BMJ Open

Social Determinants and Individual Health Seeking Behavior among Women in Kenya: A Breast Cancer Cohort Study Protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023171
Article Type:	Protocol
Date Submitted by the Author:	02-Apr-2018
Complete List of Authors:	Gakunga, Robai; Independent Research Scientist Ali, Zipporah; Kenya Hospices and Palliative Care Association Korir, Anne; Kenya Cancer Association; Kenya Medical Research Institute Kinyanjui, Asaph; Kenya Hospices and Palliative Care Association Ochieng', Emily; Kenya Cancer Association Gikaara, Nancy; Kenya Hospices and Palliative Care Association Kivuva, Florence; Kenya Cancer Association Subramanian, Sujha; RTI International,
Keywords:	Breast tumours < ONCOLOGY, Epidemiology < ONCOLOGY, SOCIAL MEDICINE, Adult palliative care < PALLIATIVE CARE

Title:

Social Determinants and Individual Health Seeking Behavior among Women in Kenya: A Breast Cancer Cohort Study Protocol

Authors:

Robai Gakunga[1] – robaigakunga@yahoo.com

Zipporah Ali[2] – zippy@kehpca.org

Anne Korir[3] – annkorir@yahoo.com

Asaph Kinyanjui[2] – asaphkinyanjui@kehpca.org

Emily Ochieng'[3] – eochieng@kenyacancer.org

Nancy Gikaara[2] - ngikaara@yahoo.com

Florence Kivuva[3] – flokivuva2006@yahoo.com

Sujha Subramanian[4] – ssubramanian@ rti.org

[1] Independent Research Scientist, Nairobi, Kenya

[2] Kenya Hospices and Palliative Care Association (KEHPCA)

[3] Kenya Cancer Association (KENCANSA)

[4] RTI International

Word Count: 3020

Corresponding Author:

Dr. Robai Gakunga

robaigakunga@yahoo.com

Key Words:

Breast Cancer, Cohort Studies, Follow-up Studies, Social Determinants of Health, Patient Acceptance of Healthcare

ABSTRACT

Introduction

A catastrophic 66% increase in the burden of breast cancer in Kenya has been predicted by 2025. Mitigating this burden is critical and local research is necessary to generate the evidence to inform policy, public health and medical practice. Most of the knowledge available has been derived from studies in high income countries which are not directly applicable due to economic, social, cultural and ethnic differences. At the time of writing this paper, we had no knowledge of any longitudinal cohort studies in sub-Saharan Africa of both breast cancer survivors and a matching cohort of women who have never had a diagnosis of cancer. We aim to pilot cohort studies in Kenya that not only consider clinical characteristics but also social determinants and individual health seeking behavior.

Methods and analysis

This will be a two-pronged, prospective mixed methods comparative cohort study where quantitative and qualitative data will be collected concurrently, then analyzed separately and together to enrich understanding of concepts by triangulation. We aim to include 800 women aged 30-60 years; 400 in the survivorship cohort and 400 in the comparative cohort. The initial contact will be face-to-face interviews followed by outreach through telephone approximately 3 months later. Two focus group discussions from each cohort will be carried out to enhance understanding of concepts and to guide recommendations.

Ethics and dissemination

Independent ethical approval was obtained from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee and the Research Triangle Institute (RTI) International Independent Review Board. Only consenting participants will be enrolled in the cohorts and counselling support, debriefing discussions and referral for formal support services, will be available for both the participants and the research assistants. Findings will be disseminated by publication in peer reviewed journals and through oral and poster presentations for various audiences.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is a pilot cohort study that includes women who have had a diagnosis of breast cancer and a comparative group of women who have never had a diagnosis of breast cancer.
- Our questionnaires are based on previously tested concepts and questions that will be adapted for the local setting, and subjected to cognitive testing to ensure appropriate language is used to facilitate comprehension.
- To perform a comprehensive assessment, we include data elements to capture social determinants and individual health seeking behavior.
- For the survivorship group, recall bias will be minimized by limiting the inclusion criteria to 3 years since diagnosis.
- The study will be conducted in Nairobi (the capital city of Kenya) and its environs where cancer management services are concentrated and our findings may not be a true reflection of the entire country but a reasonable starting point for extension to other regions.

BACKGROUND

Breast cancer is a leading cancer in incidence among women in Kenya and a substantial contributor to early mortality. Globocan 2012[1] statistics show that breast cancer incidence rate in Kenya is estimated at 38.3 per 100,000 with a mortality rate of 17.3 per 100,000. The annual incidence of breast cancer in Kenya is about 4,500 (11% of all new cancer cases), and the annual mortality is about 2,000 (7% of all cancer deaths). By 2025, it is predicted that the annual incidence of breast cancer in Kenya will increase to 7,396 (66% increase) with an annual mortality of 3,258. In comparison, the breast cancer incidence rates in the United States of America and the United Kingdom are much higher at 92.9 and 95.0 per 100,000 respectively but the mortality rates are a much lower at 14.9 and 17.1 per 100,000 population respectively. These statistics highlight the huge burden in the incidence to mortality ratio for Kenya, a lower-middle income country, versus that for the USA and UK, high income countries. Additionally, women are diagnosed at a younger age in Kenya. The median age at breast cancer diagnosis in the USA is 62 years[2] while in Nairobi, which is the capital city of Kenya, the highest age specific incidence rate (per 100,000) is among those 45-49 years of age *(unpublished data – Nairobi Cancer Registry, 2007-2011).*

The current burden and the predicted catastrophic future increase in incidence and mortality of breast cancer in Kenya may be mitigated by advancing research into breast cancer risk factors, including genetics, and management to support prevention, control, treatment and survivorship. The Kenya National Cancer Control Strategy (2017-2022) has been developed by a collaborative stakeholder approach led by the country's Ministry of Health to "serve as the blue print to reduce the incidence, mortality of cancer, down-staging and improve survival rate and quality of life of cancer patients in Kenya". It consists of five strategic pillars with one of pillars detailing the prioritized research agenda for the country. The priorities include epidemiological research on human behavioural factors, environmental and occupational risk factors and treatment options including their effectiveness and costs[3].

Paucity of breast cancer research in Kenya and the sub-Saharan African region in general, has resulted in an inadequate local evidence pool of knowledge that could be referred to for locally relevant interventions and resource planning. Breast cancer related interventions are currently

planned using a top-down approach rather than a bottom-up consultative approach that systematically evaluates the factors that impact health-seeking behaviour in the targeted population. There is growing acknowledgement that the social determinants of health affect self-care and health behaviours. Social determinants are the conditions in which people are born, grow, live, work, and age. They include factors like socioeconomic status, education, the physical environment, employment, and social support networks, as well as access to health care[4]. Understanding individuals' social determinants is essential to creating programs that address potential barriers to health care and improve overall health. For example, socioeconomic status can determine whether cost is a key barrier to obtaining health services; education levels can impact health literacy and self-care behaviours; and social support networks can perpetuate stigma and delays in seeking care. Social and cultural obstacles, if not considered, may impede the success of any cancer care program[5]. In addition, there is limited knowledge on individual level breast cancer risk factors including family history, reproductive history and lifestyle factors.

Cohort studies could provide evidence based knowledge to understand and address these factors that impact access to high quality care. In 2010, Holmes *et al*. published the need to establish cohorts in Africa in order to explain disease aetiology, and to support the development of prevention and control measures specific to the region[6]. Optimal design tailored to the local environment can support longitudinal data collection. In 2015, Dalal et al.[7] found that it was feasible to conduct large cohort studies in Sub-Saharan Africa and mobile telephony with its growing penetration and accessibility into communities, may be particularly useful. In their study face to face interviews were very successful in Uganda, use of postal services or email were a challenge in Tanzania with low return of questionnaires by post attributed to relative scarcity of post offices. Intermittent internet access in the region may also hinder questionnaire distribution and return. Despite the growing evidence on approaches to improve cohort studies in Sub-Saharan Africa, there have been very few breast cancer cohort studies[8, 9]. These studies have only enrolled women already diagnosed with cancer which does not provide opportunities to systematically evaluate the ability to prevent and screen for breast cancers. To address this gap, the current study includes both breast cancer survivors and a matching cohort of women who have never had a diagnosis of breast cancer.

OBJECTIVES

Our overall goals are to explore feasibility of conducting a breast cancer cohort study in Kenya and assess ability to collect information on social determinants and individual health seeking behavior. We intend to identify barriers and propose interventions to improve women's access to cancer prevention, treatment and survivorship care services in Kenya.

Our specific objectives include:

1. To establish feasibility of identifying and recruiting individuals to participate in a cohort study who have had a diagnosis of breast cancer within the past 3 years at the time of recruitment to minimize recall bias and a similar group of women who have never had a diagnosis of breast cancer.
2. To determine the ability to maintain contact for follow-up assessments by conducting outreach by telephone (preferable mobile phones) at 3 months after initial contact.
3. To obtain baseline information on social determinants of health, breast cancer risk factors, health seeking behaviour related to breast cancer screening and treatments received.

METHODS

Study Design and Conceptual Framework

This is a prospective mixed methods comparative cohort study where both quantitative and qualitative data will be collected concurrently, then analyzed separately and together to enrich understanding of concepts by triangulation.

Figure 1 presents the framework for assessing social determinants, and individual preferences, risk factors and treatment patterns in impacting breast cancer outcomes. This framework served as the theoretical underpinning for developing the data collection instruments. Understanding the causal pathways of the determinants of health are essential to identify the root cause of health problems and to identify tailored interventions[10-12]. Over the long term, policies can also be implemented to drive structural changes to modify the social determinants themselves; for example, increasing the overall education level in the target population. In this study, we will capture information regarding social determinants, risk factors and health seeking behavior to identify potential hypothesis that can be evaluated in future studies to develop targeted interventions and policies.

Questionnaire Development

The questionnaires to be used in this study were largely based on prior surveys and include several validated instruments. Table 1 summarizes the components included in the questionnaires and provides details on the source of the questions.

Table 1: Kenya Breast Cancer Cohort Study - Components of the Questionnaire

Components	Cohort		Source of questions
	Breast Cancer	Non- Breast Cancer	
Background Information To collect details such as (1) demographics, (2) socioeconomic status, (3) health status	√	√	Kenya Demographic and Health Survey (2014)[14]
Breast Cancer Risk Assessment	√	√	Breast Cancer Risk Assessment Tool - Cancer Research UK https://www.cancer.gov/bcrisktool/ [15]
Insurance status and Employment	√	√	Investigator developed questions
Breast Cancer Knowledge		√	Breast Cancer Awareness Measure (Breast CAM) Toolkit Updated 09.02.11 (Modified) [16]
Cancer Treatment and breast cancer symptom assessment	√		Investigator developed questions and the NCCN FBSI-16 (Version 2) (http://www.facit.org/facitorg/questionnaires) [17]
Qualitative feedback. Questions to obtain suggestions on how to improve self-care behaviors and health care delivery	√	√	Investigator developed questions

We reviewed published literature on key concepts and also solicited expert opinion to further tailor the content for the Kenyan setting. Using the questionnaires, we will obtain information on patient demographics, socioeconomics, risk factors, breast cancer treatment and access to care. We included multiple questions that address the same construct to ensure comprehensive data collection and to assess internal consistency.

Cognitive testing will be performed to support reliability and validity of the questionnaires. We will conduct one-on-one interviews of about 60 minutes each to perform cognitive testing with

10 individuals with a diagnosis of breast cancer and 10 individuals without a diagnosis of breast cancer. The cognitive testing will assess clarity and the ability of the interviewees to understand the questions and provide accurate responses. Participants will be instructed to listen to each question and then convey to the interviewer which response or responses applied and justify the selection of their response so comprehension can be assessed. Following the completion of the questionnaire, the interviewer will probe the interviewer on any aspects of the questionnaire that proved difficult or confusing for the respondent. We will also ask each participant some additional debriefing questions about the length and burden of the questions and their feelings about the content of the questions. The findings from the cognitive testing will be used to tailor the wording in the draft questionnaires to clarify the information required and remove any ambiguity. We will also take steps to reduce the length of the survey if the number of questions prove to be burdensome to the participants. In addition to this, we will also perform one-on-one interviews with up to 20 women to ensure the content of the questionnaire adequately addresses issues faced by women diagnosed with breast cancer. A maximum of 40 participants will be included in the cognitive testing.

Study Participants

The study targets women aged 30-60 years in four purposively selected counties of Kenya; Nairobi, Kiambu, Machakos and Nyeri. This age group has a high incidence and prevalence of breast cancer and they are recommended to undergo breast screening via clinical breast exams or mammograms. We will include women who voluntarily give consent and are able to provide contact information so that we can conduct 3-month follow up interviews over the telephone. We will exclude women who do not speak and understand the study languages – English and Kiswahili. Kiswahili is the national language and majority of women between the ages of 30 – 60 years are conversant in either English or Kiswahili.

Sample size calculation

We determined that a sample size of 400 each would be adequate for the cancer and non-cancer cohorts based on a 95% confidence interval where the margin of error is ± 5%.

Our sample size is based on the following calculation:

Sample Size = (Z-score) ^{2} * p*(1-p) / (margin of error)^2

Sample Size adjusted = (Sample Size) / (1 + [(Sample Size – 1) / population])

Z-score = 1.96 for confidence level 95%

Proportion (p) is not known, so we used 0.5 based on common practice.

Margin of error=5%

We estimate that 1,500 women were diagnosed with breast cancer during the previous 3-year period (*based on unpublished data by Nairobi Cancer Registry)* and will meet our inclusion criteria in the four counties targeted by this study. We assumed 60% five -year survival rate based on published literature of survival of breast cancer patients in Africa[13].

The above calculation gives us a sample size of 306 for the cancer cohort. We assumed that 80% of the cohort will be contacted via telephone to perform follow up interviews to bring the sample required to 383. We included a 5% mark up for non-response that results in 402 respondents and we rounded this to 400 patients. We will select an equal number of cancer and non-cancer patients for a total of 800 women overall.

Recruitment

After eligibility assessment, consecutive women meeting the recruitment criteria will be approached by the trained research assistants for consent to participate. The research assistants will provide information as per prepared consent forms. Face-to-face interviews will be held either at the same location on the same day of recruitment or at a later time or day with an appointment; in each case consent will be obtained immediately before the interview. Research assistants will obtain signatures or thumb prints for those who can write and those who cannot write respectively. Participants will be given a copy of the consent form and will be offered financial support to travel to the interview site. Recruitment and data collection will be from November 2017 to June 2018.

Patient and Public Involvement

Partner organizations, Kenya Cancer Association (KENCANSA) works directly with patients as they provide navigation and palliative care services and Kenya Hospices and Palliative Care

Association (KEHPCA) works closely with hospices and palliative care units across the country. This study was conceptualized based on priorities, experiences and preferences that women exhibited or shared during these interactions. We will recruit patients from KEHPCA and KENCASA membership lists and affiliated support groups, from Kenyatta National Hospital (the main referral hospital in Kenya), private hospitals, and palliative care units. We will not maintain contact information of the study participants beyond the period necessary for the data collection. We therefore do not plan to share the study findings directly with the patients. The findings will be presented in meetings organized by KENCANSA and KEHPCA, and we will also disseminate the results in peer-reviewed journal publications.

DATA ANALYSIS

Quantitative Data Analysis

Data processing and analysis will start in the field by checking for completeness of the data and performing quality control checks and sorting the data by instrument used. Data from the breast cancer and non-cancer cohorts will be compared for any similarities and differences in terms of demographics, socioeconomic factors, breast cancer risk, insurance and financial burden, employment status, access to treatment and comorbidities. We will conduct, chi-square tests, t-tests, ANOVAs or appropriate nonparametric tests to determine differences between the cohorts. These differences will be further explored using multivariate analysis to control for potential confounders between the two groups. Additionally regression analysis will be conducted to evaluate health seeking behavior, factors impacting decision making concerning cancer care and patient self-care attitudes. Furthermore, we will assess quality of life among breast cancer survivors using the standardized scoring for the National Comprehensive Cancer Network Functional Assessment of Cancer Therapy – Breast Cancer Symptom Index – 16 ***(NCCN FBSI-16)*** (Version 2) and compare with scores available from other breast cancer survivors. We will also determine the level of breast cancer knowledge among the non-cancer cohort by analysing the concepts in the Breast Cancer Awareness Measure ***(Breast CAM).***

Potential confounders in this cohort study would be age and economic stability, cancer stage at diagnosis, comorbidities and treatment options applied. We have minimized on over-exclusion to retain sufficient sample size - women of 30-60 years of age are included. In the questionnaires

we have stratifier questions on economic stability, cancer stage at diagnosis, comorbidities and treatment options applied. At analysis we will adjust for these confounders.

Qualitative Data Analysis

We plan to conduct four focus groups discussions; two focus groups with breast cancer survivors and another two with those without a previous diagnosis of cancer. We will recruit 8-10 participants per group. We have developed focus group discussion guides to explore key concepts related to breast cancer screening, diagnosis, treatment and survivorship care for breast cancer. Barriers and facilitators will be specifically explored during these focus group discussions. This information will help us with contextual details to interpret the quantitative data that will be collected.

We will use NVivo to develop coding tables to categorize the unstructured qualitative data. Two grant researchers will independently assess the crosswalk between the codes and qualitative information to determine consistency. We will also use flow charts, concept mapping, word clouds, and concept counts to explore the data visually. Qualitative feedback from the focus group discussions and the individual interviews will inform the study conclusions and recommendations.

ETHICS AND DISSEMINATION

This is a collaborative study by RTI International, KEHPCA and KENCANSA. Independent Scientific and Ethical approval was obtained from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee and the Research Triangle Institute (RTI) International Independent Review Board. Only consenting participants will be included and plans are in place to refer participants to a hospice or palliative care unit for counselling in the event that they feel psychologically or emotionally distressed during the discussions or interview. Data collectors will also have access to hospices and palliative care units for debriefing.

Findings will be disseminated by publication in peer reviewed journals and through oral and poster presentations for various audiences including scientific meetings.

DISCUSSION

In this study we will conduct a prospective, comparative cohort study of women with and without a diagnosis of breast cancer in Kenya to pilot test the approach of using face-to-face interviews and follow-up telephone calls to collect longitudinal data. We will also expand traditional data collection beyond demographics and clinical information to also obtain data on social determinants and individual health seeking behavior. Social determinants as described in the background of this paper and individual health seeking behavior have a direct impact on the implementation of interventions for reducing the burden from breast cancer. Interventions developed with disregard to these determinants may face low uptake or even rejection. There is need to embrace implementation science research which addresses determinants of intervention adoption in the real-world setting.

Cohort studies have not been previously established in Kenya and many other Sub Saharan Africa countries because of the challenges in maintaining participant contact and the high cost of running these studies. With increased mobile telephony, we presume that continued re-contact of participants is feasible. The high cost of cohort studies needs to be evaluated against their benefits if findings could inform optimal interventions for disease mitigation. Cancer incidence and mortality is rising at an alarming rate and there is need to find ways of reversing this trend using various evidence-based approaches.

Stigma associated with breast cancer may limit women's willingness to participate in this study but we will ensure proper communication of research procedures and benefits. We will maximize recruitment through close collaboration with breast cancer support groups, palliative care service providers, and healthcare workers in both public and private institutions. The study locations are within or in close proximity to Nairobi county and therefore our findings may not be generalizable to the entire country –the findings from this study will serve as a baseline assessment which can be extended to other counties in the future. We will collect data on cancer treatment and therefore there could be recall bias; we have specifically decided to interview women who have received treatment in the past three years to minimize recall bias. Women interviewed may not want to respond to all questions posed and therefore there could be missing data for certain fields as we analyze the data collected.

The findings and lessons learnt from this pilot study of 800 participants will provide a road map for future cohort studies in Kenya and the region. Local evidence on breast cancer prevention, screening and treatment is critical for tailored public health and medical interventions to address the growing burden of breast cancer.

References

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer incidence and mortality worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr

2. Surveillance, Epidemiology and End Results Programme [Internet] National Institute of Health, National Cancer Institute; 2017 [cited 2018 Feb 23] Available from: https://seer.cancer.gov/statfacts/html/breast.html

3. National Cancer Control Strategy 2017-2022 [Internet]. Ministry of Health; 2017 [cited 2017 Nov18] Available from: http://kehpca.org/wp-content/uploads/KENYA-NATIONAL-CANCER-CONTROL-STRATEGY-2017-2022.pdf

4. Marmot M, Friel S, Bell R, et al. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health. The lancet. 2008 Nov 14;372(9650):1661-9.

5. Anderson BO, Yip CH, Ramsey SD, et al. Breast cancer in limited-resource countries: health care systems and public policy. The breast journal. 2006 Jan 1;12(s1).

6. Holmes MD, Dalal S, Volmink J, et al. Non-communicable diseases in sub-Saharan Africa: the case for cohort studies. PLoS medicine. 2010 May 11;7(5):e1000244.

7. Dalal S, Holmes MD, Laurence C, et al. Feasibility of a large cohort study in sub-Saharan Africa assessed through a four-country study. Global health action. 2015 Dec 1;8(1):27422.

8. Kantelhardt EJ, Zerche P, Mathewos A, et al. Breast cancer survival in Ethiopia: a cohort study of 1,070 women. International journal of cancer. 2014 Aug 1;135(3):702-9.

9. Galukande M, Wabinga H, Mirembe F. Breast cancer survival experiences at a tertiary hospital in sub-Saharan Africa: a cohort study. World journal of surgical oncology. 2015 Jul 19;13(1):220.

10. Dow WH, Schoeni RF, Adler NE, Stewart J. Evaluating the evidence base: Policies and interventions to address socioeconomic status gradients in health. Annals of the New York Academy of Sciences. 2010 Feb 1;1186(1):240-51.

11. Braveman P, Egerter S, Williams DR. The social determinants of health: coming of age. Annual review of public health. 2011 Apr 21;32:381-98.

12. Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. Health affairs. 2002 Mar 1;21(2):60-76.

13. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet (London, England). 2015;385(9972):977-1010. doi:10.1016/S0140-6736(14)62038-9.

14. Kenya National Bureau of Statistics. Kenya Demographic and Health Survey 2014. Nairobi; 2015 p. 440-441.

15. Breast Cancer Risk Assessment Tool [Internet]. Cancer.gov. 2017 [cited 19 July 2017]. Available from: https://www.cancer.gov/bcrisktool/

16. Linsell L, Forbes LJ, Burgess C, et al. Validation of a measurement tool to assess awareness of breast cancer. European Journal of Cancer. 2010 May 31;46(8):1374-81.

17. Questionnaires [Internet]. Facit.org. 2017 [cited 19 July 2017]. Available from: http://www.facit.org/facitorg/questionnaires

Authors' contributions:

RG, SS, ZA and AN conceptualized and designed the study. RG and SS carried out literature review and drafted the manuscript. EO gave considerable input on data analysis procedures. ZA and AK made substantial input on ethical considerations. AK,NK and FK contributed to mapping of study sites, reviewing and editing of study tools. All authors have read the manuscript for its intellectual content and given approval for submission.

Acknowledgements:

RTI International

Kenya Hospices and Palliative Care Association (KEHPCA) their membership and affiliated Palliative Care Units

Kenya Cancer Association (KENCANSA) their membership and affiliated support groups

Funding statement:

This work was supported by RTI International

Competing interests statement.

The authors declare that there is no conflict of interest

Figure 1: Social determinants, and individual preferences and risk factors to improve breast cancer outcome

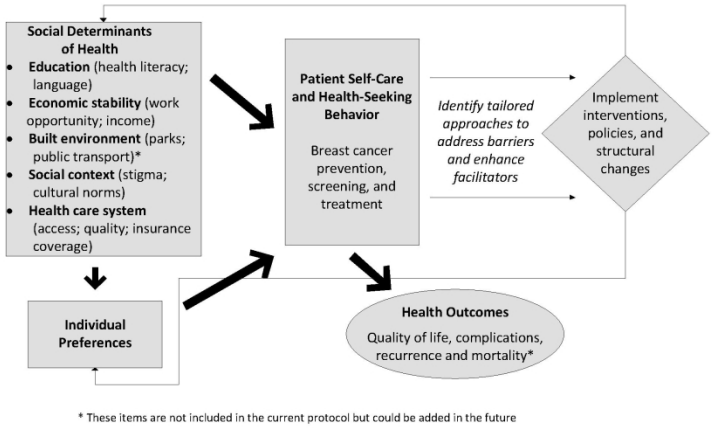

Figure 1: Social determinants, and individual preferences and risk factors to improve breast cancer outcome

215x279mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	#1 and #2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	#2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#4 and #5
Objectives	3	State specific objectives, including any prespecified hypotheses	#6
Methods			
Study design	4	Present key elements of study design early in the paper	#7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#9 and #10
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	#9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	#9 and #10
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#11 and #12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#11
Bias	9	Describe any efforts to address potential sources of bias	#6
Study size	10	Explain how the study size was arrived at	#9 and #10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	#11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#11 and #12
		(*b*) Describe any methods used to examine subgroups and interactions	#11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	#9 and #11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	#13 and #14
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	N/A
Generalisability	21	Discuss the generalisability (external validity) of the study results	#13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Social Determinants and Individual Health Seeking Behavior among Women in Kenya: Protocol for a Breast Cancer Cohort Feasibility Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023171.R1
Article Type:	Protocol
Date Submitted by the Author:	10-Jul-2018
Complete List of Authors:	Gakunga, Robai; Independent Research Scientist Ali, Zipporah; Kenya Hospices and Palliative Care Association Korir, Anne; Kenya Cancer Association; Kenya Medical Research Institute Kinyanjui, Asaph; Kenya Hospices and Palliative Care Association Ochieng', Emily; Kenya Cancer Association Gikaara, Nancy; Kenya Hospices and Palliative Care Association Kivuva, Florence; Kenya Cancer Association Subramanian, Sujha; RTI International,
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Epidemiology, Public health, Oncology
Keywords:	Breast tumours < ONCOLOGY, Epidemiology < ONCOLOGY, SOCIAL MEDICINE, Adult palliative care < PALLIATIVE CARE

Title:

Social Determinants and Individual Health Seeking Behavior among Women in Kenya: Protocol for a Breast Cancer Cohort Feasibility Study

Authors:

Robai Gakunga[1] – robaigakunga@yahoo.com

Zipporah Ali[2] – zippy@kehpca.org

Anne Korir[3] – annkorir@yahoo.com

Asaph Kinyanjui[2] – asaphkinyanjui@kehpca.org

Emily Ochieng'[3] – eochieng@kenyacancer.org

Nancy Gikaara[2] - ngikaara@yahoo.com

Florence Kivuva[3] – flokivuva2006@yahoo.com

Sujha Subramanian[4] – ssubramanian@ rti.org

[1] Independent Research Scientist, Nairobi, Kenya

[2] Kenya Hospices and Palliative Care Association (KEHPCA)

[3] Kenya Cancer Association (KENCANSA)

[4] RTI International

Word Count: 3416

Corresponding Author:

Dr. Robai Gakunga

robaigakunga@yahoo.com

Key Words:

Breast Cancer, Cohort Studies, Follow-up Studies, Social Determinants of Health, Patient Acceptance of Healthcare

ABSTRACT

Introduction

A catastrophic 66% increase in the burden of breast cancer in Kenya has been predicted by 2025. Mitigating this burden is critical and local research is necessary to generate the evidence to inform policy, public health and medical practice. Most of the knowledge available has been derived from studies in high income countries which are not directly applicable due to economic, social, cultural and ethnic differences. At the time of writing this paper, we had no knowledge of any longitudinal cohort studies in sub-Saharan Africa of both breast cancer survivors and a matching cohort of women who have never had a diagnosis of cancer. We aim to assess feasibility of cohort studies in Kenya that not only consider clinical characteristics but also social determinants and individual health seeking behavior.

Methods and analysis

This study aims to inform best practices for initiating a longitudinal cohort study in Kenya. It is a two-pronged, prospective mixed methods comparative study of women with and without a diagnosis of breast cancer with baseline data collection and one follow-up data collection approximately 3 months later by telephone. Quantitative and qualitative data will be collected concurrently, analyzed separately and together to enrich understanding of concepts by triangulation. We aim to include 800 women aged 30-60 years; 400 in the survivorship cohort and 400 in the non-cancer cohort. Two focus group discussions from each cohort will be carried out to enhance understanding of concepts and to guide recommendations.

Ethics and dissemination

Independent ethical approval was obtained from Kenyatta National Hospital-University of Nairobi Ethics and Research Committee and the Research Triangle Institute (RTI) International. Only consenting participants will be enrolled. Counselling support, debriefing discussions and referrals for formal support services will be available for both participants and research assistants. Findings will be disseminated through publications, websites and presentations.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is a feasibility cohort study that includes women who have had a diagnosis of breast cancer and a comparative group of women who have never had a diagnosis of breast cancer.
- Our questionnaires are based on previously tested concepts and questions that will be adapted for the local setting, and subjected to cognitive testing to ensure appropriate language is used to facilitate comprehension.
- To perform a comprehensive assessment, we include data elements to capture social determinants and individual health seeking behavior.
- For the survivorship group, recall bias will be minimized by limiting the inclusion criteria to 3 years since diagnosis.
- The study will be conducted in Nairobi (the capital city of Kenya) and its environs where cancer management services are concentrated and our findings may not be a true reflection of the entire country but a reasonable starting point for extension to other regions.

BACKGROUND

Breast cancer is a leading cancer in incidence among women in Kenya and a substantial contributor to early mortality. Globocan 2012[1] statistics show that breast cancer incidence rate in Kenya is estimated at 38.3 per 100,000 with a mortality rate of 17.3 per 100,000. The annual incidence of breast cancer in Kenya is about 4,500 (11% of all new cancer cases), and the annual mortality is about 2,000 (7% of all cancer deaths). By 2025, it is predicted that the annual incidence of breast cancer in Kenya will increase to 7,396 (66% increase) with an annual mortality of 3,258. In comparison, the breast cancer incidence rates in the United States of America and the United Kingdom are much higher at 92.9 and 95.0 per 100,000 respectively but the mortality rates are much lower at 14.9 and 17.1 per 100,000 population respectively. These statistics highlight the huge burden in the incidence to mortality ratio for Kenya, a lower-middle income country, versus that for the USA and UK, high income countries. Additionally, women are diagnosed at a younger age in Kenya. The median age at breast cancer diagnosis in the USA is 62 years[2] while in Nairobi, which is the capital city of Kenya, the highest age specific incidence rate (per 100,000) is among those 45-49 years of age *(unpublished data – Nairobi Cancer Registry, 2007-2011).*

The current burden and the predicted catastrophic future increase in incidence and mortality of breast cancer in Kenya may be mitigated by advancing research into breast cancer risk factors, including genetics, and management to support prevention, control, treatment and survivorship. The Kenya National Cancer Control Strategy (2017-2022) has been developed by a collaborative stakeholder approach led by the country's Ministry of Health to "serve as the blue print to reduce the incidence, mortality of cancer, down-staging and improve survival rate and quality of life of cancer patients in Kenya". It consists of five strategic pillars with one of the pillars detailing the prioritized research agenda for the country. The priorities include epidemiological research on human behavioural factors, environmental and occupational risk factors and treatment options including their effectiveness and costs[3].

Paucity of breast cancer research in Kenya and the sub-Saharan African region in general, has resulted in an inadequate local evidence pool of knowledge that could be referred to for locally relevant interventions and resource planning. Breast cancer related interventions are currently

planned using a top-down approach rather than a bottom-up consultative approach that systematically evaluates the factors that impact health-seeking behaviour in the targeted population. There is growing acknowledgement that the social determinants of health affect self-care and health behaviours. Social determinants are the conditions in which people are born, grow, live, work, and age. They include factors like socioeconomic status, education, the physical environment, employment, and social support networks, as well as access to health care[4]. Understanding individuals' social determinants is essential to creating programs that address potential barriers to health care and improve overall health. For example, socioeconomic status can determine whether cost is a key barrier to obtaining health services; education levels can impact health literacy and self-care behaviours; and social support networks can perpetuate stigma and delays in seeking care. Social and cultural obstacles, if not considered, may impede the success of any cancer care program[5]. In addition, there is limited knowledge on individual level breast cancer risk factors including family history, reproductive history and lifestyle factors.

Cohort studies could provide evidence based knowledge to understand and address these factors that impact access to high quality care. In 2010, Holmes *et al*. published the need to establish cohorts in Africa in order to explain disease aetiology, and to support the development of prevention and control measures specific to the region[6]. Optimal design tailored to the local environment can support longitudinal data collection. In 2015, Dalal et al.[7] found that it was feasible to conduct large cohort studies in Sub-Saharan Africa and mobile telephony with its growing penetration and accessibility into communities, may be particularly useful. In their study face to face interviews were very successful in Uganda, use of postal services or email were a challenge in Tanzania with low return of questionnaires by post attributed to relative scarcity of post offices. Intermittent internet access in the region may also hinder questionnaire distribution and return.

There is an urgent need to conduct breast cancer studies in Africa and the objective of this study is to assess the feasibility of initiating a breast cancer cohort study in Kenya. We will recruit patients, perform baseline assessment and conduct short-term follow up at approximately 3 months after baseline data collection. Findings from this study will provide important lessons to

tailor future longitudinal studies to the local environment to ensure successful recruitment and long-term follow up. The few breast cancer cohort studies conducted in sub- Saharan Africa [8,9,10,11] have only enrolled women already diagnosed with cancer which does not provide opportunities to systematically evaluate the ability to prevent and screen for breast cancers. To address this gap, the current study will include both breast cancer survivors and a cohort of women who have never had a diagnosis of breast cancer. The cohort of women with a diagnosis of breast cancer will provide important evidence on access to breast cancer treatment and patient experiences. On the other hand, the cohort of women without a diagnosis of breast cancer will provide valuable information on access to breast cancer screening services and their knowledge of breast cancer symptoms to enable early stage diagnosis.

OBJECTIVES

Our overall goals are to explore feasibility of conducting a breast cancer cohort study in Kenya and assess ability to collect information on social determinants and individual health seeking behavior. We intend to identify barriers and propose interventions to improve women's access to cancer prevention, treatment and survivorship care services in Kenya.

Our specific objectives include:

1. To establish feasibility of identifying and recruiting individuals to participate in a cohort study who have had a diagnosis of breast cancer within the past 3 years at the time of recruitment to minimize recall bias and a similar group of women who have never had a diagnosis of breast cancer.
2. To determine the ability to maintain contact for follow-up assessments by conducting outreach by telephone (preferable mobile phones) at 3 months after initial contact.
3. To obtain baseline information on social determinants of health, breast cancer risk factors, health seeking behaviour related to breast cancer screening and treatments received.

METHODS

Study Design and Conceptual Framework

We are conducting a feasibility study to inform best practices for initiating longitudinal cohort studies in Kenya. The study will include women with and without a diagnosis of breast cancer in separate cohorts. We will collect baseline data and conduct one follow-up data collection (at approximately 3 months by telephone). We will use a mixed method approach and collect both qualitative and quantitative data.

Figure 1 presents the framework for assessing social determinants, and individual preferences, risk factors and treatment patterns in impacting breast cancer outcomes. This framework served as the theoretical underpinning for developing the data collection instruments for baseline data collection. Understanding the causal pathways of the determinants of health are essential to identify the root cause of health problems and to identify tailored interventions[12-14]. Over the long term, policies can also be implemented to drive structural changes to modify the social determinants themselves; for example, increasing the overall education level in the target population. In this study, we will capture information regarding social determinants, risk factors and health seeking behavior to identify potential hypothesis that can be evaluated in future longitudinal cohort studies to develop targeted interventions and policies.

Questionnaire Development

The questionnaires to be used in this study were largely based on prior surveys and include several validated instruments. Table 1 summarizes the components included in the questionnaires and provides details on the source of the questions.

Table 1: Kenya Breast Cancer Cohort Study - Components of the Questionnaire

Components	Cohort		Source of questions
	Breast Cancer	Non- Breast Cancer	
Background Information To collect details such as (1) demographics, (2) socioeconomic status, (3) health status	√	√	Kenya Demographic and Health Survey (2014)[15]
Breast Cancer Risk Assessment	√	√	Breast Cancer Risk Assessment Tool - Cancer Research UK https://www.cancer.gov/bcrisktool/ [16]
Insurance status and Employment	√	√	Investigator developed questions
Breast Cancer Knowledge		√	Breast Cancer Awareness Measure (Breast CAM) Toolkit Updated 09.02.11 (Modified) [17]
Cancer Treatment and breast cancer symptom assessment	√		Investigator developed questions and the NCCN FBSI-16 (Version 2) (http://www.facit.org/facitorg/questionnaires) [18]
Qualitative feedback. Questions to obtain suggestions on how to improve self-care behaviors and health care delivery	√	√	Investigator developed questions

We reviewed published literature on key concepts and also solicited expert opinion to further tailor the content for the Kenyan setting. Using the questionnaires, we will obtain information on patient demographics, socioeconomics, risk factors, breast cancer treatment and access to care**.** We included multiple questions that address the same construct to ensure comprehensive data collection and to assess internal consistency.

Cognitive testing will be performed to support reliability and validity of the questionnaires. We will conduct one-on-one interviews of about 60 minutes each to perform cognitive testing with

10 individuals with a diagnosis of breast cancer and 10 individuals without a diagnosis of breast cancer. The cognitive testing will assess clarity and the ability of the interviewees to understand the questions and provide accurate responses. Participants will be instructed to listen to each question and then convey to the interviewer which response or responses applied and justify the selection of their response so comprehension can be assessed. Following the completion of the questionnaire, the interviewer will probe the interviewer on any aspects of the questionnaire that proved difficult or confusing for the respondent. We will also ask each participant some additional debriefing questions about the length and burden of the questions and their feelings about the content of the questions. The findings from the cognitive testing will be used to tailor the wording in the draft questionnaires to clarify the information required and remove any ambiguity. We will also take steps to reduce the length of the survey if the number of questions prove to be burdensome to the participants. In addition to this, we will also perform one-on-one interviews with up to 20 women to ensure the content of the questionnaire adequately addresses issues faced by women diagnosed with breast cancer. A maximum of 40 participants will be included in the cognitive testing.

Study Participants

The study targets women aged 30-60 years in four purposively selected counties of Kenya; Nairobi, Kiambu, Machakos and Nyeri. This age group has a high incidence and prevalence of breast cancer[19] and they are recommended to undergo breast screening via clinical breast exams or mammograms. We will include women who voluntarily give consent and are able to provide contact information so that we can conduct 3-month follow up interviews over the telephone. We will exclude women who do not speak and understand the study languages – English and Kiswahili. Kiswahili is the national language and majority of women between the ages of 30 – 60 years are conversant in either English or Kiswahili.

Sample size calculation

We determined that a sample size of 400 each would be adequate for the cancer and non-cancer cohorts based on a 95% confidence interval where the margin of error is ± 5%.

Our sample size is based on the following calculation:

Sample Size = (Z-score) ² * p*(1-p) / (margin of error)²

Sample Size adjusted = (Sample Size) / (1 + [(Sample Size – 1) / population])

Z-score = 1.96 for confidence level 95%

Proportion (p) is not known, so we used 0.5 based on common practice.

Margin of error=5%

We estimate that 1,500 women were diagnosed with breast cancer during the previous 3-year period (*based on unpublished data by Nairobi Cancer Registry)* and will meet our inclusion criteria in the four counties targeted by this study. We assumed 60% five -year survival rate based on published literature of survival of breast cancer patients in Africa[20].

The above calculation gives us a sample size of 306 for the cancer cohort. We assumed that 80% of the cohort will be contacted via telephone to perform follow up interviews to bring the sample required to 383. We included a 5% mark up for non-response that results in 402 respondents and we rounded this to 400 patients. We will select an equal number of cancer and non-cancer patients for a total of 800 women overall.

Recruitment

We will recruit women diagnosed with breast cancer through the membership lists maintained by our partner organizations, Kenya Cancer Association (KENCANSA) and Kenya Hospices and Palliative Care Association (KEHPCA). We will also recruit breast cancer survivors from Kenyatta National Hospital (the main teaching and referral hospital in Kenya), private hospitals, and palliative care units. The group of women not diagnosed with breast cancer will be recruited through members of KENCANSA and KEHPCA and also through general outreach. After eligibility assessment, consecutive women meeting the recruitment criteria will be approached by the trained research assistants for consent to participate. The research assistants will provide information as per prepared consent forms. Face-to-face interviews will be held either at the same location on the same day of recruitment or at a later time or day with an appointment; in each case consent will be obtained immediately before the interview. Research assistants will obtain signatures or thumb prints for those who can write and those who cannot write respectively. Participants will be given a copy of the consent form and will be offered financial

support to travel to the interview site. The initial face-to-face baseline interviews will be followed by a one-time follow up by telephone approximately 3 months later. Two focus group discussions (one from a higher and another from a lower socio-economic population) from each cohort will be carried out to enhance understanding of key issues of concern and to better interpret results from the quantitative analysis. Recruitment and data collection will be from November 2017 to June 2018.

Patient and Public Involvement

This study was conceptualized based on priorities, experiences and preferences that women exhibited or shared during interactions with partner organizations, KEHPCA and KENCANSA, and individual study team members. The study team includes one breast cancer survivor and one family care giver of breast cancer survivors. We have described focus groups in the study protocol to ensure patient (breast cancer survivors) and public (individuals without breast cancer diagnosis) feedback will be incorporated in interpreting the study quantitative findings.We plan to share the study results through postings on KEHPCA and KENCANSA websites.

DATA ANALYSIS

Quantitative Data Analysis

Data processing and analysis will start in the field by checking for completeness of the data and performing quality control checks and sorting the data by instrument used. Data from the breast cancer and non-cancer cohorts will be compared for any similarities and differences in terms of demographics, socioeconomic factors, breast cancer risk, insurance and financial burden, employment status, access to treatment and comorbidities. We will conduct, chi-square tests, t-tests, ANOVAs or appropriate nonparametric tests to determine differences between the cohorts. These differences will be further explored using multivariate analysis to control for potential confounders between the two groups. Additionally regression analysis will be conducted to evaluate health seeking behavior, factors impacting decision making concerning cancer care and patient self-care attitudes. Furthermore, we will assess quality of life among breast cancer survivors using the standardized scoring for the National Comprehensive Cancer Network Functional Assessment of Cancer Therapy – Breast Cancer Symptom Index – 16 ***(NCCN FBSI-16)*** (Version 2) and compare with scores available from other breast cancer survivors. We will

also determine the level of breast cancer knowledge among the non-cancer cohort by analysing the concepts in the Breast Cancer Awareness Measure ***(Breast CAM).***

Potential confounders in this cohort study would be age and economic stability, cancer stage at diagnosis, comorbidities and treatment options applied. We have minimized on over-exclusion to retain sufficient sample size - women of 30-60 years of age are included. In the questionnaires we have stratifier questions on economic stability, cancer stage at diagnosis, comorbidities and treatment options applied. At analysis we will adjust for these confounders.

Qualitative Data Analysis

We plan to conduct four focus groups discussions; two focus groups with breast cancer survivors and another two with those without a previous diagnosis of cancer. We will recruit 8-10 participants per group. We have developed focus group discussion guides to explore key concepts related to breast cancer screening, diagnosis, treatment and survivorship care for breast cancer. Barriers and facilitators will be specifically explored during these focus group discussions. This information will help us with contextual details to interpret the quantitative data that will be collected.

We will use NVivo to develop coding tables to categorize the unstructured qualitative data. Two grant researchers will independently assess the crosswalk between the codes and qualitative information to determine consistency. We will also use flow charts, concept mapping, word clouds, and concept counts to explore the data visually. Qualitative feedback from the focus group discussions and the individual interviews will inform the study conclusions and recommendations.

ETHICS AND DISSEMINATION

This is a collaborative study by RTI International, KEHPCA and KENCANSA. Independent Scientific and Ethical approval was obtained from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee and the Research Triangle Institute (RTI) International Independent Review Board. Only consenting participants will be included and plans are in place to refer participants to a hospice or palliative care unit for counselling in the event that they feel

psychologically or emotionally distressed during the discussions or interview. Data collectors will also have access to hospices and palliative care units for debriefing.

Findings will be disseminated by publication in peer reviewed journals, through oral and poster presentations for various audiences, websites and scientific meetings.

DISCUSSION

This is a prospective, comparative cohort study of women with and without a diagnosis of breast cancer in Kenya to evaluate the approach of using face-to-face interviews and follow-up telephone calls to collect longitudinal data. This short follow-up study will provide valuable feedback on the feasibility and best practices to establish longitudinal cohorts in Kenya and the region. Additionally, we will also expand traditional data collection beyond demographics and clinical information to also obtain data on social determinants and individual health seeking behavior. Social determinants as described in the background of this paper and individual health seeking behavior have a direct impact on the implementation of interventions for reducing the burden from breast cancer. Interventions developed with disregard to these determinants may face low uptake or even rejection. There is need to embrace implementation science research which addresses determinants of intervention adoption in the real-world setting.

Cohort studies have not been previously established in Kenya and many other Sub Saharan Africa countries because of the challenges in maintaining participant contact and the high cost of running these studies. With increased mobile telephony, we presume that continued re-contact of participants is feasible. The high cost of cohort studies needs to be evaluated against their benefits if findings could inform optimal interventions for disease mitigation. Cancer incidence and mortality is rising at an alarming rate and there is need to find ways of reversing this trend using various evidence-based approaches.

Stigma associated with breast cancer may limit women's willingness to participate in this study but we will ensure proper communication of research procedures and benefits. We will maximize recruitment through close collaboration with breast cancer support groups, palliative care service providers, and healthcare workers in both public and private institutions. The study locations are within or in close proximity to Nairobi county and therefore our findings may not be generalizable to the entire country –the findings from this study will serve as a baseline assessment which can be extended to other counties in the future. We will collect data on cancer treatment and therefore there could be recall bias; we have specifically decided to interview women who have received treatment in the past three years to minimize recall bias. Women

interviewed may not want to respond to all questions posed and therefore there could be missing data for certain fields as we analyze the data collected.

The findings and lessons learnt from this feasibility study of 800 participants with short-term follow-up will provide a road map for future cohort studies in Kenya and the region. Local evidence on breast cancer prevention, screening and treatment is critical for tailored public health and medical interventions to address the growing burden of breast cancer.

References

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer incidence and mortality worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr

2. Surveillance, Epidemiology and End Results Programme [Internet] National Institute of Health, National Cancer Institute; 2017 [cited 2018 Feb 23] Available from: https://seer.cancer.gov/statfacts/html/breast.html

3. National Cancer Control Strategy 2017-2022 [Internet]. Ministry of Health; 2017 [cited 2017 Nov18] Available from: http://kehpca.org/wp-content/uploads/KENYA-NATIONAL-CANCER-CONTROL-STRATEGY-2017-2022.pdf

4. Marmot M, Friel S, Bell R, et al. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health. The lancet. 2008 Nov 14;372(9650):1661-9.

5. Anderson BO, Yip CH, Ramsey SD, et al. Breast cancer in limited-resource countries: health care systems and public policy. The breast journal. 2006 Jan 1;12(s1).

6. Holmes MD, Dalal S, Volmink J, et al. Non-communicable diseases in sub-Saharan Africa: the case for cohort studies. PLoS medicine. 2010 May 11;7(5):e1000244.

7. Dalal S, Holmes MD, Laurence C, et al. Feasibility of a large cohort study in sub-Saharan Africa assessed through a four-country study. Global health action. 2015 Dec 1;8(1):27422.

8. Kantelhardt EJ, Zerche P, Mathewos A, et al. Breast cancer survival in Ethiopia: a cohort study of 1,070 women. International journal of cancer. 2014 Aug 1;135(3):702-9.

9. Galukande M, Wabinga H, Mirembe F. Breast cancer survival experiences at a tertiary hospital in sub-Saharan Africa: a cohort study. World journal of surgical oncology. 2015 Jul 19;13(1):220.

10. Cubasch H, Dickens C, Joffe M, Duarte R, Murugan N, Chih MT, Moodley K, Sharma V, Ayeni O, Jacobson JS, Neugut AI. Breast cancer survival in Soweto, Johannesburg, South Africa: A receptor-defined cohort of women diagnosed from 2009 to 11. Cancer epidemiology. 2018 Feb 28;52:120-7.

11. Effi AB, Aman NA, Koui BS, Koffi KD, Traoré ZC, Kouyate M. Immunohistochemical determination of estrogen and progesterone receptors in breast cancer: relationship with clinicopathologic factors in 302 patients in Ivory Coast. BMC cancer. 2017 Dec;17(1):115.

12. Dow WH, Schoeni RF, Adler NE, Stewart J. Evaluating the evidence base: Policies and interventions to address socioeconomic status gradients in health. Annals of the New York Academy of Sciences. 2010 Feb 1;1186(1):240-51.

13. Braveman P, Egerter S, Williams DR. The social determinants of health: coming of age. Annual review of public health. 2011 Apr 21;32:381-98.

14. Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. Health affairs. 2002 Mar 1;21(2):60-76.

15. Kenya National Bureau of Statistics. Kenya Demographic and Health Survey 2014. Nairobi; 2015 p. 440-441.

16. Breast Cancer Risk Assessment Tool [Internet]. Cancer.gov. 2017 [cited 19 July 2017]. Available from: https://www.cancer.gov/bcrisktool/

17. Linsell L, Forbes LJ, Burgess C, et al. Validation of a measurement tool to assess awareness of breast cancer. European Journal of Cancer. 2010 May 31;46(8):1374-81.

18. Questionnaires [Internet]. Facit.org. 2017 [cited 19 July 2017]. Available from: http://www.facit.org/facitorg/questionnaires

19. Korir A, Okerosi N, Ronoh V, Mutuma G, Parkin M. Incidence of cancer in Nairobi, Kenya (2004–2008). International journal of cancer. 2015 Nov 1;137(9):2053-9.

20. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet (London, England). 2015;385(9972):977-1010. doi:10.1016/S0140-6736(14)62038-9.

Authors' contributions:

RG, SS, ZA and AN conceptualized and designed the study. RG and SS carried out literature review and drafted the manuscript. EO gave considerable input on data analysis procedures. ZA and AK made substantial input on ethical considerations. AK,NK and FK contributed to mapping of study sites, reviewing and editing of study tools. All authors have read the manuscript for its intellectual content and given approval for submission.

Acknowledgements:

RTI International

Kenya Hospices and Palliative Care Association (KEHPCA) their membership and affiliated Palliative Care Units

Kenya Cancer Association (KENCANSA) their membership and affiliated support groups

Funding statement:

This work was supported by RTI International

Competing interests statement.

The authors declare that there is no conflict of interest

Figure 1: Social determinants, and individual preferences and risk factors to improve breast cancer outcome

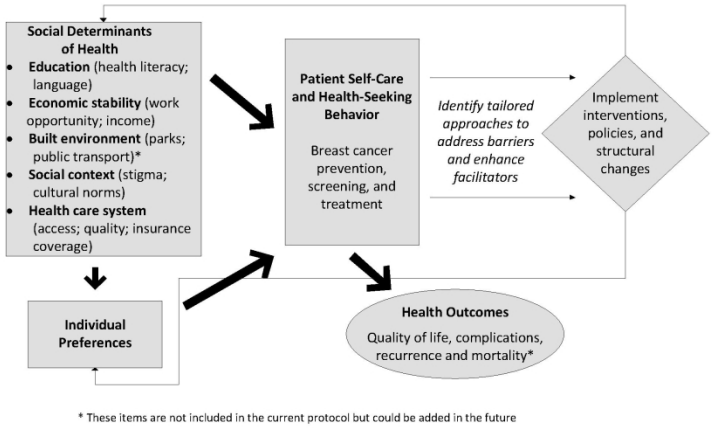

Figure 1: Social determinants, and individual preferences and risk factors to improve breast cancer outcome

215x279mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	#1 and #2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	#2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#4, #5 and #6
Objectives	3	State specific objectives, including any prespecified hypotheses	#6
Methods			
Study design	4	Present key elements of study design early in the paper	#7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#9, #10 and #11
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	#9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#11 and #12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#11
Bias	9	Describe any efforts to address potential sources of bias	#6
Study size	10	Explain how the study size was arrived at	#9 and #10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	#11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#11 and #12
		(*b*) Describe any methods used to examine subgroups and interactions	#11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	#9 to #11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	#14
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	N/A
Generalisability	21	Discuss the generalisability (external validity) of the study results	#14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Social Determinants and Individual Health Seeking Behavior among Women in Kenya: Protocol for a Breast Cancer Cohort Feasibility Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023171.R2
Article Type:	Protocol
Date Submitted by the Author:	16-Oct-2018
Complete List of Authors:	Gakunga, Robai; Independent Research Scientist Ali, Zipporah; Kenya Hospices and Palliative Care Association Korir, Anne; Kenya Cancer Association; Kenya Medical Research Institute Kinyanjui, Asaph; Kenya Hospices and Palliative Care Association Ochieng', Emily; Kenya Cancer Association Gikaara, Nancy; Kenya Hospices and Palliative Care Association Kivuva, Florence; Kenya Cancer Association Subramanian, Sujha; RTI International,
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Epidemiology, Public health, Oncology
Keywords:	Breast tumours < ONCOLOGY, Epidemiology < ONCOLOGY, SOCIAL MEDICINE, Adult palliative care < PALLIATIVE CARE

Title:

Social Determinants and Individual Health Seeking Behavior among Women in Kenya: Protocol for a Breast Cancer Cohort Feasibility Study

Authors:

Robai Gakunga[1] – robaigakunga@yahoo.com

Zipporah Ali[2] – zippy@kehpca.org

Anne Korir[3] – annkorir@yahoo.com

Asaph Wang'ombe Kinyanjui[2] – asaphkinyanjui@kehpca.org

Emily Ochieng'[3] – eochieng@kenyacancer.org

Nancy Gikaara[2] - ngikaara@yahoo.com

Florence Kivuva[3] – flokivuva2006@yahoo.com

Sujha Subramanian[4] – ssubramanian@ rti.org

[1] Independent Research Scientist, Nairobi, Kenya

[2] Kenya Hospices and Palliative Care Association (KEHPCA)

[3] Kenya Cancer Association (KENCANSA)

[4] RTI International

Word Count: 3549

Corresponding Author:

Dr. Robai Gakunga

robaigakunga@yahoo.com

Key Words:

Breast Cancer, Cohort Studies, Follow-up Studies, Social Determinants of Health, Patient Acceptance of Healthcare

ABSTRACT

Introduction

A catastrophic 35% increase in the burden of breast cancer in Kenya has been predicted by 2025. Mitigating this burden is critical and local research is necessary to generate the evidence to inform policy, public health and medical practice. Most of the knowledge available has been derived from studies in high income countries which are not directly applicable due to economic, social, cultural and ethnic differences. At the time of writing this paper, we had no knowledge of any longitudinal cohort studies in sub-Saharan Africa of both breast cancer survivors and a matching cohort of women who have never had a diagnosis of cancer. We aim to assess feasibility of cohort studies in Kenya that not only consider clinical characteristics but also social determinants and individual health seeking behavior.

Methods and analysis

This study aims to inform best practices for initiating a longitudinal cohort study in Kenya. It is a two-pronged, prospective mixed methods study of women with and without a diagnosis of breast cancer with baseline data collection and one follow-up data collection approximately 3 months later by telephone. Quantitative and qualitative data will be collected concurrently, analyzed separately and together to enrich understanding of concepts by triangulation. We aim to include 800 women aged 30-60 years; 400 in the survivorship cohort and 400 in the non-cancer cohort. Two focus group discussions from each cohort will be carried out to enhance understanding of concepts and to guide recommendations.

Ethics and dissemination

Independent ethical approval was obtained from Kenyatta National Hospital-University of Nairobi Ethics and Research Committee and the Research Triangle Institute (RTI) International. Only consenting participants will be enrolled. Counselling support, debriefing discussions and referrals for formal support services will be available for both participants and research assistants. Findings will be disseminated through publications, websites and presentations.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is a feasibility cohort study that includes women who have had a diagnosis of breast cancer and a group of women who have never had a diagnosis of breast cancer.
- Our questionnaires are based on previously tested concepts and questions that will be adapted for the local setting, and subjected to cognitive testing to ensure appropriate language is used to facilitate comprehension.
- To perform a comprehensive assessment, we include data elements to capture social determinants and individual health seeking behavior.
- For the survivorship group, recall bias will be minimized by limiting the inclusion criteria to 3 years since diagnosis.
- The study will be conducted in Nairobi (the capital city of Kenya) and its environs where cancer management services are concentrated and our findings may not be a true reflection of the entire country but a reasonable starting point for extension to other regions.

BACKGROUND

Breast cancer is a leading cancer in incidence among women in Kenya and a substantial contributor to early mortality. Globocan 2018 statistics show that breast cancer incidence rate in Kenya is estimated at 40.3 per 100,000 with a mortality rate of 17.8 per 100,000. The annual incidence of breast cancer in Kenya is about 5,985 (12.5% of all new cancer cases) and the annual mortality is about 2,553 (7.7% of all cancer deaths). By 2025, it is predicted that the annual incidence of breast cancer in Kenya will increase to 8,052 and an annual mortality of 3,448 (35% increase for both). In comparison, the breast cancer incidence rates in the United States of America and the United Kingdom are much higher at 84.9 and 93.6 per 100,000 respectively but the mortality rates are much lower at 14.9 and 14.4 per 100,000 population respectively [1]. These statistics highlight the huge burden in the incidence to mortality ratio for Kenya, a lower-middle income country, versus that for the USA and UK, high income countries. Additionally, women are diagnosed at a younger age in Kenya. The median age at breast cancer diagnosis in the USA is 62 years[2] while in Nairobi, which is the capital city of Kenya, the highest age specific incidence rate (per 100,000) is among those 40-49 years of age[3].

The current burden and the predicted catastrophic future increase in incidence and mortality of breast cancer in Kenya may be mitigated by advancing research into breast cancer risk factors, including genetics, and management to support prevention, control, treatment and survivorship. The Kenya National Cancer Control Strategy (2017-2022) has been developed by a collaborative stakeholder approach led by the country's Ministry of Health to "serve as the blue print to reduce the incidence, mortality of cancer, down-staging and improve survival rate and quality of life of cancer patients in Kenya". It consists of five strategic pillars with one of the pillars detailing the prioritized research agenda for the country. The priorities include epidemiological research on human behavioural factors, environmental and occupational risk factors and treatment options including their effectiveness and costs[4].

Paucity of breast cancer research in Kenya and the sub-Saharan African region in general, has resulted in an inadequate local evidence pool of knowledge that could be referred to for locally relevant interventions and resource planning. Breast cancer related interventions are currently planned using a top-down approach rather than a bottom-up consultative approach that

systematically evaluates the factors that impact health-seeking behaviour in the targeted population. There is growing acknowledgement that the social determinants of health affect self-care and health behaviours. Social determinants are the conditions in which people are born, grow, live, work, and age. They include factors like socioeconomic status, education, the physical environment, employment, and social support networks, as well as access to health care[5]. Understanding individuals' social determinants is essential to creating programs that address potential barriers to health care and improve overall health. For example, socioeconomic status can determine whether cost is a key barrier to obtaining health services; education levels can impact health literacy and self-care behaviours; and social support networks can perpetuate stigma and delays in seeking care. Social and cultural obstacles, if not considered, may impede the success of any cancer care program[6]. In addition, there is limited knowledge on individual level breast cancer risk factors including family history, reproductive history and lifestyle factors.

Cohort studies could provide evidence based knowledge to understand and address these factors that impact access to high quality care. In 2010, Holmes *et al*. published the need to establish cohorts in Africa in order to explain disease aetiology, and to support the development of prevention and control measures specific to the region[7]. Optimal design tailored to the local environment can support longitudinal data collection. In 2015, Dalal et al.[8] found that it was feasible to conduct large cohort studies in Sub-Saharan Africa and mobile telephony with its growing penetration and accessibility into communities, may be particularly useful. In their study face to face interviews were very successful in Uganda, use of postal services or email were a challenge in Tanzania with low return of questionnaires by post attributed to relative scarcity of post offices. Intermittent internet access in the region may also hinder questionnaire distribution and return.

There is an urgent need to conduct breast cancer studies in Africa and the objective of this study is to assess the feasibility of initiating a breast cancer cohort study in Kenya. We will recruit patients, perform baseline assessment and conduct short-term follow up at approximately 3 months after baseline data collection. Findings from this study will provide important lessons to tailor future longitudinal studies to the local environment to ensure successful recruitment and

long-term follow up. The few breast cancer cohort studies conducted in sub- Saharan Africa [9,10,11,12] have only enrolled women already diagnosed with cancer which does not provide opportunities to systematically evaluate the ability to prevent and screen for breast cancers. To address this gap, the current study will include both breast cancer survivors and a cohort of women who have never had a diagnosis of breast cancer. The cohort of women with a diagnosis of breast cancer will provide important evidence on access to breast cancer treatment and patient experiences. On the other hand, the cohort of women without a diagnosis of breast cancer will provide valuable information on access to breast cancer screening services and their knowledge of breast cancer symptoms to enable early stage diagnosis.

OBJECTIVES

Our overall goals are to explore feasibility of conducting a breast cancer cohort study in Kenya and assess ability to collect information on social determinants and individual health seeking behavior. We intend to identify barriers and propose interventions to improve women's access to cancer prevention, treatment and survivorship care services in Kenya.

Our specific objectives include:

1. To establish feasibility of identifying and recruiting individuals to participate in a cohort study who have had a diagnosis of breast cancer within the past 3 years at the time of recruitment to minimize recall bias and a similar group of women who have never had a diagnosis of breast cancer.
2. To determine the ability to maintain contact for follow-up assessments by conducting outreach by telephone (preferable mobile phones) at 3 months after initial contact.
3. To obtain baseline information on social determinants of health, breast cancer risk factors, health seeking behaviour related to breast cancer screening, treatments received and quality of life.

METHODS

Study Design and Conceptual Framework

We are conducting a feasibility study to inform best practices for initiating longitudinal cohort studies in Kenya. The study will include women with and without a diagnosis of breast cancer in separate cohorts. We will collect baseline data and conduct one follow-up data collection (at approximately 3 months by telephone). We will use a mixed method approach and collect both qualitative and quantitative data.

Figure 1 presents the framework for assessing social determinants, and individual preferences, risk factors and treatment patterns in impacting breast cancer outcomes. This framework served as the theoretical underpinning for developing the data collection instruments for baseline data collection. Understanding the causal pathways of the determinants of health are essential to identify the root cause of health problems and to identify tailored interventions[13-15]. Over the long term, policies can also be implemented to drive structural changes to modify the social determinants themselves; for example, increasing the overall education level in the target population. In this study, we will capture information regarding social determinants, risk factors and health seeking behavior to identify potential hypothesis that can be evaluated in future longitudinal cohort studies to develop targeted interventions and policies.

Questionnaire Development

The questionnaires to be used in this study were largely based on prior surveys and include several validated instruments. Table 1 summarizes the components included in the questionnaires and provides details on the source of the questions. We reviewed published literature on key concepts and also solicited expert opinion to further tailor the content for the Kenyan setting. Using the questionnaires, we will obtain information on participant's background (demographics, socioeconomics, health status), risk factors (using breast cancer risk assessment tool), insurance status and employment, breast cancer knowledge (using breast cancer awareness measure tool), breast cancer treatment and quality of life (using NCCN FBSI-16 (Version 2) tool for physical, emotional and functional wellbeing) and access to care**.** We included multiple questions that address the same construct to ensure comprehensive data collection and to assess internal consistency.

Table 1: Kenya Breast Cancer Cohort Study - Components of the Questionnaire

Components	Cohort		Source of questions
	Breast Cancer	Non- Breast Cancer	
Background Information To collect details such as (1) demographics, (2) socioeconomic status, (3) health status	√	√	Kenya Demographic and Health Survey (2014)[16]
Breast Cancer Risk Assessment (to estimate a woman's risk of developing invasive breast cancer over the next 5 years and up to age 90 (lifetime risk)	√	√	Breast Cancer Risk Assessment Tool - Cancer Research UK https://www.cancer.gov/bcrisktool/ [17]
Insurance status and Employment	√	√	Investigator developed questions
Breast Cancer Knowledge (assesses, knowledge of breast cancer symptoms, age-related risk, and frequency of breast checking)		√	Breast Cancer Awareness Measure (Breast CAM) Toolkit Updated 09.02.11 (Modified) [18]
Breast Cancer treatment and symptom assessment (quality of life assessment – physical, emotional and functional wellbeing)	√		Investigator developed questions and the NCCN FBSI-16 (Version 2) (http://www.facit.org/facitorg/questionnaires) [19]
Qualitative feedback. Questions to obtain suggestions on how	√	√	Investigator developed questions

to improve self-care behaviors and health care delivery			

Cognitive testing will be performed to support reliability and validity of the questionnaires. We will conduct one-on-one interviews of about 60 minutes each to perform cognitive testing with 10 individuals with a diagnosis of breast cancer and 10 individuals without a diagnosis of breast cancer. The cognitive testing will assess clarity and the ability of the interviewees to understand the questions and provide accurate responses. Participants will be instructed to listen to each question and then convey to the interviewer which response or responses applied and justify the selection of their response so comprehension can be assessed. Following the completion of the questionnaire, the interviewer will probe the interviewee on any aspects of the questionnaire that proved difficult or confusing for the respondent. We will also ask each participant some additional debriefing questions about the length and burden of the questions and their feelings about the content of the questions. The findings from the cognitive testing will be used to tailor the wording in the draft questionnaires to clarify the information required and remove any ambiguity. We will also take steps to reduce the length of the survey if the number of questions prove to be burdensome to the participants. In addition to this, we will also perform one-on-one interviews with up to 20 women to ensure the content of the questionnaire adequately addresses issues faced by women diagnosed with breast cancer. A maximum of 40 participants will be included in the cognitive testing.

Study Participants

The study targets women aged 30-60 years in four purposively selected counties of Kenya; Nairobi, Kiambu, Machakos and Nyeri. This age group has a high incidence and prevalence of breast cancer[20]. Data from the Nairobi Cancer Registry for the 5 year period 2007 – 2011[3], shows that the highest percentage of breast cancer diagnoses was among women in the 40-49 age group, at 29%. Ten years before and 10 years after was 20% and 24% respectively. This makes a total of 73% of all the breast cancer diagnoses in that period, and this age group is recommended to undergo breast screening via clinical breast exams or mammograms. We will include women who voluntarily give consent and are able to provide contact information so that we can conduct 3-month follow up interviews over the telephone. We will exclude women who do not speak and understand the study languages – English and Kiswahili. Kiswahili is the national language and

majority of women between the ages of 30 – 60 years are conversant in either English or Kiswahili.

Sample size calculation

We determined that a sample size of 400 each would be adequate for the cancer and non-cancer cohorts based on a 95% confidence interval where the margin of error is ± 5%.

Our sample size is based on the following calculation:

Sample Size = (Z-score) ^{2} * p*(1-p) / (margin of error)^2

Sample Size adjusted = (Sample Size) / (1 + [(Sample Size – 1) / population])

Z-score = 1.96 for confidence level 95%

Proportion (p) is not known, so we used 0.5 based on common practice.

Margin of error=5%

We estimate that 1,500 women were diagnosed with breast cancer during the previous 3-year period[3] and will meet our inclusion criteria in the four counties targeted by this study. We assumed 60% five -year survival rate based on published literature of survival of breast cancer patients in Africa[21].

The above calculation gives us a sample size of 306 for the cancer cohort. We assumed that 80% of the cohort will be contacted via telephone to perform follow up interviews to bring the sample required to 383. We included a 5% mark up for non-response that results in 402 respondents and we rounded this to 400 patients. We will select an equal number of cancer and non-cancer patients for a total of 800 women overall.

Recruitment

We will recruit women diagnosed with breast cancer through the membership lists maintained by our partner organizations, Kenya Cancer Association (KENCANSA) and Kenya Hospices and Palliative Care Association (KEHPCA). We will also recruit breast cancer survivors from Kenyatta National Hospital (the main teaching and referral hospital in Kenya), private hospitals, and palliative care units. The group of women not diagnosed with breast cancer will be recruited

through members of KENCANSA and KEHPCA and also through general outreach. After eligibility assessment, consecutive women meeting the recruitment criteria will be approached by the trained research assistants for consent to participate. The research assistants will provide information as per prepared consent forms. Face-to-face interviews will be held either at the same location on the same day of recruitment or at a later time or day with an appointment; in each case consent will be obtained immediately before the interview. Research assistants will obtain signatures or thumb prints for those who can write and those who cannot write respectively. Participants will be given a copy of the consent form and will be offered financial support to travel to the interview site. The initial face-to-face baseline interviews will be followed by a one-time follow up by telephone approximately 3 months later. Two focus group discussions (one from a higher and another from a lower socio-economic population) from each cohort will be carried out to enhance understanding of key issues of concern and to better interpret results from the quantitative analysis. Recruitment and data collection will be from November 2017 to June 2018.

Patient and Public Involvement

This study was conceptualized based on priorities, experiences and preferences that women exhibited or shared during interactions with partner organizations, KEHPCA and KENCANSA, and individual study team members. The study team includes one breast cancer survivor and one family care giver of breast cancer survivors. We have described focus groups in the study protocol to ensure patient (breast cancer survivors) and public (individuals without breast cancer diagnosis) feedback will be incorporated in interpreting the study quantitative findings.We plan to share the study results through postings on KEHPCA and KENCANSA websites.

DATA ANALYSIS

Quantitative Data Analysis

Data processing and analysis will start in the field by checking for completeness of the data and performing quality control checks and sorting the data by instrument used. Data from the breast cancer and non-cancer cohorts will be compared for any similarities and differences in terms of demographics, socioeconomic factors, breast cancer risk, insurance and financial burden, employment status, access to treatment and comorbidities. We will conduct, chi-square tests, t-

tests, ANOVAs or appropriate nonparametric tests to determine differences between the cohorts. These differences will be further explored using multivariate analysis to control for potential confounders between the two groups. Additionally regression analysis will be conducted to evaluate health seeking behavior, factors impacting decision making concerning cancer care and patient self-care attitudes. Furthermore, we will assess quality of life among breast cancer survivors using the standardized scoring for the National Comprehensive Cancer Network Functional Assessment of Cancer Therapy – Breast Cancer Symptom Index – 16 ***(NCCN FBSI-16)*** (Version 2) and compare with scores available from other breast cancer survivors. We will also determine the level of breast cancer knowledge among the non-cancer cohort by analysing the concepts in the Breast Cancer Awareness Measure ***(Breast CAM).***

Potential confounders in this cohort study would be age and economic stability, cancer stage at diagnosis, comorbidities and treatment options applied. We have minimized on over-exclusion to retain sufficient sample size - women of 30-60 years of age are included. In the questionnaires we have stratifier questions on economic stability, cancer stage at diagnosis, comorbidities and treatment options applied. At analysis we will adjust for these confounders.

Qualitative Data Analysis

We plan to conduct four focus groups discussions; two focus groups with breast cancer survivors and another two with those without a previous diagnosis of cancer. We will recruit 8-10 participants per group. We have developed focus group discussion guides to explore key concepts related to breast cancer screening, diagnosis, treatment and survivorship care for breast cancer. Barriers and facilitators will be specifically explored during these focus group discussions. This information will help us with contextual details to interpret the quantitative data that will be collected.

We will use NVivo to develop coding tables to categorize the unstructured qualitative data. Two grant researchers will independently assess the crosswalk between the codes and qualitative information to determine consistency. We will also use flow charts, concept mapping, word clouds, and concept counts to explore the data visually. Qualitative feedback from the focus group discussions and the individual interviews will inform the study conclusions and recommendations.

ETHICS AND DISSEMINATION

This is a collaborative study by RTI International, KEHPCA and KENCANSA. Independent Scientific and Ethical approval was obtained from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee and the Research Triangle Institute (RTI) International Independent Review Board. Only consenting participants will be included and plans are in place to refer participants to a hospice or palliative care unit for counselling in the event that they feel psychologically or emotionally distressed during the discussions or interview. Data collectors will also have access to hospices and palliative care units for debriefing.

Findings will be disseminated by publication in peer reviewed journals, through oral and poster presentations for various audiences, websites and scientific meetings.

DISCUSSION

This is a prospective, cohort study of women with and without a diagnosis of breast cancer in Kenya to evaluate the approach of using face-to-face interviews and follow-up telephone calls to collect longitudinal data. This short follow-up study will provide valuable feedback on the feasibility and best practices to establish longitudinal cohorts in Kenya and the region. Additionally, we will also expand traditional data collection beyond demographics and clinical information to also obtain data on social determinants and individual health seeking behavior. Social determinants as described in the background of this paper and individual health seeking behavior have a direct impact on the implementation of interventions for reducing the burden from breast cancer. Interventions developed with disregard to these determinants may face low uptake or even rejection. There is need to embrace implementation science research which addresses determinants of intervention adoption in the real-world setting.

Cohort studies have not been previously established in Kenya and many other Sub Saharan Africa countries because of the challenges in maintaining participant contact and the high cost of running these studies. With increased mobile telephony, we presume that continued re-contact of participants is feasible. The high cost of cohort studies needs to be evaluated against their benefits if findings could inform optimal interventions for disease mitigation. Cancer incidence and mortality is rising at an alarming rate and there is need to find ways of reversing this trend using various evidence-based approaches.

Stigma associated with breast cancer may limit women's willingness to participate in this study but we will ensure proper communication of research procedures and benefits. We will maximize recruitment through close collaboration with breast cancer support groups, palliative care service providers, and healthcare workers in both public and private institutions. The study locations are within or in close proximity to Nairobi county and therefore our findings may not be generalizable to the entire country –the findings from this study will serve as a baseline assessment which can be extended to other counties in the future. We will collect data on cancer treatment and therefore there could be recall bias; we have specifically decided to interview women who have received treatment in the past three years to minimize recall bias. Women

interviewed may not want to respond to all questions posed and therefore there could be missing data for certain fields as we analyze the data collected.

The findings and lessons learnt from this feasibility study of 800 participants with short-term follow-up will provide a road map for future cohort studies in Kenya and the region. Local evidence on breast cancer prevention, screening and treatment is critical for tailored public health and medical interventions to address the growing burden of breast cancer.

References

1. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2018). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [15/10/2018].

2. Surveillance, Epidemiology and End Results Programme [Internet] National Institute of Health, National Cancer Institute; 2017 [cited 2018 Feb 23] Available from: https://seer.cancer.gov/statfacts/html/breast.html

3. Nairobi Cancer Registry Report (2007-2011). Breast Cancer Incidence Among Women in Nairobi, Kenya. Kenya Medical Research Institute; 2018

4. National Cancer Control Strategy 2017-2022 [Internet]. Ministry of Health; 2017 [cited 2017 Nov18] Available from: http://kehpca.org/wp-content/uploads/KENYA-NATIONAL-CANCER-CONTROL-STRATEGY-2017-2022.pdf

5. Marmot M, Friel S, Bell R, et al. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health. The lancet. 2008 Nov 14;372(9650):1661-9.

6. Anderson BO, Yip CH, Ramsey SD, et al. Breast cancer in limited-resource countries: health care systems and public policy. The breast journal. 2006 Jan 1;12(s1).

7. Holmes MD, Dalal S, Volmink J, et al. Non-communicable diseases in sub-Saharan Africa: the case for cohort studies. PLoS medicine. 2010 May 11;7(5):e1000244.

8. Dalal S, Holmes MD, Laurence C, et al. Feasibility of a large cohort study in sub-Saharan Africa assessed through a four-country study. Global health action. 2015 Dec 1;8(1):27422.

9. Kantelhardt EJ, Zerche P, Mathewos A, et al. Breast cancer survival in Ethiopia: a cohort study of 1,070 women. International journal of cancer. 2014 Aug 1;135(3):702-9.

10. Galukande M, Wabinga H, Mirembe F. Breast cancer survival experiences at a tertiary hospital in sub-Saharan Africa: a cohort study. World journal of surgical oncology. 2015 Jul 19;13(1):220.

11. Cubasch H, Dickens C, Joffe M, Duarte R, Murugan N, Chih MT, Moodley K, Sharma V, Ayeni O, Jacobson JS, Neugut AI. Breast cancer survival in Soweto, Johannesburg, South Africa: A receptor-defined cohort of women diagnosed from 2009 to 11. Cancer epidemiology. 2018 Feb 28;52:120-7.

12. Effi AB, Aman NA, Koui BS, Koffi KD, Traoré ZC, Kouyate M. Immunohistochemical determination of estrogen and progesterone receptors in breast cancer: relationship with clinicopathologic factors in 302 patients in Ivory Coast. BMC cancer. 2017 Dec;17(1):115.

13. Dow WH, Schoeni RF, Adler NE, Stewart J. Evaluating the evidence base: Policies and interventions to address socioeconomic status gradients in health. Annals of the New York Academy of Sciences. 2010 Feb 1;1186(1):240-51.

14. Braveman P, Egerter S, Williams DR. The social determinants of health: coming of age. Annual review of public health. 2011 Apr 21;32:381-98.

15. Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. Health affairs. 2002 Mar 1;21(2):60-76.

16. Kenya National Bureau of Statistics. Kenya Demographic and Health Survey 2014. Nairobi; 2015 p. 440-441.

17. Breast Cancer Risk Assessment Tool [Internet]. Cancer.gov. 2017 [cited 19 July 2017]. Available from: https://www.cancer.gov/bcrisktool/

18. Linsell L, Forbes LJ, Burgess C, et al. Validation of a measurement tool to assess awareness of breast cancer. European Journal of Cancer. 2010 May 31;46(8):1374-81.

19. Questionnaires [Internet]. Facit.org. 2017 [cited 19 July 2017]. Available from: http://www.facit.org/facitorg/questionnaires

20. Korir A, Okerosi N, Ronoh V, Mutuma G, Parkin M. Incidence of cancer in Nairobi, Kenya (2004–2008). International journal of cancer. 2015 Nov 1;137(9):2053-9.

21. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet (London, England). 2015;385(9972):977-1010. doi:10.1016/S0140-6736(14)62038-9.

Authors' contributions:

RG, SS, ZA and AK conceptualized and designed the study. RG and SS carried out literature review and drafted the manuscript. EO gave considerable input on data analysis procedures. ZA and AK made substantial input on ethical considerations. AWK, NG and FK contributed to mapping of study sites, reviewing and editing of study tools. All authors have read the manuscript for its intellectual content and given approval for submission.

Acknowledgements:

RTI International

Kenya Hospices and Palliative Care Association (KEHPCA) their membership and affiliated Palliative Care Units

Kenya Cancer Association (KENCANSA) their membership and affiliated support groups

Funding statement:

This work was supported by RTI International

Competing interests statement.

The authors declare that there is no conflict of interest

Figure 1: Social determinants, and individual preferences and risk factors to improve breast cancer outcome

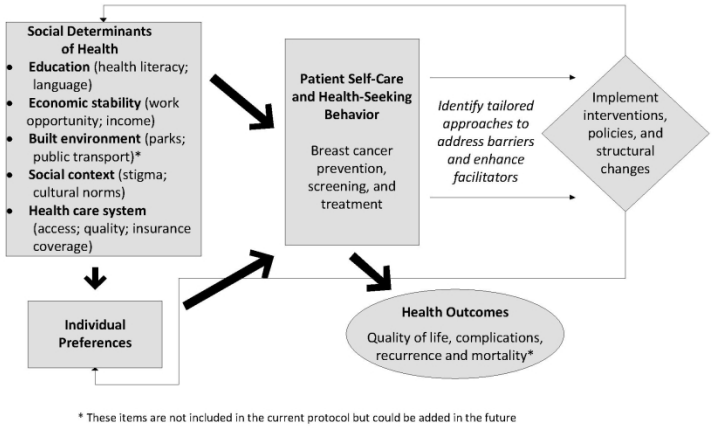

Figure 1: Social determinants, and individual preferences and risk factors to improve breast cancer outcome

215x279mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	#1 and #2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	#2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#4, #5 and #6
Objectives	3	State specific objectives, including any prespecified hypotheses	#6
Methods			
Study design	4	Present key elements of study design early in the paper	#7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#9, #10 and #11
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	#9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#11 and #12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#11
Bias	9	Describe any efforts to address potential sources of bias	#6
Study size	10	Explain how the study size was arrived at	#9 and #10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	#11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#11 and #12
		(*b*) Describe any methods used to examine subgroups and interactions	#11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	#9 to #11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	#14
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	N/A
Generalisability	21	Discuss the generalisability (external validity) of the study results	#14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.