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Breast and cervical cancer patients' experience in Addis Ababa city, Ethiopia: a follow-up study protocol

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ABSTRACT

Introduction Cancer is an emerging public health problem in Ethiopia, with breast and cervical cancers accounting for over half of all newly diagnosed cancers in women. The majority of women with breast and cervical cancer are diagnosed at late stage of the disease and most patients do not receive care consistent with global standards. However, little is known about the health-seeking behaviours, barriers to early detection and treatment, patient-reported outcomes, financial burden and survival of women with breast and cervical cancer in the country. Therefore, this study aims to document the experience of women with breast and cervical cancer from recognition of symptoms to diagnosis, treatment and survivorship/mortality in Addis Ababa city, Ethiopia.

Methods and analysis A prospective follow-up study using mixed methods (both quantitative and qualitative) will be employed. All women newly diagnosed with breast and cervical cancer from 1 January, 2017 to 30 June 2018 in Addis Ababa will be included in the study. Interviewer-administered questionnaires will be used to collect information about medical consultations after recognition of symptoms, health-seeking behaviours, treatment received, barriers to early detection and treatment, and survivorship care. In-depth interview will be conducted on purposefully selected women with breast and cervical cancer. The primary outcomes of the study are time intervals (patient and diagnostic waiting times), stage at diagnosis and survival. Multivariable analysis will be employed to determine the contributions of independent variables on the outcomes of interest. HRs with 95% CIs will be calculated for time-to-event outcomes. Qualitative data will be analysed using thematic analysis.

Ethics and dissemination This protocol is ethically approved by Institutional Review Board of Addis Ababa University. Verbal informed consent will be obtained from study participants. Results will be disseminated in international peer-reviewed journals and presented in relevant conferences.

Strengths and limitations of this study

- This study is the first prospective follow-up study in Ethiopia which will allow us to test the temporal relationship between the explanatory variables and outcome of the study.
- The study is multicentre study which will recruit incident cases from the major public and private health facilities in the city so that generalisation about women with breast and cervical cancer in the city will be possible latter.
- The study will use mixed methods; the qualitative design will help to understand the patients' experience in the course of their illness.
- The retrospective nature of collecting information about dates of symptom recognition, and medical consultations might be prone to recall bias.
- Under-reporting of time delays and over-reporting of desirable behaviour such as self-breast examination, and selection bias due to lost to follow-up are anticipated in the study.

INTRODUCTION

Breast and cervical cancers are the most commonly diagnosed cancers and the leading causes of cancer death among women in Ethiopia and in other parts of sub-Saharan Africa,[1–3] accounting for about half of all cancer cases and deaths.[4] These cancers have significant public health and societal implications not only because they represent more than half of all cancer cases in women but also because they most frequently occur in young or middle age[5 6] when patients are in the workforce, raising children and supporting other family members.

The morbidity and mortality associated with breast and cervical cancer can be mitigated through early detection and receipt of evidence-based, high-quality care.[7] However, based on limited data, a substantial proportion of women with breast and cervical cancer in Ethiopia present with advanced-stage disease. For instance, about 71% of the breast cancer cases[6] and 84% cervical cancer cases[5] in Ethiopia were diagnosed at advanced stage largely because of prolonged patient intervals in seeking medical care after recognition of symptoms and provider/health systems intervals in referral of patients to cancer treatment centres.[8 9] Further, most women with breast and cervical cancer in the country do not

receive treatments consistent with the global standard of care.[3]

In addition to early detection and receipt of standard treatments, survivorship care is an important component of high quality of care across the cancer continuum. This could be assessed through patient-reported outcomes (PROs) as well as physician ratings of patients' well-being,[10] though PROs are found to be better predictors of patients survival and are thought to be more useful for making clinical decision about patient management.[10 11] There is, however, limited information on barriers to early detection and receipt of and completion of treatment and PROs among women with breast and cervical cancer in Ethiopia to guide public health policies and patient management.[12]

Previous studies from Ethiopia have reported limited knowledge about breast and cervical cancer, including about prevention, early detection and treatment, among healthcare professionals[13–16] and the general population.[17–27] This limited awareness likely contributes to the high proportion of disease detected at advanced stage in the country.[5 6] Notably, there are also studies conducted on women with breast and cervical cancer.[5 6 8 9 28–33] Two of the studies[8 28] examined patient or diagnostic interval among women with breast cancer in Ethiopia and found long waiting times to initiate medical consultation (average about 18 months). Similarly, Tadesse reported that about 30% (56/198 patient) of women with cervical cancer visited three or more health facilities before being referred to Tikur Anbessa Specialized Hospital (TASH), a referral public hospital, for cancer-directed treatment and 20% (46) of the patients waited for more than 6 months from first healthcare visit before they were first seen at TASH.[34]

The aforementioned studies, however, were limited because of small sample sizes,[8 28] and reliance on data from chart review[6 28–30] and data were collected from only one hospital, TASH, which houses the only radiotherapy centre in the country.[5 6 8 28–30 32] These all could make them prone to incompleteness and limit their generalisability to elsewhere in Ethiopia. Moreover, none of the studies examined the factors contributing to patient and diagnostic intervals, PROs, the relationship between patient/diagnostic intervals and stage at diagnosis as well as its effect on the survival of women with breast and cervical cancer in Ethiopia. To help address this information gap, we have established a cohort of newly diagnosed patients with breast and cervical cancer in Addis Ababa, capital city of Ethiopia. This paper describes the protocol of the study, the first prospective follow-up study on cancer patients' experience in the country and perhaps in Africa.

METHODS

Aim of the study

1. To explore barriers to early diagnosis of women with breast and cervical cancer.
2. To estimate the duration of patient, diagnostic and treatment initiation intervals of women with breast and cervical cancer.
3. To assess factors associated with patient, diagnostic and treatment initiation time intervals of women with breast and cervical cancer.
4. To examine the association between patient/diagnostic interval and stage at diagnosis.
5. To determine PROs (levels of fatigue, pain, sleep disorder and depression).
6. To describe treatment patterns and adherence by sociodemographic factors.
7. To document survivorship care (eg, surveillance for recurrence and late effects of treatment).
8. To estimate the financial burden of breast and cervical cancer on patients and their families.
9. To estimate the 2-year survival rates and their associations with patient, diagnostic and treatment initiation intervals, receipt of treatment, sociodemographic factors, financial burden and other PROs.

Study setting

This study will be conducted in the Addis Ababa, which has a population of about 3.5 million.[35] The city is served by 11 public and 33 private hospitals, 88 public and 6 non-governmental health centres, and 777 private clinics.[36] According to a national survey, the main healthcare provider for outpatients was government health facilities (77%), followed by private health facilities (20%), traditional and religious healers (2%), and non-governmental organisation (1%).[37] A population-based cancer registry has been in place since 2011 in Addis Ababa, with incident cases collected from 20 health facilities including referral hospitals, higher clinics and diagnostic centres.[4] Our study will recruit all women with breast and cervical cancer aged ≥18 years diagnosed from 1 January 2017 to 30 June 2018 in seven major health facilities. Of which, two are public (TASH and St. Paul Hospital Millennium Medical College) and five are private (United Vision Medical Services Center, Hallelujah General Hospital, Betezata Hospital, Legehar Hospital and Landmark Hospital). These health facilities capture more than 90% of all women with breast and cervical cancer reported to the cancer registry in Addis Ababa. Recruitment of the study participants has been started on 20 March 2017.

Study designs and sample size

The study design is a prospective follow-up study, using mixed methods (both quantitative and qualitative). The quantitative component involves both cross-sectional and prospective follow-up study designs, while the qualitative study is phenomenological study. The latter study design will help to understand the breast and cervical cancer patients' experience of their life before and after diagnosis, and during the course of treatment.[11] We expect to recruit about 450 patients with breast and 250 patients with cervical cancer, based on the number of breast and

cervical cases recorded each year in the city over the past 2 years,[38] and they will be followed for 2 years.

The adequacy of the above-estimated cohort of 450 patients with breast and 250 patients with cervical cancer to address the stated specific objectives of the study was assessed. For instance, to estimate the sample size for the second specific objective (duration of patient and diagnostic waiting times), we used single population proportion formula. Taking expected proportion (p=31.7%) of patient interval (>3 months) from a similar study,[39] 95% confidence level ($Z\alpha/2=1.96$) and a 5% precision, a minimum of 333 patients are required for the study. In contrast, the minimum sample sizes for the third (factors associated with patient and provider time intervals), fourth (the association between patient or provider interval and stage at diagnosis) and ninth specific objective (survival rate of the patients) were estimated using two population proportion formula assuming 95% confidence level and 80% power, the estimates were found to be 422, 354 and 178 patients, respectively. To increase the precision of the estimates of the different outcomes of the study, all of the cohort of 450 breast and 250 cervical cancer cases will be considered in the analysis of each of the specific objectives.

Data collection tools and techniques

Three data collection tools will be used to address the objectives of the project: an interviewer-administered questionnaire (online supplementary file), an in-depth interview guide and a medical record data extraction tool. The tools are being developed in English, translated into Amharic and back translated into English. The Amharic version will be used for conducting the interview.

The interviewer-administered questionnaire is organised into two parts. The first part of the questionnaire addresses participants' sociodemographic characteristics, medical history and pathway to diagnosis which is adapted from a questionnaire for a similar study in Rwanda.[40] In addition, this first phase of questionnaire also includes questions about PROs (levels of fatigue, pain, sleep disorder and depression). Depression was assessed using a validated Patient Health Questionnaire-9.[41] While the questions for fatigue, pain and sleeping disorder were adopted from National Cancer Institute.[42 43] This questionnaire will be administered face to face by trained interviewers at the time of participants' recruitment.

The second tool which will be administered at about 1 year after the diagnosis of the cases investigates receipt of and adherence to treatments, financial hardship and survivorship care (online supplementary file). The questions are adapted from different standardised tools developed by the National Cancer Institute,[42 43] the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention of the US Department of Health and Human Services.[44] To improve the validity of the questions, the adapted questionnaire was reviewed by local and international experts on the research subject and cancer care. Further, a pretest was performed to enhance the clarity of the tool. Patients will be interviewed about 1 year after their cancer diagnosis by a trained interviewer, in person when possible and by telephone otherwise. Phone calls will be made at least three times at different times of the day, evening and weekends to increase the response rate of the study participants. Those patients, who are not interviewed through this mechanism, will be considered as lost to follow-up.[45] For patients who died or are too ill to be interviewed, a surrogate (relative or household member) familiar with their cancer care will be interviewed.

The medical record data extraction tool will be used to collect information about date of diagnosis, tumour characteristics (eg, stage at diagnosis, metastasis and recurrence), initiation and completion of treatments, and vital status from the medical charts of the patients. Medical record review will occur at about 1 and 2 years after diagnosis.

In addition to the interviewer-administered questionnaire and extraction tool, a semistructured interview guide will be developed and used for in-depth interviews. This instrument will include patients' knowledge and perception of breast and cervical cancer, and the patients' experience from the recognition of first symptom of the disease to diagnosis and treatment. Interviews will be conducted in local language (Amharic). The principal investigator and two trained data collectors who have experience in collecting qualitative data will conduct the in-depth interviews. Interview guide and tape recorder will be used. The interviewers will use probing and question-rephrasing techniques to clarify questions and obtain details from the respondents. The number of interviews will be determined based on information saturation.

Term definitions and measurements

Independent variables: Demographic variables (age at diagnosis, marital status and age at first child birth), socioeconomic variables (level of education, occupation, monthly family income and source of medical expenses), method of initial detection, time of first symptom/sign detection, participant's appraisal of first symptom/sign, participants immediate action to the first symptom, triggers to seek medical care, health facility of the first medical consultation, number of healthcare facilities visited before diagnosis, number of visits to healthcare facility before diagnosis, clinical presentation at time of diagnosis, time of medical care sought, family history of breast/cervical cancer, self-reported comorbidities and traditional medicine use will be obtained through in-person face-to-face interview.

The existing literature lacks consistency in the definition of the time intervals for cancer diagnosis and treatment delays, and traditionally has been classified as 'patient delay' and 'system delay'.[46] For consistency, the Aarhus statement[47] recommended classifying these as 'patient interval', 'diagnostic interval', 'treatment interval' and 'total interval'. Our study is based on this framework. Patient interval is defined as the interval from

the date of first recognition of symptoms (the time point when first bodily changes and/or symptoms are noticed) to the date of first clinical presentation (the date at which the patient first presented to a healthcare provider after first recognition of symptoms).[47] Waiting for >3 months before consulting a healthcare provider will be considered to be a long patient interval.[48–50]

We will consider using local events to help patients recall the date of first symptom recognition and presentation. If the participants are unable to recall the exact date of first symptom recognised or date of first medical consultation made, they will be asked to provide a month, or year (was it at the beginning, middle or end of the year). If they remembered the month, the date will be estimated as the 15th of that month; if the participants only said the beginning, middle or end of the year, the estimated date will be 15th of February, June or October of the year, respectively. While for those who are only able to provide the year, the estimated date will be June 30th of that year.[40]

Diagnostic interval is defined as the interval from the date of first clinical presentation to the date of pathological diagnosis (the date at which the first histological or cytological confirmation of this malignancy was reported). Treatment interval will be computed by subtracting the date of confirmation from the date of treatment initiation. Total interval will be computed by subtracting the date of first time recognition of symptom from the date of treatment initiation.[47] The date of diagnosis and treatment initiation will be taken from the medical chart of the patients.

Stage at diagnosis will be grouped into early stage (patient presented with clinical stage II and below) and advanced stage (patients presented with clinical stage III or above) diseases.[51 52]

Data quality assurance mechanism

Several measures will be taken to maintain the quality of the research starting from designing the tool to data analysis and interpretations of the findings. Tool translation and back translation will be done to ensure the consistency of the survey tools. In addition to this, the questionnaire will be pretested and relevant corrections will be made.

Data collectors and supervisor will be recruited based on the level of education, ability to communicate using the working language and experience on data collection. Moreover, they will be trained on the objectives of the study, data collection tools, interviewing techniques and ethical procedures before the implementation of the project.

In addition to the training of the data collectors, they will be supervised by the supervisor and principal investigators. Filled questionnaires will be checked for their completeness and consistency on daily bases by the supervisor. Biweekly meetings will be held with the supervisor of the data collectors and the investigators to discuss and solve any problems encountered in the data collection process.

To minimise errors during data entry, templates will be developed using Epi Info using check codes. After the entry is completed, the sample of the questionnaires will be rechecked for correctness against the raw data, and necessary corrections will be made before the analysis.

To maintain the trustworthiness of the qualitative data, interviews will be collected, transcribed and analysed by individuals experienced in qualitative data collection and analysis. All interviews will be tape recorded to grasp all the points during the interview. Moreover, data will be transcribed by the data collectors on a daily bases to maintain the consistency and context of the discussion, and checked for errors by listening back to the audio-recording and reading the transcripts simultaneously. Finally, the transcribed data will be coded using NVivo software to facilitate the reduction of the qualitative data without missing the central idea.

Data management and analysis plan

Qualitative data analysis

Specific objective 1: For the qualitative data, audio data will be transcribed verbatim into Microsoft Word files and translated from the local language to English. Before the analysis, the text will be read through several times to obtain a sense of the whole and familiarise with the data. Then word transcript of the data will be imported into NVivo software V.11[53] and coded line by line. The codes will be compared based on differences and similarities and sorted into categories, and categories will be grouped in themes. Finally, the result will be presented in themes.

Quantitative data entry, cleaning and management

De-identified data will be entered to the predesigned template with appropriately programmed skipping patterns using Epi Info V.3.5.1. Cleaned data will be exported to Stata V.14 software to calculate summary descriptive statistics, including mean (SD) and median (IQR) for continuous variable and proportions for categorical variables. Estimates of population parameters will be presented with their 95% CI. Statistical significance will be declared at $p<0.05$. Follows analytical methods for each of the specific objectives:

Specific objective 2: (to determine the duration of patient, diagnostic and treatment initiation intervals) a descriptive analysis will be used. We will present means with their SD for those with normal distribution, and median and IQR for those variables with skewed distributions. In addition, we will calculate proportions with their 95% CI for patients who waited >3 months before seeking medical care and for those patients who waited more than a month before receipt of diagnosis confirmation following date of presentation.

Specific objective 3 and 4: To determine factors associated with patient and diagnostic intervals, and the association between patient/diagnostic intervals and stage at diagnosis, we first run bivariate analyses to select

candidate explanatory variables. Variables reported as having an impact on longer interval and survival in the literature, and those variables p<0.25 with the dependent variable in the bivariate analysis will be entered into the multivariable logistic regression model to identify their independent effects. Before fitting the binary logistic regression model multicollinearity among the independent variables, outliers and model fitness will be checked. OR with its 95% CI will be calculated for each independent variable against the dependent variable.

Specific objective 5 (to determine PROs): prevalence of cancer caused pain, fatigue and sleeping disorder will be computed. Depression will be measured by nine items. Each item is rated on a 3-point scale, giving maximum scores of 27. The total depression score will be determined, and variation of depression scores at two time points (during diagnosis or treatment and after treatment) will be assessed using repeated measures analysis. Then we will test for the presence of statistical difference of the score across different participants' characteristics and receipt of treatment.

Specific objective 6 and 7 (to describe treatment patterns, adherence and survivorship care): descriptive statistics will be used to characterise the treatment pattern received by the patients and level of adherence. We will compute the proportion (with 95% CI) of patients who received radiotherapy, chemotherapy, hormonal therapy and survivorship care. In addition, multivariable logistic regression analysis will be conducted to examine the association between participants characteristics and three separate outcomes: (1) receipt of radiotherapy and chemotherapy; (2) adherence to chemotherapy and hormonal therapy and (3) receipt of survivorship care. Variables with p<0.25 on bivariate analysis will be retained in the final multivariable logistic regression.

Specific objective 8 (to estimate the financial burden of breast and cervical cancer on patients and their families): data will be analysed descriptively and both the direct and indirect patient-related costs will be computed. The mean or median cost of illness will be computed. Financial difficulties and coping mechanisms made by the patients will be described.

Specific objective 9 (to compute the 2-year survival rates and the determinants of survival): survival will be estimated using the Kaplan-Meier method and compared using the log-rank test. The time to event for the following three types of survival rates will be computed as follow[54] :

- Disease-free survival (DFS) will be computed for stage I–III cases treated with curative intention from the date of primary treatment to the date of local, contralateral or distant recurrence or death from breast or cervical cancer.
- Distant DFS will be computed from the date of primary treatment to the date of distant metastasis or death from breast or cervical cancer.
- Overall Survival (OS) will be computed from the date of diagnosis to the date of death.
- For patients who remained alive and disease-free, data will be censored at the date of the last contact.

We will also compute HR for time-to-event outcomes, with its corresponding 95% CIs, and associated p values. Cox's proportional hazard model will be used to identify factors associated with the survival of the patients. OS will be estimated using the Kaplan-Meier method and compared using the log-rank test. The proportional hazards assumption will be checked using graphical method and goodness-of-fit test. Multivariable Cox regression analysis will be used to estimate the hazard of all-cause HR associated with the preselected various prognostic factors that we are studying.

Patient and public involvement

Neither patients nor the public were involved in the design of the study, the types of research questions and study outcomes or recruitment of participants. However, we conducted a rapid ethical assessment among women with breast and cervical cancer, family members and healthcare providers for designing consent of study participants. We plan to disseminate the results of this research to study participants, staff of healthcare facilities where the study participants are recruited, Addis Ababa Health Bureau, Federal Ministry of Health, cancer control advocates, media and researchers through preparation of fact sheets for lay audience, publications in international peer-reviewed journals and presentations in conferences.

Ethical considerations and result dissemination

Prior to the start of study subjects' recruitment, we conducted rapid ethical assessment to design our consent process.[55] Based on this assessment, we found that most of the participants were not comfortable to written consent for different reasons. Accordingly, we decided to use verbal consent, which has been approved by the Institutional Review Board of College of Health Science of Addis Ababa University. Eligible patients will be verbally informed, by trained research personnel, regarding the nature and purpose of the study, and given time to decide whether or not to participate in the follow-up study. Enrolment will be fully based on the voluntary participation of the study participants and respondents who are interested to avoid specific questions or discontinue the interview will be allowed to do so. In the event, family members are grieving when contacted for vital status, we will offer our condolences and ask then them if they will be willing to speak with us at a later time.

Confidentiality of any information related to the patient and her clinical history will be maintained by keeping both the hard copy and softcopy of every collected data in a locked cabinet and password-secured computer. Only the principal investigators will have access to the de-identified data that will be kept in a secure place. All data will be coded without personal identifiers. All analyses will be on de-identified and coded data.

We intend to present the results of our follow-up study via scientific publications in peer-reviewed journals as well

as through presentation to stakeholders including the public, patients, clinicians and policy-makers.

Information gathered from this study will inform clinical guidelines and public health policies improve the quality of cancer patients' care delivered in the city, as well as other parts of the country. It will also be used to produce fact-based materials to develop 'stories' that illustrate the compelling need for increased resources to reduce suffering and death from cancer. Experience of the survivors will become available and presented to the public to enrich awareness campaigns and show that cancer is not a death sentence[56] but patients can as well be cured. Furthermore, this collaborative project will provide research collaboration opportunities for several graduate students, residents, and junior and senior faculty members of Addis Ababa University and in doing so will enhance the capacity of the university in conducting cancer care delivery and epidemiological research.

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REFERENCES

1. Torre LA, Islami F, Siegel RL, *et al*. Global cancer in women: Burden and trends. *Cancer Epidemiol Biomarkers Prev* 2017;26:444–57.
2. Kantelhardt EJ, Muluken G, Sefonias G, *et al*. A review on breast cancer care in Africa. *Breast Care* 2015;10:364–70.
3. Jemal A, Bray F, Forman D, *et al*. Cancer burden in Africa and opportunities for prevention. *Cancer* 2012;118:4372–84.
4. Timotewos G, Solomon A, Mathewos A, *et al*. First data from a population based cancer registry in Ethiopia. *Cancer Epidemiol* 2018;53:93–8.
5. Kantelhardt EJ, Moelle U, Begoihn M, *et al*. Cervical cancer in Ethiopia: survival of 1,059 patients who received oncologic therapy. *Oncologist* 2014;19:727–34.
6. Kantelhardt EJ, Zerche P, Mathewos A, *et al*. Breast cancer survival in Ethiopia: a cohort study of 1,070 women. *Int J Cancer* 2014;135:702–9.
7. World Health Organization. *Global status report on noncommunicable diseases 2010*. Geneva, Switzerland, 2011. https://www.who.int/nmh/publications/ncd_report2010/en/. (Accessed on Oct 15 2018).
8. Dye TD, Bogale S, Hobden C, *et al*. Experience of initial symptoms of breast cancer and triggers for action in Ethiopia. Hindawi Publishing Corporation. *International Journal of Breast Cancer* 2012;2012:1–5.
9. De Ver Dye T, Bogale S, Hobden C, *et al*. A mixed-method assessment of beliefs and practice around breast cancer in Ethiopia: implications for public health programming and cancer control. *Glob Public Health* 2011;6:719–31.
10. Montazeri A. Quality of life data as prognostic indicators of survival in cancer patients: an overview of the literature from 1982 to 2008. *Health Qual Life Outcomes* 2009;7:1–21.
11. Montazeri A. Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007. *J Exp Clin Cancer Res* 2008;27:1–31.
12. The Federal Democratic Republic of Ethiopia Ministry of Health. Health Sector Transformation Plan 2015/16 - 2019/20. 2015 file:///C:/Users/user/Downloads/ethiopia-health-system-transformation-plan.pdf (Accessed on Dec 2018).
13. Lemlem SB, Sinishaw W, Hailu M, *et al*. Assessment of knowledge of breast cancer and screening methods among nurses in university hospitals in addis ababa, ethiopia, 2011. *ISRN Oncol* 2013;2013:1–8.
14. Azage M, Abeje G, Mekonnen A. Assessment of factors associated with breast self-examination among health extension workers in west gojjam zone, northwest ethiopia. *Int J Breast Cancer* 2013;2013:1–6.
15. Dulla D, Daka D, Wakgari N. Knowledge about cervical cancer screening and its practice among female health care workers in southern Ethiopia: a cross-sectional study. *Int J Womens Health* 2017;9:365–72.
16. Wondimu YT. Cervical cancer: Assessment of diagnosis and treatment facilities in public health institutions in addis ababa, ethiopia. *Ethiop Med J* 2015;53:65-74.
17. Hailu T, Berhe H, Hailu D, *et al*. Knowledge of Breast Cancer and Its Early Detection Measures among Female Students, in Mekelle University, Tigray Region, Ethiopia. *Science Journal of Clinical Medicine* 2014;3:57–64.
18. Legesse B, Gedif T. Knowledge on breast cancer and its prevention among women household heads in Northern Ethiopia. *Open J Prev Med* 2014;04:32–40.
19. Birhane N, Mamo A, Girma E, *et al*. Predictors of breast self - examination among female teachers in Ethiopia using health belief model. *Arch Public Health* 2015;73:4–7.
20. Shiferaw N, Brooks MI, Salvador-Davila G, *et al*. Knowledge and awareness of cervical cancer among hiv-infected women in ethiopia. *Obstet Gynecol Int* 2016;2016:1–8.
21. Aweke YH, Ayanto SY, Ersado TL. Knowledge, attitude and practice for cervical cancer prevention and control among women of childbearing age in Hossana Town, Hadiya zone, Southern Ethiopia: Community-based cross-sectional study. *PLoS One* 2017;12:e0181415.
22. Tefera F, Mitiku I. Uptake of cervical cancer screening and associated factors among 15-49-year-old women in dessie town, northeast ethiopia. *J Cancer Educ* 2017;32:901–7.
23. Mitiku I, Tefera F. Knowledge about cervical cancer and associated factors among 15-49 year old women in dessie town, northeast ethiopia. *PLoS One* 2016;11:e0163136.
24. Getahun F, Mazengia F, Abuhay M, *et al*. Comprehensive knowledge about cervical cancer is low among women in Northwest Ethiopia. *BMC Cancer* 2013:13:2.
25. Bayu H, Berhe Y, Mulat A, *et al*. Cervical cancer screening service uptake and associated factors among age eligible women in mekelle zone, northern ethiopia, 2015: A community based study using health belief model. *PLoS One* 2016;11:e0149908.
26. Birhanu Z, Abdissa A, Belachew T, *et al*. Health seeking behavior for cervical cancer in Ethiopia: a qualitative study. *Int J Equity Health* 2012:11:83.
27. Belete N, Tsige Y, Mellie H. Willingness and acceptability of cervical cancer screening among women living with HIV/AIDS in Addis Ababa, Ethiopia: a cross sectional study. *Gynecol Oncol Res Pract* 2015;2:2.
28. Ersumo T. Breast Cancer in an Ethiopian population, Addis Ababa. *East and Central African Journal of Surgery* 2006;11:81–5.
29. Abate SM, Yilma Z, Assefa M, *et al*. Trends of breast cancer in ethiopia. *Int J Cancer Res Mol Mech* 2016;2:1–5.
30. Kantelhardt EJ, Mathewos A, Aynalem A, *et al*. The prevalence of estrogen receptor-negative breast cancer in Ethiopia. *BMC Cancer* 2014;14:1–6.

31. Hailu A, Mariam DH. Patient side cost and its predictors for cervical cancer in Ethiopia: a cross sectional hospital based study. *BMC Cancer* 2013;13:1–8.
32. Dye TD, Bogale S, Hobden C, *et al*. Complex care systems in developing countries: breast cancer patient navigation in Ethiopia. *Cancer* 2010;116:577–85.
33. Gizaw M, Addissie A, Getachew S, *et al*. Cervical cancer patients presentation and survival in the only oncology referral hospital, Ethiopia: a retrospective cohort study. *Infect Agent Cancer* 2017.12.
34. Tadesse SK. Socio-economic and cultural vulnerabilities to cervical cancer and challenges faced by patients attending care at Tikur Anbessa Hospital: a cross sectional and qualitative study. *BMC Womens Health* 2015;15:1–12.
35. Federal Democratic Repeblic of Ethiopia Centeral statistics Agency. Population Projection of Ethiopia for all regions at wereda level from 2014 – 2017. 2013 www.csa.gov.et/ (Assessed on 23 Nov 2016).
36. Federal Democratic Republic of Ethiopia Ministry of Health. Health and Health Related Indicators 2007 E.C. 2015http://www.dktethiopia.org/publications/health-and-health-related-indicators-2007-ec-2015. 2015 (Accessed on 25 Feb 2019).
37. Ethiopia Federal Ministry of Health. *Ethiopia's Household Health Services Utilization and Expenditure Survey Briefing Notes*. 5. Addis Ababa, Ethiopia, 2014. Accessed from. https://www.hfgproject.org/wp-content/uploads/2014/04/Ethiopia-NHA-Survey-Briefing-Notes.pdf.
38. African Cancer Regisrty Network. Addis Ababa population Based cancer registery. Addis ababa city cancer registry - african cancer registry network. http://afcrn.org/membership/members/100-Addisababa. (Accessed on 27 Jun 2017).
39. Harirchi I, Karbakhsh M, Hadi F, *et al*. Patient delay, diagnosis delay and treatment delay for breast cancer: Comparison of the pattern between patients in public and private health sectors. *Arch Breast Cancer* 2015;2:15–20.
40. Pace LE, Mpunga T, Hategekimana V, *et al*. Delays in Breast Cancer Presentation and Diagnosis at Two Rural Cancer Referral Centers in Rwanda. *Oncologist* 2015;20:780–8.
41. Hanlon C, Medhin G, Selamu M, *et al*. Validity of brief screening questionnaires to detect depression in primary care in Ethiopia. *J Affect Disord* 2015;186:32–9.
42. National Cancer Instutite and Northern California. Assessment of Patients' Experience of Cancer Care (APECC) Study. https://healthcaredelivery.cancer.gov/apecc/.
43. National Cancer Instutite U. S. Department of Health and Human Services National Institutes of Health. Adolecent and Young Adult Health Outcome and Patient Experiance. Follow-up survey.
44. The Agency for Healthcare Research and Quality and The Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services. Medical Expenditure Survey. Your Experiences with Cancer. https://healthcaredelivery.cancer.gov/meps/.
45. Harlan LC, Lynch CF, Keegan TH, *et al*. Recruitment and follow-up of adolescent and young adult cancer survivors: the AYA HOPE Study. *J Cancer Surviv* 2011;5:305–14.
46. Freitas AG, Weller M. Patient delays and system delays in breast cancer treatment in developed and developing countries. *Cien Saude Colet* 2015;20:3177–89.
47. Weller D, Vedsted P, Rubin G, *et al*. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. *Br J Cancer* 2012;106:1262–7.
48. Sharma K, Costas A, Damuse R, *et al*. *The Haiti Breast Cancer Initiative: Initial Findings and Analysis of Barriers-to-Care Delaying Patient Presentation*. Journal of Oncology: Hindawi Publishing Corporation, 2013:1–6.
49. Ramirez AJ, Westcombe AM, Burgess CC, *et al*. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. *Lancet* 1999;353:1127–31.
50. Sharma K, Costas A, Shulman LN, *et al*. A systematic review of barriers to breast cancer care in developing countries resulting in delayed patient presentation. *J Oncol* 2012;2012:1–8.
51. Edge SB. *AJCC cancer staging manual*. 7th ed. New York: Springer, 2010. https://cancerstaging.org/references-tools/deskreferences/Documents/AJCC%207th%20Ed%20Cancer%20Staging%20Manual.pdf. (Accessed on Jan 2018).
52. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. *Int J Gynaecol Obstet* 2009;105:107–8.
53. Hamunyela RH, Serafin AM, Akudugu JM. Strong synergism between small molecule inhibitors of HER2, PI3K, mTOR and Bcl-2 in human breast cancer cells. *Toxicol In Vitro* 2017;38:117–23.
54. Hudis CA, Barlow WE, Costantino JP, *et al*. Proposal for standardized definitions for efficacy end points in adjuvant breast cancer trials: the STEEP system. *J Clin Oncol* 2007;25:2127–32.
55. Gebremariam A, Yalew AW, Hirpa S, *et al*. Application of the rapid ethical assessment approach to enhance the ethical conduct of longitudinal population based female cancer research in an urban setting in Ethiopia. *BMC Med Ethics* 2018;19:1–12.
56. Azubuike SO, Muirhead C, Hayes L, *et al*. Rising global burden of breast cancer: the case of sub-Saharan Africa (with emphasis on Nigeria) and implications for regional development: a review. *World J Surg Oncol* 2018;16:1–13.