[redacted]

[redacted]

APPLICANT INFORMATION

Project ID	[redacted]
Name	[redacted]
Primary Institution	[redacted]
Address	[redacted]
Phone Number	[redacted]
E-mail Address	[redacted]
[redacted]	[redacted]

TRAINING and APPOINTMENT DATES

Please note: If you do not have a faculty appointment at an academic institution, please click the "N/A" box.	
What date did you complete or will you complete your final medical subspecialty training program?	[redacted]
Indicate if N/A	
What date did you begin your initial full-time faculty appointment?	[redacted]
Indicate if N/A	

PROJECT INFORMATION	
Project Title	[redacted]
Abstract	Background Low income countries (LICs) such as those found in African face a growing burden of cancer and a pressing need to strengthen cancer care delivery systems. Value-based cancer care is of particular importance in LICs. Notable efforts with varying levels of success have aimed at modifying guidelines developed in high-income countries to the healthcare capacities and infrastructures in LICs, some with emphasis on Africa. Suboptimal compliance to consensus-based national guidelines is not uncommon on the continent, and could lead to substantial, otherwise avoidable waste of resources. [redacted] in oncology was initiated by the American [redacted] in 2012 to identify and reduce avoidable low-value practices in cancer diagnosis and management. The CW movement is driven by specialist physicians and surgeons who through a consensus-based process identify common medical practices that do not offer benefit to patients and may cause harm. [redacted] was published with a list of 10 recommendations in 2018. In 2019, [redacted] reported their list. [redacted] represented the first CW initiative in LICs. Drawing from the three mentioned publications and under the guidance of my mentor [redacted] who has co-led the [redacted] initiatives, I co-led the recently completed [redacted] project. The manuscript will soon be submitted for publication. During the proposed ASCO LIFe Fellowship I will build on this work to study the implementation of CWA recommendations. Objectives: 1. To understand barriers/enablers to adoption of CWA recommendations. 2. To measure concordance of current practice with CWA recommendations. Methods: Consistent with the goals of Choosing Wisely, in the next phase of work we will study the implementation of the CWA recommendations. In this fellowship project we will use mixed methods to: 1) Disseminate an electronic survey to African oncologists to understand the acceptability of CWA recommendations and barriers/enablers to their adoption; and 2) Use prospective data capture to measure concordance with CWA recommendations at 6 major African cancer centres across 6 different Africa countries ([redacted]. 3)Undertake semi-structured interviews at a subset of centres to contextualize and validate survey findings. This proposed work builds on our existing work in Choosing Wisely Africa with a team that has already worked together and has the necessary expertise to see the project through to successful completion. The survey and prospective data capture activities will very likely lead to improved awareness of the CWA recommendations on their own. However, it is envisioned that the proposed work is one step towards implementation of CWA. Results from this study will allow our research team to identify gaps in care and future areas that require

	targeted knowledge translation activities.
Specific Aims	

[redacted]	[redacted]
Prior Application	

CLASSIFICATION

Subject Area	Health Services Research If Other: Choosing Wisely

Focus Area(s)	Health Services Research, Health Outcomes, Delivery of Cancer Care, Global Oncology If Other:

ASSURANCES

Animal Use

Animal Use	No
Assurance Status	Not Applicable
IACUC Approval Date	
IACUC Expiration Date	
Assurance Number	

Human Use

Human Use	Yes
Assurance Status	[redacted]
IRB Approval Date	
IRB Expiration Date	
Assurance Number	
Exemption Number	

CLASSIFICATION

Subject Area	Health Services Research If Other: Choosing Wisely

Focus Area(s)	Health Services Research, Health Outcomes, Delivery of Cancer Care, Global Oncology If Other:

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Animal Use	No
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IACUC Approval Date	
IACUC Expiration Date	
Assurance Number	

Human Use

Human Use	Yes
Assurance Status	[redacted]
IRB Approval Date	
IRB Expiration Date	
Assurance Number	
Exemption Number	

PERSONAL STATEMENT	
Background (LIFe)	In 1997, my [redacted] was diagnosed with cervical cancer. Little did I know that the following years, my childhood and ultimately my career path would change when she passed on in 1998. Retrospectively, her passing somewhat makes sense given the lack of medications, trained physicians and related vessels of cancer care that was evident. However, today such deaths have no explanations. When I graduated from medical school in 2013, I worked at [redacted] where I continued to see several patients of all ages succumbing to cancer. In 2018, I completed my residency at [redacted] in [redacted] My profound experience in both countries inspired me to pursue this particular fellowship. In both countries I observed various approaches to patient care. I witnessed several unacceptable medical practices that were based on physicians' discretion and with little to no evidence, this deeply disturbed me. For the longest of time, this in addition to lack of proper local guidelines created a series of harmful practices. For instance, in both [redacted] where I practiced, we would put patients with metastatic breast cancer on palliative combination chemotherapy drugs even when a single agent would suffice. After I was awarded the [redacted] grant in [redacted], I visited my mentor [redacted], who introduced me to [redacted] One recommendation from the ASCO [redacted] stood out to me and informed my current practice in [redacted]. It stated, "Don't use combination chemotherapy instead of chemotherapy with one drug when treating an individual for metastatic breast cancer …". Later on, I met Dr [redacted], who at the time had published [redacted] and was working on [redacted]. He inspired me to start [redacted], under his guidance we have been able to come up with 10 choosing wisely list specific to African settings especially low-income countries.
Benefit to Your Home Country (LIFe)	In summary this fellowship will address both clinical oncology and cancer research gaps at my centre and in my country at large. The focus of this fellowship is a

	rigorous training on research specifically cancer research. Over the past 2 decades, [redacted] has made remarkable progress in building human research capacity. However, most research has focused on infectious diseases, with little attention to noncommunicable diseases, including cancer. [redacted] has a shortage of cancer specialists and cancer researchers. This fellowship will equip me with advanced clinical & research skills to help address this shortage. After my fellowship I will establish a research department within our newly established cancer center. The research department role will be to invest research skills among my colleagues and also create a hub for cancer research in [redacted] The ultimate goal will be to improve cancer researchers' skills and ultimately increase cancer-related research output among oncologists and cancer researchers in [redacted] During this fellowship I will also have a clinical role as a fellow in both medical and radiation oncology. This will include attending clinics with my mentors and other staff, attending multidisciplinary clinics and conferences, and participating in journal clubs and grand rounds. Our Cancer Center recently acquired two linear accelerator radiotherapy machines equipped with latest technology with VMAT capacity. Most oncologists at the center were trained on machines with 2D or 3D conformal radiotherapy capacities , this fellowship will provide me with experience using this new technology and the resulting skills developed will be transferred to my colleagues back home. The center currently has a functional radiotherapy unit, a nearly complete chemotherapy infusion unit and a designated space for research department.
Mentor (LIFe)	It is rare to come across a great mentor like [redacted] In early 2018, I won a travel grant to attend and present at the inaugural [redacted], after which I spent a month at [redacted] shadowing Dr. [redacted] in her practice. Dr [redacted] knew my interests in health services research and she introduced me to Dr. [redacted] I shadowed Dr. [redacted] in [redacted] and on several occasions, we discussed our research interests. It is from here that our mentee-mentor relationship began and we have since collaborated on several projects many of which have been published in peer-reviewed journals. Of recent, Dr [redacted] and I embarked on a new project [redacted]'. Dr. [redacted] had co-led similar

	projects including [redacted] Together we identified 10 oncology practices that should be routinely avoided on the continent given their lack of evidence. Based on our partnership and past work, Dr. [redacted] is the perfect mentor to provide guidance and expertise on the implementation of choosing [redacted] recommendations. Dr. [redacted] understands the challenges and nuances to practicing oncology in resource constrained settings. He has experience working as a visiting scientist at the [redacted] and continues to work closely with his [redacted] colleagues on various projects focused on improving accessibility and quality of cancer care. His dedication to his trainees goes beyond ensuring the trainees get adequate clinical and didactic curricular; he instills a culture that facilitates professional and personal growth. His prior trainees have gone on to illustrious early careers; and they consistently attribute their successes to the excellent mentorship they received from Dr. [redacted]

BUDGET and JUSTIFICATION

	Year 1	Year 2	Year 3	Total
Passion Grant Amount	$0	$0	$0	$0
Approved Passion Grant Amount	$0	$0	$0	$0
Indirect Costs	$15,000	$0	$0	$15,000
Indirect Costs	$0	$0	$0	$0
Indirect/Facilities and Administrative Costs	$0	$0	$0	$0
Institution Overhead	$15,000	$0	$0	$15,000
Direct Costs	$100,000	$0	$0	$100,000
Consortium/Contractual Costs	$0	$0	$0	$0
Consultant Costs	$0	$0	$0	$0
Equipment	$0	$0	$0	$0
Fringe Benefits	$3,000	$0	$0	$3,000
Other Expenses	$0	$0	$0	$0
Patient Care Costs (Inpatient)	$0	$0	$0	$0
Patient Care Costs (Out-patient)	$0	$0	$0	$0
Personnel Costs	$0	$0	$0	$0
Research Costs	$20,000	$0	$0	$20,000
Salary	$70,000	$0	$0	$70,000
Subcontracts	$0	$0	$0	$0
Supplies	$0	$0	$0	$0
Travel	$7,000	$0	$0	$7,000
Total Direct Costs	$100,000	$0	$0	$100,000
Total Indirect Costs	$15,000	$0	$0	$15,000
Total	$115,000	$0	$0	$115,000

Budget Notes

Year	Note
Year 1	[redacted]

Category	Note
Passion Grant Amount	
Approved Passion Grant Amount	
Indirect Costs	
Indirect Costs	
Indirect/Facilities and Administrative Costs	
Institution Overhead	[redacted]
Direct Costs	
Consortium/Contractual Costs	
Consultant Costs	
Equipment	
Fringe Benefits	Requested funds will be used for health insurance covering 12 months, life insurance.
Other Expenses	
Patient Care Costs (Inpatient)	
Patient Care Costs (Out-patient)	
Personnel Costs	
Research Costs	Funds requested here will be used to carry out the proposed research. This will include paying research assistants in the selected cancer centres both for the prospective chart review and also for the semi structured interviews. Also funds in this category will be used to pay for REDCap software that we shall use to design and also disseminate the survey which will be sent to all practicing oncologists on the continent.
Salary	Funds requested here will be used to cover my monthly salary for the 12 months.
Subcontracts	
Supplies	
Travel	This will be used to travel twice between [redacted] and also twice to ASCO Conferences.

CONTACTS

Contacts-Personnel

Primary	Role	Name	Organization Name
Yes	Principal	[redacted]	[redacted]

Contacts-Other

Role	Name	Organization Name
Mentor	[redacted]	[redacted]

UPLOADS FROM APPLICANT

The following pages contain the uploads provided by the applicant:

Upload Type	Uploaded By	Uploaded Date
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: [redacted]

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

In 1997, my [redacted] was diagnosed with cervical cancer. Little did I know that the following years, my childhood and ultimately my career path would change [redacted] passed on in 1998. Retrospectively, [redacted] passing somewhat makes sense given the lack of medications, trained physicians and related vessels of cancer care that was evident. However, today such deaths have no explanations.

When I graduated from medical school in 2013, I worked at [redacted] where I continued to see several patients of all ages succumbing to cancer. In 2018, I completed my residency at [redacted] in [redacted] My profound experience in both countries inspired me to pursue this particular fellowship.

In both countries I observed various approaches to patient care. I witnessed several unacceptable medical practices that were based on physicians' discretion and with little to no evidence, this deeply disturbed me. For the longest of time, this in addition to lack of proper local guidelines created a series of harmful practices. For instance, in both [redacted] where I practiced, we would put patients with metastatic breast cancer on palliative combination chemotherapy drugs even when a single agent would suffice.

After I was awarded the [redacted], I visited my mentor [redacted], who introduced me to [redacted]. One recommendation from the [redacted] stood out to me and informed my current practice in [redacted]. It stated, "Don't use combination chemotherapy instead of chemotherapy with one drug when treating an individual for metastatic breast cancer …". Later on, I met Dr [redacted] in 2018, who at the time had published [redacted], and was working on [redacted]. He inspired me to start [redacted] under his guidance we have been able to come up with 10 choosing wisely list specific to African settings especially low-income countries.

My prior experience in managing grants and projects like these leaves me well situated to manage this type of project. In 2015 through an organization that I founded called [redacted] which raises awareness of childhood cancers, together, with International Health Initiative Inc. we applied and won a [redacted] Grant for which I was a co- Principle Investigator. We carried out a situational analysis to understand the childhood cancers needs across [redacted] In 2015, I won a $10,000 [redacted]t to carry out a project that was aimed to train breast cancer survivors who later trained their peers in advocacy. In this same project we also established breast cancer support groups in two regions in [redacted]. In 2018 I won the ASCO [redacted] where we used the fund to establish [redacted] in [redacted] These projects and several others that I supported have given me the experience needed to run similar projects in low-income settings.

B. Positions and Honors

Positions

[redacted]

Honors

- [redacted]

C. Contributions to Science

1. [redacted]

D. Additional Information: Research Support and/or Scholastic Performance

Conference Presentations

- [redacted]

[redacted]

[redacted]

Dear Sir/Madam,

[redacted]

[redacted] graduated from [redacted] and joined the [redacted] as a junior consultant Oncologist in January 2019. As the head of Oncology department, I have known Dr [redacted] for the past four years, first as a young medical officer treating cancer patients before joining oncology training in [redacted] and I continued to follow his progress during his residency program.

[redacted] as varsity knowledge of cancer care in poor settings and has been involved in research, publishing both peer reviewed articles and numerous cancer related editorials. This is an impressive work rate given his young clinical age. [redacted] is very active cancer patient advocate and founded [redacted] Relief an organization that advocates for children with cancer and raises the awareness of childhood cancers. He is an enthusiastic learner, always asking questions and looking to improve his depth of understanding.

I have every confidence and expectation that at the end of this fellowship, [redacted] would return with many new research and clinical skills and with new relationships that will be valuable to him and others involved in cancer care and research in [redacted] In particular the new cancer center at [redacted] is growing its research wing hence this fellowship comes at an important stage of our department. Dr [redacted] kills learnt from this fellowship will be put to work as he will help the center's research department to grow. A part from research skills, as detailed in his fellowship plan he will spend time in the clinics at [redacted] where he will learn advanced and current techniques in brachytherapy and external beam radiotherapy and new advances in cancer management in general, as a center we shall benefit from this upon his return.

The institution will support Dr [redacted] o complete this fellowship, his position and employment status after fellowship is guaranteed.

It is truly an honor to recommend him to attend this important fellowship and please feel free to contact me should you have any questions.

Yours Sincerely

[redacted]

[redacted]

[redacted]

Abstract

Background. East Africa is one of the fastest growing regions in the world and faces a rising burden of cancer; however, few people are equipped to effectively conduct research in this area.

Materials and Methods. A 31-item questionnaire was distributed to current trainees and recent graduates of the Master in Medicine in Clinical Oncology Program at [redacted] Areas that were assessed included (a) demographic information, (b) prior research training, (c) prior and current research activities, (d) attitudes toward the importance of research, and (e) supports and barriers to inclusion of research in an oncology career path.

Results. A total of 30 individuals responded to the survey, of whom 53% (n = 16) were male and 70% (n = 21) identified as current trainees. Among the majority of respondents, attitudes toward research were strongly favorable. Although only 37% (n = 11) reported receiving any formal training in research methodology, 87% (n = 26) reported intentions to incorporate research into their careers. The absence of protected time for research and lack of access to research funding opportunities were identified by a majority of respondents as critical barriers.

Conclusion. A majority of current or recent oncology trainees in Tanzania desire to incorporate research into their careers, but most also lack adequate training in research methodology and longitudinal mentorship. Our future collaboration will focus on creation of appropriate research training curriculums and fostering an environment that catalyzes interprofessional development and transforms and extends context-specific cancer research in East Africa[redacted]

Implications for Practice: Current and recent oncology trainees in East Africa expressed a high enthusiasm for research, driven by a sense of urgency related to the burden from cancer that the region faces. This highlights the need for cancer research training and mentorship in this setting. This work hypothesizes that African principal investigators can operate effectively if proper attention is given to selection and provision of high-quality foundational didactic training to learn the theory and implementation of research as well as to the development of an environment conducive to mentoring.

Introduction

Africa is facing unprecedented growth in cancer burden and is inadequately prepared to meet this public health challenge. By 2030, 1.27 million new cancer cases per year are expected, with approximately 1 million expected deaths [1].

In 2011, ministers of health for countries in the World Health Organization African Region affirmed their awareness of this mounting disease burden by adopting the Brazzaville Declaration on Non-communicable Diseases Prevention and Control [2]. The signatories to this declaration agreed to develop strategies for prevention and control to strengthen health systems and reduce noncommunicable disease (NCD) burden, to source finances necessary to fight NCDs, and to enable national health information systems to generate data on risk factors and on disease burden from NCDs. However, progress in the development of evidence-based cancer control strategies has been slow since this declaration and has been outpaced by the increasing severity of the problem.

Over the past 2 decades, institutions in sub-Saharan Africa have made remarkable progress in building human research capacity. However, most research has focused on

[redacted]

infectious diseases, with little attention to noncommunicable diseases, including cancer [3]. In the context of limited prevention and health care resources in Africa, it is imperative to formulate cancer control policies that are evidence-based and targeted to cancers with the highest incidence, morbidity, and mortality rates in the local region [4]. However, there are many factors, including the scarcity of trained health professionals, differences in the infrastructure for clinical care, and unique cancer epidemiology, that pose challenges for extrapolating clinical trial and other data from oncology research performed in resource-rich settings [5]. Research conducted by those closest to care delivery will ultimately be necessary to address the etiology of cancers unique to East Africa and to develop locally appropriate strategies to prevent and treat cancers. Thus, it will be necessary to equip oncologists who practice in resource-constrained settings with research skills and longitudinal mentorship to enable them to perform high-quality cancer research that is relevant to the context in which they provide care.

With a population of more than 150 million in 2014, East Africa is one of the fastest growing regions in the world [6]. The rapid growth and projections for increased cancer burden related to industrialization and changes in dietary and lifestyle patterns pose challenges that demand the development of research skills and capacity to address the needs of the region [7]. To tackle the growing burden of cancer, the region requires competent, well-trained African researchers with supportive infrastructure and environments to enable generation of local evidence by local investigators to inform cancer control planning.

Currently, oncology is a nascent medical specialty in East Africa, and very few individuals are equipped with both the clinical training and research skills to effectively conduct research in this area. The Master of Medicine (MMed) in Clinical Oncology program at Muhimbili University of Health and Allied Sciences (MUHAS) is one of the first programs in East Africa to train doctors to become specialists in clinical oncology, combining training in radiation and medical oncology at the Ocean Road Cancer Institute (ORCI) in Dar es Salaam, Tanzania. Since its inception in 2010, it has emerged as an oncology training hub for the East African region and beyond. Current international oncology trainees at MUHAS originate from Rwanda, Ethiopia, Kenya, Comoros Islands, the Democratic Republic of Congo, and Nigeria, all of whom will return to practice oncology in their home countries as part of a new cadre of oncology leaders in East Africa. In light of the critical need to improve research training and ultimately increase cancer-related research output among oncologists in East Africa, we sought to evaluate the attitudes and barriers toward research among current and recent oncology trainees at a regional training hub in East Africa.

Materials and Methods

Study Design and Population

A descriptive cross-sectional study was conducted in February 2018 targeting current trainees and recent graduates of the MMed in Clinical Oncology Program at MUHAS (n = 34).

Data Collection

We adapted a 31-item questionnaire, which has been used to assess attitudes and barriers to conducting research in other medical subspecialty training programs [4, 5], to focus on oncology research. Areas that were assessed included (a) demographic information, (b) prior research training, (c) prior and current research activities, (d) attitudes toward the importance of research, and (e) supports and barriers to inclusion of research in an oncology career path. Attitudes toward the importance of research were scored on a five-point Likert scale (1 = strongly agree; 5 = strongly disagree).

After informed consent was provided, an electronic questionnaire was sent out to all participants in English, which is the language of the medical school curriculum and the common language in this multinational group of current and recent trainees. Participants entered deidentified responses directly into Research Electronic Data Capture, a secure web-based application for data storage.

Statistical Analysis

Descriptive statistics were used to summarize the level of knowledge, attitude, and research practice among the study participants. Categorical variables were presented as both totals and percentages. Continuous variables were presented with median values and ranges. Fisher's exact tests were performed to evaluate associations between demographic characteristics, including gender, nationality, and rank (trainee vs. faculty), with particular attitudes and barriers. All analysis was performed with Stata statistical software version 15 [8].

Ethical Considerations

The study was considered exempt from review by both the [redacted] use of minimal risk to participants. All participants provided written informed consent prior to completing the survey.

Results

Out of 34 current trainees and recent graduates that were invited to participate, the overall response rate was 88% (n = 30), of whom 53% (n = 16) were male, 70% (n = 21) were current trainees, and 53% (n = 16) originated from [redacted] Demographic characteristics, research experiences, and career aspirations of the 30 respondents are summarized in Table 1. Respondents who identified as currently in a faculty role were more likely to be of [redacted] nationality (50% vs. 7%, p = .01).

Of 30 respondents, 37% (n = 11) reported receiving some form of dedicated research training prior or in addition to the training provided during the MMed in Clinical Oncology curriculum; seven individuals reported prior completion of a master's degree (M.Sc. or M.P.H.), and four reported completion of research coursework in a nondegree program. Among seven respondents who reported that they began doing research prior to beginning their oncology training, six reported that the prior research resulted in a publication. Among practicing faculty, the median time in practice was 4 years (range: 1–5 years).

Table 1. Demographic characteristics, research experiences, and career aspirations of oncology trainees and recent graduates of a clinical oncology training program in Tanzania (n = 30)

Characteristics	*n* (%)
Gender	
Male	16 (53)
Female	14 (47)
Current position	
Trainee	21 (70)
Faculty	9 (30)
Nationality	
Tanzanian	16 (53)
Other	14 (47)
Prior formal training in research	
Yes	11 (42)
No	15 (58)
Unknown	4
Research experience prior to oncology residency	
Yes	7 (27)
No	19 (73)
Unknown	4
Currently able to identify a research mentor	
Yes	4 (22)
No	14 (78)
Unknown	12
Career aspiration	
Private practice oncology care	4 (14)
Clinical oncology care at a referral hospital	2 (7)
A mix of clinical care and academic research	21 (72)
Research only	2 (7)
Unknown	1
Plan to conduct research in the future	
Yes	26 (90)
No	3 (10)
Unsure	1

Respondents who identified as current faculty oncologists at ORCI were less likely to report prior research experience, compared with respondents who identified as current trainees (0% vs. 39%; p = .04). Of the 18 respondents who responded to a question about existing mentorship, 22% (n = 4) identified as having a relationship with a research mentor.

A total of 23 respondents completed all or most questions regarding their attitudes toward research, which are summarized in Figure 1. Respondents of Tanzanian nationality were more likely to disagree with the statement that research increases burden, compared with respondents of other nationalities (85% vs. 30%; p = .01). There were no other statistically significant differences in demographic characteristics, background, opinions on the impact of research, or opinions on mentorship between respondents of Tanzanian origin versus other nationalities or between researchers who are faculty versus current residents. There were no statistically significant differences in background, opinions related to the impact of research, or opinions on mentorship between female and male respondents.

The reported availability of resources to support research development is summarized in Table 2. Of the 18 participants who provided responses regarding available resources to support research development, more than half reported adequate availability of computers (56%), office space (72%), and opportunities to present research (72%). In contrast, only 28% reported adequate protected time away from clinic work, and 28% reported adequate access to funding opportunities for research. Only one respondent (6%) identified availability of access to institutional support for preparation of a grant application ("pre-award support"). In response to an open-ended question asking respondents to identify the "greatest needs" for developing a research career, themes of "research training" and "mentorship" were consistently identified by 67% and 61% of respondents, respectively.

A total of 18 participants responded to questions regarding their impressions about the institutional research environment, which are summarized in Figure 2.

Discussion

The findings of our survey of all current trainees and recent graduates of one of the first clinical oncology training programs in East Africa reflect a very strong motivation to actively engage in cancer research. Despite consistent identification of barriers and challenges to conducting research throughout the survey, 77% of respondents identified that they aspired to a career path that allowed for research or a mix of clinical care and academic research, confirming our impression of high levels of enthusiasm toward the development of cancer research training opportunities.

This finding is in stark contrast, however, with the current availability of infrastructure and institutional supports to effectively support fulfillment of these aspirations. Specifically, protected time for research away from clinical responsibilities, coursework in research methods, research support, and mentorship were identified by a majority of respondents as currently unavailable. These significant barriers echo those published by the American Society of Clinical Oncology International Affairs Committee, which previously reported that lack of financial support was the primary barrier to conducting clinical cancer research in both high-income countries and low- and middle-income countries (LMICs) [9].

The reported scarcity of available mentorship is particularly notable but not surprising in what is a relatively novel field of study in East Africa [10]. Structured and longitudinal mentorship from a competent and dedicated mentor is critical both during the primary educational experience and, especially, during the period that follows [11–13]. Thus, development of investigators with effective mentorship skills is a necessary first step toward the development of broader initiatives to create and enhance conditions that foster the upward mobility of East African scholars in cancer

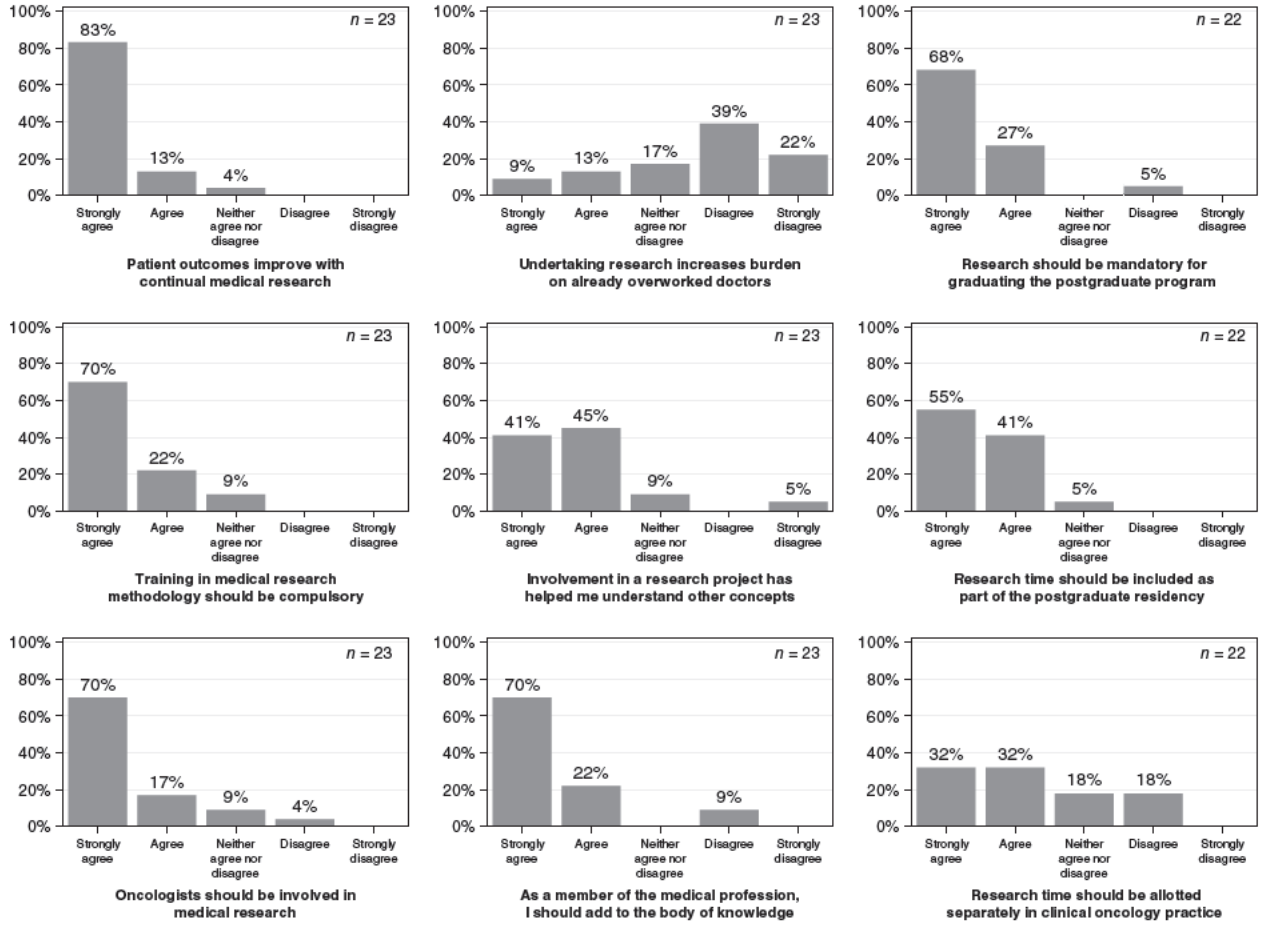

Figure 1. Self-reported attitudes toward research among current and recent oncology trainees in Tanzania.

Table 2. Reported resources currently available to support research development among oncologists in Tanzania (n = 18)

Resources	n (%)
Protected time away from clinical responsibilities	5 (28
Computers	10 (56)
Office space	13 (72)
Coursework in research methods	6 (33)
Research support	4 (22)
Mentorship	6 (33)
Funding opportunities	5 (28)
Pre-award support	1 (6)
Institutional merit or recognition	6 (33)
Opportunities to present research work	13 (72)

research. In addition to the requisite acquisition of research skills through dedicated training, formal training in mentorship techniques has been repeatedly shown to enhance mentor and mentee outcomes in academic settings [11–20]. Attention will need to be paid in effort to identify context-specific challenges in mentoring affecting trainees from LMICs, which could possibly include difficulties finding suitable mentoring; hierarchical structures that discourage mentee-driven processes; feeling invisible; facing prejudice; feeling devalued; cultural inconsistencies; a lack of altruism in mentoring due to extreme academic pressure on local faculty; and/or a lack of knowledge associated with existing, but hidden, rules and customs common to academic settings.

The MMed in Clinical Oncology program at MUHAS currently requires trainees to complete and defend a dissertation as a compulsory component of the training program. Didactic coursework provides exposures to epidemiology, biostatistics, and medical ethics; however, the content of the existing curriculum rarely leads to independent research by the graduates of the training program. This is evidenced by limited publications of dissertation research or other research by recent graduates, and it is consistent with a previously published report that even those African scientists who achieve master's or doctorate-level training remain noncompetitive for external funding sources, with fewer than 2% receiving two or more grants within 15 years after training. Low research productivity from the region is exemplified in the stagnant number of research publications and low citation counts from East Africa between 1999 and 2008 [21]. Notably, the absence of a prevailing academic culture that assigns merit to research accomplishment was identified by a majority of respondents in our study and merits further assessment. Moreover, we acknowledge that research may be deprioritized as trainees transition into the workforce in a specialty that is still heavily impacted by scarcity of trained health care professionals.

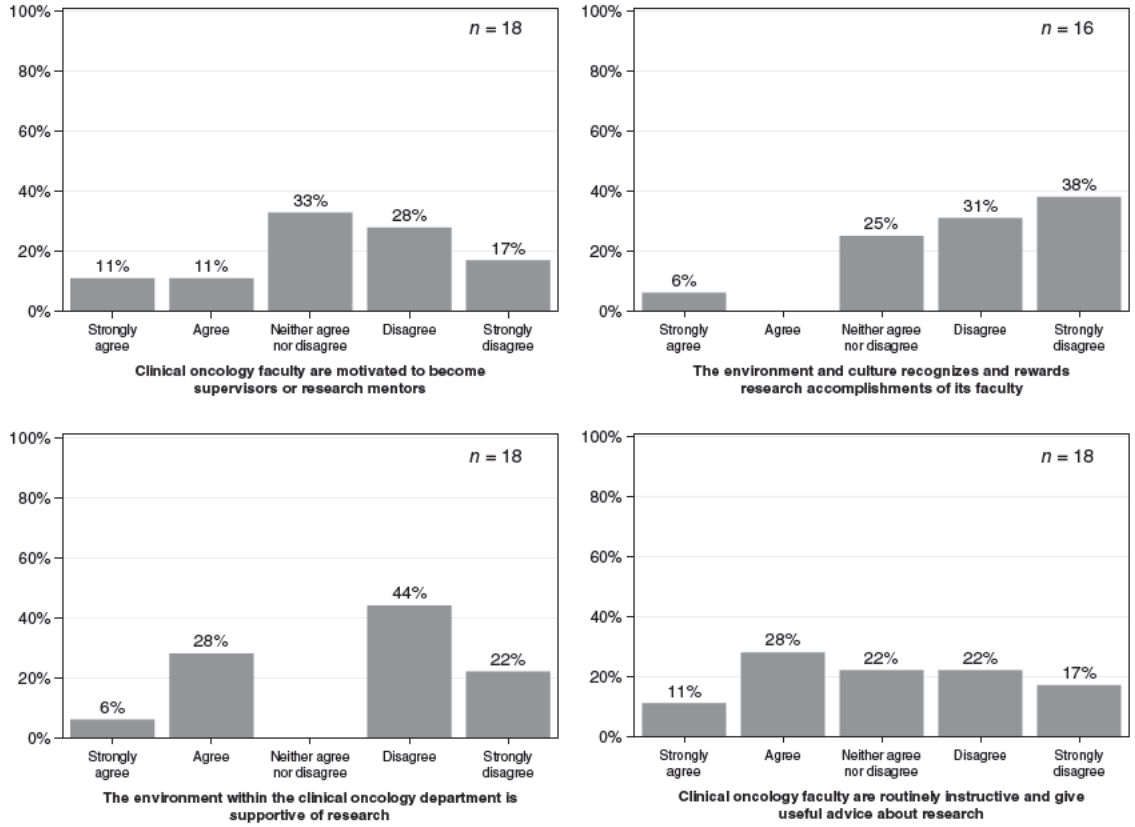

Figure 2. Self-reported impressions of institutional supports for research among current and recent oncology trainees in Tanzania.

There are several limitations to this study that should be acknowledged. First, this analysis is based upon a small sample; however, this sample reflects the majority of current trainees and recent graduates of one of the first clinical oncology training programs in East Africa. Of note, the study population may not be representative of the preceding generation of oncologists in Tanzania or East Africa more broadly who were trained previously in clinical oncology training programs outside of Tanzania.

In addition, not all participants completed all components of the survey. For reasons that are unknown, only 18 of 30 respondents completed the entire survey, contributing to a high degree of missingness. Although the survey was administered in English rather than in Tanzania's official national language of Swahili, this is the language of the medical school curriculum; thus, language barriers were unlikely to account for the high incompletion rate. Significant attrition was noted in the questions related to the institutional environment; we speculate that concerns regarding confidentiality of the responses may have contributed to significantly lower response rates in this section of the questionnaire. Also, the survey tool was not previously validated; although it was primarily designed by local researchers, differences in how the participants interpreted and responded to survey questions may have impacted completeness of the responses. Finally, the study was primarily intended to be descriptive in nature, and findings of statistical significance may have been impacted by numerous potential confounding factors and therefore should be interpreted with caution.

Conclusion

We identified a striking contrast between the aspirations for incorporation of research into career development and the research training that is currently available to oncologists and oncology trainees at a regional training hub in East Africa. Despite consistent identification of barriers and challenges to conducting research, an impressive 77% of respondents identified that they aspire to a career path that allows for academic research, confirming our impression of high levels of enthusiasm toward the development of cancer research training opportunities in Tanzania. The results of this study underscore a resounding message regarding the readiness for cancer research training and mentorship in this setting, driven by a sense of urgency related to the burden from cancer that East Africa faces.

There is currently a critical need to establish a cadre of investigators in East Africa who are capable of conceptualizing, gaining funding for, implementing, analyzing, and publishing original research focused on cancer. We hypothesize that African principal investigators can operate effectively if proper attention is given to selection and provision of high-quality foundational didactic training to learn the theory and implementation of research as well as to the development of an environment conducive to mentoring. While we continue our partnership to develop a research curriculum and mentoring programs, we also plan to perform a needs assessment to inform steps necessary to create an institutional environment that catalyzes interprofessional development and transforms and extends cancer research in East Africa.

Acknowledgments

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the
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.

Author Contributions

Conception/design:

Data analysis and

Manuscript writing:

Final approval of manuscript:

Disclosures

The authors indicated no financial relationships.

References

abstract

Purpose Children with acute lymphoblastic leukemia (ALL) in low-income countries have disproportionately lower cure rates than those in high-income countries. At Butaro Cancer Center of Excellence (BCCOE), physicians treated patients with ALL with the first arm of the Hunger Protocol, a graduated-intensity method tailored for resource-limited settings. This article provides the first published outcomes, to our knowledge, of patients with ALL treated with this protocol.

Methods This is a retrospective descriptive study of patients with ALL enrolled at BCCOE from July 1, 2012 to June 30, 2014; data were collected through December 31, 2015. Descriptive statistics were used to calculate patient demographics, disease characteristics, and outcomes; event-free survival was assessed at 2 years using the Kaplan-Meier method.

Results Forty-two consecutive patients with ALL were included. At the end of the study period, 19% (eight) were alive without evidence of relapse: three completed treatment and five were continuing treatment. Among the remaining patients, 71% (30) had died and 10% (four) were lost to follow-up. A total of 83% (25) of the deaths were disease related, 3% (one) treatment-related, and 13% (four) unclear. Event-free survival was 22% (95% CI, 11% to 36%), considering lost to follow-up as an event, and 26% (95% CI, 13% to 41%) if lost to follow-up is censored.

Conclusion As expected, relapse was the major cause of failure with this low-intensity regimen. However, toxicity was acceptably low, and BCCOE has decided to advance to intensity level 2. These results reflect the necessity of a data-driven approach and a continual improvement process to care for complex patients in resource-constrained settings.

BACKGROUND

Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer worldwide.[1] In high-income countries, survival rates have drastically improved from < 30% to 90% in the past 50 years.[2-5] However, therapy remains challenging: most children require 2 to 3 years of ongoing therapy, and intensive supportive care is often needed during the early phases. In low- and middle-income countries (LMICs), conversely, survival rates remain poor—often < 35%.[6-10] This reflects many challenges, including gaps in implementation of care, delayed or incorrect diagnosis, comorbid conditions, lack of needed treatment components, increased relapse rates, abandonment of therapy, death from toxicity, and suboptimal supportive care.[1,8,11,12]

Monitoring ALL outcomes can provide a useful metric of a program's capacity to address delivery of complex longitudinal oncology care. Successful models for treating ALL in resource-limited settings have been reported in South America. For example, 5-year event-free survival (EFS) rates in a Brazilian hospital increased from 32% to 63% from 1980 to 2002 because of improvements in clinician training, patient social support, supportive care, and treatment availability and standardization.[13] Data on similar models in sub-Saharan Africa are limited, but a Tanzanian cohort of 81 patients following the United Kingdom Acute Lymphoblastic Leukaemia 2003 (UKALL2003) protocol had a 2-year EFS rate of 26%.[14] Obstacles included availability and affordability of chemotherapy and supply of blood products.

Located in northern rural Rwanda, Butaro Cancer Center of Excellence (BCCOE) is housed in the Ministry of Health's Butaro District Hospital and provides free cancer care in partnership with Partners In Health/Inshuti mu Buzima and the

Table 1. Disease Work Up

Assessment	No.	%
No. of patients	42	
Pathology		
Bone marrow biopsy or aspirate	41	97.62
Biopsy, lymph node	3	7.14
Other biopsy	4	9.52
Imaging		
Chest x ray	31	73.81
Abdominal ultrasound	12	28.57
CT chest	3	7.14
CT abdomen	2	4.76
Other		
CNS assessment (LP, CT brain, other)	1	2.38
Testicular examination		
Number of males	23	
Examinations documented	1	

Abbreviations: CT, computed tomography; LP, lumbar puncture.

Dana-Farber/Brigham and Women's Cancer Center. BCCOE has been described in greater detail elsewhere.[15,16] After a national consensus meeting in March 2012, BCCOE began treating patients with ALL in accordance with the graduated intensity regimen proposed by Hunger et al,[17] an approach developed specifically for low-resource settings. Treatment facilities begin with regimen 1, a low-intensity medication regimen, and advance to an increased medication regimen only after demonstrating that treatment-related toxicity is acceptably low (less than one death for every 25 patients). To our knowledge, no prior studies have reported on this regimen in a low-resource setting. Therefore, the objective of this study is to report the outcomes of using regimen 1 of the Hunger protocol on pediatric patients at BCCOE, as well as the quantitative measures of resource demands and delays in care.

METHODS

Setting and Treatment

During the study period, BCCOE treated 169 pediatric oncology patients, in whom ALL was the second most common diagnosis (after nephroblastoma). At the time of this study, BCCOE offered patients with ALL basic imaging (x-ray and ultrasound), laboratory tests, bone marrow biopsy, and pathology processing. In addition, social services covered costs for transportation and nutritional support. Pathologists at Brigham and Women's Hospital (Boston, MA) or Rwandan referral hospitals or visiting pathologists at BCCOE interpreted tissue specimens.

BCCOE used regimen 1 of the Hunger protocol, composed of vincristine, prednisone, cyclophosphamide, intrathecal methotrexate, 6-mercaptopurine, dexamethasone and L-asparaginase (Appendix Table A1). There is no anthracycline administered in level 1 of this protocol. Given health system limitations, patients were not uniformly evaluated for CNS involvement, bone marrow response to therapy, or prednisone response, factors often required for clinical risk stratification, but in regimen 1 all patients receive identical therapy. Most patients remained continuously hospitalized during induction and consolidation, given the frequent chemotherapy doses and associated adverse effects. On-site visiting Dana-Farber/Brigham and Women's Cancer Center nurses trained Rwandan nurses in chemotherapy preparation and management of patients with cancer. Radiotherapy was not included in the protocol, and currently there is no radiotherapy care available in Rwanda.

Data Management and Analysis

Data were collected for consecutive patients with ALL presenting at BCCOE from July 1, 2012 to December 31, 2015. Patients were identified and data were collected using the electronic medical records system OpenMRS; additional data were collected from patient charts using a structured chart abstraction form. Analysis was performed using STATA v12 (StataCorp, College Station, TX). This study was approved by the Rwanda National Ethics Committee, the Inshuti Mu Buzima Research Committee, and the Institutional Review Board at Partners Healthcare, Boston, Massachusetts.

Patients were considered to start a phase of treatment once the first chemotherapy agent was administered. A phase of treatment was considered complete if documented in the medical record. Documented treatment delays were those that postponed chemotherapy administration for any duration. Disease-related deaths were defined as occurring either before treatment began or after relapsed or refractory disease. Relapse was confirmed by clinical symptoms, derangement of CBC,

Table 2. Duration Between Pathology Specimen and Report

Institution	No.	Median Days (IQR)
Overall, average per patient*	22	16 (8 26)
Brigham and Women's Hospital	18	21 (15 27)
Other pathology institutions	6	3.5 (3 5)

NOTE. As documented on pathology report.
*Some patients had reports from different institutions.

Table 3. Patient Demographics and Disease Characteristics

Demographic or Characteristic	No.	%
No. of patients	42	
Male	23	54.76
Age, years, median (range)		10.04 (0.38 0.35)
Country		
Rwanda	36	85.71
Burundi	6	14.29
Prior health facility		
Referral hospital	31	73.81
District hospital	5	11.90
Outside Rwanda	6	14.29
Prior chemotherapy		
Allopurinol and steroids	12	28.57
Steroids	7	16.67
Allopurinol	3	7.14
None	20	47.62
Duration of symptoms, weeks, median (IQR)	36	10.5 (4 20)
Presenting symptoms		
Lymphadenopathy	32	76.19
Fever	32	76.19
Malaise/fatigue	24	57.14
Bleeding	15	35.71
Infection	15	35.71
Weight loss	15	35.71
Arthralgia	10	23.81
Extramedullary involvement		
Lymphadenopathy	33	78.57
Splenomegaly	28	66.67
Hepatomegaly	23	54.76
Mediastinal mass	9	21.43
Immunophenotype		
B cell	9	21.43
T cell	8	19.05
Unknown	25	59.52
Reason leukemia type unknown		
Total	25	
Report unavailable	18	72.00
Subtype not reported	4	16.00
Technical issues	2	8.00
Sample of poor quality	1	4.00

Abbreviation: IQR, interquartile range.

and presence of blasts in the peripheral blood film after a period of remission. Refractory disease was defined as failure to achieve remission after completion of either induction or consolidation. The remaining deaths were deemed either treatment related (those after initiation of chemotherapy) or unclear (treatment failure clinically suspected but not confirmed before death). Loss to follow-up (LTFU) was strictly defined as missing the most recent appointment.

EFS from intake for all patients diagnosed with pathology was assessed at 2 years using the Kaplan-Meier method. This was calculated twice. First, events were death from any cause, relapsed disease, and LTFU. Second, events were death from any cause and relapsed disease; LTFU was right-censored.

RESULTS

Patient Demographics and Disease Characteristics

Fifty-four patients were evaluated or treated for ALL from July 1, 2012 to June 30, 2014. Diagnoses of eight patients were not pathologically confirmed before exiting the program, three patients had prior treatment presenting with relapsed or residual disease, and one patient was treated with an alternative protocol because of stroke. The remaining 42 patients had newly diagnosed, pathologically confirmed disease and were started on level 1 of the Hunger protocol at BCCOE.[17] Forty-two patients were evaluated with a new pathologically confirmed diagnosis of ALL (Tables 1 and 2). Median age was 10 years (range, 0.38 to 40.35 years), and 55% (23) of patients were male. Eighty-six percent (36) of patients lived in Rwanda, and 14% (six) lived in Burundi (Table 3). Seventy-nine percent were HIV negative, 5% were positive, and 17% had unknown HIV status. Seventy-four percent (31) were transferred to Butaro from national referral facilities. Before arriving at BCCOE, 29% (12) of patients received allopurinol and steroids (17% [seven] steroids, 7% [three] allopurinol), and 48% (20) of patients received no prior cancer-directed treatment.

Patients presented to BCCOE a median of 10.5 weeks (interquartile range [IQR], 4-20 weeks) after onset of symptoms, the most common of which were lymphadenopathy 76% (32), fever 76% (32), and malaise 57% (24). The most common extramedullary sites of involvement were lymph nodes 80% (33), spleen 67% (28), and liver 55% (23).

Disease immunophenotype was unknown for 60% (25) of patients, 21% (nine) had B-cell, and 19% (eight) had T-cell. In addition to subtype, other information, such as CNS involvement, was often unavailable (Tables 1 and 2). Using the limited information available for stratification, > 75% of

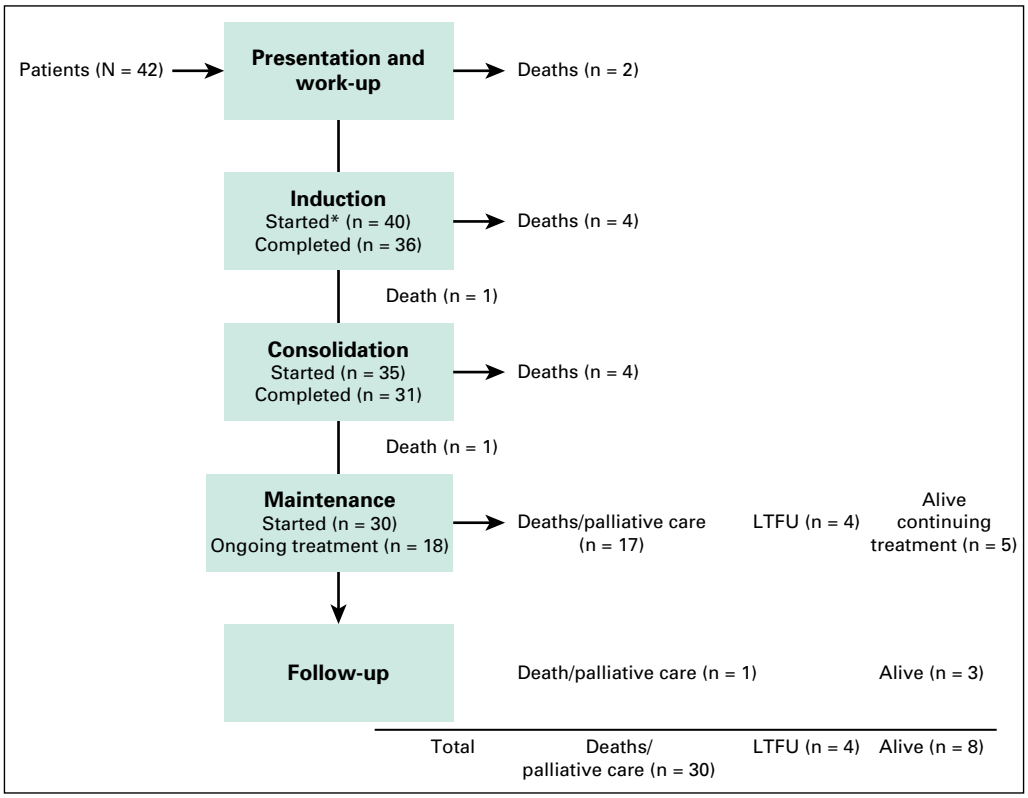

Fig 1. Treatment and patient events. (*) Started phase of induction, consolidation, and maintenance defined as having received chemotherapy. LTFU, lost to follow up.

patients in the study would have been classified as high or very high risk (Appendix Table A5).

Treatment and Outcomes

Of the 42 patients who began therapy for ALL, 95% (40) initiated induction, 83% (35) consolidation, and 71% (30) maintenance (Fig 1). At the end of the analysis period, 19% (eight) of patients were alive without evidence of relapse: three completed treatment and were in follow-up and five were still receiving treatment. Seventy-one percent (30) had died, and 10% (four) were LTFU (Table 4). When LTFU was considered an event, estimated 2-year EFS was 22% (95% CI, 11% to 36%); when LTFU was right-censored, estimated 2-year EFS was 26% (95% CI, 13% to 41%). Overall, the median time from enrollment at BCCOE to time of event was 9 months (IQR, 2-19 months).

For patients alive at time of analysis, treatment duration was a median of 699.5 days (IQR, 577-1,168.5 days). Of the 30 deaths, 83% (25) were disease related (16 relapsed, seven were refractory, and two died before treatment initiation), 3% (one) were treatment-related, and 13% (four) were unknown. Deaths occurred throughout all phases of treatment, although concentrated in two periods: within the first 2 months after presentation, and 6 to 8 months after initiation of therapy, most frequently during the first cycles of maintenance (Fig 2).

Resource Demands of Treatment

Even with this low-intensity approach, many resources were required to support these patients with ALL (Appendix Table A2). For the 42 patients evaluated before initiating therapy, 52% (22) required packed red blood cells and 43% (18) required platelets. Throughout, the median hemoglobin was 8.3 g/dL (IQR, 7.7-9.8 g/dL; n = 31) and the median platelet level was 25.5 $\times$ $10^3/\mu$L (IQR, 12-51 μL; n = 30). For the 40 patients who started induction therapy, 63% (25) required packed red blood cells and 50% (20) required platelets (Fig 3).

The most common cause of treatment delay was thrombocytopenia, present in 55% (23) of patients (Fig 3), and delayed platelet availability as products were transported from blood banks at offsite locations. Fluctuations in supply of two chemotherapy drugs, L-asparaginase and methotrexate, led to rescheduling of treatment cycles affecting care in 38% (16) of patients (Appendix Table A3). Medical-related delays included infections, neutropenia, elevated liver transaminases, neutropenic fever, and bleeding. Of note, delays resulting from

Table 4. Outcomes

Outcome	No.	%	Median Days (IQR)
No. of patients	42		
Status			
Alive	8	19.1	
Deceased*	30	71.4	
LTFU†	4	9.5	
Alive			
Total	8		
Continuing treatment	5		
Completed treatment	3		
Treatment duration‡			699.5 (577.0 1,168.5)
Causes of death			
Total	30		
Disease related	25		
Relapsed	16		
Refractory	7		
Before treatment	2		
Treatment related	1		
Unclear§	4		

Abbreviations: IQR, interquartile range; LTFU, lost to follow up.
*Relapsed patients categorized under deceased.
†LTFU defined as missed most recent appointment; LTFU occurred for both patients during maintenance.
‡Treatment duration calculated from intake until December 31, 2014 (end of analysis period).
§Unclear deaths often occurred once patient started treatment but not due to relapse or refractory disease.

socioeconomic barriers to care were few (one from lack of money for transport and one from illness of the patient or family member). Socioeconomic-related delays, however, were likely not fully captured in this retrospective review.

DISCUSSION

ALL is the most common hematologic malignancy in children,[1] and the ability to provide care for patients with ALL is an essential component of oncology programs serving LMICs. However, given the duration of therapy, the recurrent periods of neutropenia, and the supportive care requirements, including transfusions and antibiotics, delivery of care requires a robust medical infrastructure. To our knowledge, our results represent the first published outcomesfrom a rural cancer center in a low-income country using the strategy proposed by the Hunger group[17] that restructures treatment into stratified levels of therapeutic intensities. This model recommends an initial, low-intensity regimen and data capture to assess the incidence of treatment-related deaths. Once care can be demonstrated to be safely provided, intensity of care can be increased.

We piloted this approach at BCCOE, a rural-based cancer center where care is provided by pediatricians, internists and general practitioners follow strict treatment protocols, and there is support from visiting on-site oncologists and regular remote support from affiliated oncologists. As expected, given the initial low-intensity and anthracycline-free regimen, relapse was the major cause of treatment failure and led to survival rates similar to the 26% estimated 2-year EFS and 8.1 month median survival of a Tanzanian cohort.[14] In North American cohorts, an estimated 5% to 25% of patients with ALL receive cranial radiation for treatment and prophylaxis of CNS lymphoma.[18] In our patient cohort, 53% of patients experienced relapse. Given this high relapse rate in patients receiving low-intensity treatment, it is likely the low-intensity treatment was insufficient for long-term survival. For some critically ill patients, the precise cause of mortality was difficult to determine when signs of infection coincided with treatment initiation. Nevertheless, definitive treatment-related toxicity was sufficiently low to advance to the next level of therapy per Hunger guidelines.[17]

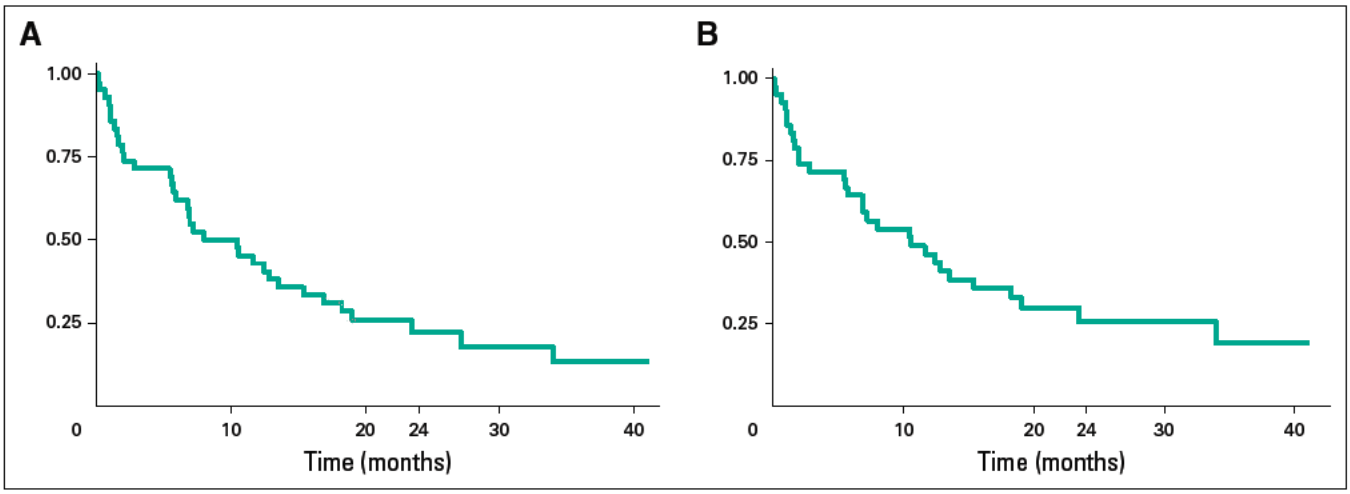

Fig 2. Censored event free survival (EFS; N 42). (A) Estimated 2 year EFS lost to follow up (LTFU) as event: 22% (95% CI, 11% to 36%). (B) Estimated 2 year EFS LTFU censored: 26% (95% CI, 13% to 41%).

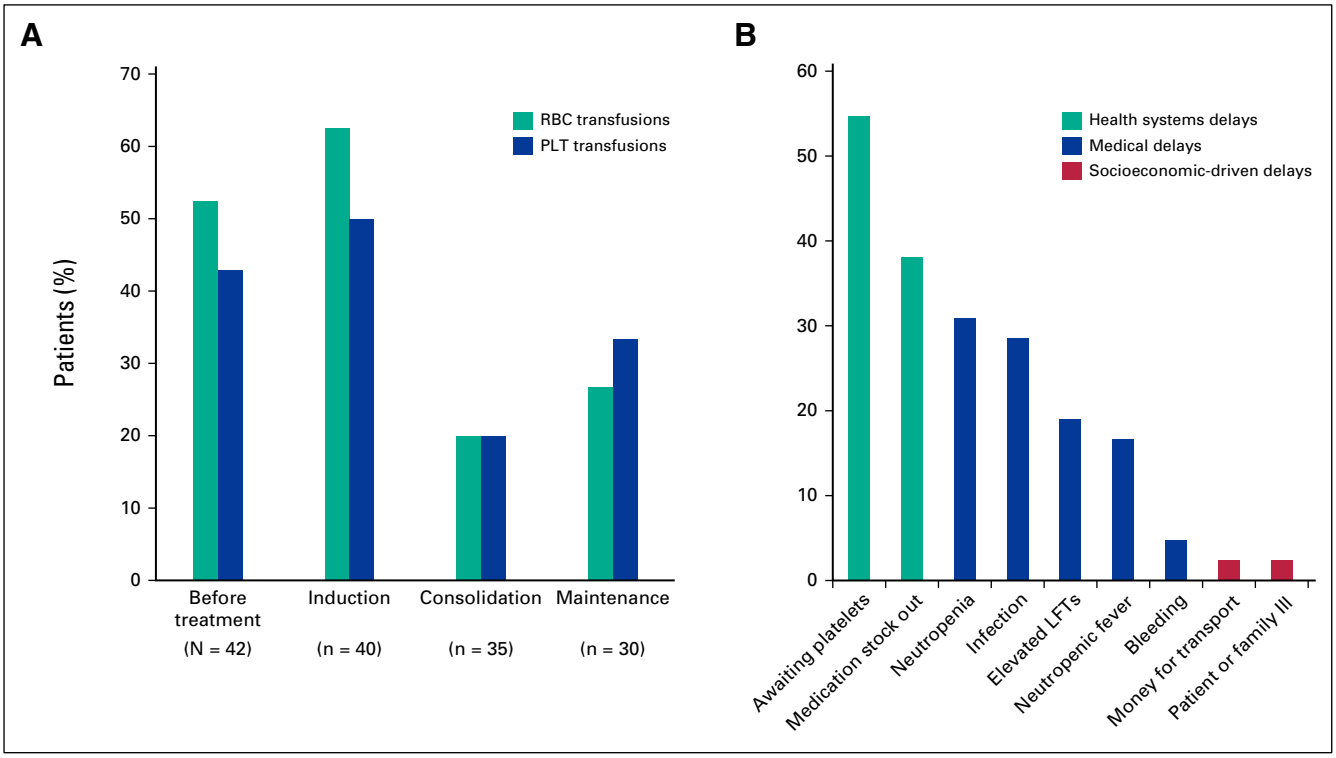

Fig 3. Treatment related resource demands. (A) Patients requiring blood products. (B) Causes of chemotherapy delay (N 42). LFTs, liver function tests; PLT, platelet.

Intensification of treatment, however, requires disease stratification, a challenge given the limited number of physicians, inconsistent access to CSF diagnostics, difficulties in reliably obtaining immunophenotyping, and delays in pathology reports (Tables 1 and 2).[8,14] In addition, the lack of in-country radiation therapy poses financial and operational challenges. When disease stratification can be achieved along with simultaneous training of hospital personnel, strengthening of supportive care, and standardizing of treatment regimens, outcomes can markedly improve, as was seen with the 63% 5-year EFS in Brazil.[13] This data-driven approach to improving care can only be achieved in the context of collecting and analyzing high-quality patient data, a challenge in all health care settings and particularly in a resource-constrained environment.

Treatment abandonment, often cited as a cause of treatment failure for patients with ALL, was uncommon at BCCOE. Although additional follow-up will be needed, the 10% lost to follow-up rate was modest compared with 35% in Indonesia[19] and 22% in El Salvador.[8] Patient social support, such as coverage of transportation and chemotherapy costs as provided at BCCOE, have helped in similar settings and have led to lower abandonment rates of 9% in Tanzania[14] and 0.5% in Brazil.[13] Given its mission to provide care to all patients, both social and clinical, BCCOE has also noted low levels of abandonment and delays in treating other cancers, such as nephroblastoma.[20]

In the presented approach to classifying delays, health system delays, such as waiting for blood products and availability of chemotherapy agents, were the most common in our patient population. Inconsistent sources for both blood products and some chemotherapy (Appendix Table A3) were major challenges. An estimated 8 million units of blood are needed in sub-Saharan African countries annually, and only 3 million units are collected.[21] At BCCOE, > 40% of patients who started treatment required transfusions; this drastically underscores the importance of a reliable system to provide supportive clinical care.[13,14,22] Quantitatively documenting this need could serve as a tool to predicting and planning for future transfusion needs in similar settings. Some minor lapses in availability of chemotherapeutics led to additional delays. Alterations in chemotherapy regimens because of lack of drug availability have led to poorer survival in both resource-rich and resource-constrained settings,[14,23] and, therefore, more accurate predictions and a reliable supply chain for ALL medications and transfusions has become a crucial goal at BCCOE.

In the context of Rwanda's dedication to providing cancer care, the Rwandan Ministry of Health has hosted regular national consensus meetings for cancer protocol development. The BCCOE clinical team presented these data at the pediatric protocol meeting in the spring of 2015. After reviewing the results, the committee supported intensifying

the national ALL treatment protocol, given the high relapse rate and acceptable treatment-related death rate. This data-driven approach that focuses particularly on resource demands of care is critical to patient outcomes in this and other resource-constrained settings.

In conclusion, this study details our experience treating patients with ALL in a rural Rwandan cancer center and to our knowledge reports the first published outcomesusing the lowest intensity level of the Hunger ALL protocol. As expected with a low-intensity regimen, a high rate of disease-related mortality occurred, interestingly clustering in two time periods. However, treatment-related toxicity was below the threshold suggested for increasing treatment intensification. In addition to supplementing the limited literature on ALL care in sub-Saharan Africa, the quantification of transfusion needs and classification of treatment delays can be used to predict challenges to care in similar settings.

Overall, we have demonstrated that an iterative model of cancer care, delivered by nononcologists with remote oncological support, where implementation is followed by analysis of outcomes and subsequent evidence-based changes for improvement of care, allows for accountable delivery of ALL treatment in LMICs using the Hunger approach. We are now risk-stratifying patients and advancing to regimen 2 for high-risk patients after an intensive educational program for providers. These results point to the necessity of a data-driven approach to optimize care for complex patients in resource-constrained settings.

[redacted]

AUTHOR CONTRIBUTIONS

[redacted]

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

[redacted]

[redacted]

Affiliations

[redacted]

REFERENCES

1. [redacted]

12. [redacted]

APPENDIX

Table A1. Regimen 1

Drugs	Dose	Duration
Induction (4 weeks)		
Prednisone prophase	60 mg/m^2/d	Days 1 7
Prednisone	40 mg/m^2/d	Days 8 29
Vincristine	1.5 mg/m^2	Days 8, 15, 22, 29
L asparaginase	6,000 IU/m^2 × 3 weeks starting at day 8	
Extra IT MTX on days 15, 22 if CNS3		
Consolidation (4 weeks)		
Vincristine	1.5 mg/m^2	Day 1
6 mercaptopurine	75 mg/m^2	Day 1 28
IT MTX days 1, 8, 15		
Maintenance (84 day cycles until 30 months from start of therapy)		
Dexamethasone	6 mg/m^2/d	Days 1 5, 29 33, 57 61
Vincristine	1.5 mg/m^2	Days 1, 29, 57
6 mercaptopurine	75 mg/m^2	Days 1 84
MTX	20 mg/m^2	Starting day 1
IT MTX Days 1, 29 for first four cycles then day 1 only (omit oral MTX when IT MTX given)		

Abbreviations: IT, intrathecal; MTX, methotrexate.

Table A2. Resource Availability, 2012 to 2014

[redacted]

Supportive care	
Whole blood transfusions,	Intermittently available at Transfusion Center, with delays of days
Platelet transfusions	Intermittently available at Transfusion Center, with delays of days
Fresh frozen plasma	Intermittently available at Transfusion Center
Ketoconazole, amphotericin,	[redacted]
Trimethoprim/sulfamethoxazole, ceftriaxone, gentamicin	
Cancer therapeutics	
Bone marrow transplant	Not available
Radiation therapy	Not Available
Dexamethasone	[redacted]
Vincristine	
Methotrexate	
6 mercaptopurine	
Cyclophosphamide	
Cytarabine	
L asparaginase	
Etoposide	
Prednisolone	
Staffing	
Nursing:patient ratio	1:15 in day, 1:30 at night
Pediatrician	Consistently available at BCCOE, mentored remotely by DFCI pediatric oncologist
Social worker	One available for all cancer wards and outpatients at BCCOE
Facilities	
Radiology	[redacted]
Pediatric ICU	
Housing for caregivers/family	Not available
Food packages	[redacted]
Transport	

[redacted]

[redacted]

Table A3. Medication Stock Out

Medication	No. of Patients Whose Chemotherapy Was Delayed by Medication Unavailability
Stock out	16 (38.1%)
IT MTX	10
PO MTX	3
L asparaginase	4
VCR	1

Abbreviations: IT, intrathecal; MTX, methotrexate; PO, orally; VCR, vincristine.

Table A4. Limited Stratification

Lower Risk	Higher Risk	Very High Risk
B-precursor ALL and age 1.00-9.99 years and initial WBC count < 50,000/μL and prednisone good response and CNS 1 or CNS 2 and day 15 M1/M2 marrow and day 29 M1 marrow	CNS 1 or CNS 2 **and T-cell ALL and WBC count < 100,000/μl OR** CNS 1 or CNS 2 **and B-precursor ALL with age < 1 or > 9.99 years or WBC count > 50,000/μL** and prednisone good response and day 15 M1/M2 marrow and day 29 M1 marrow	Prednisone poor response or CNS3 **or T-cell ALL and WBC count > 100,000/μL or** day 15 M3 marrow or day 29 M2/M3 marrow

NOTE. Bold factors were included in stratification; regular factors were not included because of unavailable/ limited information.
Abbreviation: ALL, acute lympholastic leukemia.

Table A5. Butaro ALL Patients (N 42)

Risk	N	%
Standard	6	14.29
High	9	21.43
Very high	2	4.76
Unclassified	25	59.52
Could be standard, pending ALL type	5	11.90

NOTE. 75% to 85% of patients would be high or very high risk per Hunger protocol.
Abbreviation: ALL, acute lympholastic leukemia.

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INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY

A. Personal Statement

The focus of my research program relates practice patterns and outcomes of patients with cancer in the general population. I lead programs of research in . Our research unit (the) has been an international leader for over two decades in using large administrative health databases to describe outcomes and processes of care. Our multidisciplinary group includes principal investigators that are physician scientists (medical/radiation oncology, surgery), epidemiology, health policy/economics, and biostatistics. On the strength of my research program and the support of our Unit I have been successful in securing ~$3.0 million in research funding as principal investigator (career scientist awards and operating grants). The two early career awards I was awarded included the In 2014 I was awarded a in Population Cancer Care, this was successfully renewed in 2019. My research program is funded by operating grants from , the , and the . To date I have published 216 peer-reviewed papers; 48 as first author and 106 as senior author. My work has been cited 8008 times (Google Scholar) and my h-index is 40. I have published first/senior author papers in have supervised 21 trainees including medical students (n=2), residents/clinical fellows (n=15), MSc/PhD students (n=3), and post-doctoral fellows (n=2). Under my supervision these trainees have published 38 peer-reviewed papers; in 27 of these publications the trainee was first author. My current trainees have an additional 7 first-author papers currently under peer review. The work of my trainees has been recognized with 9 research awards. I have been nominated for 5 teaching awards (1 national, 1 provincial, 3 and 1 mentorship award). While many of my trainees are still completing their clinical training, 6 are now pursuing independent careers as academic faculty. In 2016 I spent a sabbatical as a visiting scientist at the continue to work closely with colleagues in and on various projects to improve accessibility and quality of cancer care. I serve as an Advisor (Health Services Research) to the , am Co-Chair of the initiative, and a member of an expert committee at the to advise regarding the value of cancer drugs on the Essential Medicine List.

B. Positions and Honors

Positions

[redacted]

Honors

[redacted]

C. Contributions to Science

[redacted]

3) [redacted]

[redacted]

5) [redacted]

D. Additional Information: Research Support and/or Scholastic Performance

[redacted]

[redacted]

[redacted]

Host Institution: [redacted]s one of [redacted] leading universities and a world leader in clinical cancer research. Dr. [redacted] s academic home for the LIFe Fellowship will be within the [redacted] is an internationally regarded transdisciplinary research unit. There are 14 full members of the Division of [redacted] including epidemiologists, biostatisticians, cognitive psychology, and clinician scientists representing radiation oncology, medical oncology and surgery. There is no other comparable unit in [redacted] and only a handful of similar units in the United States. [redacted] located on the same campus as [redacted] is a tertiary care referral centre with a comprehensive cancer centre. The cancer program includes 13 radiation oncologists, 16 medical/hematologic oncologists, and an extensive program in surgical oncology.

Dr. [redacted] primary mentor at [redacted] will be Dr. [redacted] Dr. [redacted] is Professor of Medical Oncology and holds the [redacted]. He runs an internationally recognized program in cancer health services research and in the past five years has built a major program in global oncology. In 2016 Dr. [redacted] h spent a sabbatical as a visiting scientist at the [redacted]. Dr. [redacted] serves as an [redacted] to the [redacted] of the [redacted] He is a member of the [redacted]. Dr. [redacted] has published [redacted] manuscripts and served as research supervisor for >25 trainees.

Educational Opportunities: Dr. [redacted] will take two graduate courses in epidemiology He will also have ample opportunities to attend other lectures and graduate seminars on research methods that are widely available to fellows at the [redacted]. In addition to his LIFe Fellowship project related to [redacted] will develop and lead 2-3 smaller projects in cancer health services research at [redacted]. These hands-on projects will give him training in literature searching, epidemiologic research methods and analyses, biostatistics, and scientific writing. He will attend weekly research methods meetings with Dr. [redacted] research team and will also have the opportunity to attend Research in Progress Seminars which take place every Wednesday at [redacted] From a clinical perspective, he will have the opportunity to attend 2 half-day oncology clinics/week as an observer. He will also attend weekly Grand Rounds, Journal Clubs, and disease-specific tumour boards.

Benefits for Applicant and Home Country: Dr. [redacted] a rising star in the [redacted] cancer system with substantial leadership and academic potential. To date he has had only limited training in research methods. In March 2020 he will be attending a one week intensive cancer research methods [redacted]). Health services research [redacted]) is widely recognized as a critical element in strengthening emerging cancer systems in Low- and Middle-Income Countries. [redacted] one of the oldest and most successful cancer HSR units in the world. Moreover, there are already established links between the group at [redacted] and Dr. [redacted]. It is therefore a fitting match for him to spend one year at [redacted] where he will develop advanced training in clinical cancer research. The focus of his research will relate to access to care, quality of care and outcomes in routine clinical practice. This is incredibly relevant for cancer system strengthening in s[redacted]. With these skills he will be able to launch his own program of research in [redacted] and more importantly will be able to serve as a mentor to other investigators in Africa as he seeks to build capacity across the continent. This will have tremendous benefit for his own career and will also directly benefit his home country by building capacity in cancer research. Finally, the LIFe fellowship will further strengthen the long-term collaborative relationship between [redacted], Dr. [redacted] and other colleagues working with [redacted].

[redacted]

To: ASCO LIFe Fellowship Selection Committee

Re: Letter of Support for [redacted]

I am pleased to write a letter in strong support of Dr. [redacted] application for a 2020 ASCO LIFe Fellowship. I am a Professor of Medical Oncology and [redacted]r in Population Cancer Care at [redacted], [redacted] I lead a program in cancer health services research that is based in [redacted]ut also includes extensive work in [redacted] on the recently completed Choosing [redacted]. I initially met him when he spent a one month clinical rotation at [redacted]. Since then I have engaged with him regularly as a research collaborator and mentee. I spent one week with him in [redacted] in November 2019 at the biannual conference of the [redacted] DR. [redacted] and I were co-speakers at a very well attended [redacted] symposium in value in cancer care. In March 2020 I will spend one week with him at the [redacted] workshop in [redacted]

Dr [redacted] is a rising star in Global Oncology. He recently completed his clinical training at [redacted]; this is one of the most prestigious training programs on the [redacted] [redacted]t. Dr. R[redacted] aptitude and potential for leadership in the global cancer community have been recognized with numerous major international awards from [redacted]. He also has a very impressive track record of publishing clinical cancer research. With 10 publications (5 as first author) including a first-author paper in [redacted] CV is very strong. This is even more impressive when one considers that major lack of research infrastructure and methods training across most African training programs. Dr. [redacted] has independently sought collaborators and diverse expertise within [redacted] and globally as he seeks to build his own research program.

Dr. [redacted] is hardworking and creative. He was a driving force behind the [redacted] He has excellent communication skills and works well in a multidisciplinary team. His writing is exceptional for his level of training. Moreover, I believe his research interests address the most pressing issues in Global Oncology; namely, how to improve access to care and quality of care in emerging cancer systems so that we can begin to address the major gap in outcomes seen worldwide.

In summary, [redacted] has tremendous potential to be a leader in global cancer research. He already has a longstanding and fruitful relationship with our health services research unit at [redacted] The LIFe Fellowship represents a critical opportunity for him to fully develop his research potential. As his primary mentor I will ensure that he continues to have world class training and opportunities in this field. Global Oncology is now the strategic focus of my own research program and I will continue to support him in every way possible including site visits to his own centre in Rwanda. There is tremendous momentum in our Global Oncology program at [redacted] where we have recently recruited several very talented investigators from diverse backgrounds; one of whom is [redacted] Dr. [redacted] was recently awarded the [redacted] This speaks to the quality of our unit and the excitement in moving forward [redacted] initiatives. Dr. [redacted] would thrive as a member of this team and I look forward to working closely with him in the coming years. I cannot think of any more deserving candidate for the LIFe Fellowship.

Sincerely,

[redacted]

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Institutional Approval Face Sheet

[redacted]

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Conquer Cancer may use and process the information submitted through this application form for several purposes, including but not limited to: 1) evaluating the application, 2) communicating with you regarding your application and other opportunities that may be of interest to you, 3) publishing information regarding Conquer Cancer's grants and awards program on an anonymous basis, and 4) informing Conquer Cancer's grant making strategies and policies. Information submitted through this application form will be kept on secure servers accessible to Conquer Cancer personnel and third parties authorized by Conquer Cancer to perform functions on Conquer Cancer's behalf.

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By submitting an application form to Conquer Cancer, the applicant grants Conquer Cancer the right to use all application information submitted, outside of the research proposal, in aggregate and de-identified form, for any purpose.

If an applicant is selected for an award, the applicant grants Conquer Cancer permission to deposit grantee information collected in any documents or communications related to the application (including but not limited to investigator name, degree(s), clinical specialty, Open Researcher and Contributor ID (ORCID), institution and institutional information, project title, abstract, grant start date and duration, and grant amount) into the Health Research Alliance (HRA) online database (HRA Reporter) of privately funded grants.

If an applicant is deemed fundable but Conquer Cancer does not have funding available, the applicant grants Conquer Cancer permission to share the full proposal to potential supporters.