

Opinion paper

Suubi4Cancer: A protocol for an innovative combination intervention to improve access to pediatric cancer services and treatment adherence among children living with HIV/AIDS in Uganda

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ABSTRACT

Youth Living with HIV (YLWHIV) are at high risk for cancer. Sub-Saharan Africa (SSA) has some of the worst pediatric cancer survival rates due to barriers to accessing cancer services and treatment adherence. This protocol describes a study that aims at: 1) *Identifying confirmed and suspected cancer cases in a cohort of >3000 HIV positive youth*; 2) *Examining the short-term preliminary outcomes of an evidence-based Economic Empowerment (EE) intervention*, Suubi (“hope” in a local Ugandan language), on access to pediatric cancer diagnosis and care, and treatment adherence among YLWHIV with suspected cancers in Uganda; and 3) *Exploring multi-level factors impacting intervention participation and experiences*. The proposed Suubi4Cancer intervention combines savings-led EE through family development accounts (FDA) with financial literacy and management (FLM) and cancer education (CE). The study will review medical charts in 39 clinics in Southwest Uganda to identify confirmed and suspected cancer cases. Subsequently, Suubi4Cancer will be evaluated via a randomized-controlled trial design (FDA + FLM + CE versus Usual Care) targeting a total of 78 youth ages 10-to-24 and their caregivers. Assessments at baseline and 9 months will examine change in cancer treatment access; cancer treatment adherence; and knowledge, attitudes, and beliefs about cancer and cancer treatment. Semi-structured interviews with the intervention group will explore their intervention experiences. To our knowledge, Suubi4Cancer will be the first study to test the preliminary impact and acceptability of a combination intervention to increase access to cancer diagnosis and treatment services for YLWHIV.

Trial registration: Clinical Trials NCT03916783 (Registered: 04/16/19).

1. Introduction

Worldwide, there are ~2.1 million HIV-infected youth <15 years old with over 90% living in sub-Saharan Africa (SSA) [1]. HIV-infected youth, also known as *Youth Living with HIV (YLWHIV)*, are a particularly vulnerable group at high risk for numerous social and disease outcomes including cancer [2]. Cancer risk in YLWHIV is markedly increased relative to HIV negative youth [3–5]. Yet, cancer studies in YLWHIV in SSA are rare with only one large scale South African study reported to date [6]. In Uganda, there are no prevalence data available for pediatric cancer among YLWHIV. Moreover, survival from pediatric cancer in YLWHIV is low in SSA [7]. Thus, the overall goal for this study is to tailor and explore the short-term preliminary outcomes of an existing evidence-based Economic Empowerment (EE) Intervention,

Suubi (meaning “hope” in Luganda, a local Ugandan language), on access to pediatric cancer diagnosis, care, and treatment adherence in YLWHIV with suspected cancers in Uganda.

The Suubi EE has been tested to address adherence to HIV treatment among YLWHIV in Southern Uganda (Suubi + Adherence; R01HD074949). The intervention promotes family income-generating activities (IGAs) for poor HIV positive adolescents and their families to meet financial-specific needs associated with managing clinic visitation appointments and fees (e.g., transportation to clinic appointments, and food and nutritional supplements). Our prior studies show that Suubi EE is acceptable, feasible, and efficacious at improving adherence to anti-retroviral (ART) medication with YLWHIV [8]. Thus, given the successful implementation of the Suubi EE intervention, coupled with reports of cancer-related deaths among YLWHIV in the region (resulting from non or late diagnosis), the next logical step in caring for this

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Abbreviations	
ABC	Attitudes and Beliefs about Cancer
ART	Anti-retroviral Therapy
BARS	Brief Adherence Rating Scale
BSC	Bolstered Standard of Care
CAM	Cancer Awareness Measure
CASS	Cancer Stigma Scale
CE	Cancer Education
CSQ-8	Client Satisfaction Questionnaire
EE	Economic Empowerment
ESS	Effective Sample Size
FDA	Family Development Account
FLM	Financial Literacy and Management
GLMM	Generalized Linear Mixed Models
HIV	Human Immunodeficiency Virus
ICC	Intracluster Correlation
IGAs	Income-generating Activities
KS	Kaposi's Sarcoma
LMM	Linear Mixed Models
MMAS	Morisky Medication Adherence Scale
MRs	Medical Records
OVC	Uganda Orphans and Vulnerable Children
RCT	Randomized Control Trial
SSA	Sub-Saharan Africa
SS-B	Social Support Behaviors Scale
UCI	Uganda Cancer Institute
VI	Vulnerability Index
YLWHIV	Youth Living with HIV

vulnerable group is to ensure optimal care for comorbidities, with cancer being one of them. Moreover, there are currently no community-level efforts, to our knowledge, to improve early diagnosis, treatment and adherence to treatment among this vulnerable population. The proposed study, titled **Suubi4Cancer**, will enhance the Suubi EE intervention through incorporation of cancer education *addressing cultural misconceptions (in terms of beliefs, values, norms and attitudes) regarding cancer tumors*.

In the Suubi4Cancer study, we test the theory that youth and their families' cognitive and behavioral change is influenced by economic stability. In addition, we will examine if enhanced cancer knowledge through intra-familial support and communication will help maintain positive behavioral health functioning and reinforce engagement in care and treatment. Suubi4Cancer combines family EE with cancer education for all family members addressing cultural misconceptions regarding cancer that largely impede service use. The suggested efforts are within the Uganda Ministry of Health intervention framework that calls for improving family involvement in cancer management [9].

Suubi4Cancer will leverage the Suubi + Adherence R01 to collect pilot data needed to explore acceptability and short-term preliminary outcomes of the enhanced intervention. Using medical records (MRs), we will recruit at least 78 youth ages 10–24 years with suspected malignancies from ~3000 HIV positive youth receiving care in 39 clinics (~2 youth/clinic from a 6-month medical record). More specifically the study aims are:

Aim 1. Identify confirmed and suspected cancer cases in a cohort of >3000 HIV positive youth (ages 10–24) seen at 39 clinics in 7 districts heavily affected by HIV/AIDS in southern Uganda.

Aim 2. Enhance the Suubi EE intervention by including a component addressing misconceptions (in terms of beliefs, values, norms and attitudes) regarding cancer and explore the acceptability and preliminary impact of the enhanced intervention (Suubi4Cancer) on short-term outcomes, specifically:

- 1) change in youth and caregivers' beliefs, attitudes, and behavior toward cancer testing and treatment;
- 2) access to cancer diagnosis, care and treatment;
- 3) adherence to prescribed cancer care and treatment; and
- 4) psychosocial outcomes of youth and their caregivers.

Aim 3. Explore multi-level factors (individual, family, cultural) impacting participation in and experiences with the Suubi4Cancer intervention (satisfaction, facilitators, barriers, recommendations).

2. Background

2.1. Cancer risks in HIV-infected youth

Prior to ART, cancer risks were reported at >40-fold higher in HIV positive youth [10], with the greatest risks for Kaposi's sarcoma (KS), Non-Hodgkin's lymphoma [5,11,12], and Burkitt's lymphoma [13]. In the post-ART era, 4–14 fold higher pediatric cancer risks have been reported in South Africa [3,6]. Cancer studies among YLWHIV in SSA are rare with one recent study reporting that even after anti-retroviral therapy (ART), HIV positive youth from SSA are at high risk for KS [14]. Although ART is available to all Ugandan HIV positive youth, only 47% were on ART in 2016 [15]. Moreover, in our on-going Suubi + Adherence study, at least 27 youth died in the first four years of study implementation, suggesting incomplete ART compliance. It is likely that some of these youth may have died from cancer with verbal autopsy reports conducted by the study team suggesting possible tumors before their death.

2.2. Barriers to pediatric cancer diagnostic testing, care, and treatment adherence in SSA

Globally, some of the worst pediatric cancer survival rates are in SSA, with a majority dying from their disease [16,17]. These dismal odds are influenced by barriers to accessing cancer services and staying in treatment, including cultural misconceptions about cancer, and inadequate patient/family level resources [18–20]. Although financial barriers have been commonly identified [20–22], we know of no interventions addressing financial stress faced by families of youth with a suspected cancer who are seeking diagnosis and treatment. For example, in Uganda, youth with suspected tumors are referred to the Uganda Cancer Institute (UCI) in Kampala for diagnosis and treatment. To a family living in poverty, a trip to Kampala means sacrificing resources for food and school fees. Many patients may forego/abandon cancer diagnosis and care due to logistical and financial complexities.

2.3. Conceptual model for improving access to cancer services among YLWHIV

Based on our prior study findings among YLWHIV, we hypothesize that the main barriers to uptake of available cancer diagnostic testing, care and treatment adherence are financial and that through increased household and financial stability, we can improve engagement with the health care system and seeking cancer care when confronted with a possible diagnosis (see Fig. 1). Although this approach does not address all issues associated with receiving adequate cancer care, family economic empowerment augmented with information addressing cultural

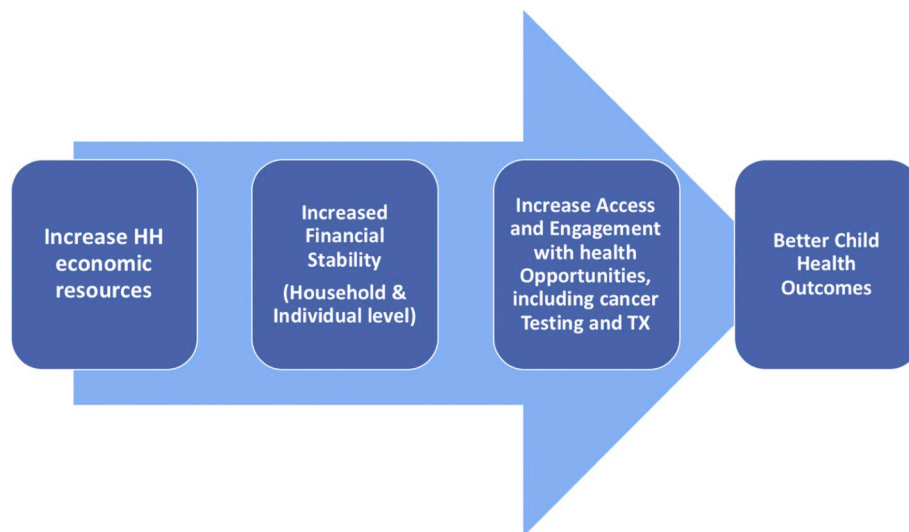


Fig. 1. Impacting long-term change among HIV positive youth with a potential cancer diagnosis.

misconceptions about cancer may improve cancer diagnostic testing, care, and treatment adherence.

3. Methods

This is multi-stage study that will identify suspected and recently diagnosed (but not necessarily having initiated treatment) pediatric cancer cases in a large cohort of HIV positive youth in a poor region heavily affected by HIV/AIDS in Uganda (**Aim 1**); followed by enhancing and testing the acceptability and preliminary outcomes of a combination intervention, Suubi4Cancer, (**Aim 2**) aimed at addressing two primary patient-level factors needed for timely cancer diagnosis, care, and treatment adherence: 1) financial stress that may hinder families' ability to access diagnostic testing and/or adherence to treatment following a diagnosis, 2) cultural misconceptions about cancer; and an examination of multi-level factors (individual, family, cultural) impacting participants' participation in and experiences with Suubi4-Cancer (**Aim 3**).

3.1. Theoretical framework

Asset Theory [23,24] that guides this study posits that economic assets may yield a range of outcomes, including increased economic stability, and improved household economic circumstances. These, in turn, may mutually enhance non-economic assets [25,26]. In this study, asset theory recognizes that there may be psychological, behavioral and social asset improvements (e.g., self-efficacy, social support, access to services) as a result of being offered an EE opportunity. Asset theory has been successfully applied in microcredit interventions for poor youth and their families in Uganda [27–31], resulting in positive health behaviors, including engagement with health services. Based on our earlier work, we propose the following pathway for behavioral change resulting from EE intervention: EE creates financial stability in a household. Financial stability in turn leads to increased access to and engagement with healthcare (in this case, testing for cancer and adhering to prescribed treatment regimens), leading to better health outcomes. (see Fig. 1). With greater resources, the youth consider the future worth living, thus influencing positive health behaviors.

3.2. Study setting

Participants will be selected from 39 clinics in the Suubi + Adherence study in five districts of southern Uganda, all heavily impacted by HIV/AIDS [30], and where the research team has multiple on-going

NIH-funded studies (see <http://ichad.wustl.edu>). The clinics serve over 3000 HIV positive youth. The study would benefit from the institutional mechanisms and support established in these EE studies for AIDS-impacted youth (see Table 1) [27–31].

3.3. Study inclusion criteria

Our target population is YLWHIV and their caregivers enrolled in care at one of the 39 clinics. Youth inclusion criteria are: 1) HIV positive (confirmation by medical report); 2) living within a family (defined broadly, not necessarily with biological parents); 3) between 10 and 24 years old; 4) attending one of the 39 clinics; and 5) did not access services or expressed unwillingness and/or inability to do so. Youth's caregivers will be eligible to participate if they have a YLWHIV under their care attending one of the 39 clinics, with a suspected cancer. Potential participants will be excluded if the research team determines that the participant cannot comprehend the study and participant rights or if they refuse to participate.

Ethics approval

All study procedures have been approved by Washington University in St. Louis Institutional Review Board (IRB; # 201905016), and by the in-country local IRB in Uganda: Uganda Virus Research Institute (GC/127/18/09/719). The study team has received training on Good Clinical Practices (GCP) and completed the Collaborative Institutional Training Initiative (CITI) certificate for protection of research participants.

3.4. Recruitment of participants

Aim 1. Medical record (MR) review will be conducted at the 39 health clinics. Following published guidelines [32], trained research assistants will conduct the MR reviews to retrospectively identify known and suspected cancer cases using a structured chart abstraction form developed in REDCap software [33,34]. We will also capture retrospective cases by linking our MR cohort to the UCI registry using a list of patient identifiers to locate potential matches. Youth with suspected malignancies (not yet diagnosed at UCI) in the last six months and their families identified through this process and prospective suspected malignancy cases identified by clinic staff while our study is underway will be eligible for Aim 2. All other youth will be included in the registry initiated as part of this project for calculation of prevalence.

Aim 2 (intervention enhancement and testing). Participants will be recruited from those identified from Aim 1 as having a suspected

Table 1
Results from authors' EE studies.

Manuscript	Outcomes	Results
Bermudez et al. (2018). <i>Journal of AIDS and Behavior</i> : Suubi + Adherence study Grant # 1R01HD074949-01.	Adherence to medication and Viral Load suppression	1. At 24-months post intervention initiation, the proportion of virally suppressed participants in the intervention cohort increased tenfold ($\Delta_{T2-T0} = +10.0$, $p = 0.001$) relative to the control group ($\Delta_{T2-T0} = +1.1$, $p = 0.733$). 2. Economic Empowerment (EE) was significantly associated with lower odds of intervention adolescents having a detectable viral load at both 12-months (OR = 0.424; 95% CI = 0.248, 0.723; $p = 0.002$) and 24-months (OR = 0.299; 95% CI = 0.161, 0.554; $p < 0.001$)
Ssewamala et al. (Under review). <i>PLOS One</i> : Suubi + Adherence study	Viral Load suppression	1. EE significantly increased the incidence of undetectable VL among intervention participants (adj. HR = 1.56, CI: 1.18–2.06, $p < 0.00$). 2. Girls were more likely to attain undetectable VL (adj. HR = 1.27, CI: 1.00–1.61, $p = 0.05$)
Bermudez et al. (2016) <i>Journal of AIDS Care: Suubi + Adherence Study</i>	Equity in Adherence to ART	1. Owning assets greatly increased the odds of self-reported adherence (OR 1.69, 95% CI: 1.00–2.85). 2. Youth living close to a health clinic were more likely to report optimal adherence (OR 1.49, 95% CI: 0.92–2.40). 3. Adolescents with greater economic advantage in ownership of household assets, financial savings, and caregiver employment had higher odds of adherence by a factor of 1.70 (95% CI: 1.07–2.70).
Cavazos-Rehg et al. (Under review). <i>Journal of AIDS and Behavior</i> : Suubi + Adherence Study	Economic equity, family cohesion and Mental health	1. Social and economic equity predicted lower depressive symptoms. Specifically, family assets and employment ($\beta = -0.28$, $t(38) = -2.48$, $p = 0.018$), food security ($\beta = -0.60$, $t(38) = -3.15$, $p = 0.003$) and social equity ($\beta = -0.35$, $t(38) = -2.54$, $p = 0.015$) were all associated with reduced depressive symptoms. 2. Family cohesion was also shown to be a factor associated with better mental health outcomes ($\beta = 0.16$, $t(38) = 6.57$, $p < 0.001$).
Nabunya et al. (under review). <i>Journal of AIDS and Behavior</i> : Suubi + Adherence study	Adherence self-efficacy to ART	1. The study found that family cohesion ($\beta = 0.397$, $p = 0.000$) and child-caregiver communication ($\beta = 0.118$, $p = 0.026$) were significantly associated with

Table 1 (continued)

Manuscript	Outcomes	Results
Wang et al. (2018). <i>Journal of Policy Analysis and Management</i> : Bridges to the Future study Grant #R01 HD070727	Savings outcomes and material well-being	adherence self-efficacy to ART. 1. Using administrative bank data, we found that (1) receiving a higher savings incentive (<i>Bridges PLUS</i>) only led to a higher frequency of deposits relative to receiving a lower savings incentive (<i>Bridges</i>) during the first intervention year. 2. Results showed evidence that the intervention increased the odds of owning a small business and the levels of asset holding. Specifically, families of the intervention condition had significantly higher odds of owning a small business at the 24-month follow-up (for <i>Bridges</i> : OR = 2.28; 95% CI = 1.05, 4.95; for <i>Bridges PLUS</i> : OR = 2.95; 95% CI = 1.38, 6.29) than children in the control condition.
Ssewamala et al. (2018). <i>Journal of Adolescent Health</i> : Bridges to the Future study	Health, mental health and self-efficacy	1. At the 24-month post intervention initiation, children in the two treatment arms showed better results in health (increase of .34–.36 standard deviation), and mental health (decreased their levels of depression by .25–.29 standard deviations and levels of hopelessness by .18–.23 standard deviations), and self-efficacy (improved adolescents' self-concept by .23–.37 standard deviation and self-efficacy by .31–.35 standard deviation) when compared to the usual care condition

cancer before they seek diagnosis and treatment. *After* identifying eligible participants (**Aim 1**), we will identify caregivers and their child (ren) who were referred to UCI with a suspicion of cancer within up to past 6 months but did not seek UCI services. To rule out participants who may not have sought UCI services at the time of the study simply because they were referred more recently (e.g. in the past month) and have not had a chance to get to UCI (but probably would in a reasonable time frame), we will screen to include in our sample only those potential participants that likely would, for several reasons, **not seek** UCI services. These are the participants that will invited to participate in the study. Clinic staff will present the study to adult caregivers of eligible youth during adolescent clinic days. If caregivers are interested, verbal consent will be obtained by research staff who are on-site during adolescent clinic days. Caregivers expressing interest will attend a one-on-one meeting with the study coordinator to learn about the project. After speaking with the study team, interested caregivers will provide written consent for youth participation. Research staff will then talk to youth separately to avoid potential coercion. Youth will be provided with the same details as the caregivers. If the child expresses interest, they will go through the informed consent/assent process. Recruitment will continue for at least three months following MR extraction initiation.

Table 2
Variables and instruments.

Variable	Measurement	Reliability	Time point
Demographics (C; Y)	Socio-demographic questionnaire	n/a	B
Family support; Social support (C; Y)	Social Support Behaviors Scale (SS-B) [28,36]	0.77	B, 9
Child vulnerability in the household (Y)	Uganda Orphans and Vulnerable Children (OVC) Vulnerability Index (VI)	n/a	B, 9
Savings deposits	Bank statements	n/a	B, 9
Financial literacy (C; Y)	Financial Literacy knowledge [35]	0.80	B, 9
Access to cancer services (C; Y)	RBA services ⁵⁶	0.66–0.83	B, 9
Adherence (C; Y)	Clinic appointments; pill count; prescription refill; Morisky Medication Adherence Scale (MMAS); Brief Adherence Rating Scale (BARS) [37,38]	MMAS; 0.83 BARS; 0.92	B, 9
Child and caregiver knowledge, attitudes, and behavior about cancer and treatment (C; Y)	Composite Measure adopted from the <i>Attitudes and Beliefs about Cancer (ABC)</i> , <i>Cancer Awareness Measure (CAM)</i> , <i>Cancer Stigma Scale (CASS)</i> , and the <i>Family CARE Project Baseline Questionnaire</i> . [39–41]	ABC; 0.80 CAM; 0.70 CASS; 0.80 <i>Family CARE Project Baseline Questionnaire</i> ; n/a	B, 9
Intervention feedback (C; Y)	Semi-structured interviews Client satisfaction survey (CSQ-8) [42]	n/a	9

Key: C-Children; Y-Youth; B-Baseline.

The team will recruit youth and their caregivers **who have not yet sought** cancer services from UCI after a reported suspected cancer and referral from the clinic, as well as those participants who will, during the screening process, express unwillingness and/or inability to access UCI services (see above). Specifically, given the number of clinics involved in the study, and the prevalence of referrals from the region (the greater Masaka region), we conservatively expect on average 2 cases per clinic over a 6 month period for a total of 78 potential participants across the 39 clinics in the five study districts. It is important to note that this number (n = 78 across 39 clinics) excludes youth who will have been referred to UCI and accessed services).

Based on our prior studies, our relationships with the local clinics, and the trust the research team has built in the region through on-going studies, we expect all individuals who screen into the study to agree to study participation. The team has partnered with 39 clinics. All participants in the treatment arm will be invited to participate in semi-structured interviews (**Aim 3**).

3.5. Randomization

The randomization will be done at the clinic level. All selected families in 19 clinics (n = ~38 families) will be placed in a control condition receiving bolstered standard of care (BSC) comprising of psychosocial counseling bolstered with literature addressing cultural misconceptions (*beliefs, values, norms and attitudes*) regarding cancer that largely impede service use and overall pediatric cancer education (using materials available at UCI). Families in the 20 clinics (n = ~40 families) will be assigned to the treatment condition (delivered over 9 months) to receive BSC plus a family EE intervention comprising of a matched family development account (FDA) for health-related expenses, including transport to UCI, food/nutrition, and health insurance. Data

will be collected at baseline and at 9-month post-intervention initiation. Youth in the same clinic will be assigned to the same study condition to avoid contamination.

3.6. Informed consent

The same consenting procedures will be used for Aims 2 and 3. During the meeting with the research team, the caregiver will sign a consent form to participate and for their child to participate. Youth (<18 years old) will sign an assent form. The field research team, including the Project Coordinator will answer any questions that come up. For youth under 18 years of age, if either the youth or the caregiver refuses to participate, the dyad will not be enrolled. The consent/assent forms (translated in Luganda) will state that the youth or caregiver can withdraw from the study at any time, for any reason, without explanation, and will not be penalized. Participants will keep a copy of the signed consent. Consent will be sought by a researcher, not medical staff to avoid coercion. Youth >18 years old will not need parental consent.

3.7. Study conditions

Suubi4Cancer: Family EE Using Matched Family Development Accounts (FDAs). Although akin to conditional cash transfer interventions, which have become increasingly popular in the social development field by enabling families and individuals to meet basic needs while incentivizing pro-social behaviors [27–31], Family EE interventions that emphasize matched savings accounts (which is the case with Suubi EE) go beyond incentivizing behavior. They emphasize long-term investment and promote life-long financial inclusion by forming savings habits and establishing partnerships between the participating family, local financial institutions and the actual intervention program. For the Suubi4Cancer study, participants in the treatment arm will receive Bolstered Standard of Care (BSC) plus a combination intervention comprising of family EE intervention in the form of a matched Family Development Account (FDA) for medical-related expenses and fees, including transport to UCI, paying for health insurance, and food/nutritional supplement expenses, combined with a cancer education component to address *misconceptions (beliefs, values, norms and attitudes) regarding cancer tumors*.

Specifically, for FDAs, savings will be housed at a local bank and deposits made by the youth and family will be matched by the intervention to encourage savings. Each youth in the EE intervention will receive a FDA held in their own name in a bank registered by the Central Bank (Bank of Uganda). For the on-going Suubi + Adherence study, the research team partnered with three national banks operating in the study area with multiple easily accessible branches: Centenary Rural Development Bank, DTB Bank, and Kakuuto Microfinance. Recently, the team has added Barclays bank to the list of partner banks. These are the banks the team will use for this study. Any of the youth's family members, relatives, or friends will be allowed and encouraged to contribute towards the FDA. The account will then be matched with money from the program. The maximum family contribution to be matched by the program will be an equivalent of US \$20 per month per family or US \$180 for the 9-month intervention period. Prior studies by the research team indicate that the partner financial institutions have multiple and easily accessible deposit locations in the study area, and that families can save these amounts [27–31].

Youth who save the maximum amount will have saved a total of \$540 by the end of the intervention period (\$180 in savings plus \$360 from the match: a 1:2 match. Each \$1 saved up to an equivalent of \$20 in saving cap per month, a participant will receive \$2 in savings match). These amounts would be enough to pay for no less than 12 trips to UCI (\$10 per trip or \$120 in total for the 12 trips to UCI) leaving a balance of \$420 to meet any additional required medical treatment, including health insurance—which costs an equivalent of \$180 a year.

As in the studies informing this application, each month, a bank

account statement will be generated for every family to note their accumulated savings. The statements are intended to act as “morale boosters” for the enrolled youth/family. Unique to this study, though, is our innovative spending model, which empowers families (with a child with a suspected cancer) with agency to make informed financial decisions. During the intervention period, families will have direct access to both their personal savings deposited in the accounts and the match provided by the study. This is different from the research team’s prior studies that required the participants’ own savings and the match to be kept in separate accounts and to get approval by the research team to access the match [27–31]. This added unconditional component provides families and the child with a safety net to address short-term medical needs and financial and consumption emergencies if they arise. Families will be provided with financial literacy sessions tailored specifically to the needs of poor youth suspected of having cancer in Uganda. The research team expects youth and their families to be equipped with the knowledge to make well-informed consumption and expenditure decisions, but also feel supported in case of immediate medical needs. The research team will monitor, but not restrict, how families spend their match via assessment questions and qualitative interview questions. Additionally, the study team will have access to and review participants’ bank statements to ascertain deposit and withdrawal frequency (throughout the 9-month intervention period).

Combined with Family EE will be four sessions of Financial Literacy and Management (FLM) [35] and two sessions of cancer education. The FLM session will cover the importance of savings, budgeting and debt management. Session 1: Why Save and Set Savings Goals, including a focus on medical expenses; Sessions 2–3: Budgeting: Examine Money Management and Set Financial Goals; Describe Importance of Budgeting; Staying within one’s Budget; Session 4: Savings: Increase Your Savings, Save for Emergencies, health care and Make a Savings Plan, including investing in health insurance. The sessions will be conducted over a 4-week period.

The two cancer specific education sessions will use UCI materials to address: 1) definitions of cancer, potential causes, signs and symptoms, and importance of cancer testing; 2) debunking cultural explanations for the causes of cancer and misconceptions (*beliefs, values, norms and prevailing attitudes*) regarding cancer that largely impede service use. The sessions will also re-emphasize the role and need to invest in health insurance. The sessions will be conducted over a 2-week period during adolescent clinic days for HIV care.

As was the case with the research team’s earlier studies, participants from the same health clinic will be assigned to the same group during training, which will occur on adolescent clinic days. The team will ascertain the extent to which the adolescent clinics days training schedule facilitates or hinders participation. The sessions will be conducted by trained community extension workers paired with community health care workers at the parish level.

The control condition. Participants in this condition will receive bolstered Standard of Care (BSC) comprising of psychosocial counseling bolstered with a cancer education component *to address misconceptions regarding suspected cancers* (see above) to be delivered during adolescent clinic days by community health care workers.

3.8. Data collection

Aim 1. The research team will collect information contained on the Ministry of Health’s HIV CARE/ART blue card as well as information contained in the patient’s files on referrals for suspected cancers. In addition, if there are any other pertinent notes relevant to suspected or known cancers included in the patient files, the team will include that information in the database. The data collected for Aim 1 will be used to create a regional HIV pediatric and adolescent database and identify eligible participants for Aims 2 and 3.

Aim 2. Participants will be interviewed at baseline and at 9-month post intervention initiation. Youth and caregiver assessments will be

conducted by a trained research assistant at each clinic (in a private location) and will take approximately 60 minutes and will be administered in Luganda, the local language of the region (see Table 2). Assessments will be translated and back-translated into Luganda from English by a certified translator. Member of the research team are fluent in Luganda, which will be helpful in cross-checking the translated documents. Careful screening of participants will partially contribute to reliability of the data. Standardized measures have been validated in SSA context. The team will carry out content and construct validity and for all measures to ensure their cultural validity in Uganda.

Process measures will be used for fidelity and quality control of intervention implementation. Participants will also be asked for feedback on intervention acceptability and relevance via semi-structured interviews upon intervention completion as described in Aim 3 (see Aim 3 for further details).

Aim 3. Semi-structured in-depth interviews will be conducted upon intervention completion with caregivers and youth (separately) for intervention acceptability and relevance. The interview will focus on: 1) Participants’ experiences with the intervention and its specific components (i.e. savings, financial literacy, and cancer education—including *beliefs, values, norms and attitudes about cancer*) and 2) Key multi-level (individual, family, contextual, and programmatic) influences that affected their participation and their decision to access services for diagnosis and treatment adherence. All participants in the treatment arm ($n = 40$) will be invited to participate in the interviews. This sample size will be sufficient for theoretical saturation [43,44], which will allow us to identify common patterns and variations in participants’ experiences. Interviews will be conducted in English or Luganda based on participants’ preference. Questions will be translated (English to Luganda) and back-translated by two proficient team members. Each interview will last about 60 min and will be audio-taped for feedback on intervention acceptability and relevance via semi-structured interviews upon intervention completion.

3.9. Data analysis

Aim 1. The team will review the MRs of ~3000 HIV positive youth, which will comprise database for identifying newly recorded suspected cancer cases (within the last six months) for Aim 2. The team will calculate the prevalence of confirmed cases (number [#] of individuals documented with confirmed diagnoses through MR and UCI divided by the total # of individuals in the recruited cohort). The team will calculate prevalence of suspected and confirmed cases as well as prevalence by cancer type to estimate known and possible cases, which will contribute to the sparse data in SSA.

Aim 2. The team will monitor recruitment rates and staff level effort, number of individuals undergoing diagnosis at UCI, proportion eligible and agreed to enroll in the Family EE intervention. Enrollment of 70% or higher in both study arms will be considered feasible. The team will also record number of rescheduled, cancelled and missed cancer diagnosis visits at UCI to inform estimation of staffing needs and retention protocols for a subsequent R01 trial.

Acceptability. The team will modify satisfaction surveys, including the Client Satisfaction Questionnaire (CSQ-8) to assess acceptability [42]. Items include: “How satisfied were you with the program?”, “How helpful was the program in addressing barriers to access to cancer services?” and “How likely are you to recommend this program to other families where youth may be referred to UCI for further examination?” Given the expected modest sample size, quantitative analyses of intervention data will be largely descriptive and concentrate on tabulating and summarizing satisfaction outcomes.

Hypotheses and methods for preliminary outcomes/exploratory analyses. Exploratory hypotheses will be evaluated to assess study feasibility. The team expects that following intervention (at 9-month time point), relative to the control group, intervention participants will have **higher:**

H1. mean count of cases accessing cancer services (both diagnosis and treatment following a positive diagnosis);

H2. mean levels of youth's reported adherence to prescribed cancer treatment. We will plot means by group over time to describe overall patterns of change.

Secondarily, we also hypothesize that mean levels of positive mechanisms of change such as knowledge, attitudes, and behaviors as well as psychosocial outcomes will be higher for intervention participants relative to control participants following the completion of the intervention.

To evaluate the proposed preliminary hypotheses the team will use linear mixed models (LMM) for continuous outcomes (e.g., mechanisms of change and psychosocial outcomes measured by continuous indices and scales) and generalized linear mixed models (GLMM) for semi-continuous data such as counts of patients accessing treatment. GLMMs fitted to count outcomes will use the best-fitting distribution from the Poisson family (e.g., Poisson, negative binomial; zero-inflated Poisson; zero-inflated negative binomial) with the log link function. The team will fit mixed models to ensure that all requisite information is available to perform the types of analyses typically undertaken in a formal RCT of intervention efficacy and to obtain valuable effect size information. These models will include dummy variables indicating clinic membership to control for clinic-based effects. Due to the expected modest sample size, significance testing will be de-emphasized.

Power analyses. Although the study purpose is to determine preliminary acceptability rather than conduct formal hypothesis tests, the team conducted several power analyses using NCSS PASS to supply additional information. For the enrollment proportion to assess feasibility: assuming a starting sample of 78 youth at baseline, and an attrition rate of 10% during study period, $\alpha = 0.05$, power = .80, 70 participants retained at the final time point following 10% estimated attrition, the width of the confidence interval for single proportions is 22.5% (standardized distance to the limit: 0.25). For continuous standard normal variables to assess acceptability (e.g., CSQ-8), the distance from the mean to the confidence limit is 0.24, which is between a small (0.20) and medium (0.50) effect size.

For preliminary efficacy exploratory inferential analyses assuming two time-points, minimum detectable standardized mean differences for continuous outcomes ranges from 0.52 to 0.64 for within-subjects correlations r ranging from 0.20 to 0.80. The above scenarios assume an extreme of no correlation of data from participants within clinics. The opposite extreme is if the correlation of data from participants within clinics is perfect (i.e., intraclass correlation [ICC] $\rho = 1$), leading to an effective sample size (ESS) of 35 instead of 70. In that scenario, the minimum detectable distance to the limit for proportions is 32.1% (standardized distance: 0.37), the same distance for means is 0.34, and minimum detectable mean differences for the pretest-posttest group difference interaction effect range from 0.73 to 0.90.

In sum, the Suubi4Cancer study is powered to detect small to medium distances to confidence limits for descriptive statistics and medium to large longitudinal analysis effects, though formal hypothesis testing will not be the study focus.

Aim 3. Interviews will be transcribed and uploaded to QSR NVivo11 analytic software. Analytic induction techniques will be used for coding [45–47]. Initially, five interview transcripts randomly selected will be read multiple times and independently coded by the team using sensitizing concepts and identifying emergent themes (open coding) [45–47]. Broader themes will be broken down into smaller, more specific units until no further subcategory is necessary. Potential themes include barriers and facilitators at the individual-level (e.g., time constraints, motivation, readiness to change); family-level (e.g., competing demands, support); program-level (e.g., content relevance; interaction with program participants); and contextual (e.g., cultural norms, stigma). Analytic memos will be written to further develop categories, themes, and subthemes, and to integrate the ideas emerging from the

data. Codes and the inclusion/exclusion criteria for assigning codes [45–47] will be discussed as a team to create the final codebook in NVivo. Each transcript will then be independently coded by two investigators using the codebook. Inter-coder reliability will be established. A level of agreement ranging from 66 to 97% based on level of coding indicates good reliability [43,44,48]. Disagreements will be resolved through team discussions. The secondary analysis will compare/contrast themes within and across participants for similarities, differences, and relationships among findings. Member checking, peer debriefing, and audit trail will be used for rigor [48].

4. Discussion

Some of the worst pediatric cancer survival rates are in SSA, with a majority dying from their disease [16,17]. Recent reviews highlight the urgent need for “better data” and the “paucity of epidemiologic information” on pediatric cancer in HIV-infected youth from regions with a high burden of HIV/AIDS [3,49]. This study will contribute to the existing literature by identifying potential pediatric cancer cases in an HIV-infected cohort in the poor SSA country of Uganda and contribute to sparse data on pediatric cancer burden; and creating a regional database for youth living with HIV/AIDS (YLWHIV) for cancer research. Our work is also complementary to existing activities in SSA focused on building infrastructure to support optimal cancer care [50] with its primary focus on minimizing barriers to accessing care and treatment among families.

The Suubi4Cancer study will be the first to test a combination intervention, integrating a family EE intervention with pediatric cancer education **addressing cultural misconceptions regarding cancers** among an HIV positive population in Uganda (and SSA). The intervention model to be tested is intended to enhance economic stability for poor YLWHIV with newly suspected cancers so that sufficient income exists to meet their cancer-related medical needs and fees (e.g. costs associated with transportation to cancer diagnosis and other related medical appointments). EE interventions, specifically savings-led income-generating activities (akin to a conditional cash transfer), are a highly innovative form of social intervention. The findings from this study will add to our understanding of the short-term impact of combination interventions addressing access to cancer diagnosis, care, and treatment adherence among YLWHIV in SSA.

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Trial status

Study recruitment has not started yet.

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