The Traditional Medicine Practitioner's Concept of Cancer, Herbal medicine use and the Patients Perceived benefits (Clinical outcomes) in Selected Districts of Central Uganda: An Exploratory Study Protocol

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Abstract

Background: In sub-Saharan Africa, herbal medicine for cancer is dispensed by traditional medicine practitioners (TMPs) to a large extent, who may not have adequate knowledge about the disease and this has been found to contribute to the late presentation of cancer patients to clinics and hospitals leading to poor patient outcomes.

Aim: This study will investigate the traditional medicine practitioner's concept of cancer, its care, herbal medicine use, and the patients' perceived benefits (clinical outcomes) in selected districts of Central Uganda.

Methods: This study will use a convergent parallel mixed-method design. TMPs claiming to treat cancer, with at least 10 years of experience will be recruited and interviewed about their understanding of cancer as a disease (grounded theory design) and the herbs used in cancer treatment (ethnobotanical survey). We will also conduct a prospective observational study to obtain the data on the perceived clinical outcomes of using herbal medicine. Adult patients (>18years) with a medical diagnosis of cancer signposted by TMPs will be recruited and followed up at baseline, 3, and 6 months. Study outcomes will include a change in the quality of life score, cancer symptoms score, perceived benefits score, and adverse reactions. The researcher will analyze qualitative data using Open, axial, selective coding techniques. We will analyze the quantitative data using descriptive statistics and results presented in frequencies, percentages and measures of central tendency (mean) where applicable. Additional analyzes such as bivariate (paired t-test and one-way repeated measures ANOVA), and multivariate (linear mixed effects model) analysis for the repeated measures data shall be undertaken to analyze the prospective observational data. P- Values of <0.05 will be considered statistically significant.

Discussion: This study will aid researchers in further understanding the TMPs' conceptualization of cancer, how that links to the treatment dispensed to their patients, and ultimately the patient-perceived outcomes.

Introduction

Among non-communicable diseases (NCDs) cancer is a significant public health problem. Globally, there was a rise in cancer incidence from 14million in 2012 to 18.1million new cases in 2018 (1). WHO (2018) estimates that 1 in 6 women and 1 in 5 men develop cancer in their lifetime. This burden of cancer is rising in Africa partly because of chronic infections (e.g., HIV/AIDs) and consumption of food containing aflatoxins (1). Uganda, a country in development transition, recorded a rise in cancer incidence from 140 to 210 per 100,000 between 1990 and 2010 (WHO, 2014). As of 2018, there were about 56,238 cancer cases in Uganda (1).

Herbal medicine use as a core element of traditional medicine among patients with cancer remains uncontested (2). Indeed, among the complementary and alternative medicine (CAM) modalities, herbal medicines are the most used form especially following a cancer diagnosis (3–7). About 35% and 50% of

patients with cancer from developed and developing countries use herbal medicines during cancer treatment (8). A recent systematic review shows that about 22% of patients with cancer use herbal medicine to manage cancer especially from Africa (40%) and Asia (28%, (2).

The reasons for herbal medicines use among patients with cancer are categorized as health care or system-related (e.g., limited and high cost of conventional cancer care), patient or disease-related (e.g., a belief that herbal medicine is safe and efficacious against cancer), geographical or topological factors (e.g., rich or diverse medicinal flora especially in Africa, Asia, and South America), and cultural or historical factors (2). In Africa and Asia, the centuries-old, rich, and popular traditional medicine systems such as Ayurveda, Siddha, Unani, acupuncture, traditional Chinese medicine, and African traditional medicine continue to be responsible for Herbal medicine use among cancer patients (9–11).

The consumption of herbal medicines with nutritional value to humans to prevent and treat cancer has been a popular practice throughout human history and population studies suggest a reduced risk of cancer-associated with it (12). Clinical and laboratory-based studies conducted in Asia, and Europe indicate that herbal medicines' use in cancer improves the quality of life of cancer patients, increases the survival of patients with certain cancers (lung cancer), and has cancer chemo-toxic or preventive activity (13–17). In Africa, however, the clinical outcomes (perceived benefits) of most of the herbal preparations used in cancer are unknown (18).

Research conducted in Africa reports that patients with cancer obtain herbal medicine from either herbalists or traditional healers (Traditional Medicine Practitioners, TMPs) (19). Therefore, their concept or understanding of cancer as a disease is key in the proper management of patients with cancer using herbal medicine. However, literature paints a mixed picture of this subject as studies conducted in South Africa and Malaysia indicate TMPs had relevant (good) knowledge related to cancer disease definition, and risk factors, in situations where TMPs received formal pieces of training about the disease (9, 20). On a contrary, poor knowledge of TMPs on cancer regarding the definition and risk factors was reported in studies conducted in Malaysia and Nigeria-where having cancer was defined by TMPs as having high cholesterol levels or having a formed abscess (9, 21). Similarly, misconceptions such as demonic attacks or ghost interference, hot spicy foods, and dry mouth were mentioned as risk factors (causes) to the acquisition of cancer (9, 21). Literature and anecdotal evidence in Uganda show that the understanding of cancer among TMPs is inadequate and based on local knowledge and patient symptoms (22). This inadequacy in the understanding of cancer among TMPs is partly responsible for the late presentation of cancer patients to clinics and hospitals, leading to poor patient outcomes.

Some herbs or natural products dispensed by TMPs are undoubtedly a key source of materials or leads for newer drugs with anti-cancer properties. Recently, over 3000 natural products with reported anti-cancer properties have been discovered (11). In addition, over 60% of the current proven treatments for cancer (vinca alkaloids, epipodophyllotoxins, taxane, and camptothecin) are from natural products, of which 75% of these medicines were discovered following folk claims (11, 23). In Africa, particularly Uganda, there are few specific and comprehensive ethno-medicinal survey(s) conducted in cancer, thus, some

herbs used by TMPs to treat cancer remain undocumented (18). In addition, despite the advancement in drug discovery and development technologies, the current classical or pharmacological (laboratory to the clinic) approach to drug discovery is inefficient and ineffective which has resulted in fewer chemical and molecular entities approved by international and national drug authorities (24). Therefore, there has been a call for a change in approach to the discovery of drugs for cancer; from the pharmacological to reverse pharmacological (clinic to laboratory) approach that favors cancer drug development from herbal medicines (25, 26). This study aims to contribute to drug discovery by using the reverse pharmacological approach or philosophy (from clinic to laboratory). Particularly stage one and two of the reverse pharmacological approach which involves the collection of information on herbs used to treat cancer, the clinical use and safety of herbal remedies, observation of the clinical effects, and confirmation of the herbal medicine safety among others (24).

Therefore, this study seeks to investigate the following research questions; 1) how do the traditional medicine practitioners (TMPs) define or explain the concept of cancer and its care in selected districts of central Uganda? 2) What herbs do the TMPs use to manage the various cancer and 3) what are the clinical outcomes in patients with cancer treated by TMPs? The researchers envisage that findings from this study will help various stakeholders understand the cancer care provided by the TMPs and received by cancer patients. This may help translate and integrate some elements of cancer care into practice, provide a basis for further research geared towards cancer drug development from certain herbs by pharmacologists using the reverse pharmacological approach and research related to cancer care in African traditional medicine, identify training gaps for traditional medicine practitioners, and inform policies on traditional medicine use in cancer in Uganda and other African countries.

Methods

Study design and Objectives

The study utilizes a convergent parallel mixed method design (Figure 1). A qualitative study employing a grounded theory approach will explore the concept of cancer and its care in traditional medicine as perceived by traditional medicine practitioners (TMPs). In addition, an ethnobotanical survey will document the herbs used by traditional medicine practitioners (TMPs) to treat or manage cancer. The two studies will indirectly aid in the selections of the TMP(s) with excellent knowledge of cancer and treatment whose patients the researcher will follow up in a prospective observational study, to determine the perceived clinical outcomes of using herbal medicine. The findings from the three studies will be reported separately, but will be compared and contrasted during discussion.

Study sites

The researcher will conduct the study in three purposively selected districts of central Uganda, namely Kampala (capital city, urban), Mukono (semi-urban), and Kiboga District (rural, Figure 2). These districts contain traditional medicine structures (traditional medicine village committees). Anecdotal evidence also indicates that the three districts have a larger number of TMPs and patients with cancer (researchers'

professional experience or observations). Particularly, medicinal plants used to treat cancer by TMPs will be collected from Mukono and Kiboga only because Kampala is largely an urban setting. The two districts are further selected based on the documented plant biodiversity. Specifically, the Mukono district is located 21 km east of Kampala (Capital city). Mukono District geographical coordinates include 00°28'50.0"N, 32°46'14.0"E (Latitude: 0.480567; Longitude: 32.770567) and is found at 1,200 m (3,900 ft) above sea level. Mukono district is rich in flora and fauna, has a favorable climate and abundant rainfall. It hosts natural forest reserves, waterfalls, and part of Lake Victoria (www.mukono.co.ug). Kiboga district is located 120 km from Kampala capital city and lies at 01 00N, 31 46E (Latitude: 1.0000; Longitude: 31.7667). The district contains an uneven landscape composed of savannah grasslands, undulating rugged hills, swamps, and lies at an altitude of 1400-1800m above sea level (www.kiboga.go.ug). We will collect data from all the counties of the two districts.

Data collection Procedure/ Recruitment.

Figure 3 shows the summarized study data collection procedure. After ethical approval, clearance to conduct the study will be obtained from local, regional, and the TMPs umbrella organizations, who will link the researcher to the TMPs. TMPs that meet the eligibility criteria shall be recruited and consented. The researcher shall pretest all study tools with about 5 to 10 TMPs and patients.

In the qualitative study, the researcher will collect data from the TMPs at a community setting in two phases (Figure 3). The first phase (face-to-face in-depth interviews) will obtain tentative theoretical concepts and their meaning, which will be verified in the second phase (Three focus group discussions with the same TMPs (n=15). The in-depth interviews and FGDs shall take approximately 45 to 60 minutes.

Similarly, after the in-depth interviews in phase one, TMPs or any other community member will be interviewed about the medicinal plants they use in the management of cancer. With the help of selected herbalists or traditional healers, and a botanist, we shall harvest those medicinal plants from the field and deposit them at Makerere University Herbarium for identification.

In the prospective observational study, the first two months will be used to recruit participants signposted by TMPs. Also, potential participants will be identified through village health teams (VHTs), area associations of people with cancer, area cancer institute or center, and primary health facilities in the study area. The researcher shall inform, screen, consent, and invite the study participants from their respective homes. Each participant will then be reviewed after three months and six months. During each study visit, the researcher shall: take history and observe the patients' general condition (general survey) and also ask patients to report any of the side/adverse effects of the herbal medicine, interview patients on the clinical outcomes (quality of life, perceived benefits, symptom distress), and remind participants to refill, take, and adhere to their treatment. The researcher will call the patient (via telephone or send SMS) monthly to remind them about adherence to their herbal treatment. Patients who will cease to take up herbal treatment during the observational period, re-locate to districts outside the study districts, become severely ill or die, will be assumed to be lost to follow-up.

Participants' selection: Eligibility, sample size and sampling methods

1) Qualitative study

To explore the concept of cancer**,** we will interview herbalists and traditional healers who are: 1) known and trusted by the community, 2) practicing traditional medicine, treating, or caring for patients with any form of cancer with a minimum of 10 years of experience. 3) Consent to take part in the study. The study shall exclude potential participants who will be sick or unavailable during the data collection period. In line the grounded theory research design, we shall interview about 20 to 30 TMPs and we will select these using theoretical sampling (27).

2) Ethno-botanical survey

Data on herbs used in the treatment of cancer will be obtained from traditional healers, herbalists, and adult members of the community who meet criteria outlined above in this section. Well-known plants used as nutritional supplements shall be included in the study, but no herbarium specimen will be collected. An ethnobotanist or plant taxonomist will help in the collection, preparation of the herbarium specimen, and identification of the plants with anti-cancer properties. The ethnobotanist or plant taxonomist shall possess at least 1) a degree or diploma in botany or plant taxonomy 2) have at least five years of ethnobotanical practice. The researchers will contact 88 TMPs in total. We estimated this sample size using the Cochran (1963) formula for calculating the sample size for large unknown study populations, with the key study outcome measured as a proportion (28). The total proportion of TMPs with knowledge on herbs used in cancer was assumed to be 50% (p=0.5). A 95% confidence level, which corresponds to a standard normal Z-value of 1.96, and a ±5% precision (e=0.05) was pre-set. The accrued total sample size of 385 was later reduced using the finite population correction formula on an assumption that 100 (N) participants (TMPs) from the three (3) districts manage patients with cancer (28), giving a sample size of 80 TMPs. Considering a 10% non-response rate, the final sample size/target that will be used in this study will be 88 participants (66 TMPs and 22 adult members of the community). Purposive and snowball sampling techniques will also be used to select the study participants until we realize the sample size.

3) Prospective observational study

TMPs will signpost patients with cancer at community clinics owned by the shortlisted10 traditional healers identified during the qualitative and ethnobotanical survey studies. TMPs that will signpost patients with cancer shall be purposively selected based on the criteria outlined above in this section. In addition, TMPs must be of any sex, above 40 years of age, have regular patients, and shall declare and consent that they do not adulterate their herbal remedies with conventional chemotherapeutic agents. During this study, TMPs may or may not disclose the herbal constituents of their treatment.

Snowball and consecutive sampling techniques will be used to obtain patients for follow-up based on their medical diagnosis of cancer (clinical signs and symptoms and histo-pathological laboratory

findings), irrespective of the time since diagnosis. These patients must also be adults (>18 years), of both sexes, and from any type of cancer treated by TMPs. All patients should have consented to participate in the study and to allow for comparative descriptive analysis, patients or clients may or may not use other conventional therapies or have other chronic diseases (e.g., hypertension, diabetes, extra) as long as they do not interfere with their follow up. This study will exclude any patient if 1) they have an uncontrolled psychiatric/ mental disorder that may affect their ability to comply with the follow up (unable to communicate) 2) involved in any clinical trial in the last one month (30 days), and 3) chronic substance abuser such as a habitual alcohol intake. The researcher will follow 345 participants in total up for 6 months. The sample size was determined using Cochran (1963) formula. The researcher considered the total proportion of patients with cancer taking herbal medicine as 28.6%, (p=0.286) based on a study conducted in Ghana (6). In the sample size (314) we obtained, we factored in a ten (10) percent loss to follow up. A 95% confidence level, which corresponds to a standard normal Z-value of 1.96, and a ±5% precision (e=0.05) was also pre-set.

Data collection Procedure/ Recruitment.

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In the prospective observational study, the first two months will be used to recruit participants signposted by TMPs. Also, potential participants will be identified through village health teams (VHTs), area associations of people with cancer, area cancer institute or center, and primary health facilities in the study area. The researcher shall inform, screen, consent, and invite the study participants from their respective homes. Each participant will then be reviewed after three months and six months. During each study visit, the researcher shall: take history and observe the patients' general condition (general survey) and also ask patients to report any of the side/adverse effects of the herbal medicine, interview patients on the clinical outcomes (quality of life, perceived benefits, symptom distress), and remind participants to refill, take, and adhere to their treatment. The researcher will call the patient (via telephone or send SMS) monthly to remind them about adherence to their herbal treatment. Patients who will cease to take up

herbal treatment during the observational period, re-locate to districts outside the study districts, become severely ill or die, will be assumed to be lost to follow-up.

Data collection instruments

1) Qualitative study:

A semi-structured interview guide and audio recorders will be used as data collection tools. The semi-structured interview guide will comprise open-ended questions on participants' understanding of cancer and its care. Specifically, TMPs will be requested to discuss their understanding of cancer (In terms of definition and cause), day-to-day activities regarding caring for patients with cancer (care roles), actual cancer care experiences, feelings and beliefs about cancer and its care, and all the meaning attached to cancer and its care. However, these research questions will be temporary, and will thus be modified based on information obtained from the initial study participants' (29,30).

2) Ethno-botanical survey

Data collection tools will include a semi-structured survey questionnaire, GPS machine, and plant harvesting tools. The semi-structured survey questionnaire will contain questions on the participant profile, and details of medicinal plants used to treat cancer such as the plant part (s) harvested and used, how it prepared, used, and stored.

3) Prospective observational Study

Independent and dependent variables that will be included in the study tools and analysis are explained first. All study outcomes shall be measured three times at baseline, 3 and 6 months.

i) Study Outcomes

Dependent variables

The changes in MD Anderson symptom inventory tool score and the quality of life (EORTC QLQ-C30) score from baseline to 3 and 6 months will be measured as the primary outcomes of this study. Secondary outcomes will include the changes in the perceived benefits tool score and the percentage of patients reporting any side effects related to the use of herbal medicine in cancer from baseline to 3 and 6 months.

Independent variable

The independent variables will include socio-demographic characteristics (e.g., residence, education level gender, level of income, and age), disease/prognostic characteristics (e.g., type of cancer, stage of cancer, tumor size, and metastasis), presence of comorbidities (e.g., hypertension, diabetes, and kidney disease), use of conventional treatment (chemotherapy, radiotherapy, and surgery), use of other drugs for

management of comorbidities, presence of surgical, chemo and radio-therapeutic side effects, and multiple herbal products use.

ii) Study instruments/tool

Patient clinical records.

Clinical records will be used to obtain information on the general patient history and examination, comorbidities, treatments given, and any other health concerns as conducted by the allopathic doctors and TMPs. Detailed clinical records data shall be gathered at the study baseline, whereas complementary health histories shall be obtained during home visits or follow-ups.

The MD Anderson Symptom Inventory-Traditional Chinese medicine tool

The changes in symptoms following intake of herbal medicine will be obtained using the MD Anderson symptom inventory tool for traditional Chinese medicine (www.mdanderson.org). Because of the concomitant herbal medicine use with conventional therapies, this tool was developed and validated to monitor and evaluate the effectiveness of treatment taken with traditional Chinese medicines (www.mdanderson.org). It is also used to measure the severity of the symptoms among patients with cancer who opt for traditional Chinese medicines and the impact of those symptoms on daily functioning. The tool also measures the seven side effects specific to traditional Chinese medicine which include bitter taste, palpitations (racing heart), constipation, sweating, feeling cold, heat in the palms or soles of the feet, and coughing. The Cronbach alpha (reliability) was found to range from 0.88 to 0.91 (www.mdanderson.org). This tool was selected for this study because medicinal plants from Uganda and those of China may bear similarities in terms of phytochemical or secondary metabolites of the herbal crude extracts such as terpenoids, phenolics, flavonoids, alkaloids and glycosides-which may be responsible for the above side effects measured in the tool (31,32). The lowest and highest scores are 0 (not present/did not interfere) and 10 (as bad as you can imagine/ interfered completely). We will expect lower total scores at subsequent measurements to conclude that herbal medicine has beneficial effects on patients in this study.

Perceived Benefits Tool.

The researcher developed an overall perceived benefit tool basing on the literature related to the benefits of using herbal medicine by patients with cancer. This tool includes items on the amelioration of eight symptoms common among patients with cancer (diarrhea, sleep disturbance, fatigue, appetite loss, nausea, vomiting, dyspnea, and constipation). Statements of the benefits of herbal medicine on amelioration of those symptoms will be presented to the patients. The patient will then rate their level of agreement on a 4-point scale *(1=strongly disagree, 4= strongly agree).* A high score will mean a high likelihood of the herbal medicine being beneficial to the patient.

Quality of life tool (EORTC QLQ-C30).

The European organization for research and treatment of cancer quality of life questionnaires (EORTC QLQ-C30) will be used to collect data on the patients' overall quality of life (QoL). The EORTC QLQ-C30 is the most common QoL tool used in oncology research, to measure the quality of life of the patients with cancer on treatment (33). The EORTC QLQ-C30 measures the overall physical, psychological, emotional, and social well-being of patients with cancer. Nine multi-item scales form the EORTC QLQ-C30, namely: a global health status/QoL scale, three symptom scales (fatigue, nausea/vomiting, and pain) , and five functional scales (role, physical, emotional, cognitive, and social functioning). Included also is a Six single-item scale (appetite loss, dyspnea, constipation, diarrhea, insomnia, and financial difficulties). The validity, reliability, and sensitivity of the EORTC QLQ-C30 tool in cancer have been tested and found appropriate (34). The EORTC QLQ-C30 Baseline values may serve as a prognostic indicator. For instance, they predict response to treatment, survival, and nausea and vomiting. The total scores on the EORTC QLQ-C30 range from 1 (not at all) to 4 (very much) and a lower score on the EORTC QLQ-C30 indicates a high Qol of the study participants.

Adverse Drug side effects report forms

Based on the general side effects of the herbal medicines as reported in the literature and what the TMPs will report during the ethnobotanical survey, an adverse side effects report tool will be developed for surveillance and referral of patients with the possible adverse side effects of herbal medicines. A sample of this tool that will be adapted has been obtained from the MUST-REC website (www.must.ac.ug). All tools used in this study shall be pretested, modified where appropriate, and re-validated before use. Below is the study visit schedule (Table1).

Table 1: Study visit schedule

	Baseline	3 months	6 months
Recruitment	X		
Inclusion criteria	X		
Exclusion criteria	X		
Informed consent	X		
Clinical characteristics	X	X	X
Outcomes			
Symptom inventory scores	X	X	X
Quality of life scores	X	X	X
Perceived benefits scores	X	X	X
Adverse effects recorded	X	X	X
Medications	X	X	X
Herbal remedies	X	X	X
Cancer treatments (surgery, chemotherapy, radiotherapy)	X	X	X
Comorbidities and their drugs	X	X	X

Quality Assurance

1) Qualitative study

The study will ensure the trustworthiness in the qualitative study through the four principles namely credibility, transferability, confirmability, and dependability (27). Credibility refers to the extent to which the study findings are believable or accurately reflect the multiple realities of the phenomenon (27). To ensure credibility, the researcher plans to have prolonged engagement with the informants in the field (about 3-6months). The findings of in-depth interviews will also be compared and triangulated with those from the focused group discussions (Method triangulation). Similarly, data captured from traditional healers will be compared with that of the herbalists (participant triangulation). Dependability measures the stability of the data over time and under different circumstances (35). Therefore, a second external reviewer/inquiry auditor (traditional medicine or qualitative study expert) shall reexamine the data to ensure that the findings emerge from the data gathered and analyzed (35,36). Confirmability refers to the extent to which others can confirm the findings of a qualitative study in the field. Hence, an audit trail containing audiotapes, verbatim transcripts, field notes, codes, and memos will be kept and reviewed by

an external reviewer/inquiry auditor and this study supervisors' who are experts in traditional medicine. Last, transferability refers to the applicability of one set of findings to another setting (27). Therefore, the researcher also plans to share verbatim transcripts of the individual interviews, and drafts of the emerging codes, concepts, and categories, to ensure future researchers make determinations about the practical application of this inquiry in other settings.

2) Ethnobotanical Survey.

Voucher plants collected will include their vegetative and reproductive structures, such as flowers, fruit, or both, to make their future identification easier. We shall press specimens in the field and wet-dried. The specimen shall be determined and registered at the Makerere University Herbarium.

3). Prospective Observational study

To minimize the risk of loss to follow-up of patients, participants will receive monthly herbal medicine adherence reminders (e.g., via SMS, call). Last, all tools of this study have been translated into the local language (Luganda). All tools used in this study shall be pretested, modified where appropriate, and re-validated before use. The internal consistency (reliability, Cronbach alpha) of the tools shall be measured before use.

Data Management

The researcher will transcribe narrative data both in the local (Luganda) and English languages using a language expert. Data shall be entered in Microsoft word 2010, then password-protected, and managed by the principal investigator. The completed consent forms and transcribed interviews in paper form will be locked in a safe cupboard and stored for one year, before destruction. The researcher, research supervisors, botanists, data analysts or statisticians, and external reviewers will access data.

Data analysis

We will analyze qualitative data using data analysis procedures outlined by Strauss & Corbin, (1990) that include: open, axial, and selective coding in ascending order respectively (35,36). In the ethnobotanical and prospective observational study, we will enter data in excel and analyzed using SPSS (version 20). The descriptive statistical analysis shall be undertaken and data shall be summarized as frequencies and presented in tables. Additional analyzes such as bivariate, multivariate (confounder), trend, and comparative analysis for the repeated measures data shall be undertaken, for the prospective observational study data. Prior to analysis, negatively worded items (e.g., those in Qol tool) will be reversed. A paired T test, and a repeated measures one way ANOVA statistics will be used to establish if the observed differences in the scores across the time measurement points are statistically significant. Preliminary analyzes, such as a normality test, will be conducted for each outcome at every time point. Violation of the assumption of normality will mean the author will use Wilcoxon signed rank test and Friedman test (non-parametric). We will eliminate from the analyzes participants with any missing data

points due to with drawl from the study or loss to follow up. Linear mixed effects model analysis will used to control for any confounding. P- Values will be reported at a 95% confidence level.

Ethical considerations

The Faculty of medicine research ethics committee, Mbarara University of Science and Technology research ethics board (#05/02-21), and Uganda National Council of science and technology approved this study. Clearance to collect data shall be obtained from the traditional healer's umbrella organizations, such as the national council of traditional healers' association (NACOTHA), the regional and area leaders. We will seek written and verbal informed consent from the study participants. All study tools shall be translated and back-translated from the local language to English. On the study tools, names or telephone contacts shall not be used to identify the study participants. However, a separate word document template with phone numbers shall be kept aside for follow-up purposes only. During home visits, any cases of patients with cancer observed by the researcher to be worsening or developing severe adverse side effects shall be referred to an oncologist at Uganda Cancer Institute with at least five years of experience. However, the respective TMP responsible for the herbal medicine shall be informed of the decision to refer their patient. The researcher shall also require TMPs or any clinicians to obtain consent from their clients before signposting them to the researcher. To minimize the risk of intellectual property or business (customer) loss related to sharing knowledge on herbal medicine (herbs) or signposting, the researcher shall re-assure the TMPs about the purpose of the study as documented in the consent form, as well as, sign a confidentiality/non-disclosure agreement. We shall compensate all TMPs and patients directly involved in the study, for their time in the study.

Discussion

Owing to the limited comprehensive studies evaluating the treatment claims of traditional healers and herbalists, research about African traditional herbal medicine for cancer remains behind that of the Chinese herbal medicine. In addition, given that disease concepts are dynamic and key in evaluating treatment claims, there is also scarce literature on the understanding of cancer as a disease untraditionally prevalent and treated by traditional medicine practitioners in Uganda. On a whole, most of the current studies on herbal medicine for cancer have used the pharmacological approach. This has generated many laboratory-based studies with few clinic-based studies, which are also needed to validate traditional treatment claims. In line with the pragmatic paradigm, this study, therefore, uses the mixed-method approach and follows the reverse-pharmacological philosophy to evaluate some of those treatment claims from the TMPs and patient perspectives in Uganda. The findings of this study have future implications for patients, traditional medicine practitioners (herbalists and traditional healers), policymakers, conservationists, researchers, and clinical/medical practitioners regarding the integration of traditional medicine into cancer care. The study findings have the potential to guide future reverse pharmacological researchers in herbal medicine in sub-Saharan Africa.

From a practical perspective, although the 3-month follow-up period in the prospective observational study is appropriate to evaluate the treatment claims, given that cancer is a chronic disease with a delayed treatment response time, nevertheless, the study has limitations. First, since we have no control group in the study, we intend to make association rather than cause-effect (efficacy) conclusions. Second, since the study participants that will be recruited are already taking herbal medicine, their findings may not be similar to studies where participants are randomly selected. Third, there are multiple confounders in the study, such as multiple treatments and comorbidities, which may introduce clinical heterogeneity. However, extensive statistical control for confounders will be undertaken during data analysis.

In sum, this study will aid researchers to further understand the TMPs' conceptualization of cancer in sub-Saharan Africa, how that links to the treatment dispensed to their patients, and ultimately the patient-perceived outcomes.

Declarations

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

The pharm-biotechnology and traditional medicine center (PHARMBIOTRAC) at the Mbarara University of Science and Technology will fund this study. PHARMBIOTRAC will not take part in the design, data collection, analysis, and interpretation of data in this manuscript.

Authors' contributions

AJB. Conceived the idea, drafted the protocol and manuscript. PBP, ECA, MMK, GN, CUT, PEO, and AMS: supervised, revised the study protocol, and manuscript. All authors read and approved the final manuscript.

Abbreviations

FREC	Faculty of Medicine Research Ethics Committee
GLOBOCAN:	Global Cancer

MUST-REC: Committee	Mbarara University of Science and Technology Research Ethics
NACOTHA	National council of traditional healers' association
QoL	Quality of life
TMPs:	Traditional Medicine Practitioners
UNCST:	Uganda National Council of Science and Technology
WHO:	World Health Organization

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Figures

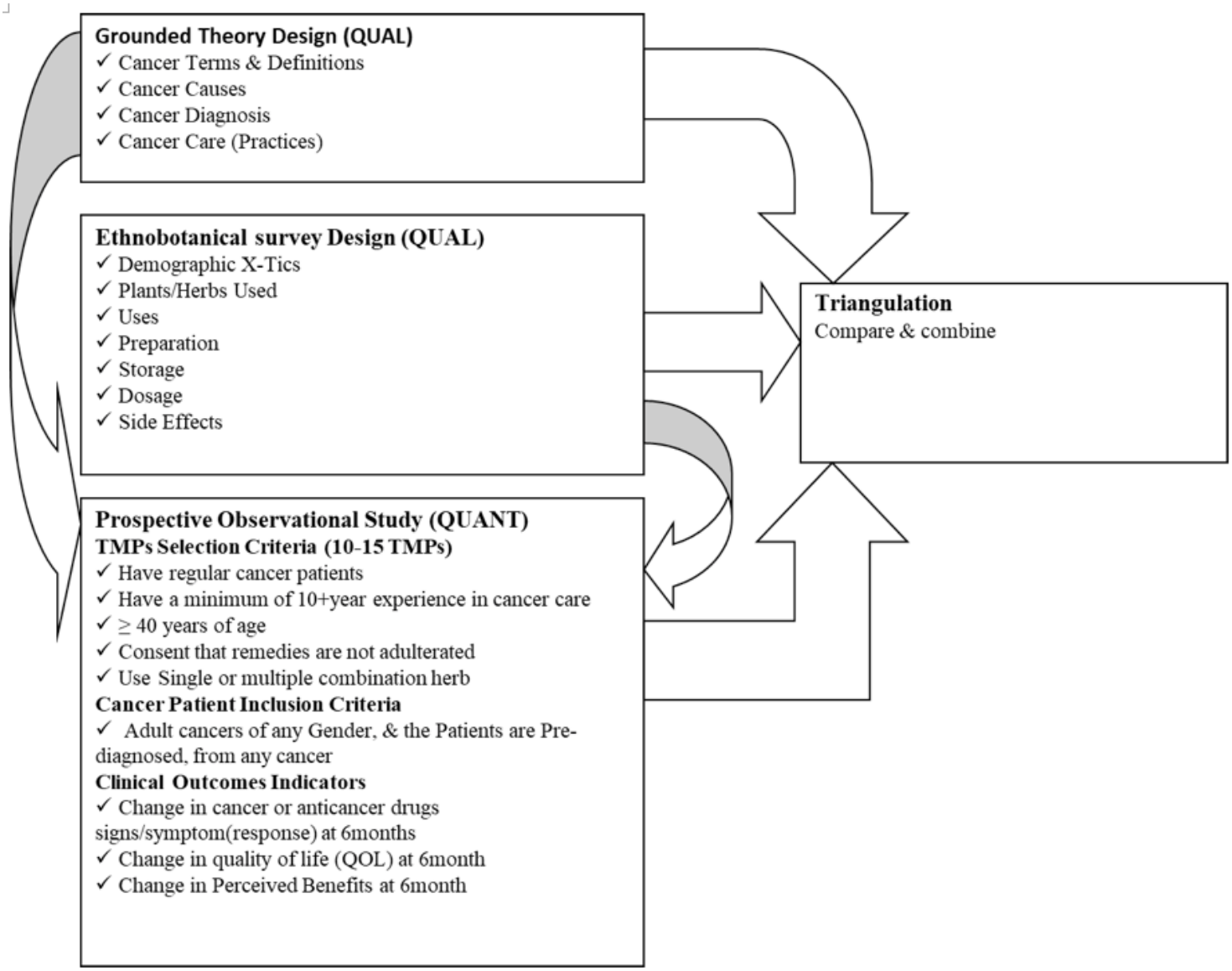

Figure 1

Study design. Note. QUAL=qualitative. QUANT=quantitative. TMPs =Traditional medicine Practitioners. Inside each box are the possible study outcomes.

Figure 2

Map showing the study sites (Kampala, Mukono, and Kiboga in Central Uganda). Source: https://www.nationsonline.org/oneworld/map/uganda-administrative-map.htm

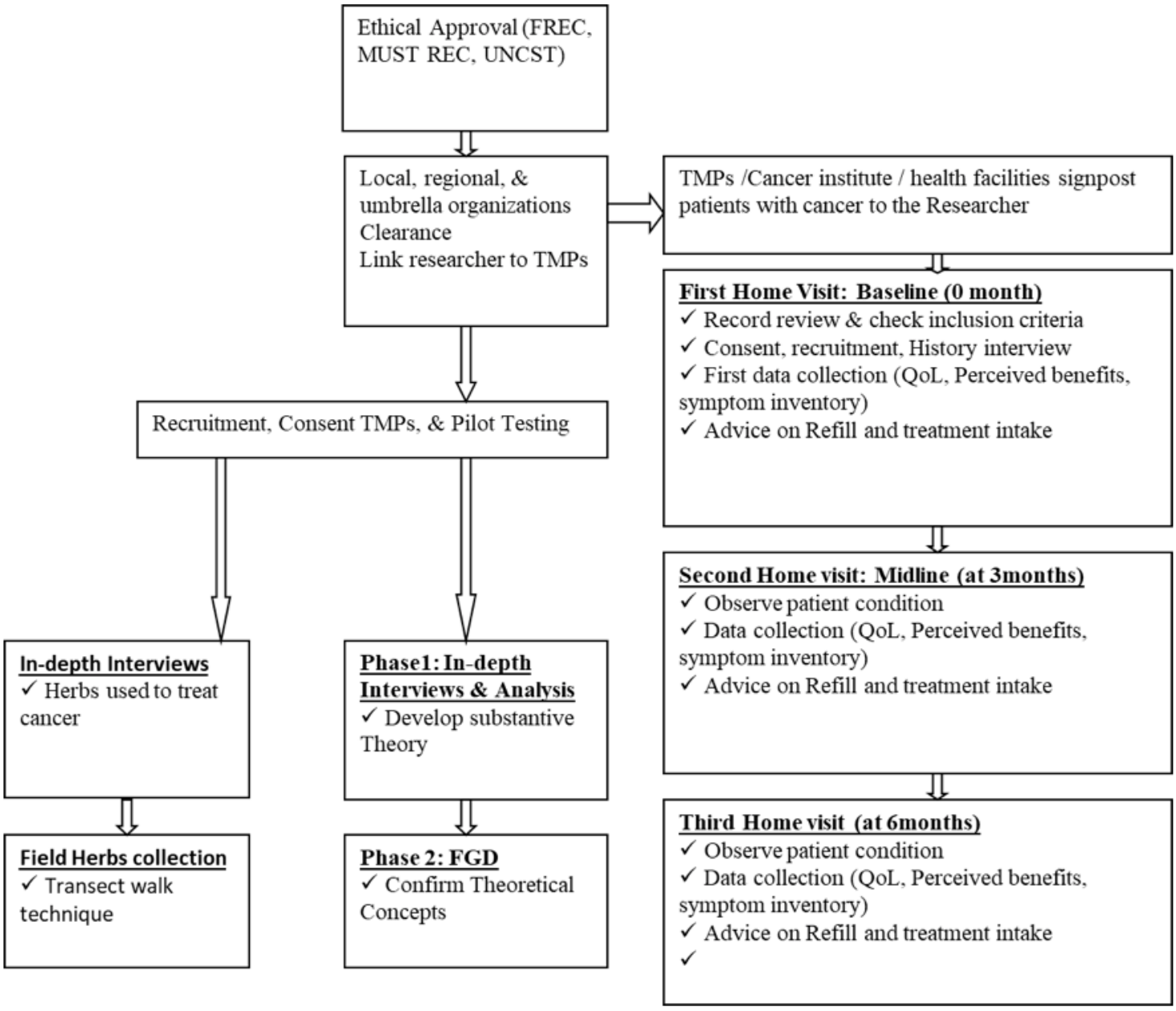

Figure 3

Data collection Procedure. Note. FREC=Faculty of medicine research ethics committee, MUST-REC=Mbarara university of Science and Technology research ethics committee, UNCST=Uganda National Council of Science and Technology, FGD=Focus group discussion, Qol=Quality of life. TMPs =Traditional medicine Practitioners.