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## From ‘intuitive’ pragmatic interventions to a systematic approach – Using implementation science to improve childhood cancer survival in low-income settings: The CANCaRe Africa experience

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### ABSTRACT

Implementation science is a relatively young field of study and is the science of delivering evidence-based interventions into routine health care. RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) is an evaluation-type implementation science framework. CANCaRe Africa is preparing a project to assess the implementation and effectiveness of a cash incentive intervention to support families with out-of-pocket costs to prevent treatment abandonment and increase childhood cancer survival in sub-Saharan Africa. Our strategy is to enhance the dissemination of our research findings to local policymakers who can support the scale-up of evidence-based clinical interventions and locally effective implementation strategies. It can be done best by embedding implementation science into our clinical research approaches.

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Survival rates of children with cancer residing in low- and middle-income countries (LMICs) are lower than those in most high-income countries (HICs) [1,2]. The difference is particularly stark in sub-Saharan Africa, where many countries are in the lowest income categories and per capita expenditure in healthcare is limited [3,4]. Despite the resource constraints, survival rates of children with cancer can improve through the implementation of evidence-based interventions that directly address modifiable factors associated with mortality. The challenge is to identify and scale up effective implementation strategies that address known health system and community barriers and build a resilient and sustainable system for health, including investment in a trained

workforce and healthcare infrastructure. The latter usually brings wider benefits to the local health system for children beyond cancer care.

The World Health Organization's (WHO's) Global Initiative for Childhood Cancer (GICC) has set a target of increasing pediatric cancer survival worldwide to 60% by 2030, with an initial focus on six common and curable ('tracer') childhood cancers for which survival is currently 85–95% in HICs [5]. To achieve this target, the GICC has prioritized interventions that are viewed as cost-effective, as much as possible, based on local evidence from LMIC settings [5]. It has also developed a comprehensive menu of tools and policy options that countries can adopt to improve their childhood cancer services [5]. These include developing national standards of care and clinical management guidelines, monitoring and evaluation frameworks, and recommendations to invest in cancer research. Despite these efforts, the estimated overall childhood cancer survival remains poor in many countries in sub-Saharan Africa, where it is estimated to be below 20% [1,6]. The relative importance of

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**Abbreviation**

LMIC	Low- and middle-income country
HIC	High-income country
GICC	Global Initiative for Childhood Cancer
WHO	World Health Organization
CANCaRe Africa	Collaborative African Network for Childhood Cancer Care and Research
RE-AIM framework	Reach, Effectiveness, Adoption, Implementation, Maintenance

non-communicable diseases such as childhood cancer is increasing as the burden and mortality of infectious diseases in Africa decreases.

The treatment strategies for childhood cancer in LMICs are usually based on treatment guidelines derived from results of clinical trials conducted in HICs, with some adaptations to make them more appropriate and feasible in the local settings [7,8]. These adaptations are essential if treatment is to be delivered safely and effectively. The vast majority (>90%) of the world's children live in LMICs, yet <10% of research on childhood cancer research is conducted in these countries [9]. Hence, there is a pressing need to do more locally relevant research in LMICs to increase survival rates.

CANCaRe Africa – the Collaborative African Network for Childhood Cancer Care and Research is an established multi-center regional network in sub-Saharan Africa, built upon work done in and coordinated from the center in Blantyre, Malawi. It was initiated in 2014 to address the survival gap between HICs and LMICs and is a platform for improving outcomes through research, capacity building, and clinical care [10,11]. The vision of CANCaRe Africa is that the survival of children in Africa with common and curable childhood cancer types will increase to 60%, aligned with the GICC 2030 goal. Since its inception, CANCaRe Africa has a strong track record in clinical research and implementing pragmatic interventions, which have had a significant impact on the care and survival of children with cancer [12–15].

These interventions have been implemented 'intuitively' rather than following a systematic approach. CANCaRe Africa is led by a group of clinicians working in sub-Saharan Africa for decades and thus have vast experience with the local context. For them, taking the local context into account is common sense. These local leaders have been at the forefront of assessing feasibility, sustainability, and planning of interventions. For example, procedures have always been kept as simple as possible, respecting the limited staff and time available. Data collection has been simple, clinically relevant, and built-in within the processes of the clinical care team. CANCaRe has given priority to interventions that were expected to increase the survival of children with cancer in the long term. Its strategy explicitly included appreciating the local context and aiming for optimal coverage of locally appropriate evidence-based interventions. Still, until recently, it had not used the tools and methodology available within implementation science. For example, we never did a systematic analysis beforehand of potential barriers or enablers of the implementation. We did not include any assessment of the success or failure of the implementation of the intervention. Including that into our approach will create language and consideration that we can share with our community, including professionals with less experience 'on the ground.'

Implementation science is a relatively young field of study and is the science of delivering evidence-based interventions into routine health care. The field recognizes that without effective implementation, even the most effective interventions have little to no

impact. The focus of implementation science is to reduce the gap between what we know and what we do (often referred to as the "know-do gap") [16]. By understanding local contextual barriers and facilitating factors, implementation science helps to identify appropriate strategies that improve the utilization of evidence-based practice and research findings into routine use by clinical practitioners and healthcare policymakers. When evidence-based practices, such as cancer care, are implemented without considering the local context, they often do not produce the expected health benefits for patients. For these reasons, CANCaRe Africa has adopted implementation science to improve pediatric cancer outcomes [17]. We now include an implementation science approach to all our new projects, collaborate with partners who also actively use implementation science, and explicitly look for funding and educational opportunities to build local – implementation science-based research capacity.

One of the key elements of implementation science is the use of models, theories, and frameworks to guide implementation. RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) is an evaluation-type framework originally published in 1999 and refined over time [18]. The purpose of RE-AIM is to direct the planning and evaluation of complex interventions, such as cancer care, to maximize public health impact in the real world. This framework helps researchers collect information needed to translate research into effective practice in a standardized, comparable way that may also be used to guide implementation and potential scale-up activities. Researchers can use common approaches to evaluate the implementation of policies and practices by employing an implementation framework like RE-AIM. Is it important to utilize these common approaches and language to describe local challenges and solutions to improve fit. By doing this, generalizable knowledge will be created that can be applied in other similarly low-resourced settings.

The approach to CANCaRe Africa's most recent project may illustrate how we adopted implementation research as a tool to improve childhood cancer outcomes in our setting. We are currently preparing a project to assess the implementation and effectiveness of a cash incentive intervention to support families with out-of-pocket costs to prevent treatment abandonment and increase childhood cancer survival in sub-Saharan Africa. Evidence shows that a cash incentive intervention is cost-effective and likely sustainable in sub-Saharan Africa to prevent treatment abandonment, reduce catastrophic costs for caregivers, and increase survival [19–23]. For this project, we use the RE-AIM implementation science framework to guide the preparation, implementation, and evaluation of the project. In addition to traditional methods of measuring success, such as clinical **effectiveness**, defined in this project as survival with no evidence of disease at the end of planned first-line treatment and no treatment abandonment, we will also assess implementation measures, including reach, maintenance, and adoption. In the preparation phase, we will describe the views of stakeholders (policymakers, health providers, and clients) on the acceptability, feasibility (**adoption**), and affordability of the intervention. In the implementation phase, we will assess "**reach**" by determining the proportion of eligible caregivers that access all planned mobile money installments throughout the course of treatment. We will also indirectly assess "**maintenance**" (or sustainability) by assessing the cost-effectiveness of the intervention within the health system of participating countries by WHO-CHOICE standards, defined as a cost less than three times the annual per capita income per disability-adjusted life year (DALY) averted.

The mission of CANCaRe Africa is to 'develop, implement and assess locally appropriate treatment guidelines and to reduce both 'treatment abandonment' and death during treatment to less than

ten percent.' Our approach also includes enhancing the dissemination of our research findings to local policymakers who can support the scale-up of evidence-based clinical interventions and locally effective implementation strategies. It can be done best by embedding implementation science into our clinical research approaches, as described in this commentary.

#### Patient's/Guardian's consent

Not applicable.

#### Ethical clearance

Not required.

#### Declaration of competing interest

None.

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