

**MODELLING THE EFFECTS OF MINDFULNESS BASED STRESS ON
BREAST CANCER SURVIVAL RATE AMONG WOMEN IN MERU AND
NYERI COUNTIES, KENYA, USING COX PROPORTIONAL HAZARD
MODEL**

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**A Thesis Submitted to the Graduate School in Partial Fulfilment of the
Requirements for the Award of the Degree of Master of Science in Applied
Statistics of Chuka University.**

CHUKA UNIVERSITY

SEPTEMBER, 2019

DECLARATION AND RECOMMENDATION

Declaration

This Thesis is my original work and has not been presented for the award of a degree or diploma in any other university or institution.

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Recommendation

This Thesis has been examined, passed and submitted with our approval as university supervisors.

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DEDICATION

This study is dedicated to my husband John Murianki, my parents Mr. and Mrs. Mutwiri and my son Jayden Zawadi who gave me the encouragement and motivation to press on.

ACKNOWLEDGEMENT

My sincere gratitude to God Almighty for giving me the grace, good health, ability and strength to accomplish this task. Am indebted to my supervisors Dr. Moses M. Muraya and Dr. Lucy Kawira Gitonga who accorded me professional assistance by their guidance, suggestions and critical insight.

My gratitude to the Chuka University for allowing me to undertake this project. Thanks to my classmates who walked with me all through in developing this project. My sincere gratitude to my family for their financial support, motivation and encouragement all through.

My gratitude goes to the hospital's nurse service managers for their assistance and links to the respective offices. The palliative care nurses and records officers at both Meru and Nyeri hospitals who accorded all the help I required. The medical practioners who filled the questionnaires and all the breast cancer survivors. I also appreciate anyone who assisted me in any way and by all means in the process of carrying out the study.

ABSTRACT

Breast cancer remains the most commonly diagnosed cancer among women, affecting 34 women per every 100,000. This has led to high number of fatalities annually, which need to be mitigated. The main interest among many cancer survivors and their families is establishing other conventional therapies they can engage in to improve their prognosis and survival. Among some of the key therapies is the interest in working on mindfulness-based stress (MBS) that patients undergo after diagnosis as complementary and alternate measures. Regardless of this, there is little that is known about the effects of MBS factors on breast cancer survival. Management of breast cancer can be enhanced through modelling the effects of MBS on breast cancer survival rate. However, there is limited information on accuracy of existing models. This study focused on developing a model to predict the effect MBS factors have on breast cancer survival rate among women in Meru and Nyeri Counties. Both Primary data and Secondary data were used. Primary data was obtained using a structured questionnaire from the breast cancer survivors and the medical practioners while secondary data was obtained from records at Meru teaching and referral hospital and Nyeri level five hospital on the MBS variables (cost burden of treatment, stress on diagnosis, prolonged time taken to access treatment, poor diet, alcohol use, physical activity and lack of awareness) among breast cancer patients for the period 2012 to 2017. Mixed method research design was used in the study. Both quantitative and qualitative data used in the study was analysed using R software. Cox proportional hazard model was used in establishing the survival rates, with the breast cancer survival rate being dependent variable while MBS factors were the independent variables. Kaplan-Meier estimators were used in determining the varying effects which the MBS factors have on survival rate. Log-rank test was used to perform comparisons of survival curves using hypothesis tests on the patients' survival rate considering age. The likelihood ratio test showed that MBS factors are significant in predicting hazard rates ($\chi^2 = 66.7$, $p = 0.0000119$). Treatment period was highly statistically significant ($p = 0.00014$) as compared to other covariates. Lack of awareness ($p = 0.0010124$), ease of coping with stress ($p = 0.000514$) and observing the right diet ($p = 0.04092$) were also found to significantly affect survival rate. Access of treatment immediately after diagnosis, availing the right information to the patients, helping patients to cope easily with stress and observing the right diet were found to be the best estimators in increasing breast cancer survival rate. The study therefore recommends use of the model in predicting breast cancer survival rates which can greatly improve breast cancer prognosis.

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LIST OF ABBREVIATIONS

BC	Breast Cancer
BCSR	Breast Cancer Survival Rate
KM	Kaplan-Meier
LRT	Log Rank Test
MBS	Mindfulness Based Stress
MBSR	Mindfulness Based Stress Reduction
PH	Proportional Hazard
RS	Relative Survival
UC	Uncensored
ECM	Extended Cox Model
PHM	Proportional Hazard Model

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Cancer remains the primary cause of mortality worldwide in countries of all income levels and is expected to continue growing precipitously as populations increase, age, and adopt lifestyle behaviors that are likely to increase cancer risk (Lindsey *et al.*, 2016). Cancer is expected to rapidly grow in low- and middle-income countries (LMIC) due to the economic changeover, which comprises greater mechanization of transport and labor, cultural shifts in the roles of women, and increased exposure and access to international markets (Lindsey *et al.*, 2016). Cancer continues to pose a great health care burden in the world with 60% of the world's new cases being diagnosed in developing countries (Ruff *et al.*, 2016). Cancer results from excessive cell growth (Nordqvist, 2018). Interventions for prevention and control are therefore urgently required. In Kenya, Cancer ranks third among the main causes of mortality and morbidity (Kenya Cancer Statistics and National Strategies (KCSNS), 2016). Cancer death rate has increased by 7% per year which is double the population growth rate of almost 3% annually, which is a great cause of alarm to the country (KCSNS, 2016). The annual estimate of new cancer cases in Kenya is 39,000 and more than 27,000 deaths with 60% comprising individuals who are younger than 70 years old (KCSNS, 2016).

Breast cancer remains the most common form of cancer among women worldwide and the second main cause of death in women, after lung cancer (Nordqvist, 2018). In the US female breast cancer is fairly common with new cases estimated at 252,710 and deaths at 40,610 in 2017 (Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review 2010-2014 cancer.gov). Nordqvist (2018) found out that the probability of any woman succumbing to breast cancer in the United State is around 1 in 37, which is 2.7 percent. Breast cancer and prostate cancer are classified as the leading types of cancers in Kenya with standardized incidence rate (SIR) of 40.6 and 51.7 per 100,000, respectively (Korir *et al.*, 2015). Female breast cancer is the most widespread among women in Meru County at 26% (Muchui, 2016). However, all is not lost since improvements in early screening and timely treatment have dramatically improved survival rates since 1989 (Nordqvist, 2018). Nordqvist (2018) observed that

there are approximately 3.1 million breast cancer survivors in the United States (U.S.).

Mindfulness-Based Stress is a condition experienced by person going through a difficult time, for example, through pain, illness and stress (WebMD, 2005-2017). Every breast cancer survivor battle with the disquiet of a cancer recurrence or developing a new cancer. This may cause anxiousness, lack of sleep and depression that may lead to high blood pressure or high blood sugar levels (Musiala *et al.*, 2011). Diagnosis of breast cancer is normally experienced as one of the difficulty situations which may result to a high level of emotional strain (Musiala *et al.*, 2011). To work on the 'existential plight' brought about by a cancer diagnosis therapeutic interventions should be employed including use of mind-body medicine (Musiala *et al.*, 2011).

Pain control measures, essential equipment, appropriate diet and assistance in upkeep are often not easily accessible and affordable, leading in considerable many unmet physical needs which increase the mindfulness based stress (Murray, 2003). Considering patients' experiences and provision of care in conflicting cultural settings can highlight gaps in framework of cancer care (Murray, 2003). In some parts of the counties patients will always try to conceal their ailment from their families to shield them from the financial burden involved in paying doctors consultations, hospital bills, and buying medicines. The community with its network of church volunteers and health can adequately care for the patients but lacks the right information and adequate resources (Murray, 2003). All these factors will always increase the MBS.

The purpose of many medical studies is prognostic factors of patients' survival time grounded on clinical categorisation (Chai *et al.*, 2015; Lo *et al.*, 2017). Regression models have been widely used in clinical studies and prognosis. Peretti *et al.*, (2016) used logistic regression model in breast cancer prediction and found the model to be very efficient. In the study, two versions were developed. The first version gave 85% of the right response while the second and the most optimized version gave 91% of the good responses. A conclusion was made that the two versions can open better scenario for future studies.

Survival data analysis may be considered to be application of parametric statistical methods, if distribution is known, or semi parametric methods, if distribution is unknown (George *et al.*, 2014). The Cox proportional hazard regression model is the most widely used semi parametric survival model in health sciences, because it depends on fewer postulations compared to other parametric models (Georgousopoulou *et al.*, 2015). The model was helpful in this study in eliminating variables which had little or no significant effect on survival rate and eventually end up with a survival rate model containing variables with significant effect on breast cancer survival rate (Smith, 2011).

A number of studies have indicated the beneficial association between stress reduction and quality of life associated with simultaneous improvement of the immune system following mindfulness-based stress reduction practice (Cecile *et al.*, 2009; Andrea *et al.*, 2015). Most studies done on mindfulness-based stress involved using randomized blocks, where breast cancer patients were distributed into different groups (blocks), different ways on how to work on MBS (treatments) were applied to different groups and studied over a period of time. A study on MBS reduction by evaluating the mindfulness and contemplation as mediators of change in depressive symptoms was done where changes in mindfulness and rumination were postulated to mediate the effect of Mindfulness Based Stress Reduction using randomization. However limited research has been done on developing models to determine cancer survival rate by considering Mindfulness Based Stress.

This study therefore aimed to work on breast cancer survival rate by developing a statistical model that will analyse the impact of mindfulness-Based stress on breast cancer survival rate. A statistical model is a way of approximating reality and optionally makes predictions from the approximation (George *et al.*, 2014). The MBS variables considered were: costly burden of treatment, stress on diagnosis, prolonged time taken to access treatment, poor diet, poor lifestyles, alcohol use, physical activity, other diseases such as diabetes and lack of awareness. The cox proportional hazard model was used to help determine the variables that have significant effect on breast cancer survival rate. The model is popular in survival analysis because it can be

estimated semi-parametrically (Bradburn *et al.*, 2003). It is also flexible in that it allows assumption of the baseline hazard function, and the coefficient estimates can be obtained through the partial likelihood function (Bradburn *et al.*, 2003).

1.2 Statement of the Problem

Breast cancer survival rate is very key to any one diagnosed with breast cancer. This is because survival of breast cancer patients can help to reconsider grounds for adjuvant treatment and give hope to breast cancer patients. Once diagnosed with breast cancer the patients will always be under one stressing factor or another ranging from costly burden of treatment, stress on diagnosis, prolonged time taken to access treatment, poor diet, poor lifestyles, alcohol use, physical activity, other diseases such as diabetes and lack of awareness on how to handle the disease. This means the patients can not only be helped by giving treatment alone and failing to work on such issues which can lead one to the grave in a single day as many cases have been reported in these counties. Working on the mindfulness based stress and helping the patient to accept their condition and be positive to help them fight the disease is the biggest challenge. Statistical modelling therefore becomes very key because they are capable of integrating biological knowledge in predicting the hazards rates. Cox Proportional hazard model was therefore found most reliable in estimating the hazard ratios and establishing the significant covariates that could increase breast cancer survival.

1.3 Objectives of the Study

1.3.1 General Objective

The general objective of this study was to develop a model that can be used to estimate female breast cancer survival rate by mitigating mindfulness-based stress among women in Meru and Nyeri Counties, Kenya.

1.3.2 Specific Objectives

- i. To establish onset of mindfulness-based stress following breast cancer diagnosis.
- ii. To develop a statistical model predicting breast cancer survival rate based on mindfulness-based stress

- iii. To determine the effects of mindfulness-based stress on breast cancer survival rates using Cox proportional hazard model.

1.4 Hypothesis

- i. H_{01} : There is no statistical significance between female breast cancer diagnosis and onset of mindfulness based stress
- ii. H_{02} : There is no statistical model for predicting breast cancer survival rate based on mindfulness-based stress
- iii. H_{03} : There is no statistical effect of mindfulness-based Stress on breast cancer survival rate using cox proportional hazard regression model.

1.5 Significance of the Study

Most residents are reluctant to go for early diagnosis and only attend health facilities when it is too late. This is mainly due to fear of the unknown where some fear to be told they have the disease, some collapse on receiving the news that they have the disease. This leads to diagnosis when the disease is at an advanced stage. This has led to an overwhelming number of patients seeking treatment at the Meru and Nyeri Referral facilities leading to longer waiting period before one is able to access the essential treatment. This causes a lot of stress to the patients who are in much pain, financial strain as they make several trips to the facility and fatigue increasing the MBS.

The study therefore becomes very key in encouraging the BC patients to strive in maintain healthy lifestyles as the model determine survival rates depending on how well one handles the mindfulness based stress factors. Most health facilities in Kenya do not concentrate on ascertaining the real causes of deaths among BC patients since it may be accelerated from the stress the patient may be going through apart from the effects of the disease itself. The major steps after unsurpassed treatment are palliative care services given to the patients. This study therefore concentrated on working on support that can be offered to the patients hence leading to reducing mortality rates. Once adopted can be useful by the medical practitioners in offering advice to the government on how to support the patients and also advice the patients to live right. The study objective is in line with the world Cancer Report which emphasize the need for early detection, treatment and palliative care. The report urges all the countries to

establish comprehensive national cancer control programs which should be aimed at reducing the prevalence of breast cancer and refining the eminence of life for cancer patients and their families.

CHAPTER TWO

LITERATURE REVIEW

2.1 Breast Cancer Incidence and Mortality

Breast Cancer is a major health burden in the society with high incidence and mortality rate and the prominent source of cancer-related deaths among females worldwide (Bozorgi *et al.*, 2016, Lindsey *et al.*, 2016). Globally, about 25% and 15% of all registered new cancer instances and cancer mortality rates registered among females were due to breast cancer (Azubuike 2018). United States registers the highest mortality rates which is prevalent among the Black women with the lowest rates registered among Korean women (Lindsey *et al.*, 2016). Patterns in the incidence and mortality from breast cancer are contributed by a variety of controls including screening systems some of which were employed in several European countries as early as the late 1980s (Botha *et al.*, 2013) Breast cancer ranks high among the common cancers affecting women with 571,000 deaths worldwide (Siegel *et al.*, 2017). Female breast cancer prevalence rates differ with different populations and ages with the highest rates in Western Europe and the United States and the lowest rates percentages experienced in Africa and Asia with an exception of Israel, which has among the highest rates (Lindsey *et al.*, 2016).

By the end of 2017, 1,688,780 new breast cancer cases and 600,920 cancer deaths were estimated to have occurred in the United States (US), where cancer incidence rate is 20% higher in women than in men. In 2017, the estimated number of new cases of female breast cancer was 252,710 while 40,610 patients were estimated to have succumbed to the disease (Siegel *et al.*, 2017). In 2018, the estimated mortality rates were 29 per 100,000 women in Washington, D.C., 22 per 100,000 women in Alabama and 20 per 100,000 women in California (Susan, 2018). In 2019, the estimate of new cases of invasive female breast cancer among U.S. women is 268,600 and an approximate 41,760 breast cancer deaths with California projected to have the highest number of breast cancers deaths at 4,560 (Susan, 2019).

The estimated new cases of cancer in Europe in 2018 were 3.9 million and 1.9 million deaths from cancer with the most common cancer sites being the female breast (523,000 cases), followed by colorectal (500,000), lung (470,000) and prostate cancer (450,000) (Ferlay *et al.*, 2018). Malvezzi *et al.* (2019) predicted cancer deaths in

Europe to about 1 410 000 for 2019, corresponding to age-standardized rates of 130.9/100 000 in men (5.9%) and 82.9 in women (3.6%). The projected mortality rate for breast cancer was at 13.4. Ferlay *et al.* (2018). noted that there was a decrease in breast cancer mortality with the largest decline in mortality noted among women in the age bracket of (50–69) by 16.4%), i.e. the age group covered by screening and was also seen in the age bracket of (20–49) at 13.8%). Malvezzi *et al.* (2019) further predicted cancer mortality to continue falling in both men and women with breast cancer rates expected to fall steadily This is mainly contributed by use of hormone replacement therapy improvements in screening, early diagnosis and treatment. However, owing to population ageing, the number of breast cancer deaths may not significantly decline (Malvezzi *et al.*, (2019).

The risk of breast cancer incidence has been found to be increasing with age, with the highest incidences registered among women in the age bracket of between 40 and 59 years (Salah *et al.*, 2010). Breast cancer ranks number one among cancers affecting Indian females with age adjusted rate as high as 25.8 per 100,000 with mortality rates at 12.7 per 100,000 women (Shreshtha *et al.*, 2018). During the period 2008-2012 India had a 11.54% increase in incidence and 13.82% upsurge in mortality rates due to breast cancer (Shreshtha *et al.*, 2018). This could likely be contributed by lack of enough breast cancer screening facilities, identification of the disease at an advanced stage and unavailability of appropriate medical facilities. In India, breast cancer mortality-to-incidence ratio is as high as 66% in rural registries whereas in urban registries it is as low as 8% with the young age being at a major risk factor for breast cancer in Indian women (Malvia *et al.*, 2018). Breast cancer prediction for India by 2020 is as high as 1797900 hence there is a dire need for established health awareness, accessibility of breast cancer screening systems and breast cancer management facilities to work on creating a positive and favorable clinical picture in the country (Malvia *et al.*, 2018).

Breast cancer remains the most common cancer affecting women in sub-Saharan Africa (SSA), with 94,000 new cases of breast cancer and 48,000 deaths due to breast cancer occurring in 2012 (McKenzie *et al.*, 2016). This burden was predicted to double between 2012 and 2030 due to population ageing and expansion (McKenzie *et*

al., 2016). Azubuike (2018) and Cumber *et al* (2017) observed that mortality statistics showed that Africa had the highest age-standardized mortality rate associated with breast cancer in the world. Azubuike (2018) also provided evidence showing relatively low breast cancer incidence in Africa has been rising over the years with several cases undetected, with southern African sub-region having the highest incidence rates and western Africa was found to have the highest burden of cancer on considering both the incidence and mortality rates. Davies *et al.* (2018) found out that breast cancer incidence in North Africa was higher at 29.3 per 100 000 (95% CI 20.0-38.7) as compared to the Sub-Saharan Africa (SSA) which was found to be at 22.4 per 100 000 (95% CI 17.2-28.0). Davies *et al.* (2018) further observed that in both North Africa and Sub-Saharan Africa registries, incidence rates increased considerably between 2000 and 2015.

Among the African countries, Kenya has been found to have the highest risk of breast cancer with breast cancer incidence and mortality rates increasing significantly since 1980s (Sawe *et al.*, 2016). Breast cancer is the leading type of cancer among women in Kenya at 23.3% of registered cancer instances (Ministry of Public Health and Sanitation & Ministry of Medical Services [MPHS & MMS], 2010). In Nairobi, Kenya 51.7 per 100,000 women are diagnosed of breast cancer annually (Korir *et al.*, 2015). The high number is largely contributed by the increasing habit of adopting a Western lifestyle, which includes; changes in foods consumed, delayed first childbirth, lower parity, and shorter periods of breastfeeding, which are contributors to a higher incidence of breast cancer among those regions (Franco & Rodriguez 2018). Breast cancer remains the highest cause of death among females in developing countries with Kenya not being an exceptional (Torre *et al.*, 2015). Patients present themselves for screening at late stages of the disease when little can be done since even the diagnosis and treatment amenities are limited (Kanyeria, 2017) Low awareness levels are greatly linked to the late presentation of cancer cases where curative treatment cannot reverse the situation (MPHS & MMS, 2010).

The growing breast cancer problem has disturbing severe consequences for women due to gender intolerance, stigma, cultural taboos as well as well-founded fears of abandonment (Ginsburg, 2013). Ginsburg (2013) observed that most breast cancer

patients face major obstacles in dealing with the cancer menace. This include accessing adequate healthcare infrastructure, lack of enough financial resources ,expertise needed for diagnosis and treatment and overcoming the social stigma associated with cancer among others which contributes to the mindfulness based stress.

2.2 Analysis of onset of Mindfulness-Based Stress following Breast Cancer Diagnosis

Being diagnosed of breast cancer remains one of the most stressing things a woman can accommodate (Wu *et al.*, 2019). Breast cancer diagnosis leads to high a degree of emotional strain, psychological and physical symptoms such as anxiety and depression, fear of recurrence, fatigue and sleep disturbance even to the point of traumatization (Frauke *et al.*, 2011; Diana, 2017). The patient gets a lot of worry due to the uncertain future, the uncertainty of the cancer prognosis and the expected financial difficulties (Frauke *et al.*, 2011). One may also be apprehensive about how they would look like after mastectomy, hair loss from chemotherapy, and possible skin changes-including darkening and thickening of one's skin-from radiation therapy (Komen, 2018). Al-Azri *et al.* (2014) observed that patients were also worried of the likelihood of their daughters getting the disease. Breast cancer can affect ones overall health by weakening the immune system and increasing the risk of getting sick with other infections (Standish *et al.*, 2008). It also raises the risk for depression and making unhealthy choices that can interfere with advanced breast cancer treatment (Diana, 2017). After breast cancer diagnosis, it's normal to feel a range of confusing emotions, ranging from despair to rage. For some, a serious mental health issue may develop even after the initial confusion and grief have dissipated. (Wu *et al.*, 2019). Breast cancer diagnosis therefore leads to mindfulness-based stress which need an urgent and timely response.

Managing advanced breast cancer and its treatment may be one of the most stressful experiences in life (Diana, 2017). Factors such as lack of adequate finances, family responsibilities, and work stress level bring a lot of pressure to the patients (Diana, 2017). Psychosomatic worry associated with breast cancer diagnosis can lead to an array of psychological experiences, varying from sorrow and hopelessness to disquiet and depression (Rachel *et al.*, 2012). Trauma may provoke a number of biological

changes which constitutes; endocrine responses, that is likely to increase angiogenesis, cell proliferation and migration; disruptions in circadian rhythms and secretion of stress-related hormones such as glucocorticoids and catechol amines; and immune function, resulting in decreased natural killer cell and cytotoxic T-cell activity and increased levels of circulating inflammatory cytokines (Rachel *et al.*, 2012). These biological responses are likely to increase the risk of chronic diseases with time and influence breast cancer mortality (Rachel *et al.*, 2012). Women who were able to receive cognitive behavioural stress management (CBSM) immediately after surgery for early-stage breast cancer reported improved quality of life and lower indications of depression for as long as 15 years after treatment (Anna, 2015). Antoni, 2018 observed that depressive signs during breast cancer management lead to greater chances of mortality within the successive 8 to 15 years. Anna 2015 found out that the CBSM measures impacted positively on long-term depressive signs which may have positive implications on survival (Anna, 2015).

Use of alcohol among breast cancer survivors is an increased risk to developing a breast cancer reappearance. For example, alcohol can increase the levels of oestrogens in the body, which might increase the risk for breast cancer recurrence (LoConte *et al.*, 2017). In people who have already been diagnosed with cancer, alcohol intake could also affect the risk of developing a new cancer (LoConte *et al.*, 2017). Diana (2017) established that breast cancer risk is “dose-dependent,” on alcohol meaning that the more one drinks, the more one exposes themselves to the risk. Diana (2017) established that taking a drink a day increases to 10 percent breast cancer risk. Excessive consumption of alcohol which is defined as greater than 2 U/day to 3 U/day (1 U equals a half-pint of beer [300mL], a glass of wine [100 mL], 1 shot of distilled spirits [25mL]), is likely to increase the danger of an osteoporotic fracture by up to 40% compared to those maintaining moderate or no alcohol intake (Fred, 2017). Too much alcohol intake leads to destruction of bone-forming cells and calcium metabolism. Alcohol intake associated with numerous nutritional insufficiencies, including vitamin D₃ deficiency, which may lead to increased secretion of parathyroid hormone, thereby increasing bone reabsorption, thus further weakening BMD (Fred, 2017). Reducing alcohol consumption therefore may be an important way many women can embrace in lowering the risk of breast cancer (Fred, 2017). American

Cancer Society (ACS) recommends to breast cancer patients going through active treatment to totally avoid alcohol since it can aggravate the side effects or adversely interfere with the drugs used in cancer treatment (Diana, 2017). Some studies have different findings on the effect of alcohol use on breast cancer survival. Gou *et al.*, (2013) found out that alcohol use was not associated with increased breast cancer mortality but with alcohol consumption higher than 20 grams per day.

The escalating breast cancer mortality in developing countries is largely contributed by the lack of awareness and early detection systems (Tazhibi & Feizi, 2014). Failure to comprehend by the patient the significance of taking medication aimed at controlling recurrence and mortality may lead to noncompliance (Jimmy and Jose 2011). This has largely been attributed to inadequate communication by health care practitioners regarding risk vs. benefit of the regimens (Jimmy and Jose 2011). Al-Azri *et al.* (2014) found out that some women with breast cancer are so desperate to get well that they agree to the advice of the people in the Omani community of using traditional medicine in the form of "Wasam" in hope of being cured. This form of management is associated with impediments including burns and infections affecting largely survival (Al-Azri *et al.*, 2014). Patients who may not understand the significance of taking their oral medications are likely not to adhere to the dosage. (Komen, 2016). Having the right information among individuals would lead to early detection enabling diagnosis at early stages, which would potentially improve the probability of survival and treatment with simpler and more cost effective treatment. It therefore becomes very key to develop public screening and educational programs through the health care system to help put more emphasis on early screening programs. As years of breast cancer management progress, overt symptoms of a malignancy or disease may not be clearly evident patients may therefore develop a sense of complacency thinking they are completely free from the disease resulting in further complications which would largely decrease the survival rates (Komen, 2016). Health care professionals working with breast cancer women should therefore educate and make sure the women are aware of the risks or complications that could result if the patients chose to skip, stop or seek traditional medicines (Al-Azri *et al.*, 2014).

The high cost of treatment and medications may largely contribute to noncompliance (Steven, 2016). Most of breast cancer patients experience financial challenges. Improvements in breast cancer management have greatly increased survival rates, but still many patients don't access these lifesaving therapies because of the financial hardships (Jennifer, 2018). The financial burden instigated by cancer treatment, upsets nearly half of cancer patients even among those with health insurance because of the financial restrictions and unreachability to the crucial facilities (Steven, 2016). Cancer care costs are higher for patients with adverse treatment effects, such as breast cancer-related lymphedema, and comorbidities. Patients with poor health care coverage or high co-payments may not be at a position to afford the costs of the vital oral agents over the required period. (Jennifer, 2018). Many patients are forced to file for bankruptcy due to the staggering cost of cancer care bringing about stress which may play a role in facilitating their untimely death (Steven, 2016). Most breast cancer patients end up receiving poor treatment because of the shortage of high-quality facilities due to lack of adequate financial resources especially in developing countries (Franco & Rodriguez, 2018). This makes it very urgent to come up with measures in developing countries that can be locally modified to create public policy programs directed at improving breast cancer medical attention with an intention of reducing mortality rates (Franco & Rodriguez, 2018).

The period between disease identification and beginning of treatment is defined as time between date of pathological diagnosis and start of treatment (Yoo *et al.*, 2016). Receiving treatment at an opportune time decreases the danger of the cancer spreading to other parts and increases the chances of breast cancer survival rate (Morante *et al.*, 2018). According to Yoo *et al.*, (2016), an interval of 60 days between diagnosis and beginning of treatment or shorter period does not adversely affect disease-free survival (DFS) in breast cancer. This means that one can take a period of less than 60 days when preparing about seeking the treatment immediately after diagnosis. Delay in cancer identification may originate from either the patient or health provider while delay in treatment is commonly connected to the health system. This is common in developing countries which have limited number of cancer centres, challenges in getting health covers, lower socioeconomic status of patients and long postponements of surgery and adjuvant therapy (Samur *et al.*, 2002). Survival can

significantly be influenced by sticking to a shorter period between biopsy to surgery and from surgery to adjuvant chemotherapy (Samur *et al.*, 2002). However, Richards *et al.* (1999) argued that within individual stages, longer delay had no adverse impact on survival.

Physical exercise is a very important therapy to breast cancer survivors particularly when combined with the appropriate diet (Hannah *et al.*, 2015). Consistent exercise coupled with taking at least five portions of vegetables and fruits per day have been found to decrease breast cancer reappearance risk thus improving survival (Hannah *et al.*, 2015). A sedentary lifestyle leads to obesity consequently increasing physical activity may help decrease a patient's Body Mass Index (Nelson *et al.*, 2014). Therefore, breast cancer patients should be encouraged to engage in physical exercises since an increased body mass index is linked to larger size tumours which is likely to lead to breast cancer advancement and mortality (Sun *et al.*, 2018). Kaufman *et al.* (2017) established that regular exercise does not only decrease the BMI but it also decreases the danger of developing Breast cancer-related lymphedema (BCRL). This is a chronic, adverse, and much feared complication of breast cancer treatment, which affects approximately 20% of patients following breast cancer treatment (Sun *et al.*, 2018). Physical exercise has significant beneficial influence in cancer rehabilitation and has been found to increase the overall survival especially when combined with high vegetable and fruit consumption (Hannah *et al.*, 2015). Hypertension is a potential risk factor for BCRL which can be rehabilitated by an effective nutrition and exercise program. Obesity and hypertensive states are potential risks of cardiovascular diseases. During adjuvant chemotherapy and follow-up care for breast cancer patients, both high and moderate-intensity exercise programs are secure and valuable (Wengstrom *et al.*, 2017). Kathryn and Rebecca (2010) established that engaging in physical exercise among breast cancer survivors was significantly associated with decreased mortality, increased biological functions, and changes in metabolic biomarkers. It is a reasonable intervention towards decreasing insulin and leptin levels in the breast cancer patients' bodies by increasing the physical activity and decreasing body fat aimed at potentially influencing breast cancer prognosis.

Failure to observe the right diet among the breast cancer patients may lead to poor survival. This is because different foods contain an exceptionally composite combination of critical nutrients and other mixtures that could impact breast cancer danger and recurrence (Holmes & Willett, 2004). Foods and its constituents play a major role in the nourishing and health condition of breast cancer patients (Wengstrom *et al.*, 2017). Schwedhelm *et al.* (2016) stated that a good diet should compose of high intake of fruit, vegetables and whole grains but low in red and processed meat, refined grains, and high-fat foods can be appropriate for a breast cancer patient. An altered nutritional status in breast cancer patients could increase the risk of postoperative complications and mortality (Holmes & Willett, 2004). It is therefore necessary for the health care professionals to follow up their patient's diet patterns (Wengstrom *et al.*, 2017). Schwedhelm *et al.* (2016) pointed out that the current dietary advice for cancer survivors is to receive personalized nutritional care from a trained professional and to follow current recommendations for breast cancer survival. This is because adherence to a healthy dietary pattern is inversely associated with overall mortality (Schwedhelm *et al.*, 2016).

2.3 Overview of Mindfulness Based Stress Reduction Measures on Breast Cancer Patients Well being

Several studies have been done on Mindfulness Based Stress reduction measures by using different modelling techniques depending on the objectives of the study. Ledesma *et al.* (2009) carried a systematic review using Cohen's *d* as measure of effect on immediate post-intervention data (6–15 weeks); Results showed Mindfulness Based Stress Reduction showed an effect on patient's mental health (Cohen's *d* = 0.48) and less convincing effects on patient's physical health (Cohen's *d* = 0.18). It was therefore noted that patients' mental and physical health improved when patients were engaged in stress reduction activities.

Shennan *et al.* (2010) carried quantitative and qualitative studies (January 2007 to September 2009) with mindfulness intervention as the core part of the intervention and improvement of anxiety, depression, stress levels, sexual problems, physiological arousal, immune function, as well as other subjectively perceived benefits where most study participants were female. Shennan *et al.* (2010) observed that mindfulness interventions seemed to provide a useful tool in the treatment of cancer patients He

therefore advocated for longer follow-ups, as well as qualitative studies in order to increase the understanding of the mediators of effect.

Frauke *et al.* (2011) studied a structured Mindfulness Based Stress Reduction programme of at least 6 weeks duration, to involve cancer patients, and to report at least 1 quantitative standardized outcome measure related to Quality of life, mood, or distress. Frauke *et al.* (2011) found out that mindfulness based stress reduction measures improved mood and distress in cancer patient.

Sahar *et al.* (2014) found out that Logo therapy was effective on reducing anxiety level in women with breast cancer among Iranian women. Sahar *et al.* (2014) further concluded that an explanation of comprehensive approaches in the treatment and management of cancer symptoms, would be an important step in improving psychological components in the lives of breast cancer patients.

Richard *et al.* (2017) did a study to identify symptom clusters among post-treatment breast cancer patients and determine symptom cluster improvement following the Mindfulness-Based Stress Reduction for Breast Cancer program. He found out that four symptom clusters emerged at baseline: pain, psychological, fatigue, and cognitive. From baseline to six weeks, the study demonstrated evidence of Mindfulness based stress reduction measures effectiveness in both the psychological (anxiety, depression, perceived stress and Quality of Life (QOL), emotional well-being) ($P < 0.007$) and fatigue (fatigue, sleep, and drowsiness) ($P < 0.001$) clusters.

2.4 Breast Cancer Survival Rate

Survival rate is defined as the per cent of people who survive a disease such as cancer for a specified amount of time after diagnosis (Lynne, 2018). Breast cancer survival rate is very important because it helps doctors to advice the patients on prognosis (Lynne, 2018) Survival depends on mortality. An assumption is made that at the beginning there is 100 percent of the people in the group and computed as shown according to Susan, 2018) $100 \text{ percent} - \text{mortality rate} = \text{survival rate}$. Breast cancer survival rates are computed in 5-year period as shown in the Table 1

Table 1: Year Breast Cancer survival rates

Breast Cancer Stage	5-Year Survival rate
0	100%
I	100%
II	93%
III	72%
IV	22%

2.5 Survival Analysis

Survival analysis involves the consideration of the time between a fixed starting point (e.g. diagnosis of cancer) and a terminating event (e.g. death) (Bradburn *et al.*, 2003)

Survival Analysis relies on the Survival Function $S(t)$.

Survivor function is computed as follows according to Xie & Liu (2005);

$$S(t) = P[T > t] \dots\dots\dots (1)$$

where T is the elapsed time until the occurrence of a specified event and t is the failure time.

Assuming that T is a continuous random variable with probability density function $f(t)$ and cumulative distribution function $F(t) = \Pr \{T \leq t\}$ giving the probability that the event has occurred by duration t .

$$f(t) = \lim_{\Delta t \rightarrow 0} \frac{p(t \leq T < t + \Delta t)}{\Delta t} \dots\dots\dots (2)$$

The Hazard function $h(t)$ is used to measure the failure rate for very small intervals (or continuous) time. This provides a crucial link between survival analysis and proportional Hazard models in assessing the instantaneous risk of demise at time t , conditional on survival to that time:

$$h(t) = \lim_{\Delta t \rightarrow 0} \frac{[p(t \leq T < t + \Delta t) / T \geq t]}{\Delta t} \dots\dots\dots (3)$$

Equation (3) shows the probability that a unit which survives to t will succumb to the event in the next instant.

In terms of the survival function:

$$\begin{aligned}
 h(t) &= \frac{f(t)}{s(t)} \dots\dots\dots(4) \\
 &= -\frac{d}{dt} \ln S(t) \\
 &= \text{how many (in \%) die at time } t
 \end{aligned}$$

There are three non-parametric methods for describing time to event data, which are:

- a) the Kaplan-Meier method
- b) the Life table method
- c) the Nelson-Aalen method

a) The Kaplan-Meier method

Kaplan-Meier were used in plotting survival curves for different patient groups (Bradburn *et al.*, 2003).

Kaplan-Meier estimator of survival at time t is shown as according to

$$\begin{aligned}
 S(t_i) &= \prod_{0 \leq j \leq n} Pr(T > t_i / T \geq t_i) \dots\dots\dots(5) \\
 &= S_{t_{j-1}} Pr(T > t_j / T \geq t_j) \\
 &= S_{t_{j-1}} \frac{n_j - m_j}{n_j} \text{ for } 0 \leq t \leq T
 \end{aligned}$$

here $j = 1, 2, \dots, n$ is the total set of failure times recorded, T is the failure time with distribution F and density f , m_j is the number of failures at time t_j and n_j is the number of individuals at risk at time t_j . Kaplan-Meier estimate was used to come up with survival curves in the study.

The general KM-formula according to Linda and Alexandros (2011) for plotting the K-M curves is as follows;

$$\hat{s}(t_{(j)}) = \prod_{i=1}^j \hat{p}r(T > t_{(i)} / T \geq t_{(i)}) = \hat{s}(t_{(j-1)}) \cdot \hat{p}r(T > t_{(j)} \mid T \geq t_{(j)}) \dots \dots \dots (6)$$

In the case of no censoring this reduces to

$$\hat{s}(t_{(j)}) = \frac{\text{surviving past } t_j}{\text{total number of people at the beginning}} = \frac{R(t_{(j+1)})}{R(t(0))} \dots \dots \dots (7)$$

b) Life Table Method

The life table method (the actuarial or Cutler Ederer method) is an approximation of the Kaplan-Meier method. It is based on grouped survival times and is suitable for large data sets (Hoem, 2001). This method also assumes that the rate of failure within an interval is the same for all subjects and is independent of the probability of survival at other time periods.

c) Nelson-Aalen Estimators

The Nelson - Aalen estimator can be used to provide a non-parametric estimate of the cumulative hazard rate function (Enrico *et al.*, 2002) Instantaneous hazard is defined as the proportion of the population present at time t that fail per unit time. The relationship between cumulative hazard and survival is as follows:

$$H(t) = -\ln[S(t)]$$

or

$$S(t) = e^{-H(t)} \dots \dots \dots (8)$$

The Nelson-Aalen estimator for the cumulative hazard rate function at time t is defined as follows according to (Enrico *et al.*, 2002):

$$\hat{A}(t) = \sum_{j:t_j \leq t} d_j / r_j, \dots \dots \dots (9)$$

Where r_j is the number of individuals at risk just prior to time t_j and d_j is the number of individuals who die at t_j .

This expression helps in estimating the hazard at each distinct time of death t_j as the ratio of the number of deaths to the number exposed. The cumulative hazard up to time t is simply the sum of the hazards at all death times up to t , and has a nice interpretation as the expected number of deaths in $(0; t]$ per unit at risk. This estimator has a strong justification in terms of the theory of counting processes.

Cox proportional hazard model was used to analyse effects of the stated independent variables on MBS (covariates) on patient's survival rate (Laura & Joanna, 2007). Since every independent variable had its own coefficients, they were varied to test their effect on the survival rate.

2.5.1 Log-Rank Test

The log rank test is used to test the null hypothesis that there is no difference between the populations in the probability of an event (here a death) at any time point. The analysis is based on the times of events (here deaths) (Martin & Douglas, 2004). The goal of using LRT is to find an expression from which we know the distribution (or at least approximately) under the null hypothesis. Test statistics is computed as follows according to Linda and Alexandros (2011);

$$\frac{(\sum O - \sum E)^2}{\sum E^2} \dots\dots\dots (10)$$

where O = Observed total failures
 E = expected failures

The log rank test is based on the same assumptions as the Kaplan Meier survival curve namely, that censoring is unrelated to prognosis, the survival probabilities are the same for subjects recruited early and late in the study, and the events happened at the times specified. Deviations from these assumptions matter most if they are satisfied differently in the groups being compared, for example if censoring is more likely in one group than another.

The log rank test is most likely to detect a difference between groups when the risk of an event is consistently greater for one group than another. It is unlikely to detect a

difference when survival curves cross, as can happen when comparing a medical with a surgical intervention. When analysing survival data, the survival curves should always be plotted. Because the log rank test is purely a test of significance it cannot provide an estimate of the size of the difference between the groups or a confidence interval.

2.6 Overview of the Proportional Hazard Model

The purpose of the model is to evaluate simultaneously the effect of several factors on survival. The proportional hazard model is given by according to (Laura and Joanna, 2007)

$$h(t/X) = h_0(t) \exp(X_1 \beta_1 + \dots + X_p \beta_p) \dots \dots \dots (11)$$

The predictors (covariates), X_1, \dots, X_p are assumed to act additively on $\log h(t|x)$

In the study the covariates were; treatment period, alcohol use, costly burden of treatment, stress on diagnosis, awareness and physical exercise.

$\log h(t/X)$ changes linearly with β_s

The effect of the predictors is the same at all times t .

The hazard function, which is denoted by $h(t)$, represents the instantaneous failure rate given that an individual has survived up to time t ; this can be written as:

$$h(t) = \lim_{\Delta t \rightarrow 0} \frac{p(t \leq T < t + \Delta t | T \geq t)}{\Delta t} \dots \dots \dots (12)$$

where Δt denotes an interval of time.

The hazard ratio for a subject with a set of predictors X^* compared to a subject with a set of predictors X is

$$hr(X^* : X) = \frac{\exp(X^* \beta)}{\exp(X \beta)} = \exp \{ (X^* - X) \beta \} \dots\dots\dots (13)$$

The point estimate for the hazard ratio is;

$$\widehat{hr}(X^* : X) = \frac{\exp(X^* \widehat{\beta})}{\exp(X \widehat{\beta})} = \exp \{ (X^* - X) \widehat{\beta} \} \dots\dots\dots (14)$$

Where $\widehat{\beta}$ is the maximum likelihood estimate of β .

The survival function, denoted as $S(t)$, is used to describe the probability that a person can survive longer than the specified time t . Theoretically, as time changes from 0 to infinity, the survival probability decreases from 1 to 0. The relationship between the survival function and the hazard function is expressed as:

$$S(t) = \exp \left[-\int_0^t h(u) du \right] \dots\dots\dots (15)$$

$$h(t) = \frac{dS(t)/dt}{S(t)}$$

= how many (in %) die at time t

This can be interpreted by considering an individual alive at time t . The chances of dying in a small interval $[t, t + \Delta t)$ are then given by:

$$q_t = \frac{S(t) - S(t + \Delta t)}{S(t)} \approx h(t) \Delta t \dots\dots\dots (16)$$

This can be alternatively written as;

$$h(t) = \frac{\text{No of deaths in } [t; t + \Delta t)}{\text{No of person-years at risk in } [t; t + \Delta t)} \dots\dots\dots (17)$$

$H(t) = \int_0^t h(u) du$ denotes the cumulative hazard risk.

The modelling of survival data usually employs a hazard function or the log-hazard. Assuming a constant hazard, $h(t) = \vartheta$ which implies an exponential distribution of survival times, with density function $p(t) = \vartheta e^{-\vartheta t}$

2.6.1 Cox Proportional Hazard Model Estimation

One of the reasons the proportional model is popular in literature is because it can be estimated semi-parametrically (Bradburn *et al.*, 2003). Parameter estimates in the Cox Proportional Hazard model are obtained by maximizing the partial likelihood.

Assume the observation for the i^{th} subject is denoted as

(x_{i1}, \dots) . Consider the conditional probability that an individual dies at time t_j given that t_j is one of the k observed death times $\{t_1, t_2, \dots, t_k\}$. Individuals are assumed to respond independently as shown below:

$$\frac{P(\text{individual with values } x_{(j)} \text{ dies at } t_{(j)})}{\sum_{k \in R} P(\text{individual } k \text{ dies at } t_{(j)})} \dots \dots \dots (18)$$

Since the baseline hazard has an arbitrary form, intervals between successive deaths times provide no information about the effects of covariates on the hazard function.

On replacing the probability of death at time t_j with probability of death in the interval, $[t_{(j)}, t_{(j)} + \Delta)$

$$\frac{\frac{P(\text{individual with values } x_{(j)} \text{ dies at } [t_{(j)}, t_{(j)} + \Delta])}{\Delta}}{\frac{\sum_{k \in R} P(\text{individual } k \text{ dies at } [t_{(j)}, t_{(j)} + \Delta])}{\Delta}} \dots \dots \dots (19)$$

Contribution to the likelihood is;

$$\frac{h_j t_{(j)}}{\sum_{k \in R} h_k t_{(j)}} = \frac{h_0 t_{(j)} \exp x_{j\beta}^T}{\sum_{k \in R} t_{(j)} h_0 t_{(j)} \exp x_k^T} \dots \dots \dots (20)$$

On cancelling the baseline function equation 18 reduces to;

$$= \frac{\exp x_{j\beta}^T}{\sum_{k \in R} t_{(j)} \exp x_k^T} \dots \dots \dots (21)$$

The joint partial likelihood is

$$l_p(\beta) = \prod_{j=1}^n \left[\frac{\exp x_{j\beta}^T}{\sum_{k \in R} t_{(j)} \exp x_k^T} \right] \delta_j \dots \dots \dots (22)$$

Where δ_j is the censoring indicator, with 1 as event and 0 as censoring.

The partial likelihood for the uncensored is given by:

$$L(\beta) = \prod_{Y_i UC} \frac{\exp(X_i \beta)}{\sum_{Y_j \geq Y_i} \exp X_j \beta} \dots \dots \dots (23)$$

Log partial likelihood is given by

$$l(\beta) = \text{Log } L(\beta) = \sum_{Y_i UC} \{ X_i \beta - \log [\sum_{Y_j \geq Y_i} \exp X_j \beta] \} \dots \dots \dots (24)$$

The joint likelihood is;

$$\prod_{i=1}^n [f_i(t_{(i)})]^{\delta_i} [S_i(t_{(i)})]^{1-\delta_i} \dots \dots \dots (25)$$

$$= \prod_{i=1}^n [h_i(t_{(i)}) S_i(t_{(i)})]^{\delta_i} [S_i(t_{(i)})]^{1-\delta_i}$$

$$= \prod_{i=1}^n [f_i(t_{(i)})]^{\delta_i} [S_i(t_{(i)})]^{1-\delta_i}$$

$$= \prod_{i=1}^n \left[\frac{\exp x_{j\beta}^T}{\sum_{k \in R(t_{(j)})} \exp x_k^T} \right]^{\delta_i} \times \prod_{i=1}^n [\sum_{k \in R(t_{(i)})} h_i(t_{(i)})]^{\delta_i} [S_i(t_{(i)})] \dots \dots \dots (26)$$

2.6.2 Model Assumptions Checking Techniques

Testing the cox proportional hazard model assumption is equal to testing the coefficient β . The following methods have been used in checking the proportional hazard assumption with a valid testing procedure and p-value; the likelihood ratio test, the Schoenfeld residuals test, the scaled Schoenfeld residuals test, the Lin *et al.* (2006) score test, and the martingale-based residuals test.

a) Likelihood ratio test

In the PH model, the likelihood ratio test can be used to compare the goodness of fit of the null and alternative models using hypothesis testing. The main criterion for this test is that one model is nested in the other, with the nested model being the null hypothesis. The likelihood ratio can be interpreted as how many times more likely the data are under one model than the other. To test the PH assumption, Cox (1972) suggested adding a time-dependent variable, $X_2(t)$, in the model. The form of this variable can be the product of time, $g(t)$, and the variable of interest. Considering

g (t) =t with extended-Cox model and PH model,

$$L_{PHM} \text{ is } h(t, X(t)) = h_0(t) \exp(\beta_1 X_1 + \beta_2 X_2) \dots \dots \dots (27)$$

$$L_{ECM} \text{ is } h(t, X(t)) = h_0(t) \exp(\beta_1 X_1 + \beta_2 (X_2 * t)) \dots \dots \dots (28)$$

The test statistic is

$$LR = -2 \log(L_{PH} \text{ model}) - (-2 \log L_{ECM}) \sim X_p^2 \dots \dots \dots (29)$$

The test statistics follow a chi-squared distribution with p degrees of freedom,

Where p is equal to $df_{ECM} - df_{L_{PH} \text{ model}}$

One may also consider the test statistics as

$$D = -2 \ln \frac{L(x_0 | t, \beta)}{L(x_1 | t, \beta)} \dots \dots \dots (30)$$

$$= -2 \ln (\text{Likelihood of Null Model}) + 2 \ln (\text{Likelihood of Composite Model})$$

b) Schoenfeld residuals test

Schoenfeld residuals are partial residuals that can be used to check the PH assumption. Schoenfeld residuals are obtained by substituting the partial likelihood estimator of the coefficient. The Schoenfeld residual for the i^{th} subject on the p^{th} covariate is:

$$\hat{r}_{ip} = \delta_i (x_{ip} - \hat{x}_{wi,p}) \quad \text{where} \quad \hat{x}_{wi,p} = \frac{\sum_{j \in R(ti)} x_{jp} e^{x_j \beta_p}}{\sum_{j \in R(ti)} e^{x_j \beta_p}} \dots \dots \dots (31)$$

The result is the covariate value of a person who gets the event at time t minus the expected value of the covariate and is not defined for censored individuals.

Schoenfeld residuals against time should be scattered randomly around zero, so testing time-dependent covariates is equivalent to testing a non-zero slope in a generalized linear regression of the Schoenfeld residuals on functions of time

c) Scaled Schoenfeld residuals test

Grambsch and Therneau (1994) suggested using scaled Schoenfeld residuals to test time-dependent variables. Scaled Schoenfeld residuals are:

$$\hat{r}_{ip}^* = 1/ [\widehat{var}(\hat{r}_{i1}, \hat{r}_{i2}, \dots, \hat{r}_{ip})] (\hat{r}_{ip}) \dots \dots \dots (32)$$

Grambsch and Therneau (1994) also suggested that $E(\hat{r}_{ip}^*) + \hat{\beta}_p \approx \beta_p(t_i)$, so on assuming that the PH assumption is valid, $\hat{\beta}_p = \beta_p(t_i)$ and $E(\hat{r}_{ip}^*) = 0$

which means that scaled Schoenfeld residuals are a random walk across the time scale. So the null hypothesis for the test is that the regression coefficient between the scaled Schoenfeld residuals and a function of time should be zero. Once the scaled Schoenfeld residuals are created, the p-value of the correlation between the scaled Schoenfeld residuals and ranked time can be obtained.

d) Lin *et al.* (2006) score test

Lin *et al.* (2006) by Saegusa and Chen (2014) propose “score-type” tests for the proportional hazards assumption in the PH model by using a natural smoothing spline representation of the corresponding non-parametric functions of time or covariate. The function of time doesn’t have to be defined. The alternative model is considered as:

$$h(t | x_1, x_2) = h_0(t) \exp\{X_1\beta + X_2\gamma(t)\} \dots \dots \dots (33)$$

Where,

- $h_0(t)$ is baseline hazard,
- X_2 is a scalar covariate of interest
- X_2 is considered as a time-dependent variable,
- $\gamma(t)$ as an arbitrary smooth function of time.

Smoothing spline (t) is considered as;

$$\gamma(t) = \sum_{k=1}^m \delta_k \varphi_k(t) + \sum_{l=1}^r a_l R(t, t_l^0) \dots \dots \dots (34)$$

Where $m \geq 1$ is an integer, $t^0 = (t_1^0, \dots, t_r^0)$. T is the $(r \times 1)$ vector of ordered and r is the total number of events

Assuming $0 < t_1^0 < \dots < t_r^0 < 1$.

δ_k and a_l are constants

$\{\varphi_k(t)\}_{k=1}^m$ is a basis for the space of (m-1) th-order polynomials and

$$R(t,s) = \int_0^1 t - u^{m-1+s} - u^{m-1} / \{(m-1)!\}^2 du \dots \dots \dots (35)$$

γ is the corresponding vector of $\gamma(t)$ evaluated at each element of t^0 .

$$\gamma = H\delta + \sigma a$$

$$H = \begin{pmatrix} \varphi_1 t_1^0 & \dots & \varphi_m t_1^0 \\ \vdots & \ddots & \vdots \\ \varphi_m t_r^0 & \dots & \varphi_m t_r^0 \end{pmatrix} \quad \sigma = \begin{bmatrix} R(t_1^0, t_1^0) & \dots & R(t_1^0, t_r^0) \\ \vdots & \ddots & \vdots \\ R(t_r^0, t_1^0) & \dots & R(t_r^0, t_r^0) \end{bmatrix}$$

e) Martingale-based residuals test

Therneau and Hongzhe (1999) proposed martingale-based residuals to check the PH model assumption. The martingale residuals can be interpreted as the differences at time t between the observed and expected numbers of events for the *i*th subject

$$\widehat{M}_i(t) = N_i(t) - \int_0^t Y_{ii}(u) \exp(\beta' X_i) d\widehat{h}_0(u) \dots \dots \dots (36)$$

Here $\widehat{M}_i(t)$ is shorthand for $\widehat{M}_i(\infty)$, $N_i(t)$ is the number of events for the *i*th subject experienced over time t, and \widehat{h}_0 is the cumulative baseline hazard.

Plotting the cumulative martingale residuals against follow-up time may check the violation of the PH assumption.

For all methods described above, a significant p-value (p<0.05) implies the variable of interest is a time-dependent variable, which is not constant over time, so the PH assumption is violated.

2.6.3 Cox Proportional Hazards Regression Model Characteristics

- i. Is a semi parametric model.
- ii. Makes no assumptions about the form of h(t) (nonparametric part of model)
- iii. Assumes parametric form for the effect of the predictors on the hazard.
- iv. The cox ph model is well-suited .in parameter estimates than the shape of the hazard.

2.7 Application of Modelling in Breast Cancer

Several models have been used in modelling different types of cancer. This include: mathematical and statistical models, deterministic models, graphical models among others. Mathematical and Statistical models are widely used in clinical studies because they are capable of integrating biological knowledge that is outside of the observational data (Rachael *et al.*, 2012).

Salah *et al.* (2010) did a study on statistical modelling of the incidence of breast cancer and found out that the incidence is highest among women in the age group (40-59). Yuan, 2005 came up with a survival model for estimating lung cancer survival by using the proportional hazard regression model. The findings were that the score function provided a good indication for the risk of death from lung cancer. This backs up the cox regression for β estimation. However he recommended larger volume of hospital data for more stable β estimation.

Ileana *et al.* (2006) used cox-Aalen model for breast cancer survival. An additive term was introduced to the model as opposed to using only the multiplicative term. It was found out that during the first 18 months after diagnosis its effect was not significant, later it became an important predictor of death. A recommendation was done that the period of study should be lengthened. This study sought to improve on the previous studies by using cox proportional hazard model, using substantial amount of data and ensuring the period of study is reasonably appropriate (5 years).

CHAPTER THREE

METHODOLOGY

3.1 Study Area

This study was conducted in Meru and Nyeri counties which were selected purposively. In Meru County, the study was conducted at Meru level 5 hospital while in Nyeri County, in Nyeri referral hospital. These facilities were selected for this study because they are the largest in the respective counties and they also have equipped facilities and specialists to handle breast cancer cases. Survivors from these and neighbouring counties receive treatment from these facilities. Meru level 5 hospital is located in Meru town, which is approximately 226 km North-East from Nairobi. Its latitude and longitude are ($0^{\circ}3'4.68''S, 37^{\circ}39'13.68''E$). Nyeri referral hospital is approximately 151.7 km North-East from Nairobi and its latitude and longitude are ($0.4259^{\circ} S, 36.9636^{\circ} E$).

3.2 Research Design

Mixed method research design was used for this study because multiple ways of collecting data were applied. This research design is appropriate when both quantitative and quality data sets are used in handling a research problem (Creswell & Clark, 2017).

3.3 Population of the Study

The target population was the breast cancer patients who had attended Meru level 5 hospital and Nyeri referral hospital between the periods 2012 to 2017. The medical practitioners who attended to the breast cancer patients in the two health facilities were also of interest to this study. Further, the breast cancer survivors in the two Counties also provided information used in this study. The population estimates as obtained from the two hospital records were; 1350 breast cancer patients, 415 care providers and 200 breast cancer survivors for the period 2012 – 2017.

3.4 Sampling Procedure and Sample Size

Selection of subjects from the hospital records was done by simple random sampling. This method ensured that the sample obtained was a representative of the whole population and each subject in the population had an equal chance of being included in the sample. The medical practitioners and the breast cancer survivors were also

selected using simple random sampling. The sample sizes of the three groups of subjects were determined using the formula by Kathuri and Pals (1993) (Appendix iv). The resulting sample sizes obtained for this study are shown in table 1.

Table 2: sample random sampling sizes

Group	Population	Sample Size
Patients from hospital records	1350	300
Medical practitioners	415	200
Breast cancer survivors	200	120
Total	1965	620

3.5 Inclusion and Exclusion Criteria

The study targeted the female breast cancer patients and survivors who we are younger than 80 years. These were the ones who had attended the two medical facilities considered in this study in either of the cancer stages. Exclusion criteria were: those with other types of cancers different from breast cancer; those with abnormal renal function tests, those who had developed other types of cancers, and them that were not willing to work on MBS factors.

3.6 Instrument Validity and Reliability

3.6.1 Pilot Survey

A pilot study was done at Embu level 5 hospitals which is of the same level as the Meru level 5 and Nyeri referral hospital. For this reason, the experiences of the breast cancer survivors and the care givers were expected to be similar. The purpose of the pilot study was to determine the reliability of the instrument used in this study. Furthermore, it helped to detect and correct any defects, confusion or omission that could have been found in the study (Turner, 2010).

3.6.2 Validity Test

Validity of the instruments in this study was done by incorporating experts' opinion. Validity is a measure of whether the results from a research study reflects the phenomenon being investigated (Babbie, 2013). The experts in the field of breast cancer treatment scrutinized the instruments for face validity, construct validity and content validity. The experts also evaluated the appropriateness of the issues that were to be investigated. Their input was put into consideration and necessary adjustments were made before the instrument was used.

3.6.3 Reliability Test

Reliability of the research instruments was tested by administering the same instrument twice to the same group of subjects at two separate times with a time lapse between the first and second test. This helped establish the extent in which an instrument yields consistent results or information after repeated trials (Henn & Foard, 2006). The study used Pearson's product moment correlation coefficient formula to determine the correlation between the two set scores. A coefficient of 0.70 or more showed that there was high reliability of data (Ratner, 2009).

3.7 Data Collection

Both primary and secondary data was collected for this study. Secondary data was obtained from the hospital records of the two facilities for the period 2012 – 2017. The data was obtained on breast cancer patients who had attended the facility during that period. The secondary data was collected using a checklist. Primary data was collected by administering questionnaires to the breast cancer survivors in the two counties and care givers at the two health facilities (Appendix 1; Appendix 2). The variables that were of interest to this study and obtained from both the primary and secondary data included age of the patient, whether the patient was still alive or dead, alcohol and drug use, stress after diagnosis, adherence to prescribed diet, access to treatment, burden of treatment, regular exercise after diagnosis and awareness of how to handle the disease after diagnosis. Data collected from the medical practioners involved years of service in the facilities, the number of breast cancer patients handled, their feeling on the MBS factors on study and other stressors experienced by the patients. These variables were then used for analysis in the study.

3.8 Data Analysis

The data collected was coded and entered into Statistical Package for Social Sciences (SPSS) version 16. The data was then imported into R software which was used for analysis in this study. Data analysis involved generation of descriptive statistics and inferential statistics. Descriptive statistics generated were inform of tables and graphs. The inferential statistics generated included the Kaplan Meir curves and the log rank tests. Kaplan –Meier curves were used to represent the differences in survival among different covariates and their outcomes. Log rank tests were used to determine

significance of different covariates. This involved determining the p values of different covariates. The covariates with p values less than 0.05 were statistically significant in predicting breast cancer survival rate. The breast cancer survival rate model was generated using the obtained data by the help of cox proportional hazard model.

3.8.1 Statistical Model

The study utilized the cox proportional hazard model. In a proportional hazards model, the unique effect of a unit increase in a covariate is multiplicative with respect to the hazard rate.

The model formula is as follows

$$h(t) = h_0(t) \exp(X_1 \beta_1 + \dots + X_p \beta_p) \dots \dots \dots (37)$$

Where $h(t)$ is the expected hazard at time t , the x 's are the covariates (costly burden of treatment - X_1 , stress on diagnosis - X_2 , poor diet- X_3, \dots, X_7). $\beta_1, \beta_2, \dots, \beta_7$ are their respective coefficients and the baseline hazard function is $h_0(t)$. The constant in this model represents a kind of log-baseline hazard, since $\log h(t) = \log h_0(t)$ when all of the x 's are equal to zero.

The model is sometimes expressed relating the relative hazard which is the ratio of the hazard at time t to the baseline hazard, to the risk factors:

$$\frac{h(t)}{h_0(t)} = \exp(X_1 \beta_1 + \dots + X_p \beta_p) \dots \dots \dots (38)$$

Natural logarithm can be taken on each side to show a relationship between the log of the relative hazard to the linear function of the predictors

$$\ln \left\{ \frac{h(t)}{h_0(t)} \right\} = (X_1 \beta_1 + \dots + X_p \beta_p) \dots \dots \dots (39)$$

The estimated coefficients in the cox proportional hazards regression model represents the change in the expected log of the hazard ratio relative to the change in X_s holding all other covariates constant.

The goal is to test whether or not the model $h(t | x)$ is improved with the inclusion of the different MBS covariates. Beginning with the null hypothesis $H_0: \beta_1 = 0$ and a

composite Hypothesis $H_1: \beta_1 \neq 0$ at $\alpha = 0.05$. This is essentially testing whether a proposed covariate has significant effect on the model;

$$h(t | x_1) = h_0(t)e^{\beta_1 x_1}$$

This is done by using the test statistics below;

$$D = -2 \ln \frac{L(x_0 | t, \beta)}{L(x_1 | t, \beta)} \dots \dots \dots (30)$$

Reject H_0 if $D > \chi^2$ which is always equal to 3.84 with 95% confidence level ($\alpha = 0.05$). Comparing the difference of a single parameter in the model is done at 1 degree of freedom for the $\chi^2 >$ test statistic. If $D > 3.84$, H_0 is rejected, concluding that a certain covariate is an important factor in determining survival rate. The Log-Rank test was used to perform comparisons of survival curves using hypothesis tests on the patients' survival rate considering age.

Survival Function is conventionally denoted by $S(t)$, for some time t and T (usually representing time of death or failure) be a continuous random variable with cumulative distribution function $F(t)$ on the interval $[0, \infty)$. Its survival function is

$$\begin{aligned} S(t) &= P(T > t) \\ &= \int_0^\infty f(u) du \\ &= 1 - F(t) \dots \dots \dots (36) \end{aligned}$$

Assuming T is a continuous random variable, with probability density function $f(t)$ and cumulative distribution function $F(t) = \Pr\{T \leq t\}$ giving the probability that the event has occurred by duration t .

$$\lim_{\Delta t \rightarrow 0} P(t \leq T < t + \Delta t) / \Delta t \dots \dots \dots (37)$$

Kaplan-Meier estimators played a crucial role in determining the varying effects which the MBS variables have on survival rate. The Kaplan-Meier curves helped in

showing a plot of percentage survival (y-axis) against time (x-axis). They are often used in survival analysis to provide a very digestible graphical output, which can be easily interpreted by those less familiar with the statistical concepts at work. The Kaplan-Meier method is based on individual survival times and assumes that censoring is independent of survival time (that is, the reason an observation is censored is unrelated to the cause of failure).

Kaplan-Meier estimator of survival at time t is shown below;

$$\begin{aligned}
 S(t_i) &= \prod_{0 \leq j \leq n} \Pr(T > t_i | T \geq t_i) \\
 &= S(t_{j-1}) \Pr(T > t_j | T \geq t_j) \\
 &= \frac{S(t_{j-1})(n_j - m_j)}{n_j} \text{ for } 0 \leq t \leq T \dots\dots\dots
 \end{aligned}$$

(38)

Here $t_{i,j} = 1, 2, \dots, n$ is the total set of failure times recorded, T is the failure time with distribution F and density f , m_j is the number of failures at time t_j , and n_j is the number of individuals at risk at time t_j .

3.8.2 Model Adequacy and Validation

The goodness of fit of the log rank tests was done using the probability values. If the probability value was less than the level of significance, the test was adequate. The adequacy of the cox proportional hazard model was determined using the likelihood ratio value and the probability value. Model validation was done by dividing the collected data into two sets. One set was used in fitting the model and the other set was used to test if the model fitted produced similar results with a different data set.

3.10 Modelling Process

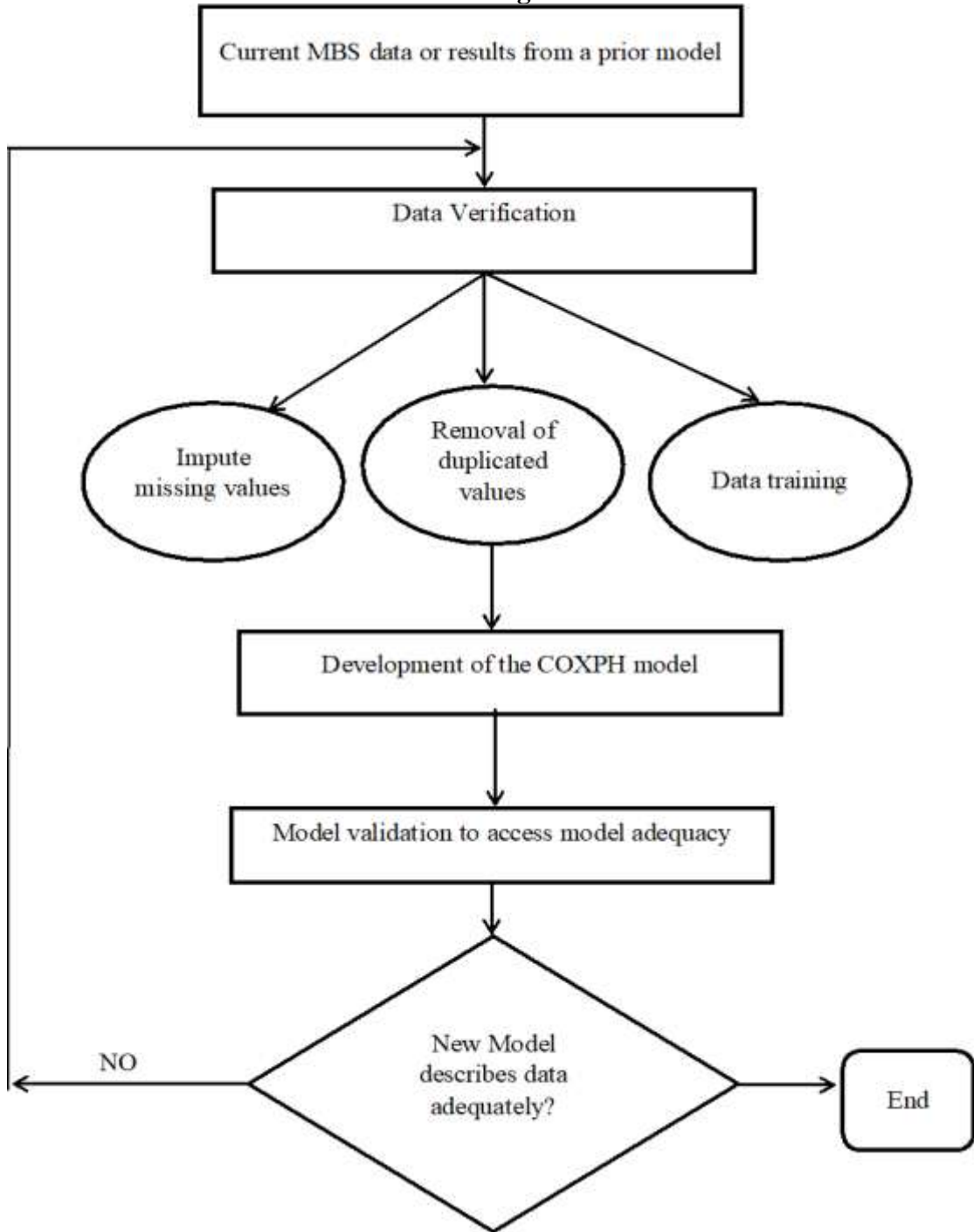


Figure 1: Modelling Process

3.11 Ethical Considerations

A research clearance was obtained from the Chuka University Ethics committee before data collection was done (Appendix IV). A research permit was also obtained from National Commission for Science, Innovation and Technology (Appendix V). Permission to collect data was obtained from the hospital's matrons. Confidentiality and security of the secondary data obtained was adhered to. The researcher acquired informed consent from all study participants by clearly explaining to participants what the study was investigating and their required participation. Autonomy was guaranteed with participants allowed to be engaged in the study at their own free will.

CHAPTER FOUR
RESULTS AND DISCUSSION

4.1 Preliminary Analysis

The average age of the respondents was 52.23 years (Table 3). The skewness and the kurtosis values showed that the data satisfied the normality assumptions. The average number of fatalities from breast cancer reported by medical practitioners was on average 42.19 per year (Table 3). The average time of survival for the breast cancer patients was 3.77 years (Table 3). The percentage of censored patients was 66.7% with the remaining 33.33% having succumbed to breast cancer. This implied that there is high mortality rate from breast cancer.

Table 3: Summary statistics for data on the breast cancer patients and the medical practitioners

Statistic	Number of fatalities	years worked	Time	Patient Age
Mean	42.19	6.44	3.77	52.23
Standard Deviation	16.41	5.56	2.03	10.74
Median	39	5	4	53
Skewness	0.42	2.2	0.36	-1.3
Kurtosis	-0.17	5.7	0.04	4.19
Maximum	90	31	10	75
Minimum	1	1	1	3

The findings of this study were in agreement with other studies. For example, with respect to the average age of the breast cancer patients was in the age group of 40 – 69 years. This indicated that this age group is more prone to breast cancer as compared to other age groups. This finding is in agreement with what was found at Cancer.net (2017). Cancer .net (2017) found out that if the cancer is located only in the breast, the 5-year survival rate of women with breast cancer is 99% and decreases to 27% if it has spread to other parts of the body. In addition, the findings on the survival rate of the breast cancer patients was in agreement with the five year overall survival rate for breast cancer patients that does not exceed 60% for any low and middle –income country in Africa (Vanderpuye *et al.*, 2017). Five-year breast cancer-specific survival shows the percentage of people who have not died from breast cancer 5 years after diagnosis (Komen, 2019). Vanderpuye *et al.* (2017) study involved search through electronic databases from 1999 to 2016 and found out that breast tumors are diagnosed at earlier ages and later stages in developing countries as compared to high income countries. This greatly reduces the breast cancer survival rate hence the low

survival rate. Vanderpuye *et al.* (2017) did not use any statistical design and so this study improves on the former by employing mixed research design that helped achieve data triangulation and more reliable results by using cox proportional hazard model.

Pizot *et al.* (2016) used the random effects model to study the five year survival rate for women with breast cancer in Canada and found that the survival rate was at 87%. This is higher than the survival rates obtained in this study which may mean that developed countries have been able to establish the right systems to fight the disease. The lowest mortality rates for breast cancer are found in China and Japan with the rates approximately to 6% and 7% respectively which are lower than the ones obtained in this study which could be due to the better established health systems in developed countries (Steven, 2016). However, the mortality rates obtained in this study may be said to be more reliable due to the use of cox proportional hazards model when compared to the results by Steven (2016) where the reliance is only on descriptive statistics. Chen *et al.* (2018) estimated new cancer cases and deaths using calculated incidence and mortality rates and corresponding national population stratified by area, sex, age group and cancer type and noted decreased mortality rates among Chinese women which concurs with the earlier observation for mortality rates in developed countries. The results of this study however, is an improvement of the ones obtained by Chen *et al.* (2018) due to application of a statistical model apart from just the analysis for the incidence and mortality rates. The average 10 year survival rate for breast cancer patients in the United States of America was found to be 83% which meant that the survival rates decreased with increase in the number of years since diagnosis which contrasts the findings of this study (American cancer society, 2019). This could be attributed to the reason that, developed countries have been able to adequately deal with reducing breast cancer fatalities. In general, the results from this study are slightly above the overall survival rate for low and middle income countries but below the survival rates for developed countries. This may be attributed to increased awareness and campaign done in these counties about coping with the disease and provision of better health care (Muchui, 2019).

4.2 Analysis of Mindfulness-Based Stress following Breast Cancer Diagnosis

Medical practitioners' sentiment was that being diagnosed with cancer stressed the patient both financially and emotionally (Table 4; Figure 2). The practitioners also tended to agree that patients' observing the diet prescribed helped them feel better and patients accessing treatment within the shortest time possible made their journey easier (Table 4; Figure 2). However, the practitioners seemed not sure if regular exercises made the patients feel better, if the patients getting the right information helped them to face the disease bravely and if the patients' abstaining from alcohol use facilitated their healing (Table 4; Figure 2).

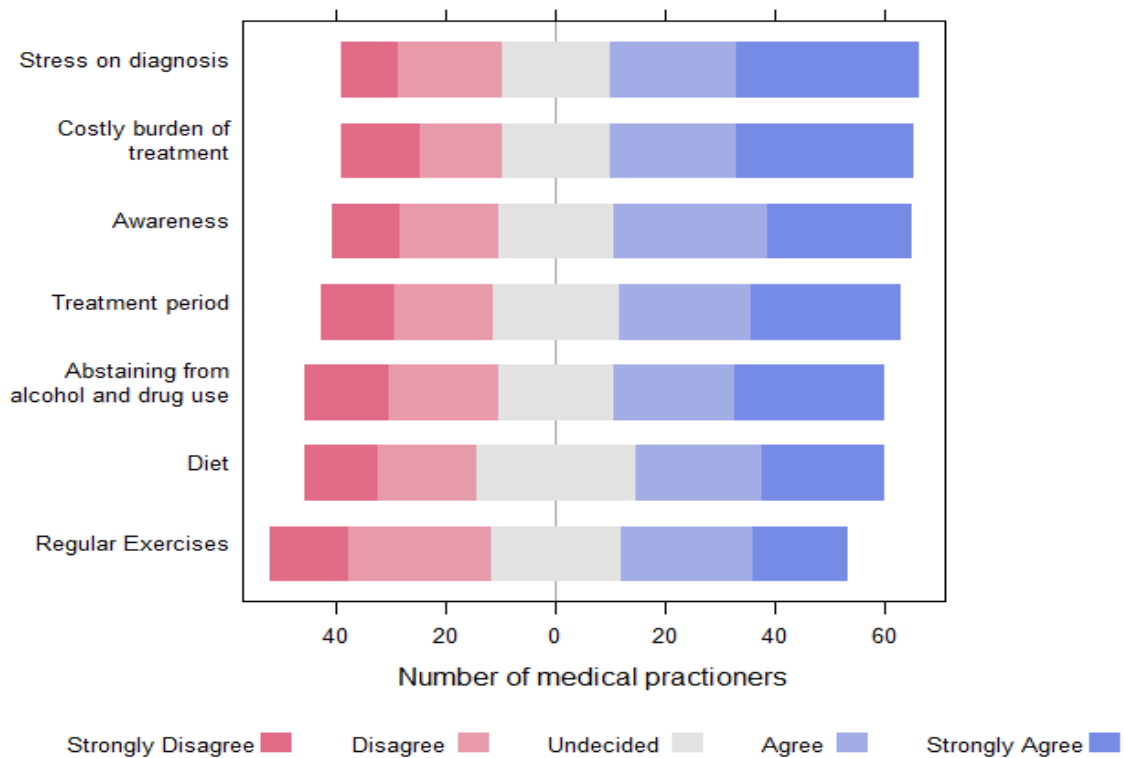


Figure 2: Diagrammatic representation of mindfulness-based stress following breast cancer diagnosis as analysed from practitioners' perspective

Table 4: Mindfulness-based stress following breast cancer diagnosis as analysed from practitioners' perspective

Variable	S. D		D.		U.		A.		S. A		M	M.d
	N	%	N	%	N	%	n	%	N	%		
Stress	44	14.67	33	11	36	12	91	30.33	96	32	4	5
Diet	31	10.4	40	13.42	75	25.17	79	26.51	73	24.5	4	4
Regular-exercise	30	10.07	52	17.45	81	27.18	67	22.48	68	22.82	3	3
Treatment-period	27	9.09	36	12.12	78	26.26	73	24.58	83	27.95	4	5
Awareness	28	9.33	45	15	81	27	65	21.67	81	27	3	3
Cost-burden	18	6	15	5	21	7	10.0	33.33	14.6	48.67	4	5
Drug use	46	15.38	69	23.08	82	27.42	55	18.39	47	15.72	3	3

S.D. Strongly Disagree, D. Disagree, U= Undecided A=Agree S.A = Strongly Agree, M= Median and M.d = Mode

Patients tended to agree with the statement that diagnosis of cancer stresses them financially, observing the diet prescribed helped them feel better and accessing treatment within the shortest time possible made their journey easier (Table 5; Figure 3). However, they were not sure if regular exercises made them feel better, if regular exercises made the patients feel better and if abstaining from alcohol use facilitated their healing (Table 5; Figure 3).

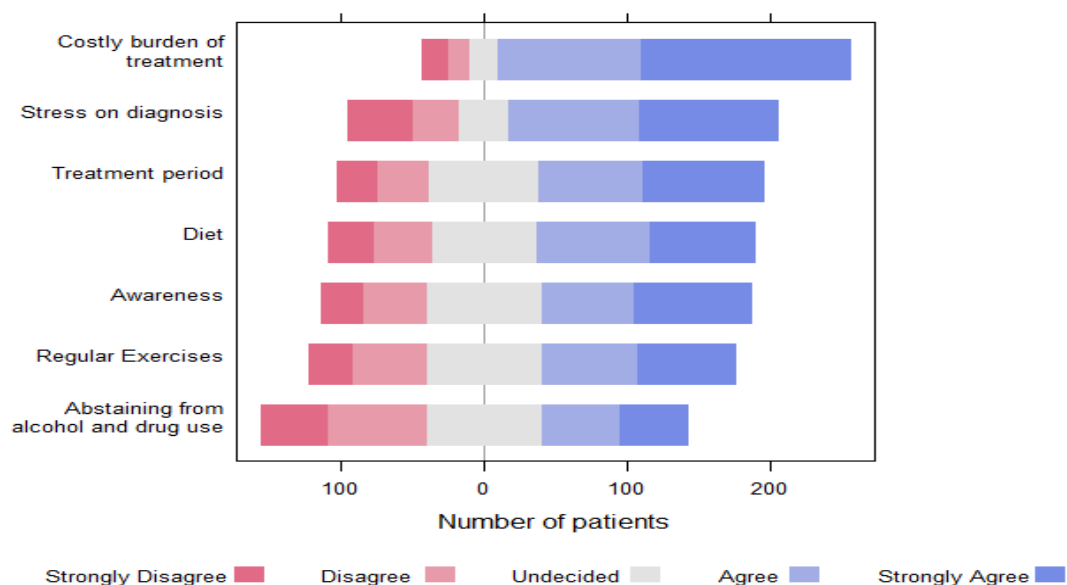


Figure 3: Diagrammatic representation of mindfulness-based stress following breast cancer diagnosis as analysed from patients' perspective

Table 5: Mindfulness-based stress following breast cancer diagnosis as analysed from patients' perspective

Variable	Strongly Disagree		Disagree		Undecided		Agree		Strongly Agree		Me di an	Mo de
	N	%	N	%	N	%	n	%	N	%		
Stress	44	14.67	33	11	36	12	91	30.33	96	32	4	5
Diet	31	10.4	40	13.42	75	25.17	79	26.51	73	24.5	4	4
Regular exercise	30	10.07	52	17.45	81	27.18	67	22.48	68	22.82	3	3
Treatment period	27	9.09	36	12.12	78	26.26	73	24.58	83	27.95	4	5
Awareness	28	9.33	45	15	81	27	65	21.67	81	27	3	3
Cost burden	18	6	15	5	21	7	100	33.33	146	48.67	4	5
Drug use	46	15.38	69	23.08	82	27.42	55	18.39	47	15.72	3	3

In summary, the mindfulness based stress that seemed to affect the breast cancer patients in the areas of study were alcohol use, stress after diagnosis, adherence to prescribed diet, access to treatment, burden of treatment, engaging in regular exercises after diagnosis and awareness of how to handle the disease after diagnosis (Table 4; Table 5; Figure 2; Figure 3). These findings concur with what has been found by other researchers (Shennan *et al.*, 2010, Frauke *et al.*, 2011 & Sahar *et al.*, 2014). Shennan *et al.* (2010) found out that the mindfulness based stress factors that affected the cancer patients were anxiety, depression, stress, sexual problems, and psychological arousal and immunity problems. However, Shennan *et al.* (2010) did not use any statistical model which was addressed in this study. Frauke *et al.* (2011) highlighted poor quality of life, moods and distress as the mindfulness based stress among those patients who had been diagnosed with cancer but never confirmed whether the found factors were significant using statistical modelling and that was improved in this study. Anxiety was also found as mindfulness based stress factor in a study by Sahar *et al.* (2014) but it was never applied in any statistical modelling to find if it was significant and that was addressed in this in this study.

4.3 Effects of Mindfulness-Based Stress on Breast Cancer Survival

Analysis using the Kaplan Meier survival function curve and the survival table showed that 6 patients died within a year after diagnosis (Table 6). The percentage of the patients who survived within the first year was 98%. By the second year, 9% of the patients had succumbed to breast cancer and 91.33% had survived (Table 6). Only 53.1% of the patients had remained by the 8th year. Twenty one patients were at risk of succumbing to breast cancer by the end of the 8th year. The five year survival rate for the breast cancer patients in this study was at 68.38 %.

Table 6: Overall survival table for the breast cancer patients

Time	Survival	Deaths	Survival SE	Number at risk
0	0.9800	6	0.0081	299
1	0.9133	20	0.0162	294
2	0.8594	15	0.0204	254
3	0.7994	15	0.0241	215
4	0.6839	24	0.0300	166
5	0.5852	15	0.0349	104
6	0.5310	5	0.0392	54
7	0.5310	0	0.0392	21

The finding of this study showed improved survival rate when compared to finding of Valderpuye *et al.* (2017), which concluded that the five year survival rate for the low and middle income countries in Africa do not exceed 60%. Valderpuye *et al.* (2017), used secondary data (2009-2016) whereas this study used both secondary and primary data hence having probability of more accurate results. This could also be attributed to the positive changes that have been happening in Kenya since the adoption of devolution in 2013. These changes are such as the availability of equipment, drugs and personnel necessary for handling cancer patients across the country. However, these findings are far below the statistics obtained from studies done in developed countries. For example, Pizot *et al.* (2016) found out the five year survival rate for the breast cancer patients in Canada was at 87 %. In China and Japan the five year survival rates for the breast cancer patients was 94 % and 93 % respectively (Steven *et al.*, 2018). In the United States of America, the five year and ten year survival rates for the breast cancer patients was 90 % and 83 % respectively (American cancer society, 2019). These statistics shows that the developed countries are still ahead of the developing countries in managing breast cancer.

The effect of alcohol use as a mindfulness- based stress on breast cancer patients' survived was analysed using the Kaplan Meier survival curve (Figure 4). The results indicated that 55% of those who disagreed that alcohol and drug use did not improve their wellbeing had survived up to 9 years after diagnosis while about 70% of those who were undecided if abstaining from alcohol and drug use had survived up to 10 years after diagnosis. Those who agreed that abstaining from alcohol increases their wellbeing had all perished by year 8 (Figure 4). These indicate that alcohol use for the breast cancer patients reduced their time of survival after diagnosis.

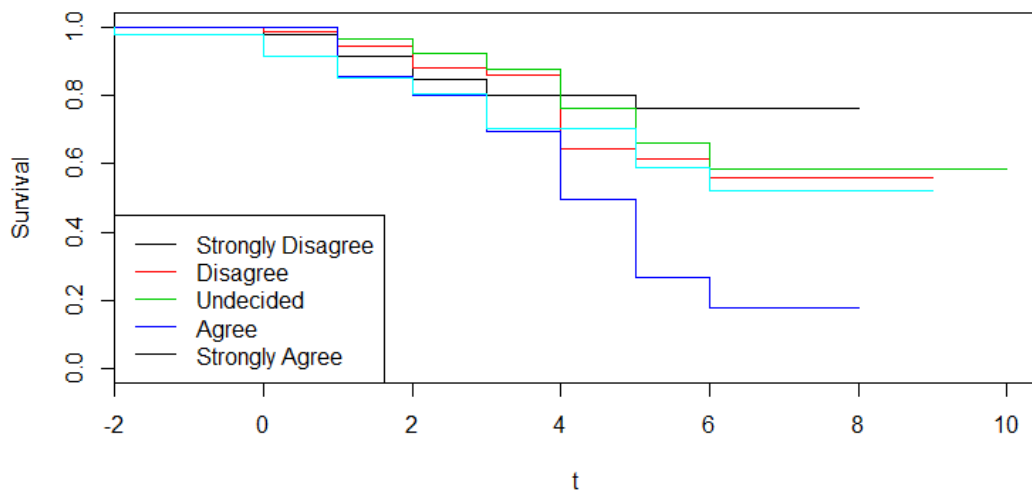


Figure 4: Kaplan-Meier estimate for effect of alcohol use on survival of breast cancer patients

Table 7: Log-rank Test for effect of alcohol use on survival of breast cancer patients

Variable	n	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$
Alcohol use_1	1 44	15	14.7	0.0053	0.00683
Alcohol use_2	2 33	10	12.2	0.4079	0.51310
Alcohol use_3	3 36	10	12.9	0.6335	0.80129
Alcohol use_4	4 91	31	29.5	0.0782	0.12228
Alcohol use_5	5 96	34	30.7	0.3524	0.55879

$\chi^2 = 1.6$ on 4 degrees of freedom, $p = 0.803$

The effect of alcohol use on the survival of breast cancer patients was also investigated inferentially using the log-rank test (Table 7). The chi-square value obtained was 1.6 at 4 degrees of freedom and a P – value ($p = 0.803$) showing there was no significant difference between the survival times in the different groups that had different views on how abstaining from alcohol affected their wellbeing after being diagnosed with cancer (Table 7). The findings agreed with most studies that alcohol use can't significantly increase mortality rates while others disagreed that alcohol use increases breast cancer recurrence and mortality rates. Diana (2016) did a study that found out that for those who had been diagnosed and treated for breast cancer, moderate alcohol use after a breast cancer diagnosis did not always lead to a lethal recurrence like death. Lowry *et al.* (2017) also concluded that consumption of alcohol before or after breast cancer diagnosis did not increase risks of overall or cause-specific mortality but observed that use of alcohol increases the risk of breast

cancer even at moderate levels of intake. These findings could be contributed by the fact that many women involved in the study were not using alcohol and so could not figure any significance they got from abstaining from alcohol use. The studies that disagreed with the findings (Gou *et al.*, 2011; Li *et al.*, 2015; Jayasekara *et al.*, 2016 and Singletary *et al.*, 2001) supported that alcohol use beyond certain limits increase breast cancer recurrence and mortality.

Effect of coping with stress on survival of breast cancer patients was also analysed using the Kaplan-Meier curve (Figure 5) and also inferentially using the chi-square test. The results indicated that about 55% of those who had agreed that breast cancer diagnosis stressed them survived up to the 7th year after diagnosis. Forty five percent of those who strongly agreed that the diagnosis stressed them also survived up to the 7th year after diagnosis. Fifty five percent who were not sure if the diagnosis stressed them survived up to the 9th year after diagnosis (Figure 5). The chi-square value obtained was 19.9 at 4 degrees of freedom and a P – value ($p= 0.000514$) meaning there was significant difference between the survival and coping well with stress. This showed that if the patient can be assisted in managing different stressors they can live long.

The findings were supported by several studies that found managing of stress increases breast survival rate. Spiegel (2012) did a randomized trial of psycho-educational groups for women and concluded that interventions that provide emotional and social support and improve stress management at the end will have a positive impact on physiological stress-response systems that affect survival. Kanani (2015) observed that breast cancer patients with depression and bipolar recorded in routine hospital data have worse overall survival than those without these mood disorders. Spiegel (2011) observed that emotional support is not only psychologically beneficial but also medically efficacious and thus he concludes that the palliative care intervention also improved the quality of life by reducing depression in breast cancer patients. American cancer society (2019) found out that depression experienced during or after breast cancer diagnosis make it harder for the patient to cope with the breast cancer treatment. That meant that patients who suffer depression after diagnosis tend to have a lower survival as compared to those patients who do not suffer

depression or are able to manage it after diagnosis (American cancer society, 2019). From all the above studies it becomes evident that those who could easily cope with stress had chances of surviving long. Those who were undecided meaning they weren't overwhelmed by stress ended living long past 9 years (Figure 7)

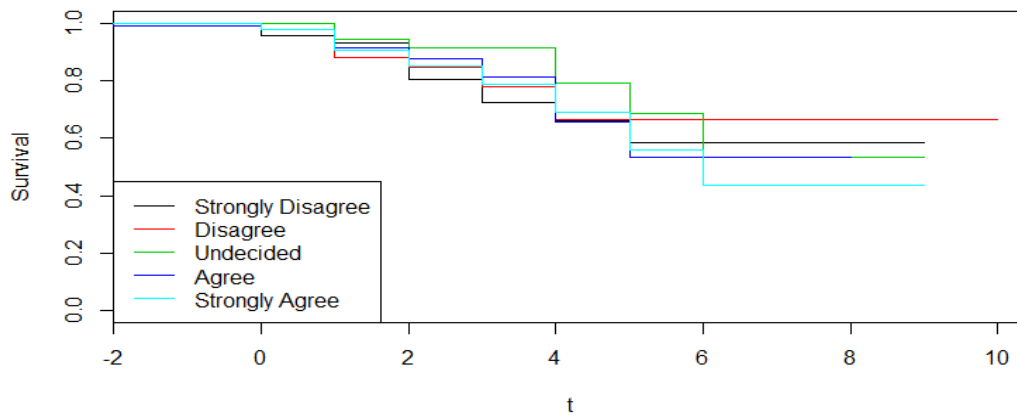


Figure 5: Kaplan-Meier curve for effect of coping with stress on survival of breast cancer patients

Kaplan-Meier curve was also used to study effect of adherence to the prescribed diet on survival of the breast cancer patients (Figure 6). The results indicated that 50% of those who strongly disagreed that prescribed diet had a significant effect on their wellbeing had passed on by the 5th year. The percentage of those who survived up to 6th year having disagreed that prescribed diet had a significant effect on their wellbeing was about 27%. The percentage of patients surviving after the 5th year who would not accurately tell if prescribed diet had a significant effect on their wellbeing was about 60%. Fifty percent of those who agreed that prescribed diet had a significant effect on their wellbeing were still surviving by the 5th year while 63% of those who strongly agreed that prescribed diet had a significant effect on their wellbeing were still surviving by 5th year (Figure 6). Log rank test showed that there was a significant difference between survival curves of those in different groups of diet, that is, those who felt diet improved their wellbeing and those who did not feel that diet increased their wellbeing. The chi-square value obtained was 9.5 at 4 degrees of freedom and a p – value of 0.04092, showing significance between observing the right diet and breast cancer survival rate.

These results agreed with findings from several studies carried out to establish effect of observing the right diet in improving survival rate such as a study by Kathleen (2019) that showed that breast cancer survivors may increase their years of survival after diagnosis by simply being physically active and eating a healthy diet. However, the study by Kathleen (2019) just relied on descriptive statistics as a basis of their findings and this study applied statistical modelling to improve this finding. Statistical modelling improved the results based on descriptive statistics since the significance of the independent variables was determined. Other studies that have investigated the relationship between diet and survival among the breast cancer patients were a study on the relationship between fat intake and survival of breast cancer patients found no association (Cao *et al.*, 2016), a study that showed that consumption of soy was found to reduce mortality due to breast cancer (Chen *et al.*, 2016) and a study where mortality due to breast cancer was also found to be reduced by consumption of high levels of fruits and vegetables (Jung *et al.*, 2013; Emaus *et al.*, 2016 & Farvid *et al.*, 2016) which concurred with the results of this study. However, all these studies used descriptive statistics as a basis of their findings and this was improved in this study by applying statistical modelling. Other studies that also used descriptive statistics and obtained similar findings were; a study where blood with highest levels of carotenoids was found to have reduced risk of mortality due to breast cancer (Eliassen *et al.*, 2015; Wang *et al.*, 2015, Bakker *et al.*, 2016) and studies on effect of diet on survival in breast cancer patients target aspects such as exposure, risk differences by tumour hormone and the specific dietary components (Bakker *et al.*, 2016).

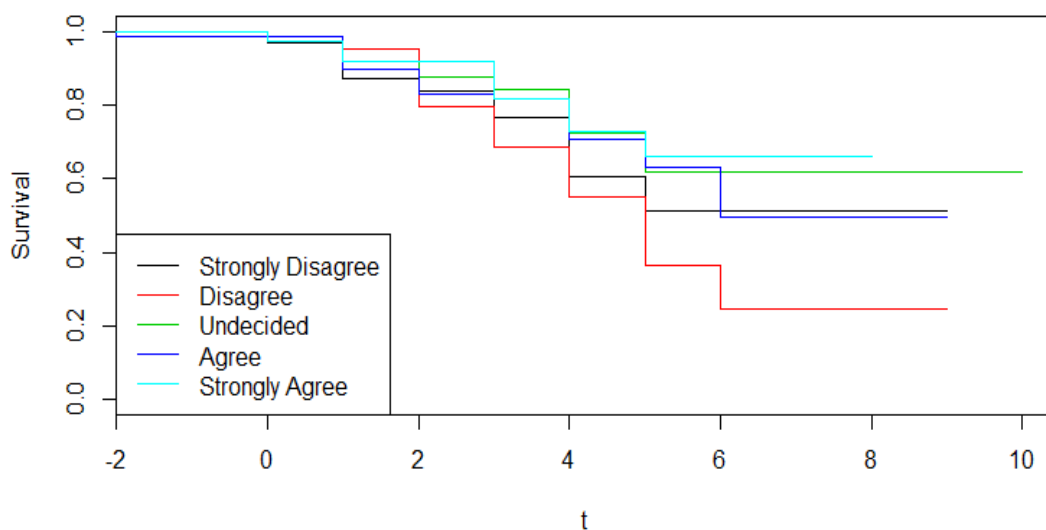


Figure 6: Kaplan-Meier curve for effect of adherence to prescribed diet on survival of breast cancer patients

Access to treatment as a mindfulness based stress and its effect on survival of breast cancer patients was analysed also using the Kaplan – Meir curve (Figure 7) and the log rank test. The results revealed that more patients who agreed that accessing treatment within the shortest time possible made their journey easier lived longer as compared to those who disagreed (Figure 7). Log rank test showed that there was a significant difference between those in different groups of views on how fast one accessed treatment The chi-square value obtained was 12.5 at 4 degrees of freedom and a P – value ($p= 0.0143$). Treatment period with a chi-square value of 12.5 at 4 degrees of freedom and a p value of $P = 0.0143$. This means that if the patients are able to access treatment immediately after diagnosis, survival can be increased which is supported by Morante *et al.* (2018) who found that the impact of delayed adjuvant chemotherapy in the outcome of triple negative breast cancer which represents a high risk group. However, Morante *et al.* (2018) did not use statistical modelling to find out if access to treatment was significant in increasing survival of breast cancer patients. Other studies that showed similar results but needed improvement by applying statistical modelling were; a study that showed that delay in presentation or total delay more than 12 weeks was associated with more advanced disease and inferior survival (Samur *et al.*, 2002) and a study where Rajan *et al.* (2015) found that cancer patients who had access to timely treatment after diagnosis exhibited improved survival rates as compared to patients who did not get timely access to treatment. Yoo *et al.* (2016) used Kaplan Meier survival analysis and the cox proportional hazards regression model and found out that delay in treatment initiation of breast cancer did not adversely affect the survival outcome of breast cancer (Yoo *et al.*, 2016) which agreed with the results of this study.

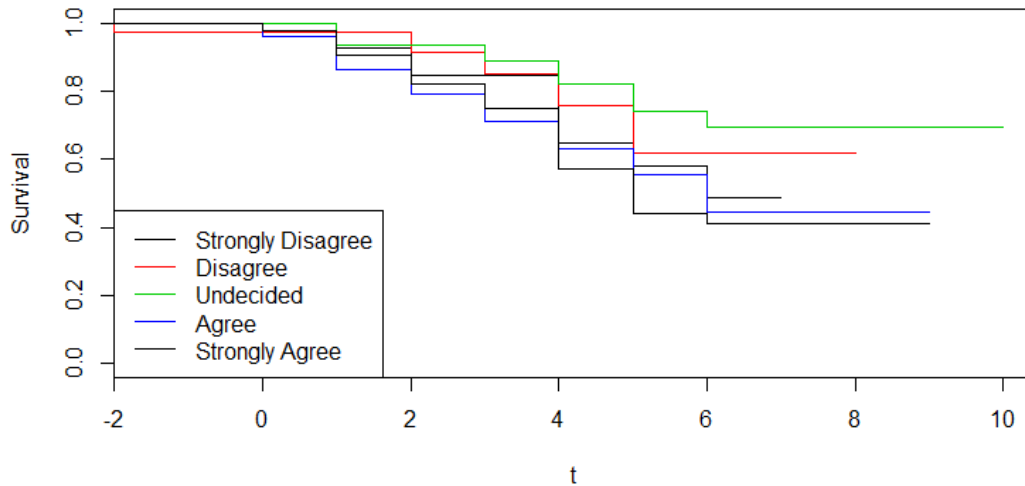


Figure 7: Kaplan-Meier curve for access to treatment and its effect on survival of breast cancer patients

Analysis for burden of treatment and its effect on survival of breast cancer patients revealed more survival on the patients who did not agree that the diagnosis was a burden as compared to those who agreed that the diagnosis was a burden in terms of treatment cost (Figure 8). Log rank test showed that there was no significant difference between those who were undecided, those agreeing and those strongly agreeing that ability to afford the cost of treatment improved their wellbeing of the patients. The chi-square value obtained was 9.5 at 4 degrees of freedom and a P – value ($p= 0.369$). This study’s findings that burden of treatment does not significantly affect breast cancer survival rate could be attributed to that, the communities in the two counties focus on the occurrence of the diseases of an individual as a community or family problem. Organising fundraisers are a common practice to solicit funds to help the individual seek treatment. Thus explaining the reason why several survivors felt that the burden of treatment was not a major concern to them. This study’s findings did not agree with most other studies that supported that treatment burden had significant effect on breast cancer survival rate.

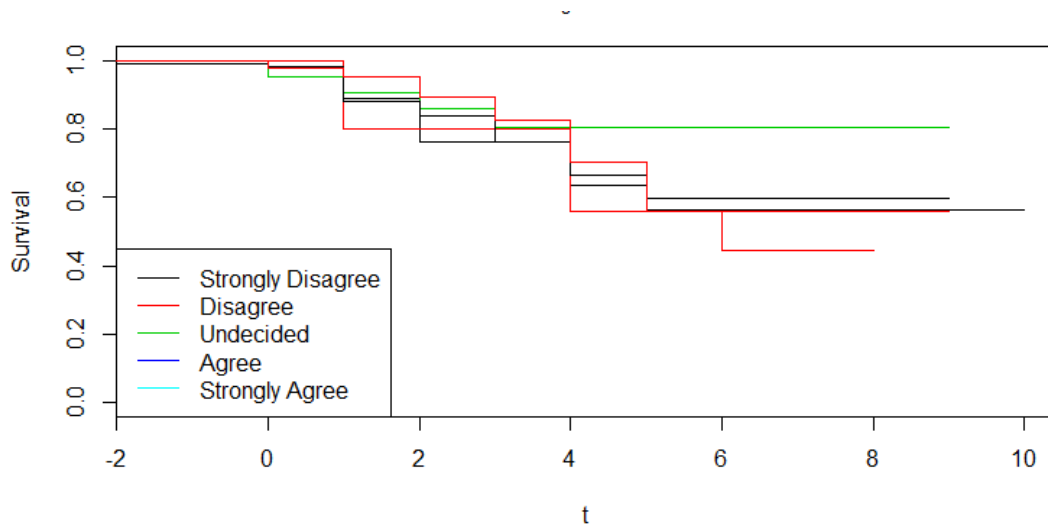


Figure 8: Kaplan-Meier curve for burden of treatment and its effect on survival of breast cancer patients

According to a study carried out by Stephanie *et al.* (2018) used descriptive statistics to establish the financial impact of breast cancer in black versus white women it was found out that disproportionate financial strain may contribute to higher stress, lower treatment compliance, and worse outcomes since black women with breast cancer experience a significantly worse financial impact which was similar to the results obtained in this study. Ryan (2018) observed that nearly one-third of cancer survivors report making changes in their prescription drug use like skipping doses, taking less medicine delaying filling a prescription and asking for lower-cost because of financial reasons which interferes with the medical schedule like surveillance for disease recurrence, screening for additional cancers thus affecting survival and despite the result being similar to the one from this study, statistical modelling would be used to make an improvement. Another similar investigated the effect of financial barriers on the access of quality care among the breast cancer patients found out that the patients found out that the patients who came from households with lower incomes had worse clinical outcomes as compared to patients who hailed from higher economic brackets which concurred with the findings of this study (James, 2017). However, the result by James (2017) could be improved by use of the Kaplan Meir curves and the cox proportional hazards model to find out if the financial burden was a significant factor.

Breast cancer patients who exercised regularly had better survival than the ones who did not exercise regularly (Figure 9). However, the log rank test showed that there

was no significant difference (p-value of 0.229) in the survival proportions in the different groups who had different views on the effect regular exercises on survival of the breast cancer patients (Table 9).

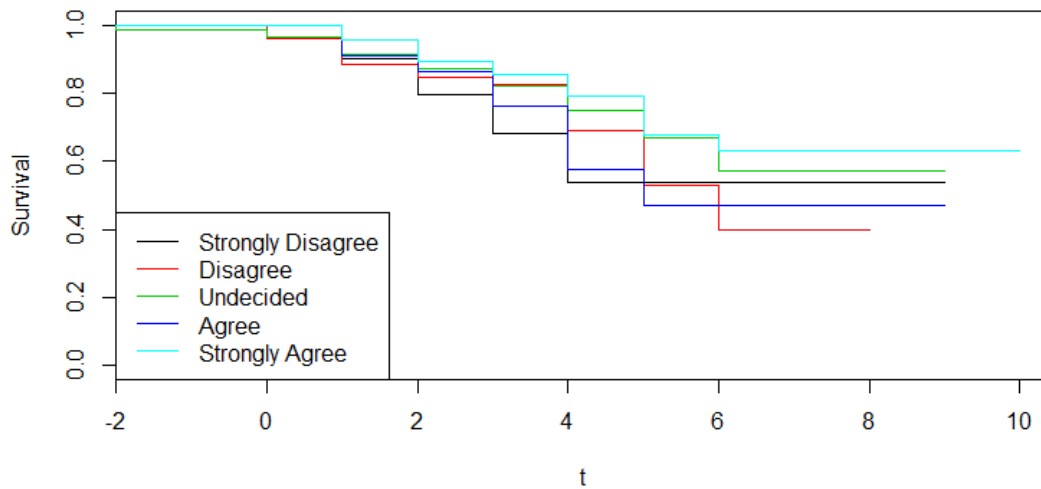


Figure 9: Kaplan-Meier curve for regular exercise and its effect on survival of breast cancer patients

Table 8: Log-rank Test for effect of regular exercise on survival of breast cancer patients

Variable	n	Observed	Expected	(O-E) ² /E	(O-E) ² /V
regular_excercise_1	30	12	9.54	0.637	0.773
regular_excercise_2	52	20	17.37	0.397	0.529
regular_excercise_3	81	22	25.94	0.598	0.891
regular_excercise_4	67	28	22.24	1.489	2.111
regular_excercise_5	68	17	23.91	1.995	2.897

$\chi^2 = 5.6$ on 4 degrees of freedom, $p = 0.229$

A study by Hannah *et al.* (2015) concluded that regular exercise combined with eating at least five servings of vegetables and fruit per day have been shown to lower breast cancer recurrence risk which concurred with the results of this study. Since, Hanna *et al.* (2015) based their finding on descriptive statistics, this study applied statistical modelling to make an improvement to this result by testing the significance of the independent variable. Physical activity reduces the risk of mortality due to breast cancer by about 10 – 20 % which concurs with the descriptive statistics obtained in this study (Pizot *et al.*, 2016). Other similar finding showed that mortality due to breast cancer is greatly reduced when the amount of exercise increases or when physical activity becomes more vigorous (Hildebrand *et al.*, 2016.) The findings by Hanna *et al.* (2015), Pizot *et al.* (2016) and Hildebrand *et al.* (2016) were all based on

descriptive statistics and they were similar to the descriptive statistics results from this study. However, physical activity had an insignificant effect (p value > 0.05) on survival of breast cancer patients.

Patients who showed lack of awareness portrayed less survival than those who had awareness of breast cancer (Figure 10). This result was confirmed inferentially using the log rank test. The log rank test results were; chi-square value of 18.439521 at 4 degrees of freedom and a p -value ($P = 0.0010124$.) This showed that there were significant different survival proportions for the different awareness groups. This means that if a survivor is fully aware what to do in fighting breast cancer, they are likely to live long.

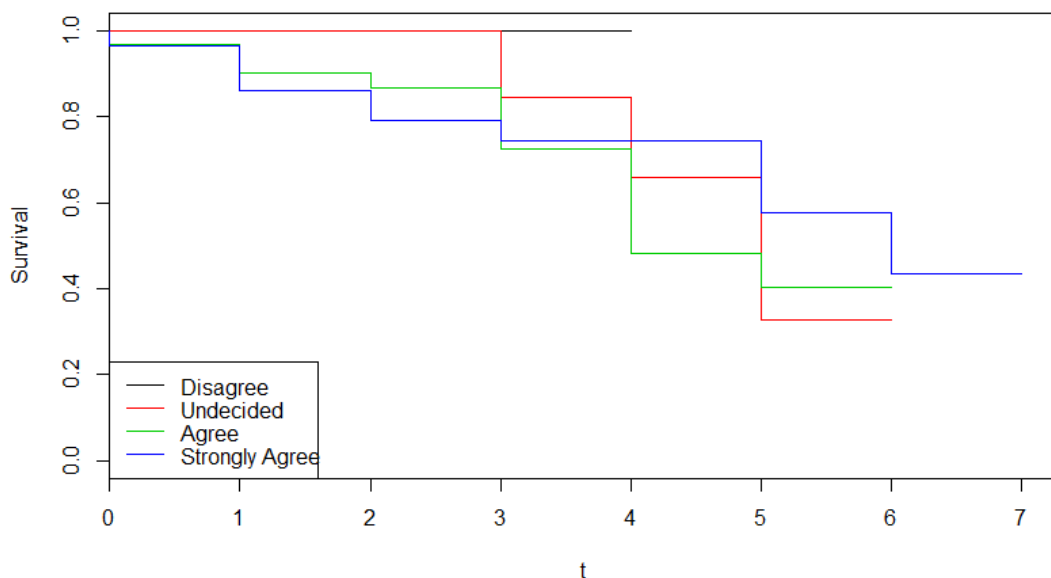


Figure 10: Kaplan-Meier curve for lack of awareness and its effect on survival of breast cancer patients

The findings of this study are in agreement with a study by Tazhibi and Feizi (2014) who conducted a research to find out the effect of awareness among Iranian women and found out that awareness would lead to early detection and reduce the stage at diagnosis, potentially improving the odds of survival and cure with simpler and more cost effective treatment. Komen (2016) found out that lack of awareness among young African American women on their risk for breast cancer is often a factor into why they have more harsh outcomes which was similar to the results of this study. However, the studies by Tazhibi and Feizi (2014) and Komen (2016) were improved

by testing the significance of the independent variable under investigation inferentially. Other similar findings were made by Mahony *et al.* (2013), Akram *et al.* (2017) and Niksic *et al.* (2016). Akram *et al.* (2017) investigated awareness of breast cancer was found to have a positive impact on recognition and screening of breast cancer which in return was observed to lead to increased survival rates while Niksic *et al.* (2016) investigated whether cancer survival was associated with cancer symptoms awareness found out that the awareness had a significant impact on breast cancer survival.

4.4 Cox Proportional Hazard Model

The Cox proportional hazard model was used to investigate how several mindfulness based stress affected the hazards of succumbing to breast cancer (Table 9; Table 10). The likelihood ratio test value for the model was 17.4 and with a probability value of $p = 0.0000119$. These values indicate that the overall model was significant. The mindfulness based stress factors that were significant in the model were diet, awareness, and cost of treatment burden and treatment period (Table 10) The most highly statistical significant coefficients were access to treatment ($p= 0.00014$) and ability to work on stress ($p= 0.000514$) (Table 10)

Table 9: Cox Proportional Hazard Model Summary

Variables	Coef	exp(coef)	se(coef)	Z	p
stress2	0.3054337	0.7368038	0.4260715	0.7168602	0.0636625
stress3	0.5865294	0.5562545	0.4686214	1.2516063	0.3098143
stress4	0.1254778	1.1336900	0.3572049	0.3512768	0.0000266
stress5	0.0781929	0.9247860	0.3515676	0.2224122	0.0095962
diet2	0.7228825	2.0603637	0.4023171	1.7967978	0.0723677
diet3	0.1906592	0.8264142	0.3987844	0.4781011	0.6325783
diet4	0.0523518	0.0537464	0.3844883	0.1361596	0.8916951
diet5	0.1280030	0.8798507	0.3944284	0.3245280	0.7455384
regular_excercise2	0.3336016	0.7163391	0.4092474	0.8151588	0.4149814
regular_excercise3	0.3918727	0.6757901	0.4070606	0.9626890	0.3357036
regular_excercise4	0.0328456	0.9676879	0.3677216	0.0893220	0.9288260
regular_excercise5	0.7066343	0.4933017	0.4015523	1.7597564	0.0784491
awereness2	1.1643320	0.3121311	0.4760576	2.4457798	0.0144539
awereness3	1.1813812	0.3068546	0.4176557	2.8286005	0.0046752
awereness4	0.0780022	0.9249624	0.3767364	0.2070471	0.8359731
awereness5	0.5754583	0.5624470	0.3773989	1.5248012	0.1273087
cost_burden2	0.2314046	1.2603691	0.6430587	0.3598499	0.7189594
cost_burden3	0.7506953	0.4720382	0.7251326	1.0352524	0.3005511
cost_burden4	0.0873911	1.9163186	0.4513698	0.1936131	0.8464789
cost_burden5	0.0547216	0.9467487	0.4364036	0.1253922	0.9002131
alcohol_use2	0.7794422	2.1802559	0.4202895	1.8545364	0.4734604
alcohol_use3	0.4176308	1.5183599	0.4112110	1.0156118	0.2107134
alcohol_use4	1.6932928	5.4373551	0.4030935	4.2007440	0.7253807
alcohol_use5	1.1439328	3.1390896	0.4416647	2.5900483	0.8239930
treatment_period	0.1845982	1.2027351	0.0941169	1.9613708	0.0498358

Table 10: Analysis of variance for the cox proportional hazard model

Variables	Loglik	χ^2	df	p-value
NULL	-510.2693	NA	NA	NA
Stress	-509.2708	1.997022	4	0.000514
Diet	-505.2957	7.950151	4	0.04092
regular_excercise	-503.0311	4.529208	4	0.229
Awareness	-493.8113	18.439521	4	0.0010124
cost burden	-492.4187	2.785297	4	0.36090
alcohol use	-478.9313	26.974668	4	0.803
treatment period	-476.9424	3.977828	1	0.000143

The interpretation of the mindfulness based stress factors and their effects on the hazards of succumbing to breast cancer was done using the odds ratios (Table 9). For instance, a patient who got stressed after diagnosis of breast cancer increased their hazards of succumbing to breast cancer with a factor of 1.1336900 on average which is 13.4 % as compared to a patient who did not get stressed after diagnosis (Table 9).

This results are supported by Wengstrom *et al.* (2017) who found out that adherence

to prescribed diet was found to reduce the risk of mortality due to breast cancer. In this case, failing to get stressed was used as the reference level with all the other covariates being held constant. Further, adhering to the prescribed diet reduced the hazards of succumbing to breast cancer by a factor 0.0537464 on average or a percent of 93.64 % as compared to not adhering to the prescribed diet. Failing to adhere to the prescribed diet was used as a reference level with all the other covariates being held constant (Table 9). The findings of this study are in agreement with what was found by Hannah *et al.* (2015) who found out that a combination of regular exercise and a healthy diet was found to reduce rate of mortality among the breast cancer patients.

Holding all the other covariates constant and taking failing to exercise as the reference level, regular exercising after diagnosis decreased the hazards of succumbing to breast cancer with a factor 0.9676879. Taking lack awareness as the reference level and holding all the over covariates constant, awareness of how to handle breast cancer reduced the hazards of succumbing to the disease with a factor 0.9249624. Holding all the other covariates constant, patients who are burdened financially by breast cancer have their hazards of succumbing to the disease increase by a factor 1.9163186 with having no financial burden being taken as the reference level. Stephanie *et al.* (2018) also observed that increased mortality in patients who experienced financial burden after diagnosis. It was explained that financial burden caused emotional stress among the patients which was then associated to increased mortality. Alcohol use increases the hazards of succumbing to breast cancer with a factor 5.4373551. This is when all the other covariates are held constant and lack of alcohol use taken as the reference level (Table 9).

The results of this study were an improvement on the findings by Gou *et al.* (2011), Spiegel (2011), Tazhibi & Feizi (2014), Hannah *et al.* (2015), Lowry *et al.* (2017), and Stephanie *et al.* (2018) who relied on descriptive statistics as a basis of their findings. The improvement involved testing the significance of the independent variables using statistical modelling. Gou *et al.* (2011) found out that alcohol consumption was associated with breast cancer mortality which agrees with the study since alcohol use increased the rate of succumbing to cancer with a factor of 5.4373551. Lowry *et al.* (2017) however found no association between mortality due

to breast cancer and alcohol consumption. Stress after diagnosis was found to increase mortality due to breast cancer according to results from a study by Spiegel (2011) which agrees with this study which found that stress increases hazard with a factor of 1.1336900. Awareness of how to deal with breast cancer after diagnosis made the patients take the necessary measure which was then associated to reduce mortality among the breast cancer patients (Tazhibi & Feizi, 2014).

4.4.1 Model selection

Model selection was done by the help of Akaike information criterion (AIC). On fitting all the estimators the AIC was 1001.47. The burden of treatment was dropped to achieve an AIC value of 994.55. The stress was further dropped to achieve an AIC of 991.55. The next covariate to be dropped was regular exercise and awareness level, alcohol use and treatment period were found to be the best estimators since they gave the least AIC (989.30). The final model selected is presented in summarised in Table 11 and 12.

Table 11: Cox Model summary of the fitted Model

Variables	Coef	Exp(coef)	Se(coef)	Z value	p-value
Awareness_2	-0.8406	0.4315	0.4482	-1.875	0.0607
Awareness_3	-0.8554	0.4251	0.3999	-2.139	0.0324
Awareness_4	0.2456	1.2784	0.3572	0.687	0.4918
Awareness_5	-0.6919	0.7267	0.3650	-0.1.716	0.3817
Alcohol_use_2	0.3192	1.9974	0.4031	1.875	0.0861
Alcohol_use_3	0.3390	1.4036	0.4035	0.840	0.4008
Alcohol_use_4	1.3858	0.3628	0.3871	4.125	3.7e-05
Alcohol_use_5	0.3263	0.9365	0.3628	0.899	0.3685
Treatment period_2	-0.3068	0.7358	0.4644	-0.661	0.5089
Treatment period_3	-0.7094	0.4919	0.4070	-1.743	0.0814
Treatment period_4	0.2579	1.2942	0.3736	0.690	0.4900
Treatment period_5	0.3263	1.3858	0.3628	0.899	0.3685

Table 12: Summary Statistics of the fitted Model

	Statistics	χ^2	df	p-value
Fitted Model	Loglk	55.24	12	0.0000002
	Waldtest	53.32	12	0.0000004
	Logrank test	56.33	12	0.0000001

The fitted cox proportional hazard model is summarized as:

$$\ln(\text{odds of hazard rate/ succumbing to breast cancer}) = 0.4315 \text{ Awareness_2} + 0.4215 \\ + 1.2784 \text{ Awareness_3} + 0.7267 + 1.9974 \text{ Alcohol use_ 2} + 1.4306 \text{ Alcohol use_ 3} + \\ 0.3628 \text{ Alcohol use_ 4} + 0.9365 \text{ Alcohol use_ 5} + 0.7358 \text{ Treatment period_ 2} + 0.4919 \\ \text{Treatment period_ 3} + 1.2942 \text{ Treatment period_ 4} + 1.3858 \text{ Treatment period_ 5}$$

The likelihood-ratio, Wald and Score (Log rank) tests are asymptotically equivalent tests of the omnibus null hypothesis that all the β s are zero.

CHAPTER FIVE

SUMMARY, CONCLUSION AND RECOMMENDATIONS

5.1 Summary

Breast cancer diagnosis was found to accelerate occurrence of Mindfulness based among breast cancer survivors. Breast cancer diagnosis remains a huge emotional shock and patients often find it hard to accept this fact making it difficult to implement an effective treatment plan. This is largely contributed by the fact that breast cancer survival still remains very low in most developing countries. The main factors considered in accelerating the Mindfulness based stress were the stress involved in accepting the condition and living with the disease, the period taken for the patient to receive treatment, the financial burden involved in breast cancer treatment, ability to work on the right diet, having the right information to fight the disease and taking regular exercises. From the practitioners responses, working on stress, having the right information, getting timely treatment and observing the diet prescribed made the patients journey easier thus reducing the Mindfulness Based stress they experience. Regular exercises and abstaining from alcohol were not found to be of great relieve to the patients by the medical practitioners. Patients attributed to receiving much stress from the financial burden of treating breast cancer, getting the right treatment and accessing the right diet. Mindfulness-Based Stress Reduction measures can be considered a promising alternative for the treatment of breast cancer symptoms when combined with the right treatment. However, such measures have been faced with challenges in the counties studied due to the low education among women. Shyness and strong cultural practices hinders them from doing constant self-examination before and after diagnosis.

On analysing the data collected from several respondents ranging from the breast cancer survivors, medical practitioners and accessing available records from the hospitals some covariates were found to significantly affect survival rate while others had little impact. The mindfulness Based Stress found to significantly influence breast cancer survival rate in both Nyeri and Meru counties were stress, working on the right diet, getting the right information and assessing timely treatment with p-values were less than 0.05 within the range of 0.000143 and 0.04092. Patients who were able to adhere to strict discipline, frequently meet doctors, consult and undergo the necessary treatment procedures, turn to friends and family when one has a bad day, and using

ones favourite outlets to release pent-up frustration were able to give breast cancer a good fight. The study therefore supports that breast cancer survivors should undergo several counselling sessions until they are able to accept their condition enabling them to courageously fight the disease. Families and friends play a crucial role in ensuring that the patient stays positive about the treatment, enjoys constant support and receives the best medical care to fight the disease and emerge victorious.

A predictive model was developed to estimate breast cancer survival rate. The model was found to significantly predict survival rate with a probability value of $p = 0.0000119$. The model was used in determining breast cancer hazard rates which can be of great help to patients in working on survival. The study largely recommends patients to work on stress levels since failure to manage stress increased their hazards of succumbing to breast cancer with a factor of 1.1336900 which is 13.4%. The selected model was fitted with three covariates that give the least A.I.C value (989.30) which were alcohol use, awareness and treatment period.

Limitations encountered in the study were the inconsistent and inaccurate data given by breast cancer survivors and the scanty data gotten from the hospital's records. The records could not accurately capture all the MBS factors appropriately hence several observations were deleted due to inconsistency and hence excluded from the study failing to give the actual situation. The medical practitioners could not accurately identify the patients who strictly followed the diet and the regular exercises as advised.

5.2 Conclusion

Cox proportional hazard model was confirmed significant in predicting breast cancer survival rate among women in Meru and Nyeri Counties. Data was collected from Nyeri Referral and Meru teaching and referral hospitals. Most of the respondents found in these facilities were residents of neighbouring counties. Nyeri referral hospital attracted majority of the survivors from different counties since it's the largest in the eastern region and the vital chemotherapy services are among the services offered. The likelihood ratio test showed that MBS factors are significant in predicting hazard rates with a chi-square value of 66.7 and a p-value ($p = 0.0000119$). Factors that were found to significantly affect survival were coping well with tress, being able to access treatment as soon as diagnosis has been made, observing the right diet and being aware of how to handle the disease. Treatment period ($p = 0.000143$) was found to significantly affect survival rate compared to other covariates; lack of awareness ($p = 0.0010124$), ease of coping with stress ($p = 0.000514$) and observing the right diet ($p = 0.04092$).

To sum it all, fighting cancer is not only through treatment but also working on mindfulness-based stress will work well alongside treatment procedures since they affect the mind of the survivors directly. A patient who can manage stress, is able to observe the right diet, knows what to do and when and is able to access treatment the right time will have a pleasant outcome. The Kenya society should therefore concentrate on the best ways support can be rendered to the survivors in all ways possibly extending a helping hand, emotional support , compassion, hope to those women in our lives with breast cancer.

5.3 Recommendations

From the findings of this study the following were recommended:

- i. Use of Cox PH model with other statistical Models in estimating breast cancer survival rate and the hazard rates.
- ii. Comprehensive records of the patients' ability to cope with the Mindfulness-Based factors by the palliative care centres.
- iii. Thorough counselling and follow ups in palliative care centres and by other government agencies to help patients work on the Mindfulness-Based factors that were found to be statistically significant in improving the survival rate.

5.4 Further Research

From the findings, the following area was suggested for further research

1. Use of randomized block designs over a period not less than 9 months to help the researcher accurately study the patients' journey and their battle with MBS factors.

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APPENDIX I

THE MEDICAL PRACTITIONER QUESTIONNAIRE

Date.....

Introduction: The study involves developing a model to estimate Breast Cancer survival rate considering mindfulness-based stress. Please take a few minutes to fill in this questionnaire

Q1. How long have you been in this hospital?

Below one year [] One year [] between 1 and 5 [] above 5 years []

Q2. Approximately, how many breast cancer patients do you handle per year?

.....

Q3. What are some of the commonly Mindfulness-based Stress factors that patients often complain of in their battle with cancer?

.....
.....
.....

Q4. According to patient's follow-up records, how does working on the following factors affect the patient's well-being?

1) Diet Poor [] Average [] Good [] Excellent []

2) Physical activity Poor [] Average [] Good [] Excellent []

3) Alcohol intake Poor [] Average [] Good [] Excellent []

4) Costly burden of treatment Poor [] Average [] Good [] Excellent []

5) Treatment Period Poor [] Average [] Good [] Excellent []

6) Stress on diagnosis Poor [] Average [] Good [] Excellent []

7) Lack of awareness Poor [] Average [] Good [] Excellent []

Q5. How many fatalities do you record annually from breast cancer?

100 [] 200 [] between 200 and 500 [] above 500 []

Q6. What do you think facilitates to the high Breast Cancer mortality rate in Meru County?

.....
.....
.....

Q7. In your opinion what do you think should be done in trying to reduce female breast cancer mortality rates in Meru County?

APPENDIX II: THE BREAST CANCER SURVIVORS QUESTIONNAIRE

Date.....

Introduction: The study involves developing a model to estimate Breast Cancer survival rate considering mindfulness-based stress. Please take a few minutes to fill in this questionnaire. Please respond to all questions and do not write your names.

- 1) What is our age?
 - a) 18-25 years [] b) 26-35 years [] c) 36-45 years [] d) 46-55 years [] e) above 56 years []
- 2) For how long have you battled with breast cancer?
 - a) 1 year [] b) 2-3 years [] c) 4-5 years [] d) 6-8 years [] e) above 10 years []
- 3) How did you know that you are suffering from breast cancer?
 - a) Regular screening [] b) pain associated with disease [] c) other []
- 4) Are you receiving palliative care services?
 - a) Yes [] b) No []
- 5) Please read through the following statements and tick appropriately about how you have been able to cope with MBS factors

KEY: 1.Strongly Disagree 2.Disagree 3.Undecided 4.Agree 5.Strongly Agree

Statements on MBS factors	1	2	3	4	5
Once diagnosed with breast cancer I felt as if everything had come to an end					
Regular exercises makes me feel better					
Observing the diet prescribed helps me feel better					
Accessing treatment within the shortest time possible made my journey easier					
Getting the right information helped to face the disease bravely					
Making the treatment services cheaper would help reduce the heavy breast cancer burden					
Abstaining from alcohol use facilitated to my healing					

Thank you for your participation.

APPENDIX III: THE SIZE OF A RANDOMLY CHOSEN SAMPLE

The table for determining the size of a randomly chosen sample for a given population of N cases such that the sample proportion is within ± 0.05 of the population within a 95% level of confidence.

N	S	N	S	N	S
10	10	220	140	1200	291
15	14	230	144	1300	297
20	19	240	148	1400	302
25	24	250	152	1500	306
30	28	260	155	1600	310
35	32	270	159	1700	313
40	36	280	162	1800	317
45	40	290	165	1900	320
50	44	300	169	2000	322
55	48	320	175	2200	327
60	52	340	181	2400	331
65	56	360	186	2600	335
70	59	380	191	2800	338
75	63	400	196	3000	341
80	66	420	201	3500	346
85	70	440	205	4000	351
90	73	460	210	4500	354
95	76	480	214	5000	357
100	80	500	217	6000	361
110	86	550	226	7000	364
120	92	600	234	8000	367
130	97	650	241	9000	368
140	103	700	248	10000	370
150	108	750	254	15000	375
160	113	800	260	20000	377

Extracted from Kathuri and Pals (1993), Introduction to Educational Research, Njoro: Egerton University Press.

APPENDIX IV: CLEARANCE LETTER FROM THE ETHICS COMMITTEE

CHUKA

Telephones: 020 2310512
020 2310518



UNIVERSITY

P.O. Box 109
Chuka

**OFFICE OF THE CHAIRMAN
INSTITUTIONAL ETHICS REVIEW COMMITTEE**

Our Ref: CU/IERC/NCST/18/19

11th October , 2018

**THE CHIEF EXECUTIVE OFFICER
NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY AND INNOVATION
P.O. BOX 30623-00100
NAIROBI**

Dear Sir/Madam,

**RE: RESEARCH CLEARANCE AND AUTHORIZATION FOR MWENDWA N.
MUTWIRI. REG NO SM18/28963/16**

The above matter refers:

The Institutional Ethics Review Committee of Chuka University met and reviewed the above MSC, Research Proposal titled Modeling of the Effect of Mindfulness based Stress on Breast Cancer Survival Rate among Women in Meru County, using Cox Proportional Hazard Model” The Supervisors are Dr. Moses Muraya and Dr. Lucy Gitonga

The candidate has amended the issues which were highlighted in the check list, the permit should therefore be issued

Kindly assist the student get the research permit.

Yours faithfully,

A handwritten signature in blue ink, appearing to read 'Adiel Magana', is written over a horizontal line.

Prof. Adiel Magana

**CHAIR
INSTITUTIONAL ETHICS REVIEW COMMITTEE**


cc: BPGS

APPENDIX V: NACOSTI AUTHORIZATION


THIS IS TO CERTIFY THAT:
MS. NANCY MWENDWA MUTWIRI
of CHUKA UNIVERSITY, 109-60400
CHUKA, has been permitted to conduct
research in Tharaka-Nithi County


on the topic: MODELLING OF THE
EFFECTS OF MINDFULNESS BASED
STRESS ON BREAST CANCER SURVIVAL
RATE AMONG WOMEN IN MERU
COUNTY, KENYA, USING COX
PROPORTIONAL HAZARD MODEL

for the period ending:
25th July, 2020


Applicant's
Signature

Permit No : NACOSTI/P/19/62642/31366
Date Of Issue : 26th July, 2019
Fee Received :Ksh 1000




Director General
National Commission for Science,
Technology & Innovation

APPENDIX VI: NACOSTI PERMIT



NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY AND INNOVATION

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2241349,3310571,2219420
Fax: +254-20-318245,318249
Email: dg@nacosti.go.ke
Website : www.nacosti.go.ke
When replying please quote

NACOSTI, Upper Kabete
Off Waiyaki Way
P.O. Box 30623-00100
NAIROBI-KENYA

Ref No. **NACOSTI/P/19/62642/31366**

Date: **26th July, 2019**

Nancy Mwendwa Mutwiri
Chuka University,
P.O. Box 109-60400,
CHUKA.

RE: RESEARCH AUTHORIZATION

Following your application for authority to carry out research on "*Modelling of the effects of mindfulness based stress on breast cancer survival rate among women in Meru County, Kenya, using cox proportional hazard model*" I am pleased to inform you that you have been authorized to undertake research in **Tharaka Nithi County** for the period ending **25th July, 2020**.

You are advised to report to the **County Commissioner, the County Director of Education and the County Director of Health Services, Tharaka Nithi County** before embarking on the research project.

Kindly note that, as an applicant who has been licensed under the Science, Technology and Innovation Act, 2013 to conduct research in Kenya, you shall deposit a **copy** of the final research report to the Commission within **one year** of completion. The soft copy of the same should be submitted through the Online Research Information System.

**GODFREY P. KALERWA MSc., MBA, MKIM
FOR: DIRECTOR-GENERAL/CEO**

Copy to:

The County Commissioner
Tharaka Nithi County.