THE COST BURDEN OF BREAST CANCER TREATMENT AT KENYATTA NATIONAL HOSPITAL: A PATIENT'S PERSPECTIVE

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A thesis submitted in partial fulfillment of the requirements for the award of the degree of Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance of the University of Nairobi.

SEPTEMBER, 2015

DECLARATION

I declare that this thesis is my original work and has not been presented for award of a degree in any university or published anywhere.

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DEDICATION

To my Parents, Dr. David Gitonga and Margaret Wanjiku; You have believed in me and sacrificed in one way or another all the way.

ABSTRACT

Background

Breast cancer ranks highest among the cancers affecting women in Kenya. Treatment involves surgery, adjuvant chemotherapy and radiotherapy. The therapy has significant cost implications. Associated procedures including diagnostic and routine laboratory tests and management of adverse effects of surgery and chemotherapy increases the direct cost to patients and costs to the society given the poor resource setting that Kenya is in.

Objective

The main objective was to evaluate the direct total medical costs incurred by breast cancer patients at Kenyatta National Hospital from a patient's perspective. The secondary objective was to identify significant cost components.

Methodology

This was a hospital based retrospective cohort study. Patients diagnosed with breast Cancer at Kenyatta National Hospital registry and who had undergone mastectomy, chemotherapy and radiotherapy during the period January 2010 and December 2014 were identified. Ninety three patient files were sampled by systematic random sampling. A customized pre tested data collection tool was used to collect socio-demographic, clinical and cost data from patient files. Descriptive and exploratory data analysis was done using STATA Version 10. A micro ingredient approach was used for costing. From patients' records and the billing department, all the resources used by patients were identified and quantified. The units cost was obtained from the procurement department. These were used to compute the total costs incurred by each patient. The median total cost was then computed. Exploratory data analysis was done to determine associations between categorical variables. A cost function for a patient was obtained by linear regression forward stepwise model building. Ethical approval to conduct the study was given by the Kenyatta National Hospital and University of Nairobi Research and Ethics committee. All costs were converted to international dollars (int $), using the purchasing power parity for Kenya against the United States dollars. The 2014 conversion rate of 40.43 Kenya shillings = 1 international dollars was used.

Results

The median total cost of treatment to a patient in 2015 for breast cancer was 2658.92 international dollars with an inter quartile range of [2122.24, 2834.67]. The equivalent cost in Kenya shillings was shs 107500 with an inter quartile range of [85748, 114578] The main cost drivers and their contribution to the total treatment cost were surgery (38.5%), laboratory and radiological tests (25.1%), chemotherapy (9%), and management of side effects (14%) arising from the various treatment modalities. Patient and disease related variables that had a significant effect on total cost were stage of the disease (p=0.046), comorbidities (p=0.039) and presence of bone metastasis (p= 0.01). The menopausal status and parity of the participants had no significant effect on the total cost.

Discussion

The median cost of Breast cancer treatment in Kenyatta National Hospital was int$ 2658.92 which is 15 times the country's average wage monthly wage level of int$ 177.84. Surgical procedures and laboratory investigations collectively are responsible for 60% of all the costs incurred by the patient. The choice of chemotherapeutic agents explains 15% of cost variation in the total cost model. Patients start therapy late and this contributes to high cost of therapy. New treatments such as transtuzumab are extremely costly

Conclusion

The total cost of breast cancer treatment is well above the countries wage level and subsidization is required

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ABBREVIATIONS

AC-T	Adriamycin Cyclophosphamide and A Taxane (Docetaxel/Paclitaxel)
BC	Breast Cancer
BMI	Body Mass Index
BSA	Body surface Area
CAF	Cyclophosphamide, Adriamycin (Doxorubicin), Fluorouracil,
CMF	Cyclophosphamide, Methotrexate, Fluorouracil
CTC	Cancer treatment centre
ET	Endocrine therapy
ER	Oestrogen Receptor
Int $	International dollars
KNH	Kenyatta National Hospital
MBC	Metastatic Breast Cancer
NHIF	National Hospital Insurance Fund
PR	Progesterone Receptor
S	Surgery
Ksh	Kenya shilling
WHO	World Health Organization

DEFINITION OF TERMS

Cost driver	A factor that directly causes a change in the cost of a treatment activity, and which is generally based on varying the levels of activity
Cancer	Malignant neoplasm which usually invades surrounding tissues may metastasize to several sites and is likely to recur after attempted removal and to kill patient unless adequately treated.
Health Care costs	A cost that can be directly or indirectly attributed to a specific treatment process, health provider or medication therapy.
Cost model	A formula for estimating the cost of a treatment process.
Direct medical cost	Costs of resources used in prevention, diagnosis, treatment and rehabilitation of a disease such as cost of drugs, hospitalization and diagnostic procedures
Direct non-medical costs	Cost of all other resource used related to the diseases such transportation costs and costs for social services
Intangible costs	The cost of pain and suffering as a result of illness or treatment
Patient's perspective	The study perspective that determines relevant costs incurred by a patient that need to be accounted for during analysis

CHAPTER ONE: INTRODUCTION

1.1 Background

Breast cancer (BC) is the most prevalent cancer among Kenyan women (1). There has been increasing incidence of BC but with improved clinical outcomes over the last few decades. This has been attributed to advances in early detection, prevention, and treatment strategies. However, there have been differences in the survival of BC patients in wealthy nations and regions with limited resources. Under developed countries have lower BC incidences but a majority of patients present with advanced disease at the time of diagnosis (2).

Underdeveloped countries have generally not identified cancer as an urgent health care issue because infectious diseases are the predominant public health threats. Nonetheless, resources are spent on cancer treatment when patients seek medical care. Kenyatta National Hospital is the only government referral hospital in the country that offers comprehensive cancer treatment where cancer treatment centre (CTC). Patients are referred from other departments within the hospital or from other hospitals across the country. Most patients receive their chemotherapy treatment as outpatients. National Hospital Insurance (NHIF) did not previously cater for the cost of outpatient treatment until mid 2015 when it was introduced. Previously patients had to fund their treatment (3).

Cancer has becomes an increasing problem as the control of communicable diseases improves and life expectancy increases (4). WHO has observed that guidelines defining optimal breast care and services have limited utility in resource constrained countries (5).

Estimation of the direct medical costs of breast cancer can help payers of healthcare to understand the burden of breast cancer on their limited financial resources as well as the society. For health providers, they can choose among alternative modalities that meet the treatment objectives cost effectively.

The increase in survival rates and improved quality of life among patients in developed countries has been credited to early detection and aggressive treatment. Many of the newer treatment alternatives are expensive and beyond the reach of many women in Kenya with the majority of Kenyans living below a dollar a day. Given the increase in the number of new cases of BC, allocating resources to purchase products would impact negatively on the

already overstretched health budget. Patients with infectious diseases in Kenya such as tuberculosis malaria and HIV/AIDS tend to access free treatment from the government and international donors (6). Cancer programs do not benefit from donor funding.

1.2 Problem Statement

Consistent research and development of new treatment technologies and targeted drugs has an impact on overall cost of cancer management (7). Heavy investments required in the pharmaceutical industry for production and marketing of these technologies increases the final cost incurred by the consumer (8). In addition, clinicians tend to prescribe expensive drugs and technologies if incentives are given by marketers. The overall cost, if borne by health insurance industry, leads to increased premiums on patients. Patients are susceptible as they may be under-insured leading to financial catastrophy (9). The trend in recent years is that an increasing number of patients are unable afford high quality cancer treatment alternatives (10).

As the development and adoption of targeted therapy such as use of monoclonal antibodies becomes widespread, costs will continue to increase in comparison to traditional non-oncology products due to a limited market. Anti-cancer treatments account for a high percentage of drug expenditures in hospitals and outpatient clinics whereas inpatient use of cancer therapeutics is dominated by supportive care agents such as hematopoietic growth factors and anti-emetics. There are variations in physicians prescribing patterns (11). The reasons for these variations have not been well documented. One explanation for variation in chemotherapy treatment has been reimbursement practices. A study reported that, once a decision to give chemotherapy was taken, physicians receiving more generous insurance reimbursements used more costly treatment regimens (11).

In Kenya the main financiers of healthcare is the Government of Kenya; directly through acquisition of drugs, equipment and payment of staff emoluments (6). The policy makers have mainly concentrated on infectious diseases. Consequently there are no well funded cancer programs in Kenya. The cost burden of various cancer treatment options which include chemotherapy, radiotherapy and surgery. Data is needed for a comprehensive cost assessment that ultimately lead to better planning of cancer care programs by the policy makers. Estimation of the cost burden on patients may inform the National Insurance Agency, (NHIF) to provide reimbursements for cancer care. This study sought to estimate the

cost burden of breast cancer management from a patient's perspective.

1.3 Conceptual framework

In Kenya a major yard stick used to evaluate affordability of breast cancer treatment option to the patient is the total direct medical cost of services and health products. The overall cost is dependent on various cost drivers in the treatment process which include surgical medication and radiotherapy costs, bed charges, doctors' fees and diagnostic charges among others. The overall cost is a function of these cost drivers as presented in Figure 1.

The study sought to establish these drivers and establish a cost function. In conceptualizing, the researcher attempted to point out the interaction of the cost drivers and how affected the overall cost of breast cancer treatment. It is hoped that the findings of this study will justify additional cover for cancer patients by NHIF.

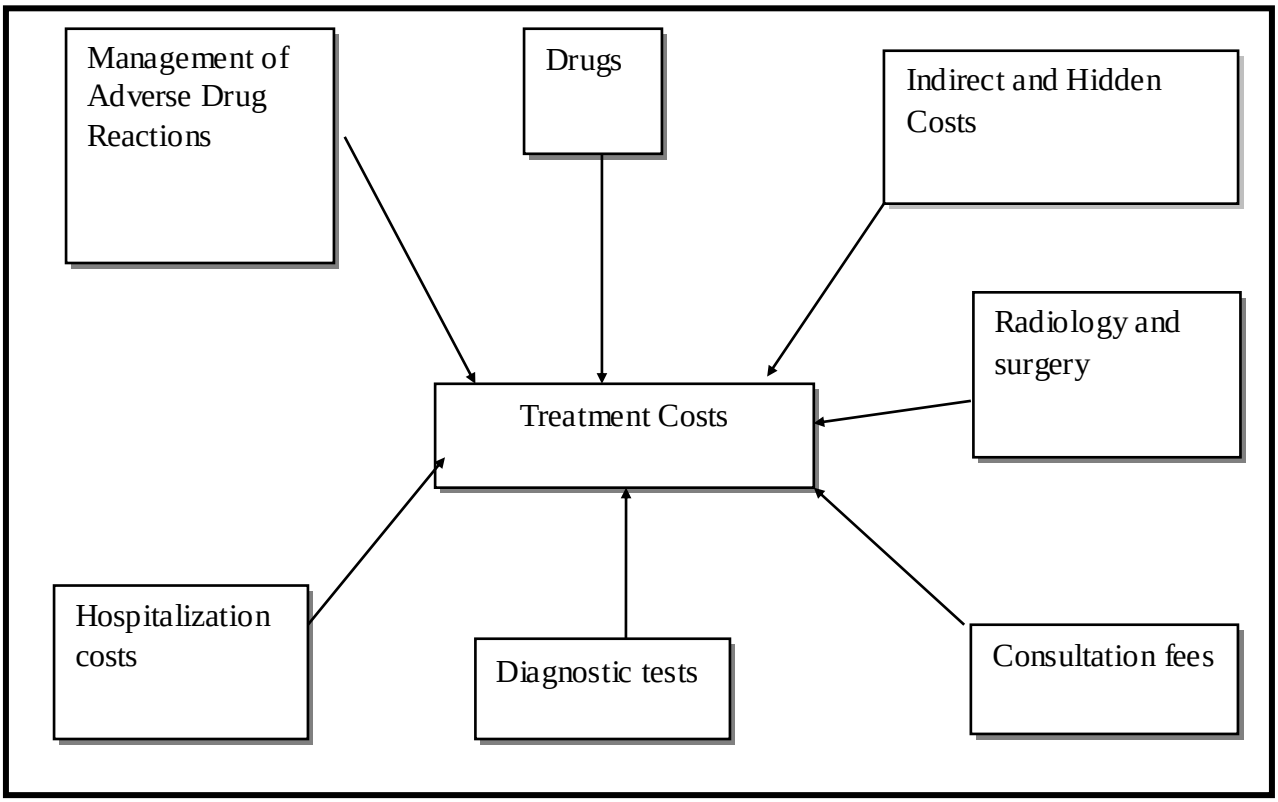


Figure 1 Conceptual framework of total medical cost and various determinants

1.4 Study Justification

There is a possibility that management of BC patients in Kenya has not been optimized, in Kenya's public hospitals. This is as a result of lack data on availability and cost of resources required in diagnosis and treatment of the disease. Direct medical costs play a significant

role in patients' perception on cost of treatment. Studies to identify and quantify direct medical costs of treatment of breast cancer have not been done in Kenyatta National Hospital, a national referral hospital. There was need for these studies to identify how much a patient incurs in seeking treatment at the hospital. The study aims to estimate of the direct medical costs of breast cancer from the patient's perspective.

1.5 Research question

1. What is the total direct medical cost of treating a breast cancer patient at Kenyatta National Hospital from a patient's perspective?
2. Which cost categories contribute most to the overall cost?
3. What patient factors influence variation in the total cost?
4. What causes variation in the inter-patient costs?

1.6 Study Objectives

1.6.1 General Objective

To estimate the direct medication cost of breast cancer treatment at Kenyatta National Hospital from a patient's perspective.

1.6.2 Specific Objective

The specific objectives were to

a) Quantify the direct medical cost burden over the duration of treatment
b) Identify the determinants of medication costs and create a total cost function model.
c) Identify how different treatment options and patient characteristics affects the total cost.

1.7 Significance of the study

The findings of this study are useful to the government in planning and budgeting for cancer care. To promote equitable provision of health, these findings may sensitize health insurance providers to provide more funding for cancer care. To healthcare providers, these findings will enable them choose best treatment options in order to minimize costs.

CHAPTER 2: LITERATURE REVIEW

2.1 Epidemiology of breast cancer

Breast cancer (BC) is the most common cancer in women both in the developed and less developed world. In 2012, BC caused an estimated 521,000 deaths worldwide (12). There has been an increasing incidence yearly. The risk factors include a familial history of breast cancer (13), "reproductive factors associated with prolonged exposure to endogenous estrogens, such as early menarche, late menopause and late age at first childbirth" (14), and modern lifestyles such as alcohol use and obesity, and physical inactivity (14). In Kenya BC accounts for 23.3% of all cancers (15).

2.2 Breast cancer diagnosis

The early and precise diagnosis of BC increases chances of proper treatment (4). A screening mammogram may reveal a lump or nodule in the woman's breast during a clinical examination. Follow up tests for definitive diagnosis include imaging tests such as ultra sound, magnetic resonance imaging (MRI) and diagnostic mammography (13). Different types of biopsies are also done where the sample is analyzed by a pathologist. Molecular testing of the tumour is also done to determine the appropriate treatment plan to increase chances of remission. They include estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2) profiling (16).

2.3 Staging of Breast cancer

Staging refers to the grouping of patients according to the apparent extent of their tumours. It can be based on either clinical or pathologic findings. The most widely used staging system for BC is that of the American Joint Committee on Cancer (AJCC). Tumour size, lymph node status (N), histopathology type and tumour grade should be documented for all cases because of their limited cost and important prognostic significance (14).

The extent of axillary lymph node involvement in BC is the dominant prognostic indicator for later systemic disease. Tumour size, and the presence or absences of distant metastases are additional factors that predicts outcome of the disease as indicated in Table 1.

Table 1: Staging of Breast cancer

Adapted from the *AJCC Cancer Staging Manual*, 7th Edition is (17).

Stage	Tumour size (T)	Lymph node status (N)
0	Tis (Carcinoma in situ)	N0 (No regional lymph node metastasis
IA	T1 Tumor > 1 mm but ≤ 5 mm	N0
IB	T0 Tumor > 5 mm but ≤10 mm	N1mi (Micrometastasis in movable ipsilateral axillary lymph nodes)
IC	T1 Tumor > 10 mm but ≤20 mm	N1mi
IIA	T0	N1
	T1 (Tumor >20 mm)	N1
	T2 (Tumor > 20 mm but ≤50 mm)	N0
IIB	T2 (T 20-50mm	N1 (< 4 axillary nodes)
	T3 (Tumor > 50 mm)	N0
IIIA	T0	N2
	T3	N2
IIIB	T4 Tumor of any size with direct extension to the chest wall and/or to the skin	N0
	T4	N1 (spread to < 10 axillary Nodes)
	T4	N2
IIIC	Any T	N3 (Metastasis in ipsilateral infraclavicular lymph nodes)
IV	Any T	Any N with distant metastasis present

2.4 Treatment of breast cancer

Local treatment of early stage BC involves either mastectomy or breast-conserving surgery followed by whole-breast irradiation (18). The pathologic and biologic properties of a woman's BC may be used to estimate her probability for recurrence of and death from BC, as well as the magnitude of benefit she is likely to receive from adjuvant endocrine therapy or chemotherapy (19).

Chemotherapy is one of three pillars of cancer treatment along with surgical treatment and radiation therapy. Chemotherapy treatment can be used for the following intents: curing,

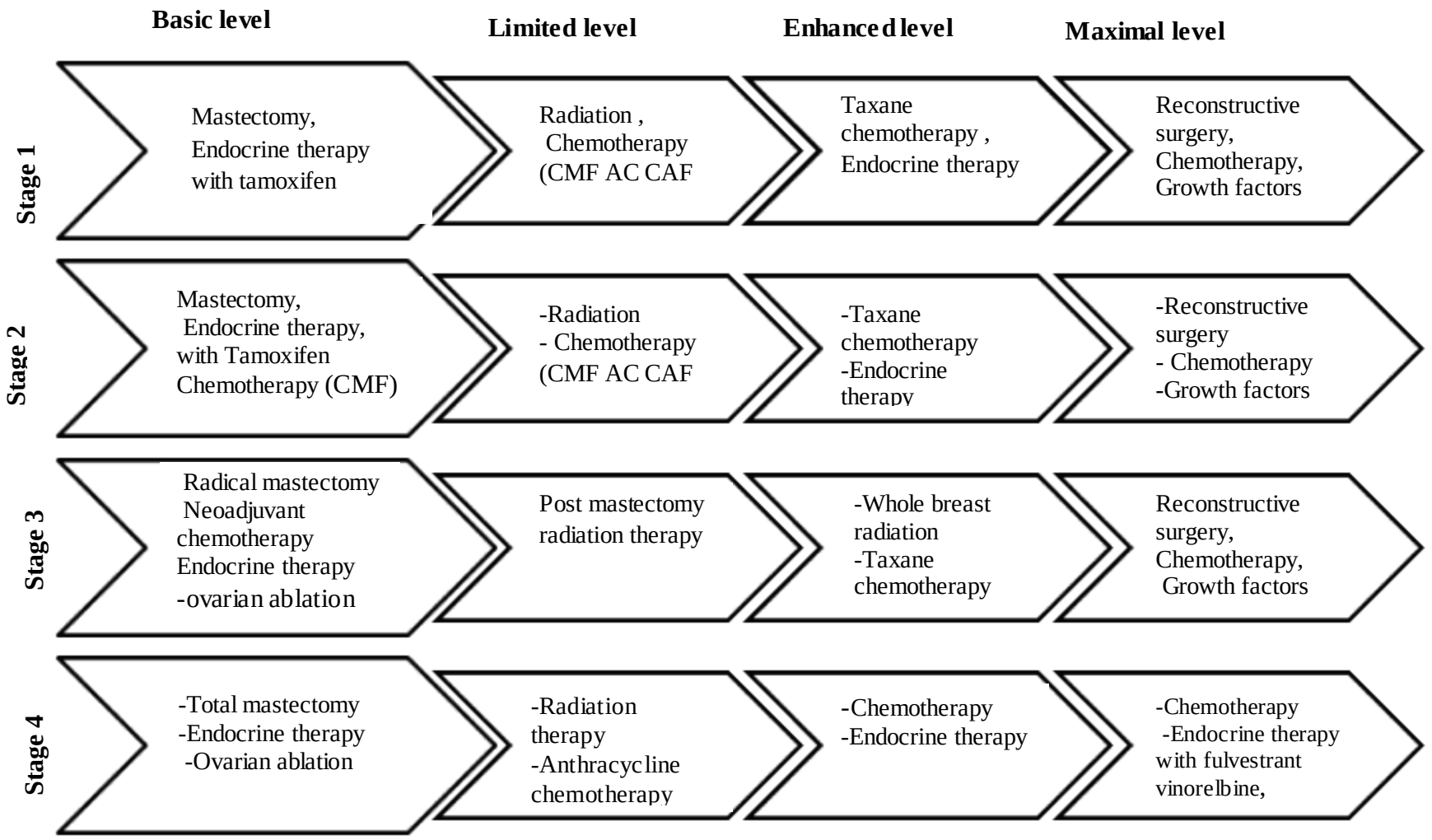
prolonging survival, or palliative care. Clinical recommendations for cancer treatment depend on the type and stage of cancer along with patient characteristics. Regimens for chemotherapy depend on whether the disease is non-metastatic or metastatic (20) as well as prior chemotherapy attempts and responses (3).

Breast Cancer is responsive to all major classes of anticancer medicines including alkylating agents, antimetabolites, mitotic inhibitors and antitumor antibiotics either as single agents or in combination (21). Combination chemotherapy, which is one of the modern approaches in the pharmacological control of cancer, has been shown to be superior to single agent chemotherapy in some tumours. Its use, involves reduction in the dose of each agent compared to the dose of a single agent (22). Combination chemotherapy is associated with improved response rates and is therefore the basis for adjuvant therapy in operable BC where cure is the objective (23). Endocrine therapy is the first line of treatment in BC for hormone receptor (HR) positive patients

The Breast Health Global initiative (BHGI) is an international breast cancer clinical improvement initiative (24). BHGI considered factors affecting the value of a given BC therapy. These factors include; disease free survival, quality of life, and cost. Each therapy was assigned to one of four incremental levels basic, limited, enhanced, or maximal. BHGI mapped out a sequential and flexible approach for planning, establishing, and expanding BC treatment services (25). Figure 2 presents the proposed treatment strategy for breast cancer.

Compared with the treatment for early BC, the treatment for advanced BC is more resource intensive and generally has poorer outcomes. This underscores the benefit of early detection and diagnosis, in terms of conserving resources and in reducing morbidity and mortality (26).

Figure 2: Proposed treatment strategy levels by Breast Health Global initiative (25)



2.5 Cost determinants in Treatment of breast cancer for the patient

The costs associated with BC treatment differ greatly based on the perspective, time profile and patients under study. The strategies that are effective in management of breast cancer in high income countries may be inappropriate for countries which have lower breast cancer incidences, fewer resources, and competing demands from high incidence health problems such as communicable diseases (27). A societal perspective includes cost categories such as loss of productivity and opportunity cost by patient in calculation of costs. Costs vary with time. They may be lower or higher depending on the prevailing conditions. Lifetime costs can be high depending on where the patient lives.

From a patient's perspective, there are several cost drivers for BC patients who are receiving care (28). They include: cost of chemotherapeutic drugs, chemotherapy-related admissions costs; consultation and procedure fees and laboratory costs. In addition, there are costs of management of chemotherapy induced side effects whereby anti-emetics, haematinics and antibiotics as a result of secondary infections may be used. These may require inpatient care (10).

2.6 The cost burden of breast cancer treatment on patients

A 2006 United States National Survey of cancer patients and their family members showed that among those with insurance, 25% of people reported that they used up all or most of their savings dealing with cancer, and 33% of families reported a problem paying their cancer bills. The study also showed that among those individuals who were uninsured, 27% reported that they or their family member delayed or decided not to obtain care for cancer because of the cost (29).

As personal costs increase, under insured or uninsured patients may be less likely to seek care, and hospitals are less likely to provide charity care (30). Studies have also shown that women with lower socio-economic status have lower breast cancer survival rates (31). Socioeconomic status influences cancer burden in four ways (31). A lower socioeconomic status increases exposure to cancer risk factors such as higher rates of smoking, heavy drinking, obesity, physical inactivity, and exposure to environmental carcinogens. Secondly it reduces the likelihood of cancer screening and early detection. Thirdly, lower socioeconomic status reduces the likelihood of timely treatment and finally lower

socioeconomic status is associated with less effective contextual support for the cancer patient.

2.7 Direct medical costs of treating breast cancer

Assessment of direct medical costs of breast cancer has been done in some other countries (29,30,31) but it is not always possible to compare the results of these studies because of varing methodologies used to calculate the cost of treatment, different perspectives and various socio-economic conditions. African studies on direct medical costs of cancer treatment are available

In Iran, the average cost of treating woman with breast cancer, regardless of the disease stage was USD 10,905.37 in 2010 (33). The results of this study also show that the direct treatment costs in the stages III and IV were significantly higher than treating the early stages. A study in Brazil in 2010, the direct costs of treatment for each patient for stages I-IV were USD 21658, 48295, 63,662 and 63,697 respectively (34).

Transtuzumab is used for targeted therapy for HER2 positive metastatic breast cancer, it is a significant cost component for a patient who receives it as part of endocrine therapy. Comparison of the price of Trastuzumab in different countries in the year 2014 is depicted in Table 2

Table 2 Comparison of the price of Trastuzumab in different countries

Country	Yearly Cost in USD	Equivalent in local currency
Kenya	16190	Ksh 1,700,000
France	39629	EUR 27,594
USA	70000	USD 70,000
Morocco	26280	MAD 204,000
United kingdom	41247	GBP 25,866

In another study in the US in 2004, the mean direct cost of treatment per patient was USD 35568 and the mean total direct cost per patient per month was USD 2896 (8). In a study in Sweden in 2005, the mean direct cost of treatment for patients in stage IV was 93700

Euros,(35) this was higher than this cost in Iran USD 8934. This difference was attributed to low-cost health services in Iran where oncologists did not prescribe expensive drugs.

The total direct medical cost for a 5-year treatment course for breast cancer in central Vietnam was estimated at USD 975 per patient with a range of USD 11.7–3,955. The initial treatment cost, particularly the cost of chemotherapy, accounted for the greatest proportion of total costs (64.9%). Among the patient characteristics studied, stage at diagnosis was significantly associated with higher total treatment costs (36).

Government sponsored health care systems may deny patients access to expensive medications, judging them cost-ineffective. In Kenya, a recently licensed, expensive anticancer agent bevacizumab is unlikely to be adopted by the National Hospital Insurance Fund. Very little has been done to develop evidence-based guidelines on cost-effective cancer treatment for use in poorly funded health care systems. The WHO established a database on the cost-effectiveness of more than 700 health-related interventions, using a standard measure, disability-adjusted life-years (DALYs). This enables the comparison of interventions within a particular field. For example, the cost for treating early-stage breast cancer is USD 78 per DALY with surgery and radiotherapy vs. USD 4,986 per DALY with systemic chemotherapy for metastatic disease (37).

CHAPTER 3: METHODOLOGY

3.1 Study Design

This was a hospital based retrospective cohort study that involved review of patient files who had surgery and had completed five to seven cycles of first line chemotherapy and all sessions of radiotherapy. This is equivalent to about six months of follow up.

3.2 Study Location

The study was carried out at Kenyatta National Hospital (KNH) in Nairobi Kenya. It is the largest teaching and referral hospital in East Africa and the main referral hospital in Kenya for treatment of breast cancer. About 4200 cancer patients are seen yearly of whom 22% have breast cancer.

3.3 Study population

The study population comprised BC patients registered in the oncology clinic and had received treatment at the KNH between 1st January 2010 to 31st December 2014. Patients who registered but had not completed treatment were excluded.

3.3.1 Time horizon

Treatment modalities do not run consecutively. Surgery is the first choice depending on staging of disease followed by radiotherapy and chemotherapy. Patients who completed five to seven cycles of first line chemotherapy which are three weeks each on average. This is equivalent to seven months of follow up.

3.3.2 Study perspective

The costs were considered from a patient's perspective.

3.4 Eligibility criteria

For patients to be considered eligible they must have undergone surgery; completed all cycles of radiotherapy; and had undergone 5- 7 first line Chemotherapy sessions depending on their regimen. Patients who did not meet all these criteria were considered ineligible.

3.5 Sample Size determination

Since the study was a one arm study with a continuous outcome, the following formula was used for sample size calculation

$$n = \left(\frac{Z\sigma}{E}\right)^2$$

Where;

n = Sample size

Z = 1.96 Standard normal deviation at required confidence level of 95%

Ϭ = The expected standard deviation of the outcome variable (24500)

E = The desired margin of error (5000)

The above formula gives a sample size of 93. Adjusting for expected proportion of files with incomplete data (estimated at 10%) yielded a final target sample size of 103 patients.

3.6 Sampling Procedure

A list of all patients with breast cancer who were seen between January 2010 and December 2014 was obtained from the oncology department. File numbers of every twentieth patient were listed on a separate sampling form (Appendix 1). A copy of the sampling form was made and used to retrieve patient files from the general medical records office. If it did not meet the criteria, the next patient file in the oncology department list was considered. A study number was assigned to each patient file. It shall be recorded on the data collection form.

3.7 Data Collection

Data was extracted from patients' medical records using a data collection form (appendix 3). It included demographic, diagnostic and treatment data. Costs for health services and products consumed by the patients were obtained from 2014-2015 year price listings in the respective hospital departments. The unit cost of surgery included the procedure, theatre consumables and hospitalization costs. It was obtained from the billing department for each identified patient.

3.8 Costing methodology

A micro-ingredient pricing approach was used. Only direct medical costs were considered. The direct medical costs of health-care services are the cost of services used in prevention, diagnosis, treatment and rehabilitation of illness or disorder in question; these include the cost of drugs, medical visits, hospitalization and diagnostic services. The direct medical cost was calculated for each patient's group separately based on their utilized services. Indirect cost such as loss in productivity, intangible costs and future costs were not considered.
Resources used by individual patients were determined and costs apportioned. Medication Costs, the Costs of surgery, radiotherapy, laboratory and diagnostic services and physicians' visits for each patient were calculated based on respective departmental price lists in 2015.

The costs were presented in Kenya shilling first before conversion into international dollars using purchasing power parity rates. The 2014 conversion rate of 40.43 Kenya shillings = 1 international dollars was used.

Figure 3 presents the steps followed in collection of cost data. The cost of medication was calculated for each patient according to the type of chemotherapy regimen, type of prescribed medication and supportive therapy, hormonal drugs and the cost of managing adverse reactions resulting from chemotherapy.

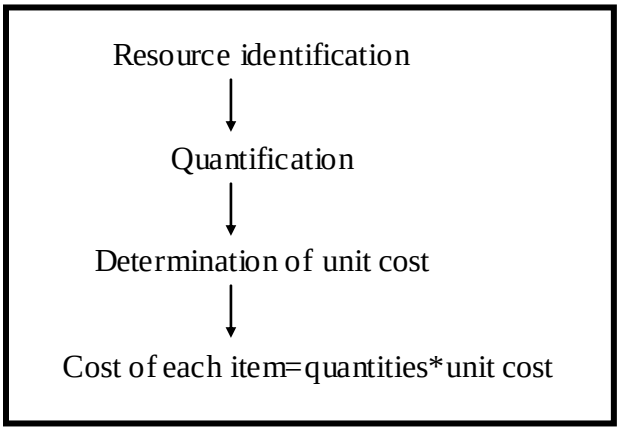


Figure 3 Steps followed in costing

Total direct medical cost were determined using the equation:

$$TC = \sum_{x=1} Q_x P_n$$

TC	denotes	Summation of all medical cost of treating a patient
Q	denotes	Units of product or service of a given product or service utilized by patient receiving treatment
P	denotes	Cost of the product or the service using the 2015 price list
n	denotes	Total number of products and services utilized by an individual patient

3.9 Data analysis

The Shapiro-Wilk test was performed to determine whether the continuous variables were normally distributed. Descriptive data analysis was then performed. Normally distributed continuous variables were summarized as the mean and standard deviation of the mean. Continuous variables that were not normally distributed were summarized as median, inter quartile range and range. Categorical variables were summarized as counts and percentages.

Exploratory data analysis was performed to determine if there were any significant correlations between continuous variables and associations between categorical variables.
Rank based Non parametric tests used were Wilcoxon Ranksum test for determination of associations between two groups and Kruskal-Wallis H test, to allow the comparison of more than two independent groups.

Linear regression analysis was performed to adjust for confounding and to identify the influence of social demographic factors and disease related characteristics and treatment modalities on total cost. Because the total cost had a large variance, it was log transformed and regressed against covariates with robust estimation of the parameters. The coefficient of determination was used to evaluate goodness of fit.

Bivariable regression analysis was first conducted to identify variables to be considered for multivariable analysis. Variables whose $P<0.1$ on bivariable analysis are considered for multivariable analysis. Multivariable analysis was carried out by forward stepwise building in order to obtain the parsimonious model. Analysis of data was done using STATA version 10 software. P-values less than or equal to 0.05 were considered statistically significant.

3.10 Quality assurance and Data Management

Pre-testing of the data collection tool was carried out before the study commenced at Kenyatta National Hospital oncology pharmacy. A sample of 10 patient files was used. Any errors noted were appropriately corrected. Data was collected and entered into the Microsoft Excel database on the same day, cleaned and stored safely with a password. A backup was performed every 5 days and a copy stored separately in an external hard drive.

3.11 Ethical Considerations

Permission to carry out the study was obtained from University of Nairobi/ Kenyatta National Hospital Research and Ethics Committee. The letter of approval to conduct the study ref KNH-ERC/A/187 is appended (Appendix 2). All the information obtained during the study was handled confidentially and only used for the intended purposes. The review of patient files was done within the oncology clinic and the general records office to ensure confidentiality and safety of the patient records. Only details relevant to the study were obtained from the patients' files. Any information that would be used to identify a patient including patient names was not recorded. Study number were used to identify patients and conceal their identity

CHAPTER 4: RESULTS

4.1 Baseline participant Socio-Demographic characteristics

A total of 93 files met the eligibility criteria. The baseline characteristics of the patients are depicted in Table 3. All the patients identified were female. The mean weight of the participants was 65.5 kg with a standard deviation of 14.6. The mean height was 157.9 cm with a standard deviation of 7.9.

The mean Body Mass Index (BMI) for the patients was 26.9 (5.6). Majority of the patients, 33 (35.5%) were overweight while 25 (26.5%) were obese. Those who had a normal BMI were 30 (32.3%) while a minority 5 (5.4%) patients were considered underweight as they had a BMI of less than 18.5

Most patients 68 (73.1%) were above 50 years of age. Those who were less than 40 years were 11(11.9%). Patients who were above 70 years accounted 17.2% of the patients studied. Over half of the women 66 (71.7%) had a parity of more than 3 children with 22 (23.9%) having more than five children each. Those with 2 children or less accounted for 28.3% of the participants

Most patients came from Nairobi and Central regions of Kenya 32 (34.4%). Patients from Rift Valley region were 19 (20.4%). The least number of patients 11(11.8%) were from Eastern and NorthEastern regions. The cumulative total from Coast, Nyanza and Western regions was 31 (33.4%) of the participants patients.

Table 3: Baseline socio-demographic characteristics of participants

Variable	Mean	Standard deviation
Weight (kg)	65.5	14.6
Height (m)	157.9	7.9
BMI	26.9	5.6
	n	**Percentage**
BMI group		
Underweight <18.5	5	5.4
Normal 18.5-24.9	30	32.3
Overweight 25-30	33	35.5
Obesity >30	25	26.9
Age group(years)		
20-30	2	2.2
31-40	9	9.7
41-50	14	15.1
51-60	19	20.4
61-70	33	35.5
>70	16	17.2
Parity		
0-2	26	28.3
3-5	44	47.8
>5	22	23.9
Region of Residence in Kenya		
Nairobi and Central	32	34.4
Coast	14	15.1
Nyanza and Western	17	18.3
Rift Valley	19	20.4
Eastern and Northeastern	11	11.8

BMI - Body Mass Index

4.2 Clinical presentation of Breast Cancer in the study participants

The largest proportion of patients, 81(91%), had stage III or IV disease at the time of diagnosis. Patient with Stage III comprised the majority 48 (51.6%). Those with stage I and II accounted for 9% as presented in Table 4.

Patients who tested positive for human epidermal growth factor receptor 2 (HER-2) comprised 33(66.3%) of patients. Estrogen receptor (ER) was detected in 20 (21.5%) of the patients. Progesterone receptor was detected in 34 (36.6%) patients.

The largest proportion of the patients had breast cancer affecting the left breast at the time of diagnosis 45 (48.9%) as compared to right breast alone 33 (35.9%) and those having bilateral breast cancer accounted for 13 (15.2%). Nine patients had bone metastasis. The majority, 84 (90.1%), did not have any metastasis of the tumor to bone.

Majority of patients 62 (66.7%) did not suffer from other co-morbidities during the treatement period. The most prevalent co-morbidity was hypertension which affectded 15% of the patients as presented in Table 4. The prevalence of Diabetes Mellitus, HIV and pyschiatric illnesses were 8.6 at 6.5 and 3.2% repectively.

Table 4 Clinical presentation of Beast Cancer in study participants

Variable	Frequency	Percentage
Tumor Stage		
I	1	1.1
II	7	7.5
III	48	51.6
IV	37	39.8
HER-2		
Positive	19	20.4
Estrogen receptor		
Positive	20	21.5
Progesterone receptor		
Positive	34	36.6
Breast affected		
Left	45	48.9
Right	33	35.9
Bilateral	13	15.2
Bone metastasis		
Present	9	13.1
Co-morbidities		
None	62	66.7
Diabetes	8	8.6
Hypertension	14	15.0
Psychiatric	3	3.2
HIV	6	6.5

HER-2 - human epidermal growth factor receptor 2

4.3 Methods used for diagnosis of breast cancer in the cohort

Abdominal pelvic ultrasound was conducted on 69, (74.1%),of the participants with a mean of two tests per patient. Mammography was conducted on 58.1% of the patients. Only 14, (15.1%) patients had an Electrocardiogram (ECG) done and 22 (23.7%) had a Radionuclide

Bone Scan performed. Sixty four patients had a chest X-ray done and 37 (39.8%) underwent a Computed tomography (CT) scan.

All the patients had a Full Blood Counts done. On average each patient had 7 tests done during the time span of the study. Urea, Electrolytes and Creatinine test was also done on all of the patients with each patient undergoing 6 tests on average as presented on Table 5.

Testing for the enzymes Aspartate Transaminase (AST) and Alanine Transaminase (ALT) was done in 90.3% of the patients with each undergoing 6 tests on average. Testing for serum calcium was done in less than 50% of the patients.

Table 5: Diagnostic Laboratory and Radiological tests conducted on Breast Cancer patients

Test	Number of patients	Percentage
Radiological procedures		
Abdominal Pelvic Ultrasound	69	74.1
Mammography	54	58.1
Electrocardiogram (ECG)	14	15.1
Radionuclide Bone Scan	22	23.7
Chest X-ray	64	68.8
CT scan	37	39.8
Routine biochemical parameters		
Full Blood Count	93	100
Urea, Electrolytes Creatinine	93	100
AST/ALT	84	90.3
Serum Calcium	36	38.7
CT scan	37	39.8

AST - Aspartate transaminase *ALT - alanine transaminase*

CT - Computed tomography

4.4 Treatment modalities stratified by stage of disease

Forty patients had a simple mastectomy. This was 43.0% of all patients and comprised all the patients with stage I and 32 (66.7%) of those with stage II disease. All 37 patients with stage IV breast cancer had a modified radical mastectomy while 30.1% of those with Stage III disease underwent this procedure. Above 50% of patients had a modified radical mastectomy done as indicated in Table 6.

All patients 93 (100%) received radiotherapy. The first line chemotherapy regimen Cyclophosphamide, Adriamycin, 5-fluorouracil (CAF), was the most commonly used chemotherapeutic regimen, with 42 (45.5%) of all patients receiving it. Majority of the patient with stage IV disease (86.7%) received the first line regimen. Cyclophosphamide, Methotrexate, 5-fluorouracil (CMF) was given to a third of the patients with 54.2% of those having stage III disease receiving it. Adriamycin and Cyclophosphamide followed by Docetaxel (AC-D) was the third first line chemotherapeutic regimen and less than a quarter of all patients 22 (23.7%) received it. The majority 6 (75%) of patients with stage I breast cancer received this regimen.

Table 6 Treatment modalities stratified by stage of disease

Treatment modality	Stage of disease [number (%)]			
	I and II	III	IV	Total
	n=8	n=48	n=37	n=93
Surgery				
Simple mastectomy	8 (100%)	32 (66.7%)	0 (0.0%)	40 (43.0%)
Modified Radical Mastectomy	0 (0.0%)	16 (30.1%)	37(100%)	53 (57.0%)
Radiotherapy	8(100%)	48 (100%)	37 (100%)	93 (100%)
Chemotherapy				
AC-T	6 (75%)	14 (29.3%)	1 (2.7%)	22 (23.7%)
CAF	2 (25%)	8 (16.7%)	32 (86.7%)	42 (45.2%)
CMF	0 (0.0%)	26 (54.2%)	3 (8.1%)	29 (31.2%)
Endocrine therapy				
Anastrazole	1(12.5%)	1 (12.5%)	0 (0.0%)	3 (3.3%)
Megesterol acetate	0 (0.0%)	2 (4.2%)	0 (0.0%)	2 (2.2%)
Tamoxifen	7 (87.5%)	40 (83.3)	14 (37.8%)	61 (64.5%)

AC-T Adriamycin and cyclophosphamide followed by a taxane(Docetaxel or paclitaxel

CAF: cyclophosphamide, Adriamycin, 5-fluorouracil

CMF: cyclophosphamide, methotrexate, 5-fluorouracil

4.5 Management of Adverse drug reactions of chemotherapy

More than half of the patients (66.7%) of the patients received the antiemetic ondasetron. Patients who received Granisetron were 12, (12.9%) as depicted in Table 7. Less than 50% of the patients received filgrastim for treatment of Neutropenia while 44.1% of the patients received recombinant erythropoietin for treatment of chemotherapy induced anemia. patients who received Beta lactams were 44, (47.3%). The least prescribed class of antibiotics were macrolides with (17.2%) of the patients receiving them. Majority of the patients 37 (39.8%) were on Non Steroidal Anti Inflammatory Drugs compared to those on Narcotic analgesics at (25.8%).

Table 7: Agents used in management of adverse drug reactions

Agents used	Frequency	Percentage
Antiemetics		
Ondansetron	62	66.7%
Granisetron	12	12.9%
	74	79.6%
Heamatinics		
Filgrastim	33	35.5%
Erythropoietin	41	44.1%
	74	79.6%
Antibiotics		
Beta lactams	44	47.3%
macrolides	16	17.2%
Fluoroquinolones	22	23.7%
	82	88.2%
Analgesics		
Narcotics	24	25.8%
NSAIDS[a]	37	39.8%
	61	65.6%

a - nonsteroidal anti inflammatory drugs

4.6 Unit costs of diagnostic tests

All costs were converted to international dollars, using the purchasing power parity for Kenya

against the United States dollar in 2014. Purchasing power parity conversion factor is the number of units of a country's currency required to buy the same amounts of goods and services in the domestic market as a U.S. dollar would buy in the United States. The 2014 conversion rate of 40.43 Kenya shillings = 1 international dollars was used.

The highest diagnostic cost was that of a determination of tumor markers. It cost 185.50 international dollars (int $) this is equivalent to keya shillings. The second highest diagnostic cost was a Radionuclide bone scan at int$ 148.40. Testing for serum calcium levels had the least cost of int $ 7.42. Biopsy for a large specimen was priced at int $ 49.2 while that of a small specimen was int $ 17.31. The cost of mammography, electrocardiogram and chest x-ray were similar at int $ 11.2 as presented in Table 8. On average, it cost a patient int$ 33.6 for routine full blood count and int $ 67.2 for Urea electrolytes and creatinine test during the treatment cycle.

Table 8: Costs of diagnostic tests

Test	Unit cost Ksh[a]	Unit cost Int$[b]	Average number of tests per patient	Total cost in Ksh[a]	Total cost in Int$[b]
Biopsy					
Large specimen	2000	49.47	1	2000	49.47
Small specimen	700	17.31	1	700	17.31
Tumor Markers	7500	185.50	1	7500	185.50
Full blood count	300	7.42	7	2100	51.94
Urea electrolytes & Creatinine	700	17.31	6	4200	103.88
AST/ALT	700	17.31	6	4200	103.88
Serum Calcium	100	2.47	3	300	7.42
Abdominal Pelvic Ultrasound	1800	44.52	1	1800	44.52
Mammography	700	17.31	1	700	17.32
Electrocardiogram	700	17.31	1	700	17.31
Radionuclide bone scan	6000	148.40	1	6000	148.40
Chest x-ray	700	17.31	1	700	17.31
CT scan	4000	98.94	1	4000	98.94

a-Ksh Kenya shilling b - Int$ - International Dollars

4.7 Cost of treatment modalities

Modified radical mastectomy had a higher average cost int$ 985.39 than simple mastectomy (int$ 1374.92). The average cost was obtained by identifying all component item costs including hospitalization after surgery and consumables. This is depicted in Table 9. The cost of surgery was the highest of all the treatment modalities.

The first line chemotherapeutic regimen Adriamycin and Cyclophosphamide followed by Docetaxel (AC-D) had the highest cost of int$ 498. It cost almost twice as much as the second regimen Cyclophosphamide, Adriamycin, 5-Fluorouracil (CAF) whose cost was int $ 433.34 and 6 times as much for the third regimen Cyclophosphamide, Methotrexate, 5-Fluorouracil (CMF) whose cost was int $ 135.42. The cost of Transtuzumab was int $ 54909.71. It was the highest cost of any individual drug or procedure. The monthly cost of Anastrazole was int $581.86. This is 13 times the cost of Tamoxifen and 5 times that of Megesterol acetate in endocrine therapy.

Table 9: Cost of treatment modalities

Item	Unit cost Ksh	Unit cost int$	Courses required	Total cost in Ksh	Total cost in Int$
Surgery					
Simple mastectomy	39836.25	985.39	1	39836.25	985.31[a]
Modified Radical Mastectomy	55588.13	1374.93	1	55588.13	1374.92 [a]
Radiotherapy	2000	49.47	4	8000	197.87
Chemotherapy					
AC-T	7790.84	192.70	4	31163.36	770.79[a]
CAF	2920	72.22	6	17520.00	433.34 [a]
CMF	912.50	22.57	6	5475.00	135.42 [a]
Endocrine therapy (monthly)					
Anastrazole	3918.75	96.93	6	23512.50	581.56
Megesterol acetate	800	19.78	6	4800.00	118.72
Tamoxifen	300	7.42	6	1800.00	44.52
Transtuzumab	185000	4575.81	12	2220000	54909.71

a – obtained after component cost analysis was done (appendix 4)

AC-T Adriamycin and cyclophosphamide followed by by a taxane (Docetaxel or paclitaxel)

CAF: cyclophosphamide, Adriamycin, 5-fluorouracil CMF: cyclophosphamide, methotrexate, 5-fluorouracil

4.8 The total cost of treatment

The total cost of treatment was the sum of individual costs for all services and health products. These are laboratory and radiological diagnostic tests, cost of surgery, chemotherapy and endocrine therapy and cost of treatment of adverse effects.

The median total cost of treatment for each patient incurred during was int$ 2658.92 and an inter- quartile range of [2022, 2834]. The total cost was not normally distributed but was slightly skewed to the right as presented in the histogram in Figure 3.

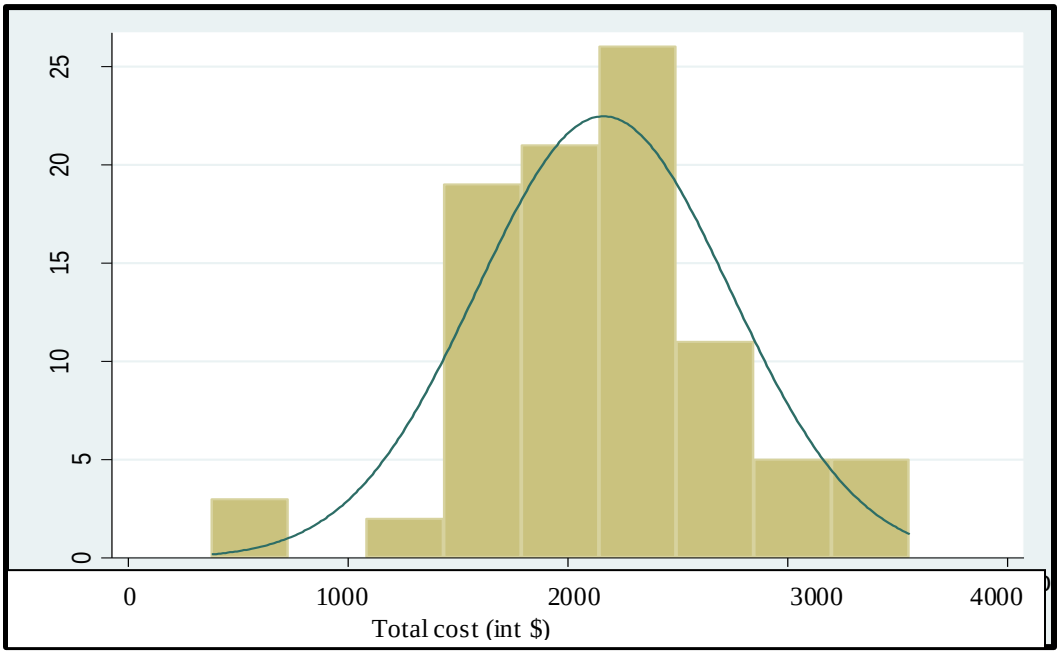


Figure 4: Histogram showing total Cost of treatment for Breast Cancer

4.9 Proportional contributions of cost categories to the Total Cost of Treatment

Surgical costs accounted for the largest proportion of the total costs incurred by the patients at 38.5%. This was followed by laboratory and radiological diagnostic procedures at 25.1%. These two costs collectively accounted for 63.6% of the total costs. Figure 5 depicts proportional contribution of cost categories to the total cost.

Medications accounted for less than 30% of the total cost. The smallest cost categories were radiotherapy and histology which together comprised 4.8% of the total cost. Of the drugs, chemotherapeutic agents were the most costly.

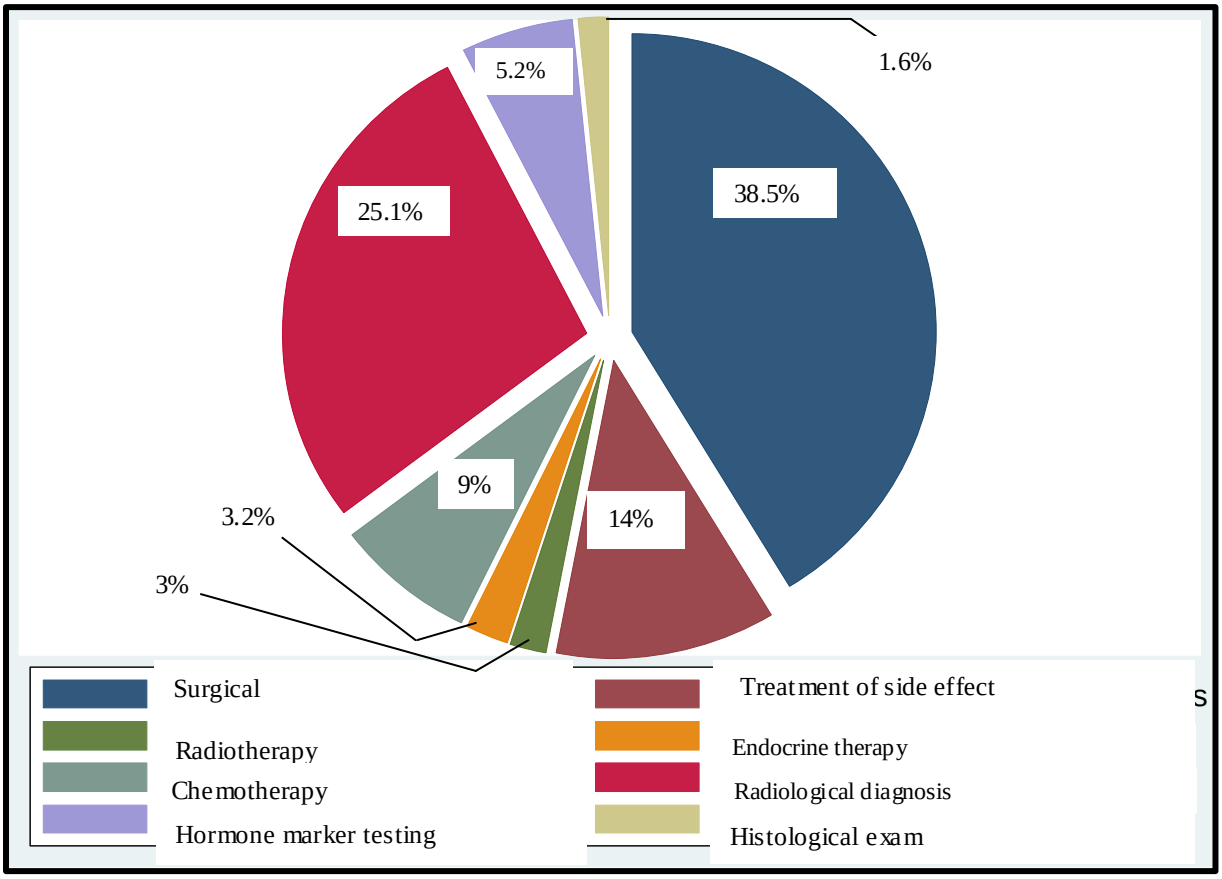


Figure 5: Proportional contributions of cost categories to the Total Cost of Treatment

4.10 Differences in Total cost incurred by Patients

There was a significant difference in Total costs incurred across categories of the Body Mass Index ($p = 0.029$). Similarly a significant difference was observed across the Stages of disease ($p = 0.046$). The difference in total cost was significant between presence and absence of metastasis ($p = 0.049$) as shown in Table 10.

There were no significant difference in the total costs incurred across the following categorical variable; parity ($p = 0.309$), menopausal status ($p = 0.114$), position of the breast affected ($p = 0.94$) and presence of co-morbidities ($p = 0.9$). Patients who had bone metastasis spend more money by about 208 international dollars. Obese patients incurred the greatest cost. As the disease progressed in stage, cost incurred by patients increased. Patients in stage IV spent about 300 international dollars more than patients in stage III disease. Patients without metastasis incurred lower total costs by about 210 international dollars.

Table 10 Differences in Total cost by Patients and Disease characteristics

Variable	n	Median cost (IQR) Int$			P value
BMI					
Underweight	5	2442.49	[2216.79,	2558.43]	
Normal	30	2773.31	[2334.28,	2811.95]	**0.029**[b]
Overweight	33	2864.51	[2589.35,	3108.76]	
Obesity	25	2869.15	[2679.01,	3204.61]	
Parity					
0-2	6	2496.59	[2210.61,	2912.44]	
3-5	25	2853.69	[2488.86,	3145.86]	0.305[b]
>5	4	2819.68	[2320.36,	2691.38]	
Menopausal status					
Pre-menopause	26	2470.31	[2195.15,	2912.44]	0.114[a]
Post-menopause	61	2768.67	[2768.67,	3145.86]	
Stage of disease					
I	1	2768.67	[2768.67,	3145.86]	
II	7	2130.22	[1327.91,	2553.79]	**0.046**[b]
III	44	2522.87	[2470.31,	3328.28]	
IV	37	2870.70	[2779.49,	3196.88]	
Breast affected					
Left	45	2691.38	[2230.75,	3057.75]	
Right	33	2663.55	[2250.80,	2937.17]	0.943[b]
Bilateral	13	2675.92	[2230.70,	2867.61]	
Co-morbidities					
Has Co-morbidities	31	2971.18	[2488.86,	3417.94]	**0.039**[a]
No Co-mobidities	62	2832.22	[2673.45,	3240.44]	
Side effects					
Experienced	91	2683.65	[2207.51,	3050.02]	0.90[a]
No side effects	1	2612.54	[2612.54,	2612.54]	
Bone metastasis					
Had metastasis	11	2963.45	[2768.6,	3396.30]	**0.049**[a]
No metastasis	73	2641.91	[2230.70,	3028.38]	

a - Wilcoxon Ranksum test b – Kruskal-Wallis H test

4.11 Differences in Total cost by Treatment Modalities

There were statistically significant differences in total cost incurred across all categories of treatment modalities as depicted in Table 11. Chemotherapy (p = 0.001), Surgery (p = 0.0004) and Endocrine therapy where p = 0.049. Anastrazole was the most costly type of endocrine therapy while the most costly first line chemotherapeutic regimen was Adriamycin and cyclophosphamide followed by a taxane (Docitaxel or paclitaxel).

Table 11 Differences in total cost by Treatment Modalities

Variable	N	Median cost (IQR) Int$			P value
Chemotherapy					
AC-T	22	2912.44	[2561.53,	3241.71]	**0.001**[b]
CAF	42	2776.40	[2655.82,	3023.74]	
CMF	29	2380.66	[2167.33,	2570.80]	
Surgery					
Simple	40	2369.84	[2171.96,	2804.23]	**0.0004**[b]
MRM[c]	53	2938.72	[2680.56,	3241.71]	
Endocrine therapy					
Anastrazole	3	2683.65	[2209.07,	3039.20]	**0.049**[b]
Megesterol acetate	2	2641.91	[2108.58,	3025.29]	
Tamoxifen	61	2456.41	[2141.05,	2890.80]	

a - Wilcoxon Ranksum test

b – Kruskal-Wallis H test

c - MRM modified radical mastectomy

AC-T Adriamycin and cyclophosphamide followed by a taxane (Docitaxel or paclitaxel)

CAF: cyclophosphamide, Adriamycin, 5-fluorouracil

CMF: cyclophosphamide, methotrexate, 5-fluorouracil

4.12 Bi-variable linear regression of individual variables against log Total Costs

The results of bivariable regression analysis are presented in Table 12. The total cost

incurred by individual patients was log transformed because it had a large variance. The variables that were statistically significant were stage of disease, chronic illness, cost of laboratory and radiological tests, radical Mastectomy, chemotherapy Regimen, cost of chemotherapy given and type of endocrine therapy.

Table 12: Relationship between total cost and individual variables

Variable	β coefficient (95% confidence interval)	P value	Adjusted R^2
Body mass index	0.14 (-0.15, 0.42)	0.35	1.3%
Parity	0.02 (-0.009, 0.047)	0.06	3.9%
Menopausal status	0.07 (-0.001, 0.16)	0.16	1.2%
County	0.002 (-0.002, 004)	0.31	2.0%
Breast affected	-0.01 (-0.07, 0.06)	0.86	0.04%
Stage of disease	0.08 (0.02, 0.14)	**0.01**	**5.9%**
ER positive	0.03 (-0.09, 0.16)	0.60	0.5%
PR positive	0.1 (-0.012, 0.219)	0.08	5.0%
HER-2 positive	0.015 (-0.08, 0.12)	0.78	0.13%
Chronic illnesses	0.04 (-0.00, 0.07)	**0.051**	**5.8%**
Bone metastasis	-0.10 (-0.2, 0.001)	0.053	2.6%
Cost of laboratory and radiological tests	0.00 (0.00, 0.00)	**0.00**	**5.3%**
Simple Mastectomy	0.00 (0.00, 0.00)	0.81	0.03%
Radical Mastectomy	0.00 (0.00, 0.00)	**0.00**	**2.4%**
Chemotherapy regimen	0.045 (0.02, 0.06)	**0.041**	**3.81%**
Cost of chemotherapy	0.0006 (0.0002, 0.0008)	**0.00**	**15.6%**
Type of Endocrine Therapy	0.065 (0.03, 0.076)	**0.00**	**3.3%**
Cost of Endocrine Therapy	0.00 (0.00, 0.0002)	**0.00**	**9.34%**
Cost of Radiotherapy	0.002 (0.001, 0.003)	0.51	0.01%
Cost of Treating Side effects	0.00 (0.00, 0.00)	0.83	0.01%

The cost of chemotherapy determined the largest amount of variation in the total cost incurred by the patient.

4.13 Parsimonious model for determination of the total cost function

The forward selection regression model building was used to fit a parsimonious model that explains variation in the dependent variable $\log_{10}$ (Total Cost) with independent variables identified. The total cost function obtained shown in equation 1.

Equation 1: Total cost function

$$\textbf{Log}_{10}\textbf{(Total Cost)} = \textbf{10.53} + (8*10^{-5})\textbf{A} + (5*10^{-5})\textbf{B} + (2*10^{-5})\textbf{C} + (6*10^{-5})\textbf{D} + (5*10^{-5})\textbf{E} + \varepsilon$$

Where:

A= Chemotherapy cost

B= Laboratory and Radiological Cost

C = Endocrine therapy Cost

D = Surgical cost

E = Costs of side effects management

ε = Error term

Exponentiation of the Y intercept (10.53) results to int$ 419. This implies that if all the above costs were equal to zero, the patient would still incur a cost equivalent to int$ 419. The inter patient variation in the total cost incurred by individual patients is best explained by the type of chemotherapy regimen they are treated with (15.6%) followed by the number of laboratories tests conducted

CHAPTER 5: DISCUSSION

Using oncology clinic records and general hospital records, we examined healthcare costs among patients with breast cancer treated in Kenyatta National Hospital. Most patients presented with Stage III and Stage IV disease at diagnosis. This observation is similar to a study which indicated that most patients seek medical help at a late state with advanced cancer (38).

We found that patients who started therapy at the advanced stage incurred more cost. The early and accurate diagnosis of breast cancer is important for optimizing treatment. The treatment of early breast cancer is more cost-effective and generally has superior outcomes, compared with the treatment of more advanced breast cancer. Due to the advanced stage of disease at presentation it was not possible to do breast conserving surgery. Early detection of breast cancer and initiation of treatment at has the potential of reducing costs incurred by the patients.

From this study the median total cost a patient incurred in 2015 for breast cancer treatment was 2658.92 international dollars with an inter quartile range of [2122.24, 2834.67]. The equivalent cost in Kenya shillings was shs 107500 with an inter quartile range of [85748, 114578]. These are the out-of-pocket fees and the perspective is that of the patient. It includes diagnostic cost, cost of surgery, first line chemotherapy, radiotherapy, endocrine therapy and treatment of chemotherapy side effects in an outpatient setup at Kenyatta National Hospital. There are no available comparative studies in Kenya and East African region. A study in United States estimated economic costs to patients with metastatic breast cancer; from diagnosis to death, to range from $41,590 to $82,973 (adjusted to 2005 US dollars). Treatment costs in Kenya is much lower than US costs. Expenditure in Kenya is subsidized. Caution should be exercised in comparing these findings with those reported by others, due to and differences in study populations and methods of estimating the economic costs

This cost is expected to increase yearly as adoption of new technology and treatment regimens continues. The most common mode of payment used by patients for outpatient services is out-of-pocket with few patients utilizing health insurance cover. Targeted endocrine therapy regimens still remain out of reach for majority of the patients. There is an opportunity for researchers, decision makers and policy makers to create sustainable financing for Breast cancer treatment.

More than 60% of the women were overweight or obese from this study. Obesity and reduced physical activity were observed to be risk factors for breast cancer (39) with the American cancer society recommending maintaining a healthy body weight as a strategy to reduce cancers in general (40). Obese patients incurred higher total treatment costs than those with a normal body mass index by 100 international dollars.

Menopausal status is important in planning and choice of endocrine therapy which subsequently contributes to total cost incurred by the patient. Most of the patients studied were above 61years (>50%). This is comparable to a similar studies (41) which indicate that menopause had a strong influence on the incidence of cancer. This study differs from one done in Congo (42) which reported the mean age at diagnosis for Congo women was 43.1 years. Patients over 61 years cannot be employed. This implies that many depend on relatives and savings for treatment. They therefore need NHIF and other mechanisms to fund treatment.

This study was reviewed using a patient's perspective with cost drivers presented in eight categories to yield a total cost for a duration lasting from diagnosis to completion of scheduled chemotherapy and radiotherapy sessions. A similar study (43) found that surgical costs were the highest of all treatment modalities. This was due to additional cost of hospitalization, consumables and nursing care post surgery.

The effect prescription of adjuvant chemotherapy to total cost was statistically significant. A similar study (43) indicated the significance of chemotherapy as a cost driver on total treatment cost. Chemotherapy was mostly administered in the outpatient setting and Costs obtained were those of the drugs. Additional consumables such as syringes and medical gloves were not considered as part of chemotherapy costs. Costs can be minimized by selection of chemotherapeutic agents that are cost effective or quality generics.

Presence of any type of co-mobiditites resulted in a increase in the median total cost incurred. The most common co-mobidity was hypertension. This is similar to a results from a study on co-mobidities prevalent in breast cancer patients (44) indicating hypertension being the most prevalent. Comorbidities may interact with the breast malignancy and its treatment. Breast Cancer treatment alternatives may be limited by the comorbidity resulting in less aggressive interventions at the outset.

The short-term side effects of chemotherapy usually include nausea, vomiting, stomatitis, and diarrhoea hair breast cancer loss, neutropaenia, myalgia, neuropathy, fatigue and myelosuppression in general. Management consisted mainly of use of filgrastim (colony stimulating factor), erythropoietin, antibiotics, anti-emetics, and the combined category of analgesics, and antidepressants. One study (46) estimated the additional hospital payments due to neutropenia associated with breast cancer chemotherapy at 8% of total cost. These are mostly administered in an outpatient setting. Ninety one percent of the patient had a chemotherapy related side effect. This is higher than a prior study (47) which indicated that 61% of patients receiving chemotherapy have one or more side effects which sometimes may necessitate hospitalization. Hospitalization results in additional cost to the patient. Managing adverse effects increased total cost by 14%. Dose reduction and selection of equivalent cost effective drugs for managing adverse effects would reduce the total cost

Surgery, diagnostic tests and chemotherapy accounted for a significant proportion of the total cost. Cost of surgery comprises additional costs of hospitalization. It agrees with studies that have revealed that hospitalization can account to as much as 32% to 52% of total costs in treatment of breast cancer (48).

Kenyatta National Hospital is owned by the Kenya government. It adopts a cost sharing approach of healthcare financing. A quarter of total spending on health care comes from out-of-pocket expenses (49). Only 20% of Kenyans have access to some sort of health insurance coverage with the majority being excluded from quality health care. The government pays salaries and subsidizes services thus offering financial protection to patients who can access services without the risk of a financial ruin. The price Trastuzumab, a targeted therapy for HER2 positive metastatic breast cancer, is 4565 international dollars (Ksh 185,000) per dose in a country where the 2014 Gross domestic product per capita according to the world bank was 2776.03 international dollars (50) equivalent to shs 111041.20. It is therefore beyond reach of majority of patients without health insurance in Kenya. In addition frequent breakdowns of radiotherapy machines due to aging increase the direct non- medical costs such as transport for the patients.

5.1 Study Limitations

This study relied on pre-recorded information on patient files. Incomplete patient records and missing files from the filing area was a limitation. Any shared overhead costs such as

consumables during chemotherapy radiotherapy and in performing diagnostic tests were ignored. Direct non-medical costs such as transport and food were not measured. The study had a short time horizon of 6 months. Lifetime costs were not considered.

5.2 Implications for policy

This study can be used to persuade policy makers provide more funding for management of breast cancer particularly for the elderly and very poor who do not have access to health insurance. A comprehensive study needs to be done on total cost from a healthcare provider's perspective and another on societal perspective in breast cancer treatment. In addition the economic analysis should involve considerations such as patient outcomes, quality of life, cost-effectiveness and cost-benefit and cost-utility so as to reduce the cost burden for patients.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The median cost of breast cancer treatment in 2015 at Kenyatta National Hospital is 2658.92 international dollars equivalent to Kenya shillings 107,500. This is ten times the country's minimum wage monthly wage level of shs 10954.80. Surgical procedures and laboratory investigations collectively are responsible for 60% of all the costs incurred by the patient. The choice of first line chemotherapeutic agents explains 15% of the cost variation. Patients start therapy when disease is advanced and this contributes to high cost of therapy.

6.2 Recommendations for policy and future research

We recommend adoption of health insurance for breast cancer outpatient services by the National Hospital Insurance Fund. This will increase uptake of hospital services from the very poor who default sometimes due to inability to afford fees charged.

Further research on acquisition costs of new treatment modalities should be undertaken. Life-time costs can be estimated using Markov modeling approaches

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APPENDICES

APPENDIX 1: DATA COLLECTION FORM

Study number: **Date filled:**

1. BIO – DATA

Date of first appointment: _____

Sex: ☐ Female ☐ Male

Weight ———————— height ———————— BMI ————————

Parity: _____

Menopausal status: ☐ Menopausal ☐ Premenopausal ☐Not specified

Age at diagnosis (years): _____

Highest Educational level attained

☐No formal schooling ☐primary ☐secondary ☐tertiary

Eligibility yes ☐ no☐

3. DISEASE AND DIAGNOSTIC INFORMATION

Breast affected: ☐ Left ☐ Right ☐ Bilateral

Histologic classification: ☐ Done ☐ Not done Cost.....

Stage of disease at diagnosis: ☐Stage I ☐Stage II ☐Stage III ☐StageIV

Hormone markers status: ☐ Done ☐ Not done Cost.....

Result

Oestrogen receptor (ER) ☐ Positive ☐ Negative

Progestogen receptor (PR) ☐ Positive ☐ Negative

Her2 neu expression: ☐ Done ☐ Not done Cost.....

Result: ☐ Positive ☐ Negative

Other Chronic illnesses: ☐ Diabetes ☐ Hypertension ☐ Asthma ☐None

☐ Other (Specify)……

Routine Laboratory and radiological tests and costs

Test	Cost/ test	No of tests done	Total cost
Lab tests			
Full blood count			
Serum creatinine			
enzymes SGOT			
Prothrombin time			
Others			
Radiological tests			
Xray			
Bone scan			
Ultrasound			
CT scans			
Others			

4. TREATMENT INFORMATION

☐ **Surgery**

Surgical procedure	Scheduled sessions	Cost per session	Total cost
lumpectomy			
Total mastectomy			
Skin sparing mastectomy			
Radical mastectomy			

☐ **Chemotherapy and endocrine therapy**

Drugs and drug Regimen used	Cost per regimen	Scheduled sessions	Associated costs(gloves syringes swabs etc)	Total cost
AC				
CAF				
CMF				
Other options				
transtuzumab				

rituximab				
tamoxifen				
anastrazole				
Megesterol acetate				
Goserelin				

☐ **Radiotherapy**

Dose selected (gray)	Scheduled sessions	Cost per session	Total cost
20-40			
40-60			
60-80			

Management of side effects of chemotherapy surgery and radiotherapy

Side effects	Medication used	Unit cost	Total units used	Total cost
Nausea and vomiting	Ondansetron Granisetron Other			
Neutropenia	Filgrasim Other			
Anemia	Erythropoietin Alfa Other			
Infections				

5. Physician review and Hospital Admission

Reviewed by consultant: ☐ Yes ☐ No

Nature of consultancy	**Number of times of consultation**	**Cost per consult**	**Overall cost**

Oncologist			
Surgeon			
Dermatologist			
Other			

Hospital admissions

	Duration of admission (days)	Bed charges per day	**Total charges**
Private wards			
Public wards			

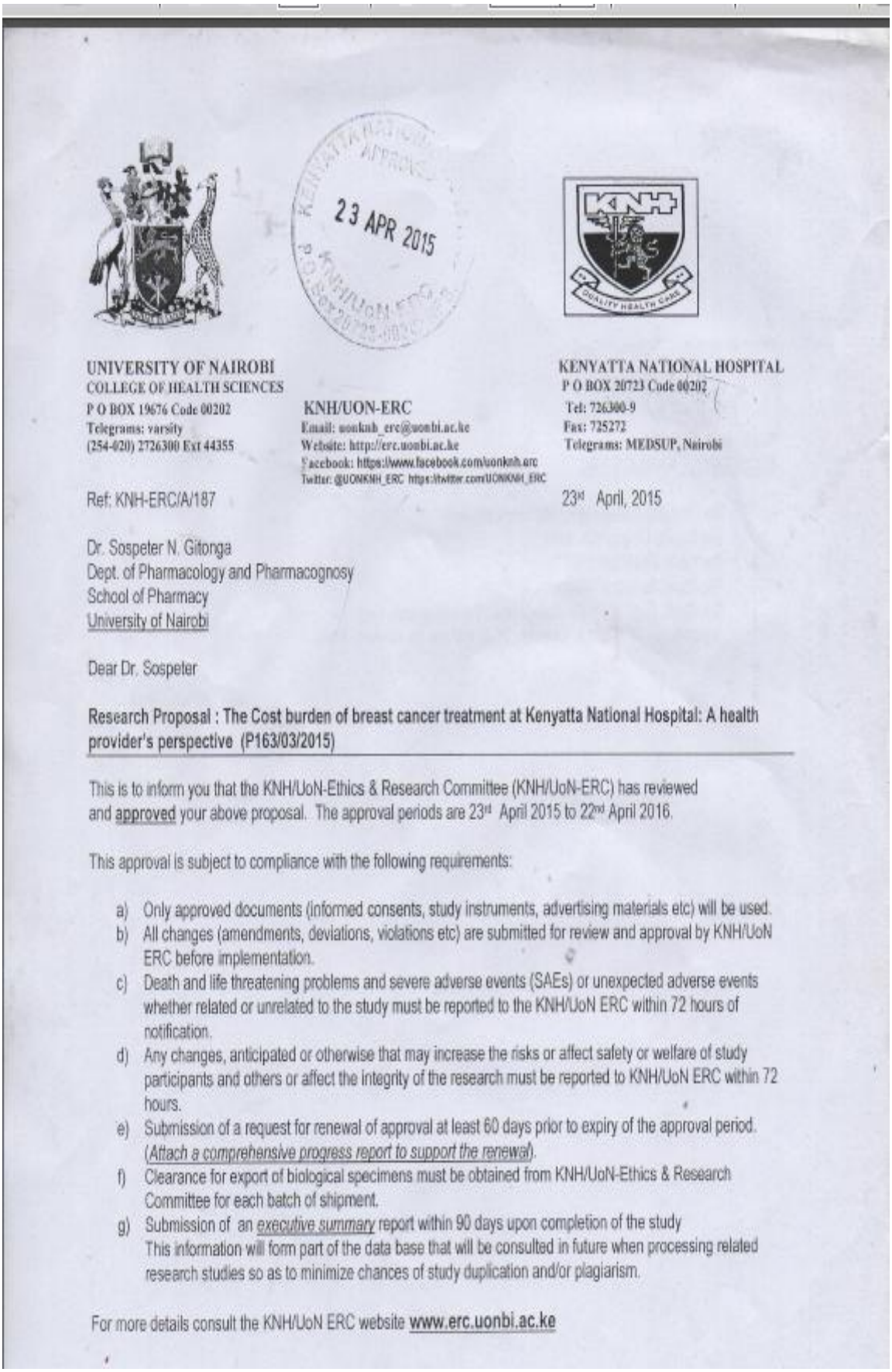
Outcome of breast cancer treatment at end of review period

☐ Remission

☐ Disease progression

☐ Other (Specify) …….. ……

APPENDIX 2: Ethical Approval



23 APR 2015

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23rd April, 2015

Dr. Sospeter N. Gitonga
Dept. of Pharmacology and Pharmacognosy
School of Pharmacy
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Dear Dr. Sospeter

Research Proposal : The Cost burden of breast cancer treatment at Kenyatta National Hospital: A health provider's perspective (P163/03/2015)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and approved your above proposal. The approval periods are 23rd April 2015 to 22nd April 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.erc.uonbi.ac.ke**

APPENDIX 3: Component cost of surgical procedure and chemotherapy

Surgical procedure

Description	Unit cost Int$
Admission procedure	2.24
Daily bed charges	8.96
Anaesthesia fees	56
General surgery fees	Varies depending on procedure but ranges from (196 to 280)
Nursing charge	Varies depending on bed days and procedure undertaken including IV drug administration, observation of vital signs etc
Theatre consumables	Varies depending on patient consumption
Pharmacy drugs	variable
Central sterile supply fees	16.8
Discharge procedure	2.24

Chemotherapy

First line Chemotherapy regimen	Cost of medication based on average Body surface area per session (int$)	Scheduled cycles	Total costs
Adriamycin and cyclophosphamide then Docetaxel (AC –D)	87.2	4	340
Cyclophosphamide, Adriamycin, 5-Fluorouracil, (CAF)	32.7	6	196.2
Cyclophosphamide, Methotrexate, and 5-Fluorouracil (CMF)	10.1	6	63.1