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CARE study: prospective cohort study on supportive care among paediatric oncology patients in western Kenya—a study protocol

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ABSTRACT

Introduction Childhood cancer presents significant challenges in low- and middle-income countries (LMICs), as survival rates remain substantially low. Supportive care, including nutritional support and infection prevention plus management, is crucial in improving outcomes of childhood cancer patients. To develop evidence-based interventions improving supportive care and survival, insight is needed into local prevalences of malnutrition, colonisation and infections, their association with clinical outcomes and the attitude of parents or legal guardians towards nutritional care and infection prevention. The overall aim of this prospective cohort study is to identify modifiable nutritional and infection-related determinants of clinical outcomes at 6 months in children with cancer (1–15 years of age) treated with curative intent at the Paediatric Oncology ward of the Shoe4Africa Children's Hospital at the Moi Teaching and Referral Hospital in Eldoret, Kenya.

Methods and analysis We will conduct a prospective cohort study on 150 children aged 1–15 years who are newly diagnosed with cancer and treated with curative intent. During 6 months of follow-up, we will collect clinical data, perform nutritional assessments and monitor pathogen exposure, colonisation and infections. Parents or legal guardians will receive one questionnaire to assess attitudes towards supportive care. Six-month mortality is the primary outcome. Other outcomes include the prevalence and characteristics of malnutrition, rectal colonisation with bacterial and fungal pathogens, infections and neutropenic fever episodes. Statistical analyses will include descriptive statistics, chi-square tests, logistic regression and thematic analysis.

Ethics and dissemination The Institutional Research and Ethics Committee has approved the study protocol (FAN: 0004674, protocol version 1.0). Informed consent from parents or legal guardians and assent from children ≥12 years will be obtained. Findings will be disseminated through peer-reviewed publications, presentations at academic conferences and engagement with local and national policymakers and stakeholders. Data from this study could guide the development of locally informed, evidence-based supportive care interventions, with the ultimate goal to improve overall survival for children with cancer in LMICs.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study investigates various aspects of modifiable supportive care elements, known to adversely affect outcomes in resource-limited countries.
⇒ Integration of quantitative clinical data with caregiver questionnaires enables a comprehensive assessment of supportive care practices during childhood cancer treatment.
⇒ Multidisciplinary involvement of clinicians, microbiologists and nutritionists enhances methodological thoroughness and ensures a nuanced examination of various aspects of supportive care.
⇒ Variability in medical record completeness, delays in obtaining cultures before antibiotic administration and potential loss to follow-up may limit data completeness or introduce bias.

INTRODUCTION

Annually, over 400 000 children develop cancer worldwide.[1–5] Survival for children with cancer has improved substantially over the last decades in high-income countries (HICs) due to advances in diagnostics, treatment protocols and supportive care.[6] In contrast, in low- and middle-income countries (LMICs), which bear at least 80% of the childhood cancer burden, survival rates are merely 20%.[1] Multiple factors contribute to this disparity, including delayed diagnosis, treatment abandonment and limited access to adequate supportive care.[4 7 8]

Supportive care, aimed at enhancing patients' quality of life and managing disease- and treatment-related complications, is integral to childhood cancer management. A structured and risk-based

approach to supportive care is key to reducing morbidity and mortality worldwide.[9] However, LMICs face challenges in delivering comprehensive supportive care, particularly concerning nutritional support and infection prevention and management. Malnutrition is associated with impaired immunity and greater susceptibility to infections.[10–13] Children with malnutrition in general have a six times higher chance of mortality, both as inpatients as well as post-discharge regardless of childhood cancer.[14] Malnutrition is highly prevalent among paediatric oncology patients in LMICs (approximately 30–60%),[15 16] and these patients have an even higher chance of a poor outcome.[17] Early identification and targeted interventions for children with cancer and malnutrition could improve outcomes and enable more efficient use of scarce resources.[18]

Infections also remain a major cause of treatment-related mortality (TRM): a recent systematic review attributed over 70% of TRM to sepsis or infection in children with cancer.[19] TRM prevalence was inversely related to country income group.[19] Children with cancer in LMICs are up to 20 times more likely to die of infections as compared with those in HICs, partly due to delayed recognition and limited access to diagnostics and appropriate antimicrobials.[20 21] Identifying patients at high risk of infections is crucial for prevention and treatment strategies,[10 12] and the impact of nutritional status on the risk of infection-related mortality has not been evaluated. While active surveillance cultures and risk-adapted management are crucial and standard in HICs,[22 23] such practices are rarely available in LMIC settings.

To reduce global disparities in childhood cancer survival, there is an urgent need for targeted and locally adapted supportive care interventions.[19] Understanding the impact of malnutrition, colonisation status and infections on clinical outcomes and parents or legal guardians' knowledge and attitudes regarding supportive care is essential for guiding context-appropriate interventions. The CARE study is a prospective cohort study to investigate these determinants to inform the development of evidence-based, locally adapted nutritional interventions, fever and infection management, and risk stratification tools for children with cancer at a large, tertiary referral children's hospital in Kenya.

Aims and objectives

Aim

The overall aim of this prospective cohort study is to identify modifiable nutritional and infection-related determinants of clinical outcomes at 6 months in children with cancer (1–15 years of age) treated with curative intent at the Paediatric Oncology ward of the Shoe4Africa Children's Hospital at the Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. This study protocol manuscript followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[24]

Secondary objectives

Nutrition

- 1.To determine the prevalence of malnutrition according to WHO definitions at the time of cancer diagnosis in this patient population.
- To assess associations between nutritional status according to WHO definitions and clinical outcomes at 6 months from diagnosis, including treatment completion, morbidity and all-cause mortality.
- To evaluate adequacy of observed daily dietary intake compared with estimated needs during treatment.
- To assess associations between nutritional status of the child and caregiver knowledge, attitudes and practices regarding nutritional care.

Infection

- To establish the prevalence of bacterial and fungal (yeast) colonisation status and intestinal parasitic infections at diagnosis, 3 and 6 months.
- To assess associations between infection-related characteristics and 6-month clinical outcomes, including treatment completion, morbidity and all-cause mortality.
- To describe the incidence, aetiology and outcomes of febrile neutropenia episodes.
- To examine the attitudes, knowledge and practices of parents or legal guardians involved in the care of cancer patients, regarding infection prevention, and their associations with infection-related outcomes.

Exploratory objective

To characterise gut microbiome variability at baseline and at 3 months, and to examine their associations with patient demographic and clinical factors. (Detailed analytic plans will be reported in a separate microbiome-specific protocol).

METHODS AND ANALYSIS

Study design

This is a prospective cohort study of children aged 1–15 years receiving childhood cancer treatment with curative intent at the Paediatric Oncology ward of the Shoe4Africa Children's Hospital at MTRH in Eldoret, Kenya. A total of 150 participants will be followed for 6 months after childhood cancer diagnosis. Study enrolment started in November 2024, and the expected time of completion is 18 months to 2 years.

Patient and public involvement

Patients or the public were not involved in the design, conduct or reporting. At the time of protocol development, formal patient and public involvement was not common practice, and no patient organisation or national paediatric oncology consortium was present in the study setting. However, the importance of meaningful patient and public involvement in health research is increasingly recognised. In the current study centre,

patient and caregiver engagement is now being incorporated more frequently into research activities, and future studies building on the CARE cohort will seek to involve patients and caregivers in the development and dissemination of supportive care interventions. We, however, plan to involve caregivers and participants in the dissemination plan by giving caregiver feedback and through publications.

Setting

This study will be conducted at the paediatric oncology department of MTRH. MTRH is a level six public referral hospital, the largest government referral hospital in Western Kenya, and serves a population of over 20 million. The paediatric oncology ward includes 35 beds, distributed across six rooms, with an average bed occupancy rate of 250%, which means beds are often shared. Approximately 300 children are diagnosed with cancer annually, as per unpublished cancer registry data of 2023 of MTRH. Surgery, chemotherapy and radiotherapy are available.

Nutritional supportive care is limited. Since January 2024, a dedicated nutritionist has been performing routine nutritional assessments for all paediatric oncology patients, including measurement of mid-upper arm circumference (MUAC), following a routine standard practice. Nutritional supplements are scarce, nasogastric feeding is infrequently used, and total parenteral nutrition is not available.

Infection prevention and management resources are constrained. A recently implemented, locally adapted fever treatment guideline and sepsis screening tool are in use but pending review with an aim to improve infection management.[21] Access to infectious disease consultation is limited, the intensive care unit has only five paediatric beds, supplies of antimicrobials are inconsistent, and blood culture results are delayed and often obtained after antibiotic administration.

Eligibility criteria

Inclusion criteria are as follows: children aged 1–15 years, newly diagnosed with cancer who are receiving treatment with curative intent at the paediatric oncology ward of the Shoe4Africa Children's Hospital at MTRH, in Eldoret, Kenya. Parents or legal guardians must be able to understand the study and provide written informed consent in English or Kiswahili. Exclusion criteria are as follows: children with suspected or confirmed congenital syndromes, such as Down syndrome, are excluded because these conditions are associated with distinct treatment protocols, increased susceptibility to treatment-related toxicity, and supportive care needs that cannot be adequately met in the resource-limited setting, resulting in care pathways that differ from standard protocols. Children with relapsed cancer are excluded because, in the study setting, relapse is typically managed with palliative intent rather than curative, whereas this study focuses specifically on patients receiving treatment with curative intent.

Participation in the guided surveys: Eligibility is limited to the parents or legal guardians of children enrolled in the study.

Recruitment and informed consent

Potentially eligible patients will be identified through the paediatric oncology ward's daily admissions. A trained research clinician will screen all newly admitted patients with a confirmed diagnosis of childhood cancer for eligibility based on the inclusion and exclusion criteria.

Eligible patients and their parents or legal guardians will be approached individually in a private setting, after the child's diagnosis and treatment plan have been discussed by the medical team. The research clinician will explain the purpose, procedures, risks and potential benefits of the CARE study. Written informed consent will be obtained at diagnosis (within 2 weeks of diagnosis or start of treatment) from parents or legal guardians of eligible participants. Children aged 12 years and older will be invited to provide assent after receiving an age-appropriate explanation of the study. Assent will be obtained verbally, and children will be informed that participation is voluntary and that declining will not affect their medical care. If a child aged 12 years or older declines to provide assent, the child will not be enrolled in the study, even if parental or guardian consent has been obtained. Children may withdraw their assent at any time during the study without consequences for ongoing treatment. Consent forms will be available in Kiswahili and English and will include permission for storage and future use of biological samples. Participation is entirely voluntary, and refusal to participate will not affect the medical care provided. Participants may withdraw from the study at any time without consequence. A screening log will be maintained to document all eligible patients, reasons for non-enrolment and refusals.

Quantitative data collection

Timeline of clinical data and sample collection

The schedule of study assessments and sample collection is summarised in figure 1. Assessments occur at seven time points: T0 – baseline, T1 – 2 weeks, T2 – 4 weeks, T3 – 6 weeks, T4 – 8 weeks, T5 – 12 weeks and T6 – 24 weeks. Clinical data will be collected by manual abstraction from the medical record by the trained research staff (eg, research clinician, medical officer, paediatric oncologist). The clinical data will be entered in the electronic case report form (eCRF) in CASTOR.[25] Additional data collection, such as febrile neutropenia (FN) episodes, will occur throughout the study whenever relevant. If a patient is at home at the scheduled time point, data or samples will be collected at the next hospital visit, ideally 2 weeks before or after the scheduled study time point. Microbiological assessments are displayed in figure 2. Data measurements will be outlined below in chronological order. All CRFs can be found in online supplemental file 1).

	T0, diagnosis	T1, 2 weeks	T2, 4 weeks	T3, 6 weeks	T4, 8 weeks	T5, 3 months	T6, 6 months	Troughout the study
Informed consent	X							
CRF baseline characteristics	X							
CRF Clinical assessment data	X	X	X	X	X	X	X	
Cardiac ultrasound	X						X	
CRF neutropenic fever episode								X
Guided questionnaire		X						
CRF dietary assessment			X		X	X		
CRF 24-hour diatary recall					X			
Blood sample chemistry	X	X	X	X	X	X	X	
Serum sample (for serology)	X							
Stool sample (2x: parasitology + DNA microbiome)	X					X		
Surveillance culture (rectum/ perineum)	X					X	X	
Serum sample and blood culture in case of neutropenic fever								X
CRF conclusion form							X	

Figure 1 Schedule of assessments. Yellow: clinical assessments, orange: questionnaire, blue: dietary assessments, green: microbiology assessments, purple: conclusion form. CRF, case report form.

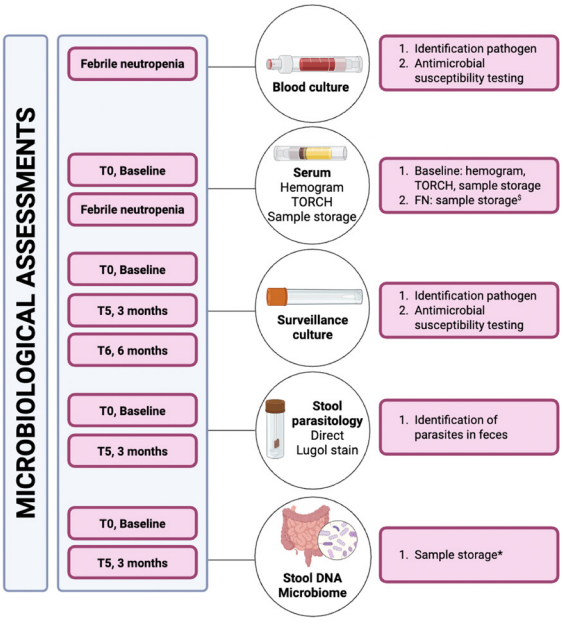

Figure 2 Overview of microbiological sample collection and analysis. All cultured micro-organisms are considered potentially relevant for this study. $Samples will be stored for future DNA/RNA detection of bacterial, viral and fungal infections. *Stool samples collected at baseline and at 3 months will be stored for future microbiome sequencing and analysis. TORCH, *Toxoplasmosis; Others, including HIV, ParvoB19, varicella; Rubella, Cytomegalovirus and herpes simplex.*

Clinical assessments

Baseline characteristics

At T0, baseline characteristics will be collected from the patient file, by the trained research staff. These include date of birth, sex, medical history, working diagnosis, presenting complaints, physical examination, suspected chronic conditions, TB screening, malaria testing, HIV status and immunisation. Missing data will be requested from the parents or legal guardians by the study team.

Clinical assessment data

Clinical assessment data is to be collected at baseline (T0), 2 weeks (T1), 1 month (T2), 6 weeks (T3), 2 months (T4), 3 months (T5) and 6 months (T6) (CRF 'Clinical assessment data'). This form contains information on clinical symptoms (eg, respiratory distress, shock, bleeding, dehydration, diarrhoea, vomiting), vitals (eg, oxygen saturation, respiratory rate, heart rate), lab results, and nutritional parameters (MUAC, height, weight). Nutrition status will be assessed in all children by a qualified nutritionist and categorised as no malnutrition, moderate acute malnutrition or severe acute malnutrition based on WHO criteria (table 1).[26] MUAC cutoffs for children above 5 years of age will be guided by Mramba *et al*.[27] Nutritional support will be provided as per the nutritional care standards at the department, in accordance with the National Kenyan Nutrition guidelines, which are based on the WHO 10-step management of malnutrition. These data will be collected from the patient file by the

Table 1 Malnutrition defined by the WHO[26]

	MAM	SAM
Age below 5 years	WH <–2SD and >–3 SD MUAC >11.5–12.5 cm	WH ≤–3 SD MUAC ≤11.5
Age 5–9 years*	WA or BMI ≤–2SD and >–3 SD MUAC ≤–2SD and >–3 SD	WA or BMI ≤–3 SD MUAC ≤–3 SD
Age 10 years and above*	BMI ≤–2 SD but >–3SD MUAC >–2SD and >–3 SD	BMI ≤–3SD MUAC ≤–3 SD

If there is a mass present: MUAC is used to determine the classification; otherwise, the most severe parameter is used.
*MUAC – the most appropriate cut-off values still need to be determined for this age group. The values above still require formal validation but may be helpful for screening.
BMI, body mass index; MAM, moderate acute malnutrition; MUAC, mid-upper arm circumference; SAM, severe acute malnutrition; WA, weight for age; WH, weight for height.

trained research staff. Missing data in the patient file can be requested from the parents or legal guardians by the study team.

Cardiac evaluation

A 2D transthoracic echocardiogram, performed by an echocardiographer of the MTRH, will be performed at baseline (T0) and at 6 months (T6; only in case of abnormalities), regardless of treatment regimen. This is a study-specific assessment. Data collected include heart structure and function.

Laboratory and sample collection

Blood chemistry

Standard-of-care laboratory tests including electrolytes, kidney function tests, liver function tests, glucose and C-reactive protein, will be taken at baseline (T0), 2 weeks (T1), 1 month (T2), 6 weeks (T3), 2 months (T4), 3 months (T5) and 6 months (T6).

Serum sample

Serum samples will be collected at diagnosis (T0) and in case of FN. This is not standard of care, but a study-related procedure. Three millilitres of blood in each tube will be collected. The (T0) sample tube will be processed for serology analysis for TORCH infections and EBV at the MTRH lab. Other samples in case of FN will be processed and stored at the AMPATH lab for future RNA/DNA detection for bacteria, viruses and fungi. Nanopore sequencing (Oxford Nanopore Technologies) will be used which will enable comprehensive genome assembly, identification of antimicrobial resistance genes and virulence determinants, and detection of mixed or emerging infections.[28]

Stool sample

Two stool samples will be collected at baseline (T0) and at 3 months (T5). One fresh stool sample will be directly analysed for parasitology at the MTRH lab. The microscopy for gastrointestinal parasites is a standard diagnostic method that involves examining stool samples under a microscope to detect various parasitic infections such as helminths (eg, roundworms, whipworms, hookworms) and protozoa (eg, Giardia, *Entamoeba histolytica*). Stool samples for microbiome will be directly collected in OM-200 collection tubes. This is a study-specific assessment. The samples will directly be frozen (−80°C) and stored for future analysis. At the end of the study, all faecal samples for DNA microbiome analysis will be sent to the Netherlands.

Rectal surveillance culture

A rectal surveillance culture will be collected at baseline (T0), at 3 months (T5) and 6 months (T6). The surveillance culture will be performed using Sigma Transwabs. The sample will be inoculated on two different media: blood agar and MacConkey agar. The study micro-organisms of interest will be *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter* spp., all *Candida* spp. and Enterobacterales, including a phenotypic assessment of extended-spectrum beta-lactamase (ESBL) production based on automated susceptibility testing. These are study-specific assessments.

Febrile neutropenia

In the case of FN, defined as a temperature of ≥38.5 °C measured once or ≥38.0 °C in two consecutive readings at least 1 hour apart, accompanied by an absolute neutrophil count of <0.5 * 10^9/L,[29] the CRF 'FN' will be filled out. This form contains information on the temperature, clinical presentation, anthropometry, antibiotic prophylaxis and treatment, blood culture results, empirical antibiotic therapy, and whether the antibiotic therapy is adjusted according to the micro-organisms cultured. Drawing a blood culture is part of standard clinical care during FN. Three millilitre of blood will be collected in the BACTEC bottle by the research clinician or phlebotomist. When positive, the blood culture will be subcultured on blood agar and MacConkey agar in the microbiology lab to identify and characterise the microorganism involved and to perform susceptibility testing according to local laboratory protocols. Additionally, malaria testing by rapid test will be performed during all FN episodes. If positive, microscopy (thick smears) will be performed to confirm malaria positivity.

Nutritional and dietary assessments

Guided survey on active parents' or legal guardians' participation

At 2 weeks (T1), parents or legal guardians will complete a study-specific semi-structured survey to assess parents' or legal guardians' knowledge, attitudes and practices related to nutritional support and dietary management for their child during cancer treatment. This semi-structured survey is administered in person by the research clinician or nutritionist in Kiswahili or English.

Nutritional and dietary assessment

All children will be evaluated by standard anthropometrics including weight, height and MUAC (table 1).[26 27] A dietary assessment will be performed at 1 month (T2), 2 months (T4) and 3 months (T5). The research clinician or nutritionist will administer a guided questionnaire together with the parents or legal guardians of the patient. The questionnaire will be provided in Kiswahili or English.

24-hour dietary recall

A 24-hours dietary recall, based on Food and Agriculture Organization (FAO)/WHO Guidelines for Measuring Household and Individual Dietary Diversity (2011) extracted from the national nutritional guidelines, is used.[30] These validated tools enable standardised evaluation of nutrient intake and diet quality among study participants and will be taken at 2 months (T4) after diagnosis. The research clinician or nutritionist will administer a guided questionnaire together with the parents or legal guardians of the patient. The questionnaire will be provided in Kiswahili or English.

Conclusion form (6-month follow-up after diagnosis)

The participant's status (dead, alive, lost to follow-up) will be assessed on day 180 of study follow-up. If participants are not in follow-up at this time point, the reasons for non-completion are identified. Details regarding the circumstances of death or withdrawal will be documented through the patient file or verbal autopsy when not available. Collected symptom and circumstance data will be coded by the study team according to the International Classification of Diseases, 11th Revision (ICD-11), enabling systematic and comparable cause-of-death assignment across the study population. For those remaining in the study at day 180, their status will be determined based on the hospital visit at that time or through confirmation via telephone contact with family or guardians.

Sample size

The patient recruitment period will be approximately 18 months. The unit admits approximately 300 new patients with cancer a year, 75% of whom are expected to be treated with curative intent. With this recruitment period, we estimate that we shall include approximately 150 patients, while considering that not all eligible patients will participate and that some patients might drop out. Although a strict sample size calculation is not required for this type of study, the chosen convenience sample size is adequate to achieve the study objectives, allowing for descriptive analyses and exploration of associations between nutritional status and infection outcomes while maintaining feasibility within the clinical setting. With an expected 150 participants and an anticipated 6-month mortality of 25–30%, yielding approximately 40 primary endpoints, we can reliably examine 3–4 key determinants in multivariable models following the 10 events per variable guideline.

Data management

All quantitative data will be recorded in CRFs and subsequently entered into a secure, password-protected CASTOR database by a trained research assistant.[31] Access will be restricted to authorised study personnel only. Microbiology test results, analysed at the MTRH microbiology lab, will be entered in the CASTOR database. To ensure data quality, regular consistency checks will be performed by a data manager, and queries will be resolved by the study team.

Data will be handled in line with the Institutional Research and Ethics Committee (IREC) and the principles of the Declaration of Helsinki. Agreements about access to and ownership of data among the affiliated research institutes were formalised in research collaboration agreements. Following data analysis and publication, data will be stored in a password-protected drive for a minimum of 7 years. Only de-identified data will be shared outside the study team, and any data sharing will be subject to ethical and institutional approval.

Data analysis

Quantitative clinical data will be cleaned and imported into STATA V.16.0/R for analysis, with oversight from a local data manager and statistician at the Trial and Data Centre of the Princess Máxima Centre. Statistical significance is defined as a $p<0.05$. Effect sizes will be reported as ORs or hazard ratios.

Descriptive statistics will summarise baseline characteristics, nutritional status and prevalence of infection including bacterial and fungal colonisation, intestinal parasitic infections at baseline and prevalence of FN during treatment.

Associations between clinical characteristics and outcomes will be examined using chi-square tests and logistic regression models. Time-to-event outcomes, including 6-month mortality and incidence and time of first FN episode, will be assessed using Kaplan–Meier survival curves and Cox proportional hazards regression. Dietary intake across nutritional status groups will be compared using ANOVA, and linear regression models will explore associations between nutritional status, dietary achievements and treatment outcomes.

Qualitative data from parents or legal guardians' semi-structured survey will undergo thematic analysis following Braun and Clarke's six-step framework.[32] An inductive coding approach will identify themes related to health literacy, nutritional practices and infection prevention.

Two researchers will independently code the data. Data will be managed using NVivo V.14. Quantitative associations between parents' or legal guardians' health literacy and clinical or infection-related outcomes will be assessed using chi-square tests.

Microbiome analyses will be treated as exploratory endpoints. Stool samples collected at baseline and at 3 months will be stored for future microbiome sequencing and analysis. Because microbiome data require specialised analytical approaches (eg, measures of alpha and beta diversity, taxonomic composition and functional profiling), a detailed microbiome-specific analysis plan will be developed and published separately. Therefore, the present protocol does not outline specific statistical methods for microbiome analysis.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the ethical principles of the Declaration of Helsinki and relevant national and institutional guidelines. Ethical approval has been obtained from the IREC of MTRH (FAN: 0004674; 14 February 2024) and the Clinical Research Committee of the Princess Máxima Centre for Paediatric Oncology (PMC CRC 2023–044; 6 February 2024).

This study includes minimal risks associated with participation. Samples taken (serum samples in case of FN, stool samples for microbiome analysis and rectal surveillance cultures) might induce slight inconvenience. The study team will ensure that the participation of the subjects does not interfere with their medical care. Monthly meetings with the coordinating investigators, nutritionist and research assistant will be held to oversee study conduct, including patient recruitment, data collection and adherence to the protocol. All study data will be handled in accordance with approved procedures to safeguard confidentiality and participant welfare.

All data will be de-identified and assigned unique identifiers. Physical and electronic records will be stored securely, with access restricted to authorised personnel. Biological samples will be stored for up to 5 years in accordance with institutional policies to allow for potential future analyses approved by ethics committees.

While there may be no direct benefit to individual participants, findings will contribute to improved infection management and nutritional care, for example, by informing antibiotic selection during neutropenic fever episodes and performing regular nutritional assessments. This study will also have a public health benefit, as we will be able to develop an evidence-based supportive care guideline for children in Eldoret, Kenya, which might be applicable for other childhood cancer departments in sub-Saharan Africa.

Findings from the CARE study will be disseminated through multiple channels. Academic dissemination will include publication in peer-reviewed open access journals and presentations at national and international conferences on paediatric oncology and global health. Locally, results will be shared with clinicians and hospital administrators at MTRH through departmental meetings and clinical workshops. For patients, families and caregivers, we will provide information on the study's key findings and implications in a layman's language.

DISCUSSION

This protocol outlines the CARE study, a prospective cohort study on supportive care among paediatric oncology patients in Western Kenya treated with a curative intent. Despite growing recognition that malnutrition and infections contribute substantially to TRM in low-resource settings, prospective data remain scarce. By integrating clinical, nutritional and microbiological assessments and caregiver perspectives, this study aims to identify modifiable nutritional and infection-related determinants of clinical outcomes at 6 months in children with cancer.

Existing evidence shows the complexity of undernutrition as well as infection-related outcomes in paediatric oncology in LMICs like Kenya. A recent systematic review on undernutrition among children newly diagnosed with cancer in an LMIC setting showed prevalence of up to 80%.[17] Undernutrition was significantly associated with inferior overall survival.[17] The complexity of infection-related outcomes among paediatric oncology patients in Kenya is shown by outcomes of febrile episodes in children with cancer, showing a low total bloodstream infection (BSI) incidence of only 6%, likely confounded by the fact that most blood cultures (94%) were obtained after antibiotic administration.[33] On the other hand, a cross-sectional study from Kenya analysing bacterial isolates from blood cultures during FN reported 28% positivity, predominantly due to gram-positive microorganisms.[34] Findings are comparable to global results, as Gram-positive cocci are described as the most common pathogen found in FN. Gram-negative organisms are less common but can cause a more fulminant clinical course due to the presence of endotoxins and other virulence factors.[35] These contrasting results highlight the need for prospective, systematic data collection on infection epidemiology, sampling practices and clinical outcomes in this setting.

The CARE study also incorporates an assessment of dietary adequacy and caregiver knowledge, attitudes and practices related to both nutrition and infection prevention. These dimensions are particularly important in low-resource settings, where caregiver understanding, food insecurity and household infection risks can influence treatment tolerance and survival. Collecting these data prospectively will provide essential context for designing feasible, patient-centred interventions and for strengthening supportive care guidelines.

This study has several anticipated challenges. Variability in medical record completeness, delays in obtaining cultures before antibiotic administration and potential loss to follow-up may limit data completeness or introduce

bias. To mitigate these risks, the protocol includes standardised data collection procedures, monthly monitoring meetings and use of both paper CRFs and a secure electronic database.

Despite these limitations, the CARE study will generate critical evidence to inform supportive care priorities in paediatric oncology in Kenya and other similar low-resource settings. By characterising nutritional status, infection patterns and caregiver-related factors in a prospective manner, the study will provide a foundation for developing locally relevant, evidence-based interventions aimed at reducing treatment-related morbidity and mortality.

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REFERENCES

1 Ward ZJ, Yeh JM, Bhakta N, *et al*. Estimating the total incidence of global childhood cancer: a simulation-based analysis. *Lancet Oncol* 2019;20:483–93.
2 Ward E, DeSantis C, Robbins A, *et al*. Childhood and adolescent cancer statistics, 2014. *CA A Cancer J Clinicians* 2014;64:83–103.
3 Lam CG, Howard SC, Bouffet E, *et al*. Science and health for all children with cancer. *Science* 2019;363:1182–6.
4 WHO. The global initiative for childhood cancer: increasing access, advancing quality. 2018. Available: https://www.who.int/initiatives/the-global-initiative-for-childhood-cancer#:~:text=The%20World%20Health%20Organization%27s%20Global,reducing%20their%20suffering%20and%20improving
5 Howard SC, Zaidi A, Cao X, *et al*. The My Child Matters programme: effect of public-private partnerships on paediatric cancer care in low-income and middle-income countries. *Lancet Oncol* 2018;19:e252–66.
6 Loeffen EAH, Kremer LCM, Mulder RL, *et al*. The importance of evidence-based supportive care practice guidelines in childhood cancer-a plea for their development and implementation. *Support Care Cancer* 2017;25:1121–5.
7 Israels T, Afungchwi GM, Klootwijk L, *et al*. Fever and neutropenia outcomes and areas for intervention: A report from SUCCOUR - Supportive Care for Children with Cancer in Africa. *Pediatr Blood Cancer* 2021;68:e29224.
8 Hafez HA, Soliaman RM, Bilal D, *et al*. Early Deaths in Pediatric Acute Leukemia: A Major Challenge in Developing Countries. *J Pediatr Hematol Oncol* 2019;41:261–6.
9 Sung L, Aplenc R, Alonzo TA, *et al*. Effectiveness of supportive care measures to reduce infections in pediatric AML: a report from the Children's Oncology Group. *Blood* 2013;121:3573–7.
10 Walson JL, Berkley JA. The impact of malnutrition on childhood infections. *Curr Opin Infect Dis* 2018;31:231–6.
11 Triarico S, Rinninella E, Cintoni M, *et al*. Impact of malnutrition on survival and infections among pediatric patients with cancer: a retrospective study. *Eur Rev Med Pharmacol Sci* 2019;23:17009:1165–75:.
12 Israëls T, van de Wetering MD, Hesseling P, *et al*. Malnutrition and neutropenia in children treated for burkitt lymphoma in Malawi. *Pediatric Blood & Cancer* 2009;53:47–52.
13 Rogers PC, Barr RD. The relevance of nutrition to pediatric oncology: A cancer control perspective. *Pediatric Blood & Cancer* 2020;67:e28213.
14 Diallo AH, Sayeem Bin Shahid ASM, Khan AF, *et al*. Childhood mortality during and after acute illness in Africa and South Asia: a prospective cohort study. *Lancet Glob Health* 2022;10:e673–84.
15 Huibers MHW, Manda G, Silverstein A, *et al*. The Burden of Malnutrition in Childhood Cancer in Malawi - Risk Regardless of Age. *Nutr Cancer* 2022;74:3322–8.
16 Barr RD, Stevens MCG. The influence of nutrition on clinical outcomes in children with cancer. *Pediatric Blood & Cancer* 2020;67:e28117.
17 Makamo N, Schoon S, Ozuah N, *et al*. Prevalence of undernutrition in children with cancer in low-income and middle-income countries: a systematic review. *BMJ Glob Health* 2025;10:e019345.
18 Viani K, Trehan A, Manzoli B, *et al*. Assessment of nutritional status in children with cancer: a narrative review. *Pediatric Blood & Cancer* 2020;67:e28211.
19 Ehrlich BS, McNeil MJ, Pham LTD, *et al*. Treatment-related mortality in children with cancer in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Oncol* 2023;24:967–77.

20 Todurkar N, Trehan A, Bansal D. Time to antibiotic administration in children with febrile neutropenia: report from a low middle-income country. *Indian J Med Res* 2021;154:615–22.
21 Nessle CN, Njuguna F, Dettinger J, *et al*. Barriers to and facilitators of effective management of fever episodes in hospitalised Kenyan children with cancer: protocol for convergent mixed methods study. *BMJ Open* 2023;13:e078124.
22 Lehrnbecher T, Robinson PD, Ammann RA, *et al*. Guideline for the Management of Fever and Neutropenia in Pediatric Patients With Cancer and Hematopoietic Cell Transplantation Recipients: 2023 Update. *J Clin Oncol* 2023;41:1774–85.
23 Biswal M, Angrup A, Kanaujia R. Role of surveillance cultures in infection control. *Indian J Med Microbiol* 2020;38:277–83.
24 von Elm E, Altman DG, Egger M, *et al*. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *The Lancet* 2007;370:1453–7.
25 EDC C. Castor electronic data capture. 2019. Available: https://castoredc.com
26 Organization WH. WHO guideline on the prevention and management of wasting and nutritional oedema (acute malnutrition) in infants and children under 5 years. 2023.
27 Mramba L, Ngari M, Mwangome M, *et al*. A growth reference for mid upper arm circumference for age among school age children and adolescents, and validation for mortality: growth curve construction and longitudinal cohort study. *BMJ* 2017;358:j3423.
28 Technologies ON. Rapid metagenomic sequencing for surveillance of bacterial, fungal and viral pathogens using sqk-rpb114.24 know-how document. 2025. Available: https://nanoporetech.com/document/requirements/rapid-metagenomic-sequencing-for-surveillance-of-bacterial-fungal-and-viral-pathogens-using-sqk-rpb114-24-know-how-document
29 Baden L, Bensinger W, Angarone M. NCCN clinical practice guidelines in oncology: prevention and treatment of cancer-related infections. *Version* 2014;2:882–913.
30 Kennedy G, Ballard T, Dop M. Guidelines for measuring household and individual dietary diversity: FAO. 2011.
31 CASTOR. 2024 Available: https://www.castoredc.com
32 Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3:77–101.
33 Kipchumba S, Busby K, Njenga D, *et al*. Severe outcomes and risk factors of non-neutropenic fever episodes in hospitalized children with cancer in Kenya. *Front Oncol* 2025;15:1575714.
34 Kipchumba SK, Njuguna FM, Nyandiko WM. Bacterial Isolates and Characteristics of Children With Febrile Neutropenia on Treatment for Cancer at a Tertiary Hospital in Western Kenya. *JCO Glob Oncol* 2024;10:e2300313.
35 Davis K, Wilson S. Febrile neutropenia in paediatric oncology. *Paediatr Child Health (Oxford)* 2020;30:93–7.