ASSESSMENT OF FACTORS ASSOCIATED WITH BREAST CANCER AMONG WOMEN IN NYERI COUNTY, KENYA – A CASE CONTROL STUDY

BY

JULIUS KARURI MACHARIA, B.D.S (UoN), MSC (UoN), ADM. NO. H57/7823/2001

A THESIS SUBMITTED IN PARTIAL FULFILLMENT FOR THE DEGREE OF MASTERS IN PUBLIC HEALTH OF THE UNIVERSITY OF NAIROBI, OCTOBER 2012
APPROVAL

Supervisors

This dissertation/thesis has been submitted for examination with our approval as University supervisors as part fulfillment for the award of Masters in Public Health.

Dr Peter Njoroge, MBchB; MPH
Lecturer, Health Service Management, School of Public Health University of Nairobi
Signature: .............................................. Date: 17/11/2012

Mrs Mary Kinoti, B.Ed.; MSc (Human Ecology); MSc (Biostatistics and Epidemiology)
Lecturer, Environmental & Occupational Health, School of Public Health University of Nairobi
Signature: .............................................. Date: 19/11/2012

Approved by the Director, School of Public Health

Dr Dismas Ongore, MBchB; MPH; PhD
Senior Lecturer, Epidemiology & Disease Control and Director, School of Public Health University of Nairobi
Signature: .............................................. Date: 19/11/2012
DEDICATION

This thesis is dedicated to my beloved father, the late Peter Macharia Kariuki who passed on December 20th 2008 from liver cancer.
ACKNOWLEDGEMENTS

I would like to express my sincere, whole-hearted thanks to many individuals who have supported me along the way during this long journey. Most importantly, I wish to express my appreciation and countless thanks to my mentors and supervisors Dr. Njoroge PK and Mrs Mary Kinoti for their endless support and encouragement from the day this thesis idea was suggested more than 2 years ago. I am especially grateful to Mrs Kinoti, who always believed in me from the beginning and encouraged me to ‘give birth’ to this dissertation after so many attempts. Her confidence in my abilities, expert advice and guidance, and friendship are most sincerely appreciated. I am also very grateful to her for her day-to-day patience with my requests for help, especially as I stumbled along trying to understand the workings of Stata programming.

I wish to thank my fellow students who offered me their support.

Many thanks to Chief Executives of Nyeri Provincial Hospital, Mathari, Outspan, Tumutumu, Karatina, Kerugoya, Nanyuki and Mukurwe-ini hospitals, and Nyeri hospice for allowing me to use their facilities in the course of my research. I can’t forget to thank Charity Muthoni for her encouragement and her positive attitude towards my never-ending list of visits to the homes of cancer survivors in the course of data collection. I also wish to thank my other research assistants in all the participating health facilities. Finally, I would like to express my extreme gratitude to my family, who are my constant inspiration; my children, Rahab and Macharia, who always provided me with sincere encouragement and warm hugs despite my ongoing preoccupation with finishing this thesis, and my wife, Margaret, who has supported me with constant patience, humour and understanding. It is truly her uncanny ability to always view obstacles from a positive perspective that kept me moving forward with this thesis.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Declaration</th>
<th>ii</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval</td>
<td>iii</td>
</tr>
<tr>
<td>Dedication</td>
<td>iv</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>v</td>
</tr>
<tr>
<td>Table of contents</td>
<td>vi</td>
</tr>
<tr>
<td>List of figures</td>
<td>x</td>
</tr>
<tr>
<td>List of tables</td>
<td>xi</td>
</tr>
<tr>
<td>List of abbreviations</td>
<td>xii</td>
</tr>
<tr>
<td>Definition of operational terms</td>
<td>xiii</td>
</tr>
<tr>
<td>Abstract</td>
<td>xv</td>
</tr>
</tbody>
</table>

## CHAPTER ONE: INTRODUCTION

1.1 Background information

1.2 Statement of the problem

1.3 Justification of the study

1.4 Study research question

1.5 Study objectives

1.6 Study hypothesis

## CHAPTER TWO: LITERATURE REVIEW

2.0 Introduction

2.1 Risk factors for breast cancer

2.1.1 Age at Menarche
3.2.2 Economic activities .........................................................33
3.2.3 Health facilities ............................................................33

3.3 Study population .............................................................33

3.4 Recruitment of study participants ........................................35
3.4.1 Cases ........................................................................35
3.4.2 Controls .......................................................................37
3.4.3 Sample size determination ...............................................38

3.5 Data variables ....................................................................39

3.6 Data collection ...................................................................40

3.7 Data analysis ......................................................................41

3.8 Ethical consideration ..........................................................42

3.9 Limitations .........................................................................43

CHAPTER FOUR: RESULTS ............................................................45

4.0 Introduction ......................................................................45

4.1 Goodness-of-Fit Test ..........................................................45

4.2 Comparison of cases and controls ......................................45

4.3 Description of study participants by independent variables ....47
4.3.1 Socio-demographic characteristics ..................................47
4.3.2 Anthropometrical status and behavioral practices ...............50
4.3.3 Medical, breastfeeding and family planning history ............51
4.3.4 Personal and family history of breast cancer........................................53
4.3.5 Reproductive characteristics..................................................................55
4.4 Identification of risk factors for breast cancer...........................................56
4.5 Magnitude and direction of association between breast cancer and identified risk factors by logistic regression .........................................................57
4.5.1 Results of the univariate analysis of risk factors .................................57
4.5.2 Results of the multivariate analysis of risk factors...............................61

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATION.........62

5.1 Discussion.................................................................................................62
5.2 Conclusion.................................................................................................67
5.3 Recommendation........................................................................................69

REFERENCES.................................................................................................71

APPENDICES.....................................................................................................88
LIST OF FIGURES

Figure 2.1: Analytical framework for breast cancer risk factors.........................31

Figure 3.1: Analytical framework for recruitment of study participants................36

Figure 4.1: Age distribution of all study participants ........................................46

Figure 4.2: Age distribution of study participants (Cases) ..................................48
LIST OF TABLES

Table 1.1: The most Common Cancers in Kenya in order of prevalence.................................2
Table 2.1: Approximate 5-year survival rate for breast cancer .............................................27
Table 3.1: Sample size calculation .........................................................................................38
Table 4.1: Two-sample Kolmogorov-Smirnov test for equality of distribution functions........45
Table 4.2: Distribution of study participants by socio-demographic characteristics ............49
Table 4.3: Anthropometrical measurements and behavioral characteristics of the study participants ........................................................................................................51
Table 4.4: Medical, breastfeeding and family planning history of study participant ..........52
Table 4.5: Distribution of study participants by personal and family history .......................51
Table 4.6: Distribution of study participants by reproductive characteristics ..................55
Table 4.7: Risk factors for breast cancer derived from univariate logistic regression analysis .........................................................................................................................60
Table 4.8: Risk factors for breast cancer derived from multivariate logistic regression analysis .........................................................................................................................61
LIST OF ABBREVIATIONS

ABBI - Advanced Breast Biopsy Instrument
AIDS - Acquired Immunodeficiency Syndrome
BMI - Body Mass Index
CI - Confidence Interval
CIS - Carcinoma in situ
DCIS - Ductal Carcinoma in Situ
DNA - De-oxy -ribonucleic Acid
EBRT - External Beam Radiotherapy
FNA - Fine Needle Aspiration
HRT - Hormone Replacement Therapy
IDC - Infiltrating Ductal Carcinoma
ILC - Infiltrating Lobular Carcinoma
LCIS - Lobular Carcinoma in Situ
MIBB - Minimally Invasive Breast Biopsy
PGH - Provincial General Hospital
PSA - Prostate Specific Antigen
RR - Relative Risk
TB - Tuberculosis
SE - Standard Error
WHO - World Health Organization
DEFINITION OF OPERATIONAL TERMS

• Behavioral practices: For the purpose of this study the term means beer consumption and/or cigarette smoking.

• Tumor or tumour: is synonymous with neoplasm, specifically solid neoplasm. Note that some neoplasms, such as leukemia, do not form tumors.

• Neoplasm: the scientific term to describe an abnormal proliferation of genetically altered cells. Neoplasms can be benign or malignant:
  o Malignant neoplasm or malignant tumor: synonymous with cancer.
  o Benign neoplasm or benign tumor: a tumor (solid neoplasm) that stops growing by itself, does not invade other tissues and does not form metastases.

• Invasive tumor is another synonym of cancer. The name refers to invasion of surrounding tissues.

• Lumpectomy: Removal of a small part of the breast

• Mastectomy: Removal of the whole breast

• Multi-variate analysis (MVA): - is based on the statistical principle of multivariate statistics, which involves observation and analysis of more than one statistical variable at a time.

• Uni-variate analysis: - methods for analyzing data on a single variable at a time.

• Odds ratio: The odds ratio is a statistical description and reflects how much more likely it is that the disease will occur given the exposure (e.g. twice as likely, 10 times as likely, etc.), compared with the non-exposed population

• P value: P value examines the predictive effect of each factor on the risk for breast cancer. P < 0.05 was considered as statistically significant.
- Menopausal status: Women were classified as menopausal if they had not menstruated during the 6 months preceding the date of data collection irrespective of age.
- A full-term pregnancy was a pregnancy lasting 8 months or longer.
- Pre-malignancy, pre-cancer or non-invasive tumor: A neoplasm that is not invasive but has the potential to progress to cancer (become invasive) if left untreated.
- Pre-menopause- The period before a woman stops experiencing monthly menstrual periods.
- Post-menopause- The period after a woman stops experiencing monthly menstrual periods irrespective of age.
- Screening: a test done on healthy people to detect tumors before they become apparent.
- Diagnosis: the confirmation of the cancerous nature of a lump. This usually requires a biopsy or removal of the tumor by surgery, followed by examination by a pathologist.
- Surgical excision: the removal of a tumor by a surgeon.
  - Surgical margins: the evaluation by a pathologist of the edges of the tissue removed by the surgeon to determine if the tumor was removed completely ("negative margins") or if tumor was left behind ("positive margins").
- Grade: a number (usually on a scale of 3) established by a pathologist to describe the degree of resemblance of the tumor to the surrounding benign tissue.
- Stage: a number (usually on a scale of 4) established by the oncologist to describe the degree of invasion of the body by the tumor.
ABSTRACT

Introduction: Breast cancer is the most common cancer in women in Kenya (Mulemi, 2010) and the second most common cancer among women in Nyeri County (HISR 2009), only second to cervical cancer. It is the most common cause of cancer-related mortality and morbidity among all women in the world and the commonest cause of cancer deaths in United States of America among women aged 20 to 59 years (Jemal et al, 2005). Research has long recognized risk factors for breast cancer such as a positive family history of breast cancer, early menarche, late menopause, nulliparity and lack of breastfeeding (Newcomb et al, 1994; McTiernan et al, 1992; MacMahon et al, 1973; Gunnar et al, 1987; Roxanne Nelson et al, 2009). While numerous studies have been conducted in industrialized countries to assess the epidemiology of breast cancer, few have been done in Sub-Sahara African populations; Kenya included (Mutuma and Korir 2006). Such studies are of interest because different risk profiles may help to explain the differences in occurrence of the disease in different populations. This study is therefore aimed at determining the risk factors for breast cancer in Nyeri County, central Kenya.

Method: A matched (1:3) case-control study was conducted in Nyeri County of central province in Kenya in the year 2010. Data collection was done between March and May 2010 where a total of 81 biopsy/fine needle aspiration proven cases of breast cancer and 272 controls that were matched by age within a 5 year period interval were enrolled. Statistical analysis was carried out using Stata version 10.0 software where chi square test of significance and then logistic regression with odds ratios at 95% confidence intervals were estimated.

Results: Data analysis showed the following independent risk factors that were predictive for breast cancer among women under study; family history of breast cancer and any other cancer, age at menarche, menstrual pattern, menopausal status and age at menopause.
Those women in the study who had no first-degree family history of breast cancer were reported to be 76% (OR=0.24, 95% CI: 0.11-0.55) less likely to have breast cancer compared to those who had a family history of the disease in univariate analysis and 83% (OR = 0.17, 95% CI: 0.05-0.56) in multivariate analysis respectively, p < 0.05. Equally, women with no first-degree family history of other cancer apart from breast were reported to be less likely to have breast cancer compared to those women with positive first-degree family history by 64% (OR=0.36, 95% CI: 0.20-0.66) in univariate and 73% (OR = 0.27, 95% CI: 0.10-0.68) in multivariate analysis respectively, p < 0.05.

Pre-menopausal status and late age at menopause (≥ 50 years) were reported to be protective factors and statistically significant in univariate analysis with an OR = 0.55 (95% CI: 0.33-0.90) and OR= 0.22 (95% CI: 0.05 - 0.94) respectively, p < 0.05. Early age at menarche was not statistically significant, p > 0.05.

However, contrary to other studies late menopause ≥ 50 was shown to reduce the risk of breast cancer among the women, while late age at menarche increased the risk.

For menstrual pattern, in univariate analysis, the risk of developing breast cancer increased 3-fold in women with irregular menstrual pattern compared with women with regular menses, (OR = 2.88, 95% CI: 1.45 -5.70), p < 0.05. The risk changed to increase by 1.5-fold in multivariate analysis, but not statistically significant.

**Conclusions:** This study revealed the role of some modifiable determinants of breast cancer that can be focused on by public health intervention in Nyeri district. Accordingly, those women who have one or more of the following risk factors should be followed up keenly and screened regularly for breast cancer: positive family history of breast cancer and other cancers. The role of
hormone replacement therapy, irregular menstrual pattern, age at menarche and menopausal status as risk factors for breast cancer should be investigated further.
1.1 Background information

The etiology of breast cancer remains largely unknown but as the risk factors that influence its development continue to be clarified, about 75% of the patients with the disease have no identifiable risk factors other than sex and age (Adebamowo et al, 2000). The incidence, morbidity and mortality are also on the rise globally with the rise in incidence occurring more rapidly in women in the past half century in population groups that hitherto enjoyed a low incidence of the disease (Okobia et al, 2005).

In 2005, breast cancer struck an estimated 211,000 women in the United States (American Cancer Society, 2005) and more than 1.1 million worldwide (Lodha et al, 2010). Besides skin cancer, breast cancer is the most commonly diagnosed cancer among U.S. women. More than 1 in 3 cancers in women (about 28%) are breast cancer (Breast Cancer Statistics, 2011).

It was reported to be the most common malignancy in women worldwide and the leading cause of cancer death in women in developing countries, accounting for 23% (1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths in 2008 (Ahmedin et al, 2008).

Breast cancer is set to become the newest epidemic in the developing world, claiming a vast number of lives, and there is currently limited funding available to tackle this disease. It is now the leading cause of cancer death among females in low economic
countries, which is a shift from the previous decade during which the most common cause of cancer death was cervical cancer (Ahmedin et al, 2008).

The disease is also the most common malignancy in Kenya as reported by practicing physicians and surgeons and the incidence seems to be on the increase, a fact corroborated by Nairobi Cancer Registry (Mutuma and Korir, 2006).

Studies show breast and cervical cancers to be the most common cancers among women in Kenya, with incidence rates of about 19% and 10% respectively (Mulemi, 2010).

In Nyeri, crude data from a preliminary review of the district Health Information System Registry (HISR) in 2009 showed breast cancer to be the second most common female cancer after cervical cancer at 16.4% and 6% respectively, n =143. This was a two-year unpublished report covering July 2007-June 2009. However, a discussion with many clinicians indicate that this is an underestimate which could be due to poor access to medical services, socioeconomic factors, lack of efficient population-based cancer registries and the absence of breast cancer screening programs in Kenya.

Table 1.1 shows the most common cancers in Kenya.

Table 1.1: The most Common Cancers in Kenya in order of prevalence.

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Head &amp; Neck</td>
<td>Breast</td>
</tr>
<tr>
<td>2. Esophagus</td>
<td>Cervix Uteri</td>
</tr>
<tr>
<td>3. Prostate</td>
<td>Head &amp; Neck</td>
</tr>
<tr>
<td>4. Stomach</td>
<td>Esophagus</td>
</tr>
<tr>
<td>5. Kaposi Sarcoma</td>
<td>Stomach</td>
</tr>
<tr>
<td>6. Liver</td>
<td>Ovary</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>Skin</td>
</tr>
<tr>
<td>8. Skin</td>
<td>Kaposi Sarcoma</td>
</tr>
<tr>
<td>9. Colon</td>
<td>Non-Hodgkin Lymphoma</td>
</tr>
<tr>
<td>10. Eye (Retinoblastoma)</td>
<td>Eye (Retinoblastoma)</td>
</tr>
</tbody>
</table>

Although the actual cause of breast cancer is not known, epidemiological studies have implicated some potential etiologic factors. Available evidence indicates that lifetime exposure to estrogen and environmental factors may be a critical factor in breast carcinogenesis. Increasing age, the female sex, reproductive characteristics such as age at menarche and menopause, menstrual irregularity, age at first and last childbirth, parity and breast feeding have also been linked to breast carcinogenesis (Okobia et al, 2005).

Cancer pathogenesis is well documented in literature and nearly all cancers are caused by abnormalities in the genetic material of the transformed cells. These abnormalities may be due to the effects of carcinogens, such as tobacco smoke, radiation, chemicals, or infectious agents. Other cancer-promoting genetic abnormalities may be randomly acquired through errors in DNA replication, or are inherited, and thus present in all cells from birth.

Appreciating relevant risk factors for breast cancer in the population is central to any preventive and control program aimed at reducing the burden of the disease through design and implementation of culturally sensitive interventions (Okobia et al, 2005). The study assessed the role of these factors in 81 cases of breast cancer and 272 controls recruited from hospitals in Nyeri district and its environs.

1.2 Statement of the problem

Cancer of the breast is the most common malignancy in women worldwide and the leading cause of cancer death in women in developing countries. In 2005, breast cancer struck an estimated 211,000 women in the United States (American Cancer Society [3])
2005) and more than 1.1 million worldwide (Parkin et al. 2005). Besides skin cancer, breast cancer is the most commonly diagnosed cancer among U.S. women. More than 1 in 4 cancers in women (about 28%) are breast cancer (Breast Cancer Statistics 2011). Cancer is set to become the newest epidemic in the developing world, claiming a vast number of lives, and there is currently limited funding available to tackle this disease. Although it has a low incidence in Africa compared with other continents, the ratio of mortality to incidence is among the highest in the world (Uganda Breast Cancer Working Group 2003). Some areas of Africa have seen an increase in incidence in recent years possibly being related to increased screening and awareness (Global Media 2009).

Cases of breast cancer in Kenya have been reported by practicing physicians and surgeons to be on the rise, a fact corroborated by Nairobi cancer Registry (Mutuma and Korir 2006). It is a problem of major public health concern in the country and it accounted for an estimated incidence of 1.08 per 100,000 person-years in females in the period 1981-1985 (Okobia et al 2005). Although this data on invasive breast cancer is largely based on the hospital reports, it is clear that the disease accounts for more deaths among women than from any other cancer (Mutuma and Korir 2006). The disease is thus an important cause of premature death, causing hardship far beyond its effects on the woman herself. Therefore, investing in the prevention and treatment of breast cancer would not only reduce mortality, but it has social and economic implications as well.

A number of variables associated with increased risk of breast cancer in women have been identified. Reproductive and hormonal factors have been reported to contribute most
to the development of breast cancer. Others include induced abortion/miscarriage, genetic predisposition, family history of breast cancer, radiation, obesity, alcohol, cigarette smoking and occupation exposure.

Implicated reproductive risk factors include, age at menarche, menstrual irregularity, age at menopause, age at first full-term pregnancy, parity and breastfeeding. Early menarche (before 12 years), irregular menstruation, delayed menopause and early first full-term pregnancy (before 20 years) have been reported to confer increased risk for breast cancer (Clemons and Goss, 2001; Michels-Blanck et al, 1996; Cuzick, 2003; Bernstein, 2002). Conversely, late first full-term pregnancy (after 30 years), multi-parity (over 5 children) and breast feeding have been reported to be protective (Bernstein, 2002; Okobia et al, 2006; Romieu et al, 1996).

Studies on hormone replacement therapy, genetic factors, family history of breast cancer for a first-degree relative, alcohol consumption, high doses of radiation exposure and synthetic chemicals, active/passive smoking and occupational exposures have been reported to be associated with an increased risk of breast cancer (Marcus et al, 1999; Roxanne 2008; McGregor et al, 1977; Consensus Statement on Breast Cancer and the Environment, 2009; American Cancer Society, 2009; Bioce et al, 1997; Davis et al, 1998; Morabia et al, 1996; Philip, 2006).

Induced abortion and obesity have reported conflicting results on the risk of breast cancer (Brind et al, 1996; Beral et, al 2004; Eliassen et al, 2006; Huang et al, 1997).
1.3 Justification of the study

In the recent past, there has been a notable increase of non–communicable diseases including cancer in the developing countries and Kenya is no exception. Despite this, occurrence of cancer is often neglected as a health problem of major public health concern.

The role of the risk factors under investigation in this study in the development of breast cancer in a developing country like ours is different as compared to that seen in western population (Yasmin et al, 2006). This is because for example, parity, younger age at first live birth and lactation practices are part of our culture whereas these factors are far less prevalent in western women. During literature review, the researcher could only find studies on breast cancer risk factors that are mainly done in western countries and a few African countries but none in Kenya. However, the results of some of the studies were also conflicting.

The study was therefore conducted to isolate the risk factors that are associated with the development of the disease in our population with a view to generating some recommendations that could be used to solve the growing puzzle surrounding the disease and develop strategies on how to reduce the burden. The study would also add into the body of knowledge on key intervention areas for breast cancer prevention and control.

1.4 Study research question

Are reproductive, hormonal, induced abortion/miscarriage, genetic predisposition, family history of breast cancer and other cancers, radiation, obesity, alcohol, cigarette smoking
and occupation exposure associated with the development of breast cancer among women in Nyeri County?

1.5 Study objectives

General: - The main objective of the study was to determine breast cancer risk factors among women in Nyeri County.

Specific: - The specific objectives of the study were:

➢ To describe the cases and controls by demographic variables
➢ To isolate the risk factors for breast cancer in Nyeri County
➢ To determine the magnitude and direction of risk factors for breast cancer

1.6 Study hypothesis

H₀: There is no association between reproductive, hormonal, induced abortion/miscarriage, genetic predisposition, family history of breast cancer and other cancers, radiation, obesity, alcohol, cigarette smoking and occupation exposure and the development breast cancer among Nyeri women.

H₁: There is a strong association between reproductive, hormonal, induced abortion/miscarriage, genetic predisposition, family history of breast cancer and other cancers, radiation, obesity, alcohol, cigarette smoking and occupation exposure and the development breast cancer among Nyeri women.
CHAPTER TWO: LITERATURE REVIEW

2.0 Introduction

It had been projected that in 2010, cancer was to become the world's leading cause of death, surpassing heart disease. Breast, cervical, liver and prostate as well as HIV/AIDS-related cancers have been reported to be among the most common in Africa (Newman et al 2005). In developing countries such as Kenya, cancer is among the three leading causes of death in adults. The major cancers among females in Kenya are cervical and breast cancer, which are found in the peak age group 35 to 54 years (Mutuma and Korir, 2006). This is a time when the women have a lot of family and economic responsibilities.

2.1 Risk factors for breast cancer

The etiology of breast cancer remains largely unknown but exposure to some risk factors has been associated with the developing of the disease. A risk factor is anything that increases a person's chance of developing cancer and many have been associated with breast cancer.

For the past two centuries, it has been suspected that sex hormones particularly estrogens may play some role in the etiology of breast cancer. MacMahon et al demonstrated an association between hormones and breast cancer in the early 1970s (Kathleen and Michelle, 1999). In 1983, Pike and colleagues (Henderson et al, 1988) indicated that the pre-menopausal period probably creates a fertile period for the pathophysiological processes culminating in the manifestation of the cancer.
Many studies have been conducted since then, in an attempt to explain the role of female hormone in the etiology and biological behavior of breast cancer.

A number of reproductive risk factors have also been implicated in the etiology of the disease, including age at menarche and menopause, menstrual irregularity, age at first full term pregnancy, parity, breastfeeding, and age at last childbirth. Also, hormone replacement therapy and environmental exposure to hormone-related substances (xenohormones) have been implicated. Other risk factors include family history of breast cancer and genetic predisposition and occupation exposure. These factors are discussed under the following sub-headings:

2.1.1 Age at menarche

There is strong evidence that early menarche increases the risk of breast cancer while late menarche tends to be protective. Women who experience menarche before 12 years have been reported to have a 50% higher risk for breast cancer compared to women having menarche when older than 14 years (Clemons and Goss 2001). In a study by Apter et al (1989), early menarcheal age was associated with a higher estrogen production level during post-menarcheal years. Results from a combined analysis of four Italian case-control studies showed the risk of breast cancer to be lower in women whose menarche occurred at age 15 or over, but the risk did not increase with decreasing age at menarche below age 15. The relative risk (RR) was 0.9 (95% CI 0.7-1.0) for those with menarche at age 15, 0.8 (95% CI 0.6-0.9) for menarche at 16, and 0.7 (95% CI 0.5-0.8) for menarche at age 17 or over (La Vecchia et al. 1992). A study by Garcia et al (2006) reaffirmed the known link of increased risk of breast cancer with early menarche with an estimated decrease in risk of 22% per five year delay in menarche.
This increase could be associated with estrogen which is known to initiate the proliferation of breast tissue and has a greater probability of replication errors causing preneoplastic lesions in proliferating tissue (de Waard and Trichopoulos 1988).

### 2.1.2 Menstrual Irregularity

It has been reported that the age of onset of regular menstrual cycles may have a role to play in mammary carcinogenesis and this has been supported by findings from a study by Michels-Blanck et al (1996). Women who reported having irregular menstruation at age 20 years were at reduced risk for breast cancer (Relative risk = 0.84; 95% CI 0.74-0.96). Irregular menstrual cycles or delay in the establishment of regular menses, independent of age at menarche was also associated with a decreased risk (La Vecchia et al, 1987). The lifelong irregularities in menstrual pattern were found to be less common among the cases (relative risk = 0.6, 95% CI 0.5-0.8).

### 2.1.3 Age at Menopause

Delayed menopause is associated with a breast cancer risk elevation of 3% for each delayed year (Cuzick, 2003). Results indicate that the hormonal pattern of pre-menopausal women {cyclic production of relatively large amounts of estradiol (E) and progesterone (Pg)} causes a greater increase of risk of breast cancer than the hormonal pattern in post-menopausal woman (constant low E and very low Pg). This evidence has been strengthened by the findings in a study by Feinleib (1968). A reduction in breast cancer risk has been reported to be most likely attributable specifically to removal of the ovaries which produce estradiol and progesterone, and the earlier the age at oophorectomy, the lower the risk (Feinleib 1968).
The age at menopause has been reported to be at 50 years on average in a rural Kenyan population (Noreh et al, 1997).

**2.1.4 Age at First Full-Term Pregnancy**

The importance of age at first birth as a risk factor was first established by MacMahon et al (1970) from a large international case control study. He reported that first full-term pregnancy before age of 18 years reduces the risk of breast cancer and the risk is significantly higher in women with first full term pregnancy after the age of 35 years (MacMahon et al, 1970). Most studies have also found that for first births over the entire childbearing period, the lower a woman’s age at first birth, the lower the risk (Paffenbarger et al, 1980; Lubin et al, 1982; Helmrich et al, 1983; Schatzkin et al, 1987; Yuan et al, 1988; Eva et al, 1988; Layde et al, 1989; Leon, 1989; Kelsey et al, 1993; Romieu et al, 1996; Lambe et al, 1996; Wohlfahrt et al, 2001; Hinkula et al, 2001; Palmer et al, 2003).

While some studies have reported no protective effect for early age at first full term pregnancy, others have found that age over 30 years at first childbirth was associated with an increased risk of breast cancer relative to nulliparous women (Adami et al 1990). This was reaffirmed by a study conducted by the Huiyan (2010), which revealed an increased risk of breast cancer with late age at birth of first child. Parous women whose first full-term pregnancy occurred at age 35 years or later had a 118% greater risk for breast carcinoma in situ (RR = 2.18, 95% CI = 1.36 to 3.49) and 27% greater risk for
invasive breast cancer (RR = 1.27, 95% CI = 0.99 to 1.65) than those whose first full-term pregnancy occurred before age 21 years.

### 2.1.5 Parity

A protective effect of parity independent of the effect of age at first full term pregnancy has been reported. A study by Kvale et al (1987), found a consistent and highly significant inverse association between high parity and breast cancer. In a study by Collaborative Group on Hormonal Factors in Breast Cancer (1996), women with breast cancer had, on average, fewer births than did controls, at 2.2 and 2.6 births respectively. Also, in another case control study in Nigeria (Okobia et al, 2006), parity of more than 4 births (OR, 0.50; 95% CI: 0.17-1.46) was associated with reduced risk of breast cancer.

The apparent protective effect of high parity was found in all subgroups of the patients according to demographic variables and could not be explained by other reproductive factors (Okobia et al, 2006). There appears to be consistency in this finding across studies conducted in both high-risk, intermediate-risk and low-risk areas (Okobia et al, 2006). The protective effect of parity seems stronger in post-menopausal than in pre-menopausal women, possibly on account of the confounding effect of time since last birth in younger women. The long-term protective effects of pregnancy are contrasted with the observation that the risk of carcinogenesis is actually increased in the short term after a pregnancy (Pathak and Whittemore, 1992).

### 2.1.6 Breastfeeding

A number of epidemiological studies have investigated the relationship between breastfeeding and breast cancer risk. Overall, studies suggest a 20-30 percent reduction in
risk among women who have ever breastfed (Romieu et al, 1996). More consistently, a longer duration of breastfeeding has been associated with breast cancer risk reductions as great as 40-60 percent (Yang et al, 1993). Although childbearing is known to protect against breast cancer, whether or not breastfeeding contributes to this protective effect is unclear (Collaborative Group on Hormonal Factors, 2002).

Age at first lactation has been identified as an important risk in the development of breast cancer, with an earlier age at initiation of lactation being associated with a stronger reduction in risk for premenopausal women and possibly for postmenopausal women (Freudenheim et al, 1997). However, because of the very strong correlation between age at first birth and age at first lactation, the independent effect of age at first lactation is difficult to isolate. It is notable that in countries with low risk of breast cancer, the protection conferred by lactation appears to be stronger and to be sustained throughout the post-menopausal period as well. Some studies suggest that an inverse association may exist only among pre-menopausal women particularly among those with a longer duration of breastfeeding and with early age at first breastfeeding (Furgerg et al, 1999).

2.1.7 Number of years Using Hormonal Contraceptives

The relationship between exogenous hormones, primarily hormonal contraceptives and hormone replacement therapy, to breast cancer has been researched extensively. The lack of total consistency among many studies may be attributed in part to the fact that these exposures are not static. Changes in pattern of use, reductions in hormone dose, and temporal considerations all contribute to the difficulty in comparing the many studies (Hulka, 2001).
The Collaborative Group on Hormonal Factors in Breast Cancer was set up in 1992 to gather and reanalyze data from the many epidemiological studies that have addressed this issue in an effort to provide more definitive information on the risk associated with oral contraceptive use (Collaborative Group on Hormonal Factors, 1996). The results of the analyses of data pooled from 54 studies were reassuring, with ever use of oral contraceptives associated with a very small increase in risk (relative risk 1.07).

The greatest risk was observed among current and recent users (within 4 years of diagnosis), with the risks declining with increasing time since last use. No increased risk was apparent for women who had discontinued use for 10 or more years. Duration of use, age at first use, or dose of the oral contraceptive had little effect on breast cancer risk, once recency of use was taken into account. Two studies examined the relationship between oral contraceptive use and breast cancer risk among African American adolescents and found an elevated breast cancer risk among users, particularly for first use below the age of 20 years (Marcus et al, 1999).

2.1.8 Number of years using Hormone replacement therapy

Available evidence suggests that menopausal estrogens are associated with a modest increase in breast cancer risk. Long-term use (5 years or more) among current users or recent users appears to be associated with a 30-50 % increase in breast cancer risk (Collaborative Group on Hormonal Factors, 1997). In a meta-analysis study by Steinberg et al (1991), he focused on risk of breast cancer according to duration of use and revealed no increase in risk with less than 5 years of use. However, for each year after 5 years of use, a proportional increase in relative risk of 0.015, which is a small increase, was found. The highest risk calculated was 1.3 (95% CI: 1.2 -1.6) for more than 15 years of use.
The results from the Collaborative Group study also showed an increased risk of having breast cancer diagnosed in women using hormone replacement therapy (HRT) and which increased with increasing duration of use. The effect reduced after cessation of use of HRT and largely, if not wholly, disappeared after about 5 years. Among current users of HRT or those who ceased use 1-4 years previously, the relative risk of having breast cancer diagnosed increased by a factor of 1.023 (95% CI: 1.011-1.036; 2P 0.0002) for each year of use; the relative risk was 1.35 (95% CI: 1.21-1.49; 2P 0.00001) for women who had used HRT for 5 years or longer (average duration of use in this group 11 years). This increase is comparable with the effect on breast cancer of delaying menopause, since among never-users of HRT the relative risk of breast cancer increased by a factor of 1.028 (95% CI: 1.021-1.034) for each year older at menopause. Five or more years after cessation of HRT use, there was no significant excess of breast cancer overall or in relation to duration of use.

2.1.9 Number of Induced abortions/Miscarriage

Epidemiological evidence of a positive association between induced abortion and the incidence of breast cancer was first presented by Segi et al (1957), based on cases diagnosed between 1948 and 1952. Since then, several reports have appeared in the literature that shows either no risk or an elevated risk for breast cancer following induced abortion. After an extensive and detailed meta analysis of the existing literature on the subject, Brind et al (1996), noted that a significant positive association exists between induced abortion and breast cancer risk, independent of the effect an induced abortion has in delaying first full term pregnancy.
Moreover, the increased risk is seen in both prospective and retrospective studies from around the world, in populations with the widest imaginable differences in ethnicity, diet, socioeconomic and lifestyle factors and which differ in many aspects of design and whose data extend over more than half a century in time (Brind et al, 1996).

The finding is consistent with the existing knowledge on human biology, oncology and reproductive endocrinology. It is also supported by laboratory data as well as epidemiological data on other risk factors involving estrogen excess. All these together, point to a plausible and likely mechanism by which the surging estradiol of the first trimester of pregnancy, if it is aborted, may significantly add to a woman’s breast cancer risk.

In contrast with these studies, a collaborative study by Beral et al (2004) assessed the possible relation between breast cancer and previous spontaneous and induced abortions. Pregnancies that ended as a spontaneous or induced abortion did not show increased woman’s risk of developing breast cancer. The overall relative risk of breast cancer, comparing women with a prospective record of having had one or more pregnancies that ended as a spontaneous abortion versus women with no such record, was 0.98 (95% CI: 0.92-1.04, p 0.5). The corresponding relative risk for induced abortion was 0.93 (95% CI: 0.89-0.96, p 0.0002). Induced abortion is on the increase in most urban centers in Kenya, particularly among adolescent girls who resort to induced abortion as a means of family planning (Sunday et al, 2010).
2.1.10 Genetic risk factors

About 5-10% of breast cancer cases are thought to be hereditary, resulting directly from gene changes (called mutations) inherited from a parent (American Cancer Society, 2009). The most common inherited mutations are those of the BRCA1 and BRCA2 genes. In normal cells, these genes help to prevent cancer by making proteins that help keep the cells from growing abnormally. If you have inherited a mutated copy of either gene from a parent, you are at increased risk for breast cancer. Women with an inherited BRCA1 or BRCA2 mutation have up to an 80% chance of developing breast cancer during their lifetime, and when they do it is often at a younger age than in women who are not born with one of these gene mutations. Women with these inherited mutations also have an increased risk for developing ovarian cancer (American Cancer Society, 2009).

Although BRCA mutations are found most often in Jewish women of Ashkenazi (Eastern Europe) origin, they are also seen in African-American women and Hispanic women and can occur in any racial or ethnic group. Other gene changes that might also lead to inherited breast cancers are ATM, CHEK2, p53 and PTEN gene (Joli et al, 2005). These genes do not impart the same level of breast cancer risk as the BRCA genes, and do not frequently cause familial (inherited) breast cancer. The ATM gene normally helps repair damaged DNA. Certain families with a high rate of breast cancer have been found to have mutations of this gene. The CHEK2 gene increases breast cancer risk about twofold when it is mutated (Joli et al, 2005). In women who carry the CHEK2 mutation and have a strong family history of breast cancer, the risk is greatly increased.
Inherited mutations of the p53 tumor suppressor gene can also increase the risk of developing breast cancer, as well as several other cancers such as leukemia, brain tumors, and sarcomas (cancer of bones or connective tissue).

The Li-Fraumeni syndrome, named after the 2 researchers who first described this inherited cancer syndrome, is a rare cause of breast cancer (Roxanne et al, 2009). The PTEN gene normally helps regulate cell growth. Inherited mutations in this gene cause Cowden syndrome, a rare disorder in which people are at increased risk for both benign and malignant breast tumors, as well as growths in the digestive tract, thyroid, uterus, and ovaries. Genetic testing can be done to look for mutations in the BRCA1 and BRCA2 genes (or less commonly in other genes such as PTEN or p53).

### 2.1.11 Family history of breast cancer

Women with a significant family history of breast cancer where first-degree relative (mother, sister, or daughter) have this disease approximately doubles a woman's risk, while having 2 first-degree relatives increases her risk about 5-fold, even if they are negative for the BRCA1 and BRAC2 mutations (Roxanne, 2008). Having 2 or more cases of breast cancer among close relatives younger than 50 years or 3 cases among close relatives of any age is associated with a risk for breast cancer that is 4 times greater than that seen in the general population (Roxanne, 2008).

Although the exact risk is not known, women with a family history of breast cancer in a father or brother also have an increased risk of breast cancer (Cancer R.I.D Guide, 2009). Altogether, about 20% to 30% of women with breast cancer have a family member with
this disease. This implies that 70-80% of women who get breast cancer do not have a family history of this disease. A woman with cancer in one breast has a 3- to 4-fold increased risk of developing a new cancer in the other breast or in another part of the same breast. This is different from a recurrence (return) of the first cancer (Cancer R.I.D Guide, 2009).

2.1.12 Radiation

There is abundant evidence from follow-up studies of survivors of the atomic bombs in Japan (McGregor et al, 1977), of women undergoing radiation treatment for acute post-partum mastitis and of women who underwent fluoroscopy in the course of treatment by pneumothorax for tuberculosis (Bioce et al, 1997) that radiation in high doses can cause breast cancer. Exposure of the breast to radiation while a woman is 10-19 years of age is associated with an especially high risk (McGregor et al, 1977; Bioce et al, 1997), a trend not seen in other cancers. Two reasons for this increased sensitivity might be that either the breasts are rapidly developing during these ages, or most women have not given birth to their first child at this time, and the breasts may be more susceptible before first birth occurs (McGregor et al, 1977).

2.1.13 Obesity

Obesity has been associated with a risk for breast cancer. However, obesity in childhood has not proven to have an effect on the risk of breast cancer later in life (Huang et al, 1997), but weight gain after the age of 18 or after menopause has been associated with increased risk of breast cancer among postmenopausal women (Eliassen et al, 2006).
On the contrary, a higher body mass index (BMI) at 18 years has been associated with a lower risk of breast cancer in premenopausal life and, in some studies in postmenopausal life as well (Huang et al, 1997). A high BMI (>31 vs. < 21) has also been associated with a 46% lower risk for breast cancer in premenopause (Friedenreich, 2001). One explanation given for the increased risk for breast cancer after menopause is that in obese women, there is high amount of endogenous estrogens produced in adipose tissue. Furthermore, obesity is reported to increase the circulating concentrations of insulin, which may be associated with the risk for breast cancer (Friedenreich, 2001). Tall women have also been reported to have a higher risk for breast cancer (Friedenreich, 2001). Childhood energy intake, the cumulative exposure to growth hormone and insulin-like growth factor-I, or the number of ductal stem cells in the mammary gland have been proposed as potential biologic mechanisms associated with an increased breast cancer risk among tall women.

2.1.14 Alcohol

Some studies have found a 10% increase in risk of breast cancer for women who have one drink per day compared to non-drinkers, and a 20% increase at two drinks per day (Davis et al, 1998). In a case control study where over 80% of the relevant information worldwide on alcohol and tobacco consumption and breast cancer were collated, checked and analyzed centrally, the relative risk of breast cancer was reported to be 1.32 (1.19–1.45, P<0.00001) for an intake of 35–44 g per day alcohol, and 1.46 (1.33–1.61, P<0.00001) for ≥45 g per day alcohol. The relative risk of breast cancer was reported to have increased by 7.1% (95% CI 5.5–8.7%; P<0.00001) for each additional 10 g per day
intake of alcohol, i.e. for each extra unit or drink of alcohol consumed on a daily basis. This increase was reported to be the same in ever-smokers and never-smokers (7.1% per 10 g per day, P<0.00001, in each group).

The authors concluded that if the observed relationship for alcohol is causal, then the results suggest that about 4% of the breast cancers in developed countries are attributable to alcohol. In developing countries, where alcohol consumption among controls averaged only 0.4 g per day, alcohol could have a negligible effect on the incidence of breast cancer. Alcohol also appears to increase circulating levels of estradiol. Marsha et al (1993) reported that two drinks of ethanol a day elevate serum estrogens. Alcohol may also enhance the susceptibility of mammary cells to carcinogenesis and increase the metastatic potential of breast cancer cells (Singletary and Gapstur, 2001).

2.1.15 Cigarette Smoking

Despite years of inconclusive studies, both active and passive smoking have been reported to increase the risk of breast cancer (Morabia et al, 1996). When contrasted with women who had never been exposed to smoke, passive smokers who had been exposed to 2 hours a day for 25 years had 3.2 times the risk compared to women with no such exposures and active smokers (20 or more cigarettes per day) had 4.6 times the risk of breast cancer (Morabia et al, 1996).

However, the relationship between smoking and breast cancer was substantially confounded by the effect of alcohol (Collaborative Group on Hormonal Factors, 2002). But when analyses were controlled by restriction to women with breast cancer and controls who reported drinking no alcohol, smoking was not associated with breast cancer (compared to never-smokers, relative risk for ever-smokers was 1.03, 95% CI
0.98–1.07, and for current smokers was 0.99, 0.92–1.05). However, Perera et al (1995) have demonstrated the presence of carcinogen called DNA adducts, which are biomarkers characteristic of tobacco smoke and polycyclic aromatic hydrocarbons in the breast tissue of women with breast cancer.

2.1.16 Occupation

In the last two decades, greater attention has been focused on occupational exposures that may be responsible for some proportion of breast cancer incidence. When groups of breast cancer cases occur, particularly among relatively young persons, an occupational exposure should be suspected. When all the known risk factors and characteristics are taken into account, as many as half of all breast cancer cases remain unexplained. A considerable and growing body of evidence indicates that exposure to radiation and synthetic chemicals is contributing to the epidemic of breast cancer and other cancers in the United States and other industrialized countries (Consensus Statement on Breast Cancer and the Environment, 2009). A number of chemicals induce breast cancer in rodents— including solvents, pesticides and polycyclic aromatic hydrocarbons — and these might serve as leads for studies in humans (Gwen et al, 1996).

Strong links have also been established between breast cancer risk in women and ionizing radiation. Evidence for nonionizing radiation (electromagnetic fields) exposures and breast cancer is suggestive, albeit limited (Gwen et al, 1996). In the United States about 5% of cancer in women is probably due to occupational exposures (Philip, 2006). Although there are many well-established risk factors for breast cancer, occupational exposures have not been fully explored. Yet, among the populations actually exposed, occupational cancer is a major health hazard. In a study by Betsey et al (2002), they
found that breast cancer risk varied with reported occupation. They also found that overall; the high-risk occupations were more likely to be sedentary in nature, supporting the association between low physical activity and breast cancer risk (Betsey et al, 2002). Several studies have suggested that women, who work at night such as nurses on a night shift, may have an increased risk of developing breast cancer. This is a fairly recent finding, and more studies are looking at this issue. Some researchers think the effect may be due to changes in levels of melatonin, a hormone whose production is affected by the body's exposure to light, but other hormones are also being studied (Roxanne et al, 2009).

Exposure to 60-megaHertz electromagnetic fields and to light at night have been linked experimentally with reductions in melatonin, a natural hormone that suppresses prolactin and estrogen levels. Several epidemiological studies have suggested that women with workplace exposures to electromagnetic fields are at increased risk of breast cancer, although the evidence remains inconsistent (Cos, 1996). Findings indicate that electromagnetic fields impede cellular communication and reduce melatonin levels (Cos, 1996). In another study by Cos et al (1998), results suggest that melatonin may modify DNA synthesis in MCF-7 human breast cancer cells, causing an anti-proliferative effect.

### 2.2 Breast cancer pathogenesis and Management

Nearly all cancers are caused by abnormalities in the genetic material of the transformed cells (Cancer Info Guide, 2009). These abnormalities may be due to the effects of carcinogens, such as tobacco smoke, radiation, chemicals, or infectious agents (Cancer Info Guide, 2009). Other cancer-promoting genetic abnormalities may be randomly acquired through errors in DNA replication, or are inherited, and thus present in all cells from birth. Genetic abnormalities found in cancer typically affect two general classes of
genes (Cancer Info Guide, 2009). First, cancer-promoting oncogenes are typically activated in cancer cells, giving those cells new properties, such as hyperactive growth and division, protection against programmed cell death, loss of respect for normal tissue boundaries, and the ability to become established in diverse tissue environments (Cancer Info Guide, 2009). Secondly, tumor suppressor genes are inactivated in cancer cells, resulting in the loss of normal functions in those cells, such as accurate DNA replication, control over the cell cycle, orientation and adhesion within tissues, and interaction with protective cells of the immune system (Cancer Info Guide, 2009). Cancer pathogenesis is traceable back to DNA mutations that impact cell growth and metastasis. Substances that cause DNA mutations are known as mutagens, and mutagens that cause cancers are known as carcinogens (Cancer Info Guide, 2009).

Particular substances have been linked to specific types of cancer. Many mutagens are also carcinogens, but some carcinogens are not mutagens. Alcohol is an example of a chemical carcinogen that is not a mutagen (Seitz et al, 1998). Such chemicals may promote cancers through stimulating the rate of cell division. Faster rates of replication leaves less time for repair enzymes to repair damaged DNA during DNA replication, increasing the likelihood of a mutation. Cancers are caused by a series of mutations. Each mutation alters the behaviour of the cell somewhat.

Cancer diagnosis usually requires the histologic or cytologic examination of a tissue biopsy specimen by a pathologist (Appendix III), although the initial indication of malignancy can be symptoms or radiologic imaging abnormalities.

There are several types of breast cancer (Appendix IV), although some of them are quite rare. Most these cancers can be treated and some cured (Appendix VI), depending on the
specific type, location, and stage. In some cases a single breast tumor can have a combination of these types or have a mixture of invasive and in situ cancer.

Staging (VII) is the process physicians use to assess the size and location of a patient's cancer. Identifying the cancer stage is one of the most important factors in selecting treatment options (American Cancer Society, 2005). Several tests may be performed to help stage breast cancer including clinical breast exams, biopsy, and certain imaging tests such as a chest x-ray, mammogram, bone scan, CT scan, and MRI scan. Cancers are designated the letter T (tumor size), N (palpable nodes), and/or M (metastasis). Once diagnosed, cancer is usually treated with a combination of surgery, chemotherapy and radiotherapy (American Cancer Society, 2005).

The prognosis of cancer patients is most influenced by the type of cancer, as well as the stage, or extent of the disease. In addition, histologic grading (Appendix V) and the presence of specific molecular markers can also be useful in establishing prognosis, as well as in determining individual treatments (American Cancer Society, 2005).

Breast cancer screening is an attempt to detect unsuspected cancers in an asymptomatic population. If signs of cancer are detected, more definitive and invasive follow up tests are performed to confirm the diagnosis. Screening for cancer can lead to earlier diagnosis which may in turn lead to extended life. Screening for breast cancer with mammograms has been shown to reduce the average stage of diagnosis of breast cancer in a population (National Cancer Institute, 2010). Stage of diagnosis in a country has been shown to decrease within ten years of introduction of mammographic screening programs.
(Mandelblatt et al, 2009). Screening mammography is an x-ray examination of the breasts in a woman who is asymptomatic (has no complaints or symptoms of breast cancer).

Cancer prevention is defined as active measures to decrease the incidence of cancer (Adami et al, 2001). This can be accomplished by avoiding carcinogens or altering their metabolism, pursuing a lifestyle or diet that modifies cancer-causing factors and/or medical intervention (chemoprevention, treatment of pre-malignant lesions). The epidemiological concept of "prevention" is usually defined as either primary prevention, for people who have not been diagnosed with a particular disease, or secondary prevention, aimed at reducing recurrence or complications of a previously diagnosed illness (Adami et al, 2001). There is no primary prevention for cancer. Some breast cancer risk factors are environmental or lifestyle-related in nature, leading to the claim that it is a largely preventable disease (Danaei et al, 2005). Examples of modifiable cancer risk factors include alcohol consumption, smoking, inactivity, and being overweight/obese (American Cancer Society, 2010). Based on epidemiologic evidence, it is now thought that avoiding excessive alcohol consumption and tobacco exposure may contribute to reductions in risk of breast cancers (American Cancer Society, 2010).

The concept that medications could be used to prevent cancer is an attractive one, and many high-quality clinical trials support the use of such chemoprevention in defined circumstances (Gasco et al, 2005). Daily use of tamoxifen, a selective estrogen receptor modulator (SERM), typically for 5 years, has been demonstrated to reduce the risk of developing breast cancer in high-risk women by about 50% (Gasco et al, 2005). A recent study reported that the selective estrogen receptor modulator raloxifene has similar
benefits to tamoxifene in preventing breast cancer in high-risk women, with a more favorable side effect profile (Vogel et al, 2006). In the trial, which studied almost 20,000 women, raloxifene had fewer side effects than tamoxifene, though it did permit more DCIS to form (Vogel et al, 2006).

Breast cancer has a reputation for being a deadly disease. While this certainly applies to certain particular types, the truths behind the historical connotations of cancer are increasingly being overturned by advances in medical care. Some types of cancer have a prognosis that is substantially better than nonmalignant diseases such as heart failure and stroke (Vasileios et al, 2010). Health care professionals are able to predict a patient’s survival rate based on the determined stage of breast cancer.

Table II shows an approximate survival rate for each stage of breast cancer. Percentages vary depending on individual medical situations, etc.

Table 2.1: Approximate 5-year survival rate for breast cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-year Relative Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>I</td>
<td>98%</td>
</tr>
<tr>
<td>IIA</td>
<td>88%</td>
</tr>
<tr>
<td>IIB</td>
<td>76%</td>
</tr>
<tr>
<td>IIIA</td>
<td>56%</td>
</tr>
<tr>
<td>IIIB</td>
<td>49%</td>
</tr>
<tr>
<td>IV</td>
<td>16%</td>
</tr>
</tbody>
</table>

Source: American Cancer Society, 2005

A five-year survival rate refers to the average number of patients who are still alive five years after diagnosis with a specific stage of breast cancer (American Cancer Society, 2005). After seven years, the survival rate decreases for each stage.
The average Stage I breast cancer survival rate is 92%. The Stage II survival rate is 71%, Stage III survival rate is 39%, and the Stage IV survival rate is 11%. It is important to note that these survival rates are based on averages. Some women with advanced breast cancer live significantly longer than seven years. Researchers are constantly developing new treatment alternatives to prolong breast cancer survival. Progressive and disseminated malignant disease has a substantial impact on a cancer patient's quality of life, and many cancer treatments (such as chemotherapy) may have severe side-effects (Quinn et al, 2008). In the advanced stages of cancer, many patients need extensive care, affecting family members and friends. Palliative care solutions may include permanent or "respite" hospice nursing (Appendix VIII).

2.3 Analytical framework for breast cancer risk factors

Breast cancer development depends on the complex interplay of the established risk factors. This analytical framework distinguishes between risk factors that directly cause breast cancer, those that extend the time period of vulnerability of the breast by prolonging breast development and consequent susceptibility to damage, and those that contribute to altered levels of cancer-causing exposures.

**Direct risk factors**

Ionizing radiation and inherited genetic damage are the only established risk factors for breast cancer that directly cause the disease (Rothman, 1988). Radiation and inherited defects can be said to cause breast cancer in that they produce alterations in cell growth, repair, and metabolism that are understood to be mechanistically linked with the development of breast cancer. A variety of studies indicate that the potential for aberrant
growth is dependent on two factors: the rate of cell growth and the extent of exposure (Davis et al, 1992).

**Contributing Factors**

Contributing factors can directly affect overall exposure to circulating hormones and can interact with vulnerability factors. Some hormones are potent stimulators of cell growth (Sonnenschein et al, 1995), and some hormonal metabolites can bind to DNA and trigger aberrant cell growth (Liehr et al, 1996; Telang et al, 1997). For example alcohol increases the total amount of bioavailable estradiol (Kelsey et al, 1996). Bioavailable estradiol represents the fraction of estradiol that is not readily excreted when bound to sex hormone-binding globulin (SHBG) or albumin (Mendel, 1989). This binding reduces the availability of estradiol to the cells. Thus, processes that decrease hormone binding increase circulating levels of estradiol. Contributing factors can also alter metabolism of other growth-regulating hormones that alter breast cell growth and metabolism and increase the likelihood of aberrant cell growth.

A large nurses' health study (Colditz et al, 1990), later corroborated by a women's health study (Gapstur et al, 1992), determined that postmenopausal women who consumed alcohol manifested a 40% increased risk of breast cancer with estrogen administration, while those who did not consume alcohol or consumed it at levels below the average daily intake of 5 g showed no increased risk.
Vulnerability Factors

Vulnerability factors for breast cancer are those that extend the time during which the breast is growing and the rate of this growth. For instance, early menses, no lactation, and late menopause prolong the time period during which the developing breast is potentially exposed to estradiol and deleterious agents (See Fig. 2.1). Evidence for this increased vulnerability is provided by observations of women born to mothers who had unusually high or low levels of estrogen during pregnancy. Toxemia is tied with preeclampsia and lower levels of estrogen. Women born to mothers who were toxemic had an adjusted odds ratio (OR) of 0.41 for breast cancer compared to those who underwent normal pregnancy.

In contrast, women who experienced elevated levels of hormones prenatally or neonatally were found to have an OR of 3.96 (Ekbom et al, 1997). Lactation is a potentially modifiable factor that can be considered as both vulnerability and a contributing risk factor. Premenopausal women who lactated have a reduced risk of breast cancer, with further significant reductions of risk for women who lactate earlier or for longer cumulative duration. Animal studies have demonstrated that early reproductive life breast tissue is positively influenced by lactation (Newcomb et al, 1994).
DIRECT RISK FACTORS

- Radiation Exposure
- Inherited Genetic Mutations

CONTRIBUTING FACTORS

- Alcohol Consumption
- Cigarette Smoking

VULNERABILITY FACTORS

- Age at Menarche
- Menstrual Irregularity
- Age at Menopause
- Age at First Full-Term Pregnancy
- Parity
- Breast Feeding
- Use of Hormonal Contraceptive
- Use of Hormonal Replacement Therapy
- Induced Abortion
- Obesity
- Occupation

INCREASED RISK OF BREAST CANCER

Figure 2.1: Analytical Framework for Breast Cancer Risk Factors and Outcome
CHAPTER THREE: MATERIALS AND METHODS

3.0 Introduction

This section describes the specific way in which the study was executed. It includes a short description of the study design, data variables, study area and population, sampling procedure, methods of data collection, methods of data analysis and ethical considerations.

3.1 Study Design

This was an analytical case control study on women of 20-60 years of age. The case to control ratio was 1 is to 3. The age of the cases considered was that at diagnosis of breast cancer. Matching was done by age group within 5 years interval. However, proportion of controls in each age-specific stratum was fixed in advance based on the expected age distribution of cases. The pre-determined age-specific quotas for sampling of controls were: 1%, 1%, 9%, 20%, 15%, 20%, 10%, 14%, and 10% for age groups 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59 and ≥ 60 years respectively.

3.2 Study Area

3.2.1 Administrative and Physical Location

The study area was the larger Nyeri County which is one of the seven counties of Central Kenya. It has a total area of 3,266 square kilometers and is situated between longitudes 36° and 38° east and between the equator and latitude 0° 38’ south. The county borders Laikipia County to the north, Kirinyaga Count to the east, Murang’a County to the south,
Nyandarua County to the west and Meru County to the northeast. It is divided into seven administrative districts namely Tetu, Mukurweini, Mathira, Nyeri Central, Othaya, Kieni West and Kieni East. There are 37 locations and 194 sub-locations in the county (GoK, 2002/2008). Specifically, the study was carried out in Nyeri provincial hospital, Outspan hospital, Nyeri hospice, Mathari hospital, Karatina hospital, Mukurwe-ini hospital, Kerugoya hospital, and Nanyuki hospital.

3.2.2 Economic activities

Majority of the rural population practice agriculture while the populations of the municipalities work in the informal sectors as well as in small-scale urban agriculture and livestock production.

3.2.3 Health Facilities

According to the Nyeri County Development Plan (GoK, 2002/2008), the county has fairly well distributed health facilities. It has 5 hospitals several health centres, dispensaries and clinics. The health facilities are either government or non-government sponsored and maintained. The degree of utilization of these health facilities varies, depending on various factors such as the size of the population of the catchment area, ease of communication and services rendered. The county has some sectoral policy objectives, one of them being to intensify activities aimed at control, prevention and eradication of diseases, and to promote and develop cost-effective research aimed at promotion and protection of people's health. Based on these objectives, it is appropriate to carry out the study in the district.
3.3 Study population

Data from the 1999 Population and Housing Census shows that the county had a population of 661,156 people in 1999 with an estimated annual growth rate of 0.8%. The males were 322,521 (49%) while females were 338,635 (51%). The population was expected to increase to 710,515 persons by the end of 2008 (GoK, 2001).

For the purposes of this study, women over 65 years and over were considered to be elderly and not eligible for recruitment. This represents the accepted age utilized for such analyses in most studies. In this regard, it is worthy to note that age in itself was not considered the most useful parameter but rather the concept of senescence (the passage of biologic time) as opposed to ageing (the passage of chronological time) which is of more value.

Cases

Cases were all women of age 20-60 years diagnosed with any type of breast cancer in Nyeri County and in the surrounding area. The diagnosis of breast cancer must have been made by excision, incision, core-needle or fine-needle biopsy (Appendix III). All types of breast cancer (Appendix IV) qualified for the study irrespective of the histologic grade (V) and stage of the breast cancer (Appendix VII). The Scarff-Bloom-Richardson system is the most common type of cancer grade system used today. They were also at different stages of management (Appendices VI and VIII), depending on the specific type, location, and stage.

Controls

Controls were women of 20-60 years but with no breast lump(s) or nipple discharge. The confirmation was done by use of medical history and clinical breast examination by a
medically trained research assistant and those found positive excluded from the study.

Clinical breast examination entails medical history and physical examination.

The women answered questions about their personal and family medical history which gave the research assistant information about symptoms and risk factors for breast cancer and benign breast conditions.

Next, the assistant did a thorough physical examination starting with the breast to check for any lumps and to feel their texture, size, and relationship to the skin and chest muscles. Any changes in the nipples or the skin of the breast were also noted. The lymph nodes under the armpit and above the collarbones were felt because swelling or firmness of these lymph nodes could be a sign of spread of breast cancer. If any abnormality was detected during the physical examination, the woman was disqualified from the study and referred to the nearest health facility for further investigations and management. Women with hysterectomy and artificial menopause were also excluded from the study.

3.4 Recruitment of study participants

This section deals with the recruitment of study participants and sample size determination.

Figure 3.1 shows the analytical framework for recruitment of study participants.

3.4.1 Cases

Cases were women selected from health facilities and from the Nyeri community. In the participating health facilities, selection was done by monitoring new admissions to the wards where breast cancer was treated, and by checking patients’ files from health records department to establish contact with the surviving patients. Diagnosis of breast
cancer could have been made by excision, incision, core-needle or fine needle biopsy. All women who presented with breast cancer in these facilities were recruited. Entry into the study was restricted to those women who reside within the geographical area served by the facility. Cases were also recruited from Nyeri Hospice which has a well organized system for women with breast cancer to visit regularly for counseling and palliative care.

![Analytical framework for recruitment of study participants](image)

**Figure 3.1: Analytical framework for recruitment of study participants**

The research also established contact with breast cancer survivors' support groups to assist in the recruitment of cases in the community.

The study had identified 92 cases with breast cancer but 10 (10.9%) of them were not included in the study for different reasons. This was done to minimize recall bias.

Six (6.5%) of the cases identified for inclusion in the study were difficult to contact in that, two (2) kept on switching off the phone when called, two (2) had given wrong phone
contact while two (2) refused to be interviewed. Another two (2.2%) were excluded because they were about 70 years old which is way above the 60 year age limit set in the study while two (2.2%) had died by the time of doing the study.

Of the 82 cases included in the study, five (5) were between 60-64 years which is above the 60 year set age limit but they insisted on being included and the investigator felt they were within the five year age limit used in selecting controls. One questionnaire was not fully completed because the patient was dumb and could not communicate. Efforts to trace the mother were unsuccessful and therefore only the scanty file notes were relied upon, resulting in 81 (98.78%) of fully filled questionnaires.

In all the cases, diagnosis of breast cancer had been made by excision biopsy after preliminary investigation by auxiliary tests such as fine needle aspiration or mammogram.

3.4.2 Controls

Controls were recruited from the participating health facilities within Nyeri County from among those women that were admitted in the health facilities for conditions other than cancer, obstetric and/or gynecology. Hospital staff and visitors to the facilities were excluded. Frequency matching by age was done in the selection. Sampling was done so as to have three times the number of controls to cases in the various stratified age brackets. They had to be malignancy-free and with birth dates within 5 years of their matched case at diagnosis (plus or minus five years). Like the cases, the controls were residents of the geographical area served by the facility.
Of the three hundred (300) women sampled for the controls, 28 (9.3%) were not included in the study. Of these, nineteen (6.3%) refused to participate while 9 (3%) had different conditions considered to increase risk of developing breast cancer that excluded them from inclusion in the study. The conditions ranged from breast lump(s), nipple discharge, lymphadenopathy to changes of the skin of the breast which were discovered on clinical breast examination by a trained research assistant. They were all referred to different health facilities in their respective area for further management. The number of controls was three times the number of cases in the various stratified age brackets. In all, 272 matched controls were recruited.

3.4.3 Sample size determination

Epi Info Version 3.03.17 calculator was used. Two-sided significance level (alpha) of 0.05, power (% chance of detecting) of 80%, proportion of controls with exposure of 0.4, proportion of cases with exposure equals 0.6 and a ratio of controls/cases of 3 were used (Kelsey et al 1996).

Table 3.1 shows the minimum sample size depending on the method used.

Table 3.1: Sample size calculation

<table>
<thead>
<tr>
<th></th>
<th>Kelsey</th>
<th>Fleiss</th>
<th>Fleiss with CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size- Cases:</td>
<td>65</td>
<td>65</td>
<td>72</td>
</tr>
<tr>
<td>Sample Size-Controls</td>
<td>195</td>
<td>195</td>
<td>213</td>
</tr>
<tr>
<td>Total sample size</td>
<td>260</td>
<td>260</td>
<td>285</td>
</tr>
</tbody>
</table>

Source: Kelsey et al 1986

CC = continuity correction factor. All calculations are rounded up to the nearest integer.
3.5 Data Variables

3.5.1 Dependent variable: This was the presence (Cases) or absence (Controls) of breast cancer.

3.5.2 Independent (Explanatory) variables.

Φ Socio-demographic characteristics:

▪ Age – One case marched with three controls
▪ Marital status
▪ Occupation

Φ Nutritional status and behavioral practices:

▪ Body mass index (Weight and Height)
▪ Alcohol intake
▪ Cigarette smoking

Φ Medical, breastfeeding and family planning history:

▪ History of use of estrogen containing contraceptives and hormone replacement therapy
▪ Radiation exposure
▪ Breastfeeding

Φ Personal and family history of cancer:

▪ Age at menarche
• Menstrual pattern
• First-degree breast cancer family history
• First-degree family history of other cancers

Φ Reproductive characteristics:
• Age at first full term pregnancy
• Parity
• Number of miscarriages
• Menopausal status
• Abortion

3.6 Data collection

The data collection exercise took three months to complete - from March to May 2010. With the help of the hospital matron and contact persons in the community, cases and controls were identified and interviewed. Written consent was taken from every participant (Appendix I a). A structured questionnaire (Appendix II) prepared in English and translated to the participants in a language each understood best was administered by a trained research assistant in each of the participating health facilities. A separate room was used for interviews. Since questions were phrased in order to elicit explicit answers, every informant was exposed to the same stimuli.

In addition to basic demographic details, the following information was obtained from both cases and controls: age at menarche, menstrual cycle history, first-degree family
history for cancer, age at first pregnancy, parity, number of miscarriages, age at first lactation and history of alcohol intake. Other information obtained included, number of years of use of estrogen containing contraceptives and hormone replacement therapy.

Information was sought on whether or not each woman had ever consumed alcohol. No information was sought about alcohol consumption at various ages or about the particular type of alcohol consumed. Information was also sought on whether or not each woman had ever smoked, and whether she was a current or past smoker. Passive smoking was also considered and information sought on any member of the family who was a current or past smoker with attention being given to the reported associations with environmental tobacco smoke. Information was sought on the amount smoked but not on the age when smoking started or stopped. Information was collected up to the date of interview for controls and date of diagnosis of breast cancer for cases.

3.7 Data Analysis

To obtain comparability between the women with breast cancer and similar women without breast cancer, they were all stratified by age (from 20 to 24, 25 to 29, 30 to 34, etc., up to 55 to 59). Early menarche was defined as menarche occurring at age < 12 years. Women were categorized as pre-menopausal and post menopausal status. They were further categorized on age at menopause into 30-39, 40-49 years and ≥ 50 years. Nulliparous women were assigned to a separate stratum and parous women were cross-classified according to parity (1–2, 3–4, 5–6, 7+), lactation (never vs. ever), duration of lactation and age at first birth (<20, 20–24, 25–29, 30+). Variables relating to family
history of breast cancer and other cancers, radiation exposure, alcohol consumption and cigarette smoking history (ever/never) were also included.

Data was entered into Stata version 10 software and the outcome variable which was breast cancer status (presence/absence) was coded as 1/0 where 1 indicate success (breast cancer) and 0 case failure (no breast cancer). This was necessary in order to use logistic regression which recognises 1/0 coding system in stata software. Analysis was done by each objective and results presented in tables, figures and statistical statements. In order to describe the study population, proportions (percentages) were determined. Chi square tests of significance were performed to identify any statistical association between breast cancer and predictor variables. All predictor variables found to be statistically significant were subjected to univariate and multivariate logistic regression to determine the magnitude and direction of association between the outcome variable and the predictor variables. Both odds ratio (OR) and P values at 95% confidence level were used to describe the magnitude and significance of association.

In general, results were presented as odds ratios and their appropriate standard errors. The odds ratio estimates were calculated and results given with their appropriate 95% CIs to summarize the findings.

3.8. Ethical Consideration

In order to ensure good flow of data/information between the study and the health care facilities, all research assistants were strictly bound by the public servants’ professional code of ethics which demands observing confidentiality of patient information. Information users interested in the collected data and information services were required
to obtain authority for access to data/information from the principal researcher and were mutually bound to acknowledge the principal researcher in their data usage. In order to protect confidentiality of facilities and patient information, inclusion of facility and patient identification details was restricted to coded numbers.

Permission was sought from all study participants and a consent form signed (Appendix I a). Those who declined were not included in the study. In addition, written consent was sought and granted by the Ethical and Research Committee of Kenyatta National Hospital/University of Nairobi (Appendix I b). Written permission was also sought from the heads of the study institutions.

Cases were counseled to continue with treatment and those in need of palliative care were linked up with Nyeri hospice and also supported to start support groups in their respective communities. All those controls who had different conditions considered to increase the risk of developing breast cancer were excluded from the study and referred to different health facilities in their respective area for further management.

3.9. Limitations

Although the case-control designs are more feasible to study the etiology of cancers, they are subject to incomplete or biased recall. Among the study’s potential limitations, in relation to recall, is information on independent variables such as contraceptive use which often refers to a fairly distant period of time prior to the appearance of breast cancer. As compared to controls, women with breast cancer also tend to remember more facts that may be related to the disease. In order to reduce bias, interviews of cases and respective controls were performed by the same interviewer and controls selected from
similar geographical area. The information bias due to non-comparable accuracy in assessing exposure for deceased cases was also experienced.

Because of feasibility constraints, a number of important variables were not addressed by the current study—these are genetic mutations, nutritional factors, radiation exposure and environmental exposure.

Finally, although the results cannot be generalized, the findings suggest that the associations between some of these risk factors may differ in Kenya when compared with Western countries.
CHAPTER FOUR: RESULTS

4.0 Introduction

This chapter presents the analysis of the results of the study which are organized into different sections based on the study objectives. The analysis has been done by describing the study participants by independent variables and logistic regression. A total of 353 women of which 81 were breast cancer cases and 272 were healthy controls (98.78% and 100% respectively) were enrolled in the study.

4.1 Goodness of fit

The data was categorized into small groups of five year intervals and subjected to a Two-sample Kolmogorov-Smirnov test for equality of distribution functions test.

The difference in the distribution of the study population (cases and controls) was not statistically significant with the results in table 4.1 showing there exists a tie in the combined dataset with only 14 unique values out of 354 observations ($p > 0.05$).

Table 4.1: Two-sample Kolmogorov-Smirnov test for equality of distribution functions

<table>
<thead>
<tr>
<th>Smaller group</th>
<th>D</th>
<th>P-value</th>
<th>Corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>0:</td>
<td>0.0308</td>
<td>0.888</td>
<td></td>
</tr>
<tr>
<td>1:</td>
<td>-0.0430</td>
<td>0.793</td>
<td></td>
</tr>
<tr>
<td>Combined K-S:</td>
<td>0.0430</td>
<td>1.000</td>
<td>1.000</td>
</tr>
</tbody>
</table>

4.2 Comparison of cases and controls

The study population showed a semblance of normal distribution. As shown in figure 4.1, there was no statistically significant difference between the mean age of the cases and
controls: Mean age of cases was 45.73 [standard deviation (SD) 9.38] years, minimum 23 years, maximum 64 years; Mean age of controls was 45.78 [10.24], minimum 20 years, maximum 65 years, (P > 0.05).

![Age distribution of study participants](image)

**Fig 4.1: Age distribution of study participants**

The Median is about 45 years for both cases and controls. For variability ie spread of the data set, range for cases is 41 years and for the controls 40 years.

Interquartile range (IQR) for both groups is represented by the width of the box which is equal to 17 years.

Finally as for skewness, the box plots show the shapes of both data sets to be symmetrical and therefore normally distributed.

The validity of the chi-square test depends on both the sample size and the number of cells. Several rules of thumb have been suggested to indicate whether the chi-square
approximation is satisfactory. One such rule suggested by Cochran (Gordon, 2002) says that the approximation is adequate if no expected cell frequencies are less than one and no more than 20% are less than five, both of which this study has met.

4.3 Description of study participants by independent variables

This section provides the analysis of the first objective which was: To describe the cases and controls by independent variables. The analysis involves use of descriptive statistics that include the mean and standard deviation values obtained from the interviewed participants. The analysis also employs cross tabulation on the various characteristics with a focus to comparing them between cases and controls.

Pearson's chi-square statistic was used to test the hypothesis of association between the outcome variable and the predictor variables that are postulated to influence occurrence of breast cancer. A chi-square probability of 0.05 or less was used as a justification of the rejection of the null hypothesis that the independent variable is unrelated (that is, only randomly related) to the dependent variable. The section describes the study participants by socio-demographic characteristics, behavioral practice and nutritional status, medical, breastfeeding and family planning history, personal and family history and reproductive characteristics.

4.3.1 Socio-demographic characteristics

These include age, marital status, education level and occupation. The results of tabulation and descriptive statistics are shown in Table 4.2.
As shown in figure 4.2, ten-year age groups distribution of cases showed the peak age groups with most respondents to be 35-39 and 45-49 at 19.75% and the least at 1.24% in the age groups of 20-24 and 25-29.

![Age distribution of study participants (Cases)](image)

**Figure 4.2: Age distribution of study participants (Cases)**

In terms of marital status, most of the participants were married with 85.19% of cases and 82.35% of controls respectively but there was no statistically significant difference between cases and controls observed in the characteristic (P > 0.05).

Most of the study participants had basic education (primary and secondary) with 71.60% of the cases and 65.44% of the controls respectively. There was no statistically significant difference between cases and controls observed in terms of education level (P > 0.05).
Though there was no statistically significant difference between cases and controls in terms of occupation, the participants were mainly farmers - 48.15% of cases and 39.71% of controls respectively (P > 0.05).

Table 4.2: Distribution of study participants by socio-demographic characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases</th>
<th>(%)</th>
<th>Controls</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age groups (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-24</td>
<td>1</td>
<td>1.24</td>
<td>6</td>
<td>2.21</td>
</tr>
<tr>
<td>25-29</td>
<td>1</td>
<td>1.24</td>
<td>9</td>
<td>3.31</td>
</tr>
<tr>
<td>30-34</td>
<td>7</td>
<td>8.64</td>
<td>19</td>
<td>6.99</td>
</tr>
<tr>
<td>35-39</td>
<td>16</td>
<td>19.75</td>
<td>51</td>
<td>18.75</td>
</tr>
<tr>
<td>40-44</td>
<td>12</td>
<td>14.81</td>
<td>35</td>
<td>12.87</td>
</tr>
<tr>
<td>45-49</td>
<td>16</td>
<td>19.75</td>
<td>51</td>
<td>18.75</td>
</tr>
<tr>
<td>50-54</td>
<td>9</td>
<td>11.11</td>
<td>33</td>
<td>12.13</td>
</tr>
<tr>
<td>55-59</td>
<td>11</td>
<td>13.58</td>
<td>43</td>
<td>15.81</td>
</tr>
<tr>
<td>≥60</td>
<td>8</td>
<td>9.88</td>
<td>25</td>
<td>9.18</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>81</td>
<td>100</td>
<td>272</td>
<td>100</td>
</tr>
<tr>
<td><strong>Mean±s.d</strong></td>
<td>45.73±9.38</td>
<td></td>
<td>45.78±10.24</td>
<td></td>
</tr>
<tr>
<td><strong>Chi-square</strong></td>
<td>2.25</td>
<td></td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marital status</th>
<th>Cases</th>
<th>(%)</th>
<th>Controls</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never married</td>
<td>12</td>
<td>14.81</td>
<td>48</td>
<td>17.65</td>
</tr>
<tr>
<td>Married</td>
<td>69</td>
<td>85.19</td>
<td>224</td>
<td>82.35</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>81</td>
<td>100</td>
<td>272</td>
<td>100</td>
</tr>
<tr>
<td><strong>Chi-square</strong></td>
<td>2.85</td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education level</th>
<th>Cases</th>
<th>(%)</th>
<th>Controls</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non</td>
<td>4</td>
<td>4.94</td>
<td>23</td>
<td>8.46</td>
</tr>
<tr>
<td>Primary</td>
<td>27</td>
<td>33.33</td>
<td>92</td>
<td>33.82</td>
</tr>
<tr>
<td>Secondary</td>
<td>31</td>
<td>38.27</td>
<td>86</td>
<td>31.62</td>
</tr>
<tr>
<td>Tertiary</td>
<td>19</td>
<td>23.46</td>
<td>71</td>
<td>26.10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>81</td>
<td>100</td>
<td>272</td>
<td>100</td>
</tr>
<tr>
<td><strong>Chi-square</strong></td>
<td>4.23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>Cases</td>
<td>Controls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n (81)</td>
<td>(%)</td>
<td>n(272)</td>
<td>(%)</td>
</tr>
<tr>
<td>Employed</td>
<td>16</td>
<td>19.75</td>
<td>69</td>
<td>25.36</td>
</tr>
<tr>
<td>Farmer</td>
<td>39</td>
<td>48.15</td>
<td>108</td>
<td>39.71</td>
</tr>
<tr>
<td>Business</td>
<td>9</td>
<td>11.11</td>
<td>44</td>
<td>16.18</td>
</tr>
<tr>
<td>Housewife</td>
<td>8</td>
<td>9.88</td>
<td>28</td>
<td>10.29</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
<td>11.11</td>
<td>23</td>
<td>8.46</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100</td>
<td>272</td>
<td>100</td>
</tr>
</tbody>
</table>

| Chi-square     | 4.35  |
| P-value        | 0.63  |

4.3.2 Anthropometrical status and behavioral practices

These included body mass index (BMI), beer consumption, and cigarette smoking (Table 4.3). Most of the participants were in the overweight and obese category (65.43% and 96.32% of cases and controls respectively) with a body mass index of between 25 and 30kg/m². There was no statistically significant difference between cases and controls observed in terms of body mass index (P > 0.05). Similar observation was made on beer consumption and cigarette smoking, indicating no statistically significant difference between cases and controls with a p > 0.05. Passive smoking which was represented in the study by partner smoking was not statistically significantly different between the cases and controls, p > 0.05.
Table 4.3: Anthropometrical measurements and behavioral characteristics of the study participants

<table>
<thead>
<tr>
<th>Body Mass Index (BMI) kg/m²</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (81) (%)</td>
<td>n(272) (%)</td>
<td></td>
</tr>
<tr>
<td>≤ 18.49(Underweight) 2</td>
<td>2 (2.47)</td>
<td>3 (1.10)</td>
</tr>
<tr>
<td>18.5- 24.9(Normal Weight) 26</td>
<td>26 (32.10)</td>
<td>75 (27.57)</td>
</tr>
<tr>
<td>25.0- 29.9(Overweight) 27</td>
<td>27 (33.33)</td>
<td>125 (45.96)</td>
</tr>
<tr>
<td>≥ 30(Obesity) 26</td>
<td>26 (32.10)</td>
<td>69 (25.37)</td>
</tr>
<tr>
<td>Total</td>
<td>82 (100.00)</td>
<td>272 (100.00)</td>
</tr>
</tbody>
</table>

Chi-square  4.63  
P-value  0.20

<table>
<thead>
<tr>
<th>Beer consumption</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (81) (%)</td>
<td>n(272) (%)</td>
<td></td>
</tr>
<tr>
<td>In the past</td>
<td>30 (37.04)</td>
<td>67 (24.63)</td>
</tr>
<tr>
<td>Current taking</td>
<td>4 (4.94)</td>
<td>13 (4.78)</td>
</tr>
<tr>
<td>Never</td>
<td>47 (58.02)</td>
<td>192 (70.59)</td>
</tr>
<tr>
<td>Total</td>
<td>81 (100.00)</td>
<td>272 (100.00)</td>
</tr>
</tbody>
</table>

Chi-square  4.95  
P-value  0.08

<table>
<thead>
<tr>
<th>Cigarette smoking</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (81) (%)</td>
<td>n(272) (%)</td>
<td></td>
</tr>
<tr>
<td>Ever smoked</td>
<td>4 (4.94)</td>
<td>7 (2.57)</td>
</tr>
<tr>
<td>Never</td>
<td>77 (95.06)</td>
<td>265 (97.43)</td>
</tr>
<tr>
<td>Total</td>
<td>81 (100.00)</td>
<td>272 (100.00)</td>
</tr>
</tbody>
</table>

Chi-square  1.16  
P-value  0.28

<table>
<thead>
<tr>
<th>Partner Smoking</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (81) (%)</td>
<td>n(272) (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32 (39.51)</td>
<td>126 (46.32)</td>
</tr>
<tr>
<td>No</td>
<td>49 (60.49)</td>
<td>146 (53.68)</td>
</tr>
<tr>
<td>Total</td>
<td>81 (100.00)</td>
<td>272 (100.00)</td>
</tr>
</tbody>
</table>

Chi-square  1.53  
P-value  0.47

4.3.3 Medical, breastfeeding and family planning history

This section describes the study participants by hormone replacement therapy, radiation exposure, breastfeeding and contraceptive use (Table 4.4).

Over 90% of the participants reported having never used hormone replacement therapy. However, for those who used, there was a statistically significant difference between...
cases and controls (P > 0.05). Similarly, there was no statistically significant difference between cases and controls in terms of radiation exposure, breast feeding and hormonal contraception, p > 0.05. The proportion of the participants who breastfed their children was more or less the same for the cases and controls, at 93.9% and 93.8% respectively.

Table 4.4: Medical, breastfeeding and family planning history of study participants

<table>
<thead>
<tr>
<th>Use of hormone replacement therapy</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81)</td>
<td>(%)</td>
</tr>
<tr>
<td>Never used</td>
<td>73</td>
<td>90.12</td>
</tr>
<tr>
<td>Used</td>
<td>8</td>
<td>9.88</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Chi-square: 18.95, P-value: 0.00

<table>
<thead>
<tr>
<th>Radiation exposure</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81)</td>
<td>%</td>
</tr>
<tr>
<td>Never exposed</td>
<td>77</td>
<td>95.06</td>
</tr>
<tr>
<td>Exposed</td>
<td>4</td>
<td>4.94</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Chi-square: 2.41, P-value: 0.12

<table>
<thead>
<tr>
<th>Breastfeeding</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81)</td>
<td>%</td>
</tr>
<tr>
<td>Not breastfed</td>
<td>4</td>
<td>4.94</td>
</tr>
<tr>
<td>Breastfed</td>
<td>77</td>
<td>95.06</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Chi-square: 0.19, P-value: 0.66

<table>
<thead>
<tr>
<th>Use of oral contraceptives</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81)</td>
<td>(%)</td>
</tr>
<tr>
<td>Never used</td>
<td>37</td>
<td>45.68</td>
</tr>
<tr>
<td>Used</td>
<td>44</td>
<td>54.32</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Chi square: 0.15, P-value: 0.70

<table>
<thead>
<tr>
<th>Use of injectable contraceptives</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81)</td>
<td>(%)</td>
</tr>
<tr>
<td>Never used</td>
<td>47</td>
<td>58.02</td>
</tr>
<tr>
<td>Used</td>
<td>34</td>
<td>41.98</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Chi square: 5.62, P-value: 0.43
4.3.4 Personal and family history of cancer

This section describes the study participants by age at menarche, menstrual pattern, family history of breast cancer and other cancers apart from breast cancer. The results of tabulation and descriptive statistics are shown in Table 4.5 where all the variables were reported to be statistically significant.

There was a statistically significant difference between cases and controls in terms of age at menarche ($P < 0.05$). Most of the study participants had their menarche at 13-15 years with cases at 64.20% and controls at 70.63% respectively. Similarly, there was a statistically significant difference between cases and controls in terms of menstrual pattern and first degree family history of breast cancer ($P < 0.05$). Majority of the study participants had regular menstrual pattern at 79.01% for cases and 91.54% for controls respectively. Cases were more likely than controls to have a first degree family relative with breast cancer at 16.05% and 4.41% respectively.

As for those study participants with first degree family history of other cancers apart from breast, there was a statistically significant difference between cases and controls at $p < 0.05$. Father was the most common first degree relative with other cancer apart from breast at 6.17% for cases and 5.88% for controls respectively.

Table 4.5: Distribution of study participants by personal and family history

<table>
<thead>
<tr>
<th>Age at Menarche</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n(81)</td>
<td>(%)</td>
</tr>
<tr>
<td>≤12</td>
<td>5</td>
<td>6.17</td>
</tr>
<tr>
<td>13-15</td>
<td>52</td>
<td>64.20</td>
</tr>
<tr>
<td>≥16</td>
<td>24</td>
<td>29.63</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>100.00</td>
</tr>
<tr>
<td>Chi-square</td>
<td>17.45</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Menstrual pattern</td>
<td>Cases</td>
<td>Controls</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td>n(81) (%)</td>
<td>n(272) (%)</td>
</tr>
<tr>
<td>Regular</td>
<td>64 79.01</td>
<td>249 91.54</td>
</tr>
<tr>
<td>Irregular</td>
<td>17 20.99</td>
<td>23  8.46</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

Chi-square 9.76  
P-value 0.002

<table>
<thead>
<tr>
<th>Family history of breast cancer</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n(81) (%)</td>
<td>n(272) (%)</td>
</tr>
<tr>
<td>Yes</td>
<td>13 16.05</td>
<td>12  4.41</td>
</tr>
<tr>
<td>No</td>
<td>68 83.95</td>
<td>260 95.59</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

Chi square 17.41  
P-value 0.002

<table>
<thead>
<tr>
<th>Relatives with breast cancer</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No relative</td>
<td>68 83.95</td>
<td>260 95.59</td>
</tr>
<tr>
<td>Sister</td>
<td>2 2.47</td>
<td>4  1.47</td>
</tr>
<tr>
<td>Mother</td>
<td>4 4.94</td>
<td>4  1.47</td>
</tr>
<tr>
<td>Other</td>
<td>7 8.64</td>
<td>4  1.47</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

Chi square 17.41  
P-value 0.002

<table>
<thead>
<tr>
<th>Family history of other cancer</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>24 29.63</td>
<td>36 13.24</td>
</tr>
<tr>
<td>No</td>
<td>57 70.37</td>
<td>236 86.76</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

Chi square 11.89  
P-value 0.001

<table>
<thead>
<tr>
<th>Relatives with other cancer</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No relative</td>
<td>61 75.30</td>
<td>237 87.13</td>
</tr>
<tr>
<td>Sister</td>
<td>2 2.47</td>
<td>2  0.74</td>
</tr>
<tr>
<td>Mother</td>
<td>1 1.24</td>
<td>4  1.47</td>
</tr>
<tr>
<td>Brother</td>
<td>2 2.47</td>
<td>3  1.10</td>
</tr>
<tr>
<td>Father</td>
<td>5 6.17</td>
<td>16  5.88</td>
</tr>
<tr>
<td>Other relatives</td>
<td>10 12.35</td>
<td>10  3.68</td>
</tr>
<tr>
<td>Total</td>
<td>81 100</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

Chi square 11.82  
P-value 0.04
4.3.5 Reproductive characteristics

Chi square test of significance was used to find out if there was an association between breast cancer and reproductive characteristics (Table 4.6). Among the reproductive characteristics, only age at first-fullterm pregnancy and menopausal status were found to be significantly associated ($P < 0.05$).

Table 4.6: Distribution of study participants by reproductive characteristics

<table>
<thead>
<tr>
<th>Pregnancy history</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81) (%)</td>
<td>n (272) (%)</td>
</tr>
<tr>
<td>Parous (Ever pregnant)</td>
<td>77 95.06</td>
<td>259 95.22</td>
</tr>
<tr>
<td>Nulliparous (Never pregnant)</td>
<td>4  4.94</td>
<td>13  4.78</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age at 1st full term pregnancy</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81) (%)</td>
<td>n (272) (%)</td>
</tr>
<tr>
<td>No child</td>
<td>4  4.94</td>
<td>15  5.58</td>
</tr>
<tr>
<td>15-19</td>
<td>18 22.22</td>
<td>66 24.53</td>
</tr>
<tr>
<td>20-24</td>
<td>31 38.27</td>
<td>135 50.56</td>
</tr>
<tr>
<td>25-29</td>
<td>26 32.1</td>
<td>43 15.98</td>
</tr>
<tr>
<td>≥30</td>
<td>2  2.47</td>
<td>9  3.35</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>268 100.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abortion/miscarriage</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n(81) %</td>
<td>n(272) %</td>
</tr>
<tr>
<td>Never</td>
<td>58 71.60</td>
<td>217 79.78</td>
</tr>
<tr>
<td>Ever had</td>
<td>23 28.40</td>
<td>55 20.22</td>
</tr>
<tr>
<td>Total</td>
<td>81 100.00</td>
<td>272 100.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of children</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81) (%)</td>
<td>n (272) (%)</td>
</tr>
<tr>
<td>1-3 Children</td>
<td>46 59.74</td>
<td>152 59.38</td>
</tr>
<tr>
<td>4-6 Children</td>
<td>27 35.06</td>
<td>79 30.86</td>
</tr>
<tr>
<td>7-9 Children</td>
<td>2  2.60</td>
<td>18  7.03</td>
</tr>
<tr>
<td>≥10 Children</td>
<td>2  2.60</td>
<td>7  2.73</td>
</tr>
<tr>
<td>Total</td>
<td>77 100.00</td>
<td>256 100.00</td>
</tr>
</tbody>
</table>
### Menopausal status

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81) (%)</td>
<td>n (272) (%)</td>
</tr>
<tr>
<td>Pre-menopause</td>
<td>39 (48.0)</td>
<td>171 (62.9)</td>
</tr>
<tr>
<td>Post-menopause</td>
<td>42 (52.0)</td>
<td>101 (37.1)</td>
</tr>
<tr>
<td>Total</td>
<td>81 (100.0)</td>
<td>272 (100.0)</td>
</tr>
</tbody>
</table>

Chi square 5.6
P-value 0.02

### Age at menopause

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (81) (%)</td>
<td>n (81) (%)</td>
</tr>
<tr>
<td>≤39</td>
<td>6 (10.2)</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>40-49</td>
<td>30 (50.8)</td>
<td>43 (43.5)</td>
</tr>
<tr>
<td>≥50</td>
<td>23 (39.0)</td>
<td>53 (53.5)</td>
</tr>
<tr>
<td>Total</td>
<td>59 (100.0)</td>
<td>99 (100.0)</td>
</tr>
</tbody>
</table>

Chi square 5.4
P-value 0.07

#### 4.4 Isolation of risk factors for breast cancer

This section provides the results of the second objective which was to isolate the risk factors for breast cancer in Nyeri County.

From the results of the study, the following independent variables were found to be statistically significant with the chi-square test (P-value ≤ 0.05) and were therefore isolated as associated factors for breast cancer in Nyeri County: hormone replacement therapy, age at menarche, first degree family history of breast cancer, first degree family history of any other cancer apart from breast, age at first full term pregnancy, menstrual pattern, menopausal status and age at menopause.
4.5 Magnitude and direction of association between breast cancer and identified risk factors by logistic regression

This section provides the analysis of the third objective which was to determine the magnitude and direction of the risk factors associated with breast cancer development in Nyeri county.

The independent variables that were found to be statistically significant with the chi-square test were entered into a univariate logistic regression analysis model. Univariate logistic regression analysis was used to test strength/magnitude and direction of association/relationship between outcome variable (breast cancer) and each one of the predictor variables.

Those variables/characteristics that showed statistical significance at univariate logistic regression analysis were entered into a multivariate logistic regression analysis model. The inclusion of statistically significant individual variables into a multivariate model was done to assess the combined effect based on the fact that all the variables are at play at anyone given time on an individual woman.

4.5.1 Results of the univariate logistic regression analysis of risk factors

Univariate logistic regression analysis was applied to test the magnitude and direction of association between explanatory variables found to be statistically associated with breast cancer by chi square test. Eight independent variables were found to be statistically and significantly associated with breast cancer by use of univariate logistic regression analysis (Table 4.7). These variables were: hormone replacement therapy ($p< 0.01$),
family history of breast cancer (p<0.01), history of distant relatives with breast cancer (p<0.05), family history of other cancers apart from breast (p<0.01), history of distant relatives with other cancers apart from breast (p<0.05), irregular menstrual pattern (p<0.05), post-menopausal status (p<0.05) and late age at menopause (p<0.05).

A statistically significant relationship between hormone replacement therapy and breast cancer was reported. The risk of developing breast cancer in women not exposed to hormone replacement therapy was 93% lower than that of those exposed, OR 0.07 (95% CI: 0.01-0.33), p < 0.01.

Age at menarche was not statistically significant though the risk of breast cancer increased linearly with increase in age with an OR of 1.20 (95% CI: 0.43-3.33) and 1.47 (95% CI: 0.49-4.41) at 13-15 and 16-18 years respectively, p > 0.05.

Women with no family history of breast cancer had a 76% lower risk of developing breast cancer with an OR of 0.24 (95% CI: 0.11-0.55) as compared to women with relative(s) with the disease (P < 0.01). Of those women with sisters and mothers with a history of breast cancer, a 2-fold and 4-fold increased risk of developing breast cancer with an OR of 1.91 (95% CI: 0.34-10.66) and 3.82 (95% CI: 0.93-15.68) respectively was reported. However, these were not statistically significant, p > 0.05. The risk was however reported to be statistically significant and highest on those women with distant relatives with breast cancer with a 9-fold increased risk, OR 8.92 (95% CI: 2.25-35.41), p < 0.01.
For other cancers apart from breast, the risk of developing breast cancer was 64% lower in those women who did not have a relative with cancer than those with relatives with the disease, OR 0.36 (95% CI: 0.20-0.66), p < 0.05.

Of those women with sisters and brothers with a history of other cancer, a 4-fold and 3-fold increased risk of developing breast cancer with an OR of 3.89 (95% CI: 0.54 - 28.14) and 2.59 (95% CI: 0.42 - 15.85) respectively was reported. However, these were not statistically significant, p > 0.05. The risk was however reported to be statistically significant on those women with distant relatives with breast cancer with a 4-fold increased risk, OR 3.89 (95% CI: 1.55 - 9.75), p < 0.01.

Menstrual pattern was found to be a strong risk factor. Compared with women who had regular menstrual pattern, a significantly more than two-fold increased risk with an OR of 2.88 (95% CI: 1.45 - 5.70) was reported among women who had irregular menstrual pattern, p < 0.05.

A direct relationship between menopausal status and risk of breast cancer was reported. Post-menopausal status was found to be protective against breast cancer with a 45% lower risk compared to pre-menopausal women, OR 0.55 (95% CI: 0.33-0.90), p < 0.05.

Age at menopause was not found to be statistically significantly associated with the risk of developing breast cancer in the 40-49 age group, p > 0.05. However, for those women who were 50 years and above, the risk reduced by 78%, p < 0.05.
<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone replacement therapy (Months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>Never used</td>
<td>0.07 (0.01-0.33)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age at Menarche (Yrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>13-15</td>
<td>1.20 (0.43 - 3.33)</td>
<td>0.72</td>
</tr>
<tr>
<td>16-18</td>
<td>1.47 (0.49 - 4.41)</td>
<td>0.50</td>
</tr>
<tr>
<td>≥19</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Family history of breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.24 (0.11-0.55)</td>
<td>0.001</td>
</tr>
<tr>
<td>Relatives with breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No relative</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>Sister</td>
<td>1.91 (0.34 - 10.66)</td>
<td>0.46</td>
</tr>
<tr>
<td>Mother</td>
<td>3.82 (0.93 - 15.68)</td>
<td>0.06</td>
</tr>
<tr>
<td>Brother</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Other relatives</td>
<td>8.92 (2.25 - 35.41)</td>
<td>0.002</td>
</tr>
<tr>
<td>Family history of other cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.36 (0.20-0.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>Relatives with other cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No relative</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>Sister</td>
<td>3.89 (0.54 - 28.14)</td>
<td>0.18</td>
</tr>
<tr>
<td>Mother</td>
<td>0.97 (0.11 - 8.8)</td>
<td>0.98</td>
</tr>
<tr>
<td>Brother</td>
<td>2.59 (0.42 - 15.85)</td>
<td>0.30</td>
</tr>
<tr>
<td>Father</td>
<td>1.21 (0.43 - 3.44)</td>
<td>0.72</td>
</tr>
<tr>
<td>Other relatives</td>
<td>3.89 (1.55 - 9.75)</td>
<td>0.004</td>
</tr>
<tr>
<td>Menstrual pattern</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>Irregular</td>
<td>2.88 (1.45 -5.70)</td>
<td>0.002</td>
</tr>
<tr>
<td>Menopausal status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-menopausal</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>Post-menopausal</td>
<td>0.55 (0.33-0.90)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age at menopause (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>0.35 (0.08 - 1.51)</td>
<td>0.16</td>
</tr>
<tr>
<td>≥ 50</td>
<td>0.22 (0.05 - 0.94)</td>
<td>0.04</td>
</tr>
</tbody>
</table>
4.5.2 Results of the multivariate analysis of risk factors

All predictor variables that were statistically significant at the univariate logistic regression analysis level were entered into a multivariate logistic regression analysis model and results tabulated in table 4.8. On multivariate analysis, some of the individual predictor variables retained their statistical significance on interaction while others lost. Women with no family history of breast cancer had an 83% lower risk of developing breast cancer with an OR of 0.17 (95% CI: 0.05-0.56) as compared to women with relative(s) with the disease, \( p < 0.01 \). For those women with other cancers apart from breast, the risk of developing breast cancer was 73% lower in those women who did not have a relative with cancer than those with relatives with the disease, OR 0.27 (95% CI: 0.10-0.68), \( p < 0.01 \).

Menstrual pattern, menopausal status, and age at menopause lost their significance in the multivariate logistic regression analysis modeling, \( p > 0.05 \).

Table 4.8: Multi-variate logistic regression analysis

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.17 (0.05-0.56)</td>
<td>0.004</td>
</tr>
<tr>
<td>Family history of other cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.27 (0.10-0.68)</td>
<td>0.004</td>
</tr>
<tr>
<td>Menstrual pattern</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>Irregular</td>
<td>1.48 (0.47-4.65)</td>
<td>0.50</td>
</tr>
<tr>
<td>Age at menopause (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>1.00 (ref.)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>0.37 (0.07-2.10)</td>
<td>0.27</td>
</tr>
<tr>
<td>≥ 50</td>
<td>0.36 (0.07-2.03)</td>
<td>0.25</td>
</tr>
</tbody>
</table>
CHAPTER FIVE:

DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 Discussion

Reviewed literature showed that a number of risk factors play an important role in the aetiology of breast cancer among women while this study indicated that the following factors are the only ones associated with the disease; hormone replacement therapy, family history of breast cancer, family history of other cancers, irregular menstrual pattern, menopausal status, age at menarche and age at menopause.

There was no association between breast cancer and age at first full term pregnancy, parity, number of miscarriages, breastfeeding history, alcohol intake, cigarette smoking, radiation exposure and occupation.

In respect to risk factors for breast cancer, hormone replacement therapy use, age at menarche, family history of breast cancer, family history of cancer apart from breast, irregular menstrual pattern, menopausal status and age at menopause were all found to be risk factors for breast cancer with chi square analysis.

In the current study, the risk of developing breast cancer increased linearly with increase in the age at menarche. This is inconsistent with many studies that have shown breast cancer risk to be more for women whose menarche occurs at an early age (Iwasaki et al, 2007; Shantakumar et al, 2007; Mahouri et al, 2007). In one study, early menarche (≤12 years) contributed to 44% of breast cancer cases in young and 26% of cases in older women (Gao et al, 2000). Garcia et al (2006) also reported an estimated decrease in risk
per five year delay in menarche of 22%. However, two Indian case-control studies, Gajalakashmi et al (1991) and Pakseresht et al (2009) found no association between age at menarche and breast cancer risk.

The lack of significant association between breast cancer and the other variables studied was unexpected.

For example, studies have shown that past oral contraceptive use is associated with a somewhat higher OR among young women or women who have a family history of breast cancer (Ursin et al, 2000). In a study by Collaborative Group on Hormonal Factors in Breast Cancer (2002), women who breastfed were reported to have reduced their risk compared with women who did not breastfeed with the risk decreasing by 4% for every 12 months of breastfeeding.

Sociodemographically, breast cancer cases and controls did not differ in body mass index, marital status, education level, beer consumption and cigarette smoking. However, this is contrary to studies done elsewhere. For example, in a study by Brandt et al (2000), body mass index (BMI) was reported to show nonlinear significant inverse and positive associations with breast cancer among pre- and post-menopausal women, respectively. Based on the results of the Million Women Study, an estimated 7% of breast cancers in post-menopausal women in the UK were due to overweight and obesity. In contrast, obese pre-menopausal women had a 20% reduction in breast cancer risk (Reeves et al, 2007). Concerning education, this study showed no association between level of education and breast cancer. In contrast, in a study from South Africa, women who developed breast cancer had a higher level of education compared with control groups (Coogan et al, 1999).
In respect to alcohol consumption, this study showed no association between alcohol consumption and breast cancer. This finding is inconsistent with several other studies done previously (Baan et al., 2007; Key et al., 2006; Allen et al., 2009; Collaborative reanalysis, 2002). All these other studies reported a strong association between alcohol consumption and breast cancer. For example, risk to breast cancer was reported to be elevated by alcohol consumption to between 7-12% for every beer drunk (Key et al., 2006; Allen et al., 2009).

As regards smoking, no association with breast cancer was found in this study which is inconsistent with previous studies. For example, results of a study on cigarette smoking showed that women who start smoking as teenagers and continue to smoke for at least 20 years may increase their breast cancer risk by 90% (Odiase, 2009).

Overall, the results of this study are consistent with many western literature and local literature that have shown increased risk for breast cancer if one had affected 1st degree relative (Collaborative reanalysis, 2001). From the univariate logistic regression analysis, the present study showed that a positive family history of breast cancer is a risk factor for breast cancer in Kenya. History of breast cancer in first degree relatives increased breast cancer risk by 76% in the univariate logistic regression analysis and the risk was statistically significant (P < 0.05). A 7% increased risk was noted from 76% to 83% with multivariate logistic regression analysis, which is in agreement with a number of previous studies (McMahon et al., 1973; Helmrich et al., 1983; Sattin et al., 1985; Kelsey and Gammon, 1990; Collaborative Group on Hormone Factors in Breast Cancer, 2001).

[64]
The results also correspond with research findings which indicated that a positive family history of breast cancer is a strong risk factor for breast cancer especially with young age at diagnosis (Pharoah et al, 1997 and Calle et al, 1993).

The results are further supported by a study by McPherson et al (2000) which reported that having a history of breast cancer among first degree female relatives (mothers, sisters or daughters) was independently associated with an increased risk of breast cancer.

The risk of developing breast cancer was also found to increase slightly from 64% by univariate logistic regression analysis to 73% by multivariate logistic regression analysis in women with relatives with cancer other than breast compared with women without relatives with the disease (P < 0.05). Genetic contribution to breast cancer risk could be suggested by the increased incidence of breast cancer in women with a family history of other cancer apart from breast and by the existence of families with a very high incidence of breast cancer cases. This could be similar to a family history of breast cancer in a 1st or 2nd degree relative which has been reported to be approximately 10-20% of breast cancer cases, as compared to 5-10% of age-matched, general population controls, with a relative risk of approximately 2 (Pharoah, 1997). It has been reported that, if both the mother and a sister have had breast cancer and/or if the cancer in the relative was diagnosed at an early age, the risk is higher (up to relative risk of 5-10) (Pharoah, 1997).

In this study, although univariate logistic regression analysis found statistically significant increase in risk to breast cancer among women with irregular menstrual pattern, the significance was lost in the multivariate logistic regression analysis.
On menopausal status, this study found the risk to be statistically significant and less by 45% in the univariate logistic regression analysis for women in post-menopause compared to women in pre-menopausal stage, $p < 0.05$. Concerning post-menopausal women, the risk decreased with increase in age and the risk was statistically significant in late age at menopause ($\geq 50$ years), $p < 0.05$. However, the risk was not statistically significant in multivariate analysis. These results are consistent with those from other regions in Africa which demonstrate a consistent decline in breast cancer risk following menopause, which is in sharp contrast to the rising incidence rates seen among postmenopausal women from North America and Europe (Adebamowo et al, 2000).

In a study by Trichopoulos (1972), women who had a natural menopause before the age of 45 had half the breast cancer risk than postmenopausal women of the same age, with a natural menopause after the age of 55. He also reported that women subjected to early oophorectomy had a reduced breast cancer incidence than menstruating controls (Trichopoulos, 1972). For every 5-year difference in age at menopause, the risk for breast cancer was reported to increase by about 17%.

It has been postulated that the lower postmenopausal breast cancer incidence rates observed for Africans are a consequence of demographics, especially population age and overall life expectancy (Adebamowo et al, 2000). Compared with expected longevity of American women (79 years), Ghanaian women have been reported to have a life expectancy of 58 years; Nigerian 51 years; Kenyan 50 years; and South African women, 52 years (WHO, 2000). This unfortunate truncation of lifespan precludes the ability to make robust conclusions regarding risk of postmenopausal breast cancer.
It has also been suggested that breast cancer case ascertainment is disproportionately low among older African women because of their lower literacy rates, poor socioeconomic status, and diminished awareness of breast cancer (Amir et al, 1994). Also, this sort of contrasting result might be due to recall bias because in the course of data collection, many women reported having experienced temporary or permanent menopause during chemotherapy. The results were therefore likely to be influenced by no-differential misclassification due to poor recall among older women especially the cases.

Although this research was not addressing the qualitative determinants of breast cancer, a number of socio-economic issues came up in the course of data collection that requires a brief mention. One of them is the stigma associated with breast cancer and the high cost of cancer treatment. Some women gave moving narratives of the experiences they went through after they were diagnosed with breast cancer. These ranged from stigma in the neighborhood and spouses to high cost of treatment and long distances they had to travel to Kenyatta National hospital for chem- and radio-therapy, which is the only public health hospital with cancer treatment facilities near Nyeri County. Narratives abound of women who had been divorced and others abandoned by close relatives after testing positive for breast cancer. To this end, many appealed for government intervention to lower the cost of cancer treatment in general or offer the treatment free of charge.

5.2 Conclusion

This study has demonstrated that there is an association between some risk factors and the development of breast cancer among women in Nyeri. These factors are age, hormone replacement therapy, first degree family history of breast cancer, first degree family
history of any other cancer apart from breast, age at menarche, menstrual pattern, menopausal status and age at menopause.

Risk of developing breast cancer was reported to generally increase with increase in age with a bi-modal peak age distribution between 35-39 and 45-49 age groups.

Of particular note is the significantly increased risk in breast cancer in those women whose first degree relatives have had a history of breast cancer, OR 0.24 (95% CI: 0.11-0.55), p < 0.05 and other cancers, OR 0.36 (95% CI: 0.20-0.66), p < 0.05 respectively.

This is particularly so when the relative is either a mother or a sister. Other factors associated with increased risk of breast cancer are, use of hormone replacement therapy, OR 0.07 (95% CI: 0.01-0.33), p < 0.05, irregular menstrual pattern, OR 2.88 (95% CI: 1.45-5.70), p < 0.05, menopausal status, OR 0.55 (95% CI: 0.33-0.90), p < 0.05 and late age at menopause, OR 0.22 (95% CI: 0.05-0.94), p < 0.05.

However there were inconsistencies found with the existing literature regarding early age at menarche and late age at menopause which were reported to be associated with a reduced risk of breast cancer in the study. Despite the inconsistencies, the null hypothesis stands rejected and the research question answered in the affirmative that there is an association between exposure to some of the known risk factors and development of breast cancer in Nyeri women and Kenyan women in general.

Overall, the findings of this study corroborate the results of previous investigations on analytical epidemiology of risk factors for breast cancer. This study provides important background information for designing detailed studies and interventions that aim to improve our understanding of the epidemiology and management of breast cancer in the
Nyeri population. Furthermore, the study provides the first scientific evidence for formulating targeted campaigns for prevention and early diagnosis of breast cancer in Nyeri County.

5.3 Recommendations

Based on this study, it is recommended that breast cancer public awareness and screening at community level be emphasized to achieve early diagnosis that in turn will improve treatment outcomes in Nyeri County thereby ultimately increasing the probability of survival. This can be enhanced by training community health extension workers and medical health workers to teach women in the reproductive age group (starting preferably in late 20s and early 30s) on how to do self-breast examination test, how to recognise early signs and symptoms of breast cancer and the action to take on encountering suspicious cases. This basic screening test should be done regularly on monthly basis and be continued for as long as a woman is in good health, and also to have yearly clinical breast examinations by trained health care workers at the health care facilities. Health care workers should also be sensitized on the importance of clinical breast examination on women of child bearing age at first contact.

Particular attention should be given to those women with first degree relatives with history of any cancer and be encouraged to introduce their female siblings to breast cancer screening at an early age.

To address stigma and the emotional impact of cancer diagnosis, symptoms, treatment, and related issues, health education should be enhanced at community level.
The Ministry of Health should also allocate more resources both financial and manpower to programmes in the district to deal with non-communicable diseases in an effort to scale up early cancer detection and management to reduce morbidity and mortality from the disease. This should include subsidizing the cost of treatment.

The ministry of health should also start palliative care centers in all county and sub-county health care facilities in the County. The ministry should also support the establishment of cancer support groups at community level to provide a supportive environment to help clients cope with uncertainty and body-image problems inherent in cancer treatment and gain perspective from cancer survivors.

However there were some variables whose association with breast cancer was not clear and therefore further clarification through research is needed. These include the role of age at menarche and age at first full term pregnancy. Although age at menarche was not statistically significant by univariate logistic regression analysis, the variable needs further investigations given that it is related to age at menopause and hormonal profile of a woman.

Given the reported late presentation of women with breast cancer in health care facilities, there is need for a research to be done on the possible social factors which could be hindering them from seeking breast cancer screening services and early treatment in the district.
APPENDIX Ia: RESEARCH PARTICIPATION CONSENT FORM

ASSESSMENT OF RISK FACTORS FOR BREAST CANCER IN NYERI DISRTICT: A CASE CONTROL STUDY.

PARTICIPANT’S CONSENT

"Hello, My name is.... I am standing for J.K Macharia from the University of Nairobi who is carrying out a study on breast cancer among women. I am interested to know if you have been exposed to the known disease risk factors any time in your life time. You have been randomly identified as one of our respondents in this study, and I hope that you will feel free to discuss with me. All the information that you will provide will be treated in confidence. Your name or information that may identify you as a participant shall not be given to anyone. You are not under obligation to respond to all the questions and you may withdraw at any time during the interview should you desire to do so.

Thank you for your co-operation".

Do you agree to participate?

Yes--------------------------------

No---------------------------------
APPENDIX Ib:  KNH/UoN-ETHICS & RESEARCH COMMITTEE APPROVAL

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi;
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP”, Nairobi.
Email: KNHplan@Ken.Heathnet.org

*21st January 2010*

Dr. Julius Karuri Machana
Department of Community Health
School of Medicine
University of Nairobi

Dear Dr. Macharia

RESEARCH PROPOSAL: “ASSESSMENT OF RISK FACTORS FOR BREAST CANCER IN NYERI DISTRICT, KENYA: A CASE CONTROL STUDY.”  (P2789/2009)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and approved your above cited research proposal for the period 21st January 2010 – 20th January, 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

DR. L. MUCHIRI
AG. SECRETARY, KNH/UON-ERC

C.C. Prof. K. M. Bhatt, Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Community Health, UON
The HOD, Records, KNH
Supervisors: Dr. P. K. Njorge, Dept. of community Health, UON
Mrs. Mary Kinoti, Dept. of Community Health, UON
APPENDIX II: QUESTIONNAIRE

ASSESSMENT OF RISK FACTORS FOR BREAST CANCER IN NYERI COUNTY: A CASE CONTROL STUDY.

Questionnaire Number: [___][___][___]

Name (Optional)__________________________

District: ________________________________

Location: ________________________________

Sub-location: ____________________________

Village: _________________________________

Height ___, Weight ____

Interviewer: _____________________________

Date: _________________________________

1. What is your age? [___] Years

2. What is your marital status?
   1) Never married [___]
   2) Married [___]
   3) Separated [___]
   4) Divorced [___]
   5) Cohabiting [___]

3. What is the highest level of education you have completed?
   1) None [___]
   2) Secondary [___]
3) Tertiary (Intermediate college) □
4) Higher /University □

4. What is your occupation?

(1) Teacher □
(2) Farmer □
(3) Nurse/doctor □
(4) Business □
(5) Clerical □
(6) Housewife □
(7) Other (specify) __________________________

5. At what age did you have your first menstrual period? [___ ___]

6. How was/is your monthly periods?
   Regular □
   Irregular □

7. Pregnancy history
   a) Have you ever been pregnant?
      Yes □ (Go to b)
      No □ (Go to Q. 8)
   b) How old were you on your first full-term pregnancy? [___ ___] (Go to c)
   c) How many children do you have? ______

8. Breastfeeding history
   a) How many of your children did you breastfeed? ______
   b) What was the average breastfeeding period per child? ______

9. Oral contraceptive use
a) Have you ever used Oral contraceptives for family planning purpose?
   Yes [ ] (Go to b)
   No [ ] (Go to Q. 10)

b) For how long? [ ]

10. Injectable contraceptive use
    a) Have you ever used injectable contraceptives for family planning purpose?
       Yes [ ] (Go to b)
       No [ ] (Go to Q. 11)

    b) For how long? [ ]

11. Menstrual history
    a) Had you stopped having menstrual periods at the time you were
diagnosis with breast cancer (Menopause)?
       Yes [ ] (Go to b)
       No [ ] (Go to Q. 12)

    b) What was your age then when you stopped having menstrual periods
       (Menopause)?
       [ ] [ ]

12. Hormone replacement therapy use
    a) Have you ever been on hormone replacement therapy?
       Yes [ ] (Go to Q. b)
       No [ ] (Go to Q. 13)

    b) For how long? [ ] Months
       [ ] Years

    a) Have you ever had an induced abortion/miscarriage?
Yes [ ] (Go to Q. b)

No [ ] (Go to Q. 14)

b) How many times? [ ]

14. Radiation exposure history
   a) Were you ever exposed to radiotherapy prior to developing breast cancer?
      Yes [ ] (Go to Q. b)
      No [ ] (Go to Q. 15)

   b) How many times? [ ]

15. (a) Do you have a relative with history of a breast cancer?
       Yes [ ] (Go to (b))
       No [ ] (Go to (16))

       (b) Please specify?

           (1) Sister
           (2) Mother
           (3) Brother
           (4) Father
           (5) Other relative......................... (Specify)

16. (a) Do you have a relative with history of any other cancer apart from breast cancer?
       Yes [ ] ...................... (Specify) (Go to (b))
       Yes [ ] (Go to (16))

       (b) Please specify?

           (1) Sister
           (2) Mother
17. (a) Have you ever taken beer?
   (1) In the past (Ask b)
   (2) Currently taking (Ask b)
   (3) Never (Go to Q. 18)

   (b) How bottles do/did you drink per day?
       (1) Less than 1 [ ]
       (2) 1 – 2 [ ]
       (3) 3– 5 [ ]
       (4) 5 – 10 [ ]
       5) More than 10 [ ]

18. (a) Have you ever smoked?
   (1) In the past (Ask b)
   (2) Currently smoking (Ask b)
   (3) Never (Go to stop interview)

   (b) How Many cigarettes do you smoke per day?
       (1) Less than 1 [ ]
       (2) 1 – 2 [ ]
       (3) 3– 10 [ ]
       (4) 10 – 20 [ ]
       (5) More than 20 [ ]

THANK YOU.
APPENDIX III: BREAST CANCER DIAGNOSIS

Breast cancer is initially recognized either because signs or symptoms appear or through screening. Neither of these lead to a definitive diagnosis, which usually requires the opinion of a pathologist, a type of physician (medical doctor) who specializes in the diagnosis of cancer and other diseases. The investigations include:

1. Radiography

- Diagnostic Mammography – This mammography is an x-ray examination of the breast in a woman who either has a breast complaint (for example, a breast lump or nipple discharge is found during self-examination) or has had an abnormality found during screening mammography.

- Breast Ultrasound - Breast ultrasound, also known as sonography or ultrasonography, is frequently used to evaluate breast abnormalities that are found with screening or diagnostic mammography or during a physician performed clinical breast examination. Ultrasound is excellent at imaging cysts: round, fluid-filled, pockets inside the breast.

- Breast MRI – Magnetic Resonance breast imaging (MRI, MR) is often used to investigate breast concerns first detected with mammography, physical exam, or other imaging exams. MRI is also excellent at imaging the augmented breast, including both the breast implant itself and the breast tissue surrounding the implant (abnormalities or signs of breast cancer can sometimes be obscured by the implant on a mammogram).

MRI is also useful for staging breast cancer, determining the most appropriate treatment, and for patient follow-up after breast cancer treatment.
Electrical Impedance (T-scan) – T-scan (also called electrical impedance scanning or EIS) is used as an adjunct tool to mammography in helping to detect breast cancer. T-scan uses the electrical impedance principal to measure the way electrical current passes through breast tissue and helps detect cancerous tumors. Conversely, T-scan imaging can also confirm when tumor tissue is benign (non-cancerous). T-scan impedance imaging of the breast does not use radiation such as x-rays or radionuclides, does not require compression of the breast, and does not require an injection or biopsy sampling of the breast tissue via needle or surgical incision.

2. **Nuclear Medicine (Scintimammography)**

Nuclear medicine breast imaging (also called scintimammography) is a supplemental breast exam that may be used in some patients to investigate a breast abnormality. A nuclear medicine test is not a primary investigative tool for breast cancer but can be helpful in selected cases after diagnostic mammography has been performed. Nuclear medicine breast imaging involves injecting a radioactive tracer (dye) into the patient. Since the dye accumulates differently in cancerous and non-cancerous tissues, scintimammography can help physicians determine whether cancer is present.

3. **Breast Biopsy**

A breast biopsy involves removing a sample of breast tissue to determine whether it is cancerous or benign (non-cancerous). Biopsy followed by pathological (microscopic) analysis is the only definitive way to determine if cancer is present. The tissue diagnosis given by the pathologist indicates the type of cell that is proliferating, its histological grade, genetic abnormalities, and other features of the tumor. Together, this information is useful to evaluate the prognosis of the patient and to choose the best treatment.
Cytogenetics and immunohistochemistry are other types of testing that the pathologist may perform on the tissue specimen. These tests may provide information about the molecular changes (such as mutations, fusion genes, and numerical chromosome changes) that has happened in the cancer cells, and may thus also indicate the future behavior of the cancer (prognosis) and best treatment.

There are several different methods of breast biopsy. These types include:

- Fine needle aspiration (FNA)
- Core needle biopsy
- Vacuum-assisted biopsy (Mammotome or MIBB)
- Large core surgical (ABBI)
- Open surgical (excisional or incisional)

One method of biopsy will likely be most favorable depending on a number of factors.

**APPENDIX IV: TYPES OF BREAST CANCERS**

There are several types of breast cancer, although some of them are quite rare. In some cases a single breast tumor can have a combination of these types or have a mixture of invasive and in situ cancer.

**Ductal carcinoma in situ**

Ductal carcinoma in situ (DCIS; also known as intraductal carcinoma) is the most common type of non-invasive breast cancer. DCIS means that the cancer cells are inside the ducts but have not spread through the walls of the ducts into the surrounding breast tissue. Nearly all women diagnosed at this early stage of breast cancer can be cured.

A mammogram is often the best way to find DCIS early.
Lobular carcinoma in situ

Although not a true cancer, lobular carcinoma in situ (LCIS; also called lobular neoplasia) is sometimes classified as a type of non-invasive breast cancer, which is why it is included here. It begins in the milk-producing glands but does not grow through the wall of the lobules. Women with this condition do have a higher risk of developing an invasive breast cancer in the same breast or in the opposite breast. For this reason, women with LCIS should make sure they have regular mammograms.

Invasive (or infiltrating) ductal carcinoma (IDC)

This is the most common type of breast cancer. Invasive (or infiltrating) ductal carcinoma (IDC) starts in a milk passage (duct) of the breast, breaks through the wall of the duct, and grows into the fatty tissue of the breast. At this point, it may be able to spread (metastasize) to other parts of the body through the lymphatic system and bloodstream.

Invasive (or infiltrating) lobular carcinoma

Invasive lobular carcinoma (ILC) starts in the milk-producing glands (lobules). Like IDC, it can spread (metastasize) to other parts of the body. Invasive lobular carcinoma may be harder to detect by a mammogram than invasive ductal carcinoma.

Less common types of breast cancer

Inflammatory breast cancer: This uncommon type of invasive breast cancer accounts for about 1% to 3% of all breast cancers. Usually there is no single lump or tumor. Instead, inflammatory breast cancer (IBC) makes the skin of the breast look red and feel warm and gives the skin a thick, pitted appearance that looks a lot like an orange peel. Doctors now know that these changes are not caused by inflammation or infection, but by
cancer cells blocking lymph vessels in the skin. The affected breast may become larger or firmer, tender, or itchy. In its early stages, inflammatory breast cancer is often mistaken for infection (mastitis). Because there is no defined lump, it may not show up on a mammogram, which may make it even harder to find it early. It tends to have a higher chance of spreading and a worse outlook than typical invasive ductal or lobular cancer.

Mixed tumors: Mixed tumors are those that contain a variety of cell types, such as invasive ductal cancer combined with invasive lobular breast cancer. In this situation, the tumor is treated as if it were an invasive ductal cancer.

Medullary carcinoma: This special type of infiltrating breast cancer has a rather well-defined boundary between tumor tissue and normal tissue. It also has some other special features, including the large size of the cancer cells and the presence of immune system cells at the edges of the tumor. Medullary carcinoma accounts for about 3% to 5% of breast cancers. The outlook (prognosis) for this kind of breast cancer is generally better than for the more common types of invasive breast cancer. Most cancer specialists think that true medullary cancer is very rare, and that cancers that are called medullary cancer should be treated as the usual invasive ductal breast cancer.

Paget disease of the nipple: This type of breast cancer starts in the breast ducts and spreads to the skin of the nipple and then to the areola, the dark circle around the nipple. It is rare, accounting for only about 1% of all cases of breast cancer. The skin of the nipple and areola often appears crusted, scaly, and red, with areas of bleeding or oozing. The woman may notice burning or itching.
Phyllodes tumor: This very rare breast tumor develops in the stroma (connective tissue) of the breast, in contrast to carcinomas, which develop in the ducts or lobules. Other names for these tumors include phylloides tumor and cystosarcoma phyllodes. These tumors are usually benign but on rare occasions may be malignant.

Angiosarcoma: This is a form of cancer that starts from cells that line blood vessels or lymph vessels. It rarely occurs in the breasts. When it does, it is usually seen as a complication of radiation to the breast. It tends to develop about 5 to 10 years after radiation treatment. However, this is an extremely rare complication of breast radiation therapy. Angiosarcoma can also occur in the arm of women who develop lymphedema as a result of lymph node surgery or radiation therapy to treat breast cancer. These cancers tend to grow and spread quickly.

APPENDIX V: THE SCARFF-BLOOM-RICHARDSON HISTOLOGIC SYSTEM OF GRADING BREAST CANCER

<table>
<thead>
<tr>
<th>Tubule Formation (% of Carcinoma Composed of Tubular Structures)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 75%</td>
<td>1</td>
</tr>
<tr>
<td>10-75%</td>
<td>2</td>
</tr>
<tr>
<td>less than 10%</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nuclear Pleomorphism (Change in Cells)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small, uniform cells</td>
<td>1</td>
</tr>
<tr>
<td>Moderate increase in size and variation</td>
<td>2</td>
</tr>
<tr>
<td>Marked variation</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mitosis Count (Cell Division)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 7</td>
<td>1</td>
</tr>
<tr>
<td>8 to 14</td>
<td>2</td>
</tr>
<tr>
<td>15 or more</td>
<td>3</td>
</tr>
</tbody>
</table>

Source: Courtesy of the American Medical Association (2005).
Summary of Histologic Grades of Breast Cancer

A tumor with a final sum of 3, 4, or 5 is considered a Grade 1 tumor (well-differentiated).

A sum of 6 or 7 is considered a Grade 2 tumor (moderately-differentiated), and a sum of 8 or 9 is a Grade 3 tumor (poorly-differentiated).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Score</th>
<th>5 yr. survival</th>
<th>7 yr. survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Well-differentiated breast cells; cells generally appear normal and are not growing rapidly; cancer arranged in small tubules.</td>
<td>3,4,5</td>
<td>95%</td>
<td>90%</td>
</tr>
<tr>
<td>(lowest)</td>
<td>Grade 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderately-differentiated breast cells; have characteristics between Grade 1 and Grade 3 tumors.</td>
<td>6,7</td>
<td>75%</td>
<td>63%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Poorly differentiated breast cells; Cells do not appear normal and tend to grow and spread more aggressively.</td>
<td>8,9</td>
<td>50%</td>
<td>45%</td>
</tr>
<tr>
<td>(highest)</td>
<td>Grade 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Courtesy of the American Medical Association (2005).
The most common modes of breast cancer treatment are surgery, chemotherapy, radiation therapy and immunotherapy. The choice of therapy depends upon the location and grade of the tumor and the stage of the disease, as well as the general state of the patient (performance status).

- Surgery  
  - Lumpectomy
  - Mastectomy
- Chemotherapy
- Radiation Therapy
- Hormone therapy; Breast Prostheses and Post-Mastectomy Care

**Lumpectomy**

Lumpectomy is the surgical removal of a cancerous lump (or tumor) in the breast, along with a small margin of the surrounding normal breast tissue. Lumpectomy may also be called wide excision biopsy, breast conserving therapy or quadrantectomy (this latter term is used when up to one fourth of the breast is removed). The procedure is often performed on women with small or localized breast cancers and can be an attractive surgical treatment option for breast cancer because it allows women to maintain most of their breast after surgery.

**Mastectomy**

Mastectomy is the surgical removal of a breast. Surgery is presently the most common treatment for breast cancer. Following mastectomy, immediate or delayed breast reconstruction is possible in many instances.
Chemotherapy

Chemotherapy involves using anticancer drugs to help control or prevent the growth of cancerous tumors. Chemotherapy is often used as an adjuvant (supplemental) therapy in addition to other treatments, such as surgery or radiation therapy, which are designed to achieve local (breast/chest) control of the cancer. These drugs interfere with cell division in various possible ways, e.g. with the duplication of DNA or the separation of newly formed chromosomes. Most forms of chemotherapy target all rapidly dividing cells and are not specific to cancer cells, although some degree of specificity may come from the inability of many cancer cells to repair DNA damage, while normal cells generally can.

Chemotherapy may be used to:

- cure cancer
- stop cancer from spreading to other parts of the body
- slow cancer growth
- kill cancer cells
- relieve symptoms of cancer

Radiation Therapy

Radiation therapy (or radiotherapy) uses high-energy rays to stop cancer cells from growing and dividing. It is often used to destroy any remaining breast cancer cells in the breast, chest wall, or axilla (underarm) area after surgery. Radiation therapy can be administered externally via external beam radiotherapy
(EBRT) or internally via brachytherapy. Occasionally, radiation therapy is used before surgery to shrink the size of a tumor.

**Breast Prostheses and Post-Mastectomy Care**

Breast Reconstruction- Often modified radical mastectomy patients may undergo breast reconstructive surgery during the same operation to remove the breast. Reconstructive surgery usually involves insertion of breast implant or a muscle flap. Women who do not wish to have further surgery may be fitted with an external prosthesis (an artificial breast) after healing from mastectomy.
APPENDIX VII: STAGING OF BREAST CANCER

Cancers are designated the letter T (tumor size), N (palpable nodes), and/or M (metastasis)

T: Tumor Size

The letter T followed by a number from 0 to 4 describes the tumor's size and whether it has spread to the skin or chest wall under the breast. Higher T numbers indicate a larger tumor and/or more extensive spread to tissues surrounding the breast.

TX: Tumor cannot be assessed
T0: No evidence of a tumor
Tis: Cancer may be lobular carcinoma in situ (LCIS), ductal carcinoma in situ (DCIS) or Paget's disease
T1: Tumor is 2 cm or less in diameter
T2: Tumor is between 2 and 5 cm in diameter
T3: Tumor is more than 5 cm in diameter
T4: Tumor is any size, has attached itself to the chest wall and spread to the pectoral (chest) lymph nodes

N: Palpable Nodes

The letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, whether the affected nodes are fixed to other structures under the arm.

NX: Lymph nodes cannot be assessed (lymph nodes were previously removed, etc.)
N0: Cancer has not spread to lymph nodes
N1: Cancer has spread to the movable ipsilateral axillary lymph nodes (underarm lymph nodes on same side of breast cancer)

N2: Cancer has spread to ipsilateral (same side of body as breast cancer) lymph nodes fixed to one another or to other structures under the arm

N3: Cancer has spread to the ipsilateral mammary lymph nodes or the ipsilateral (same side of body as breast cancer) supraclavicular lymph nodes

M: Metastasis

The letter M followed by a 0 or 1 indicates whether or not the cancer has metastasized (spread) to distant organs (i.e., the lungs or bones) or to lymph nodes that are not next to the breast, such as those above the collarbone.

MX: Metastasis cannot be assessed

M0: No distant metastasis to other organs

M1: Distant metastasis to other organs

Numerical Stages of Breast Cancer

The stage of a breast cancer describes its size and the extent to which it has spread. The staging system ranges from Stage 0 to Stage IV.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor Size</th>
<th>Lymph Node Involvement</th>
<th>Metastasis (Spread)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Less than 2 cm</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>II</td>
<td>Between 2-5 cm</td>
<td>No or in same side of breast</td>
<td>No</td>
</tr>
<tr>
<td>III</td>
<td>More than 5 cm</td>
<td>Yes, on same side of breast</td>
<td>No</td>
</tr>
<tr>
<td>IV</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Stage 0 or "in situ:" Cancer is contained and has not spread beyond the breast ductal system. Fifteen to twenty percent of breast cancers detected by clinical examinations or testing are in Stage 0 (the earliest form of breast cancer). Two types of Stage 0 cancer are lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS).

**LCIS:** indicates high risk for breast cancer. Many physicians do not classify LCIS as a malignancy and often encounter LCIS serendipitously (by chance) on breast biopsy while investigating another area of concern. While the microscopic features of LCIS are abnormal and are similar to malignancy, LCIS does not behave as a cancer (and therefore is not treated as a cancer). LCIS is merely a marker for a significantly increased risk of cancer anywhere in the breast.

**DCIS:** the cancer cells are confined to milk ducts in the breast and have not spread into the fatty breast tissue or to any other part of the body (such as the lymph nodes).

**Stage I:** The primary (original) cancer is 2 cm (approximately \( \frac{3}{4} \) inch) or less in diameter and has not spread to the lymph nodes.

**Stage IIA:** The primary tumor is between 2 and 5 cm in diameter and has not spread to the lymph nodes.

**Stage IIB:** The primary tumor is between 2 and 5 cm in diameter and has spread to the axillary (underarm) lymph nodes; or the primary tumor is over 5 cm and has not spread to the lymph nodes.

**Stage IIIA:** Primary breast cancer of any kind that has spread to the axillary (underarm) lymph nodes and to axillary tissues.

**Stage IIIB:** The primary breast cancer is any size, has attached itself to the chest.
wall, and has spread to the pectoral (chest) lymph nodes.

**Stage IV**: The primary cancer has spread out of the breast to other parts of the body (such as bone, lung, liver, brain).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor (T)</th>
<th>Node (N)</th>
<th>Metastasis (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage 1</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T0</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T0</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1, N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>any N</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>any T</td>
<td>any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Source: American Joint Commission on Cancer and International Union Against Cancer
Palliative care is treatment to relieve, rather than cure, symptoms caused by cancer. It can help people live more comfortably and it is an urgent humanitarian need for people worldwide with cancer and other chronic fatal diseases. It is particularly needed in places with a high proportion of patients in advanced stages where there is little chance of cure. Although the control of the symptoms of breast cancer is not typically thought of as a treatment directed at the cancer, it is an important determinant of the quality of life of cancer patients, and plays an important role in the decision whether the patient is able to undergo other treatments. Relief from physical, psychosocial and spiritual problems can be achieved in over 90% of advanced cancer patients through palliative care.

Although doctors generally have the therapeutic skills to reduce pain, nausea, vomiting, diarrhea, hemorrhage and other common problems in cancer patients, the multidisciplinary specialty of palliative care has arisen specifically in response to the symptom control needs of this group of patients. The palliative care movement, a more recent offshoot of the hospice movement, has engendered more widespread support for preemptive pain treatment for cancer patients. Some local organizations offer a variety of practical and support services to people with cancer. Support can take the form of support groups, counseling, advice, financial assistance, transportation to and from treatment, films or information about cancer. These organizations often are involved in cancer prevention, cancer treatment, and cancer research. Nyeri hospice is the only such organization in this region.
APPENDIX IX: LOCATION OF NYERI IN KENYA

LOCATION OF NYERI IN KENYA

Source: Nyera District Development Plan, 2002-2006, Fig 3.

Prepared by CRES 1999 Pop Census

This map is not authoritative, use administrative boundaries