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Priorities and Funding for Global Cancer Surgery Research

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The UN High Level Meeting on the Prevention and Control of Non-Communicable Diseases (NCDs) held in 2011 drew attention to the global burden of NCDs, including cancer. While there was no specific mention of surgery in general or cancer surgery in particular, this high level discussion brought to attention the burden of cancer and garnered international agreement to launch cancer control efforts. Further highlighting the need for global commitment to research, objective #5 of WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020 calls on all stakeholders to promote and support national capacity for high-quality research in order to achieve the target of 25% relative reduction in premature mortality from NCDs by 2025.¹ The core principle is that research, while relevant globally, must be applied locally at the regional and national levels. The Sustainable Development Goals, adopted by the UN General Assembly in 2015, include NCDs as part of the overall health goal. Several of the nine health targets included in the SDGs are related to NCD-related health issues. Target 3.4, for example, is to “reduce by one third premature mortality from NCDs through prevention and treatment, and promote mental health and well being.”

An analysis of cancer incidence and prevalence data conducted by Globocan in 2012 attests to the urgency of addressing cancer. However, access to cancer treatment, particularly access to surgery, poses a significant barrier to cancer survivorship. Approximately 5 billion people are estimated to lack access to safe, affordable surgical and anesthesia care.² This represents a major contributor to the striking global inequities in cancer survival. The Lancet Commission on Global Surgery report supported the World Health Assembly’s unanimous endorsement of a resolution regarding global surgery and anesthesia in 2015.³ This resolution also made clear that surgery should be considered an essential part of global health. Subsequently, the Lancet Oncology Commission on Global Cancer Surgery estimated that over 80% of the 15.2 million new cancer patients diagnosed in 2015 would require a surgical intervention as part of their treatment plan (Table 1).⁴ All countries are projected to lose up to 1.5% of GDP annually between 2015 and 2030 if cancer surgical systems are not strengthened. Improved surgical oncology services can minimize

catastrophic financial events for patients and their families; countries, therefore, should recognize that investment in surgical oncology services can have major positive impacts on both health and household economics of their populations.⁴

The spectrum of surgical research includes cancer diagnosis, cancer treatment, symptom management, rehabilitation, and survivorship, novel approaches to surgical training and quality control, and implementation science. The span of implementation science can include interventions to address delays in cancer diagnosis and definitive cancer surgery, interventions to improve supply chain management for surgical equipment, and interventions to improve access to multidisciplinary cancer care. Surgery is also a key component of other cancer research topics, including the evaluation of novel technology, access to tissue for pathologic research, genomics and response studies, pre-operative, intraoperative and post-operative imaging, and neoadjuvant chemotherapy trials, to name a few.

Investment in cancer surgery research overall is poor across all income settings, with only 1.3% of global cancer research spending focused on cancer surgery.⁵ Cancer surgery research in high-income countries (HIC) is overrepresented, particularly in the cancer surgery trials literature.⁴ Ninety-three percent of global cancer surgery research occurs in only 35 countries of which 27 are HIC, which leads to a large disparity between where funding is focused and the burden of cancer in LMIC. All countries are projected to lose up to 1.5% of GDP annually between 2015 and 2030 if cancer surgical systems are not strengthened.⁴ Improved surgical oncology services can minimize catastrophic financial outcomes.⁴

It is vital to make the case for cancer surgery to fit into the overarching priorities of the global development world to expand funding for cancer surgery in LMIC. Cancer surgery has multiple roles, as it can be diagnostic, preventive, curative, and palliative. Aligning with the 2015 UN Sustainable Development Goals (SDGs) are one mechanism for doing this. This is possible because of linkages that can be made between cancer and primary care issues such as diabetes mellitus screening (with combined non-communicable disease clinics). Several of the nine health targets included in the SDGs are related to NCD-related health issues. Target 3.4, for example, is to “reduce by one third premature mortality from NCDs through prevention and treatment, and promote mental health and well being.” Target 3.5 also describes the prevention and treatment of substance abuse, including alcohol abuse, which is a risk factor for multiple tumor types. The World Health Organization (WHO) has a mandate to support and coordinate global research. The WHO has four primary goals relevant to research, as follows: (i) assist with research priority settings, (ii) develop standards for good research practice, (iii) ensure quality evidence is turned into evidence-informed policies and appropriate selection of affordable technologies, and (iv) build capacity in research systems. In cancer control, the International Agency for Research on Cancer (IARC), which is the specialized cancer research agency of WHO, has led major trials globally, aided in the establishment of cancer registries to assist with planning and research, and supported training and mentoring for hundreds of cancer researchers from LMICs through fellowships, courses, and collaborative projects.

Despite progress in the knowledge of cancer generated from research in high-income countries, the benefit of research on improving health outcomes has yet to be achieved, particularly among the most vulnerable populations globally. The resultant divide between knowledge and action is known as the evidence-into-implementation gap and is compounded by deficits in the dissemination of research findings.⁶ This gap is one priority for global cancer research efforts. Both implementation research and the assessment of technology are methods to address this priority.

Implementation Research

The slow translation of research evidence into practice is a global phenomenon and has concerning implications for the quality and cost of care. Studies from HIC have shown that up to 45% of patients fail to receive treatments that are effective, and 11% of treatment is not needed or potentially harmful.⁷ A review of the evidence-into-implementation interval found that it took an average of 17 years for 14% of original research to be integrated into physician practice.⁸ These phenomena are compounded by health systems that do not respond equitably to the needs of cancer patients. Up to one-half of premature NCD deaths could be avoided if health systems were strengthened to meet the need of patients with NCDs and best practices were universally applied.^{4,9} Such benefits of effective implementation and equitable access far exceed the treatment gain of most novel anti-neoplastic medicines and would be available to a significantly greater number of patients.

Patients, providers, insurers and governmental agencies are increasingly focusing on implementation research to understand barriers to the translation of research and how to develop evidence-informed policies (Table 2). Evidence-informed policies that prioritize value-based services will increasingly dictate how and what care is delivered in the clinics and operating rooms. Examples of how policies can impact surgical practice include centralization of services to high-volume facilities, accreditation according to minimum surgeon volumes or surgeon specialization, and the availability and use of high-cost technologies like robotic surgery.

Utilizing evidence-based interventions in cancer control can ensure that available resources achieve maximal efficiency. The income level of a country or population is not a barrier to success, and research can ensure domestic and international resources are used appropriately. WHO estimates that 20–40% of health expenditure is wasted.¹⁰ Implementation research can identify where inefficient spending occurs and direct funding to high-impact, low-cost interventions universally accessible. Simply stated, cancer research is a wise investment.

In 2011, WHO published A Prioritized Research Agenda for Prevention and Control of Noncommunicable Diseases.¹¹ In cancer control, a recommendation was made to study the effectiveness and cost of cancer surgical procedures and other treatment modalities to develop effective approaches and guide policy. Two other research priorities were to study means to improve access to diagnosis and treatment as well as assess alternative technologies for tele-imaging and tele-pathology. While progress has been made in the

interval six years, significant additional research is needed to improve access and establish evidence-informed policies in cancer and surgery.

Utilizing Technology to Improve Cancer Surgery

Technology can enable and optimize surgical practice by bridging the evidence-into-implementation gap and also improving the quality of surgical care. Online platforms for continuing medical education and professional development facilitate up-to-date surgical knowledge. Advanced health information systems are being designed to interpret large volume of data and improve the quality of care. However, the consequences of meta-data and advanced technologies are not yet clear; research is needed to objectively investigate their use and impact.

Advancements in technology have also revolutionized surgical practice. Proficiency in minimally invasive procedures does not adhere to the “see one, do one, teach one” tenet. Intensive and continuous training is needed, and the value of simulation training and video-recording with real-time feedback has to be studied in greater detail.¹² Remote learning and simulation training have significant potential and is an area ripe for global surgical research, as it is unclear how these can be used to improve outcomes in LMIC.

Funding Sources

Surgeons who want to improve outcomes for cancer patients globally must understand how best to develop an individual research project, how to integrate a global health research program into an academic surgical career, and how to secure funding for global cancer research projects. This article focuses on the first and third topics; the issue of integrating a global health research program into an academic career is beyond the scope of this manuscript. Funding sources and priorities span global health, global surgery, and global cancer. For global health research, the most common funders are the US NIH, the UK-based Wellcome Trust, the UK Medical Research Council, the European Commission, and the Institut National de la Sante et de la Recherche Medicale of France.¹³ Foreign funding overall, however, for conducting research in LMIC has been limited.¹⁴ Lack of time and funding have been described as the most significant barriers to conducting cancer care research. These barriers comprise major problems for research in most countries in sub-Saharan Africa (SSA) where physician salaries are generally smaller and patient loads higher than in high-income countries (HIC).²⁰ Moreover, obtaining grant funding for projects in LMIC can be far more difficult than obtaining funding for similar projects in HIC. Hence only 10% of global research funding goes to diseases which comprise 90% of the global burden.²¹ Some of the international funding agencies have recognized the funding gap in resource sparse countries and have begun to make some opportunities available which can only be applied for by or in collaboration with researchers from LMIC.

There are multiple opportunities to apply for to obtain funding for global cancer surgery research. At the US NIH, the NCI Center for Global Health and Fogarty International Center (FIC) have issued multiple options for domestic and LMIC investigators. Some examples, not all of which are currently open to new applications, include the following:

1. *P20 (RFA-CA-15-007) Planning for Regional Centers of Research Excellence in Non-communicable Diseases in Low and Middle Income Countries.* The goal of this RFA is to facilitate the planning, designing, and initial research focus of Regional Centers of Research Excellence (RCRE) for non-communicable diseases. This RFA requires a collaborative plan between HIC and LMIC centers with a focus on at least 2 NCDs in an LMIC, with one of the NCDs cancer.
2. *R21 (PAR-16-052) Global non-communicable diseases and injury across the lifespan: Exploratory Research.* This 2-year grant can combine cancer with injury research. The focus should be on research into the cancer continuum, such as prevention, detection, diagnosis, treatment, and survivorship. This can include epidemiologic studies on risk factors for cancer, the use of mobile technologies, cancer disparities, or cancers associated with chronic infections.
3. *UG3/UH3(RFA-CA-15-024), Cancer detection, diagnosis, and treatment technologies for global health.* This is sponsored by the NCI and the National Institute of Biomedical Imaging and Bioengineering. The goal is to support cancer-relevant technologies suitable for use in LMIC. The first two years of the grant are to develop the technology and the 3rd, 4th, and 5th years of the grant are for implementation of the technology in an LMIC. The goal at the completion of the grant is a commercial point-of-care device that is cost effective in an LMIC.
4. *R21 (PAR-16-292) Mobile health: technology and outcomes in low and middle income countries.* This grant is a two-year Fogarty International Center grant with multiple NIH collaborating centers. This opportunity funds exploratory research concerning innovative mobile health (mHealth) technology oriented towards use in LMIC. The goal is to create evidence based use of mobile technology to improve outcomes. There has to be a partnership between an HIC US institution and LMIC.
5. *K43 (PAR-15-292) Fogarty Emerging Global Leader Award.* This grant provides research support and protected time to a research scientist from a low- or middle-income country (LMIC) in a junior faculty position. This is a mentored career development award for up to 5 years, with \$75,000 given per year for the salary and \$30,000 per year for research development costs.
6. *K01 (PAR-17-002) International Research Scientist Development Award.* The NIH FIC supports intensive, mentored research career development for early stage US investigators. Applications can include epidemiology studies on common risk factors for cancer, diagnostic studies, cancer registry development, translational cancer research, and implementation science. The goal is for the investigator to become independent in global health research by the completion of the award.

The International Union for Cancer Control (UICC) also has research support with its ICRETT fellowship. These fellowships are generally for one month in length; the goal is to facilitate the rapid transfer of cancer research and clinical technology, skills, and areas of

cancer control and prevention. Since 1976, over 2,500 ICRETT fellows have been appointed. The intention of this fellowship is to allow for a transfer of knowledge on a specific topic that can be used back in the fellows home country. One example of this is initiating a sentinel lymph node program for breast cancer. This can include training and observerships with surgeons, pathologists, and a nuclear medicine team to allow a physician to gain the knowledge needed to start or improve their own program.

Several societies have grants to support cancer research in LMIC. The African Organization for Research and Training in Cancer (AORTIC), in partnership with the US NIH, sponsors the Beginning Investigator Grant for Catalytic Research (BIG Cat) program. The grant awards up to \$50,000 to African investigators for a two year project. This is specifically designed for Principal Investigators that are beginning investigators who have received his or her highest degree of study within the seven years prior to the application deadline. The American Society for Clinical Oncology (ASCO) has an International Innovation Grant. This award supports novel and innovative projects that can improve the diagnosis, prevention, and treatment of cancers in low- and middle-income countries. The grant is for one year with \$20,000 support. ASCO also has an International Development and Education Award (IDEA) that supports early-career oncologists in low- and middle-income countries by pairing recipients with ASCO mentors at the annual ASCO meeting. The goal of the program is to create a long term relationship with the mentor and the mentor's facility. There are also private foundations that support cancer research. One example is Wellcome Trust, based in the UK. The Wellcome Trust partnered with the US NIH to fund genetic studies in Africa, with the Human Heredity and Health in Africa Project. The Wellcome Trust also has partnered with the Bill and Melinda Gates Foundation and the UK Department of International Development (DFID) as the Alliance for Accelerating Excellence in Science in Africa (AESA). This initiative supports Africa-led initiatives in key areas of science, particularly health research relevant to Africa.

As discussed above, global cancer surgery research must be viewed within the large fields of global surgery research, global cancer research, and global health research. The imperatives for global cancer surgery research are made clear by the WHO's priority plan for NCD research and NCD Action plan, as well as the UN Sustainable Development Goals. Surgeons should explore a variety of potential funding sources, including national government research agencies, philanthropy, and cancer-specific NGOs.

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Table 1

Overview of conclusions from the Lancet Oncology Commission on Global Cancer Surgery⁴

<ul style="list-style-type: none">• Over 80% of 15.2 million people diagnosed with cancer in 2015 will need a surgical procedure• Globally, countries will likely lose up to 1.5% of GDP annually without strengthening of cancer surgery systems• National investments in health education and training are required to strengthen the role of cancer surgery in cancer control plans• Less than 5% of global cancer research concerns cancer surgery• Global cancer surgery must become a priority for public health leaders in government and philanthropy

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Table 2

Examples of cancer surgery questions that can be addressed with implementation science

1	What are the oncologic outcomes of LMIC-specific guidelines for cancer treatment?
2	What is the value of screening high-risk patients, as opposed to average risk patients, in LMIC?
3	Are there new technologies that can be used in low resource areas that are : point of care, cost effective, durable, low maintenance?
4	Which high-income country cancer diagnostics are useful for cancer screening in LMIC?
5	How do cancer mutation analyses fit into LMIC cancer diagnosis and treatments?
6	What is the role for minimally invasive cancer surgery techniques in LMIC?

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