

Cost effectiveness of support with out-of-pockets costs to prevent treatment abandonment in Malawi and sub-Saharan Africa; lessons learnt and the way forward – a report from CANCaRe Africa

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LMIC Low- and middle-income country

GICC Global Initiative for Childhood Cancer

CANCaRe Africa Collaborative African Network for Childhood Cancer Care and Research

ALL Acute lymphoblastic leukaemia

GDP Gross Domestic Product

Commentary

With a decreasing burden and mortality of infectious diseases in Africa, the relative importance of non-communicable diseases such as childhood cancer is increasing. Great progress in childhood cancer care has been made over the past decades. Various initiatives have increased the availability of trained staff, drugs, and locally appropriate treatment guidelines in many low- and middle-income countries (LMIC), including the Global Initiative for Childhood Cancer (GICC), launched by the WHO in 2018. The GICC target is to increase survival worldwide to 60% by 2030, with an initial focus on six common and curable ('index') childhood cancer types for which survival is currently over 85- 95% in high income countries.

Estimated overall childhood cancer survival in many countries in sub-Saharan Africa is still below 20% (1, 2). Non-adherence to treatment, commonly referred to as treatment abandonment, is the most common cause of treatment failure, with reported proportions between 46% to 89% (3, 4, 5, 6). High quality evidence specific to Africa on (baseline) survival of children with cancer and sustainable impact of interventions to increase survival are lacking. There is an urgent need to close this survival and research gap.

News that a child has cancer is devastating to any family; the magnitude of the problem, the length and toxicity of treatment, the repeated visits to hospital and anxiety about the outcome are overwhelming. Families discover that even when chemotherapy is free, there are many out of pocket costs. Travel to and from hospital is costly, daily needs while in hospital with a child, loss of income if a parent must stop working and care for the rest of the family drain resources (7). Providing highly nutritious foods for their child is beyond many households (8). Even in high income countries where charities and government subsidies are available, it is estimated that when a child completes therapy, 1 in 6 families are in debt (9). This financial burden is particularly difficult for families in low-income settings. Many live far from the hospital, the mother may be responsible for several children and run a small-scale business to support the family and grow the crops that feed her family. It is not surprising that when a choice has to be made about continuing treatment for one child or serving the needs of the whole family, that treatment is left unfinished.

Thus, treatment abandonment is found to be a common cause of childhood cancer treatment failure in low-income countries. It is defined as the failure to complete treatment or interruption of treatment for more than 4 weeks for non-medical reasons (10). Reported causes worldwide include lack of hope of survival, inadequate counselling, unavailability of treatment and long travel distances to the hospital (3, 4, 5). A prospective descriptive study on treatment abandonment in the CANCaRe Africa network showed that the need to borrow money to reach the hospital was the only significant predictor of treatment abandonment (8). In sub-Saharan Africa the overriding cause is inability of the families to pay for out-of-pocket costs associated with treatment (7, 8, 11). These include costs for diagnosis and treatment, transport between home and the hospital and food and accommodation while staying at the hospital.

Analysis of cost effectiveness is important. The internationally recognized WHO-CHOICE guidelines are commonly used to define cost-effectiveness thresholds (12). Interventions that cost less than three times a country's per capita income per disability-adjusted life year (DALY averted) are considered cost-effective, while those costing less than per capita income per DALY averted are considered very cost-effective. Childhood cancer treatment was found to be very cost effective in two and cost effective in one out of four centres across sub-Saharan Africa (13). Evidence from simulations suggest that interventions to prevent treatment abandonment in sub-Saharan Africa are likely to be cost-effective (14). Cash incentives have been shown to be effective to increase adherence on the continent in other areas of health care such as treatment of TB (15). We also found that 50 USD was sufficient to cover out-of-pocket costs for 4 weeks of treatment for 50% of all families (8).

The implementation of cash incentives to primary caregivers of children with newly diagnosed common and curable cancers was piloted in Malawi in a prospective study. The intervention consisted of cash incentives for all transport costs during the whole treatment, on average 200 Euro per patient (16). Families in Malawi do not have to pay for diagnosis, treatment or accommodation while staying at the hospital. Treatment

abandonment decreased significantly from 19% (49 of 264) to 7% (10 of 150), $p < 0.001$ (16, 17). The proportion of patients alive and without evidence of disease at the end of treatment increased from 53% (139 of 264) to 61% (91 of 150) but was not statistically significant ($p = 0.1$). However, we demonstrated a significant increase in the proportion of patients alive without evidence of disease at the end of treatment from 38% (57/149) to 53% (44/83) ($p = 0.03$) in patients with the most significant decrease in abandonment (Wilms tumour, retinoblastoma and acute lymphoblastic leukaemia (ALL) (16).

Data were not prospectively collected to analyse cost-effectiveness according to established criteria. A rigorous analysis of the cost-effectiveness would require data on several parameters, including 2-year survival of children who do not abandon therapy, the real-world cost of treating a child who abandoned therapy, and the real-world cost of treating a child who did not abandon therapy. Though these data are not currently available, some parameters have been collected in other sub-Saharan African jurisdictions.

We assumed a 2-year survival of children without treatment abandonment of 30%, a comparable average cost of treating a child with cancer (\$2,400 USD) as previously demonstrated in Tanzania, and that the average cost of treating a child until the point of abandonment is 10% of the average cost (i.e., \$240) (13). Note that these assumptions are likely to be conservative as evidence and on-the-ground experience suggests that 2-year survival is higher, average cost of treatment may be lower, and the average cost of treatment until the point of treatment may be more than 10% of average treatment cost (16, 18). Conservative assumptions may in fact underestimate cost-effectiveness.

Nonetheless, with the assumptions as stated, the decrease in treatment abandonment seen in the pilot study (19% to 7%) would result in an increase in overall 2-year survival from 24% to 27.9% and an increase in the average cost of treating a patient of \$471 USD (including the cost of the abandonment intervention itself). Together, this implies that the incremental cost per life saved would be approximately \$121 USD. This is a metric well below the threshold for a very cost-effective intervention of 629 USD - the per capita Gross Domestic Product (GDP) of Malawi in that year (19).

Treatment abandonment is a common and preventable cause of childhood cancer treatment failure in sub-Saharan Africa. Out-of-pocket costs are an overriding cause. Evidence suggest that interventions to prevent treatment abandonment, including cash-incentives for caregivers, are cost-effective. Collaborative efforts are needed to increase support to families to enable them to complete the treatment of their child. Rigorous evaluation of impact of such interventions, including an analysis of cost-effectiveness and other aspects of implementation will contribute meaningfully to joint and multi-stakeholder advocacy.

Conflict of interest Statement None declared.

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