ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF PUBLIC HEALTH

DETERMINANTS OF SURVIVAL AMONG PATIENTS WITH BREAST CANCER IN HAWASSA, SOUTHERN ETHIOPIA: A RETROSPECTIVE STUDY, 2019

BY

ABEL SHITA BOGALE (BSc)

A THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCE, SCHOOL OF PUBLIC HEALTH FOR THE PARTIAL FULFILLMENT OF THE REQUIREMENTS IN MASTERS OF PUBLIC HEALTH IN EPIDEMIOLOGY AND BIOSTATISTICS.

SEPTEMBER, 2019

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Advisors:

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Abbreviations/ Acronyms

AHR	Adjusted hazard ratio
AJCC	American Joint Committee on Cancer
BC	Breast Cancer
CHR	Crude hazard ratio
cT	Clinical tumor size
CT	Computed tomography
DMFS	Distant Metastasis Free Survival
ENT	Ear, Nose and Throat
GLOBOCAN	Global organization board of cancer association network
HIV	Human Immune-deficiency syndrome
HR	Hazard ratio
HUCSH	Hawassa University Comprehensive Specialized Hospital
IBC	Inflammatory Breast Cancer
LMICs	Low to Middle Income Countries
LTF:	Loss to follow up
MFS:	Metastatic Free Survival
MRI:	Magnetic resonance imaging
MRM:	Modified radical mastectomy
NCCP:	National Cancer Control Plan
OS:	Overall Survival
SNNPR:	Southern Nation Nationalities and People Regional state
TNM:	Classification based on Tumor size, Nodal status, and Metastasis status
US:	United States
WCA:	Worst case analysis
WHO:	World Health Organization
YIMSC:	Yanet Internal Medicine Specialized Center

Abstract

Background: Breast cancer (BC) is the second most common of all cancers and the commonest in women contributing 12% of all new cancer cases and 25% of all cancers in women. It is the most prevalent cancer in Ethiopia. Even if the estimation of BC survival is beneficial to improve the current breast cancer care & treatment, studies are lacking in Ethiopia.

Objectives: To identify determinants of survival and to estimate cumulative survival probabilities of patient's with BC that are diagnosed from 2013-2018 in Hawassa University Comprehensive Specialized Hospital and Yanet Hospital.

Methods: A health facility-based retrospective study of 302 patients was conducted. The median survival was estimated by Kaplan- Meier. Log Rank test was used to compare survival among groups. Cox proportional hazards model was used to identify determinants. Results were repaired as hazard ratio (HR) along with the corresponding 95% CI. Sensitivity analysis was done with the assumption of lost to follow-ups (LTF) might die 3 months after last hospital visit.

Results: Majorities (83.4%) were presented at an advanced stage. The study participants had followed for a total of 4685.62 person-months. Their median survival is 50.61 months (IQR=18.38-50.80) declined to 30.57 months in worst case analysis (WCA), the outcome of 57 patients were unknown (majorities, 96% being advanced stage) and 67 patients were died. The overall survival (OS) of patients at two years is 69.3% (61.30, 76.03) and it declines to 51.3 % in WCA. Rural residence (AHR=2.71, 95% CI: 1.44, 5.09), travel time ≥ 7 hours (AHR=3.42, 95% CI: 1.05, 11.10), duration of symptom 7-23 months (AHR=2.63, 95% CI: 1.22, 5.64), > 23 months (AHR=2.37, 95% CI: 1.00, 5.59), advanced stage (AHR=3.01, 95% CI: 1.05, 8.59) and not taking chemotherapy (AHR=6.69, 95% CI: 2.20, 20.30) were independent predictors of death. Through WCA, rural residence, advanced stage of BC, not having breast surgery, poor adherence to chemotherapy were independent predictors of death.

Conclusion: The 2 years OS is low in Hawassa (69.3% and declines to 51.3% in WCA). Rural residence, advanced stage and poor adherence to chemotherapy were independent determinants of death. Increasing early diagnosis of BC and access to cancer treatment is mandatory.

Keywords: Breast cancer, Survival, Determinants, Ethiopia

1. INTRODUCTION

1.1. Background

Cancer is a group of diseases that cause cells in the body to change and spread out of control. Most types of cancer cells eventually form a lump or mass called a tumor and are named by the part of the body where the tumor originates (1).

According to Global organization board of cancer association network (GLOBOCAN) estimation, there would be 18.1 million new cases and 9.6 million cancer deaths worldwide in 2018(2). World Health Organization (WHO) had estimated that among all causes of death, cancer accounts for 7 % in Ethiopia (3). Among females, breast cancer (BC) is the most commonly diagnosed cancer and the leading cause of cancer death (2).

Breast cancer produces no symptoms when the tumor is small and most easily treated. Thus, screening is important for early detection. The most common physical sign is a painless lump that may spread to underarm lymph nodes and causes swelling, even before the tumor is large enough to be felt. Less common signs and symptoms include breast pain or heaviness; persistent changes such as swelling, thickening, or redness of the skin; and nipple abnormalities such as spontaneous discharge (especially if bloody), erosion, or retraction (1).

Nowadays, both the diagnosis and mortality of cancer are increasing annually and breast cancer becomes the commonest cancer, constituting 33% of the cancers in women and 23% of all cancers identified from the Addis Ababa cancer registry (4, 5).

The average 5-year survival rates of patients with BC are more than 80% in developed countries and less than 60 percent in Low to middle-income countries (LMICs). The low survival rate in LMICs can be explained mainly by late-stage disease (6, 7). The only available study in Ethiopia exposed that the two year overall survival is 53%(8) which is far below other developed and developing countries. Thus, recent studies with this regard are insufficient in Ethiopia. Therefore, studying breast cancer survival and its determinants is crucial to fill information gap, to evaluate the extent of care provided and can be an input for policymaking.

1.2. Statement of the problem

Worldwide, about two-thirds of annual cancer deaths occur among women. It was estimated that there would be 2.1 million newly diagnosed female BC cases in 2018, accounting for almost 1 in 4 cancer cases among women. BC is the most frequently diagnosed cancer in the vast majority of the countries (154 of 185) and is also the leading cause of cancer death in over 100 countries (2, 9).

For many cancers, incidence rates are generally 2 to 3-fold higher in transitioned compared with transitioning economies. It varies greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. However, the differences in mortality between these 2 regions are smaller, in part because of a higher case fatality for many cancer types in LTMICs (2).

In Ethiopia, about 7 % of mortality is due to cancer (3). The annual incidence of cancer is around 60,960 cases and the annual mortality over 44,000. The most prevalent cancers in Ethiopia among the entire adult population are BC (30.2%), cervical cancer (13.4%) and colorectal cancer (5.7%). The estimated prevalence of BC case in 2015 was 13,987 with a crude incidence rate of 28.2 per 100,000. The trend of BC significantly increased year to year among females than males (4, 10).

World Cancer Research Fund International reported that, in many countries with advanced medical care, the five-year survival rate of early-stage breast cancers is 80–90 percent, while it falls to 24 percent for advanced stage(7). Five-year survival was 89% in Hawaii, 7.3% in Brazil, 67.6% in Iran, 63% in Mexico (11-14), and 51.8% in Uganda, 24% in Nigeria (15, 16). The only available studies in Ethiopia show that it is far below other developed and developing countries. The overall 5-year metastatic free survival (MFS) is 46% and the overall 2-year survival of patients with BC is 53% in rural Ethiopia(6, 8).

Predictors of survival of patients with BC include tumor characteristics such as metastasis, advanced disease stage, lymphovascular space invasion, and extracapsular extension triple-negative tumor type, multiple metastases sites, , maintenance endocrine therapy (17-20). A study conducted in Ethiopia found that young age, advanced stage of cancer are associated with decreased MFS and lymph-node positive disease, clinical tumor size 3 and 4, and hormone receptor-negative disease are found to be associated increased OS (6, 8).

Scholars are warning, unless urgent action is taken, BC will compound Sub-Saharan Africa's disease burden, increase poverty and gender inequality as well as reverse the current global gains against maternal and neonatal mortality (21).

United nation had planned to reduce premature mortality from non-communicable diseases including cancer by one third by 2030 (22). In line with this, Ethiopia had drafted a national cancer control program (NCCP) in 2015. The strategies of the program are enhancing surveillance for cancer & its risk factors, strengthening, monitoring and evaluation of cancer control activities (9). However, even if there is a focus at the policy level, there is only one radiation therapy center in Tikur Anbesa Specialized Hospital (TASH) and very limited chemotherapy centers nationally (8). As to the knowledge of the author, there is only one study on the overall survival of BC in Ethiopia. A prospective study in western rural Ethiopia was done on 107 patients most of them treated with only adjuvant surgery (8). However, the role of adjuvant chemotherapy and stage of BC is not considered.

Hence, this study could fill the information gap by estimating overall survival and identifying its determinants in settings that have adjuvant therapies except for radiation.

1.3. Significance of the study

Reducing mortality from cancer had given focus on sustainable development goal and on Ethiopian NCCP (9, 22). The strategies of NCCP are enhancing surveillance for cancer & its risk factors, strengthening, monitoring and evaluation of cancer control activities (9). To achieve the goals of global and national programs, knowing the breast cancer patient's overall survival and its determinants will have a paramount importance.

Surveillance of cancer survival is also seen as vital by stakeholders. It is being used to formulate cancer control strategies, to prioritize cancer control measures, and to assess both the effectiveness and cost-effectiveness of those strategies (23). However, there is very little evidence in Ethiopia to support this.

Therefore, the finding of this study is aimed to feel information gap, use as a baseline for future comparison or evaluation of the progress in the quality of BC care and treatment, and it could be important for health programmers, health professionals and future researchers.

For health programmers, the finding of this study is important to design evidence-based intervention strategies for improving BC care and treatment and in turn to increase patient's

survival. Similarly, the finding is also key for health professionals to provide evidence-based counseling and interventions. The finding of the study could also be a baseline for future studies and suggest possible research questions that need further study.

2. LITERATURE REVIEW

2.1. Breast cancer

Globally, BC is the most frequently diagnosed and the leading cause of cancer mortality among women, with an estimated 1.7 million cases and 521,900 deaths in 2012. It accounts for 25% of cancer cases and 15% of cancer deaths among women worldwide. Despite LMICs like Sub Saharan Africa have lower incidence, mortality rates are higher because of diagnosis at a late stage and limited access to treatment (24).

It is also reported that the most prevalent cancers in Ethiopia among the entire adult population is BC (30.2%). A study that review sixteen years data in TASH back from 2015 revealed that the trends of BC case significantly increased year to year among females (4, 10).

2.2. Survival of patients with breast cancer

Average 5-year survival rates are more than 80% in developed countries compared with less than 60 percent in LMICs and less than 40 percent in Algeria (7), and it was 67.6 % among Iranian women as reported from a result of systematic review and meta-analysis (13). It was 77.3% in Goiânia-GO Brazil (11), 63% in Mexico (14), 89% in Hawaii (12). A study in Iran Yazd also revealed that the overall five-year survival of women with BC was 62.5%, and 1-year until 5-year cumulative survival for breast cancer patients was 95%, 86%, 82%, 76%, and 70%, respectively (25).

The five-year breast cancer survival rate in Lagos, Nigeria was 24.1% (16) and 51.8 % in Uganda (15). In Ethiopia, a study conducted in Tikur Anbesa Hospital in 2011 revealed that MFS of patients after 2 and 5 years was 74% and 46%, respectively (6)and in rural part of Ethiopia in 2016, the estimated 1- and 2-year overall survival probability rates were 78 and 53%, respectively (8).

2.3. Determinants of survival of patients with breast cancer

2.3.1. Sociodemographic variables

An international review and meta-analysis by Romi Carriere et al. showed us out of 39 studies included in a meta-analysis, 36 had found evidence of poorer cancer survival in rural areas. After aggregating results, the study concluded that rural-dwellers are 5% less likely to survive

from cancer (HR =1.05; 95% CI 1.02–1.07) (26). Similarly, a study by Mia Hashibe et al. in Utah revealed that rural residents had a five-year relative survival that was 5.2% lower than metropolitan residents and a 10% increase in the risk of death (27).

Age at diagnosis of BC was a significant prognostic factor in many studies. A study in Iran Yazd revealed that women aged less than 50 years old had better survival compared to women aged more than 50 years old. Women >60 years at the time of diagnosis were 2.6 times more likely to die before 5 years survival of BC when compared to women <60 years HR=2.6 (95% CI (p=0.009) (25). On another study in Mexico, young age (<40 years) was positively associated with metastatic breast cancer during the follow-up period. Young patients (≤ 40 years) showed a statistically significant decrease in survival than old-aged (40 years) patients (p=0.003)(14). In Ethiopia, MFS was highest in women aged 50–59 years (63.4%) and was lower in < 30 years (38.6%). The HR for distant metastasis of patients <30 years of age was higher (HR = 3.20, 95% CI 1.99, 5.14) compared with that of women aged 50–59 years (6). In western Ethiopia, there was a tendency for very young women (< 35 years) to have worse overall survival compared to patients ≥ 35 years (8). However, the age of women at diagnosis was not associated with terminal illness/death in a study in South Africa(28).

2.3.2. Clinical characteristics of the breast cancer

A study in Rwanda by Lydia E. Pace et al. showed us when compared with patients presented within 3 months after the onset of symptoms, patient delays of 6–12 months and ≥12 months increased the odds of more advanced-stage disease (p = 0.006) (29). And this, in turn, can bring decreased survival.

In Mexico, A lower 5-year survival rate (38%, p ≤ 0.001) was observed in patients with tumors greater than or equal to 5 cm when compared with patients with a tumor size <2 cm (14). The corresponding 2-year survival for patients with cT4 tumors was 25% versus 68% for patients with cT1–2 tumors (cT1–3 vs. cT4 HR 1.86; 95% CI 1.82–13.63) (8).

In Iran-Yazd, a significant difference was observed between lymph node involvement and survival rates, 40.1% of patients with lymph node involvement and only 17.5% of the patients without lymph node involvement died during the study (25). Similarly, in a study in rural Ethiopia, the 2-year survival for patients with clinically positive lymph nodes was 44%

compared to 73% for patients with lymph node-negative disease (HR=2.44; 95% CI 1.19–5.02) (8).

A study by Dawood S. et al. in a study in US explored, patients with stage IIIB and IIIC disease had a 63% (HR= 0.373, 95% CI; 0.296–0.470) and 31% (HR= 0.691, 95% CI; 0.512–0.933) decreased risk of death from IBC compared with women with stage IV disease (30). In a study in Mexico, patients on advanced stage showed the lowest survival rate (40.0%) when compared with patients at earlier stages (p<0.001) (14). A similar finding is observed in Hawaii (HR 11.2; 95% CI 4.97-25.3) (12).

In South Africa, 3-year survival was 84% for early-stage (I/II) and 56% for late-stage (III/IV) tumors (HR 2.8 (95% CI; 1.9–4.1) (28). In Nigeria, the survival of women with early-stage disease (TNM Stage I) for one, three and five years was 100%, 100%, and 71% respectively. For women with TNM Stage II, it was 95%, 74%, and 37% respectively for the same years. The worst scenario observed for one, three- and five-year survival for TNM Stage III was 95%, 50%, 28%and for TNM Stage IV 84%, 20%, and 3%. (16). In Uganda, the 2-year survival probabilities were 94% for early-stage and 56% for advanced-stage (P=0.002), whereas those for 5-year survival were 74% for early-stage and 39% for advanced stage (P=0.001). The overall 5-year survival was 56% (31). In Ethiopia, women with stage 3 disease had a considerably worse MFS than patients with stage 1/2 disease, showing an HR of 2.62 (6).

Patients with ductal histology had the best MFS (56.1 %) compared with lobular (41.8%) and other entities (33.7%). The hazard ratio for women with lobular BC was HR=1.65, 95% CI; (1.02, 2.67) when compared to ductal (6).

A study in Nigeria had also reported a better survival of postmenopausal patients (70.6%) at 36 months as compared to premenopausal (68.5%) patients (p=0.05) (32)

2.3.3. Breast cancer therapy

A single recent study in southwest china by Yuxin Xie revealed that the overall survival of stage-IV BC patients was significantly higher among patients who had surgery. Patients in the surgery group had dramatically longer OS (45.6 vs 21.3 months, log-rank p< .001). And surgery was an independent prognostic factor for OS (AHR= 0.569; 95% CI, 0.329–0.984)

(33). Similarly, a study in the US that separately studied the survival of women with an advanced stage of BC revealed that those who had surgery of primary tumor have increased the chance of survival (AHR=0.543; 95%CI, 0.416, 0.708) (30).

A retrospective study by Achim Wockel et al. showed us there is an association between guideline adherence to chemotherapy and overall survival. Those who didn't adhere to chemotherapy are 2.59 times increased risk of death and 2.12 times increased the risk to develop recurrent BC, AHR= 2.59; 95% CI, 2.02, 3.31 and AHR=2.21; 95%CI, 1.67, 2.69 respectively (34). However, a study by Hancke K. et al. revealed that adherence to chemotherapy didn't show a significant difference in the survival of women with BC ≥ 70 years (35).

Conceptual frame work

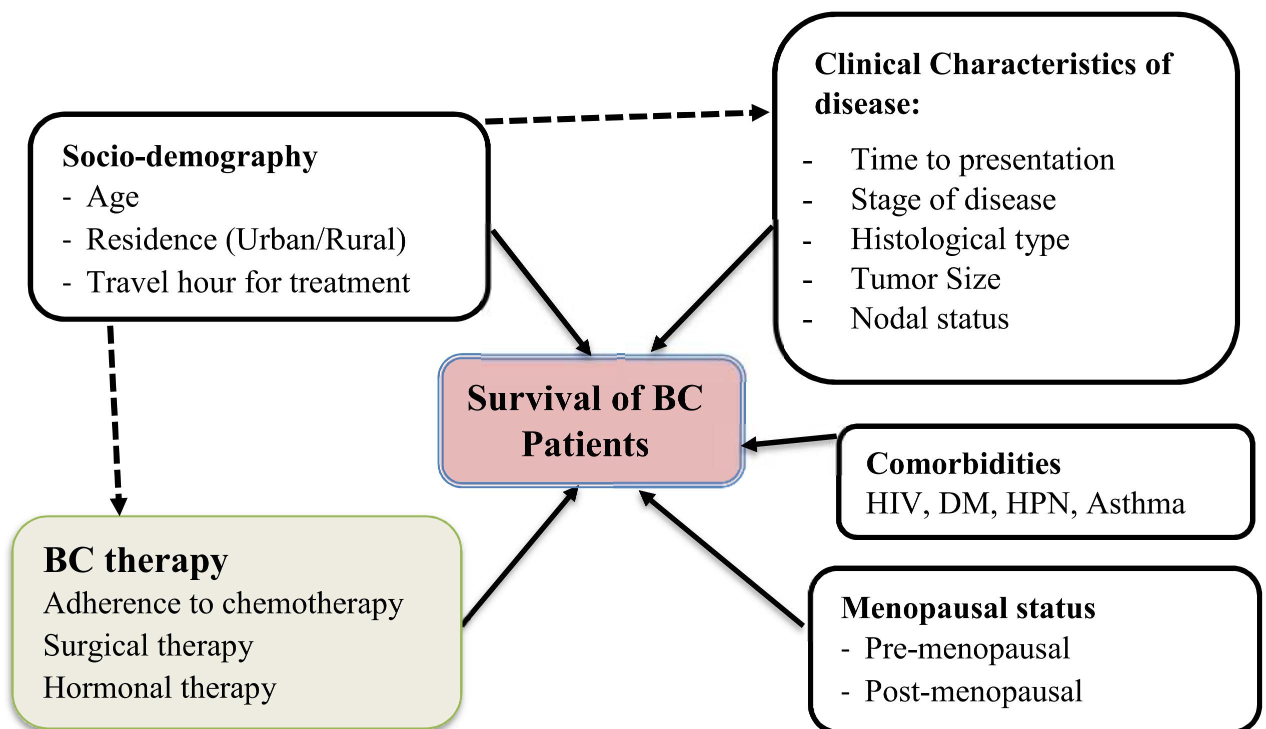

Figure 1: A conceptual framework for the determinants of survival of patients with breast cancer, developed after a review of different literatures, (Prepared, 2018).

Research question

1. How much is the cumulative probability of survival of patients with breast cancer to the end of the study?
2. What are the determinants of the survival of patients with breast cancer?

Hypothesis:

HA: Socio-demographic characteristics, clinical characteristics of tumor and breast cancer therapy can determine survival of patients with BC.

3. OBJECTIVES:

3.1. General objective

To identify determinants and estimate cumulative survival probabilities of the patient's with breast cancer that are diagnosed from 2013-2018 in Hawassa University Comprehensive and Specialized Hospital and Yanet Hospital.

3.2. Specific objectives

3.2.1. To estimate the cumulative probability of survival of patient's with breast cancer

3.2.2. To identify the determinants of survival of patient's with breast cancer

4. METHODS AND MATERIALS

4.1. Study area and period

This study was conducted in Hawassa University Comprehensive Specialized Hospital (HUCSH) and Yanet Internal Medicine Specialized Center (YIMSC) which are found in Hawassa, the capital city of SNNP Regional State. Hawassa city is 273 km from Addis Ababa to the south, 130 km east of Sodo, and 75 km north of Dilla. The city harbors 350,000 population (36).

In Hawassa, there are 6 hospitals (2 are owned by the government, 4 by private) (37). HUCSH and YIMSC are the selected institutions for this study since they offer cancer treatment.

HUCSH had started to give health services in 2006. It provides a diversity of services for about 15 million populations from all over SNNPRS and neighboring regions. The hospital offers services at general and specialized levels. It is the first hospital in south Ethiopia that launch the oncology unit initially for breast cancer in 2013(38). Recently, the oncology unit has one oncologist, one oncology trained physician, nine oncology trained nurses, four untrained nurses, and one pharmacist. Concerning investigation modalities basic laboratory tests are available, it provides FNAC and biopsy tests, CT scan gives service intermittently and a new MRI is about to begin service. However, no tumor marker is available.

Yanet Internal Medicine Specialized Center (YIMSC) is a privately-owned center which is established in 2012. It is the only privately-owned center that provides chemotherapy for cancer patients in Hawassa. It provides FNAC, biopsy and imaging services.

The study includes patients with BC that are diagnosed in HUCSH and YIMSC from January-1st, 2013- December 30th, 2018. Data was collected from February 8th to April 30th, 2019.

4.2. Study Design

A health facility-based retrospective study was employed.

4.3. Source Population

All women with breast cancer who were diagnosed in HUCSH and YIMSC.

4.4. Study Population

All women with BC who were diagnosed from January-1st, 2013- December 30, 2018 in HUCSH and YIMSC and who are eligible for the study.

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion criteria

All women patients with BC who were diagnosed and enrolled in HUCSH and YIMSC cancer treatment centers from January-1st, 2013- December 30, 2018 were included.

4.5.2. Exclusion criteria

Charts with unconfirmed BC, unknown stage of BC and recurrence at first visit are excluded.

4.6. Sample Size determination

To estimate the cumulative probability of survival of BC patients, a single population proportion formula was used. The 2-year overall survival of patients with BC in a study in rural Ethiopia is 53%(8). By assuming critical value at 95% certainty ($Z\alpha/2 = 1.96$) d = margin of error (d =0.05) the sample size was 384.

$$n = (Z\alpha/2\,)^2 * \frac{\mathbf{p(1-p)}}{\mathbf{d2}} \quad n = (1.96\,)^2 * \frac{\mathbf{0.53(1-0.53)}}{\mathbf{(0.05)2}} = \mathbf{384}$$

For the second objective, the sample size was calculated using two population proportion formula using Epi-Info version 7 for selected variables to obtain maximum sample size with the assumption of 95% confidence level, power (1-β) = 80%, and exposed to an unexposed ratio of 1.

Considering stage of disease as a factor, 15% outcome among unexposed and 34% outcome among exposed (6) and the final sample size calculated is **180.**

Outcome among unexposed (negative lymph node) is 27% and outcome among exposed 56% (8), the final calculated sample size is **102.**

Therefore, the largest of these all results **(384)** is taken as the final sample size. However, since the total number of patients is less than the calculated sample size, all patients are considered in the study.

4.7. Sampling Procedure

A total of 292 BC patient charts were obtained in HUCSH that are diagnosed from January-1st, 2013 to Dec, 30, 2018. Among these, 21 charts were excluded and a total of 271 charts were included in the study. In YIMSC, 45 patients with BC were diagnosed from July 8th,

2016 to December 30th, 2018 and only 35 patients' information was available on the database, manual patient cards were unavailable. Out of these, 4 31 patients were included in the study.

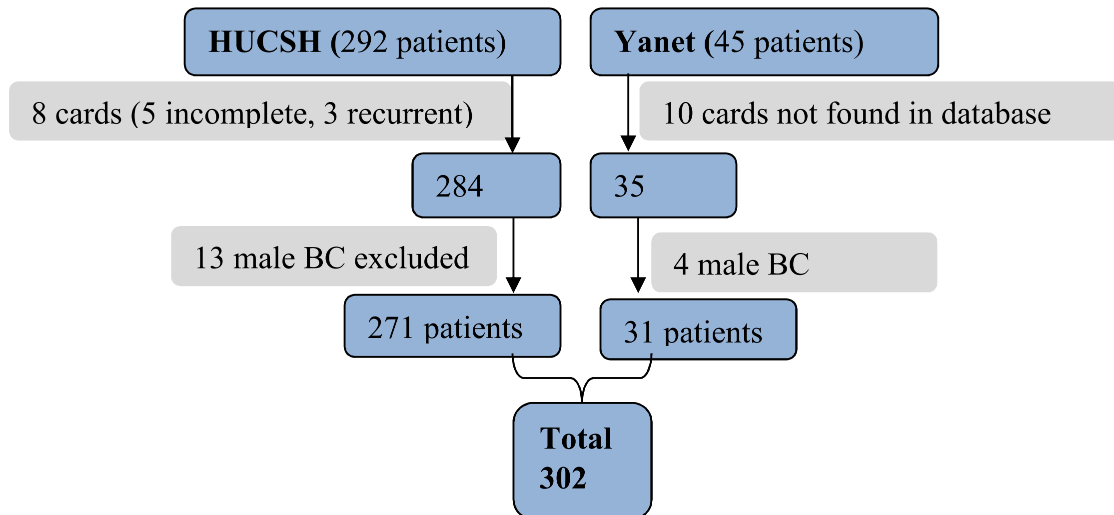

Figure 2: Sampling procedure to obtain study participants from HUCSH & YIMSC, 2018

Out of 302 patients with BC, the phone number is not found on 13 patient cards. Among 289 cards that have a telephone number, a telephone interview was made with 206 patients or with their close relatives who are > 18 years of age. The rest of the phone call trials were not successful with three and more trials. Two of them, the language they spoke is unknown, 6 of them didn't respond for three call trials, 16 were mistaken phone numbers, and others were not functional.

4.8. Study variables

4.8.1. Dependent (outcome) variable

Time to death

4.8.2. Independent variables

Socio-demographic data: age, place of residence, marital status, level of education, religion, travel time to hospital and occupation.

Clinical and pathological characteristics of the disease: duration of symptom, stage of BC at diagnosis, tumor size, histological type, nodal status, nuclear grade, and distant metastasis.

Type of BC therapy: Adherence to chemotherapy, surgical therapy and hormonal therapy.

Co morbidities: HIV, hypertension, diabetes mellitus, Asthma.

All socio-demographic data including their telephone number was taken from the patient's medical chart and it was collected by telephone interview. For some patients that are not met by telephone, it was obtained from the nursing sheet in their chart. However, most of the patient charts have no such sheet.

Residence, patients travel time to the cancer treatment center was taken from a telephone interview. For those who are not met by telephone, but have the same address with interviewed participants, the most frequent response to that residence was recorded.

The stage of BC was determined by the American Joint Committee on Cancer staging system AJCC (seventh edition) using the information on tumor size (T) and nodal status (N) and metastasis (M) (39). Two observations are used for this regard; TNM staging at the time of diagnosis and the last follow up to confirm the progression of the disease. Tumor size is primarily ascertained by clinical examination of the oncologist, if not available it was obtained from biopsy. Histological type and nuclear grading are taken from biopsy results.

Patients with non-metastatic BC are treated with 8 cycles of adjuvant chemotherapy; 4 cycles of AC (Adriamycin + Cyclophosphamide) and four cycles of Taxol. Those with metastatic BC are treated with 6 cycles of AC.

The current status of patients (alive or dead) was confirmed by telephone or taken from the chart or if the patient has a follow-up after the end date of the study, she was registered alive.

Unexposed and exposed cases in this study respectively are; early-stage BC (stage I/II) and advanced-stage breast cancer (III/IV).

4.9. Data collection tools and procedure

Data collection tool: A structured record review checklist was developed after review of the literature and by assessing the availability of information from patients' cards (Annex II). For a telephone interview, a questionnaire was prepared based on the required information in English and translated to local languages (Amharic, Sidama and Affan Oromo) and then back to English to maintain consistency by experts.

Data collectors: The information was extracted by four trained BSc nurses from the cancer treatment center and one BSc nurse supervised the process and finally, a telephone interview was done by the head of nurses of the unit.

Data collection procedure: Primarily, all cards of patients with BC were identified by their medical record number, reviewed for eligibility, and the information was extracted. A phone call to patients with BC was made to assure their current status, whether they are alive or dead.

4.10. Data quality assurance

An assessment was made before two weeks of actual data collection in HUCSH to check its consistency and any ambiguousness of the questionnaire. Then based on the result, some modification was made on the data extraction checklist. A procedural guide for medical record data abstraction and telephone interview was prepared (Annex IX) and it was used for data collection training and used as a reference during data collection. Training was given to the supervisor and data collectors on the overall objectives of the research and on how to extract the information for two days before data collection. A clear explanation of the purpose of the study was provided for the respondents at the beginning of the interview. Close supervision was carried out by the supervisor and the principal investigator during data collection procedures. The data from each respondent was checked for its completeness, clarity, consistency by the data collectors and principal investigator.

4.11. Operational definitions

Exposure-variable: Unexposed (Early stage) and exposed groups (Advanced stage)

Early-stage BC: stage I/II based on TNM classification of AJCC.

Advanced-stage BC: stage III/IV based on TNM classification of AJCC.

Event (failure): patient death regardless of its cause. In worst case analysis, LTF patients that are unavailable by telephone calls considered as they developed event after 3 months of last date of hospital visit (6, 8).

Entry date: the first date of confirmation of BC which is obtained from biopsy, or FNAC.

End date of study: December 30th, 2018.

Exit date: end date of the study for those who are alive to the end, date of death for those who are dead, or last date of follow up for those who had visited the hospitals > 6 months and unavailable by telephone call.

Lost to follow up (LTF): patients that are lost from follow up for > 6 months.

Censored: patients that are alive at the end of the study are right-censored, those who developed the event or LTF are left-censored.

Overall survival: the proportion of patients with BC who were alive for a specific time point after diagnosis of BC.

Survival time: time from date of entry to date of death or end date.

Good adherence to chemotherapy: when patients had completed all cycles of chemotherapy as per the guideline(34).

Poor adherence to chemotherapy: when patients didn't complete all cycles of chemotherapy as per the guideline(34).

Main analysis: analysis of LTF patients as left censored and alive.

Worst case analysis: analysis of LTF patients by assuming as they developed the event 3 months after last date of hospital visit (6, 40).

4.12. Data analysis procedures

Data were coded, cleaned and explored to identify outliers, missing values, and inconsistencies. The coded data were checked for completeness and entered into EpiData version 4.4.3.1 and analyzed by STATA V.14.

Descriptive statistics of numeric variables are presented in medians with interquartile range (IQR), categorical variables are presented using frequency and percentages. Normality assumption was checked for age and travel time using the Shapiro-Wilk normality test and it was significant which means the assumption of normality was violated so that we have reported the median and IQR (interquartile range) for those variables. Chi-square test ($\chi2$) is used to assess associations between the stages of BC and other covariates. The overall survival was estimated by Kaplan- Meier. Log rank test was used to compare survival among groups with a confidence interval of 95%. Missing data were handled by simple deletion from the bivariate and multivariable analysis.

Bivariate Cox regression was done for all of the predictors. The assumptions of Cox proportional hazard regression model are checked by Log (-log (St) plots, Schoenfeld residual test.

Covariates that did not violate the assumption test and have 25 % ($p<0.25$) significant level on bivariate Cox regression were considered for multivariable cox regression. Breslow test was used to handle tied failures. A P-value of < 0.05 was considered to denote statistical significance. Multi-colinearity and interaction for the main effect model was checked, and

variance inflation factor greater than 10 was considered to denote its existence. Finally, goodness of fit of the model was assessed by Cox-Snell residual plot.

4.13. Ethical considerations

Ethical clearance and support letters were taken from research and ethical committee of Addis Ababa University School of Public Health. After an in-depth explanation of the aim of the study, formal permission was obtained from HUCSH and YIMSC to review patient records and contact patients on a phone call. Verbal consent was obtained by telephone from patients and for patients who are died it was obtained from patient's relatives (father, mother, husband or children > 18 years).

4.14. Dissemination of the result

The results will be presented to the School of Public Health, Addis Ababa University and will be reported for HUCSH, YIMSC, SNNPRS Health bureau. The result will also be disseminated through presentations on specific conferences and will be published in a scientific journal.

5. RESULTS

5.1. Description of patient's with breast cancer in the retrospective cohort

There were 337 patients with BC diagnosed from January-1st, 2013 to 30, Dec, 2018 in HUCSH and YIMSC. Out of 302 patients included in the study, a telephone interview was made with 206 patients or their relatives. The second review of patient charts was made after two months of the beginning of data collection and 29 patients that are unavailable by telephone had visited the hospitals between the months and thus, they are confirmed alive. Therefore, out of 302 BC patients, the outcome of 235 (77.8%) patients was confirmed (168 were alive, 67 were died), 57 (18.8%) patients were LTF and the rest 10 patients have visited the hospital within 6 months before the end date of the study. Out of 141 alive patients contacted by telephone, 101 (71.6%) reported they were working their usual job, 35 (24.8%) were ambulatory, 5 (3.5%) were bedridden. All relatives of deceased patients with BC believe the cause of patients' death is BC.

5.1.1 Socio-demographic characteristics

Out of 263 patients, 189 (71.8%) of them were from urban areas. Their median travel time to Hawassa is 2 hours (IQR=0.30-3.30 hours). Out of 302 BC women recruited to this study, the majority of them, 177(58.6%) were within the age of 35-50 years, the median age being 39 (IQR=32-45) years, 79.1% of them were pre-menopause. Out of 208 patients, majorities 178 (85.6%) were married, 108 (51.9%) were house wife's and 78 (37.5%) can't read and write (Table 1).

5.1.2 Clinical and pathological characteristics

Two hundred eleven (69.9%) of patients were diagnosed within the years 2016-2018 and the rest within 2013-2015. About one-third of BC patients, 208 (73.5%) came with complaints of breast lump and 171 (60.4%) were presented to oncology unit within 7-23 months of a complaint. Out of 196 patients whose tumor grade is available 109 (56.2%) were grade II (moderately differentiated). Out of all 302 BC patients, 50 (16.6%) were early stage, 252 (83.4%) were presented with advanced stage at the first hospital visit, 161(53.3%) were stage III and 91(30.1%) were stage IV. About 173 patients (58.8%) had tumor size III/IV, 249 (83.4%) had ductal carcinoma, 240 (84.2%) had positive lymph node, and 56 (18.54%) had

distance metastasis at the time of diagnosis. Thirty-five patients have comorbidity out of which, 23(7.6%) have hypertension, and five (1.6%) have HIV (Table 1).

Table 1: Socio-demographic and tumor characteristics of patients with breast cancer in HUCSH & YIMSC, 2013-2018.

Covariates	Category	Total Number (%)
Resident (n=263)		
	Urban	189 (71.86)
	Rural	74 (28.14)
	Total	263 (100)
Travel time (n=263)		
	< 3 hours	197 (74.9)
	3-6 hours	51 (19.39)
	≥ 7 hours	15 (5.7)
	Total	263 (100)
Age (n=302)		
	<35	82 (27.15)
	35-50	177 (58.61)
	>50	43 (14.24)
	Total	302 (100)
Menopausal status		
	Pre-menopause	239 (79.1)
	Post-Menopause	63 (20.86)
	Total	302 (100)
Breast complaint at first visit		
	Breast lump	208 (73.5)
	Breast ulcer	34 (12.01)
	Other #	41 (14.49)
	Total	283 (100)
Duration of symptom		
	0 - 6 months	110 (38.87)
	7 - 23 months	112 (39.58)
	> 23 months	61 (21.55)
	Total	283 (100)
Histological type		
	Ductal	249 (82.45)
	Lobular	24 (7.95)
	Other*	24 (8.08)
	Total	297 (100)

Stage of BC		
	Early	50 (16.55)
	Advanced	252 (83.44)
Tumor size		
	TI/II	121 (41.16)
	TIII/IV	173 (58.84)
	Total	294 (100)
Distant -metastasis		
	Yes	56 (18.54)
	No	246 (81.45)
	Total	302 (100)
Nodal status		
	Positive	240 (84.21)
	Negative	45 (15.79)
	Total	285 (100)
Co-morbidities		
	Yes	35 (11.59)
	No	267 (88.41)
	Total	302 (100)

NB: *#=shortness of breath, axillary swelling, nipple retraction, nipple discharge.* *******=Mixed ductal & lobular, mucious*

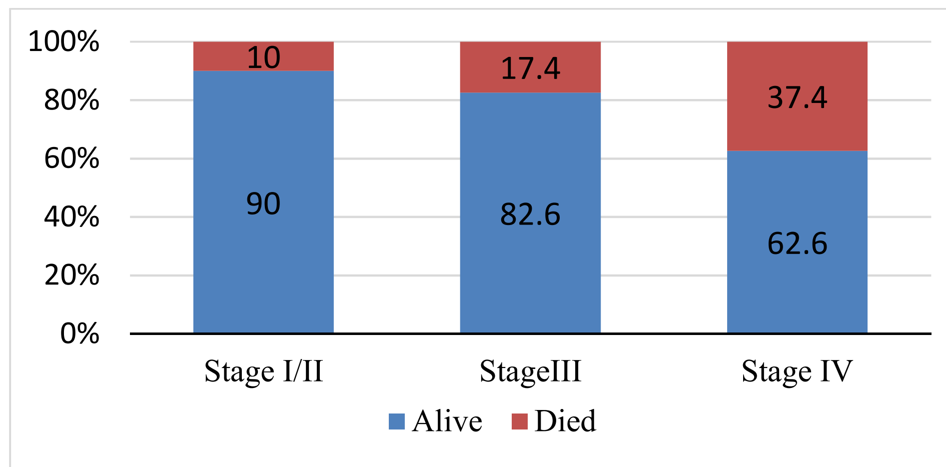

Figure 3: Stages of BC with proportions of death among patients with BC of HUCSH & YIMSC, 2013-2018.

5.1.3 Breast cancer therapy

One hundred twenty-eight (45.7%) patients had referral paper from another hospital and 69 (22.8%) are referred after they had surgery. A total of two hundred eight patients with BC were treated with breast surgery. Out of 190 patients with BC whose type of surgery is available on their chart, 173(91.05%) of them underwent MRM. Chemotherapy was

administered for 219 BC patients, out of this, 54(24.7%) had completed the treatment while 138 (63.0 %) had discontinued and 27 (12.3 %) were on schedule at the time of data collection. Out of 100 patients with BC that took hormonal therapy, 65(65%) were treated with Tamoxifen. Eight of patients with BC had taken radiation therapy at Tikur Anbesa Specialized Hospital.

Table 2: Breast cancer therapies and other characteristics of patients with breast cancer in HUCSH & YIMSC, 2013-2018.

Covariates	**Category**	**Number (%)**
Surgical therapy		
	Yes	208 (68.87)
	No	94 (31.13)
	Total	302 (100)
Type of surgery		
	MRM	173 (57.28)
	Toilet mastectomy	17 (5.63)
	No surgery	112 (37.09)
	Total	302 (100)
ACT		
	Good adherence	54 (19.64)
	Poor adherence	138 (50.18)
	No chemotherapy	83 (30.18)
	Total	275 (100)
Hormonal therapy		
	Yes	100(33.12)
	No	202 (66.89)
	Total	302 (100)
Hormonal therapy type		
	Tamoxifen	65 (21.52)
	Anastrazole	35 (11.59)
	No hormonal therapy	202 (66.89)
	Total	302 (100)
Recurrence		
	Yes	22 (7.28)
	No	280 (92.72)
	Total	302 (100)
Progression		
	Yes	40 (13.25)
	No	262 (86.75)
	Total	302 (100)

NB: ACT: *Adherence to chemotherapy*

5.1.4 Description of lost to follow-up patients with BC

Out of 57 LTF patients, 55 (96.4%) have an advanced-stage of BC. Among these, 28 (49.1%) of them have stage IV disease, and 21 (36.8%) have distant metastasis at time of diagnosis. The majority of them, 39 (68.4%) had breast surgery, even if 35 (61.4%) of them started chemotherapy, only 6 (10.5%) have had good adherence, only 9 (15.8%) were started hormonal therapy. For 84.2 % of them, their last date of contact was before the end of 2017.

5.2. Incidence density

Using the main analysis, the overall incidence density is 14.3/1000 patients per month. The mortality rate for urban and rural residents is 10.4 and 34.9 per 1000-patients per month. It is 10.5, 16.4 and 18.7 per 1000-patients per month for those who had presented before six month, 7-23 months and > 23 months respectively. The death rate for those who had good adherence, poor adherence to chemotherapy and no chemotherapy is 5.4, 12.5, and 26.8 per 1000 patient per month. The rest is presented on table 3.

Table 3: Incidence density of patients with breast cancer diagnosed in HUCSH & YIMSC, by groups of significant covariates on log-rank test, 2013-2018

Covariates	**Categories**	**Person time in months**	**Death**	**Rate (95% CI)/1000**
Residence	Urban	3447.23	36	10.4 (7.5, 14.4)
	Rural	858.28	30	34.9 (24.4, 49.9)
Travel time	<3 hours	3511.83	48	13.6 (10.3, 18.1)
	3-6 hours	595.23	12	20.1 (11.4, 35.4)
	≥7 hours	198.44	6	30.2 (13.5, 67.2)
Age in years	<35	961.45	23	23.9 (15.8, 35.9)
	35-50	3064.79	34	11 (7.9, 15.5)
	>50	659.37	10	15.1 (8.1, 28.1)
Time to presentation	0-6 months	1795.57	19	10.5 (6.7, 16.5)
	7 - 23 months	1824.76	30	16.4 (11.4, 31.1)
	> 23 months	799.63	15	18.7 (11.3, 31.1)
Stage of BC	Early	1231	5	4 (1.6, 9.0)
	Advanced	3454.61	62	17.9 (13.9, 23)
Surgical therapy	Yes	3719.63	37	9.9 (7.2, 13.7)
	No	965.98	30	31 (21.7, 44.4)
ATC	Good adherence	1091.27	6	5.4 (2.4, 12.2)
	Poor adherence	2476.92	31	12.5 (8.8, 17.7)
	No chemotherapy	1117.42	30	26.8 (18.7, 38.3)
Nodal status	Positive	3587.14	57	15.8 (12.2, 20.6)
	Negative	802.80	3	3.7 (12, 11.5)

NB: CI: *Confidence interval,* ***ATC:*** *Adherence to chemotherapy,*

5.3. Survival of patients with breast cancer

A total of 302 BC patients had followed for 4685.61-person-months or at-risk time. There were 67 confirmed deaths during follow-up period which is 72 months. The median follow-up time was 50.61 (IQR=18.38-50.80) months. The overall survival of BC patients at the end of one, two and three year is 83%, 69.3%, and 63.1%, respectively. The overall survival for early and advanced stage of BC at the end of 2 year was 89.9 % and 63.8 %, while it is 73.4% and 44.3% for stage III and IV respectively.

In the worst-case analysis, a total of 124 patients were considered as they developed event. The median survival of BC patients is 30.57 (IQR=7.23-64.23) months. The overall survival of patients at the end of one, two and three year is 67.03 %, 51.3 %, and 44.6 % respectively. The overall survival for early and advanced stage of BC at the end of 2 year is 85.1 % and 44.1 % and for stage III and IV it is 55.1% and 23.7% respectively.

Table 4: Life table of patients with breast cancer in HUCSH & YIMSC, 2013-2018

Intervals in month	BC patients at risk	Deaths	Censored	Survival	SE	95% CI	
						Lower	Upper
Early stage							
0-6	50	1	8	0.9783	0.0215	0.8555	0.9969
6-12	41	1	8	0.9518	0.0334	0.8195	0.9878
12-18	32	0	5	0.9518	0.0334	0.8195	0.9878
18-24	27	0	4	0.9518	0.0334	0.8195	0.9878
24-30	23	1	10	0.8989	0.0603	0.6934	0.9695
36-42	12	1	0	0.8240	0.0906	0.5549	0.9384
42-48	11	0	2	0.8240	0.0906	0.5549	0.9384
48-54	9	0	1	0.8240	0.0906	0.5549	0.9384
54-60	8	1	2	0.7063	0.1338	0.3637	0.8873
60-66	5	0	2	0.7063	0.1338	0.3637	0.8873
66-72	3	0	3	0.7063	0.1338	0.3637	0.8873
Advanced stage							
0-6	252	23	75	0.8928	0.0211	0.8431	0.9274
6-12	154	13	44	0.8048	0.0300	0.7379	0.8563
12-18	97	10	20	0.7123	0.0382	0.6297	0.7798
18-24	67	3	6	0.6789	0.0410	0.5911	0.7519
24-30	58	5	22	0.6067	0.0477	0.5065	0.6927
30-36	31	2	9	0.5609	0.0540	0.4488	0.6589
36-42	20	2	6	0.4949	0.0647	0.3633	0.6135
42-48	12	1	2	0.4499	0.0728	0.3048	0.5846
48-54	9	2	2	0.3375	0.0879	0.1759	0.5072
60-66	5	1	4	0.2250	0.1089	0.0597	0.4541

SE: *Standard error,* ***CI****: Confidence interval.*

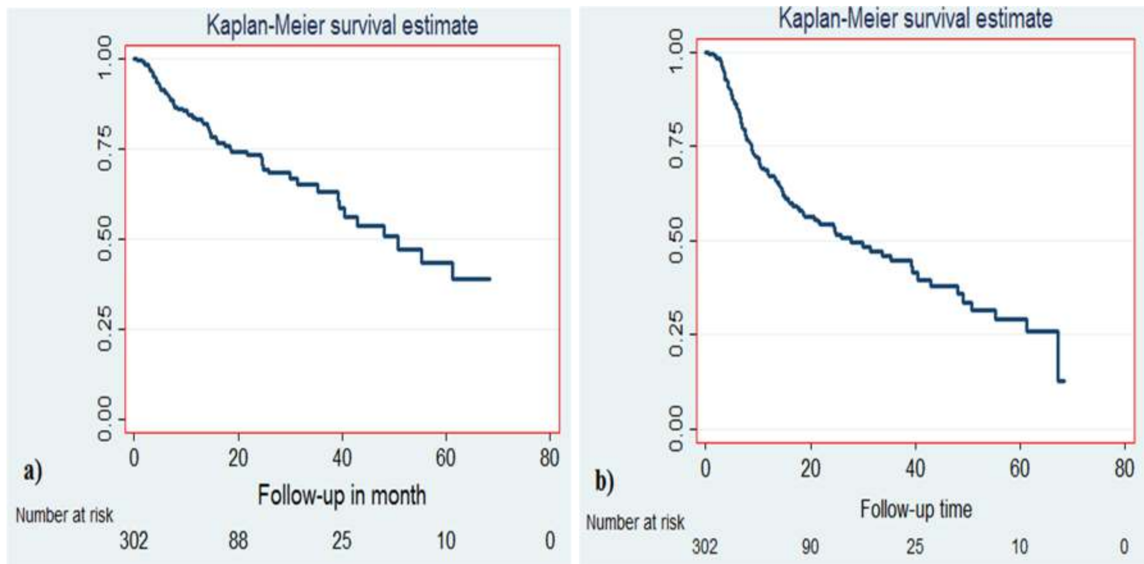

Figure 4: Kaplan-Meir curve showing time to death of patients with BC among patients of HUCSH & YIMSC, 2013-2018 a) Main analysis b) Worst case analysis

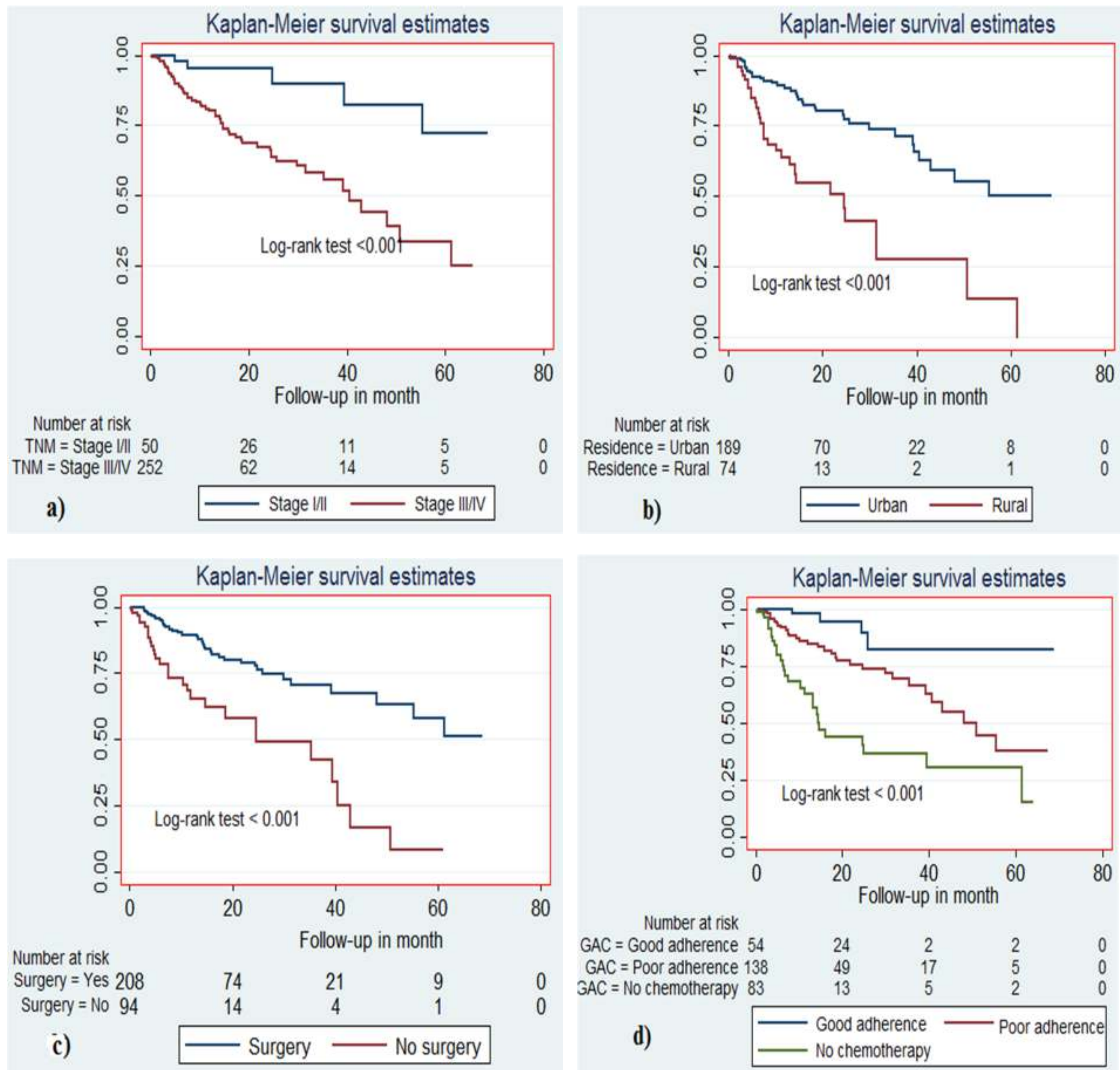

Figure 5: Kaplan-Meier survival estimates of patients with BC diagnosed in HUCSH and YIMSC 2013-2018 for significant covariates on Log-rank test, **a)** for stage of breast cancer **b)** for residence **c)** for surgical therapy **d)** for adherence to chemotherapy

5.4. Log rank test

Log-rank test for equality of survival function was made to assess the presence of a statistically significant difference in survival time between different categories of covariates. Then, it is found that there is significant difference in survival experience between categories of residence, age, stage of BC, nodal status, surgical therapy, adherence to chemotherapy, and hormonal therapy.

Table 5: Log-rank test for equality of survival function of patients with breast cancer diagnosed in HUCSH and YIMSC, 2018

Covariates	Category	Survival at 3 years (%)	Observed death	Expected death	X^2 (df)	Log-rank test (Pr > X^2)
Residence						
	Urban	71.4	36	52.13	24.5 (1)	**<0.001**
	Rural	27.5	30	13.87		
Age in years						
	<35	56.7	23	14.06	7.93 (2)	**0.019**
	35-50	70.2	34	43.65		
	>50	48.8	10	9.28		
Stage of BC						
	Early	89.8	5	17.52	12.76 (1)	**<0.001**
	Advanced	55.6	62	49.48		
Nodal status						
	Positive	58.9	57	48.74	7.75 (1)	**0.005**
	Negative	87.7	3	11.26		
Surgical therapy						
	Yes	70.5	37	53.07	23.81 (1)	**<0.001**
	No	42.0	30	13.93		
ACT						
	Good adherence	82.2	6	15.79		
	Poor adherence	66.1	31	35.27	19.33 (2)	**<0.001**
	No chemotherapy	36.6	30	15.95		
Hormonal therapy						
	Yes	85.2	13	35.64	32.36 (1)	**<0.001**
	No	41.3	54	31.36		

ACT: *Adherence to chemotherapy*

5.5. Predictors of survival of patients with breast cancer

5.5.1 Bivariate analysis

Out of all variables, nuclear grading and socio-demographic data (marital status, religion, educational status, occupation, and monthly income) have a missing value greater than 30% that, they are excluded from the analysis. From the theoretical point of view, distance metastasis and tumor size are excluded since they are considered in TNM staging of BC.

In bivariate analysis; resident category, age, stage of BC, surgical therapy and ACT were found to be significantly associated with survival of patients with BC at $p<0.05$.

Table 6: Bivariate Cox regression for predictors of survival of patients with breast cancer in HUCSH & YIMSC, 2013-2018

Covariates	Category	Died				
		Yes (%)	No (%)	CHR (95% CI)	p-value	P(PH)
Residence (n=263)						
	Urban	36 (19)	153 (81)	1		
	Rural	30 (40.5)	44 (59.5)	**3.29 (2.00, 5.24)**	**<0.001**	0.692
Travel time (n=263)						
	< 3 hours	48 (24.4)	149 (75.6)	1		
	3-6 hours	12 (23.5)	39 (76.5)	1.40 (0.73, 2.66)	0.304	0.970
	≥ 7 hours	6 (40)	9 (60)	2.22 (0.94, 5.20)	0.067	
Age in years						
	<35	23 (28)	59 (72)	1		
	35-50	34 (19.2)	143 (80)	**0.47 (0.27, 0.80)**	**0.006**	0.815
	>50	10 (23.3)	33 (76.7)	0.65 (0.31, 1.37)	0.265	
Menopausal status						
	Pre-menopause	55 (23)	184 (77)	1		
	Post-menopause	12 (19)	51 (81)	0.74 (0.39, 1.39)	0.352	0.191
Duration of symptom (n=283)						
	0-6 months	19 (17.3)	91 (82.7)	1		
	7 - 23 months	30 (26.8)	82 (73.2)	1.50 (0.84, 2.67)	0.163	0.352
	> 23 months	15 (24.6)	46 (75.4)	1.71 (0.87, 3.39)	0.119	
Stage of BC						
	Early	5 (10)	45 (90)	1		
	Advanced	62 (24.6)	190 (75.4)	**4.67 (1.85,11.76)**	**0.001**	0.557
Histological type						
	Ductal	59 (23.7)	190 (76.3)	1		
	Lobular	3 (12.5)	21 (87.5)	0.42 (0.13, 1.34)	0.146	0.840
	Other*	5 (17.2)	24 (82.8)	0.86 (0.34, 2.60)	0.758	
Nodal status (n=285)						
	Positive	57 (23.8)	183 (76.3)	1		
	Negative	3 (6.7)	42 (93.3)	**0.21 (0.06, 0.70)**	**0.011**	0.313
Co-morbidities						
	Yes	9 (25.7)	26 (74.3)	1		
	No	58 (21.7)	209 (78.3)	1.25 (0.62, 2.54)	0.525	0.604
Surgical therapy						
	Yes	37 (17.8)	171 (82.2)	1		
	No	30 (31.9)	64 (68.1)	**3.17 (1.94, 5.18)**	**<0.001**	0.722
ACT						
	Good adherence	4 (7.4)	50 (92.6)	1		
	Poor adherence	33 (23.9)	105 (76.1)	3.37 (1.19, 9.54)	**0.022**	0.224
	No chemotherapy	29 (34.9)	54 (65.1)	8.66 (3.03, 24.73)	**<0.001**	

__NB: P(PH)__ – Prob>X 2 global test for proportional-hazards assumption, __ACT:__ Adherence to chemotherapy, ***=Mixed ductal & lobular, mucious*

5.5.2 Multivariable cox regression analysis

Variables on bivariate analysis which are significant at a level of ($p<0.25$) and meet assumption test were candidates for multivariable Cox regression. Hormonal therapy and radiation therapy did not fulfill assumption tests for Cox proportional hazards model. Therefore, residence, travel time, age, duration of symptoms, stage of BC, histological type, nodal status, surgical therapy and adherence to chemotherapy fulfilled the above criteria's and are fitted to the final model. Patients' residence, travel time, time to presentation, stage of BC and adherence to chemotherapy were independent predictors of death.

BC patients that came from rural area had 2.71 increased risk of death as compared to urban dwellers (AHR=2.71, 95% CI: 1.44, 5.09). Patients with BC that travel >7 hours to Hawassa for cancer treatment had 3.42 times increased risk of death as compared to those traveled less than 3 hours (AHR=3.42, 95% CI; 1.05, 11.10). Patients that present to oncology unit within the range of 7 to 23 months after beginning of sign and symptoms of BC had 2.63 times increased risk of death (AHR=2.63, 95% CI; 1.22, 5.64) and those who came >23 months had 2.37 times increased risk of death (AHR=2.37, 95% CI; 1.00, 5.59) as compared to those patients presented within 6 months. Those who have advanced stage of disease had 3.01 times increased risk of death as compared to early stage (AHR=3.01, 95% CI; 1.05, 8.59). The hazard of death for patients that took no chemotherapy was 6.69 times (AHR=6.69, 95% CI; 2.20, 20.30) higher than those patients that have good adherence to chemotherapy.

In the worst-case analysis, significant association was observed between survival of patients with BC and residence, stage of BC, surgical therapy and adherence to chemotherapy. The hazard of death for rural residents with BC was 70% higher than urban residents (AHR=1.70, 95% CI; 1.02, 2.82). Patients that have advanced stage of BC had 4.16 times increased risk of death as compared to early stage (AHR=4.16, 95% CI; 1.62, 10.68). As compared to patients who had breast surgery those who had not breast surgery have 76% increased risk of death (AHR=1.76, 95% CI; 1.08, 2.88). The hazard of death for patients that have poor adherence was 2.45 times higher (AHR=2.45, 95% CI; 1.07, 5.59), and for those who didn't took chemotherapy was 5.57 times higher (AHR=5.57, 95% CI; 2.41, 12.87) than patients that have good adherence.

Table 7: Multivariable cox regression analysis model for survival of patients with breast cancer diagnosed in HUCSH & YIMSC, 2013-2018

Covariates	Category	Main analysis			Worst case analysis		
		CHR (95%CI)	AHR (95%CI)	p-value	CHR (95%CI)	AHR (95%CI)	p-value
Residence	Urban	1	1		1	1	
	Rural	3.29 (2.00, 5.42)	**2.71 (1.44, 5.09)**	**0.002**	2.34 (1.52, 3.53)	**1.70 (1.02, 2.82)**	**0.038**
Travel time	<3 hours	1	1		1	1	
	3-6 hours	1.40 (0.73, 2.66)	1.11 (0.52, 2.38)	0.773	1.22 (0.70, 2.11)	1.09 (0.59, 2.03)	0.772
	≥ 7 hours	2.22 (0.94, 5.20)	**3.42 (1.05, 11.10)**	**0.041**	2.19 (1.09, 4.40)	1.78 (0.72, 4.40)	0.207
Age in years	<35	1	1		1	1	
	35-50	0.47 (0.27, 0.80)	0.78 (0.38, 1.57)	0.489	0.54 (0.38, 0.83)	0.86 (0.50, 1.49)	0.608
	>50	0.65 (0.31, 1.37)	1.68 (0.65, 4.30)	0.275	0.67 (0.38, 1.19)	1.40 (0.66, 2.99)	0.373
Duration of symptom	0- 6 months	1	1		1	1	
	7-23 months	1.50 (0.84, 2.67)	**2.63 (1.22, 5.64)**	**0.013**	1.17 (0.78, 1.79)	1.29 (0.74, 2.25)	0.360
	> 23 months	1.71 (0.87, 3.39)	**2.37 (1.00, 5.59)**	**0.048**	1.59 (0.99, 2.56)	1.41 (0.76, 2.60)	0.267
Stage of BC	Early	1	1		1	1	
	Advanced	4.67 (1.85, 11.76)	**3.01 (1.05, 8.59)**	**0.040**	5.62 (2.60, 12.13)	**4.16 (1.62, 10.68)**	**0.003**
Histological type	Ductal	1	1		1	1	
	Lobular	0.42 (0.13, 1.34)	0.32 (0.07, 1.39)	0.132	0.54 (0.25, 1.18)	0.50 (0.19, 1.31)	0.162
	Other*	0.86 (0.34, 2.60)	0.18 (0.03, 1.07)	0.060	1.00 (0.53, 1.86)	0.70 (0.27, 1.80)	0.463
Surgical therapy	Yes	1	1		1	1	
	No	3.17 (1.94, 5.18)	1.57 (0.85, 2.89)	0.079	2.38 (1.65, 3.43)	**1.76 (1.08, 2.88)**	**0.025**
ATC	Good adherence	1	1		1	1	
	Poor adherence	3.37 (1.19, 9.54)	2.87 (0.96, 8.58)	0.032	3.00 (1.48, 6.04)	**2.45 (1.07, 5.59)**	**0.033**
	No CT	8.66 (3.03, 24.73)	**6.69 (2.20, 20.30)**	**0.001**	6.94 (3.40, 14.17)	**5.57 (2.41, 12.87)**	**<0.001**
Nodal status	Positive	1	1		1	1	
	Negative	0.21 (0.06, 0.70)	0.23 (0.04, 1.15)	0.075	0.67 (0.38, 1.16)	0.66 (0.25, 1.71)	0.397
Global test			***0.8358***			***0.9848***	

NB: CHR: Crude hazard ratio, AHR: Adjusted hazard ratio, ***ACT:*** *Adherence to chemotherapy, BC: breast cancer,* ***** *=Mixed ductal & lobular, mucious, No CT: no chemotherapy.*

6. DISCUSSION

Surveillance of cancer survival is seen as vital by national and international agencies, cancer patient advocacy groups, departments of health, politicians, and research agencies. It is being used to formulate cancer control strategies, to prioritize cancer control measures, and to assess both the effectiveness and cost-effectiveness of those strategies (23). This study identified determinants of survival and estimated overall survival of 302 patients with BC, most of them treated with adjuvant chemotherapy and surgery in HUCSH & YIMSC.

The overall survival at the end of two years is 69.3% (95% CI; 61.30, 76.03) and residence, travel time, duration of symptom, and adherence to chemotherapy were significant predictors of survival.
Comparing survival time especially with developed countries might lack similar reference time since almost all of them are interested in the survival of more than five years.

The two years OS in this study (69.3%) is comparable with the result of Iran's systematic review which is 67.6% (13), it is higher than the finding of a study in rural Ethiopia which revealed 2 year survival is 53% (8).The difference with a study in rural Ethiopia could be due to higher number of loss to follow-up in this study (18%) and or, due to the availability of adjuvant chemotherapy and hormonal therapy in our study setting.

In contrast to our study, a better survival is observed in South Africa and Iran. Survival after two years is 80% in Sawoto South Africa (28) and 86% in Iran Yazd (25). This discrepancy could be due to methodological difference as a study in Sawoto relied on existed records and excluded loss to follow-ups which can lead to underestimation of the number of deaths and overestimation of survival (28), and due to the availability of BC care and treatment evidenced by 67% of patients with BC had received combined treatments of surgery, chemotherapy and radiation in Iranian study (25) compared to only 50.7% in our study received surgery and chemotherapy but not radiation therapy.

In most studies of developed nations, even the five-year survival was better than the two-year survival of our study. The five-year survival in Idaho (rural state of US) is 89% and 83% for women linked and do not linked to women's health check program respectively (41).

Increased survival in developed countries could be due to earlier presentation to cancer treatment, adequate screening service and quality of care. A study in the US shows an association between increased breast cancer incidence and mammographic screening which in turn brings a shift in breast cancer stage distribution towards the earlier stage and finally bring a better survival (42).

In our study, most of patients with BC (83.4%) presented at an advanced stage. This result is in line with the finding of a systematic review that compares BC patients' survival in developing and developed countries. Only 20%-50% of patients with BC present in early-stage in LMIC. The reason for diagnosis at an advanced stage in LMICs could be due to the patient's very long delay for consultation, access barriers and quality deficiencies in cancer care and treatment, negative symptom interpretation, fear, belief in alternative medicine, social relations and networks(43, 44). A delayed presentation and diagnosis are also observed in Africa, especially in Sub-Saharan Africa (45). This is also evidenced by most studies in the developed world, an association between an advanced clinical stage of BC and delays greater than three months (43). In contrast to this study, 70% of patients with BC in most high-income countries are diagnosed in stages I and II (43).

We found that patients with BC that have advanced stage of disease have 3.01 times increased risk of death as compared to early stage. This finding is similar with findings in Mexico, Hawaii, US, Nigeria, and Uganda (12, 14, 16, 30, 31). This implies that earlier presentation or down staging of BC at time of diagnosis will have a paramount effect on survival of BC patients.

In this study, rural residents are more likely to die from BC. This is supported by a meta-analysis conducted in developed nations of US and Europe that revealed rural-dwellers are 5% less likely to survive from cancer (26). Similarly, a study in Utah revealed that rural residents had a 10% increased risk of death(27). This variation between urban and rural residents could be due to decreased health care seeking behavior in rural residents (46) and decreased awareness of BC in rural parts of Sub-Saharan Africa (47). Another reason for urban rural difference in survival can be explained by comparing urban-rural discrepancies in this study evidenced by, advanced-stage presentation (87.8 % versus 79.7%), time to presentation after 23 months (28.4%. versus 18.6 %), no chemotherapy (48.6% versus 31.6%) and good

adherence to chemotherapy (35.1% versus 47.1%) for rural and urban respectively. This result implies that awareness creation in the rural parts will be beneficial.

BC patients that present to cancer treatment centers within 7-23 months after the onset of breast complaint had 2.2 times increased risk of death as compared to those who had presented within six months. This finding is supported by a study in Rwanda that explored patient delays of 6–12 months and ≥12 months increased the odds of more advanced-stage disease when compared with patients presented within 3 months after the onset of symptoms (29). And this in turn, can bring decreased survival.

In our study, patients that travel > 7hours have increased risk of death as compared to those who travel < 3 hours to get cancer treatment. This association is not found significant in another reviewed study. This could be due to differences in awareness of the public and the facility in Wolega Ira might have good community sensitization about BC and this can increase early diagnosis (8).

Since we have 18.9% LTF, sensitivity analysis was done through worst case analysis and resident, stage of BC, surgical therapy and adherence to chemotherapy are found to be independent predictors of survival of patients with BC. Residence and stage of BC patients is discussed above under discussions of main analysis.

As compared to patients that have good adherence, patients that have poor adherence have 2.45 times increased risk of death and those who didn't take chemotherapy are 5.57 times increased risk of death. It has been reported that studies on the impact of guideline-adherent therapy in breast cancer have been sparse and lacking systematic designs (48). However, among some available studies that studied the effect of adherence to chemotherapy on overall survival of BC patients, a retrospective study at the University of Ulm, Germany revealed that patients with BC that have no guideline conformity to chemotherapy have 2.59 times higher risk of death (34). However, in another study in Germany, omitting chemotherapy did not affect the overall survival or disease-free survival of women aged > 70 years (35). This discrepancy could be due to the stance of elderly patients in the upper border of life expectancy.

In this study, breast surgery was significantly associated with better survival. Similarly, in a study in china, surgery was an independent prognostic factor for OS. Patients who had breast surgery were 47% increased chance of survival as compared to those who had not (33). The total removal of the tumor will prevent further growth and metastasis of tumor cells and thus increases the metatartaric-free, progression-free survival and finally increases the overall survival. However, since surgery is not done for stage four patients this association might be due to the early stage of BC than solely because of surgery.

6.1. Strength and limitation of the study

Strength of the study

The strength of the study is the use of all available data which can minimize sampling error. And it is the most up to date and the second of its type in Ethiopia, and the first for the study area. On the other hand, sensitivity analysis was reported.

Limitation of the study

- Since it is a retrospective study and based on records, missing data was the challenge.
- Socio-economic variables and other tumor characteristics are not well addressed due to large missing.
- Study participants might die from causes other than BC, and these rates don't take that into account.
- The outcome of 57 (18.9%) patients is unknown and they are considered as left censored and alive, this can overestimate the survival time.

7. CONCLUSION AND RECOMMENDATION

7.1 Conclusion

Most of patients with BC (83.4%) treated in Hawassa University Comprehensive Specialized Hospital and Yanet Internal Medicine Specialized Center had mainly presented with an advanced stage of BC. The overall survival after two years is below 69.3% and rural residence, advanced stage of cancer, poor adherence to adjuvant chemotherapy are independent predictors of survival.

7.2 Recommendation

For the public: Women with any breast complaint should consult health care providers immediately and follow the physician's care and treatment recommendations.

Health professionals: Health professionals shall provide health education in a way that enhances the earlier presentation of breast cancer, on availability of treatment and they shall consider earlier referral to appropriate facility.

Policymakers and program planners: Responsible body shall focus on promoting the awareness on early signs and symptoms of BC to the public and on training of first-line health professionals including health extension workers. Promotion of early referral procedures to facilitate adequate diagnosis and increasing access to treatment of BC shall be emphasized.

To HUCSH and YSIMC: Inclusion of detailed patient characteristics, active follow up of patient's outcome with a predefined schedule by telephone contact, and establishing a database will be beneficiary for quality of care, treatment, and better researches.

To researchers: There is still the need for further studies on the survival of BC patients. A study that can fill the limitations of this study preferably using prospective design and inclusion of socio-economic variables shall be emphasized. The reasons for poor adherence of patients with BC to chemotherapy also need to be investigated.

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Annexes

Annex I: Supplementary document for worst-case analysis (sensitivity analysis)

Table 8: Life table for patients with breast cancer in HUCSH & YIMSC, by worst case analysis, 2013-2018

Intervals in month	BC patients at risk	Deaths	Censored	Survival	SE	95% CI	
						Lower	Upper
Early stage BC							
0-6	50	1	7	0.9785	0.0298	0.8570	0.9969
6-12	42	3	7	0.9022	0.0466	0.7594	0.9623
12-18	32	0	5	0.9022	0.0446	0.7594	0.9623
18-24	27	0	4	0.9022	0.0466	0.7594	0.9623
24-30	23	1	10	0.8521	0.0657	0.6629	0.9396
36-42	12	1	0	0.7811	0.0908	0.5373	0.9064
42-48	11	0	2	0.7811	0.0908	0.5473	0.9064
48-54	9	0	1	0.7811	0.0908	0.5473	0.9064
54-60	8	1	2	0.6695	0.1293	0.3567	0.8555
60-66	5	0	2	0.6695	0.1293	0.3567	0.8555
66-72	3	0	3	0.6695	0.1293	0.3567	0.8555
Advanced stage BC							
0-6	252	57	41	0.7538	0.0283	0.6930	0.8043
6-12	172	23	34	0.6272	0.0337	0.5574	0.6892
12-18	100	16	14	0.5157	0.0375	0.4399	0.5863
18-24	69	4	5	0.4837	0.0384	0.4066	0.5565
24-30	58	6	21	0.4226	0.0409	0.3419	0.5010
30-36	31	3	8	0.3757	0.0444	0.2892	0.4618
36-42	20	2	6	0.3315	0.0490	0.2381	0.4276
42-48	12	2	1	0.2738	0.0549	0.1731	0.3842
48-54	10	2	2	0.2054	0.0587	0.1048	0.3293
60-66	5	2	3	0.0880	0.0599	0.0149	0.2456
66-72	1	1	0	0.0000			

SE: Standard error, **CI**: Confidence interval

Table 9: Log-rank test for equality of survival function of patients with breast cancer diagnosed in HUCSH and YIMSC in worst case analysis, 2018

Covariates	Worst case analysis				
	Survival at 3 years (%)	**Observed death**	**Expected death**	**X^2 (df)**	**Log-rank test ($Pr > X^2$)**
Resident Category					
Urban	59.2	59	75.16	16.43 (1)	**<0.001**
Rural	22.0	37	20.84		
Age in years					
<35	29.9	40	26.53	9.25 (2)	**0.009**
35-50	53.8	67	80.71		
>50	36.0	17	16.76		
Stage of BC					
Early	85.1	7	29.99	24.23 (1)	**<0.001**
Advanced	36.0	117	94.01		
Surgical therapy					
Yes	52.2	76	97.72	23.09 (1)	**<0.001**
No	24.4	48	26.28		
ACT					
Good adherence	73.7	9	29.17	43.5 (2)	**<0.001**
Poor adherence	45.9	63	69.21		
No CT	19.8	51	24.62		
Hormonal therapy					
Yes	78.2	22	63.94	60.01 (1)	**<0.001**
No	21.2	102	60.06		

ACT: *Adherence to chemotherapy,* No CT: No chemotherapy

Table 10: Bivariate cox regression using worst case analysis for predictors of survival among patients with breast cancer in HUCSH & YIMSC, 2013-2018

	Died				
	Yes (%)	**No (%)**	**CHR (95% CI)**	**p-value**	**P(PH)**
Resident					
Urban	59 (31.2)	130 (68.8)	1		
Rural	37 (50.0)	37 (50.0)	**2.34 (1.52, 3.53)**	**<0.001**	0.454
Travel time					
< 3 hours	71 (35.7)	128 (64.3)	1		
3-6 hours	16 (31.4)	35 (68.6)	1.22 (0.70, 2.11)	0.477	0.983
≥ 7 hours	9 (60)	6 (40)	**2.19 (1.09, 4.40)**	**0.027**	
Age category					
<35	40 (48.8)	42 (51.2)	1		
35-50	67 (37.9)	110 (62.1)	**0.54 (0.38, 0.83)**	**0.003**	0.520
>50	17 (39.5)	26 (60.5)	0.67 (0.38, 1.19)	0.168	
Menopausal status					
Pre-menopause	97 (40.6)	142 (59.4)	1		
Post-Menopause	27 (42.9)	36 (57.1)	0.99 (0.64, 1.52)	0.970	0.224
Duration of symptom					
< 6 months	40 (36.4)	70 (63.6)	1		
7 - 23 months	50 (44.6)	62 (55.4)	1.17 (0.78, 1.79)	0.458	0.916
> 23 months	31 (50.8)	30 (49.2)	1.59 (0.99, 2.56)	0.051	
Stage of BC					
Early	7 (14.0)	43 (86.0)	1		
Advanced	117 (46.4)	135 (53.6)	**5.62 (2.60, 12.13)**	**<0.001**	0.757
Histological type					
Ductal	106 (42.6)	143 (57.4)	1		
Lobular	7 (29.2)	17 (70.8)	0.54 (0.25, 1.18)	0.124	0.955
Other	11 (37.9)	18 (62.1)	1.00 (0.53, 1.86)	1.00	
Nodal status					
Positive	100 (41.7)	140 (58.3)	1		
Negative	15 (33.3)	30 (66.7)	0.67 (0.38, 1.16)	**0.156**	0.705
Co-morbidities					
Yes	16 (45.7)	19 (54.3)	1		
No	108 (40.4)	159 (59.6)	1.23 (0.72, 2.09)	0.431	0.493
Surgical therapy					
Yes	76 (36.5)	132 (63.5)	1		
No	48 (51.1)	46 (48.9)	**2.38 (1.65, 3.43)**	**<0.001**	0.565
ACT					
Good adherence	9 (16.7)	45 (83.3)	1		
Poor adherence	63 (45.7)	75 (54.3)	3.00 (1.48, 6.04)	0.002	
No chemotherapy	51 (61.4)	32 (38.6)	6.94 (3.40, 14.17)	**<0.001**	0.594

***NB: P(PH)** – Prob>X 2 global test for proportional-hazards assumption, **ACT:** Adherence to chemotherapy*

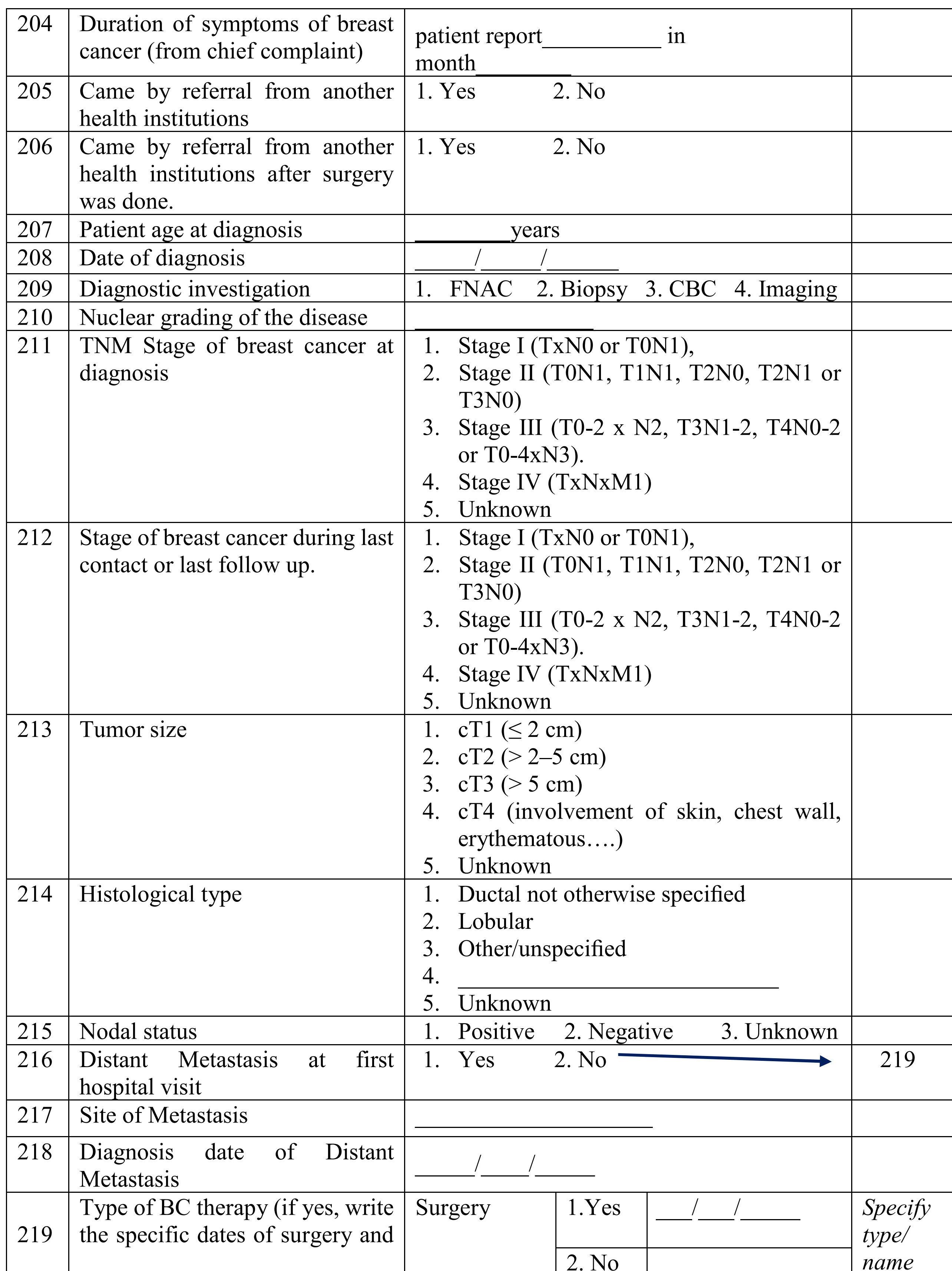
Annex II: Data extraction checklist

Data extraction checklist for the assessment of determinants of survival of breast cancer patients in Hawassa Referral Hospital and Yanet Internal Medicine Specialty Center, 2018

Code: _______________

Medical record number: ______________

SN	Variables	Response	Skip
	Part I: Socio-demographic variables		
101	Place of Residence	Region ____________ Zone ______________ Worde/city____________Kebele___________	
102	How far is your residence from Hawassa	_____________Km	
103	Residence category	1. Urban (Regional, Zonal town, Worde town) 2. Rural	
104	Travel time to hospital (to HUCSH)	__________ Hrs. ___________min	
105	Marital status	1. Single 4. Widowed 2. Married 5. Cohabitation 3. Divorced 6. Unknown	
106	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Others__________	
107	Level of education	1. No education 2. Read and write 3. Primary education 4. Secondary education 5. Diploma/ Degree 6. Master's degree and above	
108	Occupation	1. Government employee 2. Merchant 3. House wife 4. Student 5. Farmer 6. Unemployed 7. Others___________	
109	Income/Month/Birr	___________________Birr	
	Part II: Clinical Data		
201	In which hospital the patient is attending follow up?	1. HCSH 2. Yanet	
202	Date of first hospital visit for a breast cancer in concern	_____/_____/______	
203	Breast complaint at first visit	___________________________________	



No.	Question	Response	Skip
204	Duration of symptoms of breast cancer (from chief complaint)	patient report___________ in month_________	
205	Came by referral from another health institutions	1. Yes 2. No	
206	Came by referral from another health institutions after surgery was done.	1. Yes 2. No	
207	Patient age at diagnosis	_________years	
208	Date of diagnosis	______/_____/_______	
209	Diagnostic investigation	1. FNAC 2. Biopsy 3. CBC 4. Imaging	
210	Nuclear grading of the disease	_________________	
211	TNM Stage of breast cancer at diagnosis	1. Stage I (TxN0 or T0N1), 2. Stage II (T0N1, T1N1, T2N0, T2N1 or T3N0) 3. Stage III (T0-2 x N2, T3N1-2, T4N0-2 or T0-4xN3). 4. Stage IV (TxNxM1) 5. Unknown	
212	Stage of breast cancer during last contact or last follow up.	1. Stage I (TxN0 or T0N1), 2. Stage II (T0N1, T1N1, T2N0, T2N1 or T3N0) 3. Stage III (T0-2 x N2, T3N1-2, T4N0-2 or T0-4xN3). 4. Stage IV (TxNxM1) 5. Unknown	
213	Tumor size	1. cT1 (≤ 2 cm) 2. cT2 (> 2–5 cm) 3. cT3 (> 5 cm) 4. cT4 (involvement of skin, chest wall, erythematous….) 5. Unknown	
214	Histological type	1. Ductal not otherwise specified 2. Lobular 3. Other/unspecified 4. ______________________________ 5. Unknown	
215	Nodal status	1. Positive 2. Negative 3. Unknown	
216	Distant Metastasis at first hospital visit	1. Yes 2. No →	219
217	Site of Metastasis	______________________	
218	Diagnosis date of Distant Metastasis	______/_____/______	
219	Type of BC therapy (if yes, write the specific dates of surgery and	Surgery: 1.Yes ___/___/______; 2. No	*Specify type/ name*

	radiation, for chemotherapy write the beginning date)	Chemo therapy	1.Yes	___/___/_____	*Specify type/ name*
			2. No		
		Hormonal	1. Yes	___/___/_____	*Specify type/ name*
			2. No		
		Radiotherapy	1. Yes	_____/____/_____	
			2. No		
220	Last cycle of chemotherapy received.			_________________	
221	Duration of Hormonal Rx			_______year ________month	
222	Adherence to chemotherapy			1. Yes 2. No	
223	Co-morbidities (HIV, Hpn, DM...…etc.)			_________________	
224	Recurrence after surgery			1. Yes 2. No →	226
225	If yes to Q26, Diagnosis date of recurrence			_____/____/_____	
226	Diagnosis date of progression of the disease if any, (Date of Metastasis, change in stage)			_____/____/_____	
227	Diagnosis date of Distant Metastasis that develop during follow up (indicative of progression)			_____/____/_____	
228	Site of distance metastasis			_________________	
230	Status of the patient during last contact			1. Alive 2. Dead	
231	Current status of the patient (*confirmed by telephone)*			1. Alive 2. Dead	
232	If alive, functional status of the patient *(confirmed by telephone)*			1. Working 2. Ambulatory 3. Bed ridden	
233	Last date of follow up (Date of last contact)			_____/____/_____	
234	If lost to follow up, date of lost to follow up			_____/____/_____	
235	If dead, date of death			_____/____/_____	
235 a	What was the cause of death?			1. Breast cancer 2.Other: __________	

Form completed by: ________________. Sign ________________ Date: _______________

Name of supervisor: ________________. Sign _______________ Date: _______________

Annex III: Consent form and questionnaire for telephone interview (English version)

I. Consent form

Good morning/Good afternoon

My name is ______________________. I am working with Mr. Abel Shita who is doing a research as partial fulfillment for the requirement of MPH at Addis Ababa University. This study is intended to assess determinants of survival of breast cancer patients in Hawassa Referral Hospital who are under follow up for treatment in cancer treatment center from 2013 to 2018 GC.

The study is aimed to fill the information gap and provide evidence for program planners, implementers and decision makers at different levels and thereby to improve breast cancer care, treatment and control.

A formal consent was obtained from Hawassa Referral Hospital to begin the study and now we are collecting the data from patient records and by telephoning to patients.

I assure you that your information will be kept confidential and your name will not be used in the study. Your answers to any of the questions will not be given to anyone else and no reports of the study will ever identify you.

The interview is voluntary and it may take 15-20 minutes. Your right not to participate or to terminate will have no effect on services that you or your family may receive from the health service provider. However, if you participate in the interview, you will contribute a lot for improvements in cancer treatment and care.

Are you willing to participate in the study?

1. Yes 2. No

The responder is willing to take part in the study.

Name of data collector: ________________________ Signature: ______________

II. Telephone interview questionnaire (English)

Phone call trials	1st		2nd		3rd	

Is the consent form explained to participant and is she volunteer for interview? **1. Yes 2. No**

SN	Variables	Response	Skip
	Part I: Socio-demographic variables		
T01	Place of Residence	Region ___________ Zone _____________ Woreda/city___________ Kebele _____________	
T02	How far is your residence from Hawassa	____________Km	
T03	Residence category	1. Urban (Regional, Zonal town, Woreda town) 2. Rural	
T04	Travel time to hospital (to HUCSH)	_________ Hrs. __________min	
T05	Marital status	1. Single 4. Widowed 2. Married 5. Cohabitation 3. Divorced 6. Unknown	
T06	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Others__________	
T07	Level of education	1. No education 2. Read and write 3. Primary education 4. Secondary education 5. Diploma/ Degree 6. Master's degree and above	
T08	Occupation	1. Government employee 2. Merchant 3. House wife 4. Student 5. Farmer 6. Unemployed 7. Others__________	
T09	Income/Month/Birr	_________________Birr	
Part II: Others			
T10	Current status of the patient	1. Alive 2. Dead	
T11	If she is alive what is her condition right	1.Working 2. Ambulatory 3. Bed ridden	
T12	If she is dead what was the cause of	1.Breast cancer 2. Other	
T13	If she is dead date of death:	____/____/________	

Interviewer name:____________________Date:______________Signature: _____________

Annex IV፡ Consent form and questionnaire for telephone interview (Amharic)

I. <u>የህመምተኞችን ፈቃደኛነት መጠየቅያ ቅጽ</u>

ጤና ይስጥልኝ!

ስሜ______________ይባላል። በአሁኑ ሰዓት የአዲስ አበባ ዩኒቨርስቲ የማህበረሰብ ጤና ዘርፍ የሁለተኛ ዲግሪ የመመረቂያ ጥናታዊ ፅሁፋቸውን ከሚሰሩት ከአቶ አቤል ሽታ ጋር በመሆን መረጃ በመሰብሰብ ላይ እገኛለው።
ጥናቱ የሚደረገው ከ2013-2018 (እ.አ.አ) በሀዋሳ ሪፈራል ሆስፒታልና በያኔት ሆስፒታል የካንሰር ህክምና ማዕከል የጡት ካንሰር ህክምናን በመከታተል ላይ የሚገኙ ህመምተኞች ህክምና እየተከታተሉ ለረዥም ጊዜ እንዲኖሩ ወይም እንዳይኖሩ የሚያደርጉ ሁኔታዎችን ለመለየት ነው።

ጥናቱለፕሮግራምአውጭዎች፣አስፈጻሚዎችእንዲሁምውሳኔሰጪዎችጥናታዊ መረጃበመስጠትና ያለውን የመረጃ እጥረት በመቀነስየህሙማኑንየጤናሁኔታለማሻሻልጉልህአስተዋፆያደርጋል።

ስለዚህም ከሀዋሳ ሪፈራል ሆስፒታል ፈቃድ በማግኘት ለዚህው ጥናት የሚውል መረጃ ከህመምተኞች ማህደር እና ህመምተኞችን በስልክ በማግኘት በመሰብሰብ ላይ እንገኛለን።

የሚሰጡት መረጃ ሚስጥራዊነት የተጠበቀ ሲሆን፤ ስምዎትም በዚህ ጥናት ውስጥ አይገለጽም መረጃውንም ለሌላ ወገን አሳልፈን እንደማንሰጥ አረጋግጥልዎታለው። ቃለምልልሱም እስከ 10 ደቂቃ ሊፈጅ ይችላል።

ቃለምልልሱ በፈቃደኝነት ላይ የተመሰረተ ሲሆን ያለመሳተፍ ወይም በማንኛውም ሰዓት የማስቆም መብትዎ የተጠበቀነው። ይህ በመሆኑም በእርሶም ሆነ በቤተሰብዎ ላይ ከሆስፒታሉ በሚያገኙት አገልግሎት ላይ ምንም አይነት ተፅእኖ አይኖረውም። ሆኖም ግን መረጃ በመስጠት ቢተባበሩን ለጡት ካንሰር ህክምናና እንክብካቤ ላይ ለሚደረጉ ማሻሻያዎች የበኩልዎን አስተዋፆ የበረክታሉ።

ለጥናቱ መረጃ ለመስጠት ፍቃደኛ ነዎት?

1. አዎን 2. አይደለሁም

በጥናቱ ለመሳተፍ ፈቅደዋል።

የመረጃው ሰብሳቢ ስም: ___________________________ ፊርማ:_________________

II. Questionnaire for telephone interview *(Amharic)*

በስልክ የሚደረግ ቃለ መጠይቅ

የስልክ ሙከራዎች	1ኛ		2ኛ		3ኛ	

የፈቃደኝነት ቅጽ ተነበላቸው በጥናቱ ለመሳተፍ ፈቃደኛ ሆነዋል? **1. አዎ** **2. አይደለም**

ክፍልአንድ: አጠቃላይ የማህበራዊ አኗኗር ሁኔታ መረጃ ዳሰሳ		
ቁጥር	**ጥያቄ**	**መልስ**
T01	መኖርያዎት የት ነው?	ክልል: ____ ዞን: ____ ወረዳ: ____ ቀበሌ: ____
T02	መኖርያዎት ከሀዋሳ ያለው እርቀት በ ኪሜ. ምን ህል ነው?	____ ኪሜ
T03	የመኖርያ ክልል	1. ከተማ 2. ገጠር
T04	ከመኖርያ ቦታዎት ወደ ሃዋሳ ሆስፒታለ ለመምጣት ምንያ ህል ሰዓት ይፈጃል?	____ ሰዓት ____ ደቂቃ
T05	የጋብቻ ሁኔታ	1. ያላገባች 4. ባል የሞተባት 2. ያገባች 5. አብራ የምትኖር 3. የፈታች 6. አልታወቀም
T06	የየትኛው ሀይማኖት ተከታይ ነዎት?	1. ኦርቶዶክስ 2. ሙስሊም 3. ፕሮቴስታንት 4. ሌላ ካለ ይግለጹ
T07	ምንያህል ተምረዋል?	1. አልተማርኩም 4. ሁለተኛ ደረጃ (9-12) 2. ማንበብና መጻፍ ብቻ 5. ዲፐሎማ/ዲግሪ 3. የመጀመርያ ደረጃ (1-8) 6. ማስተርስ/ከዚያ በላይ
T08	ስራዎት/መተዳደርያዎት ምንድነው?	1. የመንግስት ሰራተኛ 4. ተማሪ 2. ነጋዴ 5. ገበሬ 3. የቤት እመቤት 6. ስራ የለኝም 7.. ሌላ: ____
T09	የወር ገቢዎት ምን ያህል ነው ?	____ ብር
ክፍል II: ሌሎች		
T10	በአሁኑ ሰዓት ህመምተኛዋ ያለችበት	1. በህይወት አለች 2. በህይወት የለችም → *T12*
T11	በህይወት ካለች በምን አይነት ሁኔታ ላይ ነች ?	1. ስራ ትሰራለች 2. ስራ አትሰራም፡ ትንቀሳቀሳለች 3. የአልጋ ቁራገኛ ናት
T12	በህይወት ከሌለች የሞቷ ምክንያት ምን ነበር	1. የጡት ካንሰር 2. ሌላ ____
T13	በህይወት ከሌለች ያረፈችበት ቀን	____/____/____

የጠያቂው ስም:____________ቀን:____________ፊርማ: ____________

Annex V: Consent form and questionnaire for telephone interview (Sidama language)

I. Xiwanaano Fajjo Xa'minanni borro

Keere Hedhinoonni

Summaya ____________________________Yamameemo/ ma: xaayannara addis abebu universite gido dagatate fayimmanni layinki digre maasamate xinxallo borro qixeesirani noohu kalaa Abeel shshita ledo ikkaten mashalaqe gamba assinnanni heenomoha ikkanna Xinxallo assinannihu 2013MD hanafe 2018 MD geesha, hawaasi referalete hospitaale giddo kanserete ikkiminni urinshira unuunu kansere xibbini amadantinori , ikkiminna harunsitanni seeda yanna hedhdhanno woyi hedhdhannokki gede assanno hunneta bade afateeti.

Xinxallo programe fushitannorira ,jeefissanoriranna hattono farcidhdhanorira xinxallote mashalaqe aatenna nooha mashalaqqete xeo wonshate xiwamaanote fayimma woyeesate ,ikkado kaa'lo affidhino. Konni kainohunni hawaasi riferaalete hospitaalenni fajjo afiratenni tenne xinxallora ikitanno ikkado mashalaqe xiwamaanote doosenna xiwamaano bilbila bilbilatenni mashalaqe gamba assinanni heenomo.

Uyitinaanink mashalaqe ayimma agarantinnota ekkana, summineno tenne xinxallo giddo dixawinsanni, tenne mashalaqe wole dagara sainse uyinemokkita xawinseemone. Shiqinsheenonne xamo 5 daqiiqa calla adhitannota ikkitano.

Shiqinsheenonne xamora dawaro ate kinne fajjo hasiisanokeha ikkana ,hananifummo gedenoon mereeroho urisate dandiitinanni; Konne ikkino daafira kinnerano ikko minine manni hospitaaletenni afidhinanni anshooti gido mitonka qarra diabanno. Ikkolla kayinni mashalaqe aateni kaalitininkero unuunu kansere ikkimini garigarooshe woyeesate uminne kallo assitinanni heedhdhinonnita qummi asemone.

Xinxallote mashalaqe aate fajjo'neeti?

1, ee 2. Dee'ni

II. Bilbila bilbilatenniassinannixamo

Bilbila BilbilateeWonnalisha	Umiki		layyinki		sayyiki	

Xinxallotemashalaqeaatefajjo'neeti? **1,** ee **2.** Dee'ni

Umikifile :Wommantaheesholainohunassinannixinxallo		
Kiiro	**Xamo**	**Dawaro**
SD1	Teesone mamaat?	1.Killile…………………Zone……… 3.Woreda…………Qabale………
SD2	Miniki hawassi quchuminnimaggeshafafanno	…………………………
SD3	Herattokillilemati	1. Quchumaho2. Badiyaho
SD4	TeesokinnikayyiseHawassiquchu miradayyatemeesatteeadhanno	---------------sattee-------------dakika
SD5	Adhamahajolaanoxamo	1.Semotte 4. Minanashidhinotte 2.Mine amaddenotte 5. Leedohedhanotte 3.Gursumotee 6. Diaffonitte
SD6	Hiite Ammanoharunsitinanni?	1. Ortodoxise 2. Esliminna 3. Protestante 4.Woleikkiroxawisi__________________
SD7	Me'ekifilegeesharossinooni?	1. Dirossoma 3. Layinkdirimi 2. Umidirimi 4. Diploma/digre 5. Mastersena /masterseteroore
SD8	Loosinemaat?	1. Mangisteteloosasinchoot 2. Nagaadete 3. Min amaati 4. Rosaanchote 5. Gaata Loosiregaleema 6. Loosudinoe 7. Woleikkirroxawisi……………
SD9	Aganunnimaggeshiwomasha affiratta/tto	----------------birrra
. Layyinkikifile :Wollehajolaanoxamo		
SD10	Tenneyanaraxiwamanchonooderra	. 1. Lubotteni noo 2. lubanttino
SD11	Lubotteni nohaikkirohittoheshohedhano	. 1. Loosolossanni . 2.Loosodilossanokayinillamilimiliyitano . 3. Dalassahogoxellahedhano
SD12	Lubanttinoha ikkirohittenexissonitti	. 1. Unuunu 2. Wolletenni
SD13	Lubanttinoha ikkirolubanttinoyanna/wogga	. -----------/------------/------------

Xamanchusuma……….………………………………Barra…………Malaate………….

Guca gaaffii heeyyamummaa dukkubsattootaa

Harka fuune!

Maqaan koo______________jedhama. Ani yeroo ammaa kana, yuniversiitii Finfinneetti digrii lamaffaasaanii murna saayinsii fayyaa hawaasummaadhaan hojjechaa kan jiranii fi barreeffama qo'annoo qopheessaa kan jiran obboo Abeel shittaa faana hojii odeefannoo funaanurran jira.

Qo'annichi kan adeemsifamu bara 2013 – 2018 (A.L.A) yemmuu ta'u, dhukkubsattoota kaansarii harmaatiin qabamanii wiirtuu yaalii kaansarii, Hospitaala rifaraalaa Hawaasaatti yaalamaa jiraniif, haalota dhukkubsattoonni yeroo dheeraaf jiraachuuf isaan dandeessisuu fi gufuu ta'u addaan baasuufi.

Qo'anichi, Saganteessitootaaf, qaama raawwachiiftuuf, akkasumas, murtee kennitootaaf odeefannoo saayinsaawaa kennuudhaan hanqina odeefannoo furuun, haala fayyaa dhukkubsattootaa foyyeessuuf gahee guddaa taphata.

Kanaafuu hospiaala rifaraalaa Hawaasaa eeyyamsiisuun, Galmee dhukkubsattootaa ilaaluufi dhukkubsattoota bilbilaan argachuun odeeffannoo funaannuurran jirra.

Odeefannoon isin nuu kennitan iccitummaan isaa kan eegame yemmuu ta'u, maqaan keessan qo'annoo kanarratti hin caqasamu; odeefannichas qaama biraatif dabarsinee kan hin kennine ta'uu cimsinee sinii mirkaneessina. Gaaffii fi deebichi daqiiqaa 5 fudhachuu danda'a.

Gaaffii fi deebiin heeyyema keessanirratti kan hundaa'ee waan ta'eef, hirmaachuu dhiisuu yookin immoo yeroo feetanitti dhaabuun mirga keessan. Kana gochuu keessaniif, sinirrattis ta'ee maatii keessaniif tajaajila hospitaalicha irraa argattanirratti dhiibbaa tokkollee hin qabu. Ta'us yoo odeeffannoo kennuurratti nu deeggartan, dhukkuba kaansarii harmaatiif foyyaa'iinsa yaalii fi kununsa irratti godhamuuf gahee keessan gumaachitu.

Odeeffannoo qo'anichaaf ta'u, nuu kennuuf heeyyamtanii?

1. Eeyyeen 2. Lakki

Qo'annicha irratti hirmaachuuf heeyyamaniiru.

Maqaa funaanaa odeeffannoo: ______________________________
Mallattoo:_______________

Annex VI: Questionnaire for telephone interview *(Afaan Oromoo)*

Gaaffii fi deebii bilbilaan gaggeeffamu

Yaalii bilbilaa	1ffaa		2ffaa		3ffaa	

Gucni heeyyamaa erga dubbifameefi booda, qo'anicha irratti hirmaachuuf heeyyamaa ta'aniiru? **1. Eeyyeen** **2. Miti**

Kutaa tokko: Odeeffannoo waliigalaa haala jiruuf hawaasummaa		
Lakk.	**Gaaffii**	**Deebii**
T01	Teessoon keessan eessa?	Naannoo________________ Goodina: __________ Aanaa፡ _________________ Ganda፡ __________
T02	Bakki jireenyaa keessanii magaalaa Hawaasaa irraa hammam fagaata?	KM. ___________________
T03	Bakki Jireenyaa	2. Magaalaa 2. Baadiyaa
T04	Bakka jireenya keessan irraa hospitaala Hawaasaa dhufuuf, yeroo hammamii sinitti fudhata?	Sa'aatii _________________f daqiiqaa_____________
T05	Haala Gaa'elaa	1. Kan hinheerumne 4 kan dhirsi jalaa du'e 2. kan heerumte 5. Heeruma malee kanwaliin jiraattu 3. kan hiikte 6. Hin beekamne
T06	Amantii kam hordofaa jirta?	1.Ortodoksii2. Musliima 3. Protestaantii 4. nbiraa___________
T07	Hammam barattan?	1.Hin baranne 4. Sadarkaa lamaffaa (9 - 12) 2.Dubbisuuf Barreessu qofa 5. Dippiloomaa/Digrii 3.Sadarkaa tokkoffaa (1 - 8) 6. Digrii lamaffaaf/sanaa ol
T08	Hojiin keessan maali?	1.Hojjettuu mootummaa 5. Qotee bulaa 2.Daldaltuu 6. Hojii hin qabu 3.Haadha warraa 7. Kan biraa፡ _____________ 4.Barattuu
T09	Galiin ji'aan argattan hammami?	Qarshii __________
Kutaa lama: Taateewwan biroo		
T10	Yeroo ammaa kanatti haala dhukkubsattuun keessa jirtu	1. Lubbuun jirti 2. Lubbuun hinjirtu → *T12*
T11	Luubbuun jirti taanan haala attamii irra jirti?	1. Hojii ni hojjatti 2. Hojii hin hojjattu garuu nisosochooti 3. Itilleerratti hafteerti
T12	Lubbuun hin jirtu taanaan sabibni du'uushii maal ture?	1. Kaansarii harmaa 2. Kan biraa ____________
T13	Lubbuun hin jirtu taanaan guyyaan itti boqatte	_____/____/_____

Guddaa galatoomaa!

Maqaa gaaffii dhiyeessaa:_________________ Guyyaa: __________Malattoo: _________

Annex VII: Information sheet (English version)

Research Title: Determinants of Survival of Breast Cancer Patients in Hawassa Referral Hospital, Southern Ethiopia: A Retrospective Cohort Study.

Name of principal investigator: Abel Shita

Name of the sponsor: Addis Ababa University

Introduction: This information sheet was prepared for Hawassa Referral Hospital, cancer treatment center. The aim of the form is to make the institution clear about the purpose of the research, data collection procedures and finally to get permission to conduct the research.

Purpose of the research project: Primarily, the result of the study will be submitted to Addis Ababa University School of Public Health for the requirements to get Masters of Public Health in Epidemiology and Biostatics.

Due to the fact that there are a very few studies conducted on the area of cancer in Ethiopia, the Ethiopian cancer control program had mentioned improving research capacity on cancer as one strategy to control the disease. Thus, the finding of this study will contribute its part in filing the information gap regarding breast cancer and its care by isolating factors that bring poor survival of patients so as to guide specific interventions on those factors. Therefore, it will contribute its part for policies that focus on cancer prevention, care and treatment.

Procedure: All patient cards and data base information's of breast cancer patients who are under follow up from 2013 to 2018 in Hawassa Referral Hospital cancer treatment center will be selected and a review of the required information from the records will be made using checklist. For some variables that are unavailable on records, a phone call to patients will be made and necessary information will be collected after getting their consent. Four nurses form the cancer treatment center will be trained and collect the data.

Risk/ discomfort: There will be no risk at all on patients whom their records are reviewed and phones called.

Benefits: There will be no incentive or direct benefit to patients involved in the study. In dead, they will benefit indirectly from the research when the result of the study is used for program planning to improve cancer care and treatment. Therefore, this research will have a paramount

direct benefit for health care planners and managers working on cancer prevention, care and treatment.

Confidentiality: All patient rights will be highly respected. Patients name will not be used, instead, number codes will be used for every patient. Patient's information will be kept confidentially so as no other parties can obtain except the principal investigator and it will be locked with password in a computer.

Person to contact: This research project was reviewed and approved by the institutional review board of College of Medicine and Health Sciences, Addis Ababa University. In case, if you want to know more information about the research and its undertakings, you can contact the committee through the following address.

Addis Ababa University College of Medicine and Health Science Research Review Committee

Tel: +251-115157701 or +251-115-513-099

Abel Shita (MPH Candidate): Tel: 0913820763

Permission: Therefore, you are kindly requested to permit and forward your permission to concerned body in your organization so that the researcher can get cooperation from data clerks and other responsible bodies.

With regards!

To be filled by Medical Directors:

I have properly examined the objective of the study, understood patient rights are respected patient confidentiality is assured and there will be no risks on patients related to the study. Therefore, I gave a formal permission for the study to begin on behalf of the Hawassa Referral Hospital/ YIMSC.

Medical Director Name:______________________________

Signature:___________________________

Date:_______________________________

Annex VIII: Information sheet (Amharic version)

<u>የጥናቱን አጠቃላይ ሁኔታ የሚገልጽ የመረጃ ቅጽ፡</u>

የጥናቱ ርእስ፡ በሀዋሳ ሪፈራል ሆስፒታል የጡት ካንሰር ህመምተኞችን በህይወት የመኖር እድልን የሚወስኑ ምክንያቶች፡ "Determinants of Survival of Breast Cancer Patients in Hawassa Referral Hospital, Ethiopia: A Retrospective Cohort Study"

የተመራማሪው ስም፡ አቶ አቤል ሽታ

የጥናቱስፖንሰር፡ አዲስ አበባ ዩኒቨርሲቲ

መግቢያ፡ ይህ የመረጃ ቅጽ ለሐዋሳ ሪፈራል ሆስፒታል የካንሰር ህክምና ማእከል እና ለያኔት ሆስፒታል የተዘጋጀ ነው። ዓላማውም ሆስፒታሉ የጥናቱን ዓላማ በሚገባ እንዲረዳና የመረጃ አሰባሰብ ሂደቱ ምን እንደሚመስል እንዲረዳና በመጨረሻም ጥናቱ እዲካሄድ ተቋማዊ ፈቃድ እንዲሰጥ ነው።

የጥናቱ ዓላማ፡ የጥናቱ ውጤት በኢፒዴሞሎጂና ባዮስታትስቲክስ ትምህርት ዘርፍ የማስተርስ ዲግሪ ለማግኘት ለአዲስአበባ ዩኒቨርሲቲ የማህበረሰብ ጤና ትምህርት ቤት የሚገባነው።

በሀገራችን ኢትዮጵያ በካንሰር ላይ የተሰሩ ጥናቶች እጅግ አነስተኛ በመሆናቸው ምክንያት የኢትዮጵያ የካንሰር ቁጥጥር ፕሮገራም በዘርፉ የሚደረጉ ጥናቶች እንዲበራከቱ እንደ አንድ ስትራቴጂ አስቀምጦታል።ስለዚህም የዚህ ጥናት ውጤት ስለጡት ካንሰር ህመምተኞችና ስለሚያገኙት እንክብካቤና ህክምና ያለውን የመረጃ እጥረት በማጥበብ ህመምተኞቹ ለረዥም ጊዜ በህይወት እንዳይቆዩ የሚያደርጉ ምክንያቶችን በመለየት የትግበራ ማስተካከያ ለማድረግ ያግዛል።ስለዚህም፡ የዚህ ጥናት ውጤት የካንሰር መከላከልና ህክምና እና እንክብካቤ ላይ ለሚያተኩሩ ፖሊሲዎች የበኩሉን አስተዋጾ ያረጋል።

የመረጃ አሰባሰብ ሂደት፡ በሐዋሳ ሪፈራል ሆስፒታል የካንሰር ህክምና ማዕከል ከ2013-2018 ዓም. (እ.አ.አ) ህክምና የሚከታተሉ የሁሉም የጡት ካንሰር ህመምተኞች ካርድና የዳታቤዝ መረጃ በመመርመር አስፈላጊ የሆኑ መረጃዎች ወደ ቼክሊስት ይገለበጣሉ። በተጠቀሱት የመረጃ ምንጮች ያልተገኙና ከህመምተኛው ወይም ከቅርብ ዘመድ መገኘት የሚችሉ መረጃዎችን የህመምተኛው ፈቃድ ተጠይቆ መረጃው በስልክ ቃለምልልስ ይሰበሰባል።

ጥናቱ በህመምተኞች ላይ ያለው ተጽእኖ፡ፈቃደኛ ሆነው መረጃቸው የሚሰበሰብ ወይም በስልክ ቃለምልልስ የሚያደርጉ ህመምተኞች ከጥናቱ ጋር በተያያዘ ምንም አይነት ጉዳት አይደርስባቸውም።

የጥናቱ ጥቅም፡ የጥናቱ ተሳታፊዎች ከጥናቱ ጋር በተያያዘ ምንም አይነት ድጎማ ወይም ጥቅም አያገኙም።ነገርግን የጥናቱ ውጤት የጡት ካንሰር ህመምተኞችን ህክምናና እንክብካቤ ለማሻሻል ለሚደረገው የፕሮግራም እቅድ ሲጠቅም ህመምተኞችም ቀጥተኛ ባልሆነ መንገድ ተጠቃሚ ይሆናሉ፡
:

ስለዚህ የዚህ ጥናት ውጤት በካንሰር መከላከል ህክምናና የህሙማን እንክብካቤ ላይ ለሚሰሩ የጤናው መስክ ፐላን አውጪዎችና ማኔጀሮች ቀጥተኛ ጠቀሜታ ይኖረዋል፡፡

የመረጃው ምስጢራዊነት፡ የህመምተኞች መብት በሙሉ ይከበራል፡፡የህመምተኞች ስም በፍጹም አይካተትም፡፡ ከህመምተኞች ስም ይልቅ ለያንዳንዱ ህመምተኛ ኮዶችን እንጠቀማለን፡፡የህመምተኞች መረጃ ከጥናቱ ባለቤት ውጪ ማንም እነዳያይ በምስጢር ይጠበቃል፡፡ለዚህም በኮመፒዩተር ላይ የተሞላው መረጃ በይለፍ ቃል ይቆለፋል፡፡

ለበለጠ መረጃ፡ ይህ የጥናት ፕሮጀክት በአዲስ አበባ የኒቨርሲቲ የህክምናና ጤና ሳይንስ ኮሌጅ ጥናታዊ ፕሮጅክቶችን መርምሮ በሚያጸድቅ ቦርደ / institutional review board/ ተገምግሞ ጸድቋል፡፡ ስለጥናቱ ተጨማሪ ማብራርያ ካስፈለገ የሚከተለውን አድራሻ በመጠቀም መጠየቅ ይቻላል፡፡

የአዲስ አበባ የኒቨርሲቲ የህክምናና ጤናሳይንስ ኮሌጅ የጥናታዊ ጽሁፎች ገምጋሚ ኮሚቴ
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ከምስጋና ጋር!

በሜዲካል ዳይሬክተሩ የሚሞላ፡

የጥናቱን ዓላማ የህመምተኞች መብት መጠበቁን መረጃቸው በሚስጥር እንደሚጠበቅና ከጥናቱ ጋር በተያያዘ በጥናቱ ተሳታፊዎች ላይ ምንም አይነት ጉዳት እነደማይደርስ ተረድቻለው፡፡ስለዚህም በሆስፒታሉ ስም ጥናቱ እንዲጀመር መፈቀዱን እየገለጽኩ የሚመለከታቸው ክፍሎች አስፈላጊውን ትብብር እንዲያደርጉላቸው እጠይቃለው፡፡

የሜዲካል ዳይሬክተሩ ስም፡______________________________
ፊርማ፡______________________________
ቀን፡______________________________

Annex IX: A guide for Medical Record Data Abstraction and Telephone Interview for Assessment of Determinants of BC Patients' Survival in HUCSH and YIMSC.

Introduction

First of all, potentially challenging areas during data collection are identified and this data abstraction and telephone interview guide is developed to overcome the challenge. Therefore, this guide will be used for training of data collectors, supervisor and as a reference when data collectors are abstracting data from the medical records and during or before telephone interview of breast cancer patients in HUCSH and YIMSC. This guide will explain; source of data for every variable, the most frequently used abbreviations by physicians in the hospital, protocols and steps for data collection from records and for telephone interview. Therefore, data collectors will easily perform their tasks with this reference.

Objective of the study

- To assess determinants and estimate cumulative survival probabilities of breast cancer patients that are diagnosed 2013-2018 in HUCSH and YIMSC.

Eligibility criteria

Inclusion criteria: All women patients with BC who were diagnosed and enrolled in HUCSH and YIMSC from 2013-2018 will be included.

Exclusion criteria: Charts with unconfirmed BC, unknown stage of BC and recurrence at first visit are excluded.

Sources of data: Medical records, Data base, Chemotherapy log book, Telephone interviews

Criteria for data collectors and Supervisor: data collectors and supervisor must be oncology trained BSc Nurse and who had at least one-year experience in oncology unit. The senior of them will be nominated as supervisor.

Part I: Data collection from Medical records

Time required: a maximum of 25 minutes for every patient chart.

How each variable is extracted?

1. Socio-demographic variables

- Place of residence: this can be fully or partially available on the cover page of patient chart.
- Distance from Hawassa, residence category and travel time to HUCSH are not expected to be extracted from patients' chart. So, jump them.

- Marital status, Religion, level of education, occupation and monthly income are not usually available on the patient chart. However, if there is a nursing process sheet in the chart, you can record from it.

2. Clinical data

- Date of diagnosis: taken from biopsy result, if not FNAC.
- Breast complaint and its duration: this is obtained from chief complaint of patient history on the first hospital visit.
- Referral data: get from referral papers from another health institutions if any.
- Patient age at diagnosis: take from result sheets of biopsy, FNAC, radiographic results. But not from the cover page of patients' chart since the age on the cover may be written previously for another complaint before breast complaint.
- Nuclear staging: from biopsy result
- TNM staging at diagnosis: this is directly obtained from investigation result or on the physician's assessment on continuation sheet. However, it may not be written as "stage I, II" rather, it can be written as "Tx Nx Mx" (were x is any number 0-4). In this case, search the TNM match and label the stage which is written with it. See the lists below.

Stage 1: (TxN0 or T0N1),

Stage 2: (T0N1, T1N1, T2N0, T2N1 or T3N0)

Stage 3: (T0-2 x N2, T3N1-2, T4N0-2 or T0-4xN3).

Stage 4: (TxNxM1)

- TNM Stage of BC during follow up or last contact: this is different from stage at diagnosis. This stage tells as if there is progression of disease as evidenced by a change from lower stage at diagnosis to a higher stage during follow up or at last date of follow up. It is obtained from physician's assessment on continuation sheet.
- Tumor size: Clinical examination
- Histological type and Nodal status: Biopsy result
- Distant metastasis at first hospital visit and its site & date: obtained from physicians' assessment on continuation sheet.
- Type of BC therapy:
  - Surgery: from operation not if the surgery is performed in HUCSH and from referral paper if surgery was done in another hospital.

- Chemotherapy and Hormonal therapy, cycle and duration of therapy: obtained from chemotherapy/Hormonal therapy administration record sheet.
- Radiation: record this if there is a report sheet from Tikur Anbesa Specialized hospital or patient history. Otherwise, this could be addressed by telephone interview.

- Recurrence, Co-morbidities: observe every diagnosis of physicians from beginning to last contact.
- Progression of disease: it is said to be progression of disease if there is metastasis during follow up (not at diagnosis) and/or change in TNM staging during follow up. And this can be obtained from physician's assessment or radiologic examination results.
- Status of patient during last contact: find the last date the patient visited the hospital on continuation sheet and if death is not documented there record as alive.
- Last date of follow up: the last date the patient visited the hospital on continuation sheet.

Commonly used Abbreviations on patients' chart

Dx (diagnosis), Ass (assessment), Breast Ca (breast cancer), Chemo (Chemotherapy), Met (Metastatic/ Metastasized), HPN (Hypertension), DM (Diabetes Mellitus).

Medical name synonyms

Breast cancer: benign tumor of breast, metastasized breast cancer,
Assessment (Ass): Diagnosis
Plan: Investigation
Breast Ca? Breast cancer suspected, but not confirmed.

Part II: Data Collection using telephone interview.

Who is the interviewer?

- Telephone interview is only made by the hospital's oncology unit data clerk/nurse that usually contact patients through telephone in previous trends. Other data collectors will not be involved in telephone interview.

Who can be the responder?

- The patient herself is the first-choice respondent.

- If the patient has language barrier, or not alive; patients' mother, father, husband can be interviewed. If patient's sister, brother or children are the respondent, they must be > 18 years.

What type of data obtained by telephone interview?

- Socio-demographic (Age, residence, travel time, marital status, educational status, religion.
- Patient status (alive or dead) and date of death.
- Patients are also asked if they were treated in other oncology care and treatment units and type of treatment they received there.

Principles

- Telephone call trial to get the patient will be made only three times, once a day in working hours and will be registered as telephone interview inaccessible if the three trials failed.
- Tell the respondent you are calling from HUCSH or Yanet, and ask whether the respondent is the client or client's cloth relative or husband.
- The purpose of telephone call will be explained to the one who respond for telephone call and if he/she is not the patient, his/her relation to the patient and his/her age will be asked then continue if age is >18 years.
- Never interrupt the respondents while they are talking.
- If the patient is dead, tell the responders you are sorry, reassure them and ask date of death.

Steps

1. The data collection will begin by reviewing patient's medical record and will be completed and submitted to supervisor.
2. The supervisor will attach telephone interview questionnaire and send it to the interviewer.
3. The interviewer will call to patients if phone number is available. The maximum telephone call trial will be three, only one call in a day with in formal working hours.
4. If the three-day phone call trial fail, then will be registered us phone call trials failed.
5. If phone call succeeds, first the patient will be told about why we called, the purpose of the study, and her privacy issues, verbal consent will be obtained and if patient is volunteer, she will be interviewed. If not, the interviewer will depart by giving thanks.
6. After completion of the whole interview, the interviewer will depart giving a heartfelt gratitude.

Declaration

I, the undersigned, MPH student declare that this thesis is my original work in partial fulfillment of the requirement for the Master of Public Health in Epidemiology and Biostatistics.

Name of the investigator: Abel Shita

Date: —————————— Signature __________________

Approval of the primary advisor

This thesis work has been submitted with our approval as university advisor.

Name of the primary advisor: Prof. Alemayehu Worku

Date. _____________________ Signature __________________

Name of external examiner: _____________________

Date. _____________________ Signature __________________

Name of internal examiner: _____________________

Date. _____________________ Signature __________________