The Challenges of Delivering Cost-Effective and Affordable Care to Children With Cancer in the Developing World

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The authors of this report[1] are a cohesive amalgam of experts in the relevant methods and local practitioners with the requisite experience and expertise. Indeed, the senior authors have been in the vanguard of efforts to determine the cost-effectiveness of pediatric cancer care in low- and middle-income countries (LMICs). In this study, the numerous assumptions, estimates, extrapolations, and allocations are realistic necessities in the absence of relevant information, which is so common in LMICs, and have been well defended methodologically (as with multiple sensitivity analyses). The "failure" of Kenya to reach the threshold for cost-effectiveness invites further comment. What follows is, in part, a narrative exercise in joining the dots.

Kenya, Uganda, and Tanzania were the original members of the East African Community, which now includes Rwanda and Burundi with Swahili as the lingua franca. There is a rich history of medical research in Kenya. Dr. Henry Foy (1900-1991) was educated at Oxford, where he studied physiology under Julian Huxley. He established his laboratory in Nairobi in 1949 with funding from the Wellcome Trust and with the support of his longtime colleague and companion Athena Kondi. When I came to know them in their retirement, they were affectionately named Koy and Fondi. The Kenya Medical Research Institute was established in 1979 close to Kenyatta National Hospital (KNH), which was named after the country's first president after independence from the United Kingdom in 1963.

The Kenya Medical Research Institute formed a partnership with the Wellcome Trust and the University of Oxford in 1989 and maintains numerous research programs to this day.

As a newly minted internist and budding hematologist, I arrived in Nairobi in April 1970 to join the faculty of medicine, which had been developed, in a collaboration from 1965 with the University of Nairobi, by staff from the University of Glasgow. Kenya was a highly successful country (the Kenyan pound was worth more than the pound sterling) and decidedly peaceful. However, there were no pediatricians with an interest or expertise in the care of children with blood diseases or cancer. Two internists/hematologists from McGill University and I set up a clinic at KNH to address this deficit. So began my 50-year journey in pediatric oncology.

In December 1971, I attended the annual meeting of the Association of Surgeons of East Africa in Kampala, Uganda. The meeting was opened by His Excellency, Field Marshal Idi Amin Dada, President for Life, in full military uniform. Amin was heralded subsequently as the Last King of Scotland in a book of the same name by Giles Foden,[2] and this is also the title of the related film.

While in Kampala, I had the good fortune to meet Dr. John Ziegler, who had established the Lymphoma Treatment Centre, forerunner of the Uganda Cancer Institute, in 1967. Ziegler published the results of the first randomized clinical trial in Burkitt lymphoma in Africa in 1970.[3] This demonstrated that a single dose of cyclophosphamide was as effective as multiple doses in securing durable remissions in children with localized disease, and it thus set the stage for Denburg et al[4] to demonstrate the cost-effectiveness of treating Burkitt lymphoma in Uganda almost 50 years later. Pediatric oncology in Kenya was boosted by the return to Nairobi in 1974 of Dr. Edward Kasili after training in hematology in Glasgow. He became a strong proponent of the care of children with cancer and was instrumental in the establishment in 1985 of a ward at KNH devoted to this purpose. Unfortunately, resources were scarce. KNH consumed 25% of the budget of the Ministry of Health in 1970, but in the past year this was reduced to 13% (15 billion KSh [approximately

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US $150 million] for this 1800-bed institution, with $4 million assigned to pediatric oncology). Edward died prematurely in 1994,[5] but his legacy lives on under the leadership of Dr. Jessie Githang'a, first author of the report under discussion, who trained in Glasgow also and benefitted from Professor Kasili's mentorship. Another important contribution has been made by Dr. William Macharia, who returned to Nairobi in 1992 after completing training in pediatric hematology and oncology at McMaster University, where he also received a master's degree in clinical epidemiology. Dr. Macharia became the director of the Nairobi unit of the International Clinical Epidemiology Network and in 2007 moved to Aga Khan University in Nairobi, where he is chair of the Department of Pediatrics and Child Health.

What lessons can we learn from the information provided in the report by Githang'a et al[1] and from their interpretation with respect to the circumstances at KNH? Two items in particular stand out: the cost of medications and the impact of the abandonment of therapy. The proportion of the total costs related to medication was highest in Kenya among the 4 countries in the investigations. A recent study attests to the high costs of anticancer drugs, even generic medications, for children in LMICs.[6] This burden on health care systems is mirrored in the financial toxicity experienced by families, as noted by Githang'a et al; this is a phenomenon even in high-income countries, as exemplified by Canada,[7] where health care is described as "universal access first dollar coverage" but there is no national system of pharmacare. The importance of philanthropic support cannot be overestimated. A good example is provided by the consortium of pediatric cancer care institutions in Central America, each of which has a foundation supported by a civil society.[8] However, this is a patchwork solution at the global level. At its last in-person annual meeting in Lyon, France, in October 2019, the International Society of Paediatric Oncology (SIOP) convened a meeting of major stakeholders, including the World Health Organization (WHO), with which SIOP has a formal association; St. Jude Children's Research Hospital; and Childhood Cancer International (CCI),[9] which is a network of 167 parent-driven patient support groups within 90 countries in 5 continents and is an official partner of SIOP. This group has begun to explore the development of a global funding initiative perhaps modeled on Gavi, the Vaccine Alliance, which was founded by the Bill and Melinda Gates Foundation.

Until this goal has been achieved, what can be done? SIOP's working group on essential medicines must continue to collaborate with colleagues at WHO on that organization's essential medicines list, which is a useful guide to governments on the composition of their national essential medicines lists as well as procurement practices.[10] SIOP has a strong track record in this regard.[11] The regional offices of the WHO must be encouraged to foster group purchasing of drugs; this would improve cost-effectiveness (KNH would then meet the threshold, as explained by Githang'a et al[1]). Member organizations of CCI can make representation to national governments with respect to the cost of drugs for children with cancer, as the Fundación Natali Dafne Flexer is doing in Argentina (Edith Grynszpancholc, personal communication [email], August 27, 2020). All of us with vested interests in pediatric oncology should remain vigilant for the appearance on the market of substandard or frankly fraudulent products, as in the case of preparations of asparaginase manufactured in China and distributed in Latin America with consequent harm.[12,13]

Enhancing the annual government health expenditure per capita is an uphill struggle in LMICs. From 2015 data using figures adjusted for inflation and expressed in 2011 purchasing power parity US dollars, the figures for Kenya, Zimbabwe, and Nigeria are $157, $182, and $215 (a figure for Tanzania is not available)[14] with corresponding gross national incomes per capita of $3440, $3020, and $5710[15]; these values provide ratios of 22:1, 17:1, and 27:1, respectively. For comparison, the figures in Canada are $4600 and $47,590 for a ratio of 10:1. There is a long way to go. The challenge is compounded by systemic corruption. According to the Corruption Perceptions Index,[16] the least corrupt countries are Denmark and New Zealand, which each score 87/100, and the most corrupt is Somalia (9/100). The scores for Kenya, Zimbabwe, Nigeria, and Tanzania are 27, 22, 27, and 36, respectively. When acting in concert, these influences can be catastrophic. Myanmar has a gross national income per capita of $6500 and an annual government health expenditure per capita of $58 for a ratio of 112 with a Corruption Perceptions Index score of 29 and a manifestly inflated national essential medicines list.[17]

An easier nut to crack is abandonment of therapy, a prevalent challenge encountered almost exclusively in LMICs. It is determined in large part by socioeconomic disadvantage.[18] Marked reductions in rates of abandonment have been described, such as in Central America,[8] with a common theme being effective interventions by organizations of volunteers. CCI has had a considerable impact on these endeavors. As Githang'a et al[1] have observed, reducing abandonment would augment cost-effectiveness, especially at KNH, which has a rate higher than 50% despite the added hotel costs borne by the hospital.

The authors of the report to which this editorial is related[1] will surely continue to exert a leadership role in this area of study. While expanding their investigations geographically, they will undoubtedly add utilities to disability-adjusted life-years (DALYs). Health economists and decision scientists may argue about the relative merits of DALYs and quality-adjusted life-years, which are based on quite different constructs. These approaches yield results that are not interchangeable but rather are complementarily informative.[19] The availability of utility weights for DALYs[20] allows cost utility analyses, which, while challenging in pediatric oncology even in high-income countries,[21] provide added value to assessments of cost-effectiveness.[22] It will be especially useful to revisit the sites of their studies after elements influencing cost-effectiveness, such as abandonment of therapy, have been addressed substantially. Then, it is on to resolving the dilemma of cost-effectiveness versus affordability, as the authors have recognized. They are particularly well placed to bridge this gap in knowledge.

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