with the milk making cells growing and reproducing. The shedding of breast tissue during lactation and programmed cell death following lactation may decrease risk because cells with potential DNA damage are eliminated (AICR, 2008:6).

Long periods (±16 months) of breast feeding decrease the risk for breast cancer by separation of ductal epithelial cells protecting against carcinogens and increased prolactin levels that may contribute to separation of ductal epithelial cells (Fregene & Newman, 2005:1543). There is a reduced lifetime risk of 4.3% and a reduced risk of 7% for every birth given in women breast feeding for 12 months (Celik & Aksoy, 2007:10). History of breast feeding reduces risk of breast cancer at around 55 to 64 years (Lord *et al*., 2008:1723).

Breastfed babies likely receive protection against cancer because breast feeding decreases the likelihood that a child will be overweight during early years of childhood. Protection from weight gain is important because childhood overweight have a tendency to continue into adulthood overweight (AICR, 2008:6; Samaras, 2010:88) and adults with excess body fat are at an increased risk of postmenopausal breast cancer. Breastfed babies exhibit slower growth and make the chances of developing cancer later in life lower (AICR, 2008:7). Breast feeding also helps in establishing a microbial ecosystem of the new infants since at birth the gastrointestinal tract is sterile (Heavey & Rowland, 1999:76).

2.3.2.6 Anthropometric status

Anthropometric measurements associated with risk in breast cancer risk in women include body weight, height, and waist circumference **(**Kluttig & Schmidt-Pokrzywiniak, 2009:85**).**

i) Weight

Birth weight is positively associated with the risk for breast cancer (Parodi, 2005:556; Travis & Key, 2003:243; Innes *et al*., 2000:1121) due to perinatal factors related to high concentrations of maternal oestrogen in pregnancy or high levels of oestrogens in the postnatal infancy (Travis & Key, 2003:243). While birth weight is associated with circulating oestrogen levels and IGF-1 activity, however, fetal weight is negatively associated with both fetal and maternal levels of IGF-1. Both oestrogens and IGF-1 are important in fetal growth and mammary gland development and therefore play a central role in the initiation and promotion of breast cancer (Innes *et al*., 2000:1121). Recent weight loss is associated with a reduced risk of breast cancer in all age groups (Ziegler, 1997:926; Friedenreich, 2001:19). The decrease in risk may be linked to changes in hormonal status and body fat distribution (Friedenreich, 2001:19).

ii) Height

Height reflects the number of ductal stem cells developing in the breast in utero and plays an important role in the exposure of breast cancer etiology prenatally (Friedenreich, 2001:15; Ziegler, 1997:925). Height relates to nutrition (Nemesure *et al*., 2009:391; Friedenreich, 2001:15) indicating differences in energy intake, dietary patterns in early life (Chang *et al*., 2006:337), and adiposity associated to adult energy intake leading to increased risk for breast

cancer (Chang *et al*., 2006:336; Friedenreich, 2001:15). Height also relates to genetic growth potential and hormones influencing breast cancer incidence (Friedenreich, 2001:15).

Increasing height is associated with increased risk for breast cancer (Chang *et al*., 2006:336; Fregene & Newman, 2005:1543; Wrensch *et al*., 2003:94) in both pre- and post-menopausal women (Friedenreich, 2001:20). The association is explained by factors influencing the development of both height and breast cancer (Ziegler, 1997:925). If women reach maximum height late, the breasts mature late and have less time between pubertal breast development and the breast growth protection occurring at the time of the first live birth (Friedenreich, 2001:15).

iii) Fat distribution

Typically, body fat locates to upper abdominal part or lower sites around the hips and thighs. Abdominal adiposity consists of three separate stores; the superficial subcutaneous, deep subcutaneous, and visceral components differing in their metabolic activity and contributing different levels of hormonal milieu (Rose *et al*., 2007:739). Women with central adiposity have a higher risk of breast cancer than women whose fat is distributed over the hips, buttocks, and lower extremities (Friedenreich, 2001:17). Central body fat distribution decrease fat cell size with energy reduction thereby reducing abdominal obesity and breast cancer risk (Friedenreich, 2001:19).

Fat around the waist increases risk of postmenopausal breast cancer (AICR, 2008:8; Friedenreich, 2001:17; Ziegler, 1997:927) giving a protective effect before menopause (Neilson *et al*., 2009:16). WC is a better predictor of breast cancer risk than WHR probably because it is a direct measure of abdominal adiposity (Friedenreich, 2001:17). Overweight people, especially if they are "apple-shaped", have high levels of substances circulating in their blood that stimulate cell division. This is supported by laboratory studies indicating that body fat stored by people is not motionless, and waist fat is more active in producing growth stimulants (AICR, 2007:15). Excess adipose tissue in the abdominal area leads to high blood concentrations of free fatty acids and endocrine factors such as tumour necrosis factor alpha (TNF-ά), leptin and resistin, and low concentrations of adiponectin (Dossus & Kaaks, 2008:553).

Central adiposity may also increase breast cancer risk through increasing multiple hormonal and metabolic changes including circulating insulin (MacInnis *et al*., 2004:2117; Friedenreich, 2001:4), glucose or triglycerides, decreases in SHBG, androgen levels, and conversion of androgen to oestrogen in adipose tissue (Friedenreich, 2001:17). In premenopausal women, insulin levels are positively associated with breast cancer, while in postmenopausal women adiposity is related to increased plasma glucose and hyperinsulinaemia. Nutritionally induced hyperinsulinaemia and insulin resistance are the main metabolic changes resulting in breast cancer development. Overnutrition, obesity, low physical activity, and chronic changes in the endocrine secretion of steroid hormones particularly ovarian androgens and reduced production

of SHBG by the liver is the model hypothesised to increase the risk of breast cancer development (Friedenreich, 2001:4).

Current adiposity influences the risk for breast cancer than earlier adiposity. Adiposity at the time of cancer is diagnosed is associated with an increased probability of recurrence (Ziegler, 1997:925) and a decreased survival time (Calle *et al*., 2003:1628; Ziegler, 1997:925). If adiposity enhances tumour growth after diagnosis, it is expected to promote tumour development and growth in the late stages of breast carcinogenesis even before clinical detection. Excess weight may function as a late stage promoter of breast carcinogenesis (Ziegler, 1997:926; Friedenreich, 2001:19).

High WHR is positively related to an increased risk of breast cancer (MacInnis *et al*., 2004:2117) in postmenopausal women, however, there is no association with breast cancer risk in premenopausal women (Nemesure *et al*., 2009:391). Women in their highest quintile of WHR (≥88) have a risk of one and half (1.5) times than women in their lowest quintile (<80) with the relationship being strong among women with a family history of breast cancer (Ziegler, 1997:927).

iv) Obesity

The relationship between BMI and breast cancer risk differs by menopausal status (Key *et al*., 2003:414). Obesity might increase risk in women aged 50 years or more who are postmenopausal but might decrease risk in women under the age of 50 years. The heaviest women (BMI ≥40kg/m^2) have a risk of death from breast cancer than women of normal weight (Calle *et al*., 2003:1628). The risk is increased by 30% among obese postmenopausal women (≥30kg/m^2) compared to those with a normal BMI (<25kg/m^2) (Travis & Key, 2003:240).

Obesity increases levels of circulating endogenous sex hormones, insulin, and IGF (Neilson *et al*., 2009:14; Friedenreich, 2001:13), production of proteins in blood (called cytokines causing inflammation) (AICR, 2008:8), adiponectin lowering levels of SHBG (Friedenreich, 2001:13; Neilson *et al*., 2009:14; Vona-Davis & Rose, 2009:889), increased peripheral fat conversion of estrogens to progesterone, and increased serum testosterone levels. All these chemicals increased may be associated with an increased risk of breast cancer (Adebamowo *et al*., 2003:22).

Obese premenopausal women likely have longer menstrual cycles and more anovulatory cycles than non-obese premenopausal women resulting in less exposure to estrogen and the reduced risk of breast cancer (Clemons & Goss, 2001:277). Leptin produced by adipose tissue stimulates growth of breast cancer cells, which is associated with large primary tumours (Vona-Davis & Rose, 2009:889). However, leptin also inhibit production of ovarian estrogen and contribute to reduced risk of breast cancer in heavier young women (Friedenreich, 2001:23).

2.3.2.5 Role of nutrition in the etiology of cancer

Suggested associations between diet and cancer in human are mostly based on data obtained from epidemiological studies (Grant, 2008:962; Thomas & Bishop, 2008:770). Epidemiologists look at human populations and evaluate how many people are diagnosed with cancer, the kinds of cancers they are diagnosed with, and the factors that play a role in the development of cancer (Grant, 2008:962). Epidemiologic studies include cross-sectional, case-control, prospective (cohort), and intervention trial studies (Grant, 2008:962; Thomas & Bishop, 2008:770).

Cross-sectional studies compare differences in diet and cancer prevalence, (Grant, 2008:963; Thomas & Bishop, 2008:770) either between or within populations. Observations provided indicators, but are not necessarily evidence, of cause-and-effect, as other relevant factors such as socioeconomic, demographic, genetic, cultural, and environment may influence the relationship between parameters (Thomas & Bishop, 2008:770).

Case-control studies determine differences between the diets of people who develop a specific type of cancer, and the diets of their carefully matched healthy controls (Grant, 2008:963; Thomas & Bishop, 2008:770). Variables matched may include age, sex, and other factors (Grant, 2008:963). Although this type of study creates a homogenous study population, small or not detectable dietary differences may still exist between groups in terms of age, social class, occupation, and other factors, due to limitations of dietary assessment methods. Dietary differences are difficult to clarify as to whether they existed in the early stages of cancer development, many years before, or whether they are a result of having the disease (Thomas & Bishop, 2008:770).

Prospective (cohort) studies follow initially healthy people for a long time until cancer develops, enabling dietary comparisons between those who do or do not develop the disease (Grant, 2008:963; Thomas & Bishop, 2008:771).

Randomized controlled prospective intervention trials evaluate the effects of making dietary changes and provide clear evidence of dietary benefit or risk (Thomas & Bishop, 2008:771).

While epidemiological studies may find associations between dietary factors and cancer risk, animal studies are used to help explain the mechanisms by which dietary factors may cause carcinogenesis (Grant, 2008:962; Thomas & Bishop, 2008:770). Animal studies however cannot predict dietary risk in free-living human populations where other factors operate (Thomas & Bishop, 2008:771).

2.3.2.6 Usual dietary intakes and the development of breast cancer

Dietary factors related to breast cancer risk concentrate mainly on the intake of energy, fat, protein, carbohydrates, fruits and vegetables, fibre, phytochemicals, antioxidants, phytoestrogens, coffee and tea, and methods of food preparation.

The main hypotheses regarding the effects of nutrition on breast cancer risk are that obesity and a high intake of meat, dairy products, fat, and alcohol may increase risk, while a high intake of fibre, fruits, vegetables, antioxidants, and phytochemicals may reduce risk. Possible mechanisms include nutritional effects that may affect endogenous hormone levels and impact on breast cancer risk (Key *et al*., 2003:413). For example, phytoestrogens may reduce breast cancer risk by reducing estradiol (principal form of estrogen in humans) levels or by blocking the action of estradiol (Thomas & Bishop, 2008:223; Rolfes *et al*., 2006:466; Key *et al*., 2003:413). Antioxidants in food may also reduce breast cancer risk by reducing oxidative damage to the DNA in breast epithelial cells (Thomas & Bishop, 2008:222; Key *et al.*, 2003:413).

The inter-relationship between diet and the development of cancer is complex, multifactorial (Thomas & Bishop, 2008:771; Chyz *et al*., 2001:3), and hard to unravel because of many variables involved on the disease and the dietary influences (Thomas & Bishop, 2008:771). Foods and nutrients are never eaten in isolation, therefore their effects are likely to interact (Brennan *et al*., 2010:1294) and thus the risk or benefit from one dietary component may be affected by the presence or absence of other dietary components. Although all cancers stem from DNA damage, causes for and effects of the damage vary, so that some dietary factors (e.g. non-starch polysaccharide) may be protective against one type of cancer, but have no effect on another type of cancer (Thomas & Bishop, 2008:771).

i) Energy intake

Energy restriction is known to prevent breast cancer development in animal models (Chang *et al*., 2006:334; Milner, 2003:3824). Reduced energy intake is associated with low rates of cell reproduction during premalignant and malignant stages of the cancer process (Milner, 2003:3824). Energy restriction reduces reproduction activity and suppresses tumour growth (Chang *et al*., 2006:334). The adverse influence of high energy intake on human breast cancer development was concluded from animal models of energy restriction which showed that reduced energy intake, regardless of energy source, leads to fewer and/or smaller mammary tumours (Chang *et al*., 2006:336).

Energy intake may change breast cancer risk through the interaction of hormones that control energy balance. High energy intake is associated with increased availability of insulin-like growth factor-I (IGF-I) (Dossus & Kaaks, 2008:556; Chang *et al*., 2006:337) and IGF-I may play an etiologic role in cancer development. High energy intake may also increase blood insulin

levels (Chang *et al*., 2006:337) which is associated with an increased risk of breast cancer (Chang *et al*., 2006:337; Friedenreich, 2001:26).

Increasing energy intake in a typical range of USA diets is positively associated with risk of breast cancer (Dossus & Kaaks, 2008:551; Chang *et al*., 2006:335). Women with an unfavorable energy balance (high energy intake, high BMI, and low physical activity) have twice the risk of women with a favorable energy balance (Chang *et al*., 2006:336). However, high energy intake has not been consistently linked to increased breast cancer risk in humans (Chang *et al*., 2006:335).

ii) Fat intake

Diets high in fat (40% - 45% of total energy intake) are associated with increased breast cancer risk (Carter & Church, 2009:7; Mettlin, 1999:142), although there are some populations that have a high dietary fat intake without high breast cancer rates. Use of monosaturated fat sources such as olive oil is protective against breast cancer (Lof *et al*., 2007:1570; de Pablo *et al*., 2002:948 Mettlin, 1999:142) whereas polyunsaturated fat (PUFAs) is most specifically associated with high risk (Ion *et al*., 2010:81; Mettlin, 1999:142). The mechanism how dietary fats are implicated in tumour progression is not fully yet understood (Ion *et al*., 2010:81; Carter *et al*., 2009:7).

PUFAs include the omega-3 (n-3) and omega-6 (n-3) classes, both of which play essential roles in normal physiology. Dietary fats, specifically PUFAs, are involved in the inflammatory process linked to cancer cell motility and survival. The summary of the possible biological activities performed by the PUFAs are indicated in Table 2.1.

The n-3 PUFA to n-6 PUFA ratio is what drives cancer cell biology (Carter *et al*., 2009:7). For protection against cancer development n-3 and n-6 PUFAs need to be consumed in a proportion of 1:1 or 1:2 (n-3: n-6) (Granados *et al*., 2006:44).

Table 2.1 PUFAs in foods and their possible effects in breast cancer development (Ion *et al*., 2010:81; Carter *et al*., 2009:7; Granados *et al*., 2006:44; Ray, 2005:12; de Pablo *et al*., 2002:948):

PUFA name/class	Food sources	Biological activity
Omega-3		
Alpha-linolenic acid	-flaxseed oil, canola oil, soybean oil, green leaves of purslane	-inhibit tumour growth. -decrease cell motility.
Eicosapantaenoic acid (EPA) Docosahexaenoic acid (DHA)	-cod liver oil, mackerel, salmon, sardines, crab, shrimp, oysters	-suppress development of breast cancer. -reduce growth in tumour cell lines of breast cancer.
Omega-6		-inhibits onset and promotion of tumours and possibly cancer progression.
Linoleic acid	-Polyunsaturated vegetable oils	
Arachidonic acid (AA)	- land animals	-increase cell motility and survival through inactivation of tumour suppressor.

iii) Protein intake

High intake of meat is a risk factor for breast cancer (McTiernan, 2003:330) especially red meat (beef, lamb, pork) or processed meat (AICR, 2008:7; Ray, 2005:15), but there is no evidence that connects white meat, while fish is protective against cancer risk (Ray, 2005:15). All meats (red, white, and processed) combined are associated with increased risk of breast cancer (AICR, 2008:7). Women who are high consumers of meat and low consumers of vegetables or soy and soy products have an increased breast cancer risk, which is supported by the study conducted in Asian American women by Wu and the associates (2008:1150).

A diet low in protein is low in essential amino acids and reduces serum IGF-I levels in humans. Strict vegetarian (vegan) women whose diets are low in essential amino acids have a 12% lower IGF-I concentration compared with lacto-ovo-vegetarians and meat-eaters. IGF-I is a peptide hormone that acts as a mitogen to stimulate breast epithelial cell growth in both normal and diseased tissue and may play a role in breast cancer development. A high circulating IGF-I concentration either on its own or together with its main binding protein, IGFBP-III, is predictive of breast cancer risk among premenopausal women (Dossus & Kaaks, 2008:557; Key *et al*., 2003:414). The link between essential amino acids and IGF-I is of great interest because serum levels of IGF-I are known to be sensitive to dietary changes (Key *et al*., 2003:414).

Table 2.2 gives protein foods and the types of dietary fat they contain.

Table 2.2 Protein foods and types of dietary fat they contain (Whitney & Rolfes, 2010:168)

Saturated fats	Monounsaturated fats	Polyunsaturated fats
-Bacon -Butter -Chocolate -Coconut -Cream cheese -Cream -Lard -Meat -Milk & milk products -Oils (coconut, palm, palm kernel) -Shortening -Sour cream	-Oils (canola, olive, peanut, sesame) -Avocados -Nuts(almonds, cashews, filberts, hazelnuts, macadamia nuts, peanuts, pecans, pistachios) -Olives -Peanut butter -Seeds (sesame)	-Fatty fish (herring, mackerel, salmon, tuna) -Flaxseed -Nuts (walnuts)

A Western diet is composed of high fat and low fibre foods that contribute a high percentage of energy from saturated fats (from animal sources), sugars, and refined carbohydrates. This type of diet causes increase in rates of obesity and high body fatness and an increased risk of breast cancer (Dossus & Kaaks, 2008:551). A typical traditional African diet consists mostly of grain, vegetables, high fibre, low fat and protein (AICR, 2009:Online; Fregene & Newman, 2005:1543). The African dietary pattern may be protective against breast cancer risk (AICR, 2009:Online; Fregene & Newman, 2005:1543; McTiernan, 2003:329), especially against postmenopausal breast cancer (AICR, 2009:Online). Vegetables, fruits, whole grains, and beans are low-energy dense, high-nutrient dense foods which may protect against weight gain, thus also protecting against breast cancer (AICR, 2009:Online).

iv) Milk and dairy products

Controversy exists about the association of milk intake and breast cancer risk (Hjartáker *et al*., 2001:888). However, the intake of dairy products may affect the pathways associated with carcinogenesis (Van der Pols *et al*., 2007:1722). Dairy products are a diverse food group in terms of factors that could potentially influence risk. Some dairy products, such as whole milk and many types of cheese, have a high saturated fat content which may increase risk (Moorman & Terry, 2004:5).

Components of milk such as growth factors, fatty acids, and calcium are hypothesised to play a role in the development of breast cancer (Hjartáker *et al*., 2001:888). Calcium intake has been

negatively associated with cancer risk, especially of the breast and colon. Calcium together with vitamin D may protect against development of breast cancer through its effect on the mammary gland. Milk and dairy products also contain conjugated linoleic acid (CLA) (Moorman & Terry, 2004:5) suggested to block both local growth and systematic spread of human breast cancer in animal studies (Hjartáker *et al*., 2001:892).

Dairy products may also increase breast cancer risk through their oestrogen and growth factor content (Hjartáker *et al*., 2001:892), the circulation of IGF-I, exposure to contaminants such as polychrorinated biphenyls (Van der Pols *et al*., 2007:1722) and pesticides, which have carcinogenic potential, and through the reflection of an overall dietary fat intake particularly saturated fat (Moorman & Terry, 2004:5).

The IGF-I plays a role in the regulation of prenatal and postnatal growth but also exerts a growth-promoting effect in adulthood through low apoptosis, angionesis (van der Pols *et al*., 2007:1722), and high cell proliferation (production) (Van der Pols *et al*., 2007:1722; Moorman & Terry, 2004:5). High concentrations of IFG-I are associated with increased risk of premenopausal breast cancer and other cancers such as colorectal and prostate (Van der Pols *et al*., 2007:1722).

v) Antioxidants, phytochemicals, and phytoestrogens

a) Antioxidants

Antioxidants are substances in foods that significantly decrease the adverse effects of free radicals on normal physiological functions in the human body (Whitney & Rolfes, 2010:338). Dietary anti-oxidants include minerals selenium, copper, manganese, and zinc, and vitamins E and C. Dietary anti-oxidants also include non-nutrient chemicals. Nutrients, phytochemicals, and anti-oxidants defend the body against cancer by minimising damage by limiting free-radical formation (Thomas & Bishop, 2008:222; Rolfes *et al*., 2006:391), destroying free radicals or their precursors, stimulating antioxidant enzyme activity, repairing oxidative damage, and stimulating repair of enzyme activity (Rolfes *et al*., 2006:391). Antioxidants also contain naturally occurring biological compounds which give additional protection against LDL oxidation (Vaya & Aviram, 2010:Online; Thomas & Bishop, 2008:222), DNA mutation, or inhibit abnormal cell production (Thomas & Bishop, 2008:222).

Both nutritive and non-nutritive antioxidants in fruits and vegetables neutralise harmful effects of DNA damaging of free radicals produced by metabolism and external factors such as pollution and smoking. Carotenoids and tocopherols in fruits and vegetables inhibit oxidative processes involved in carcinogenesis, carcinogen metabolism, and cell proliferation, and enhance the cellular immune system. Dietary intake of carotenoids, tocopherols, and vitamin A are associated with a reduction in breast cancer risk (Dorjgochoo *et al*., 2009:381). ßeta-carotene is effective in

protecting lipid membranes from damage by free radicals and reactive species. Lycopene is the efficient quencher of singlet oxygen species, lutein and zeaxanthin are scavengers of radical oxygen species (Nkondjock & Ghadirian, 2004:857).

Fruits have antioxidant and anti-inflammatory properties and may apply inhibitory action on tumour promoter induced carcinogenesis and associated cell signaling. The chemopreventive agents include flavonoids, ellagic acid, perillyl alcohol, and resveratrol (Ray, 2005:15). Anticarcinogenic agents found in fruits include antioxidants vitamins such as vitamins C and E and selenium, phytochemicals, and nonnutritive substances thought to influence tumourigenesis. Phytochemicals consumed from fruits have synergistic effect to inhibit cell growth through their antioxidant and anticancer properties (Grant, 2008:965).

Berries such as black raspberries, blackberries, and strawberries inhibit carcinogen induced malignancy in animal models. The chemopreventive agents in berries include vitamin C, vitamin E, folate, small amount of calcium, and selenium, beta- and alpha-carotene, polyphenols (ellagic acid, ferulic acid, *p*-coumaric acid, quercetin, anthocyanins), and phytosterols (triterpenes). Berries inhibit growth of premalignant cells through down regulating genes associated with tumour development. Berries might also have the ability to inhibit tumour development by impairing signal transduction pathways. Grapes, berries, and peanuts contain resveratrol, which is a natural food micro-component with strong chemopreventive properties regarding human diseases including cancer. Perillyl alcohol, a monoterpene found in citrus peel, is another important chemopreventive agent (Ray, 2005:18).

Cruciferous vegetables play an important role against risk of breast cancer (Terry *et al*., 2008:284). The Cruciferae are the family of plants that include a wide variety of familiar members of the species *Brassica oleracea* (e.g., broccoli, cabbage, cauliflower, parsnip, kale, kohlrabi, brussels sprouts, turnip, rutabaga) and other plants which are commonly consumed as oriental cabbage, arugula, watercress, radish, daikon, wasabi, various mustards, horseradish, kai choi, and others (Terry *et al*., 2008:284; Ray, 2005:17). Cruciferous vegetables contain flavonoids and selenium. Chemopreventive effects of cruciferous vegetables are due to high glucosinolate content which under enzymatic hydrolysis produces bioactive compound isothiocyanates. Isothiocyanates of cruciferous vegetables are inhibitors of carcinogenesis in experimental animal models. Cruciferous vegetables can also modulate oestrogen metabolism, thereby lowering the risk of oestrogen dependent cancers like breast cancer (Ray, 2005:17).

Curcumin is a yellow coloured pigment isolated from rhizome of plant *Curcuma longa*, known as turmeric. Curcumin has anti-inflammatory and antioxidant properties and may inhibit lipooxygenase activity, initiation of carcinogenesis by suppressing cytochrome enzyme activity, and increasing levels of glutathione-*S*-transferase. (Ray, 2005:19). A summary of antioxidants responsible for breast cancer prevention in humans and their possible biological mechanisms is indicated in Table 2.3.

Table 2.3: Antioxidants, phytochemicals, and phyto-oestrogens in foods and their possible effects in breast cancer prevention (Smolin & Grosvenor, 2008:395; Thomas & Bishop, 2008:233; Rolfes *et al*., 2006:466)

Phytochemical name/class	Foods sources	Biological activity
Carotenoids: Lycopene	-Apricots, carrots, cantaloupe, tomatoes, sweet potatoes, broccoli, spinach, leafy greens.	-provide antioxidant protection. -reduce cancer risks.
Curcumin **Flavonoids:** catechins, cyanins, flavonols, flavones, isoflavones.	-Turmeric, mustard. -Berries, citrus fruits, onions, margarine, pulp grape, green tea, red wine, chocolate, celery, olives, oregano, soybeans and products.	-may inhibit enzymes that activate carcinogens. -act as antioxidants. -block carcinogens & slow the growth of cancer cells.
Glucosinolates: Indoles	-Broccoli, brussels sprouts, cabbage, cauliflower, mustard greens, horseradish.	-may inhibit oestrogen action. -may trigger production of enzymes that block DNA damage from carcinogens. -inhibit enzymes that activate carcinogens.
Isothiocynates (sulforaphane)	-Broccoli, brussels sprouts, cabbage, cauliflower, mustard greens, horseradish.	-trigger production of enzymes that detoxify carcinogens. -protect animals from breast cancer.
Lignans	-Oats, barley, wheat-germ, potatoes, apples, cherries, plums, vegetable oils from: cotton seed; sunflower; corn linseed; olive; coconut.	-block oestrogen activity in cells, possibly reducing the risk of breast cancer.
Monoterpenes: limonene	-citrus fruit peels & oils.	-may trigger enzyme production to detoxify carcinogens. -inhibit speed production of carcinogen-destroying enzymes. -slow production of carcinogen-activating enzymes.

Table 2.3- continue: Antioxidants, phytochemicals, and phyto-oestrogens in foods and their possible effects in breast cancer prevention (Smolin & Grosvenor, 2008:395; Thomas & Bishop, 2008:233; Rolfes *et al*., 2006:466)

Phytochemical name/class	Food sources	Biological activity
Organosulfur compounds	-chives, garlic, leeks, onions.	-may speed production of carcinogen-destroying enzymes. -slow production of carcinogen-activating enzymes.
Phenolic acids	-coffee beans, apples, cherries, blueberries, -grapes, oranges, pears, prunes, oats, potatoes, soybeans.	-may trigger enzyme production to make carcinogens water soluble, facilitating excretion.
Phytic acids	-whole grains.	-bind to minerals, preventing free-radical formation, possibly reducing cancer risk.
Phyto-oestrogens: Genistein, daidzein, isoflavones	-soybeans, soy flour, soy milk, tofu, flax seed, rye bread, textured vegetable protein, other legume products.	-mimic effect of oestrogen. -induce cancer cell death. -slow the growth of cancer cells. -reduce risk of breast cancer.
Protease inhibitors	-Broccoli sprouts, potatoes, soybeans & other legumes, soy products.	-may suppress enzyme production in cancer cells, slowing tumour growth. -inhibit hormone binding.
Saponins	-Beans & herbs, alfalfa sprouts, other sprouts, green vegetables.	-may interfere with DNA replication, preventing cancer cells from multiplying.
Tannins	-tea, red & white wine, black-eyed peas, grapes, lentils.	-may inhibit carcinogens activation & cancer promotion. -acts as antioxidants.

Antioxidant supplements have not been proved beneficial to reduce risk of cancer in the body (Rolfes *et al*., 2006:392). The total amount of antioxidants obtained naturally in foods provide better benefits than individual antioxidants received from supplements (Svilaas *et. al*., 2008:Online). The antioxidant benefits are more visible when they come from foods rather than

from supplements because antioxidants behave differently under different conditions. At physiological levels of a healthy diet, chemicals act as antioxidants but at pharmacological doses typical supplements may act as prooxidants stimulating the production of free radicals (Rolfes *et al*., 2006:392).

b) Phytochemicals

Phytochemicals are substances in plant foods that are not essential nutrients but may have health promoting properties (Smolin & Grosvenor, 2008:393). Phytochemicals interact to provide cancer protection (AICR, 2008:9; Boyer & Liu, 2004:1186), a concept called synergy (AICR, 2009:Online; Smolin & Grosvenor, 2008:399). Phytochemicals are responsible for health promoting properties provided by variety of natural functional foods in different ways (Smolin & Grosvenor, 2008:394; Rolfes *et al*., 2006:467). Some phytochemicals are antioxidants, others provide benefits because they copy the structure or function of natural substances in the body, others are health promoting due to their ability to change the way in which cells communicate, affect DNA repair mechanisms, or influence other cell processes that may affect cancer development (Smolin & Grosvenor, 2008:394; Béliveau & Gingras, 2007:1908; Boyer & Liu, 2004:1188) while others prevent cancer-causing substances (carcinogens) from becoming active, prevent damage, or heal damage to normal cells, or trigger the "suicide" of cancer cells (AICR, 2008:9).

Phytochemicals consumed from the diet interfere with tumour development by acting on tumour cells and by changing the tumour's microenvironment (stroma) and creating physiologic conditions that are unfriendly to tumour growth (Béliveau & Gingras, 2007:1908). For example, phytochemicals may inhibit cancer cell proliferation (Boyer & Liu, 2004:1188), regulate inflammatory and immune response, protect against lipid oxidation, and the anti-inflammatory effect contributes to their anticancer properties (Béliveau & Gingras, 2007:1908). When consuming plant foods one is boosting the body's defences against cancer (AICR, 2008:9).

Fruits and vegetables also contain nonnutritive compounds (phytochemicals) that have chemopreventive effects through stimulation of cell differentiation, cessation of cell division, antioxidant potential, anti-oestrogenic effects, induction of metabolic detoxification, and enhancement of immune function (Gaudetet *et al*., 2004:1487). Fruits and vegetables are the primary sources of phytochemicals hypothesised to have anticarcinogenic properties, including carotenoids, inhibitors, plant sterols, glucosinolates, indoles, isothiocyanates, flavonoids, phenols, protease inhibitors, plant sterols, allium compounds, and limonene (Terry *et al*., 2008:285) (Table 2.3).

c) Phyto-oestrogens

Phyto-oestrogens are plant hormones that interrupt cancer development and affect health by interfering with the action of human oestrogen (Smolin & Grosvenor, 2008:397). Structurally, phyto-oestrogens are similar to human oestradiol and can either copy or block the action of human oestrogen (Thomas & Bishop, 2008:223; Rolfes *et al*., 2006:466). Phyto-oestrogens compete with endogenous oestrogens for binding to oestrogen receptor (Ray, 2005:15) making phyto-oestrogens to have beneficial effects in the prevention of steroid hormone dependent cancers such as of the breast (Thomas & Bishop, 2008:223; Rolfes *et al*., 2006:466; Ray, 2005:15).

Phytoestrogens have antioxidant activity and therefore may slow the growth of breast cancer (Rolfes *et al*., 2006:466) however, the effects are variable and may be influenced by ethnicity, type of soya, usual amount of phytoestrogen consumed, dietary composition (Thomas & Bishop, 2008:223), and the hormonal environment of the person (McTiernan, 2003:330). Soybean consumption may be responsible partly for lowering levels of ovarian hormones and decreasing breast cancer rates in Asian women compared to Western populations. Soybeans contain isoflavones, daidzein and genistein which are weak oestrogens (Lu *et al*., 2000:4112).

Foods rich in fiber are important sources of phyto-oestrogens and they may interact with and modulate the activity of oestrogen receptors hypothesised to protect against breast cancer (Sonestedt *et al*., 2008:2203). Possible protective effects are through the influence on the bioavailability and the action of oestrogens in the body. Lignin found in fibre foods block oestrogen activity in the cells, possibly reducing the risk of breast cancer. Lignin may influence the enterohepatic circulation of oestrogens, increasing the excretion of oestrogens in the faeces, and giving reduced levels of circulating oestrogens (Sonestedt *et al*., 2008:2203; Key *et al*., 2003:415). However, it is not known whether this effect results in a reduction in blood levels of oestrogens or diverts the excretion of the hormone from the urine to the faeces (Key *et al*., 2003:415).

Phytochemical supplements and fortified foods may offer some specific advantages (Smolin & Grosvenor, 2008:400) but do not provide all the benefits provided by the diet high in natural sources (Smolin & Grosvenor, 2008:400; Rolfes *et al*., 2006:392). Many phytochemical supplements contain only a portion of many phytochemicals contained in foods (Smolin & Grosvenor, 2008:400) and therefore cannot replace benefits provided by many foods due to interactions among variety of phytochemicals and nutrients in a diet (Smolin & Grosvenor, 2008:400; Rolfes *et al*., 2006:392).

vi) Coffee and tea

a) Coffee intake

Coffee is a source of caffeine, and contains polyphenols such as phyto-oestrogens (flavonoids & lignans) (Kotsopoulos *et al*., 2007:915; Baker *et al*., 2006:166), phenols (chlorogenic acid), minerals, and other phytonutrients such as tocopherols. Coffee has a higher antioxidant activity than tea based on the number of cups consumed (Kotsopoulos *et al*., 2007:915).

Coffee contains caffeic acid thought to increase and reduce risk of breast cancer. The risk with caffeine is higher with coffee intake while the risk is reduced with the use of decaffeinated coffee while there is no risk with tea intake. Carcinogenic effects of caffeine may outweigh the possible protective effects of phytochemicals present in coffee and tea including flavonoids. Caffeine intake is associated with increased risk of breast atypical hyperplasia due to accumulation of cyclic adenosine monophosphate and activation of protein kinase which leads to over production of fibrous tissue and cystic fluid (Baker *et al*., 2005:18). Caffeic acid also inhibits DNA methylation in cultured cancer cells (Nkondjock, 2009:121).

Caffeine may protect against breast cancer in women with BRCA1 mutation but not for BRCA2 mutation carriers (Kotsopoulos *et al*., 2007:912). Reduction in risk may be in the amount of coffee consumed per day having six or more cups reducing risk compared with those who never drink coffee. Intakes of caffeine are associated with altered levels of SHBG (Kotsopoulos *et al*., 2007:915; Baker *et al*., 2006:166) and oestradiol, possibly reducing the risk of developing breast cancer (Baker *et al*., 2006:166), and is negatively associated with bioavailable testosterone. Furthermore, caffeine together with theobromine and xanthine, caffeine catabolised products, has a quenching effect on the production of hydroxyl radicals and on oxidative DNA breakage by hydroxyl radicals (Kotsopoulos *et al*., 2007:915).

Caffeine has anticarcinogenic properties that include antimetastatic effects, the ability to inhibit cell growth, and enhance apoptosis (Kotsopoulos *et al*., 2007:915). Coffee also contain two diterpenes, cafestol and kahweal, which have anticarcinogenic properties including the induction of phase II enzymes involved in carcinogen detoxification, specific inhibition of the activity of phase I enzyme responsible for carcinogen activation, and stimulation of intracellular antioxidant defence mechanisms. Coffee is also a source of chlorogenic acid that contributes to its antioxidant effect, which reduces glucose concentrations in rats and intake of quinides, degradation products of chlorogenic acid, and increases insulin sensitivity (Nkondjock, 2009:121).

b) Tea intake

Tea has mechanisms thought to prevent cancer because of its substances, including polyphenolic compounds known as catechins which may inhibit growth, induce cell cycle arrest, and apoptosis in different cancer cell lines (Ray, 2005:18). Green tea is rich in catechins and contains up to 40% catechins when dry. Green tea also contains flavanols, flavandiols, flavonoids, and phenolic acids (Mukhtar & Ahmad, 2000:1699). The polyphenols in green tea activate mitogen-activated protein kinases, a potential signaling pathway in the regulation of phase II enzyme gene expression mediated by an antioxidant-responsive element. Furthermore, the anticancer activity of epigallocatechin-3-gallate (EGCG) in green tea might be due to inhibition of the enzyme urokinase (u-plasminogen activator), one of the most frequently expressed enzymes in human cancers (Mukhtar & Ahmad, 2000:1700). Black tea seems to contain up to 10% catechins (Mukhtar & Ahmad, 2000:1699) and is a mixture of caffeine, phytoestrogens, and flavonoids which exhibit anticarcinogenic properties (Baker *et al*., 2006:166).

vii) Food preparation methods

High-temperature cooking, particularly on an open flame, increases the formation of potentially carcinogenic products such as heterocyclic amines and polycyclic aromatic hydrocarbons (Pala *et al*., 2009:456) and intake of these chemicals is associated with risk of breast cancer. The production of polycyclic hydrocarbons and heterocyclic amines, which are potentially genotoxic agents, are produced when cooking foods through methods such as broiling (grilling), frying, and braaing. Foods liable for production of high mutagenic compounds include especially meat and fish. There is no evidence linking boiling or steaming with cancer risk. However, boiling food in coconut milk was associated with a two-fold increase in breast cancer risk in Philippines women (Kotsopoulos *et al*., 2006:346). The association was thought to be with the use of coconut milk due to its energy and/or fat content since coconuts are high in saturated fats.

2.4 Hormones associated with breast cancer

Hormonal factors associated with breast cancer development in women include endogenous and exogenous oestrogens, progesterone, prolactin, and testosterone.

2.4.1 Endogenous and exogenous oestrogens

Risk factors for breast cancer including early age at menarche, late age at menopause, use of HRT, and high BMI affect breast carcinogenesis by increasing breast exposure to oestrogens and other sex hormones (Woolcott *et al*., 2008:1471). Oestrogen metabolites such as oestrone, oestrone sulfate, and oestradiol influence the risk for breast cancer (Neilson *et al*., 2009:16; Dötsch *et al*., 2001:82). High SHBG reduce risk by acting as the negative modulator of oestradiol thereby reducing oestrogen bioavailability (Neilson *et al*., 2009:16). SHGB also

mediate the effects of obesity in postmenopausal women since obesity is associated with lower levels of SHGB and an opposite association has been observed between concentrations of SHGB and breast cancer in postmenopausal women (Travis & Key, 2003:241).

Throughout fertile life, ovarian oestradiol remains the major endogenous oestrogen produced by granulosa cells of growing follicle and by corpus luteum (Dötsch *et al*., 2001:85). The main source of circulating oestrogens for postmenopausal women not using HRT is from androgen aromatisation in the peripheral tissues such as the bone, brain (Neilson *et al*., 2009:16; Dötsch *et al*., 2001:85), muscle, adipose tissue (Neilson *et al*., 2009:16), the cardiovascular system, and the liver (Rice *et al*., 2007:1039; Dötsch *et al*., 2001:85).

Oestrogens are necessary for normal development of the breast (Adebamowo *et al*., 2003:22; Clemons & Goss, 2001:276; Dötsch *et al*., 2001:82) but the risk of breast cancer could be determined by the cumulative exposure of breast tissue to oestrogen (Clemons & Goss, 2001:276). The mechanism responsible for oestrogen and breast cancer association focuses on the increased cell growth caused by oestrogen through oestrogen receptor, mediated signal transduction accompanied by increased probability for mutation during DNA synthesis (Yager, 2000:67). Oestrogen is almost inactive during the development of mammary gland unless insulin-like growth factors I (IGF-I) is available (Kleinberg *et al*., 2009:51). Oestrogen enhances the action of IGF-I through a stromal epithelial interaction, thereby inhibiting IGF-I and preventing mammary development and tumour formation without reduction of cancers of oestrogen (Kleinberg *et al*., 2009:62).

The majority (70%) of breast cancers express oestrogen receptors, hence why oestrogen is considered the promoter of tumour growth (Travis & Key, 2003:241; Yager, 2000:67). The incidence rate of breast cancer increases with age regardless of the loss of ovarian hormones in postmenopausal women (Rice *et al*., 2007:1039). Susceptibility of breast cancer is through germline polymorphisms in metabolic genes especially those encoding enzymes involved in the biosynthesis and metabolism of oestrogens. Such polymorphisms are important among postmenopausal women whose oestrogen production is not homeostatically controlled by pituitary gonadotrophins (Travis & Key, 2003:241).

Hypotheses associating oestrogen to tumourigenesis are based on the general concept that cell division plays a crucial role in cancer development and the reproductive factors that increase mitotic activity in the breast epithelium also increase cancer risk (Woolcott *et al*., 2008:1471). Reproductive hormones during tumourigenesis are related to epigenetic alteration and tumour promotion. Oestrogen metabolites can bind to DNA and trigger damage suggesting that oestrogen might be a complete carcinogen that can cause genetic alteration and affect tumour initiation. The possibility is supported by the finding that women with reduced amounts of enzymes responsible for removing reactive oestrogen metabolites are at a higher risk of developing breast cancer (Huang *et al*., 1999:4871).

Multiplication effects of oestrogens are through entering the target cells and by binding to the receptor protein which then binds to hormone response elements on the nuclear DNA, activating or suppressing specific sequences in the regulatory regions of genes responsible to oestrogen controlling cell growth and separation (Travis & Key, 2003:243). The resulting growth could increase the probability of mistakes made with DNA copying and setting mistakes as mutations. Because the effects of oestrogens are mediated by oestrogen receptors, the magnitude of their effects may be determined by the level of oestrogen receptors expressed in the breast (Woolcott *et al*., 2008:1471).

Exogenous oestrogens may reduce risk by altering oestrogen metabolism away from the production of genotoxic metabolites or through non-oestrogen pathways. Exogenous oestrogens include exposure to oestrogens through use of OC, HRT, and foods rich in phyto-oestrogens particularly soybeans. The hypotheses about the possible protective effects of food rich in phyto-oestrogens in the diet of several Asian countries gives an explanation why there is an observation of low breast cancer rates in most Asian countries than in the Western Europe and the US (Travis & Key, 2003:242).

2.4.2 Progesterone

Progesterone acts through its own receptor, and its levels may be important in breast carcinogenesis. Breast epithelial cell growth is related to progesterone levels (Woolcott *et al*., 2008:1471). The cell growth of the breast is greatest during the luteal phase of the menstrual cycle when levels of progesterone are highest, suggesting that progesterone may enhance breast cell growth (Lu *et al*., 2000:4117). Progesterone is expressed in the majority of breast carcinoma tissues and considered an important mediator of hormonal additive therapy in human breast tumours (Suzuki *et al*., 2001:2251).

2.4.3 Prolactin

Prolactin was first determined as a hormone that plays an important role in the breast cancer initiation and development in rodents, and later partly in humans. In the culture there is evidence of a direct stimulatory role of prolactin on mammary epithelial cells and the breast cancer cells. Prolactin may play active roles in tumour development by stimulating angiogenesis and activating pathways involved in cellular adhesion and motility (Levina *et al*., 2009:531). Serum prolactin concentrations in some breast cancer patients and women at risk of developing familial breast cancer may be increased (Mujagic *et al*., 2009:236).

Prolactin is generated by tumours and by a variety of normal tissues, placenta being the richest source of the extrapituitary prolactin and responsible for high levels in human amniotic fluid. The immune system, uterus, brain, dermal fibroblasts (Mujagic *et al*., 2009:239), human breast tissues and cells also produce prolactin. Prolactin levels decrease with each additional pregnancy

(Mujagic *et al*., 2009:239; Travis & Key, 2003:244) and concentrations are higher in nulliporous than porous women and among women using certain types of OC (Travis & Key, 2003:244).

2.4.4 Testosterone

Normal ovary produces larger amounts of testosterone than oestradiol (Dimitrakakis *et al*., 2004:531). Adrenal derived or ovarian derived androstenedione increases testosterone levels in the ovaries, adipose, and breast before and after menopause. Androgens are the most abundant sex steroid hormones in postmenopausal women with testosterone as one of the most powerful natural forms. Testosterone binds to SHBG making it biologically inactive. The aromatase enzyme converts testosterone to oestradiol, and androstenedione to oestrone within the adipose tissue of postmenopausal women (Neilson *et al*., 2009:17). The total and bioavailable testosterone levels may be reduced in women taking OC (Dimitrakakis *et al*., 2004:532). Testosterone might have a role in the etiology of breast cancer development (Travis & Key, 2003:244) through binding to the intracellular androgen receptor which is abundant in normal mammary epithelium (Dimitrakakis *et al*., 2004:535) or by converting testosterone to oestrogen in the breast (Travis & Key, 2003:244).

2.5 Dietary recommendations for the prevention of cancer

The World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR:2007) designed the following cancer prevention recommendations in order to reduce the risk from some of the common types of cancer:

- Be as lean as possible, within the normal range (21-23kg/m^2) of body weight;
- be physically active, equivalent to brisk walking, for at least 30 minutes everyday. Limit sedentary habits such as watching television;
- limit consumption of energy-dense foods (foods processed in high sugar, low in fibre & high in fat). Consume “fast foods” sparingly, if at all;
- eat more of variety of vegetables, fruits, whole grains, and legumes (beans). Eat at least five portions or servings of non-starchy vegetable and fruits every day. Eat unprocessed cereals (grains) and/or pulses (legumes) with every meal. Limit refined starchy foods;
- limit the intake of red meat (beef, pork, lamb) and avoid processed meats. If red meat is consumed eat less than 500g a week and very little of processed meats;
- limit intake of alcoholic drinks to one a day for women if consumed at all;
- limit consumption of salty foods and foods processed with salt (sodium). Avoid salt-preserved, salted, or salty foods. Preserve foods without using salt;

- aim to meet nutritional needs through diet alone. Do not use supplements to protect against cancer because dietary supplements are not recommended for cancer prevention;
- it is best for mothers to breastfeed exclusively for six months and add other liquids and foods thereafter. It is also best for children to be breastfeed; and
- after treatment, cancer survivors should follow the recommendations for diet, healthy weight, and physical activity for cancer prevention.

These guidelines should be followed in the context of a balanced diet based on healthy eating principles (Thomas & Bishop, 2008:772).

2.6 Evaluation of dietary intake

There are various standards used to evaluate dietary intake, some of which describe the amounts of individual nutrients needed while some suggest patterns of food intake that promote health and prevent disease. The nature of each set of guidelines depends upon the population it targets, its goals, and how it will be used. There are various guidelines available, including nutrient based and food based guidelines (Smolin & Grosvenor, 2007:35). The nutrient based guidelines include e.g. the Dietary Reference Intakes (DRIs) and the Recommended Nutrient Intakes (RNIs), while the food based guidelines include e.g. food guide pyramids, food based dietary guidelines for different populations, and others. For the purpose of this study the DRIs, the United States Food Guide Pyramid (USFGP) and Dietary Guidelines for Americans (DGA) will be discussed. The use of exchange lists to calculate the macronutrient content of dietary intake will also be discussed.

2.6.1. Dietary Reference Intakes

The first dietary standards in the US were published in 1943 by the Food and Nutrition Board of the National Research Council of the National Academy of Sciences, and were called the Recommended Dietary Allowances (RDA). The goal for the development was to promote optimal health and lower the risk of nutrient deficiencies (Dodd & Bayerl, 2012:235). The recommendations were made for the intake of energy (kcalories) and nutrients at risk for deficiency of protein, vitamins, and minerals (Smolin & Grosvenor, 2007:35). The Canadian Council on Nutrition also established a Canadian Dietary standard called the Recommended Nutrient Intake (RNI) in 1939 and included recommendations for calories, protein, fat, calcium, iron, iodine, ascorbic acid, and vitamin D (Lee & Nieman, 2010:15).

After realising the need for more inclusive set of nutritional and dietary standards that adequately addressed more current nutritional concerns, the Food and Nutrition Board together with the Canadian Institute of Nutrition and Health of Canadian developed a new and expanded set of nutrient intakes known as Dietary Reference Intakes (DRIs) (Lee & Nieman, 2010:17). The

DRIs are a set of energy and nutrient intake recommendations promoting health as well as preventing nutrient deficiencies. The DRIs were designed to be used for planning and assessing the diets of the healthy people and include the values for energy, protein, micronutrients, and macronutrients (carbohydrates, proteins, & fats), as well as phytochemicals for different life-stage groups (Smolin & Grosvenor, 2007:35). The DRIs include the Estimated Average Requirement (EAR), Recommended Dietary Allowances (RDA), Adequate Intakes (AI) and Tolerable Upper Intake Levels (UL) (Murray *et al*., 2012:275):

- The Estimated Average Requirement (EAR) is the amount of a nutrient whereby approximately one half of individuals would meet their needs and one half would not. The EAR value is used to assess the nutrient adequacy of populations but not individuals;

- the Recommended Dietary Allowance (RDA) is defined as the amount of nutrient needed to meet the requirements of almost all (97% - 98%) of healthy population of individuals. The RDA is used to assess nutrient intake for individuals but not the groups;

- the Adequate Intake (AI) refers to a nutrient intake recommendation for a group of healthy people when there is insufficient scientific evidence to calculate RDA or an EAR; and

- the Tolerable Upper Intake Level (UL) is defined as the highest level of daily nutrient unlikely to have any adverse health effects on almost individuals in the general population. The UL was established in order to reduce the risk of adverse or toxic effects from intake of nutrients in concentrated forms- either alone or combined with others or from enrichment and for fortification.

The DRIs make two types of recommendations concerning energy intake, the Estimated Energy Requirement (EER) and the acceptable macronutrient distribution ranges (AMDR).

- The EER provides the average dietary energy intake (in kcalories per day) that will maintain energy balance in a person having a healthy body weight and a level of physical activity (Whitney & Rolfes, 2010:19). The variables used are age, gender, weight, height, and PAL and change in any variable changes the EER (Smolin & Grosvenor, 2007:38).

- The AMDRs are recommendations expressed as ranges of carbohydrates, proteins, and fats because healthy diets can contain many different combinations (Smolin & Grosvenor, 2007:38) which contribute to the total energy intake (Whitney & Rolfes, 2010:19). AMRDs provide flexibility in food choices based on individual preference while still providing a diet that minimises disease risk and the values have been set for specific amino acids and fatty acids. The AMRDs include 45% to 65% coming from

carbohydrates, 20% to 35% from fats, and 10% to 35% from proteins (Smolin & Grosvenor, 2007:38).

2.6.2 The USA Food Guide Pyramid

Food grouping was initiated in 1916 by the US Department of Agriculture (USDA). Since then the food grouping systems have changed in shape (wheels, boxes, & pyramids) and numbers of groupings (four, five, & seven groups) but the goal, to present an easy guide for healthful eating, remains the same. The food guidance focuses on promoting health and preventing disease, and the guides are adapted whenever the DGA guidance changes (Dodd & Bayerl, 2012:234).

The pyramid, based on the food grouping recommendations was developed, tested, and communicated in 1988 by the USDA together with a private market research firm (Smolin & Grosvenor, 2008:43). The food guide pyramid is a graphic representation of the daily food guide (Whitney & Rolfes, 2005:47) and has proved to be the most effective visual approach for communicating the messages of variety, proportionality, and moderation and was released in 1992 (Lee & Nieman, 2010:52). The pyramid shape helped to emphasise the relative contribution of each group. The larger base of the pyramid was made up of plant origin foods-grains, fruits, and vegetables while the smaller upper sections contained foods from animals-milk and dairy products; meats, fish, and eggs (Smolin & Grosvenor, 2007:43). At the apex were fats, oils, and sugars to indicate that they should be consumed sparingly as illustrated in Figure 3.1 (Smolin & Grosvenor, 2008:43). The recommended number of servings from each group was expressed as a range (Lee & Nieman, 2010:53).

Portion sizes included the following (Whitney & Rolfes, 2005:44):

- **Breads, cereals, and other grain products:** 1 slice o bread; ½ cup cooked cereal, rice, pasta; ½ cup ready-to-eat cereal; ½ bun, English muffin; 1 small roll, biscuits or muffin; 3-4 small or 2 large crackers;
- **Vegetables:** ½ cup cooked or raw vegetables; 1 cup leafy raw vegetables; ½ cup cooked legumes; ¾ cup vegetable juice;
- **Fruits:** 1 medium apple, banana or orange; ½ grapefruit, 1 melon wedge; ¾ cup juice; ½ cup berries; ½ cup diced, cooked, or canned fruit; $^{1}/_{4}$ cup dried fruit;
- **Meat, poultry, fish, and alternates:** 30g cooked lean meat, poultry, or fish; 1 egg; ½ cup cooked legumes, ½ cup nuts or seeds; 2 tablespoons peanut butter;
- **Milk, cheese, and yoghurt:** 1 cup milk or yoghurt; 30g cheese; and

- **Fats and sweets:** 2 teaspoons sugar; 2 hardboiled sweets; 10ml mayonnaise; 5ml oil; 10ml margarine (medium fat).

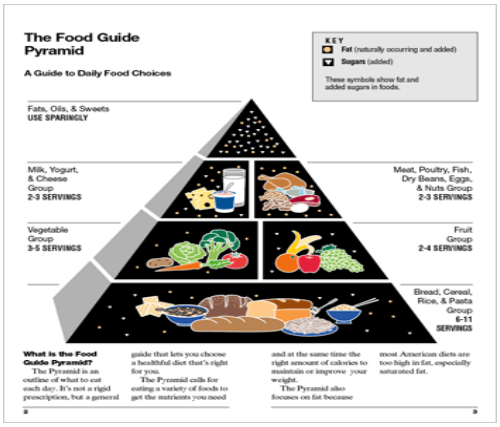

Figure 3.1. The UDSA Food Guide Pyramid (1992)

2.6.3 The Dietary Guidelines for Americans

The DGA were first released in 1980 by the US Department of Agriculture and the US Department of Health and Human Services. The guidelines reflected emerging scientific evidence about diet and health and expanded the traditional focus on nutrient adequacy to also address the impact of diet on chronic disease. Although the DGA were continuously updated, the goal for the recommendations regarding the components of a health promoting diet was maintained. The crucial goal of the guidelines is to improve the health of the current nation and future generations by facilitating and promoting healthy eating and physical activity choices in order for the behaviours to become norms among all individuals.

The newest DGAs are the 2010s which are intended for healthy Americans ranging from two years and older, including those who are at increased risk of chronic diseases. The DGA 2010 also provides resources that can be used in developing policies, programs, and educational materials. The DGA 2010 has additional appendices containing nutritional goals for age-gender groups based on DRIs and the dietary nutrient and food intake guidelines based on estimated energy needs per day by age, gender, and physical activity level (Dietary Guidelines for Americans, 2010).

The Dietary Approach to Stop Hypertension (DASH) eating plan forms part of the DGA, 2010. Foods in the DASH diet are grouped into: grains; vegetables; fruits; fat-free milk or low-fat milk and milk products; lean meats, poultry, and fish; nuts, seeds, and legumes; fats and oils; sweets and added sugars. The serving sizes as well as patterns with a sodium limits per day are indicated. The DASH diet also includes the specific number of servings per week for fat and

sugar at different energy levels that are recommended for health, which are not quantified in the USFGP, illustration in Appendix A_2. (Dietary Guidelines for Americans, 2010:83).

2.6.4 The Exchange lists

The Exchange list is a food group system that is used in planning diets to meet specific energy and macronutrient goals. The Exchange list was first developed in 1950 by the American Dietetic Association and the American Diabetes Association (Smolin & Grosvenor, 2008:59) as a meal-planning tool for individuals with diabetes. Since then, the use of the Exchange list has been expanded to planning weight-loss diets and diets in general (Whitney & Rolfes, 2010:47; Smolin & Grosvenor, 2008:59). The latest revision of the Exchange lists divided the foods into three main groups based on their macronutrient content: the carbohydrate group, the meat and meat-substitute group, and the fat group (Smolin & Grosvenor, 2008:59; Cataldo *et al*., 2003:607; Wheeler *et al*., 1996). The carbohydrate group included foods that are sources of carbohydrates: starches, fruits, milk, and vegetables. It also defined a list of other high-carbohydrate foods and indicated how to fit these foods into a diet based on exchanges (Smolin & Grosvenor, 2008:59). The meat and meat-substitute group included an exchange of list with four subgroups: very lean, lean, medium fat, and high-fat meat. The fat group included an exchange list with three subgroups of monounsaturated, polyunsaturated, and saturated fats (Smolin & Grosvenor, 2008:59; Cataldo *et al*., 2003:609).

The exchange lists are designed so that each serving within a list contained approximately the same amount of energy, carbohydrate, protein, and fat (Smolin & Grosvenor, 2008:59; Cataldo *et al*., 2003:610). Each serving in the fruit exchange list provided about 60 kcalories, 15 grams of carbohydrate, no protein, and no fat. Choices of starch list provided about 80 kcalories, 15 grams of carbohydrate, 3 grams of protein, and 0-1 gram of fat (Wheeler *et al*., 1996). The food groupings of the Exchange lists are designed to meet energy and macronutrient criteria. The exchange system can be used to design diets to meet individual tastes and preferences at specific energy and macronutrient levels (Smolin & Grosvenor, 2008:60).

2.7 Summary

Several risk factors for breast cancer have been known for years. Increasing age is one of the strongest risk factors. Mutations in BRCA1 and BRCA2 account for the majority of families with hereditary susceptibility to breast cancer. Having a family history of breast cancer increases a woman's risk, an earlier age at diagnosis and the number of relatives affected increase the risk even more. A personal history of benign breast disease, particularly, atypia is associated with substantial increase in breast cancer. Early age at menarche and late age at menopause increase breast cancer risk.

There is no evidence suggesting association between marital status and breast cancer. There is a doubling of risk of breast cancer in women living in urban areas since urban areas are characterised by western behaviours and lifestyles associated with breast cancer. Since education is a major component of socioeconomic status, it may affect breast cancer risk through influencing reproductive, lifestyle, and behavioural factors. Lifestyle and environmental factors have an important impact on breast cancer risk. Physical activity protects against postmenopausal breast cancer while sedentary behaviours increase risk. A controversy exists around the use of oral contraceptives and the risk for breast cancer. Nulliparity and late age at first birth increase breast cancer risk. Breastfeeding, particularly for long periods is associated with lower risk for breast cancer. Both height and postmenopausal BMI are positively associated with breast cancer risk while premenopausal obesity is negatively associated, at least in Western populations.

Few nutritional effects have been firmly established as important risk factors for breast cancer. The role of diet in the etiology of breast cancer remains controversial regardless of wide studies conducted, which most were in the Western white populations. The conclusions of most studies investigating risk associations in relation to nutrients suggested that any effect of diet on breast cancer may be weak. Most of the suggested associations between diet and cancer in humans were based on data from epidemiological studies that comprised of cross-sectional, case-control, prospective (cohort), and intervention trial studies. Animal studies were also used to help explain the mechanisms of carcinogenesis. High fat of the total energy intake is associated with increased risk especially the PUFA. Lignin in fibre has been hypothesized to affect breast cancer risk.

Alcohol intake is associated with an increased risk due to its ability to increase oestradiol levels. Antioxidants defend the body against cancer due to the chemical substances they contain. Phytochemicals have health promoting properties including cancer protection. Phyto-oestrogens have antioxidant activity and therefore slow the growth of breast cancer by interfering with the action of human oestrogen. There is no evidence associating cooking methods with cancer risk, however, there is evidence linking boiling food in coconut milk to breast cancer probably because coconuts are high in saturated fats. However, grilling, frying, or braaing foods, especially meats, increase risk because they produce polycyclic hydrocarbons and heterocyclic amines associated with breast cancer risk.

Most of the established risk factors for breast cancer in humans are thought to influence risk through hormone related pathways. These hormones include oestrogens, progesterone, prolactin, and testosterone. The prudent advice is to maintain normal BMI ($<25 kg/m^2$), minimise alcohol consumption, eat variety of fruit and vegetables, limit intake of foods high in sugar and, eat foods high in fibre, meet nutritional needs through diet, take regular physical exercise, extend

breast feeding period to at least one and half years, and make changes to lifestyle and reproductive behaviours.

CHAPTER 3

METHODOLOGY

3.1 Introduction

The aim of the study was to determine the prevalence of the known risk factors in women diagnosed with breast cancer at the Queen II hospital in Maseru. Valid methods were used to obtain relevant and reliable data to meet the aims of the study. A description of the study design, study population, measurement, pilot study, ethical approval and study procedures, statistical and nutritional analysis, and problems encountered during the study is given.

3.2 Study design

A descriptive study was conducted in order to determine the prevalence of the known risk factors as reported in the literature in women diagnosed with breast cancer at the Queen II hospital in Maseru.

3.3 Study population

3.3.1 Sample frame

The target population included all adult Lesotho women diagnosed with breast cancer who were treated at the Queen II hospital (and its cancer clinic), and who were referred to the Universitas hospital in Bloemfontein at the time of the study. These women, who have been diagnosed with breast cancer, included both newly diagnosed women and those on the treatment of breast cancer. All women who were younger than 19 years were excluded from the study because according to the available data from the Queen II hospital there were no patients seen who were younger than 19 years.

Exclusion criteria:

- All women not diagnosed with the disease and those younger than 19 years;
- all women not seen at the Queen II hospital and those that do not get treatment at the Universitas hospital; and
- all women who did not seek modern medicine methods because they sought help from indigenous healers.

3.3.2 Sample selection

A purposive sampling was conducted in order to determine the prevalence of the known risk factors as reported in the literature in women diagnosed with breast cancer at the Queen II hospital in Maseru. Purposive sampling allowed for selection of key or typical individuals from

the spectrum in which the researcher was interested (Jourbert & Katzenellenbogen, 2010:101; Leedy & Ormrod, 2001:219). The particular sample of participants was selected because they were already diagnosed with breast cancer.

Permission to conduct the study at the Queen II hospital and its cancer clinic (Appendix C_1) was obtained from The Director General of the Ministry of Health and Social Welfare in Lesotho. Permission was also obtained from the CEO of the Universitas hospital, Bloemfontein, where patients are referred to from Queen II hospital for treatment. All women (≥19 years) who were admitted at the Queen II hospital, or were attending their check-up at the cancer clinic at Queen II, as well as those attending treatment at the Universitas hospital during the time of the study, and who gave their informed consent, were included in the study.

The nurses who worked with the patients and knew them were asked to speak to the patients on the researcher's behalf about the study. The researcher supplied the nurses with the information documents (Appendix D_{2A}) to give to the patients or to brief the patients about the study orally. When patients gave their consent to participate in the study they were referred to the researcher in a private room where consent forms were signed and the anthropometric measurements were taken and interviews were conducted. The interviews were conducted at the Queen II hospital for in-patients, at the Queen II cancer clinic for out-patients coming for their treatment, and at the patients' homes for those who invited the researcher to do so. Patients who went for their treatment at the Universitas hospital had to report back to the Queen II hospital, where the researcher met them.

3.3.3 Sample size

Due to a limited number of patients (±25) diagnosed per year as reported by the cytology laboratory at Queen II, and the poor filing system at the hospital which does not enable easy access to the patients, the final sample included only 52 patients, willing to participate. A 53th patient who was initially included unfortunately died a day before the scheduled interview. Due to the small sample size the results of the study cannot be generalised to all Lesotho women but they could be used to indicate the tendencies for this research group.

Other studies conducted on the risk factors for breast cancer such as Pushkala and Gupta (2009) and Saweer *et al*. (2003), used somewhat larger sample sizes. Pushkala and Gupta conducted a study about the prevalence of breast cancer in menopausal blind women in Chennai in India on a sample size of 204 women. Saweer *et al*. conducted a similar study on the prevalence of risk factors among women diagnosed with breast cancer using 93 breast cancer patients obtained from the Oncology Clinic Salmaniya Medical Center. Daniels *et al*. (2004), however, also used a small sample of only 37 women in Utah, United States to conduct a study on associations between breast cancer risk factors and religious practices.

3.4 Measurement

Measurements will include the variables and work definitions, as well as techniques used in this study.

3.4.1 Variables and work definitions

The variables that were measured included non-modifiable and modifiable risk factors for breast cancer.

3.4.1.1 Non-modifiable risk factors

Non-modifiable risk factors are risk factors that cannot be changed and for this study included age at diagnosis, history of breast cancer, and menstrual history. The categories of non-modifiable risk factors for breast cancer development are shown in Table 3.1.

i) **Age** referred to the age at which a woman was diagnosed with breast cancer.

ii) **History of breast cancer**

History of breast cancer referred to family of breast cancer, thus whether a woman had a relative with the disease, either mother, father, sister, brother or aunt (Wardlaw, 1999:29; Lundy, 1994:271; Hayes & Schnitt, 1993:2.2).

iii) **Menstrual history**

Menstrual history referred to age at menarche and age at menopause.

- **Age at first menarche** meant the age at which an individual started menstruating. Menstruation is the "shedding of the outer two-thirds of the endometrium with accompanying bleeding as a result of a lowering of oestrogen secretion by ovaries at the end of the monthly cycle" (Fox, 2006:733).

- **Age at menopause** meant the age at which a woman went through menopause. Menopause referred to the cessation of menstruation (Fox, 2006:733). Women were classified as menopausal if they had not menstruated during the past year before the date of data collection (Borrell *et al*., 2006:213; Ebrahim *et al*., 2002:10) and the reason for their menstrual period stopping was "natural menopause" (Borrell *et al*., 2006:214).

3.4.1.2 Modifiable risk factors

Modifiable risk factors are the risk factors that can be changed because they represent lifestyle choices. Modifiable risk factors for this study included usual dietary intakes, socio-demographic profiles, lifestyle behaviours, reproductive factors, and anthropometric status. The categories of modifiable risk factors in terms of risk for breast cancer development are indicated in Table 3.1.

Table 3.1 Categories of non-modifiable and modifiable risk factors for breast cancer

Risk factors	Categories	Level of risk for breast cancer	Reference
Non-modifiable risk factors			
Age at diagnosis	*****35-45 years	High	
	≥46 years	Medium	
	≤34 years	Low	(Adebamowo *et al*., 2003:19 & Rambau *et al*., 2011:214)
	†>50 years	High	(Rambau *et al*.,2011:214)
History of breast cancer			
Family history	First degree relative	High	(Chen *et al*., 199:858)
	Second degree relative	Medium	
	No relative	Low	
Menstrual history			
Age at menarche	≤12 years	High	(Key *et al*., 2003:413)
	>12 years	Low	
Age at menopause	≥ 55 years	High	(Key *et al*., 2003:413)
	≤54 years	Low	
Modifiable risk factors			
Socio-demographics profiles			
Marital status	Never married	High	(Abbasis *et al*., 2009:9)
	Ever married	Medium	
Place of residence	Urban	High	(Fregene & Newman, 2005:1543)
	Rural	Medium	
Education level	High level (tertiary)	High	(Webster *et al*., 2008:1127)
	Low level (primary & high school)	Low	
Income	Middle class	High	(Shah & Shrestha, 2004:3)
	Low (low class)	Low	
Lifestyle behaviours			
Alcohol	Heavy drinker (≥3 drinks/day)	High	(Grant, 2008:966)
	Moderate drinker (1-2 drinks/day)	Medium	
	Light drinker (<1 drink/day)	Low	
	Non-drinker	Low	
Physical activity level	Sedentary (1-1.39)	High	(Grant, 2008:963)
	Low activity (1.4-1.59)	Medium	
	≥Active (1.6-2.5)	Low	

* Level of risk for African women
† Level of risk for White women

Table 3.1- continue: Categories of non-modifiable and modifiable risk factors for breast cancer

Risk factors	Categories	Level of risk for breast cancer	Reference
Reproductive factors			
Oral contraceptive use	Long-term use (>1 year) Use at early age (<18 years) Recent use (≥ 6 months) Non-use ≥30 years	High High Medium Low	(Gammon *et al*., 1999:414)
Age at first pregnancy	30 years <30 years	High Increased risk	(Travis & Key, 2003:240)
Parity	Not having children Having children	High Low	(Travis & Key, 2003:240)
Breast feeding	<6 months 6-11 months ≥12 months	High Medium Low	(Ursin *et al*., 2005:356)
Anthropometric status			
Height	>169cm 153-169cm <153cm	High Medium Low	(Chang *et al*.,2006:336)
BMI	≥26 kg/m^2 (obese) 23-26 kg/m^2 (overweight) 18.5-23kg/m^2(healthy/desirable)	High Increased risk Low	(Chen *et al*., 199:861)
Waist circumference	≥88cm 80-87.9cm <80cm	High Medium Low	(Alberti *et al*., 2009:1642)
Waist-hip ratio	≥0.85 0.80-0.84 <0.80	High Medium Low	(Alberti *et al*., 2009:1642)

i) Socio-demographic profiles

Socio-demographic profiles referred to marital status, place of residence, education level, and income (Table 3.1).

a) **Marital status** referred to whether the participant was ever married or not.

b) **Place of residence** meant urban or rural areas, where a participant had been staying for the past year before the date of data collection.

- **Urban area**: referred to villages found around towns and the city within the radius of 30 kilometers (km); and
- **Rural area**: referred to villages found outside the radius of 30 km away from the towns or city.

c) **Education level** meant the educational qualification a woman had.

d) **Income** was defined as low class or middle class. Livelihoods strategies in Lesotho were defined differently depending on the location one was based. However, low class and middle class categories were used:

- **Low class**: included the group of people in society who had less money or education, and the people in society who traditionally did physical work and earned low salaries. These included people whore were self-employed in order to survive such as those who were selling traditional beer, those producing agricultural products from the fields, and those working in the factories; and
- **Middle class**: referred to the group of people in society who were educated and worked in professional jobs. Included were teachers, nurses, technicians, and economists.

ii) Lifestyle behaviours

Lifestyle behaviours referred to alcohol intake and physical activity level.

(a) **Alcohol intake** referred to the intake of any beverage that contained alcohol. Alcohol use was categorised according to Mukamal *et al*. (2005:11):

- **Light drinker**: was the participant who consumed less than 1 drink (0.1-9.9grams) per day of alcoholic drinks, or the patient who consumed alcohol once a week.
- **Moderate drinker**: was the participant who consumed 1 to 2 drinks (10.0-29.9 grams) per day, or the participant who consumed alcohol two to three times a week.
- **Heavy drinker**: was the participant who consumed 3 or more drinks (≥30 grams) drinks daily, or who consumed alcohol more than four times a week.

(b) **Physical activity level** (PAL) referred to the ratio of total energy expenditure (TEE) to basal energy expenditure (BEE). Physical activity level was categorised as sedentary, low activity, and active (Frary & Johnson, 2008:22).

- **Sedentary lifestyle:** referred to the lifestyle with the physical activity values of 1-1.39 per day.

- **Low activity lifestyle:** referred to the lifestyle with the physical activity values of 1.4-1.59 per day.
- **Active lifestyle:** referred to the lifestyle with the physical activity values of ≥1.6 per day.

iii) Reproductive factors

Reproductive factors referred to oral contraceptive use, parity, age at first pregnancy, and breast feeding.

a) **Oral contraceptives use** referred to recent user, long-term user, and user at an early age.

- **Recent user**: was the participant who had been using oral contraceptives for six months or more.
- **Long-term user**: was the participant who had been using oral contraceptives for more than a year.
- **User at an early age**: was the participant who had been using oral contraceptives at the age younger than 18 years old.

b) **Parity** meant whether the participant had children or not.

c) **Age at first pregnancy** was the age at which a woman had her first pregnancy.

d) **Breast feeding** referred to whether a woman had breast fed her children or not. Breast feeding is the "production and secretion of breast milk for the purpose of nourishing an infant" (Whitney *et al*., 2002:485).

iv) Anthropometric status

Anthropometric status for the purpose of this study referred to height and weight in order to calculate body mass index, waist and hip circumferences in order to calculate waist-hip-ratio. The categories for anthropometric criteria are shown in Table 3.1.

a) **Height** is the overall of the body from the crown to the bottom of the feet, usually taken in the standing position.

b) **Weight** is the sum of the protein, fat, water, and bone mass in the body (Gibson, 2005:257).

c) **Body mass index (**BMI**)** is the current weight (kg) divided by height (m^2) (Gee *et al.*, 2008:532; Wardlaw, 1999:274).

d) **Waist circumference** (WC) is the "distance midway between the inferior margin of the ribs and the superior border of the iliac crest (Alberti *et al.,* 2006:478). The International

Diabetes Federation (IDF) definition for waist circumference of 80 cm and more was used.

e) **Hip circumference** is the widest point over the buttocks.

f) **Waist-hip ratio** (WHR) is the waist circumference divided by hip circumference (Gibson, 2005:279).

v) **Usual dietary intake**

a) **Usual dietary intake** referred to the types of food and number of portions from each food group usually eaten on a daily basis, the usual daily energy and macronutrients intakes, as well as variety of food and food frequency. The prudent guidelines and range perspectives for healthy people and the prevention of disease including breast cancer were used for comparison.

The usual food intakes were evaluated according to the recommendations of the Food Guide Pyramid (USDA, 1992) based on food groups (Smolin & Grosvenor, 2008:43) and the Food Exchange list (Smolin & Grosvenor, 2008:59). A usual food intake less than the recommended number of portions was considered inadequate, an intake within the recommendation was considered adequate, and an intake above the recommendation was considered high as indicated in Table 3.2. The USDA food guide pyramid was used because it is the one that had number of portions to be eaten daily.

Table 3.2 Serving recommendations according to the US Food Guide Pyramid (USDA, 1992):

Food groups	Serving portions per day
Bread and cereals	6-11
Fruit	2-4
Vegetables	3-5
Meat and meat alternatives	2-3
Milk and milk products	2-3
Fats and sweets	Use sparingly

Dietary intakes would also be evaluated according to the food groups as recommended by the DGA, 2010 and the DASH recommendations at different levels of energy intakes. The USFGP (1992) and the DGA, 2010 recommendations were used because they promote general health while the DASH pattern was used to compare fat and sugar intakes as they are not quantified in daily serving sizes in either the USFGP (1992) and the DGA, 2010. A usual food intake less than the recommended number of portions would be considered inadequate, an intake within the recommendation would be considered adequate, and an intake above the recommendation would be considered high as indicated in Appendices A_1 and A_2.

b) **Energy and macronutrient intake** referred to the total kiloJoule (kJ) intake in grams of carbohydrates, proteins, fats, and fibre according to the food exchange system. Macronutrients in grams were expressed as a percentage of total energy intake (Table 3.3). A usual macronutrient intake expressed as percentage of total energy (%TE) less than the recommended percentages was considered inadequate, an intake within the recommended percentages was considered adequate, and an intake above the recommended percentages was considered high.

Table 3.3 Macronutrient and fibre intake expressed as percentages of total energy intake (Whitney & Rolfes, 2010:192):

Nutrients	Low	Within the ranges	High
Protein	<10%	10-35%	>35%
Fat	<20%	20-35%	>35%
Carbohydrate	<45%	45-65%	>65%

The energy and macronutrients intakes were compared to the DRIs. The DRIs refer to a set of energy and nutrient intake recommendations which were designed to promote health and prevent nutrient deficiencies and were used in this study to assess adequacy of the patients' diets (Smolin & Grosvenor, 2008:35). The DRIs used in the current study included the EAR, RDA, and EER:

- The EER values for women 19 to 50 years of age were used;
- the EAR values for macronutrients for values for women 19 to 50 years were used where available; and
- the RDA values for macronutrients for values for women 19 to 50 years were used when EARs were not available.

c) **Variety of food** consumed referred to foods mostly consumed by patients on a typical day according to the 24-hour recall of usual intake.

d) **Frequency of food intake** referred to the frequency of consumption of food items according to the FFQ on the basis of per day, per week, per month, and per season.

3.4.2 Techniques

For this study anthropometric techniques and questionnaires were used. Valid techniques were important. Data was gathered under well controlled conditions in order to ensure data reliability.

Validity referred to the extent to which a measure actually measured what it was meant to measure (Katzenellenbogen *et at.,* 1997:90).

Reliability referred to the degree of similarity of the information obtained when the measurement was repeated on the same subject or the same group (Katzenellenbogen *et al.,* 1997:90).

3.4.2.1 Anthropometric techniques

Anthropometric assessment provided a fast, inexpensive method of assessing the body composition and also indicated if an individual was at risk of developing a complication (Grant & DeHoog 1991:9). The anthropometric measurements included: weight and height to calculate BMI, waist and hip circumferences to calculate waist-hip ratio.

To ensure validity, the anthropometric measurements taken were all the risk factors reported in the literature that could imply a risk in developing breast cancer.

In order to ensure reliability the scales were calibrated before use and after the 10^{th} person measured, one trained researcher took all the measurements in order to ensure consistency in measurements. The anthropometry measurements were taken according to the standard procedures recommended by Alberti (2006) for WC and Gibson (2005) for the weight, height, and hip circumference. The values were noted on a data sheet adapted from Katzenellenbogen *et al.* (1997:87) (Appendix B_1, section d).

i) Weight

Weight was determined with an electronic scale. The scale was put on hard, flat surface and checked and calibrated for zero-balance before each measurement. Measurements were taken after emptying the bladder and were done before a meal was taken. The subject stood on the centre of the platform looking straight ahead, standing unassisted, relaxed but still with the light clothing on. The body weight was recorded to the nearest 0.1kg.

ii) Height

Height was measured standing using a free-standing stadiometer. Subjects wore light clothing so that posture could be seen clearly. Shoes and socks were not worn. Before use the device was adjusted. The subject stood straight with the head in the Frankfurt plane, feet together, knees straight, and heels, buttocks and shoulder blades in contact with the vertical surface of the stadiometer or the wall. Arms hang loosely at the sides with palms facing the thighs. Subjects were asked to take a deep breath and stand tall to aid the straightening of the spine. Shoulders were relaxed. The movable headboard was gently lowered until it reached the crown on the head

and height was taken at maximum inspiration, with the examiner's eyes level with the headboard to avoid parallax errors. Height was recorded to the nearest 0.1 cm.

iii) BMI

After obtaining weight and height measurements BMI was calculated by dividing weight (kg) by height (m^2) (Gibson, 2005:259).

iv) Waist circumference

An unstretchable tape with an ungraduated extremity of 3 to 5 cm in order to properly grab the tape was used. The subject stood with her feet shoulder-width apart. The arms hang on each side of the body but out at an angle of about 30^0, or alternatively participants crossed their arms on their shoulders in a relaxed manner. A slight tension was applied to the tape (until the red mark appeared) at the moment of the reading. Waist circumference was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. The measurement was taken at the end of a normal expiration, while ensuring that the participant did not contract the abdominal muscles. The measurement was made twice and a third time if the difference between the first two measurements were greater than 5% (±1 cm). The two closest measurements were averaged. The participant untied her belt and her pants or skirt in order to remove any pressure in the abdomen. It was recommended to completely remove the blouse or shirt. The top garment was pulled and tucked under the bra (Alberti *et al*., 1998:542). The reading was taken to the nearest millimeter.

a) Hip circumference

The subject was measured standing erect with arms at the side and feet together. The measurement was taken at the point yielding the maximum circumference over the buttocks with the tape held in a horizontal plane, touching the skin but not indenting the soft tissue. The measurement was recorded to the nearest millimetre.

b) Waist-hip ratio

After obtaining waist and hip circumferences a waist-hip ratio was calculated by dividing waist circumference by hip circumference (Gibson, 2005:279).

3.4.2.2 Questionnaires

Questionnaires included usual dietary intake, socio-demographic information, lifestyle behaviours, menstrual history, reproductive patterns, history of breast cancer, and anthropometric measurements. Questions were formulated to include open and closed questions. Questionnaires were completed by one trained researcher in privacy with each patient by means of a structured interview and were done in Sesotho, the first language of the participants.

i) Usual dietary intake

The simultaneous use of food frequency and the 24-hour recall questionnaires improve the accuracy of intake estimates (Hammond, 2008:397). In order to determine the usual dietary intake an adapted 24-hour recall of usual intake was combined with the food frequency questionnaire (FFQ). The FFQ was used as a cross-control with an adapted 24-hour recall to determine the usual intake.

a) Adapted 24-hour recall of usual intake:

Dietary intake was determined by an adapted 24-hour recall of usual intake (Appendix B_2). The dietary intake questionnaire for this study was adapted from the questionnaire developed by the Department of Nutrition and Dietetics and validated for Medicine, Nursing, and Allied Health Science Students. The questionnaire was adapted by changing it from a 24-hour recall to an adapted 24-hour recall of usual intake by using the food frequency questionnaire as a cross-control in determining the usual intake. The adapted 24-hour recall included not only questions about what was eaten during the previous day, but also about what was usually eaten in 24 hours.

The adapted 24-hour recall was used to obtain information on usual food intake from individuals in order to assess usual 24-hour dietary intake (Smolin & Grosvenor, 2008:62). In the adapted 24-hour recall questionnaire, patients mentioned everything they usually ate and drank on a typical day including everything that was also added to the food. The patients included the type, amounts, and the preparation methods of each food item eaten. The adapted 24-hour recall interview was composed of three passes. The first-pass was a quick-list where subjects listed what they usually consumed. The second-pass was a detailed description where subjects clarified type of foods mentioned in the quick-pass indicating the types, what was added during the preparation, and the portion sizes consumed. The third-pass was the review where the interviewer reviewed the list of foods mentioned and probed for additional consumptions (Johnson & Hankin, 2003: 228).

b) FFQ as a cross-control with an adapted 24-hour recall:

The intake of the adapted 24-hour recall was calculated and combined with information obtained from the FFQ to estimate the usual intake of the individuals and the group. Foods which were consumed three times and more a week in the FFQ were included in the adapted 24-hour recall of the usual intake and their portion sizes were determined by the daily portion sizes given by the patients and were included in the adapted 24-hour recall questionnaire.

c) Food frequency questionnaire:

The purpose of the FFQ was to assess the usual food intake that contributed to a typical dietary food intake and be used as a cross-control with an adapted 24-hour recall, determine the top ten foods most often consumed by the participants (Smolin & Grosvenor, 2008:64), and to determine

if there were any associations between food intake and breast cancer risk (Johnson & Hankin, 2003:231). The FFQ was adapted from the questionnaire developed by the Department of Nutrition and Dietetics and validated for Medicine, Nursing, and Allied Health Science Students. The FFQ was adapted for the present study by adding foods that could imply a risk in developing breast cancer as reported in the literature and by adding typical traditional dishes used in Lesotho (Appendix B_3). Patients were asked to indicate the frequency of intake of each food item listed. The frequency was according to per day, per week, per month, or per season and intake was evaluated according to the frequency of intake per food item.

Reliability was ensured by explaining the questionnaires for usual dietary intake, socio-demographic information, lifestyle behaviours, menstrual history, reproductive patterns, history of breast cancer, and anthropometric measurements and their procedures to the participants before the interview. In order to overcome pitfalls with the dietary questionnaires, the researcher asked probing questions in order to help the subjects to remember everything they usually ate and repeated questions to check if the same answers would be obtained. The researcher also guided the subjects by asking probing questions in order to help them remember in order to respond to the socio-demographic information, lifestyle behaviours, menstrual history, reproductive patterns, and history of breast cancer questionnaire. Reliability was also ensured by repeating the same questionnaires with 10% of the same sample a month after conducting the main data collection and by using one trained researcher.

ii) Socio-demographic information, lifestyle behaviours, menstrual history, reproductive factors, and history of breast cancer factors

In order to ensure validity of the questionnaire (Appendix B_1) the questionnaire was developed based on the known risk factors in developing breast cancer as reported in the literature.

The questionnaire included socio-demographic information (section a), lifestyle behaviours (section b), menstrual history (section c), reproductive patterns (section c), history of breast cancer (section c), and anthropometric measurements (section d). The questionnaire was developed in order to include all the questions that would determine the risk in developing breast cancer as reported in the literature. The questionnaire comprised of both open-ended questions where subjects were expected to elaborate where necessary, and closed-ended questions where they were expected to choose an answer from the options provided.

3.5 Pilot study

A pilot study was conducted on four South African Sesotho speaking women who had breast cancer and attended their treatment at the National Hospital in Bloemfontein. The South African women were used because they were considered to be a representative of women residing in Lesotho and also because the researcher did not want to use women from Lesotho as they would have to be excluded from the main study and affect the sample size of the study as a result

because of the limited available Lesotho women. The participants used for pilot study were not included in the main study because they were not from Lesotho.

The purpose of the pilot study was to test the questionnaires regarding the clarity of language, to make sure that subjects understood the questionnaires and to test the data analysis on the questionnaires. The pilot study was also used to determine the length of time required to complete the questionnaires, to carry out anthropometric measurements, and to make sure that all relevant foods in the FFQ were included.

After the pilot study there were changes made to the questionnaires including clarifying questions that were unclear, adding some questions in order to get more specific information, removing some questions, and questionnaires were adjusted and finalised for the main study.

3.6 Ethical approval and study procedures

3.6.1 Ethical approval

- Ethical approval to conduct the study was obtained from The Ethics Committee of the Faculty of Health Sciences, UFS.
- Consent was obtained from The Director General of the Ministry of Health and Social Welfare to conduct the study at the Queen II hospital (and the breast cancer clinic) (Appendix C_1).
- Consent was obtained from the Universitas Hospital (Appendix C_2) from where the main study was conducted as a follow-up of patients from Lesotho for those who got their treatment at the Universitas hospital and the National Hospital (Appendix C_3) respectively, where the pilot study was conducted.
- Participants who gave their consent were seen at the hospitals or the clinic for interviews.
- Consent forms (Appendix D) were completed by the participants in Sesotho.
- Information and consent documents were issued to the participants to keep for their reference.

3.6.2 Study procedures

- Pilot study was conducted on four South African Sesotho speaking women who had breast cancer.
- Interviews were conducted at the hospital and the cancer clinic when participants came for their treatment or at the participants' homes if their places were easily accessible.

- Anthropometric measurements were taken, and the questionnaires on usual dietary intake, socio-demographic information, lifestyle behaviours, menstrual history, reproductive patterns, and history of breast cancer were completed (Appendix B_1).

- The interviews for the reliability study were conducted a month after the initial interview. Every 10^{th} participant was selected.

3.7 Statistical and nutritional analysis

3.7.1 Statistical analysis

Descriptive statistics, viz. averages and standard deviations or medians and percentiles for continuous data, and frequencies and percentages for categorical data were computed. The analysis was performed by staff from the Department of Biostatistics, UFS. Reliability analysis was conducted on repeat data gathered from a 10% sub-sample of the respondents, one month after the initial data collection, and no items were found not to be reliably measured.

3.7.2 Nutritional analysis

The overall dietary quality and adequacy was evaluated according to total energy and macronutrient intake and compared to the DRIs, variety of food intake, the USFGP, DGA, 2010, DASH diet, and the frequency of food intake. The exchange lists according to Wheeler *et al* (1996) were used to analyse the energy and macronutrient content of the diet as indicated in Table 3.4.

Table 3.4 Energy and macronutrients values of the exchange list (Wheeler *et al*., 1996):

Exchange group	Serving size	Energy (kcal)	Carbohy-drate(g)	Protein (g)	Fat (g)
Carbohydrate group					
Starch	½ cup pasta, cereal, rice; 1 slice bread	80	15	3	0-1
Fruit	1 small apple, peach, or pear; ½ banana; ½ cup canned fruit (in juice)	60	15	0	0
Milk	1 cup milk or yoghurt	90	12	8	0-3
Non-fat		120	12	8	5
Low fat		150	12	8	8
Whole					
Other Carbohydrate					
Vegetables	Serving sizes vary	Varies	15	Varies	Varies
		25	5	2	0
Meat/meat-substitute group					
Very lean	½ cup cooked; 1 cup raw				
Lean	30 grams meat of cheese	35	0	7	0-1
Medium fat		55	0	7	3
High fat		75	0	7	5
		100	0	7	8
Fat group	1 tsp butter, margarine, or oil; 1Tbsp salad dressing	45	0	0	5

3.8 Problems encountered during the study

3.8.1 Small sample size

3.8.1.1 Late start of data collection for the main study

The data collection of the main study could only start after five months since the requisition letter to conduct the study at the Queen II hospital had been submitted. The researcher made follow-ups by calls and emails checking as to how far the committee was with the approval.

The five months waiting period could have been used to collect data from the patients who were admitted in the hospital or who went for the check-up at the clinic at that time. The patients who were missed could have been added to the study and could have increased the sample size and thus add value to the study results.

3.8.1.2 Communication with the nursing staff

During the hospital visits to check for patients for the interviews, at some days the researcher would be told by the nursing staff on duty that there were no patients in the ward yet there were patients admitted with breast cancer. At some days even though the researcher was told that there were no patients, some patients who had already participated in the study would bring new patients to the researcher. At times new patients would approach the researcher themselves after being told about the study by other patients who had already participated in the study.

Although the researcher still managed to interview some patients even been told that there were no new patients, it is still believed that there were other patients who could have been missed who could have added value to the study results by increasing the sample size.

3.8.1.3 Delayed service to the patients

The diagnosis process at the hospital is very long for some patients, and it even took years for some patients in order to be confirmed with the disease. However, the matter has not been solved yet but will be reported to people in charge so that it can be rectified accordingly. If ever the diagnosis process was quicker, hopefully a larger sample size would have been obtained in order to have more stable and reliable results.

3.8.2 Recalling of dates by participants

The participants had the problem of recalling some of the dates. The dates included: birth dates, when they were diagnosed with breast cancer, when they had their last mammograms, last date when they had their breasts examined by hands by the health care professionals. In most cases participants remembered only the years and forgot about the days and months and had to try to remember an event that they associated with those dates. However, there were some participants who could not remember completely even when the researcher tried to clarify the information.

This problem could mean that when the interviews were to be repeated on the same patients, the researcher would obtain different information about the dates which would affect the reliability of the study.

3.8.3 Portion sizes and additions during food preparation

All the participants said they did not measure when cooking especially with the use of cooking oil, salt, and some spices. Only what they could tell was to indicate whether they ate a lot or just enough and the researcher probed in order for participants to at least say in measuring tools how much was consumed. The patients' responses were liable to change if the patients were to be re-interviewed and as a result the reliability of the study would be affected.

3.8.4 Food frequency

It was also not easy for participants to recall on the number of frequency of consumption for certain food items especially those that were seasonal. The participants made rough guesses when responding to the question. This problem could also affect the reliability of the study since different information would be obtained when the measurement could be repeated on the same sample or group.

3.8.5 Space for interview

At times when the researcher arrived at the hospital for interviews, there was no free room where interviews could be conducted. In order to overcome the problem, a small corner in the ward or at the corridor away from other patients would be used.

The problem affected the patients' responses and this could mean that there was information that could have been held by the patients being afraid to disclose some of their information in the presence of other patients.

CHAPTER 4

RESULTS

4.1 Introduction

The results of the study regarding the prevalence of non-modifiable and modifiable risk factors for breast cancer will be described in this chapter. Results will be presented in tables, with continuous data presented as medians and percentiles, and categorical data as frequencies and percentages. Group trends will be compared by 95% confidence interval (CI) for median differences or percentage differences. Reliability analysis was gathered from a 10% sub-sample of the participants a month after the main data collection and no items were found not to be reliably measured.

4.1.1 Non-modifiable risk factors

The medians for the non-modifiable risk factors for breast cancer are shown in Table 4.1 and categories for the non-modifiable risk factors are shown in Table 4.2.

The median age at interview was 53.5 years (min 28; max 86) (Table 4.1). The median age at diagnosis for the breast cancer patients was 48.5 years (min 24; max 86). The difference for median ages at interview and diagnosis was five years. According to Table 4.2, the majority (78.7%) of the 52 patients was 46 years and older when they were diagnosed with breast cancer, which as women from sub-Saharan Africa places them into the medium risk category for breast cancer as summarised in Table 3.3. However, 15.4% of the patients were at a high risk of breast cancer development because they were diagnosed between the age range of 35 and 45 years.

Of the 52 patients, the majority (93.8%) could still remember when they first had their menstrual period (Table 4.2). The median age at menarche for the patients was 15 years (min 9; max 20) (Table 4.1). The majority (93.9%) of the 49 patients had their first menarche at the age of 12 years and older, placing them into a low risk category (Table 4.2).

Of the 52 patients in this study, 31 had already reached menopause by the time of the interviews (Table 4.1). The median age at menopause was 49 years (min 35; max 57). Of the 31 patients who had reached their menopause, the majority (96.8%) had menopause at an age younger than 55 years, placing them into a low risk category (<54 years) for breast cancer development (Table 4.2).

The majority (77%) of the 52 patients had no relatives diagnosed with any type of cancer, which corresponds with a low risk category (Table 4.2), while only 13.5% of the patients had second-degree relatives with cancer, placing them into a medium risk category.

Table 4.1 Medians, minimum, and maximum years of onset of non-modifiable risk factors

Variable	N	Minimum	Median	Maximum
Non-modifiable factors				
Age at interview	52	28 years	53.5 years	86 years
Diagnosis age	52	24 years	48.5 years	86 years
Age at menarche	49	9 years	15 years	20 years
Age at menopause	31	35 years	49 years	57 years

Table 4.2 Categories of non-modifiable risk factors for breast cancer

Variable	Level of risk for BRCA*	n	%
Non-modifiable factors			
Age at diagnosis (N=52)			
35-45 years	High	8	15.4
≥46 years	Medium	41	78.7
<35 years	Low	3	5.8
Menstrual history			
Age at menarche (N=49)			
≤12 years	High	3	6.1
>12 years	Low	46	93.9
Age at menopause (N=31)			
≥55 years	High	1	3.2
≤54 years	Low	30	96.8
History of breast cancer Family (N=52)			
First-degree relative	High	5	9.6
Second-degree relative	Medium	7	13.5
No relative	Low	40	77

***Evaluated according to the interpretations for breast cancer risk factors and risk categories (Table 3.3)**

4.1.2 Modifiable risk factors

The modifiable risk factors for breast cancer included socio-demographic factors, lifestyle behaviours, reproductive factors, anthropometric status, and usual dietary intake.

4.1.2.1 Socio-demographic information

The distributions of breast cancer risk according to socio-demographic information are shown in Table 4.3. The majority had both a low level of education (80.8%) and income (59.6%) and was

placed into a low risk category. A low level of education referred to having a primary or high school certificate, while low income level included patients at a low or working class. The majority had been or was married (82.7%). Equal numbers resided in the rural (51.9%) and urban areas (48.1%) at the time of the interview and were placed into medium and high risk, respectively.

4.1.2.2 Lifestyle behaviours

Regarding alcohol intake, most patients were placed into a low risk category, being non-drinkers (48.6%) or light drinkers (36.5%) (Table 4.3). Alcoholic drinks consumed included beer (Hansa & Castle), traditional beer, and wines (red & white). The majority 82.6% had a sedentary lifestyle (PAL: 1- 1.39 METs) placing them into a high risk category.

4.1.2.3 Reproductive factors

The majority 88.9% used oral contraceptives (OC) for a long time (>1 year) placing them into a high risk category. The median age of OC use was 25.5 years (min 21; max 40) (Table 4.4) and thus a medium risk category. The OC used was mostly pills. The majority (80.8% & 86.8%, respectively) had children and had breastfed for 12 months or more which corresponds with a low risk category (Table 4.3). The median age at first breast feeding was 22 years (min 16; max 39) (Table 4.4).

Table 4.3 Categories for modifiable risk factors and level of risk for breast cancer

Variable	Level of risk for BRCA*	n	%
Modifiable factors			
Socio-demographic profiles			
Marital status (N=52)			
Never married	High	9	17.3
Ever married	Medium	43	82.7
Place of residence (N=52)			
Urban	High	25	48.1
Rural	Medium	27	51.9
Education level (N=52)			
High level (tertiary)	High	10	19.2
Low level (primary & high school)	Low	42	80.8
Income (N=52)			
Medium (middle class)	High	21	40.4
Low (low & working class)	Low	31	59.6
Lifestyle behaviours			
Alcohol use (N=52)			
Heavy drinker (≥3 drinks/day)	High	2	3.8
Moderate drinker (1 -2 drinks/day)	Medium	6	11.5
Light drinker (<1 drink/day)	Low	19	36.5
Non-drinker	Low	25	48.1
Physical activity level (N=52)			
Sedentary (1 – 1.39)	High	43	82.6
Low activity (1.4 – 1.59)	Medium	4	7.7
≥Active (1.6 – 2.5)	Low	5	9.6
Reproductive factors			
Oral contraceptive Use (N=52)			
Yes		18	34.6
No		34	65.4
Duration (N=18)			
Long term use (>1 year)	High	16	88.9
Recent use (6 months/more)	Medium	2	11.1
Age at OC use			
Use at early age (<18 years)	High	0	0.0
>18 years	Medium	18	100
Parity (N=52)			
Not having children	High	10	19.2
Having children	Low	42	80.8
Breast feeding (N=46)			
<6 months	High	1	2.2
6 – 11 months	Medium	5	10.9
≥12 months	Low	40	86.8

***Evaluated according to the interpretations for breast cancer risk factors and risk categories (Table 3.1)**

Table 4.4 Medians, minimum, and maximum years of onset of modifiable risk factors

Variable	N	Minimum	Median	Maximum
Modifiable factors				
Age at first breast feeding	43	16 years	22 years	39 years
Oral contraceptive use	18	21 years	25.5 years	40 years

4.1.2.4 Anthropometric measurements

The medians for anthropometric measurements are summarised in Table 4.5. The largest percentages fell into high risk categories for WHR (73.1%), WC (69.1%), and BMI (63.5%) (Table 4.6). However, based on height most patients (67.2%) fell into a medium risk category.

Table 4.5 Medians, minimum, and maximum measurements of the patients (N=52)

Variable	Minimum	Median	Maximum
Height (cm)	134	157.5	183
Weight (kg)	44	78.6	120
BMI (kg/m^2)	17.7	32.7	46.3
WC (cm)	50.3	96.3	118
HC (cm)	55	101	131.5
WHR	0.73	0.9	1

Table 4.6 Categories for height, BMI, WC, and WHR of the patients and the levels of breast cancer risk (N=52)

Variable	Categories	Level of risk for breast cancer*	n	%
Height categories (cm)				
Lowest quintile	<153	Low	16	30.7
Within quintiles	153 – 169	Medium	35	67.2
Highest quintile	>169	High	1	1.9
Body mass index categories (kg/m^2)				
Lowest quintile	<23§	Low	1	1.9
Low quintile	‡23 – 26	Low	7	13.5
Within quintiles	†27 – 30	Medium	11	21.2
Highest quintile	>30(obese)	High	33	63.5
Waist circumference categories (cm)				
Lowest quintile	<80	Low	12	23.1
Within quintiles	80 – 87.9	Medium	4	7.7
Highest quintile	≥88	High	36	69.1
Wait-hip-ratio categories				
Lowest quintile	<0.80	Low	9	17.3
Within quintiles	0.80 – 0.84	Medium	5	9.6
Highest quintile	≥0.85	High	38	73.1

*Evaluated according to Table 3.3: Interpretations for breast cancer risk factors and risk categories

†Overweight BMI category

‡Desirable/healthy BMI category

§ Underweight BMI category

4.1.2.5 Usual daily dietary intake

The usual daily dietary intakes were evaluated according to the recommendations for general health and cancer risk.

i) Evaluation of the overall quality and adequacy of usual dietary intake according to recommendations for general health

Overall dietary quality and adequacy was evaluated according to total energy and macronutrients intake, variety of foods consumed, food groups, Food Guide Pyramid (FGP), Dietary Guidelines for Americans (2010), DASH diet, and frequency of food intake. Usual dietary intake referred to the intake of types of food (variety) and number of portions from each food group in which the patients reported eating on the given day. Total energy (TE) and macronutrients were calculated and macronutrients expressed as percentages of total energy intake (%TE).

a) Total energy and macronutrients intakes

Medians of total energy and macronutrient intakes are shown in Tables 4.7.

1) Energy intakes

The median total energy intake of the patients was 5414.5 kJ (min 1690 kJ; max 63190 kJ) (Table 4.7) lower than the EER (10 044 kJ; 2403 kcal) for active adults (Lee & Nieman, 2010:233). The high maximum total energy intake indicated in Table 4.3 was due to high alcohol consumption by a minority (1.9%) of the patients.

2) Macronutrients intakes

The median intakes of macronutrients per day were 49g protein (min 12g; max 191g) higher than the RDA (46g/day) (Whitney & Rolfes, 2010:A), 210g carbohydrate (min 70g; max 633g) higher than the EAR for adults (100g/day) (Lee & Nieman, 2010:20), and 21.5g fat (min 5; max 114g).

The median for protein as calculated by grams per kilogram per day was 0.63 (min 0.2g/kg/day; max 3.8 g/kg/day). This median intake was similar to the EAR value for adults (0.66g/kg/day) (Mahan *et al*., 2012:Cover page).

Table 4.7 Medians, minimum, and maximum intakes of total energy and macronutrients for breast cancer patients (N=52)

Variable	Minimum	Median	Maximum
Total energy (kJ)	1690	5414.5	63190
Protein (g)	12	49	191
Carbohydrate (g)	70	210	633
Fat (g)	5	21.5	114

3) Macronutrients expressed as a percentage of total energy intake

The macronutrients expressed as a percentage of total energy intakes are shown in Table 4.8. The majority of patients consumed protein (92.3%) and carbohydrate (57.7%) at the recommended levels for general health. Most patients (57.7%), however, reported fat consumption at low levels of TE.

Table 4.8 Macronutrient intakes expressed as a percentage of total energy intake according to general health (N=52)

Variable	Level of risk for general health	n	%
Protein (g)			
>35% total energy (%TE)/day	High	1	1.9
10% - 35% TE/day	Medium	48	92.3
<10% TE/day	Low	3	5.8
Carbohydrate (g)			
>65% TE/day	High	30	57.7
45% - 65% TE/day	Medium	18	34.6
<45% TE/day	Low	4	7.7
Fat (g)			
>35% TE/day	High	7	13.5
20% - 35% TE/day	Medium	15	28.9
<20% TE/day	Low	30	57.7

***Evaluated according to the interpretations for breast cancer risk factors and risk categories (Table 3.3)**

b) Variety of foods consumed

Variety of different foods consumed was determined by an adapted 24-hour recall to indicate the intake that contributed to a typical dietary food intake. Table 4.9 shows foods which were mostly consumed by the patients on a typical day.

Full-cream milk was the most frequently (28.8%) consumed food among the milk and dairy products. Chicken and eggs were most frequently (32.7% & 32.7%, respectively) consumed foods from the meat and meat substitute group.

Apples and bananas were frequently (46.2% & 44.0%, respectively) consumed among the fruit group. Among the fancy vegetables pumpkin (30.8%), beetroot (19.2%), and green pepper (17.3%) were the most frequently consumed. Cabbage and spinach were the most frequently (84.6% & 73.1%, respectively) consumed among the green leafy types (moroho). Commercially ground maize papa and brown bread were the most frequently (88.6% & 59.6%, respectively) consumed among the bread and starch group.

Sunflower cooking oil was most frequently (86.5%) consumed in the fat group. Table sugar was most frequently (67.3%) consumed in the sweets and sugar group.

Tea and coffee were also consumed frequently (59.7% & 25.0%, respectively). Beer was most frequently (38.5%) consumed among the alcohol group.

Table 4.9 Variety of food intake summarised from adapted 24-hour recall of what was usually consumed by the patients (N=52)

Food	n	%
Milk & dairy products		
Milk:		
Full-cream	15	28.8
Skimmed	1	1.9
2% low-fat	3	5.8
Cheese	5	9.6
Yoghurt	3	5.7
Meat & meat substitutes		
Chicken:		
-with skin	17	32.7
-without skin	3	5.8
Peanut butter	7	13.5
Fish: pilchard	10	19.2
Polony	14	26.9
Eggs	17	32.7
Corned beef	5	9.5
Beans	12	23.1
Beef	9	17.3
Peas	3	5.8
Ham	2	3.8
Mutton	2	3.8
Pork	2	3.8
Lentils	1	1.9
Fruit		
Fancy:		
Apple	24	46.2
Banana	23	44.0
Oranges	5	9.6
Peaches	2	3.8
Pears	6	11.5
Guava	1	1.9
Paw-paw	1	1.9
Grapes	1	1.9
Juice:		
Mango	3	5.8
Guava	4	7.7
Orange	1	1.9
Indigenous		
Blackberry	6	11.5
Prickly pear	9	17.3
Gooseberry	1	1.9
Vegetables		
Fancy		
Egg plant	1	1.9
Green pepper	9	17.3
Chilies	2	3.8
Pumpkin	16	30.8
Beetroot	10	19.2
Carrots	8	15.4

Table 4.9- continue: Variety of food intake summarised from adapted 24-hour recall of what was usually consumed by the patients (N=52)

Food	n	%
Tomato	3	5.8
Green beans	3	5.8
Lettuce	2	3.8
Cucumber	3	5.8
Broccoli	1	1.9
Moroho (green leafy)		
Cabbage	44	84.6
Spinach	38	73.1
Turnip	23	44.2
Radish	26	50.0
Indigenous green leafy		
Theepe	10	19.2
Bobatsi	10	19.2
Tenane	3	5.8
Leharasoana	4	7.7
Serue	3	3.8
Papasane	5	5.8
Leshoabe	5	5.8
Mantsokoane	1	1.9
Lihaba	5	9.6
Bread & starch		
Papa (maize stiff porridge):		
-commercial grinding	46	88.6
-home grinding	7	13.5
Motoho- fermented soft porridge (sorghum):		
-commercial grinding	2	3.8
-home grinding	11	21.2
Unfermented Soft porridge (lesheleshele) (sorghum):		
-commercial grinding	4	19.2
-home grinding	10	7.7
Bread:		
-Brown	31	59.6
-White	5	9.6
-Home ground wheat	1	1.9
Breakfast cereals:		
Weetbix	7	13.5
Cornflakes	4	7.7
Branflakes	4	7.7
Oats	2	3.8
Muesli	4	7.7
Fat		
Sunflower oil	45	86.5
Rama (brick)	6	11.5
Olive oil	1	1.9
Mayonnaise	1	1.9
Sugar:		
Sugar	35	67.3
Sweeteners	2	3.8
Tea	31	59.7
Coffee	13	25.0
Alcohol:		
Traditional	8	15.4
Beer	20	38.5
Wines:		
Red	5	9.6
white	3	5.8

c) Usual dietary intake summarised in food groups according to the Food Guide Pyramid (USDA, 1992)

The usual dietary intake was quantified according to the FGP in order to assess food intake that contributed to a typical food intake. Table 4.10 shows summary of foods evaluated according to the FGP.

The majority of the patients had a low intake of milk and dairy products (92.3%), meat and meat substitutes (44.2%), and fruit (92.3%) (Table 4.10). Fruits taken were mostly apples, bananas, and pears. A third of the patients had inadequate daily intakes of vegetables, while half met the recommendations. However, vegetable intake in this group constituted mostly green leafy types in the form of moroho (cabbage, spinach, radish, turnip) and indigenous leafy types (bobatsi, theepe, leshoabe, leharasoana). Approximately 48.1% of the patients had high intakes of bread and starches, while half met the recommendations.

Fat and sugar intakes which are not quantified in daily serving portions in either the Food Guide Pyramid (1992) and the Dietary Guidelines for Americans (2010), were compared to the Dietary Approach to Stop Hypertension (DASH) recommendations at different levels of energy intake of 1400kcal (5852 kJ). The majority of the patients had adequate intake of fat (59.6%) and sugar (67.3%) per week (Table 4.10). Fat consumed was mostly cooking oil.

Table 4.10 Usual dietary intake of breast cancer patients summarised in food groups according to the Food Guide Pyramid (1992) (N=52)

Food groups	Recommended no. of portions per day	n	%
Milk & milk products			
Below recommendations	<2 servings/day	48	92.3
Within recommendations	2-3 servings/day	4	7.7
Meat & meat substitutes			
Below recommendations	<2 servings/day	23	44.2
Within recommendations	2-3 servings/day	15	28.9
High intake	>3 servings/day	14	26.9
Fruit			
Below recommendations	<2 servings/day	48	92.3
Within recommendations	2-4 servings/day	2	3.9
High intake	>4 servings/day	2	3.9
Vegetables			
Below recommendations	<3 servings/day	17	32.7
Within recommendations	5 servings/day	26	50.0
High intake	>5 servings/day	9	17.3
Bread & starch			
Below recommendations	<6 servings/day	1	1.9
Within recommendations	6-11 servings/day	26	50.0
High intake	>11 servings/day	25	48.1
Fat*			
Within recommendations	≤3 servings/week	31	59.6
Sugar*			
Within recommendations	≤3 servings/week	35	67.3

***Evaluated according to the DASH eating plan**

d) Usual dietary intake summarised in food groups according to the Dietary Guidelines 2010 and the DASH diet

The usual dietary intake was quantified according to the Dietary Guidelines 2010s in order to assess food intake that contributed to a typical food intake. Table 4.11 shows summary of foods evaluated according to the Dietary Guidelines.

As the median energy intake of these patients was 5415kJ (1289 kcal), their dietary intakes were evaluated according to the Dietary Guidelines for Americans 2010's recommendations for average daily intakes at 1400kcal (5852 kJ) per day (Table 4.11).

The majority of the patients had a low intake of milk and dairy products (100%), meat and meat substitutes (57.7%), and fruit (92.3%) (Table 4.11). The majority of the patients met the recommendations of vegetables (67.3%) and bread and starch (100%).

Table 4.11 Usual dietary intake of patients (N=52) (median energy intake =5414.5kJ [1400kcal/5852 kJ]) compared to *Dietary Guidelines 2010 and the †DASH diet

Food groups	Recommendations for energy intake of 1400 kcal/5852 kJ per day*	n	%
Milk & milk products			
Below recommendations	<2 1/2 servings per day	52	100
Within recommendations	≥2 1/2 servings per day	0	0.0
Meat & meat substitutes			
Below recommendations	<3 servings per day	30	57.7
Within recommendations	≥3 servings per day	22	42.3
Fruit			
Below recommendations	<2 servings per day	48	92.3
Within recommendations	≥2 servings per day	4	7.7
Vegetables			
Below recommendations	<3 servings per day	17	32.7
Within recommendations	≥3 servings per day	35	67.3
Bread & starch			
Below recommendations	<4 servings per day	0	0.0
Within recommendations	≥4 servings per day	52	100
Fat†			
Within recommendations	≤3 servings/week	31	59.6
Sugar†			
Within recommendations	≤3 servings/week	35	67.3

*Evaluated according to the Dietary Guidelines for Americans (2010:79)

† Evaluated according to the DASH eating plan

e) Frequency of food intake

The frequency of food intake was determined by the food frequency questionnaire to assess food intake that contributed to a typical dietary food intake. Table 4.12 shows foods which were mostly consumed by the patients either per day, per week, or per month.

Daily, maize papa and brown bread were the most frequently (100% & 67.3%, respectively) consumed foods among the bread and starch group. Papa was classified according to commercial grinding (low fibre) and home grinding (high fibre) in order to indicate fibre content. More participants (65.4%) consumed commercial ground papa than home ground papa (34.6%). Moroho (green leafy vegetables) was frequently (80.7%) consumed in the vegetable group. The green leafy types included cabbage, spinach, radish, and turnip. Cooking oil was frequently (92.3%) consumed in the fat group, mostly as cooking oil. Table sugar was frequently (71.1%) consumed in the sugar group. Sugar taken was used to sweeten tea, coffee, motoho (fermented soft porridge), and lesheleshele (unfermented soft porridge).

Weekly, eggs and legumes (beans & peas) were frequently (65.4% & 63.4%, respectively) consumed in the meat and meat substitute group. Full-cream milk was consumed frequently although by a small percentage (36.5%). Fancy fruits (apples, bananas, & oranges) were consumed frequently (23.6%) among the fruit group.

Monthly, peanut butter and chicken were the most frequently (42.3% & 23.1%, respectively) consumed among the meat and meat substitute. Fancy vegetables were frequently consumed monthly by a small percentage (19.2%). The fancy vegetables consumed included beetroot, green beans, pumpkin, onion, tomato, and carrots.

Table 4.12 Frequency of food intake on daily, weekly, and monthly basis (N=52)

Food	Per day		Per week		Per month	
	n	%	n	%	n	%
Milk & dairy products						
Milk: full-cream	14	26.9	19	36.5	7	13.5
Meat & meat substitutes						
Eggs	15	28.8	34	65.4	2	3.8
Chicken	9	17.3	31	59.6	12	23.1
Legumes (beans & peas)	4	7.7	33	63.4	10	19.2
Peanut butter	5	9.6	11	21.1	22	42.3
Fruit						
Fancy fruit (apples, bananas, oranges)	6	11.5	17	23.6	6	11.5
Vegetables						
*Fancy vegetables	5	9.6	18	34.6	10	19.2
†Moroho (green leafy vegetables)	42	80.7	0	0.0	0	0.0
Bread & starch						
Maize papa (Stiff porridge)	52	100				
-commercial grinding	34	65.4	0	0.0	0	0.0
-home grinding	18	34.6	0	0.0	0	0.0
Bread (Brown)	35	67.3	9	17.3	3	5.8
Bread (white)	8	15.4	8	15.4	2	3.8
Lesheleshele (unfermented soft porridge): (sorghum: home ground)	8	15.4	11	21.1	1	1.9
Lesheleshele (soft porridge): (sorghum: commercial ground)	7	13.4	5	9.6	3	5.8
Breakfast cereals	7	13.4	6	11.5	5	9.6
Motoho (fermented soft porridge): (sorghum: home ground)	4	7.7	0	0.0	1	1.9
Motoho(fermented soft porridge): (sorghum: commercial ground)	4	7.7	1	1.9	6	11.5
Fat						
Cooking oil	48	92.3	2	3.9	5	9.6
Sugar						
Sugar (table)	37	71.1	6	11.5	0	0.0
Tea	32	61.5	11	21.2	0	0.0
Coffee	12	23.1	7	13.4	1	1.9
Cool drinks	5	9.6	5	9.6	8	15.3

*Fancy vegetables: beetroot, carrots, green beans, pumpkin, onion, tomato.

†Moroho: cabbage, spinach, radish, turnip, and indigenous leafy vegetables (bobatsi, theepe, leshoabe, leharasoana)

ii) Evaluation of usual dietary intake according to cancer risk

The dietary energy intake of the patients was below the requirements placing them into a low risk of breast cancer. The majority had low intake of fat, meat and meat substitute, milk and dairy products, and a low risk of breast cancer. Fruit intake was low while half of the patients met the recommendations of vegetables per day. However, the patients may be at an increased risk for breast cancer due to lack of variety of fruits and vegetables consumed. Boiling was the commonly used method of cooking foods.

4.2 Summary

The entire sample of this study was of women diagnosed with breast cancer, however, the patients had demonstrated different risk categories for breast cancer. The risk categories included low (0), medium (1), and high (2) levels when valued. The risk factors for each group of factors were sub-totalled and totalled to get a total risk score. The higher the total risk factors the more at risk the person was. In total there were 21 risk factors, although age at pregnancy was not used, so the risk factors used were actually 20. Given that the high risk is 2, therefore the maximum risk score was 40 with the scores ranging from 12 and 17.

Overall the sample presented with low risk regarding non-modifiable risk factors (age at first menarche, age at menopause, and family history) and socio-demographic factors (low education level and income). Regarding non-modifiable risk factors, the sample demonstrated a low risk related to reproductive factors (having children and breast feeding), certain lifestyle behaviours (drinking habits), and certain dietary factors (energy intake, fat, meat and meat substitute consumption, and milk and dairy products intake, and food preparation methods). However, high risk factors for the development of breast cancer which were identified in the sample were mostly related to lifestyle and behaviour, including high prevalence of OC use, low activity levels, high prevalence of overweight and obesity, low intakes of fruits and vegetables and low dietary variety.

CHAPTER 5

DISCUSSION OF RESULTS

5.1 Introduction

In this chapter the most important observations of the study will be discussed and compared to the results of relevant studies of the same nature in terms of the cancer risk profile. Limitations encountered during the study will be discussed to evaluate how these may have influenced the results.

5.2 Discussion

5.2.1 Non-modifiable risk factors

5.2.1.1 Age at diagnosis

The median age at interview for the current patients was 53.5 years (min 28; max 86). The median age at diagnosis for the current patients was 48.5 years. This was similar to the median age at diagnosis of 46 years found among Tanzanian women (Rambau *et al*., 2011:214), but older than 29.1 years found among Indian women studied by Puri *et al*. (2009:3). In this study the youngest patients were 24 years and the oldest 86 years. The age range was similar to that of Ebrahim *et al*. (2002:11) whose Iranian patients ranged from 24 to 81 years. However, a Malaysian study (Norsa'adah *et al*., 2005:700) have indicated different ages at diagnosis although the youngest patients were still below 30 years, ranging from 28 to 70 years.

When age at diagnosis for the current study was stratified in the same way as in the Tanzanian (Rambau *et al*. 2011:214) and Nigerian (Ogundiran *et al*., 2010:686) studies, it was evident that 53.9% of the current patients were older than 50 years compared to 24.3% of Tanzanians and 40% of Nigerians. The age at diagnosis for the current patients was similar to that of African-Americans (Palmer *et al*., 2003:480) who were mostly (63.3%) diagnosed at 45 years and older. In contrast to Indian patients (Puri *et al*., 2009:3) who were diagnosed at 40 years and younger (34.3%), only 17.3% of the current patients were younger than 40 years.

The majority (78.7%) of the current patients were 46 years and older at diagnosis, which is older than the age range of 35 to 45 years, which was found to be the typical age of diagnosis for most African women by various researchers including Rambau *et al*. (2011:214), Akarolo-Anthony *et al*. (2010:8), Kruger and Apffelstaedt (2007:19), and Adebamowo *et al*. (2003:19). Furthermore, the age at the time of diagnosis determines risk (the earlier a woman develops a first primary breast cancer in her lifetime, the greater the risk of developing a second primary (Chen *et al*., 1999:857). Only 21.2% of the current patients were diagnosed before the age of 45 years which corresponds to a high risk for breast cancer recurrence.

Regarding age at diagnosis, the current patients thus had a risk profile for breast cancer which differed from other African women in that the Basotho women were typically older at diagnosis, more similarly to African-American women. This implies that screening for breast cancer ought to start at an age of 40 years in Basotho women in order to aim for earlier detection and treatment and thus a better probability of survival.

5.2.1.2 Age at menarche

Given that the majority (93.9%) of the current patients had their first menarche at an age older than 12 years, they were placed in a low risk category. According to Sprague *et al.* (2008:406) women who were younger at menarche (≤12 years) are at an increased risk of developing breast cancer because long menstrual history increases life time exposure to oestrogen (Friedenreich 2001:21; Sasco 2001:322).

The median age at menarche for the current patients was 15 years (min 9; max 20), this was higher than in Californian patients, who were predominantly white (Wrensch *et al*., 2003:91), whose median age at menarche was 12.6 years. In the current study only 6.1% had early menarche (≤12 years) and thus a high risk, compared to 47.6% of Indian patients studied by Shah and Shrestha (2004:2) in Jabalpur, Nepal. The higher age at menarche of the Basotho women in the current study, however, confirms findings of Walker et *al*. (1984:797), who recorded age at menarche as 14.7 years in rural black women in South African and 13.9 years in urban black women, compared to 12.6 years in white women. The current patients' median age at menarche was also similar to the 14.8 years of Northwest Indian women used by Zegeye *et al*. (2009:29). However, the current patients' age ranges (min 9; max 20) at menarche differed from that of Northwest Indian women which was 13.9 years to 15.3 years. According to Karapanou and Papadimitriou (2010:1477) age at menarche varies - with African women experiencing menarche at older ages (Fregene & Newman, 2005:1543). Reasons for variations of menarche are dependent on the interaction between genetic and environmental factors (Karapanou & Papadimitriou, 2010:1477).

The current patients, similar to that of rural black women in South African and Northwest Indian women, thus had menarche at a late age compared to white women in South Africa who have an early menarche.

5.2.1.3 Age at menopause

Women who are older at menopause (>55 years) are at an increased risk of developing breast cancer (Sprague *et al.,* 2008:406) because long menstrual history increases life time exposure to oestrogen (Friedenreich 2001:21; Sasco 2001:322). In Asian women menopausal status was, however, not associated with breast cancer risk (Wu *et al*., 2009:1149).

Of those Basotho women in the present study who had reached menopause, the majority (96.8%) (n=31) experienced menopause at the age of 54 years and younger and thus had a low risk for

breast cancer. The median age at menopause for the current patients was 49 years (min 35; max 57). This was similar to 48 years in white Americans in a study conducted by Berstad *et al*. (2010:1536), but slightly older than the African-American women in the same study who experienced the onset of menopause at 46.5 years.

The majority (90.3%) of the Basotho women in the present study experienced natural menopause while only 9.7% did not. The reasons for "unnatural menopause" included being on cancer treatment and having had a hysterectomy (removal of the uterus and associated structures) (Bosman *et al*., 2008:344). The majority (92.3%) had never used hormone replacement therapy (HRT) for menopause while the rest did not know if they had ever used HRT. Berstad *et al*. (2010:1536) had reported that age at menopause differed among HRT users and non-users having users experiencing menopause earlier than non-users, with a difference of 3.2 years among white women and 3.7 years among black women. The HRT is a source of exogenous oestrogen (Travis & Key, 2003:242) and its use affects breast carcinogenesis by increasing breast exposure to oestrogens and other sex hormones (Woolcott *et al*., 2008:1471).

The current patients thus experienced the onset of menopause at an age similar to white American women but older than African-Americans. Nine out of ten of these Basotho women experienced natural menopause and had never used HRT.

5.2.1.4 Family history

A woman is at an increased risk if her blood relatives on either her mother or father's side have had cancers of the breast (Pakseresht *et al*., 2009:137) and/or ovaries (Afonso, 2009:44). The majority (77%) of the patients in the present study reported having no relatives diagnosed with any type of cancer, which corresponds with a low risk (Abbasis *et al*., 2009:8; AICR, 2007:2). Nigerian patients (Ogundiran *et al*., 2010:687) and American women (both African-American and white) with breast cancer (Berstad *et al*., 2010:1534) were reported to be more likely to have a first-degree family history of breast cancer than their controls. Only 9.6% of the present patients had first degree relatives with cancer which placed them in a high risk category compared to 19.0% of Californian patients (Wrensch *et al*., 2003:92). About 13.3% of the present patients had second-degree relatives previously diagnosed with cancer, placing them at medium risk.

In the current study, only six out of 13 (46.2%) of the relatives with cancer were diagnosed with breast cancer, compared to 85.0% of relatives of Indian women with breast cancer (Puri *et al*., 2009:4). Other types of cancer diagnosed among the relatives of women in the present study included cancers of the cervix (38.5%), colon (7.7%), and prostate (7.7%) which according to Chen *et al*. (1999:857) also put them at an increased risk, because a family history of endometrial and ovarian cancers increase the risk of developing a second primary breast cancer. However, questions to determine whether the patients' disease was a new case, a recurrence, or a new development of a new cancer on another breast, were not included in the current study.

Only a third (30.8%) of the patients knew the ages at which their relatives were diagnosed with cancer. The finding is supported by Anyanwu (2000:123) who indicated that it is difficult to obtain family histories among African women due to decreased awareness of breast cancer in Sub-Saharan Africa, and due to the desire for secrecy sometimes found within families after a diagnosis of cancer. Some of the patients in the present study also indicated that only their husbands, children, siblings, and parents knew about their cancer diagnosis; while other relatives only knew that the patients were in hospital, but did not know the details about their disease. Using the information from those that did know the age at which their relatives were diagnosed, it was found to range from 44 years to 65 years for all types of cancer. The patients with relatives who were diagnosed at a young age were at an increased risk, because a young age at diagnosis for a relative increases the risk of developing breast cancer in women (Abbasis *et al*., 2009:8) while the risk decreases with increasing age in both the patient and the relative (Easton, 2002:179).

There was therefore a tendency of secrecy regarding family history among these Basotho women, nevertheless, the majority had reported not having relatives with cancer. The relatives had cancers of the breast, cervix, colon, and prostate.

In summary, regarding non-modifiable risk factors, the current patients had a risk profile for breast cancer which differed from other African women in that these Basotho women were typically older at diagnosis, more similar to African-American women. The current patients also had late menstrual onset, which is a profile similar to that of Indian and South African women, but different to that of white South African women. Age at menopause for the current patients was at a later age, similar to that of white American women. Nine out of ten of these Basotho women experienced natural menopause and had never used HRT. There was a tendency of secrecy regarding family history; nevertheless, the majority had reported not having relatives with cancer. The relatives with cancer, had cancers of the breast, cervix, colon, and prostate.

5.2.2 Modifiable risk factors

5.2.2.1 Socio-demographic factors

Marital status in this study referred to being married, divorced, separated, widowed, not married but living with someone, or never married (single). The majority (82.7%) of the current patients had married at the time of the interviews corresponding to a medium level of risk. However, according to Abbasis *et al*. (2009:9) and Ebrahim *et al*. (2002:11), marital status by itself does not determine the level of risk for breast cancer development.

Level of education is described in various studies as a risk factor in breast cancer development (Vona-Davis & Rose, 2009:890; Webster *et al*., 2008:1127; Hussain *et al*., 2008:166). Findings from Gibson *et al*. (2010:517) in Filipino women indicated that the risk is almost double for women who had received a tertiary education compared with those who received only a minimal education, or primary and/or high school certificates, since time spent in getting educated

followed by building a career contributes to delay in marriage and possibly conception (Celik & Aksoy, 2007:10). According to Hussain *et al*. (2008:166) the level of education may also affect other factors associated with breast cancer risk - including reproductive patterns (parity and age at first birth) and lifestyle behaviours (physical activity and diet).

In the current study the majority (80.8%) of the patients had a low level of education (defined in this study as having a primary or high school certificate) and thus a low risk for breast cancer development. Similar results were also found among Bahraini women with breast cancer in a study by Saweer *et al*. (2003:4) where 78.0% had low levels of education.

Level of income has also been associated with risk of breast cancer development (Samaras, 2010 :88). The current patients were categorised into either low or medium income class based on various variables. Variables used included: employment status (self-employed, employed, or not employed/working); type of work done; job titles held; industry worked in; amount of money spend on food per month; number of people per household; number of persons contributing to the buying of food per household; and whether the house was owned or rented. These determinants were used because livelihoods in Lesotho depend on the location where one is based (Turner *et al*., 2001:Online). In Lesotho agriculture plays an important role because it is the major contributor of livelihood of many Basotho (people from Lesotho) (FAO, 2010:11) and like other developing countries, there is still trade in resources such as sharing of food and income between families and neighbours (Meyer & Ehrlich, 2010:214).

In the present study a low income level referred to a low or working class. About six out of ten (59.6%) current patients had a low level of income placing them into a low risk category for breast cancer development, contrary to only 9.0% of Californian patients who had reported their status as "poor" (working class) or "lower middle" class (Wrensch *et al*., 2003:92). The Basotho women in the present study who were from a low income class had a low education level (primary/high school certificate) and did physical jobs such as selling traditional beer, working at the factories, cleaning offices, or being shop assistants. Approximately 40.4% of the current patients were from a medium income class compared to 36.0% of the Californian patients (Wrensch *et al*., 2003:92). In the current study, patients from the medium income class had educational qualifications enabling them to secure professional jobs, and they did jobs that included teaching, nursing, and financial advisory. The educational qualifications in the medium income class ranged from college diplomas to university Master's degrees. In the current study there were no patients from the upper middle class while in the Californian study 55.0% of patients were from the upper middle class (Wrensch *et al*., 2003:92).

Place of residence influences breast cancer risk. There is a doubling risk in women living in urban areas compared to living in rural areas. Urban areas are associated with westernised behaviours and lifestyles (Fregene & Newman, 2005:1543). Place of residence also affects patients' decision to obtain early medical help or to avoid the proposed medical therapies for cancer because people from rural areas still seek medical help from the indigenous practices.

Socioeconomic status and geographic accessibility to medical centres with oncology services (Vorobiof *et al*., 2001:127) also affect patients' decisions to obtain early help which were applicable to the current patients. Approximately equal numbers of the current patients resided in the rural (51.9%) and urban areas (48.1%) at the time of the interview placing them into medium and high risk categories, respectively.

The current patients went to the Queen II Hospital in Maseru because they could not afford to pay their own medical expenses. The Queen II Hospital is a control centre for all government hospitals in Lesotho to which new cases of cancer are referred to before they could be transferred to South African health institutions since there are no appropriate cancer treatment facilities at the Queen II hospital. The transfer process is relatively long which raises a suspicion that there were patients who might have pulled out of the process and thus affected the sample size.

To summarise, regarding socio-demographic factors these Basotho woman demonstrated a low risk of breast cancer. The majority was married or had married, and had a low level of education and low income, while approximately equal numbers of patients resided in rural and urban areas.

5.2.2.2 Lifestyle factors

Increased alcohol intake, especially about 3 units or more per day, increases risk of breast cancer (Tan *et al*., 2006:2; Key *et al*., 2003:413) while moderate drinking (1 drink/day) (Tan *et al*., 2006:2) on a regular basis increases risk of death (Grant, 2008:966; Tan *et al*., 2006:2) mainly if there is a history of alcohol use, benign breast disease, and oestrogen or HRT (Grant, 2008:966). Alcohol increases risk because it possibly increases endogenous oestrogen levels (Key *et al*., 2003:414; Travis & Key). Most patients in the current study were non-drinkers (48.6%) and light drinkers (36.5%) and thus had a low risk of breast cancer whereas Californian patients had reported a high frequency of drinking alcohol although the intake was not quantified (Wrensch *et al*., 2003:92). Ogundiran *et al*. (2010:687) also reported that Nigerian patients were more likely to have consumed more alcohol than their controls. In the present study, however, it was not determined which patients may have once used alcohol previously, but had stopped by the time of the study, and as a result these patients may have been misclassified as non-drinkers. Alcoholic drinks consumed by the current patients included beer (Hansa & Castle) (38.5%), traditional beer (15.4%), and wines (red 9.6%, white 5.8%).

In the present study, there were a few patients who were heavy drinkers (3.8%) resulting in their total energy intakes much exceeding the EER. Chronic alcohol abuse removes nutrients from the diet by replacing food intake with alcohol, as well as interfering with the body's metabolism of nutrients (Whitney & Rolfes, 2010:236). Alcohol intake has a negative impact on the nature or biological value of the dietary factors thought to be cancer protective, by reducing intakes of nutrients including folate, β-carotene, lutein or zeaxanthin, and vitamin C (Tan *et al*., 2006:3), and thus is associated with increased risk for breast cancer. Physical activity of all types protects against postmenopausal breast cancer (AICR, 2008:8) while sedentary behaviours increase

cancer risk (Kruk, 2009:443; AICR, 2007:15). The risk may be reduced by decreasing endogenous oestrogen exposure (Friedenreich, 2001:15), obesity (Goedecke *et al*., 2006:72; Popkin & Du, 2003:3899) and abdominal fat mass, and by improving immune function (Friedenreich, 2001:15).

The majority (82.6%) of the women in the present study had a sedentary lifestyle (PAL: 1- 1.39 METs) placing them into a high risk category of breast cancer compared to 29.7% of the Indian patients who were sedentary (Puri *et al*., 2009:4). A sedentary lifestyle is a level of inactivity below the threshold of the beneficial health effects of regular physical activity (Wellman & Kamp, 2008:291). The median PAL value for the current patients was 0.74 METs ranging from 0.04 METs (sedentary category) to 1.72 METs (active category). The current patients were categorised as sedentary because they were not engaged in any physical exercises, did little household activities, and used cars as their modes of transportation.

Sedentary lifestyle choices can lead to sedentary death syndrome (SeDs), a term which collectively refers to the life-threatening diseases of lifestyle such as cardiovascular disease (CVD), hypertension, diabetes, dyslipidaemia, obesity, overweight, and increased rates of death (Wellman & Kamp, 2008:292). The frequency, duration, and intensity of physical activity are associated with health benefits and can help decrease these diseases related to lifestyle (Puoane *et al*., 2008:77).

In summary, these Basotho women demonstrated a low risk for breast cancer development based on drinking habits. Regarding physical activity levels, the majority of the current patients had a low physical activity and thus a high risk for developing breast cancer as well as other diseases of lifestyle.

5.2.2.3 Reproductive factors

Contraception plays a key role in women's reproductive health through prevention of pregnancies that are too early, too close, and too many (WHO, 2001). Oral contraceptives have hormones which may have a protective anovulation effect on the breast, while on the other hand may stimulate mitotic activity in the breast tissue due to the mixture of oestrogen and progesterone (Clemons & Goss, 2001:277). Duration of OC has an impact on breast cancer risk, having a small increase with recent use (Vorobiof *et al*., 2001:126) while long-term use increases life-time exposure to oestrogen and may influence the risk of cancer by changing the endogenous hormonal milieu (Sasco, 2001:322). Sprague *et al*. (2008:406) found no risk association between duration of OC use and breast cancer development in US patients who were predominately white women, while Ozmen and associates (2009:37) found a decreased risk in Turkish women.

Most (65.4%) of the current participants had not used OC at the time of the interview and as a result had a low risk for breast cancer. About a third (34.6%) of the current patients had used OC compared to only 17.7% of North Indian breast cancer patients (Puri *et al*., 2009:4). Of the patients who used OC, the majority (88.9%) (n=18) had used them for a long time (>1 year),

although there were no patients who had started using OC before the age of 18 years. The median age of OC use for the present study was 25.5 years (min 21; max 40). The pill-form was mostly used in the present study compared to a quarter of respondents studied by Shah and Shrestha (2004:2) in Jabalpur, Nepal. Other forms of OC used by the present study sample included "natural methods", hormonal injections, and cervical caps. Multiparity reduces endogenous oestrogen levels over time thus decreasing level of risk (Fregene & Newman, 2005:1543) while nulliparity leads to high concentrations of prolactin which increases the risk for breast cancer (Travis & Key, 2003:243). However, among Turkish women Ozmen *et al*. (2009:37) had discovered that nulliparity was associated with decreased risk. About eight out of ten (80.8%) of the current patients had children at the time of the interview placing them into a low risk category. The number of children ranged from one child up to ten children per patient. According to Wrensch *et al*. (2003:92) the risk for breast cancer is reduced for women having given birth three or more times, while Sprague *et al*. (2008:406) states that having few children increases risk. In the current study the majority (65.3%) had three or more children while 34.7% had less than three children.

Breast feeding protects women against breast cancer (AIRC, 2008:5) through several ways including hormonal changes in the body (Lord *et al*., 2008:1723; Wrensch *et al*., 2003:93; Travis & Key, 2003:240), delayed ovulation, change in the hormonal environment of the breast, and excretion of carcinogenic agents (Lord *et al*., 2008:1723). Breast feeding hormonal changes are associated with delayed return of a new mother's menstrual periods thus reducing a woman's lifetime exposure to hormones such as oestrogen (AICR, 2008:5; Clemons & Goss, 2001:276) and risk for breast cancer as result. According to Fregene and Newman (2005:1543), long breast feeding (±16 months) also decreases the risk.

The majority (86.8%) in the present study had breastfed for 12 months or more corresponding to a low risk. The median age at first breast feeding was 22 years (min 16; max 39). Only 28.6% had breastfed at the age of 20 years or younger (≤20 years) while 8.5% had started breastfeeding at 30 years or older (≥30 years). Only a small percentage (8.5%) had never breastfed. Total duration of breast feeding in this study ranged from 6 months to 380 months placing patients at medium (6 – 11 months) (10.9%) and low (≥12 months) (86.8%) risk for breast cancer, respectively.

According to the analysis of the present results, patients had low risk due to their reproductive patterns. The finding is supported by Fregene and Newman (2005:1543) who indicated that women from Sub-Saharan Africa have low incidences of breast cancer due to the gynaecologic and reproductive patterns which cause them to experience fewer ovulatory cycles over a lifetime. These reproductive patterns include late menarche, multiparity, young age at child bearing, and long breast feeding which lead to lower endogenous oestrogen levels over time and thus reduce breast cancer risk. Age at first pregnancy was however not determined in this study.

Regarding reproductive factors the current patients had low risk of breast cancer because they had children and had breastfed for 12 months or more. Most Basotho women had not used OC at the time of the interview and as a result had a low risk for breast cancer.

5.2.2.4 Anthropometric measurement

Central adiposity has a higher risk of breast cancer than fat distributed over the hips, buttocks, and lower extremities (Friedenreich, 2001:17). The risk is increased through multiple hormonal and metabolic changes (MacInnis *et al*., 2004:2117; Friedenreich, 2001:4). Waist circumference (WC) of more than 88 cm is a predictor of risk for health in general for women and indicates an increased risk equal to a BMI of 25-34.9 kg/m^2 (Thomas & Bishop, 2008:63). WC together with fat percentage is an important indicator of obesity related health risks and heart failure (Gee *et al*., 2008:540). A WC of 80 cm or more also increases risk of insulin resistance and the metabolic syndrome (interrelated risk factors for CVD and diabetes including dysglycaemia, raised blood pressure, elevated triglyceride levels, low high-density lipoprotein cholesterol levels, and central obesity) in sub-Saharan African women (Alberti *et al*., 2009:1640).

Obesity is the disease whereby excess body fat has accumulated to an extent that health may be negatively affected (WHO, 2000:894) while overweight is a state in which weight exceeds a standard based on height (Gee *et al*., 2008:539). For overweight and obesity to develop extended exposure to environmental factors including high-fat diet and physical inactivity are necessary (Mollentze, 2006:44). The negative health consequences of obesity include insulin resistance, type 2 diabetes, dyslipidaemia, hypertension, coronary heart disease, hyperuricaemia, osteoarthritis, and malignancies such as cancer of the breast in postmenopausal women, endometrium, and colon (WHO, 2000:894), gallbladder disease, and mortality (Gee *et al*., 2008:541).

Approximately 73.1% of the current patients had high waist-hip-ratio (WHR) (≥0.85) and a high risk since WHR is related to an increased risk for breast cancer especially in postmenopausal women (Nemesure *et al*., 2009:391). Only 17.3% of the current patients had a WHR less than 0.80 and thus a low risk since a WHR of less than 0.80 is associated with a reduced risk (Ziegler, 1997:927). The median WHR for the present study was 0.9 (min 0.73: max 1), which is above the healthy range.

Almost seven out of ten (69.1%) patients from the present study had high WC (>88 cm) and a high risk of breast cancer. The majority (76.9%) of the current patients had a WC of 80 cm or more and as a result were at an increased risk of insulin resistance and the metabolic syndrome. Most (63.5%) of the current patients were obese (BMI >30 kg/m^2) compared to only 19.1% of Nepal patients (Shah & Shrestha, 2004:3). About two out of ten (21.2%) of the current patients were overweight (BMI 27-30 kg/m^2). Thus the majority (84.7%) of these Basotho patients had above normal BMIs, which corresponds to the prevalence of overweight and obesity reported for Lesotho women in general (FAO, 2010:3).

Only 13.5% of the current patients had a desirable or healthy BMI (23-26 kg/m^2) and thus a low risk for breast cancer. Only a few (1.9%) patients in the current study were underweight compared to 42.8% of Nepal patients (Shah & Shrestha, 2004:3). Although being underweight lowers the risk for breast cancer, it increases the risk of other diseases due to insufficient intake of nutrients or energy. Undernutrition may be caused by a deficient intake, increased requirements, or an inability to absorb or use nutrients (Smolin & Grosvenor, 2008:11). The symptoms of undernutrition include becoming extremely thin, losing muscle tissue, and becoming prone to infections and diseases (Whitney & Rolfes, 2010:21). The median BMI for the current patients was 32.7 kg/m^2 ranging from 17.7 kg/m^2 while the Californian patients had a mean BMI of 20.6 kg/m^2 ranging from 18.5 kg/m^2 (Wrensch *et al*., 2003:91) indicating that the current patients were more obese.

In Nigerian patients there was no association found between body weight and breast cancer risk (Ogundiran *et al*., 2010:688). Berstad *et al*. (2020:1534) in their study had found that African-American and white premenopausal women with a recent BMI of 35kg/m^2 or higher had a 19% lower risk of breast cancer than women reporting a recent BMI of less than 25kg/ m^2.

Most (67.2%) of the current patients had height within the recommendations (153 – 169cm) and thus a medium risk. The median height for the current patients was 157.5 cm (min 134: max 183) similar to those of the Nigerian patients (160.2 cm) as reported by Ogundiran *et al*. (2010:687) but lower than of the Californian patients (165 cm) (Wrensch *et al*., 2003:91) indicating that the current patients were shorter. Height relates to nutrition (Nemesure *et al*., 2009:391) indicating differences in energy intake, dietary patterns in early life (Chang *et al*., 2006:337), adiposity associated with adult energy intake leading to increased risk for breast cancer (Chang *et al*., 2006:336; Friedenreich, 2001:15), and genetic differences.

In summary, most patients in this study in contrast to Nepal patients were obese and overweight and as a result had a high risk of breast cancer. Height, however, was similar in the Basotho women compared to the Nigerian women, and fell within the recommendations, resulting in them having a medium risk for breast cancer.

5.2.2.5 Overall dietary intake

Overall dietary quality and adequacy will be discussed according to the intakes of total energy, fat, protein, carbohydrates, phytochemicals and micronutrients, and methods of cooking.

i) Total energy

Energy is defined as the "capacity to do work". To survive, the human body needs a regular supply of energy from carbohydrates, proteins, fats, and alcohol in the diet (Frary & Johnson, 2008:23). Carbohydrates, proteins, and fats metabolism are altered by tumour growth and tumours also have a consistent demand for glucose (Grant, 2008:968).

Energy intakes change breast cancer risk through interaction of hormones (Dossus & Kaaks, 2008:556). Low (restricted) energy intakes are associated with low rates of cell reproduction during premalignant and malignant stages of the cancer process (Milner, 2003:3824), and suppresses tumour growth (Chang *et al*., 2006:336). Thus low energy intakes correspond with a low risk for breast cancer (Chang *et al*., 2006:334; Milner, 2003:3824).

The median total energy intake (5414.5 kJ; 1295 kcal) in this study was lower than the EER for adults (10, 093 kJ; 2, 403 kcal). The EER is the average dietary energy intake predicted to maintain energy balance in a healthy person of a defined age, gender, weight, height, and level of physical activity consistent with good health (Lee & Nieman, 2010:233).In light of the fact that these patients were obese, it is possible that "flat-slope syndrome", which refers to the phenomenon that subjects with high actual consumptions often underestimate the amount of food and drink they recall (Lee & Nieman, 2010:81**)**, may have played a role. The group was also very inactive, which may have contributed to the high level of obesity despite apparent low energy intakes. Furthermore, nonexistence activity thermogenesis (NEAT) and sedentary lifestyle may be important in obesity. NEAT is the energy expended for activities that use energy such as going to work, typing, doing yard work, toe-tipping, or fidgeting, which is not included during sleeping, eating, or sports-like exercise (Gee *et al*., 2008:536). However, there is an apparent lack of association between low energy intakes and high prevalence of overweight and obesity.

Individual energy intake in the present study ranged from a minimum of 1690 kJ to the maximum of 63 190 kJ per day. The low energy intake (1690 kJ) could have been due to a low food intake due nausea and food restrictions such as low fat intake, following a mastectomy. However, one patient who reported a low food intake had a healthy BMI (23kg/m^2). The high maximum energy intake (63 190 kJ; 15 117 kcal) could have been due to the high alcohol consumption, as well as the high meat consumption reported by a minority (1.9%) of the patients. A minority of the patients were obese (29kg/m^2). High intake of alcohol moves nutrients from the diet and interferes with the metabolism of cancer protective dietary factors and lowering levels of folate, β-carotene, lutein and zeaxanthin, and vitamin C (Tan *et al*., 2003:3).

ii) Fat intake

The median fat intake in the present study was 21.5 g / day (min 5; max 114g) but there are currently no DRIs for fat intakes. The Recommended Dietary Allowances (RDA) or adequate intake (AI) is not quantified at present, since there is insufficient data available to determine total fat requirements for adults at risk of inadequacy, or to prevent chronic diseases. There is also presently no tolerable upper intake level (UL) established for total fat because there is no level identified that is specifically associated with adverse effect (Lee & Nieman, 2010:29). Instead it is recommended that fat intake should not exceed 20% to 35% of the total energy, and that no more than 10% of energy should be contributed by saturated fatty acids (Stang, 2008:251) since saturated fats are associated with the development of chronic diseases. Most (57.7%) of the current patients had a low self-reported fat intake (<20%) and thus a low risk of breast cancer

because a diet high in fat (40% - 45%) of total energy intake is associated with increased risk (Carter & Church, 2009:7). It is also possible that "flat-slope syndrome" (the phenomenon that subjects with high actual consumptions often underestimate the amount of food and drink they recall) (Lee & Nieman, 2010:81**)**, may have occurred with the reporting of fat intake in this study.

The MUFAs such as olive oils are protective against cancer (Lof *et al*., 2007:1570; de Pablo *et al*., 2002:948) while PUFAs are associated with high risk because they are involved in the inflammatory process related to cell motility and survival (Ion *et al*., 2010:81). Edefonti *et al*. (2008:611) found that Italian women with higher unsaturated fat intakes had a slightly reduced risk for breast cancer, while there was no clear trend for ovarian cancer. The unsaturated fat dietary pattern in these Italian women was rich in vegetable fat and vitamin E, MUFAs and PUFAs.

Furthermore, PUFAs can be dangerous when subjected to routine frying or cooking of which they can generate high levels of toxic aldehyde products able to promote CVD and cancer (Gallagher, 2008:59). These Basotho women, however, mostly reported boiling their foods as will be discussed later.

In the current study, olive oil (a source of predominantly MUFAs) was consumed by a minority (1.9%) of the patients but then on a daily basis. The fat source mostly consumed on daily basis in this study was sunflower cooking oil (86.5%), brick margarine (11.5%) and mayonnaise (1.9%) which are all rich sources of PUFAs associated with increased breast cancer risk.

iii) Milk and dairy products

Dairy products contain substances thought to play a protective role in the development of breast cancer and also increase risk (Hjartáker *et al*., 2001:888). The majority of patients in the present study had low intakes of milk and dairy products. Dairy products consumed were mostly full-cream (28.8%), although small percentages also consumed cheese (9.6%), yoghurt (5.7%), low-fat milk (2%), and skimmed milk (1.9%). Dairy products were mostly consumed weekly rather than daily.

The Western dietary pattern composed of high loadings of refined grains, high-fat dairy products, meat and processed meat, eggs, margarine, butter and mayonnaise, potato, French fries, sweets, soda and snacks was not significantly associated with breast cancer risk in African-American women (Agurs-Collins *et al*., 2009:624). These Basotho women's diet was mostly transitional because it was composed of low fibre foods, high in sugar, low fat, and low plant foods**.** The nutrition transition is a stepwise progression of features in dietary patterns and nutrient intakes (Vorster *et al*., 2005:761). Nutrition transition is associated with an increase of lifestyle diseases including type 2 diabetes, CVD, hypertension, obesity, cancer, and related non-communicable diseases (NCDS) (Raschke *et al*., 2009:5).

iv) Protein intake

When protein was expressed as a percentage of total energy intake, the majority (92.3%) of the current patients consumed protein at the recommended level (10% - 35%) associated with reduced risk of chronic disease while providing adequate intake of essential nutrients (Smolin & Grosvenor, 2008:38).

A diet low in protein is low in essential amino acids and reduces serum IGF-I levels in humans (Dossus & Kaaks, 2008:557; Key *et al*., 2003:414). Protein intake ranged from 12 to 191 grams indicating a low and above recommended intakes demonstrating that some patients consumed below and some above the optimum level (RDA 46g / day) (Whitney & Rolfes, 2010:A). Even though the protein intake of some patients was above the recommendations, the intake might be appropriate because some of these patients were in hospital at the time of the interview and protein and energy needs of cancer patients are elevated above those of healthy people. The protein and energy needs of hospitalised patients can increase two or more fold as a result of hypermetabolism accompanying trauma, infection, burns, and surgical recovery. Protein is the principal compound upon which the body structure and function is based (Lee & Nieman, 2010:3130), including playing roles as enzymes, hormones, immunoproteins, and for transportation (Gallagher, 2008:59). Protein-energy-malnutrition (PEM) is common in people with cancer and may be either primary (due to inadequate food intake) or secondary (due to other diseases leading to insufficient food intake, inadequate nutrient absorption or utilisation, increased nutritional requirement, and increased nutrient losses) (Lee & Nieman, 2010:3130).

The median for protein was 0.63 g/kg/day (min 0.2g/kg/day; max 3.8 g/kg/day) similar to the EAR for adults (0.66g/kg/day) (Mahan *et a*l., 2012:Cover page) while the maximum intake was above the recommendations by 3.14 grams. Protein serves as a functional component of body tissues and enzymes and as a fuel source.

Analysis of the intake of meat and meat substitutes according to the FGP (1992) and the Dietary Guidelines for Americans (2010) has indicated that the majority had low intake and thus a low risk of breast cancer. A diet composed of low intake of meat (saturated fats) and starches (energy-dense) and high in legumes was associated with a reduced risk of breast cancer in Asian women (Wu *et al*., 2009:45). However, Edefonti *et al*. (2008:611) found no association between animal dietary pattern and cancers of the breast and ovary in Italian women. The animal dietary pattern had greatest loads of animal protein and fat, calcium, cholesterol, saturated fatty acids, riboflavin, zinc, and phosphorus.

In the current study meat and meat substitutes were mostly consumed on a weekly rather than daily basis and included eggs, legumes (beans, peas, peanut butter, & lentils), and chicken (livers, heads, & feet). Other meats such as beef, mutton, and pork were also consumed but occasionally, while fish was mostly pilchards. Processed meats consumed included polony, corned beef, viennas, and ham but by small percentages. High intakes of red meat (beef, lamb,

pork) or processed meat increase the risk of cancer (AICR, 2008:7; Ray, 2005:15) but there is no evidence connecting white meat to cancer risk, while fish is protective against cancer (Ray, 2005:15). However, when all meats (red, white, and processed) are combined they are also associated with increased risk (AICR, 2008:7).

In this study eggs and chicken were mostly consumed due to their affordable price while other meats were occasionally consumed due to their high price and most often were consumed on occasions and/or only by the middle-class households. Fish consumed was mostly pilchards because it was affordable and could be stored easily without the need of cold storage.

a) Carbohydrate intake

Carbohydrates are produced by plants and are the major source of energy in the diets comprising around half the total energy (Gallagher, 2008:42). The median intake for carbohydrate was 210 grams per day and higher than the EAR (100 g/day) for adults by 110 grams (Lee & Nieman, 2010:20). The majority (57.7%) of the current patients consumed above the recommended levels (>65%) (Smolin & Grosvenor, 2008:38). Carbohydrate intake ranged from 70 grams to 633 grams per day indicating that some patients had very low intakes while others had more than the recommendations. The values of carbohydrates are based on the minimum amount of glucose needed by the brain and are typically exceeded in order for a person to meet the energy needs of the body while consuming an acceptable quantity of energy from fats and protein (Lee & Nieman, 2010:28).

The diet of the current patients was mainly based on maize papa (stiff porridge). The majority consumed maize papa and brown bread on a daily basis. Other cereal products consumed included fermented (motoho) and unfermented (lesheleshele) soft porridges which were either made of sorghum flour or maize meal. Breakfast cereals and white rice were also consumed though only by small percentages, only in the urban areas and by people in the middle-income group, while rice was mainly consumed on Sundays and/or on special occasions.

Traditionally, maize was ground using grinding stones, however, the practice is changing due to advanced milling facilities. The hammer mills are still common in the rural areas since people still produce their own cereals which include maize, sorghum, and wheat (FAO, 2010:18) while in the urban areas commercial ground maize is mostly consumed. In this study, maize and sorghum were classified as commercial (low fibre) or home (high fibre) ground in order to determine the fibre content of the products, however, the questionnaire may not have fully captured the patients' fibre intake. Although commercial ground products contain low fibre, they were consumed by the majority of the patients. The commercial products are fortified with vitamins and minerals. Fortification is the addition of nutrients which may or may not have been present in the original foods. Foods are fortified to prevent vitamin and mineral deficiencies and promote health in a population (Smolin & Grosvenor, 2008:321). Because the patients' diet was low in fibre it was, however, also low in lignin because it is found in fiber rich foods.

Most (67.3%) of the current patients consumed sugar. The sugar was used to sweeten tea, coffee, motoho, and lesheleshele.

b) Phytochemicals and micronutrients intake

Fruits and vegetables contain chemical substances which defend the body against cancer (Thomas & Bishop, 2008:222; Rolfes *et al*., 2006:391). The anticarcinogenic agents inhibit oxidative processes involved in carcinogenesis, carcinogen metabolism, and cell proliferation, and enhance the cellular immune system (Dorjgochoo *et al*., 2009:381). Although the questionnaire may not have fully captured the patients' intakes of specific antioxidants and phytochemicals, the evident pattern of low intake and low variety of these foods in the diets of these Basotho women alludes to an increased risk for breast cancer.

Patients in the current study had fruit intake lower than the recommendations while half met the recommendations of vegetables per day. Green leafy vegetables (moroho) were used as accompaniments of maize papa, included were cabbage, spinach, turnip, radish, lihaba (pumpkin green leaves), and the indigenous green leafy such as bobatsi, theepe, leshoabe, and leharasoana. However, wild vegetables and fruit are available seasonally. Other vegetables which formed part of the diet included pumpkin, beetroot, green-pepper, and carrots although they were only consumed on Sundays, special occasions, or by households in the middle class who could afford to purchase them frequently.

Fruits frequently consumed by most patients included apples and bananas. Other fruits consumed included pears, oranges, peaches, guava, paw-paw, and grapes but were by small percentages. Peaches are the most common and affordable fruit in Lesotho but are only available between October and April while other fruits are mostly imported or grown in small quantities, hence why they are not generally accessible for consumption due to their high cost (FAO, 2010:18). Indigenous fruits were also consumed when in season although it was consumed by small percentages, included were prickly pears, blackberries, and gooseberries.

Phyto-oestrogens are found in fiber rich foods (Sonestedt *et al*., 2008:2203). Phyto-oestrogens have antioxidant activity and slow the growth of breast cancer (Rolfes *et al*., 2006:466), interrupt cancer development, and affect health by interfering with the action of human oestrogen (Smolin & Grosvenor, 2008:397). Foods rich in fibre consumed in this study included; beans and peas, sorghum and wheat products, and home ground maize papa.

Lignin in fiber rich foods blocks oestrogen activity in the cells possibly reducing the risk of breast cancer and may influence the enterohepatic circulation of oestrogens, increase the excretion of oestrogens in the faeces, and give reduced levels of circulating oestrogens (Sonestedt *et al*., 2008:2203; Key *et al*., 2003:415). Sources of lignin consumed in this study were apples, sunflower cooking oil, beans and peas, sorghum and wheat products, and home ground maize papa.

Isoflavones, daidzein, and genistein are phytochemicals found in soybeans. These chemicals are weak oestrogens responsible for lowering levels of ovarian hormones and decreasing breast cancer rates in Asian women (Lu *et al*., 2000:4112). Although legumes were consumed by the current patients, soy products were excluded with only beans, peas, peanut butter, and lentils included.

Cruciferous vegetables protect against breast cancer risk due to the chemicals substances they contain (Terry *et al*., 2008:284). Cruciferous vegetables also modulate oestrogen metabolism, thus lower the risk of oestrogen dependent cancers like of the breast (Ray, 2005:17). In this study cruciferous vegetables consumed included cabbage, turnip, and radish.

Berries, grapes, and peanuts decrease breast cancer risk due to the chemopreventive substances they contain, including resveratrol, vitamins C, E, and folate, small amount of calcium and selenium, beta- and alpha-carotene, polyphenols, and phytosterols. Berries inhibit growth of premalignant cells through down regulating genes associated with tumour development (Ray, 2005:18). In the current study food sources of the above chemical substances included peanut butter, blackberries, gooseberries, and grapes although they were consumed by small percentages and only when in season.

Perillyl alcohol, a monoterpene, is an important chemopreventive agent found in citrus peel (Ray, 2005:18). Although oranges were consumed by a small percentage in the present study, it was only when they were in season. It was, however, not determined whether the patients consumed peels as well.

Thus, although some sources of phytochemicals are available to these Basotho women, they may be at an increased risk for breast cancer due to lack of variety of fruits and vegetables consumed on a regular basis., since varied diet has both genetic (antioxidant) and disease-specific effects such as tumour suppressor (Lock *et al*., 2005:104). Vegetables, fruits, whole grains, and beans are low-energy dense but high in nutrients which may protect against weight gain and breast cancer (AICR, 2009:Online).

Different studies had reported different results regarding plant foods intakes. Included were Fung *et al*. (2011:653) who found no risk between ER+ and fruit and vegetables, and whole grains intake in Nurses' Health study in the US states. Edefonti *et al*. (2008:611) found no risk associated with ovarian cancer in women consuming the highest intakes of the vitamin and fibre pattern in Italian women. The vitamin and fibre pattern had greatest loads of vitamin C and total fibre, total folate, potassium, β-carotene equivalent, soluble carbohydrates, and vitamin B_6. Agurs-Collins *et al*. (2009:624) in a Black women's health study had discovered that prudent dietary pattern and Western dietary pattern were not associated with breast cancer risk. The prudent dietary pattern was composed of higher intakes of cruciferous and other vegetables, fruit, whole grains, cereals, beans low-fat dairy products, fish, and poultry.

c) Coffee and tea

Coffee contains caffeine and cancer preventing chemicals. Caffeine is associated with altered levels of SHBG (Kotsopoulos *et al*., 2007:915; Baker *et al*., 2006:166) and oestradiol, possibly reducing the risk of breast cancer development (Baker *et al*., 2006:166). Caffeine is also negatively associated with bioavailable testosterone (Kotsopoulos *et al*., 2007:915). Coffee was consumed only by a small percentage (25.0%) of the patients in the present study.

Tea prevents cancer through chemical substances it contains, included are polyphenolic compounds (catechins) which inhibit growth, induce cell cycle arrest and apoptosis in different cancer cell lines (Ray, 2005:18), and tannins which inhibit carcinogens activation and cancer promotion and acts as antioxidants (Smolin & Grosvenor, 2008:395). Most (59.7%) patients in the present study consumed tea on a daily basis.

d) Food preparation methods

Cooking methods such as grilling (broiling), frying, and braaing are associated with breast cancer risk because they form potentially carcinogenic products such as heterocyclic amines and polycyclic aromatic hydrocarbons (Pala *et al*., 2009:456) which have potential genotoxic agents associated with breast cancer risk. There is, however, no evidence linking cooking methods such as boiling or steaming with cancer risk (Kotsopoulos *et al*., 2006:346). In the present study boiling was the commonly used method of cooking foods while other methods used were frying and steaming.

In summary, regarding the usual dietary intake the majority of the patients had low intakes of total energy, fat, milk and dairy products, and meat and meat substitutes and thus a risk of chronic diseases. The intake of fruit was also low while half met the recommendations of vegetables. However, even those that met the required amounts may still be at an increased risk of breast cancer due to an overall lack of variety in the types of fruits and vegetables consumed on a regular basis. Alcohol consumption was low on average with only a few individuals with high intakes. Tea was consumed by most patients and coffee by only one out of four. Boiling was the commonly used method of cooking.

5.3 In conclusion

Regarding the non-modifiable risk factors for breast cancer, the risk profile of these Basotho women were different from that typically reported for black women in Africa in that they were diagnosed with breast cancer at an older age. In this regard they were more similar to African-American women, although they experienced both menarche and menopause at an older age than their African-American counterparts. The current patients had few relatives with cancer compared to Nigerian and American patients who were reported to be more likely than their controls to have first-degree relatives with breast cancer. Overall these Basotho women thus seemed to score low on the non-modifiable risks to develop breast cancer – with most being

diagnosed at an older age; seemingly having a low family history of the disease; and starting and stopping menstrual cycles at older ages.

Regarding the modifiable factors for breast cancer, the current patients also had lower levels of education and income, used less OC and drank less than their North American counterparts, all of which concurs with a lower risk for breast cancer. Furthermore, most of the Basotho women were, or had been married at the time of the study, had given birth, had breastfed for substantial periods of time, and had low consumption of meat (particularly red meat), drank tea on a regular basis, and did not use cooking methods that produce cancer promoting agents - all of which also protect against breast cancer development.

However, with regard to physical activity levels, the Basotho women were very inactive –more so than breast cancer patients from other developing countries like India. Concurrently they were very obese with BMIs, WCs, and WHRs that put them at high overall risk for chronic diseases of lifestyle. While their self-reported macronutrient and energy intakes and the macronutrient distribution of the diet concurred with a low risk for breast cancer, underreporting of fat intakes cannot be guaranteed in this study group. However, low intakes of fibre rich foods, low intakes of fruit, low variety of plant foods, and increasing intakes of fat and sugar in these patients show evidence of the typical nutrition transition taking place. In Lesotho, South Africa and other developing countries this phenomenon has been well described and entails the moving away from the prudent traditional diets towards more westernised eating patterns and lifestyles associated with increased morbidity and mortality from chronic diseases of lifestyle, including cancer (Popkin & Du, 2003:3898). Specifically regarding the risk of breast cancer, the low intakes of fruits, and the low dietary variety particularly with regard to fruit, vegetables and starches in the diet, puts these Basotho women at risk of low intakes of protective antioxidants and phytochemicals.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

In this study the prevalence of the known non-modifiable and modifiable risk factors in adult Basotho women diagnosed with breast cancer at the Queen II hospital were determined. The conclusions**,** the limitations of the study, as well as the recommendations based on these conclusions are summarised in this chapter.

6.1 Conclusions

Regarding the non-modifiable risk factors for breast cancer the majority (78.7%) of Basotho women in this study were diagnosed with breast cancer at an age of 46 years and older similar to the African-American women but different from the typical profile of African women who are usually diagnosed at age range of 35 to 45 years. The Basotho women experienced menarche at an older age (>12 years) than their African-American and white South African counterparts. This observation is similar to that of rural black women in South Africa and Northwest India. These Basotho women were young at menopause (≤54 years) similar to white American women but older than African-Americans. The Basotho women reached natural menopause without the use of HRT. The Basotho women had a tendency of secrecy regarding family history, however, 33.0% of the patients had reported having relatives with cancers of the breast, cervix, colon, and prostate.

With regard to modifiable risk factors for breast cancer, the Basotho women had a low level of breast cancer risk with regard to levels of education, which was low; similar to Bahraini women in the Middle East, income which was low compared to North American women, low OC-use; and low drinking habits. The current patients were or had also been married at the time of the study, had children, breastfed for 12 months or more, had low intake of meat particularly red meat, drank tea regularly, and used cooking methods that did not produce cancer promoting agents protecting against breast cancer development as a result.

However, these Basotho women were very inactive compared to breast cancer patients from India and were also very obese having high BMI, WC, and WHR putting them at a high overall risk for chronic diseases of lifestyle. The majority (67.2%) of the Basotho women were within the recommended height (153 - 169 cm) similar to the Nigerian women therefore corresponding to a medium risk of breast cancer. The energy and macronutrient intakes were low corresponding to a low risk of breast cancer risk, nevertheless, the low intakes of plant foods especially low intakes of fibre foods, fruits, and low variety of plant foods had put the current patients at risk of breast cancer and other diseases due to low supply of protective antioxidants and phytochemicals.

6.2 Limitations of the study

The small sample size in the current study (n=52) may not have been representative of the whole breast cancer patients seen at the Queen II hospital. The small subject number could, however, not be avoided, due to time constraints (3 years) for the degree, the slow diagnosis

process of the patients, and lack of funding for the study. It is therefore recommended that this study be expanded in Lesotho to include more patients.

Unfortunately there was no control group in this study therefore it is not possible to make any judgments on whether the identified factors are any different from what may be found in healthy controls. However, this was an observational study and as a result a control group was not essential. Nevertheless, it is recommended that in an expansion of this study the prevalence of the known risk factors be determined for a control as well.

In the current study, hormone and genetic susceptibility, endogenous hormones, and environmental pollutants as risk factors for breast cancer were not determined due to lack of funds. During results analysis, it was also discovered that the questionnaire might not have fully captured certain information, namely: previous history of alcohol consumption (those who once drank but had stopped); fibre intake, intake levels of individual antioxidants and phytochemicals; personal history of breast cancer (whether the disease was a new case, recurrence, or development of a new cancer on another breast); and age at first pregnancy. It is therefore recommended that in an expansion of this study these risk factors be fully determined.

The possibility of over- and/or under-reporting was not determined for this study. The misreporting could have been calculated using the ratio of energy intake (EI) to basal metabolic rate (BMR), according to the Goldberg (1991). EI could have been calculated from the data analysis and BMR could have been estimated using the Schofield equation (Thomas & Bishop, 2007:858) based on BMI, age, and gender. According to Black (2000:1127), the Goldberg (1991) cut-offs have various limitations and were not considered, however, the cut-off values for EI:BMR used by Farajian *et al*. (2004:576), could possibly have been used for this study. . It is recommended that misreporting be explored in future studies.

6.3 Recommendations

Since the patients in this study ranged from a young age it is recommended that early detection through mammography and routine screening are practiced for those at high risk. The screening programs ought to start at an age of 40 years in Basotho women in order to aim for better probability of survival. For screening to take place training of clinicians and laboratory technicians to ensure proper tissue sampling and fixation is critical. Pathology facilities which are not in place at the moment must also be provided to process the specimens since such services are still obtainable from the neighbouring country, South Africa.

It is recommended that patients be supported financially and be transported from their residential places to the health institutes for their treatment since the majority of these patients had a low income level and had to travel long distances since the treatment facilities are located in Maseru and Bloemfontein.

The Ministry of Health and Social Welfare ought to have, and train, community health workers (CWH). The CHW's roles should include health education enclosing breast cancer

education and advocacy around curability; health services provision; and patient navigation (helping patients find their ways through the continuum of breast cancer screening, diagnosis, and treatment). There seemed to be a perception of stigma in patients diagnosed with breast cancer due to the results of the treatment especially regarding mastectomy. Therefore, education efforts need to address the reality that many women, especially those with less income and education, may not seek care when they feel a breast mass because they are not aware of what it means but are concerned about the stigma of cancer and being rejected. The CHW should create awareness of the benefits of detection and treatment and should educate women about breast health in order for women to be better poised to seek essential services. In addition to education, the CHW should also provide clinical breast examination (CBE) as a form of early detection and encourage the patients to practice breast-self examination (BSE).

The government through ministries of agriculture and health and social welfare is recommended to provide the community with nutritional education regarding the importance of good nutrition, physical activity, and maintenance of healthy body weight in order to avoid chronic diseases of lifestyle. Emphasis of good nutrition should focus on the importance of good eating habits, balanced meals, and variety of food intake especially fruits and vegetables. The community must also be encouraged to eat according to the recommendations, and to eat foods in season in order to achieve greater variety in the diet.

To address the problem of obesity, a multi-sectoral approach is needed. The approach should include changes in policy aimed at creating an environment conducive and supportive for change such as promoting physical activity and dietary education in schools in order to prevent obesity in children who are likely to become obese adults. The play of traditional games and household activities for exercise needs in young girls must also be encouraged. The prevention strategies should be culturally sensitive and include programmes to improve the education, status, and economic empowerment of women since within the black African community obesity has positive connotations including symbolising happiness, beauty, affluence, health, and negative HIV/AIDS status. The stakeholders from the government through the ministries of education and health and social welfare need to understand factors contributing to decreased physical activity among girls and adults and the effect of inactivity on health and should initiate programmes to increase activity among communities. A combination of lifestyle behaviours may improve breast cancer survival since a healthy diet and regular exercise has the potential to reduce the risk of co-morbidity (such as other cancers, cardiovascular disease, diabetes, and many other diseases associated with lifestyle behaviours) and improving quality of life through a reduction of the risk on fatigue and depression.

Media could be used to inform the concerned government ministries, non-government organisations (NGOs) dealing with health and nutrition, and the general public about the study findings in order to create awareness. Messages via emails could also be sent to ministries and NGOs to organise presentations regarding the results of the study. However, the findings of this study might not have an impact on policy change due to a small sample size used although it is a representative of the population.

In conclusion, since there has not been any study conducted in Lesotho regarding the prevalence of the known risk factors this study has provided a ground work from which other studies can be conducted. The study provides valuable information that will be useful for policy makers in the fields of health and nutrition. The study has discovered that the Basotho women had a low risk regarding non-modifiable risk factors but a high risk in modifiable risk factors. The study is also unique in the sense that it identified evidence of the typical nutrition transition taking place due to the low intakes of fibre rich foods, low intakes of fruit, low variety of plant foods, and increasing intakes of fat and sugar, and low physical activity in the patients.

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APPENDIX A: Dietary recommendations

USDA food patterns

APPENDIX A_1

For each food group or subgroup[a] recommended average daily intake amounts[b] at all calorie levels. Recommended intakes from vegetable and protein foods subgroups are per week.

calorie level of pattern[c]	**1,000**	**1,200**	**1,400**	**1,600**	**1,800**	**2,000**	**2,200**	**2,400**	**2,600**	**2,800**	**3,000**	**3,200**
Fruits	1 c	1 c	1½ c	1½ c	1½ c	2 c	2 c	2 c	2 c	2½ c	2½ c	2½ c
Vegetables[d]	1 c	1½ c	1½ c	2 c	2½ c	2½ c	3 c	3 c	3½ c	3½ c	4 c	4 c
Dark-green vegetables	½ /wk	1 c/wk	1 /wk	1½ c/wk	1½ c/wk	1½ c/wk	2 c/wk	2 c/wk	2½ c/wk	2½ c/wk	2½ c/wk	2½ c/wk
Red and orange vegetables	2½ c/wk	3 c/wk	3 /wk	4 /wk	5½ c/wk	5½ c/wk	6 c/wk	6 c/wk	7 c/wk	7 c/wk	7½ c/wk	7½ c/wk
Beans and peas (legumes)	½ c/wk	½ c/wk	½ c/wk	1 /wk	1½ c/wk	1½ c/wk	2 c/wk	2 c/wk	2½ c/wk	2½ c/wk	3 c/wk	3 c/wk
Starchy vegetables	2 c/wk	3½ c/wk	3½ c/wk	4 c/wk	5 c/wk	5 c/wk	6 c/wk	6 c/wk	7 c/wk	7 c/wk	8 c/wk	8 c/wk
Other vegetables	1½ c/wk	2½ c/wk	2½ c/wk	3½ c/wk	4 c/wk	4 c/wk	5 c/wk	5 c/wk	5½ c/wk	5½ c/wk	7 c/wk	7 c/wk
Grains[e]	3 oz-eq	4 oz-eq	5 oz-eq	5 oz-eq	6 oz-eq	6 oz-eq	7 oz-eq	8 oz-eq	9 oz-eq	10 oz-eq	10 oz-eq	10 oz-eq
Whole grains	1½ oz-eq	2 oz-eq	2½ oz-eq	3 oz-eq	3 oz-eq	3 oz-eq	3½ oz-eq	4 oz-eq	4½ oz-eq	5 oz-eq	5 oz-eq	5 oz-eq
Enriched grains	1½ oz-eq	2 oz-eq	2½ oz-eq	2 oz-eq	3 oz-eq	3 oz-eq	3½ oz-eq	4 oz-eq	4½ oz-eq	5 oz-eq	5 oz-eq	5 oz-eq
Protein foods[d]	2 oz-eq	3 oz-eq	4 oz-eq	5 oz-eq	5 oz-eq	5½ oz-eq	6 oz-eq	6½ oz-eq	6½ oz-eq	7 oz-eq	7 oz-eq	7 oz-eq
Seafood	3 oz/wk	5 oz/wk	6 oz/wk	8 oz/wk	8 oz/wk	8 oz/wk	9 oz/wk	10 oz/wk	10 oz/wk	11 oz/wk	11 oz/wk	11 oz/wk
Meat, poultry, eggs	10 oz/wk	14 oz/wk	19 oz/wk	24 oz/wk	24 oz/wk	26 oz/wk	29 oz/wk	31 oz/wk	31 oz/wk	34 oz/wk	34 oz/wk	34 oz/wk
Nuts, seeds, soy products	1 oz/wk	2 oz/wk	3 oz/wk	4 oz/wk	4 oz/wk	4 oz/wk	4 oz/wk	5 oz/wk	5 oz/wk	5 oz/wk	5 oz/wk	5 oz/wk
Dairy[f]	2 c	2½ c	2½ c	3 c	3 c	3 c	3 c	3 c	3 c	3 c	3 c	3 c
Oils[g]	15 g	17 g	17 g	22 g	24 g	27 g	29 g	31 g	34 g	36 g	44 g	51 g
Maximum Sofas[h] limit, calories (% of calories)	137 (14%)	121 (10%)	121 (9%)	121 (8%)	161 (9%)	258 (13%)	266 (12%)	330 (14%)	362 (14%)	395 (14%)	459 (15%)	596 (19%)

The DASH eating plan at various levels

APPENDIX A_2

The number of daily servings in a food group vary depending on caloric needs[a]

Food group[d]	1,200 calories	1,400 calories	1,600 calories	1,800 calories	2,000 calories	2,600 calories	3,100 calories	serving sizes
Grains	4–5	5–6	6	6	6–8	10–11	12–13	1 slice bread 1 oz dry cereal[c] ½ cup cooked rice, pasta, or cereal[c]
Vegetables	3–4	3–4	3–4	4–5	4–5	5–6	6	1 cup raw leafy vegetable ½ cup cut-up raw or cooked vegetable ½ cup vegetable juice
Fruits	3–4	4	4	4–5	4–5	5–6	6	1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit ½ cup fruit juice
Fat-free or low-fat milk and milk products	2–3	2–3	2–3	2–3	2–3	3	3–4	1 cup milk or yogurt 1½ oz cheese
Lean meats, poultry, and fish	3 or less	3–4 or less	3–4 or less	6 or less	6 or less	6 or less	6–9	1 oz cooked meats, poultry, or fish 1 egg
Nuts, seeds, and legumes	3 per week	3 per week	3–4 per week	4 per week	4–5 per week	1	1	⅓ cup or 1½ oz nuts 2 Tbsp peanut butter 2 Tbsp or ½ oz seeds ½ cup cooked legumes (dried beans, peas)
Fats and oils	1	1	2	2–3	2–3	3	4	1 tsp soft margarine 1 tsp vegetable oil 1 Tbsp mayonnaise 1 Tbsp salad dressing
Sweets and added sugars	3 or less per week	3 or less per week	3 or less per week	5 or less per week	5 or less per week	< 2	< 2	1 Tbsp sugar 1 Tbsp jelly or jam ½ cup sorbet, gelatin dessert 1 cup lemonade
Maximum sodium limit[d]	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	

DIETARY GUIDELINES FOR AMERICANS, 2010

APPENDIX B: Questionnaires

Department of Nutrition and Dietetics, UFS.

Prevalence of the known risk factors in women diagnosed with breast cancer at the Queen II hospital, Maseru

Appendix B_2

Adapted 24-hour recall questionnaire of usual intake

1. Subject number: _____ | | | | 1-3

2. Day of the week: 1. Monday 2. Tuesday 3. Wednesday 4. Thursday

5. Friday 6. Saturday 7. Sunday | | 4

3. Is this a usual day, if not, what is different?

1	Yes
2	No

	5

Elaborate:

_____ | | | 6-7
_____ | | | 8-9
_____ | | | 10-11

4. Has your diet changed ever since you were diagnosed with breast cancer?

1	Yes
2	No

	12

*If No, please skip to the next question.

5. How has your diet changed? Please elaborate.

_____ | | | 13-14
_____ | | | 15-16

Instructions

- Please tell me everything you usually eat and drink on a typical day. Please include everything that was added to the food.
- Please include the type, amounts and preparation methods of each food item eaten.

- **Food and fluid intake**

Food/Drinks and amounts	**Amount**	**Milk & milk products**	**Meat & alternatives**	**Bread , cereals & Legumes**	**Fruit**	**Vegetable**	**Fats & oils**	**Sweets/Sugar**	**Alcohol**
Breakfast and midmorning									
Lunch and mid afternoon									
Supper and late night									
Total:									

Evaluation of dietary intake according to Food Guide Pyramid (FGP):

	Interpretation of number of exchanges compared to *FGP recommendations				
	Quantity	**Below (1)**	**Within (2)**	**Above (3)**	
Milk and milk products					17
Meat and meat alternatives					18
Fruits					19
Vegetables					20
Bread, cereal & legumes					21
Fats and oils					22
Sweets/sugar					23

*Food Guide Pyramid (FGP) (USDA, 1992)

Serving recommendations according to the Food Guide Pyramid (USDA, 1992):

Food Group	Number of servings/day
Bread and cereal	6-11
Fruit	2-4
Vegetables	3-5
Meat and meat alternative	2-3
Milk and milk products	2-3
Fats and sweets	Use sparingly (≤3 servings)

* ≥ 4 servings of fats and oils and sweets are considered high.

Dietary intake evaluation according to the food exchange system to calculate energy and macronutrients:

	Quantity	**Energy**	**Protein**	**CHO**	**Fat**
Bread, cereal & legumes		285	3	15	-
Meat & meat alternatives:(very lean)		147	7	-	1
Meat & meat alternatives: (lean)		231	7	-	3
Meat & meat alternatives: (medium fat)		315	7	-	5
Meat & meat alternatives:(high fat)		420	7	-	8
Milk & milk products: Full cream		640	8	12	8
Milk & milk products: Low fat (1.5-2%)		530	8	12	5
Milk & milk products: Skimmed		340	8	12	-
Fruit		285	-	15	-
Vegetables A		-	-	-	-
Vegetables B		150	2	7	-
Fats & oils		190	-	-	5
Sweets/sugar		170	-	10	-
Alcohol	(ml)	29kJ/ml	-	-	-
Total					

Based on the American Dietetic Association Standard for Exchange Lists (Wheeler *et al*., 1996)

Calculated estimated total values for:

Carbohydrate (g)	_____	24-26
Protein (g)	_____	27-29
Fat (g)	_____	30-32
Energy (kJ)	_____	33-37

Macronutrient intake expressed as percentage (%) of total energy intake (Whitney & Rolfes, 2005:180)

Nutrient	Low	Within	High
Protein	<10%	10-15%	>15%
Carbohydrate	<45%	45-65%	>65%
Fat	<20%	20-35%	>35%

Dietary intake evaluation

ONE LEGUME PORTION PROVIDES:

21 grams of carbohydrates, 7 grams of protein, 0.7 grams of fat and 500 kJ.

Split peas (cooked).....$^1/_2$ cup (85g)
Chick peas (dried & cooked)..... $^1/_2$ cup (85g)
Lentils (whole: cooked)..... $^1/_2$ cup (90g)
Lentils (split; cooked)..... $^1/_2$ cup (90g)
Sugar beans (fried & cooked)..... $^1/_2$ cup (100g)
Kidney beans (white; dried & cooked).....$^1/_2$ cup (90g)

Canned:
Baked beans in tomato sauce..... $^1/_3$ cup (90g)
Kidney beans (white; solids & liquids)..... $^1/_3$ cup (90g)

Soy beans..... $^1/_2$ cup (80g)
Provides: 8 grams of carbohydrates, 13 grams of protein, 7 grams of fat, and 630 kJ.

PORTION SIZES-ADULTS:

Grain group
1 slice bread
$^1/_2$ cup cooked rice or pasta
$^1/_2$ cup cooked porridge
$^1/_2$ cup ready-to eat cereal
$^1/_3$ cup samp

Fats and sweets
2 teaspoons sugar
2 hardboiled sweets
10ml mayonnaise
5ml oil, 10ml margarine (medium fat)

Fruit group
1 piece fruit or melon wedge
$^1/_2$ cup juice
$^1/_2$ cup canned fruit
$^1/_2$ cup dried fruit

Milk group
1 cup milk or $^1/_2$ cup yoghurt
30g cheese

Meat group
30g cooked lean meat, poultry or fish
1 egg
$^1/_2$ cup of cooked dried beans
2 tablespoons peanut butter
(add one fat exchange)

Vegetable group
1 cup raw leafy vegetables
$^1/_2$ cup chopped raw/cooked vegetables

Department of Nutrition and Dietetics, UFS.

Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru

Appendix B_1

Socio-demographic information, lifestyle behaviours, other related factors questionnaire, and anthropometric measurements.

Section a = (socio-demographic)

1. Date of birth (dd/mm/yy): _____ | | | | | | | 1-6

2.District: _____ | | 7-8

3.Village: _____ | | 9-10

4. What is your current marital status? (Please choose one status that best describes your current situation).

1	Married	11
2	Divorced	
3	Not married, but living with someone	
4	Separated	
5	Widowed	
6	Single, never married	

5. What is the highest level of education you have completed? (Please choose one).

1	Primary school	12
2	High school	
3	Did not complete high level	
4	Technical school	
5	Bachelor's degree	
6	Honours degree	
7	Master degree	
8	Doctorate	
9	Other, please specify _____	

6. What is your current employment status?

_____ ☐☐ 13-14

***If not currently employed, please skip to question 10.**

7. If you currently work for payment or are self-employed, what type of work do you do?

_____ ☐☐ 15-16

8. What is your job title? _____ ☐☐ 17-18

9. In what kind of business or industry are you?

_____ ☐☐ 19-20

10. How much do you or your household spend of your income on food per month?

R _____ ☐☐☐☐☐☐☐ 21-27

11. How many people are there in the household?

_____ ☐☐ 28-29

12. How many people in the household contribute financially in the buying of foods?

_____ ☐☐ 30-31

13. Is the house where you live:

1	Owned by you or someone in the household?	☐ 32
2	Rented for money?	
3	Occupied without payment of money?	
4	Other, specify) _____	

Section b = (lifestyle behaviours)

14. How often do you drink alcohol?

1	Regularly	33
2	Occasionally	
3	Never	

*__If never, please skip to question 15__.

14a.Do you drink any of the following?

1	Red wine	1. Yes	2. No	34
2	White wine	1. Yes	2.No	35
3	Beer	1. Yes	2. No	36
4	Liquor	1. Yes	2.No	37
5	Other, please specify _____			38

14b. How many drinks per week do you take?

1	Red wine (glass) _____		39-40
2	White wine (glass) _____		41-42
3	Beer (glass) _____		43-44
4	Liquor (shot) _____		45-46
5	Other, specify _____		47-48

14c. Which day of the week are you taking more alcohol?

1	Week day	49
2	Week-end	
3	Both	

15. Think back to your typical day. For each of the 30 minutes periods, select a primary activity performed.

Time	Activity performed	PAL/hr			
00:00					
0:30					
1:00					
1:30					
2:00					
2:30					
3:00					
3:30					
4:00					
4:30					
5:00					
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23:00					

1	Sedentary
2	Low activity
3	Active
4	Very active

	.			50-53

List of physical activities

A: Daily activities
1. Lying quietly
2. Riding in a car
3. Light activity while sitting
4. Watering plants
5. Walking the dog
6. Vacuuming
7. Doing household tasks (moderate effort)
8. Gardening (no lifting)
9. Mowing (power mower)

B: Leisure activities: Mild
1. Walking (2 mph)
2. Canoeing (leisurely)
3. Golfing
4. Dancing (ballroom)

C. Leisure activities: Moderate
1. Walking (3 mph)
2. Cycling (leisurely)
3. Walking (4 mph)

D. Leisure activities: Vigorously
1. Chopping wood
2. Playing tennis
3. Cycling (moderate)
4. Swimming
5. Climbing hills (5-kg load)
6. Walking (5 mph)
7. Jogging (10-minutes mile)
8. Skipping rope

Section c = (other related factors)

16. How old were you when you had your first menstrual period? _____ ☐☐ 54-55

17. How old were you when your periods first became regular? _____ ☐☐ 56-57

18. Have you ever been pregnant?

1	Yes	☐ 58
2	No	
3	Do not know	

* **If No or do not know, please skip to question 27.**

19. Are you currently pregnant?

1	Yes	☐ 59
2	No	
3	Do not know	

20. How many times have you been pregnant? _____ ☐☐ 60-61

21. Of your pregnancies, how many ended before 20 weeks (5 months)? ☐☐ 62-63

_____

22. Of your pregnancies, how many lasted 20 weeks or more (include all pregnancies that ended in live births and still births).

_____ ☐☐ 64-65

23. Did you breast feed any children for at least one month?

1	Yes	☐ 66
2	No	

24. How many children did you breast feed for at least one month?

_____ ☐☐ 67-68

25. How old were you when you first breast fed a child for at least a month?

_____ ☐☐ 69-70

26. Thinking about all the children you breast fed, how many months in total did you breast feed?

_____ ☐☐☐ 71-73

27. Between the first time you had your first period and your last period, did you ever go without having a period for at least one year? (Do not count times when you were pregnant or breast feeding).

1	Yes	☐ 74
2	No	
3	Do not know	
4	Never had period	

28. Have you ever taken birth control pills for any reason? (Do not include birth control pills prescribed for menopause).

1	Yes	☐ 75
2	No	
3	Do not know	

*__If No or do not know, please skip to question 31.__

29. How old were you when you first started taking birth control pills?

_____ ☐☐ 76-77

30. In total, how long have you taken birth control pills, other than for menopause? (Please round to the nearest year).

_____ ☐☐ 78-79

31. Have you ever had a natural menstrual period during the past 12 months? (Please answer "No" if your bleeding was induced by hormone replacement therapy?

1	Yes	☐ 80
2	No	
3	Do not know	

*__If yes, please skip to question 34.__

32. Did your menstrual periods stop occurring naturally? (Please answer "No" if your periods stopped because of surgery or because you started hormone treatment therapy).

1	Yes	☐ 1
2	No	
3	Do not know	

33. At what age did your periods stop occurring? _____ ☐☐ 2-3

34. Have you ever used female hormones for menopause e.g. tablets, pills, a patch or cream?

1	Yes	☐ 4
2	No	
3	Do not know	

*__If No or do not know, please skip to question 37.__

35. Are you currently using female hormones?

1	Yes	☐ 5
2	No	

36. If yes, for how long have you taken female hormones? (Round to the nearest year).

_____ ☐☐ 6-7

37. When were you diagnosed with breast cancer (dd/mm/yy)?

_____ ☐☐☐☐☐☐ 8-13

38. Has your weight changed ever since you were diagnosed with breast cancer?

1	Yes	☐ 14
2	No	

39. What size did you wear before you were diagnosed with breast cancer?

_____ ☐☐ 15-16

40. What size do you wear now?

_____ ☐☐ 17-18

41. Are you willing to disclose your HIV status?

1	Yes	☐ 19
2	No	

***If No, please skip to question 44.**

42. Do you know your HIV status?

1	Yes	☐ 20
2	No	

43. Are you on ARVS?

1	Yes	☐ 21
2	No	

This section is about your full blooded relatives' medical histories. Please do not include family members who are related to you by marriage or adoption. (Full-blooded sisters and brothers are those who have the same two biological parents as you, as well as aunts and grandmothers). If you were adopted, please include any information that you know about your biological family.

44. Has anyone in your family been diagnosed with cancer?

1	Yes	☐ 22
2	No	
3	Do not know	

***If No or do not know, please skip to question 48.**

45. What age were they diagnosed?

Relative	Age		Relative		Age		
				23			24-25
				26			27-28
				29			30-31
				32			33-34
				35			36-37
				38			39-40

46. How many relatives were diagnosed with breast cancer?

_____ | | | 41-42

47. What kind of cancer did your relatives have?

Relative	Type of cancer	Cancer type	
			43
			44
			45
			46
			47
			48

48. Have you ever had a mammogram (a breast cancer X-ray)?

1	Yes	49
2	No	
3	Do not know	

***If No or do not know, please skip to question 49.**

48a. When was the last time you had a mammogram (dd/mm/yy)?

_____ | | | | | | | 50-55

48b. In your lifetime, in total how many mammograms have you had?

_____ | | 56-57

48c. Why did you have your last mammogram? (Please choose all that apply).

1	Family history of breast cancer	58
2	Part of regular check-up	59
3	Due to age	60
4	Previously detected lump	61
5	Breast problem	62
6	Other, please specify _____	63

49. Other than a mammogram, have you ever had your breasts examined for lumps by a doctor or health care professional?

1	Yes	64
2	No	
3	Do not know	

***If No or do not know, please skip to question 50.**

49a. When was the last time you had your breasts examined by a doctor or health care professional? (dd/mm/yy)

_____ 65-70

49b. How many times in your lifetime had you had your breasts examined by a doctor or health care professional?

_____ 71-72

50. Have you ever examined your own breasts for lumps?

1	Yes	73
2	No	
3	Do not know	

***If No or do not know, please skip to section d.**

50a. How often do you examine your breast?

1	At least once a month	74
2	Once every 2-3 months	
3	Less often than 2-3 months	

Section d = (anthropometric measurements)

1	weight (kg)				.		75-79
2	Height (cm)				.		1-5
3	Waist circumference (cm)				.		6-10
4	Hip circumference (cm)				.		11-15

Department of Nutrition and Dietetics, UFS.

Prevalence of the known risk factors in women diagnosed with breast cancer at the Queen II hospital, Maseru

Appendix B_3

Food frequency questionnaire

Instructions

- Please indicate frequency of intakes – times per day (tpd)/ times per week (tpw)/ times per month (tpm)/ times per season (tps).
- Use one option (per day, per week, per month or per season).

Food	/day		/week		/month		/season		
Bread (brown):									38-45
Bread (white):									46-53
Papa (maize-home grinding);									54-61
Papa (maize- commercial grinding);									62-69
Papa (other, specify- home grinding):									70-77
Papa (other, specify- commercial grinding):									1-8
Samp									9-16
Rice (brown):									17-24
Rice (white):									25-32
Pasta									33-40
Breakfast cereals									41-48
Motoho (maize-home grinding):									49-56
Motoho (maize-commercial grinding):									57-64
Motoho (sorghum-home grinding):									65-72
Motoho (sorghum-commercial grinding):									73-80
Lesheleshele (maize-home grinding):									1-8
Lesheleshele (maize-commercial grinding):									9-16
Lesheleshele (sorghum-home grinding):									17-24
Lesheleshele (sorghum-commercial grinding):									25-32
Peanut butter									33-40

Food	**/day**		**/week**		**/month**		**/season**		
Legumes (beans, peas, lentils):									41-48
Chicken									49-56
Red meat: (beef, mutton, pork)									57-64
Cheese									65-72
Fish (specify):									73-80
Eggs									1-8
Milk: full-cream									9-16
Milk: low-fat									17-24
Milk: Skimmed									25-32
Fancy fruit (specify):									33-40
Wild fruits (specify):									41-48
Fruit juice (specify):									49-56
Fancy vege (specify):									57-64
Fancy vege (specify):									65-72
Wild vege (specify):									73-80
Moroho (specify):									1-8
Margarine: soft									9-16
Margarine: medium									17-24
Margarine: hard									25-32
Oil (specify):									33-40
Fat: lard									41-48
Sweet/chocolates									49-56
Cake/biscuits									57-64
Cool drinks									65-72
Tea									73-80
Coffee									1-8
Sugar									9-16
Jam/syrup/honey									17-24
Western Alcohol (specify):									25-32
Traditional beer (specify):									33-40
Traditional dishes (specify):									41-48

Remarks: ……
……
……

Appendix C: Letters requesting permission to perform the study

APPENDIX C_1

The Director General
Ministry of Health and Social Welfare
Maseru- 100
Lesotho

Dear Madam,

Re: Permission to perform a research study at the Queen II hospital

I am currently a student registered for a Master's degree in Nutrition at The University of the Free State. As part of this degree, I am undertaking a research project titled "**Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru.**" I hereby apply for permission to undertake a study at the Queen II hospital and at the Breast Cancer clinic.

Results obtained in this study will be used to determine the prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital. Results might also be used to develop screening charts which can be used to create awareness in women and to the health care team as a whole.

Procedures in the study include:

1. An interview with patients, during which questionnaires regarding the patients' usual diet and food frequency will be completed.

2. Anthropometric measurements will be assessed, including: body weight and height, hip and waist circumferences.

3. Questionnaires regarding socio-demographic information, lifestyle behaviours, and other related risk factors will be completed.

The study procedures involve no foreseeable risks or harm to participants. Participation is voluntary and there will be no compensation for participation. Participants have the right to withdraw from the study at any time and without any penalties.

All of the information obtained during this study will be kept confidential, and no information or part of it will be used for purposes other than the research project. The results may be published but the participants will remain anonymous.

Questions may be addressed to the researcher at +27 828 420 995 or +266 5875 4940 and the Ethical Committee of the Faculty of Health Sciences, Ms. H. Strauss +2751 405 2812.

Sincerely

Lehlasoa 'Mamotlatsi (Ms)

APPENDIX C_2

Universitas Hospital
1 Logeman St. Universitas
Box 11595 Universitas

Dear Sir/Madam,

Re: Permission to perform a research study at the Universitas hospital

I am currently a student registered for a Master's degree in Nutrition at The University of the Free State. As part of this degree, I am undertaking a research project titled "**Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru.**" I hereby apply for permission to undertake a study at the Universitas hospital on Lesotho women who come for breast cancer treatment.

Results obtained in this study will be used to determine the prevalence of the known risk factors in women diagnosed with breast cancer at the Queen II hospital. Results might also be used to develop screening charts which can be used to create awareness in women and to the health care team as a whole.

Procedures in the study include:

1. An interview with patients, during which questionnaires regarding the patients' usual diet and food frequency will be completed.

2. Anthropometric measurements will be assessed, including: body weight and height, hip and waist circumferences.

3. Questionnaires regarding socio-demographic information, lifestyle behaviours, and other related risk factors will be completed.

The study procedures involve no foreseeable risks or harm to participants. Participation is voluntary and there will be no compensation for participation. Participants have the right to withdraw from the study at any time and without any penalties.

All of the information obtained during this study will be kept confidential, and no information or part of it will be used for purposes other than the research project. The results may be published but the participants will remain anonymous.

Questions may be addressed to the researcher at +27 828 420 995 or +266 5875 4940 and the Ethical Committee of the Faculty of Health Sciences, Ms. H. Strauss +2751 405 2812.

Sincerely

Lehlasoa 'Mamotlatsi (Ms)

APPENDIX C_3

National Hospital
P/B 20660
Bloemfontein 9301

Dear Sir/Madam,

Re: Permission to perform a research study at the National hospital

I am currently a student registered for a Master's degree in Nutrition at The University of the Free State. As part of this degree, I am undertaking a research project titled "**Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru.**" I hereby apply for permission to undertake a pilot study at the National hospital on Sesotho speaking women with breast cancer.

Results obtained in this study will be used to determine the prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital. Results might also be used to develop screening charts which can be used to create awareness in women and to the health care team as a whole.

Procedures in the study include:

1. An interview with patients, during which questionnaires regarding the patients' usual diet and food frequency will be completed.

2. Anthropometric measurements will be assessed, including: body weight and height, hip and waist circumferences.

3. Questionnaires regarding socio-demographic information, lifestyle behaviours, and other related risk factors will be completed.

The study procedures involve no foreseeable risks or harm to participants. Participation is voluntary and there will be no compensation for participation. Participants have the right to withdraw from the study at any time and without any penalties.

All of the information obtained during this study will be kept confidential, and no information or part of it will be used for purposes other than the research project. The results may be published but the participants will remain anonymous.

Questions may be addressed to the researcher at +27 828 420 995 or +266 5875 4940 and the Ethical Committee of the Faculty of Health Sciences, Ms. H. Strauss +2751 405 2812.

Sincerely

Lehlasoa 'Mamotlatsi (Ms)

Appendix D: Consent documents

Informed consent

APPENDIX D_{1A}

Dear participant,

Research: Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru

I am 'Mamotlatsi Lehlasoa, currently a student registered for a Master's degree in Nutrition at The University of the Free State. As part of this degree, I am undertaking a research project titled "**Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru**".

You are kindly requested to participate in this study. The purpose of this study is to determine the **Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital**. Results obtained in this study will be used to determine the prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital. Results might also be used to develop screening charts which can be used to create awareness in women and to the health care team as a whole.

The study was submitted for approval by the evaluation committee of the school of Allied Health Professions and the Ethics committee of the health sciences of the university. The study procedures involve no foreseeable risks or harm to you.

Procedures in the study include:

1. An interview during which questionnaires regarding usual diet and food frequency will be completed.
2. Body (anthropometry) measurements will be assessed, including: body weight and height, hip and waist circumferences.
3. Questionnaires regarding the characteristics and statistics of human populations (socio-demographic) information, lifestyle behaviours, and other related risk factors will be completed.

Data will be collected by the researcher and stored in a secure place and will not be shared with any other person without your permission. The above measurements assessment will require you to empty your bladder and wear light clothing before being taken.

Your participation in the study is voluntary and you have the right to withdraw from the study at any time without any penalty. There is no compensation for participating in this study, however should any health problem be identified, you will be referred to the relevant health care professional.

Your identity will not be revealed while the study is being conducted or when being reported or published. Questions regarding the study may be directed to the investigator at any time to the following numbers: +27 828 420 995/ +266 5875 4940 and the Ethical Committee of the Faculty of Health Sciences, Ms. H. Strauss +2751 405 2812.

I have read the consent form and I agree to participate in this study.
Subject's signature..... Date.....
Investigator's signature..... .Date.....

Tlhaloso ea kopo

APPENDIX D_{1B}

'M'e

Tloaeleho ea lintho the tsebahalang li ka ba baka lefu la mofetše oa matsoele basaling ba fumanoeng ka mofets'e sepetle sa Queen II, Maseru

'Na 'Mamotlatsi Lehlasoa, ke morutoana sekolong se seholo sa Foreisetata, teng ke etsa "Master's degree in Nutrition". E le karolo ea lengolo lena, ke etsa boithuto ka "**Tloaeleho ea lintho the tsebahalang li ka baka lefu la mofetše oa matsoele basaling fumanoeng ka mofets'e sepetle sa Queen II, Maseru".**

Mona u kupuoa ho nka karolo boithutong bona. Lebaka la boithuto bona ke ho fumana Tloaeleho ea lintho the tsebahalang li ka ba kotsi ho baka lefu la mofetše basaling. Likarabo tse tla fumanoa lipatlisisong tsena li tla sebelisoa ho fumana hore na ke lintho li fe tse tloaelehileng basaling ba nang le mofetše oa matsoele basaling ba fumanoeng ka mofets'e sepetleng sa Queen II. Hape likarabo li tla sebelisoa ho etsa "screening charts" tse tla sebelisoa ho hlokomelisa basali le ba lefapha la bophelo ka kakaretso ka mofetše oa matsoele basaling ba sepetle sa Queen II.

Boithuto bona bo hlahlobiloe ke komiti ea litlhatlhobo ea sekolo se seholo sa Foreisetata, tlasa lekala la bophelo le komiti ea litsamaiso lefapheng la mahlale le bophelo bo botle. Tsela ea tsamaiso boithutong bona ha bona letho le kabang kotsi ho uena.

Litsamaiso li kenyeletsa tsena tse latelang:

1. Kopano le motho ea etsang lipatlisiso moo lipotso mabapa le tsela eo u tloaetseng ho ja ka eona le hore na u ja khafetsa ha kae lijo tse itseng li tla botsoa;

2. Ho tla methoa likaro tse ling tsa 'mele oa hau, ho kenyeletsa: boima ba 'mele le bolele ba hau, bophara ba letheka le liqholo; le

3. Lipotso tse amanang le bophelo ba hau, tsela eo u phelang ka eona, le tse ling tse amanang le mofets'e.

Litaba tse amanang le lipatlisiso tsena li tla bokelloa ke mofuputsi 'me li bolokoe sebakeng se sireletsehileng 'me litaba tsena ha lina ho arolelanoa le motho e mong ntle le tumello ea hau. Ho methoa ha 'mele ho tla ho hloka hore u ntše metsi pele ho etsoa hape u apare liphahlo tse bobebe.

Ho nka karolo lipatlisisong tsena ke boithaopo 'me u na le tokelo ea ho tsoa ka lehare nako e fe kapa e fe ntle le qoso. Ha hona tefo ho nkeng karolo lipatlisisong tsena, empa ha ho ka hlokomeleha kotsi e fe kapa e fe e amang bophelo ba hau u tla romelloa ho mesebeletsi oa bophelo ea lokelang.

Lebitso la hau ha lena ho hlahella ho hang ha ho ntse ho etsoa lipatlisiso kapa ha liphatlalatsoa. Lipotso mabapi le lipatlisiso tsena li ka lebisoa ho motho ea etsang lipatlisiso linomorong tsena; +27 828 420 995 kapa +266 5875 4940 le ho ofisi ea komiti ea tsela ea litsamaiso sekolong se seholo sa Foreisetata lefapheng la mahlale le bophelo bo botle nomorong tsena +2751 405 2812.

Ke balile tlhaloso ena 'me ke fana ka tumello ea ho ba karolo lipatlisisong tsena.

Lebitso la monka karolo ..... Letsatsi .....

Lebitso la mofuputsi ..... Letsatsi .....

Information document

APPENDIX D_{2A}

Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru

Dear participant,

I, Lehlasoa 'Mamotlatsi (Ms), is doing research study on "**Prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital, Maseru".** Research is just the process to learn the answer to a question. In this study I want to learn about the commonness of the known risk factors in women diagnosed with breast cancer at Queen II hospital. This is a research study and involves no routine care.

You are kindly requested to participate in a research study.

A descriptive study will be conducted in order to determine the prevalence of the known risk factors in women diagnosed with breast cancer at Queen II hospital in Maseru. Your involvement in the study will entail a structured interview in privacy where you will be expected to answer the questions set and your body measurements will be assessed. You will be expected to be in the study until May 2011 when the study is completed.

The standard procedures being done in the study include a once off structured interview in private with the trained researcher. A reliability interview will be conducted a month after conducting the main data collection with 10% of the same sample. Assessment of body measurements will require you to empty your bladder and to wear light clothing.

The procedures that are being tested in the study include:

1. A structured interview during which questionnaires regarding usual diet and food frequency will be completed.

2. Body (anthropometry) measurements will be assessed, including: body weight and height, hip and waist circumferences.

3. Questionnaires regarding the characteristics and statistics of human populations (socio-demographic) information, lifestyle behaviours, and other related risk factors will be completed.

There are five South African women who will participate in the pilot study and they will be excluded from the main study because they are not from Lesotho. There will also be 50 to 100 Lesotho women to participate in the main study.

The study procedures involve no foreseeable risks or harm to you. There is no compensation for participation in the study, however should any health problem be identified, you will be referred to the relevant health care professional.

As a participant you will be given relevant information on the study while involved in the project and after the results are available. Personal information will be treated as confidential.

Your participation in the study is voluntary, and refusal to participate will involve no penalty. You may discontinue or withdraw from the study at any time without penalty.

Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

If results are published, this may lead to individual or cohort identification.

For further information or reporting of study-related adverse events please contact the researcher at any time to the following numbers, +27 8284 20995 or +266 5875 4940 and/or the Ethics Committee of Faculty of Health Sciences, UFS at +2751 405 2812.

Tokomane ea lintlha-kholo

APPENDIX D_{2B}

‘M’e

Tloaeleho ea lintho the tsebahalang li ka ba baka lefu la mofetše oa matsoele basaling ba fumanoeng ka mofets’e sepetlele sa Queen II, Maseru

‘Na Lehlasoa ‘Mamotlatsi, morutoana sekolong se seholo sa Foreisetata, ke etsa lipatlisisong sebakeng sa ho ithuta ka **Tloaeleho ea lintho the tsebahalang li ka ba kotsi ho baka lefu la mofetše oa matsoele basaling sepetlele sa Queen II, Maseru.** Lipatlisiso ke tsela ea ho fumana likarabo tsa potso e iteng. Boithutong bona ke batla ho tseba ka tloaeleho ea lintho tse ka tsebahalang li ka baka lefu la mofets’e oa matsoele basaling sepetlele sa Queen II. Sena ke liphuphutso malebana le bo ithuta ‘me ha ho ea kenyeletsa tlhatlhobo ea ka mehla.

Ka hona u kopuoa ho ba e mong ea tla nka karolo lipatlisisong tsena.

Boithuto bona bo tla hlalosa ho tloaeleha ha lintho tse ka etsang hore basali ba fumanoeng ka mofets’e oa matsoele sepetleleng sa Queen II Maseru ba be le mofetše oona. Ho nka karolo ha hau ho tla kenyeletsa lipuisano le mofuputsi lekunutung moo u tla botsoa lipotso hape le ‘mele oa hau u methoe. U tla lebelloa ho ba karolo ho fihlela liphuphutso tsena li feleli, e leng ho fihlela Mots’eanong 2011.

Tsela ea tsamaiso boithutong bona bo tla kenyetsa lipotso ha ngoe feela lekunutng le mofuputsi ea rupeletsoeng. Liphuputso tsa ho hlahloba ho tšepahala ha likarabo bo tla etsoa khoeli ka mora phuphutso ea batho bohle ‘me ho tla etsoa bathong ba leshome lekholong. Ho methoa ha ‘mele ho tla hloka hore u ntše metsi pele ho etsoa hape u lebeletsoe hore u apare liphahlo tse bobebe.

Tsela ea tsamaiso e kenyelelitse tse latelang:

1. Kopano le motho ea etsang lipatlisiso moo lipotso mabapa le tsela eo u tloaetseng ho ja ka eona le hore na u ja khafetsa ha kae lijo tse itseng;

2. Ho tla methoa likaro tse ling tsa ‘mele oa hau, ho kenyeletsa: boima ba ‘mele le bolele ba hau, bophara ba letheka le liqholo; le

3. Lipotso tse amanang le bophelo ba hau, tsela eo u phelang ka eona, le tse ling tse amanang.

Boithuto bona bo kenyeletsa basali ba Afrika Boroa ba bahlano ba tla nka karolo boithutong ba teko ‘me ba tla siuoa ha ho etsoa liphuphutso tse kholo hobane hase ba Lesotho. Basali ba Lesotho na tla nka karolo liphuphutsong tse kholo ba tlaba mashome a mahlano ho isa lekholong.

Tsela ea tsamaiso ha ena kotsi ho uena. Ha hona tefo e tla ba teng sebakeng sa ho nka karolo boithutong bona, empa ha ho ka hlokomeleha bothata ba bophelo ho uena, u tla romelloa ho mosebeletsi oa bophelo ea lokelang.

Likarabo tse tla fumanoa li tla sebelisoa ho fumana tloaeleho ea lintho tse ka bang kotsi basaling ba fumanoeng ba na le lefu la mofetše oa matsoele sepetlele sa Queen II. Se tla fumanoa hape se tla sebelisoa ho etsa "screening charts" tse tla sebelisoa ho hlokomelisa basali le ba lefapha la bophelo ka mofetše oa matsoele.

Joalo ka motho ea nkileng karolo lipatlisisong tsena, u tla fuoa litaba ka boithuto bona ha bo ntse bo etsoa pele le ha bo felile. Ha hona hoba le litaba tse u amang ka kotloloho tse tla fumaneha hoba ho tla etsoa liteko tsohle hore lebitso la hau lipatlisisong tsena le se tsebahale.

Ho nka karolo ke boithaopo 'me ho se nke karolo ha hona ho ba le kotlo. U ka khetha ho tlohela ho tsoa ka lehare lipatlisisong tsena nako e fe kapa e fe ka ntle le kotlo.

Ho tla etsoa liteko tsohle hore lebitso la hau le se phatlalatsoe lipatlisisong tsena. Empa litaba tse u amang ka bo mong bo ka hlahella haeba bo hlokuoa ke molao.

Ha liphetho li phatlalatsoa ho ka etsa hore u tsebahale ka bo mong kapa le le sehlopha.

Sebakeng sa lipotso kapa ho tlaleha mathata a bakiloeng ke liphuphutso tsena u ka letsetsa mofuputsi ka linako tsohle linomorong tsena: +27 828 420 995 kapa +266 5875 4940 kapa komiti ea tsela ea litsamaiso sekolong se seholo sa Foreisetata lefapheng la mahlale bophelong bo botle linomorong tsena +2751 405 2812.

Consent to participate in research

APPENDIX D_{3A}

You have been asked to participate in a research study.

You have been informed about the study by .....

You may contact 'Mamotlatsi Lehlasoa (Ms) at +27 8284 20995 or +266 5875 4940 at any time if you have questions about the research or if you are injured as a result of the research.

You may contact the Secretariat of the Ethics Committee of the Faculty of Health Sciences, UFS at +2751 405 2812 if you have questions about your rights as a research subject.

Your participation in this study is voluntary, and you will not be penalised or lose benefits if you refuse to participate or decide to terminate participation.

If you agree to participate, you will be given a signed copy of this document as well as the participant information sheet, which is the summary of the research.

The research study, including the above information has been verbally described to me. I understand what my involvement in the study means and I voluntarily agree to participate.

Signature of participant	Date
Signature of witness (where applicable)	Date
Signature of translator (where applicable)	Date

Kopo ea ho nka karolo patlisisong

APPENDIX D_{3B}

U kopuoa ho ba e mong oa batho ba tla nka karolo lipatlisisong tsena.

U tsebeli ka patlisiso ena ka .....

U ka letsetsa 'Mamotlatsi Lehlasoa linomorong tsena: +27 828 420 995 kapa +266 5875 4940 ka linako tsohle ha eba u na le lipotso ka patlisiso ena kapa haeba u ka tsoa kotsi ke patlisiso ena.

U ka letsetsa ofisi ea komiti ea tsela ea tsamaiso lefapheng la thuto ea tsa mahlale le bophelo bo botle sekolong se seholo sa Foreisetata linomorong tsena: +2751 405 2812 ha eba u na le lipotso mabapi le litokelo tsa hau u le karolo ea lipatlisiso.

Ho nka karolo lipatlisisong tsena ke boithaopo 'me hau na ho ahloloa kapa ho lahleheloa ke thuso eo u ntseng u e fumana hau sa nke karolo kapa u khetha ho tlohela hoba karolo ea lipatlisiso tsena ka lehare.

Hau lumela ho nka karolo lipatlisisong tsena, u tla fuoa pampiri ena e tekennoe hammoho le tokomane e hlalositseng ka patlisiso ena.

Patlisiso hammo le litaba tse hlalositsoeng ka holimo ke li hlaloselitsoe. Kea utloisisa na karolo ea ka patlisisong ena e bolelang 'me ke lumela ka boithaopo ho nka karolo.

lebitso la monka karolo	Letsatsi
lebitso la molebelli (moo ho hlokahalang)	Letsatsi
lebitso la motoloki (moo ho hlokahalang)	Letsatsi

APPENDIX E: Approval letters to conduct study

APPENDIX E_1

ID 25/09

LESOTHO

Ministry of Health and Social Welfare

Director General of Health Services

P.O. Box 514, Maseru 100

Date: 23 December 2009

Lehlasoa 'Mamotlatsi R.

PO Box 13286

Maseru 100, Lesotho

Dear Lehlasoa,

Re: Prevalence of the known risk factors in women diagnosed with breast cancer in Lesotho

Thank you for resubmitting the protocol. The Ministry of Health and Social Welfare Research and Ethics Committee having reviewed your protocol hereby authorizes you to conduct this study. The study is authorized with the understanding that the protocol will be followed as stated. Departure from the stipulated protocol will constitute a breach of the permission.

Best Regards,

Dr. M. Moteetee

Chairperson Research and Ethics Committee

Director General

Health Services

PNO
Dr Siddiqui

Please facilitate

MEDICAL SUPERINTENDENT
- 6 JAN 2010
OFFICE O. E. II

6/01/2010

1

APPENDIX E_2

health

Department of
Health
FREE STATE PROVINCE

Ref. no.: 13/2

13 August 2009

Ms MR Lehlasoa
PO Box 13286
Maseru
LESOTHO
100

Dear Ms Lehlasoa

RESEARCH PROJECTS: PREVALENCE OF THE KNOWN RISK FACTORS IN WOMEN DIAGNOSED WITH BREAST CANCER IN LESOTHO

Herewith permission for the mentioned project to be done at Universitas Academic Hospital on condition that approval is obtained from the Ethics Committee.

The Chief Executive officer must be notified if the findings of the project will be published.

Yours sincerely

DR NIC R J VAN ZYL
HEAD: CLINICALSERVICES
UNIVERSITAS ACADEMIC HOSPITAL

DR NRJ VAN ZYL
2009 -08- 13
HEAD: CLINICAL SERVICES
UNIVERSITAS ACADEMIC HOSPITAL

HEAD: CLINICAL SERVICES: DR NRJ VAN ZYL
Private Bag X20660, Bloemfontein, 9300. Tel. No.: 051-4052866,
Fax: 051-4053500, Room 1077, First Floor, Universitas Academic Hospital
E-mail: vanzylnr@fshealth.gov.za

www.fs.gov.za

APPENDIX E_3

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

Departement Onkoterapie/Department of Oncotherapy
Fakulteit Gesondheidswetenskappe/Faculty of Health Sciences
Skool vir Geneeskunde/School of Medicine

Dr MC Botha

13 August 2009

Ms Lehlasoa Mamotlatsi
P.O. Box 13286
Maseru, 100
LESOTHO

Dear Ms Mamotlatsi

RE: PERMISSION TO PERFORM A RESEARCH STUDY AT THE NATIONAL HOSPITAL

We hereby give permission for you to undertake a pilot study for your project "**Prevalence of the known risk factors in women diagnosed with breast cancer in Lesotho**" at Universitas Annex.

You can contact the department at 051 4052646 to make arrangements.

DR AC BESTER
ACTING HEAD OF DEPARTMENT/PRINCIPAL SPECIALIST
/cm

Departementshoof/Head of Department: Prof L Goedhals
Konsultante/Consultants: Dr AC Bester, Dr A Sherriff, Dr MP Kahl, Dr MC Botha, Dr MJ Strydom & Dr M Kruger
339, Bloemfontein 9300, ☎ (051) 405 2646, # 27/51/405 2646, (051) 447 5029, # 27/51/447 5029,
goedhall@fshealth.gov.za, Republiek van Suid-Afrika, Republic of South Africa

APPENDIX F: Ethics letters, UFS

APPENDIX F_{1A}

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

Direkteur: Fakulteitsadministrasie / Director: Faculty Administration
Fakulteit Gesondheidswetenskappe / Faculty of Health Sciences

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Ms H Strauss

2009-07-31

MS MR LEHLASOA
P O BOX 13286
MASERU
LESOTHO
100

Dear Ms Lehlasoa

ETOVS NR: 96/09
PROJECT TITLE: PREVALENCE OF THE KNOWN RISK FACTORS IN WOMEN DIAGNOSED WITH BREAST CANCER IN LESOTHO

- You are hereby informed that The Ethics Committee approved the above protocol at the meeting on 28 July 2009 on condition that permission has to be obtained from the Ministry of Health and Social Welfare, Universitas Hospital, National Hospital. Copies of the response letters have to be submitted to the Ethics Committee for record purposed.
- Committee guidance documents: Declaration of Helsinki, ICH, GCP and MRC Guidelines on Bio Medical Research. Clinical Trial Guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles Structure and Processes Department of Health RSA 2004; Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa, Second Edition (2006); the Constitution of the Ethics Committee of the Faculty of Health Sciences and the Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines.
- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.
- The Committee must be informed of any serious adverse event and/or termination of the study.
- A progress report should be submitted within one year of approval of long-term studies and a final report at completion of both short term and long term studies.
- Kindly refer to the ETOVS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully

.....
PROF WH KRUGER
CHAIR: ETHICS COMMITTEE

CC: Prof A Dannhauser, Dept of Human Nutrition, UFS

339, Bloemfontein 9300,RSA ☎ (051) 405 2812 gndkhs.md@ufs.ac.za
Republiek van Suid-Afrika / Republic of South Africa

APPENDIX F_{1B}

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
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Ms H Strauss

2011-07-27

REC Reference nr 230408-011
IRB nr 00006352

MS MR LEHLASOA
PO BOX 13286
MASERU
LESOTHO
100

Dear Ms Lehlasoa

ETOVS NR 96/09
PROJECT TITLE: PREVALENCE OF THE KNOWN RISK FACTORS IN WOMEN DIAGNOSED WITH BREAST CANCER IN LESOTHO

- You are hereby kindly informed that the Ethics Committee approved the above study at the meeting held on 26 July 2011 after the following was received:
  - ***Permission letters obtained from the Ministry of Health and Social Welfare; Universitas Hospital and National Hospital.***
- Committee guidance documents: Declaration of Helsinki, ICH, GCP and MRC Guidelines on Bio Medical Research. Clinical Trial Guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles Structure and Processes Department of Health RSA 2004; Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa, Second Edition (2006); the Constitution of the Ethics Committee of the Faculty of Health Sciences and the Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines.
- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.
- The Committee must be informed of any serious adverse event and/or termination of the study.
- A progress report should be submitted within one year of approval of long term studies and a final report at completion of both short term and long term studies.
- Kindly refer to the ETOVS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully

.....
CHAIR: ETHICS COMMITTEE

339, Bloemfontein 9300,RSA ☎ (051) 405 2812 StraussHS@ufs.ac.za
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SUMMARY

Breast cancer is the leading cancer in the world among women, both in industrialised and developing countries. While the USA has the highest prevalence and mortality rates of the disease, with middle prevalence rates in Eastern Europe; Africa and Asia have low rates. In South Africa breast cancer is the most common cancer and is being diagnosed with increasing prevalence among the black population. No literature is, however, currently available regarding the prevalence of breast cancer, the prevalence of the risk factors for breast cancer, or the associated mortality rates for breast cancer in Lesotho.

The aim of this study was to determine the prevalence of the known risk factors for breast cancer among adult women who were diagnosed with the disease at the Queen Elizabeth II hospital, Maseru.

A descriptive survey was conducted on 52 adult breast cancer patients seen at the Queen II hospital in Maseru, who gave informed consent. A trained researcher performed anthropometric measurements and administered a questionnaire on usual dietary intake and non-modifiable and modifiable risk factors for breast cancer, during structured interviews. Reliability was ensured by repeating the same questionnaire with 10% of the sample a month after conducting the main study.

Regarding the non-modifiable risk factors for breast cancer, the majority of the Basotho women in this study were diagnosed with breast cancer at 46 years and older (78.7%), experienced menarche at 12 years and older, (93.9%), had reached natural menopause, did not use hormone replacement therapy, and had reached menopause before the age of 55 years (96.8%).

Regarding the modifiable risk factors for breast cancer, the Basotho women had a low risk profile with low levels of education (80.8% had only primary or high school educations), low incomes (59.6%), low oral contraceptive use (65.4% had never used), and were mostly non-drinking (48.1%) and low-drinking (36.5%). Most were also, or had been, married at the time of the study (82.7%), had children (80.8%), and had breastfed for ≥12 months (86.8%).

However, these Basotho women were very inactive (82.6%), with high body mass indexes (21.1% overweight; 63.5% obese), waist circumferences, and waist to hip ratios putting them at high risk for breast cancer and other chronic diseases of lifestyle. Their self-reported median total energy and macronutrient intakes were 5414.5 kJ, 49g protein (0.63 g/kg/day), 210g carbohydrate, and 21.5g fat. Dietary intakes were evaluated according to the recommendations of the USDA Food Guide Pyramid and the Dietary Guidelines for Americans 2010. Although they had low intakes of meat, particularly red meat, drank tea regularly, and used cooking methods that did not produce cancer promoting agents, all of which protect against breast cancer development; their low intakes of fruits, and low variety of plant foods put them at risk of breast cancer and other diseases due to low supply of protective antioxidants and phytochemicals.

Particularly vegetables were mostly only consumed as green leafy types (moroho), while other vegetables were only consumed occasionally and by small percentages.

This study is the first to report on the known risk factors of breast cancer among women in Lesotho. In summary, these Basotho patients were found to have a low risk profile for breast cancer with regard to non-modifiable risk factors, reproductive history and socio-demographic factors. The main risk factors for breast cancer were inactivity and obesity, combined with a diet low in variety of protective plant foods. Intervention programmes should thus focus on addressing these modifiable risk factors.

KEY TERMS

- Breast cancer
- Prevalence
- Risk factors
- Non-modifiable
- Modifiable
- Patients
- Adult
- Basotho
- Women
- Diagnosed

OPSOMMING

Borskanker is die mees algemene vorm van kanker wat onder vroue in die wêreld voorkom – beide in ontwikkelde en in ontwikkelende lande. Die VSA het die hoogste voorkoms en mortaliteit van borskanker, met gemiddelde voorkomssyfers in ontwikkelende lande in Oos-Europa, Afrika en Asië. In Suid-Africa is borskanker die mees algemene vorm van kanker onder vroue en word met toenemende frekwensie onder swart vroue gediagnoseer. Geen literatuur is egter huidiglik beskikbaar wat die voorkoms van borskanker, die risikofaktore vir borskanker, of die gassosieerde mortaliteitssyfers, in Lesotho beskryf nie.

Die doel van hierdie studie was om die voorkoms van die bekende risikofaktore vir borskanker onder volwasse Basotho vroue wat met die siekte by die Queen Elizabeth II hospitaal, Maseru, gediagnoseer is, te bepaal.

'n Beskrywende studie is op 52 volwasse borskankerpasiente uitgevoer wat by die Queen II hospitaal in Maseru gesien is, en wat ingeligte toestemming gegee het. 'n Opgeleide navorser het antropometriese meetings uitgevoer en 'n gestruktureerde vraelys oor gewoontlike dieetinnames en die modifieerbare en nie-modifieerbare risiko's vir borskanker, tydens 'n gestruktureerde onderhoud ingevul. Betroubaarheid is verseker deur dieselfde vraelys met 10% van die steekproef 'n maand na die hoofstudie te herhaal.

Met betrekking tot die nie-modifieerbare risikofaktore vir borskanker, is die meerderheid van die Basotho-vroue in die studie in met borskanker op 46 jaar of ouer (78.7%) gediagnoseer, het vroeë menarche op 12 jaar of ouer (93.9%) beleef, het natuurlike menopause bereik, het nie hormoonvervangingsterapie gebruik nie, en het menopouse voor 55 jaar bereik (96.8%).

Met betrekking tot die modifieerbare risikofaktore vir borskanker, het die Basotho-vroue 'n lae risiko vir borskanker getoon, met lae vlakke van opleiding (80.8% het primêre- en hoërskoolopleiding gehad), lae inkomstes (59.6%), lae gebruik van orale kontrasepsie (65.4% het dit nooit gebruik nie), en was oorwegend nie-drinkers (48.1%) and lae vlak-drinkers (36.5%) was. Die meeste was ook ten tye van die studie, of voorheen, getroud (82.7%), het al kinders gehad (80.8%), en het vir ≥12 maande geborsvoed (86.8%).

Daarteenoor was hierdie Basotho-vroue egter baie onaktief (82.6%), met hoë massa-lengte-indekse (21.1% oormassa; 63.5% vetsugtig), middelomtrekke en middel-tot-heupverhoudings wat hulle in 'n hoë risikokategorie vir borskanker en ander chroniese leefstylsiektes plaas. Hul selfgrapporteerde totale energie- en makrovoedingstofinnames was 5414.5 kJ, 49 g proteïen (0.63 g/kg/dag), 210 g koolhidrate, en 21.5 g vet. Dieetinnames is volgens die aanbevelings van die "USDA Food Guide Pyramid" en die 'Dietary Guidelines for Americans 2010" geëvalueer. Alhoewel hulle min vleis, veral rooivleis, ingeneem het, gereeld tee gedrink het, en gaarmaakmetodes gebruik het wat nie kankerbevorderende substanse produseer nie (alles faktore

wat teen die ontwikkeling van borskanker beskerm), hou die lae innames van vrugte en die klein verskeidenheid van plantvoedsels in hul dieet, ‘n risiko vir borskanker en ander chroniese leefstylsiektes in weens die lae gepaardgaande inname van beskermende antioksidante en plantchemikalieë. Veral groente is meesal net as groen blaargroente (moroho) ingeneem, terwyl ander groentesoorte net per geleentheid en deur klein persentasies ingeneem is.

Hierdie is die eerste studie wat data met betrekking tot die voorkoms van die bekende risikofaktore vir borskanker in Lesotho rapporteer. Ter samevatting het hierdie Basotho-pasiënte ‘n lae risikoprofiel vir borskanker met betrekking tot nie-modifieerbare risikofaktore, reproduksiegeskiedenis en sosio-demografiese faktore getoon. Die hoofrisikofaktore vir borskanker in hierdie vroue was egter onaktiwiteit en vetsug, gekombineer met ‘n dieet wat ‘n klein verskeidenheid van beskermende plantvoedsels insluit. Intervensieprogramme behoort dus daarop te fokus om hierdie modifieerbare risikofaktore aan te spreek.

SLEUTELTERME

- Bors kanker
- Voorkoming
- Risiko faktore
- Nie-veranderlik
- Veranderlik
- Pasiënte
- Volwassene
- Basotho
- Vroue
- Diagnose