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Original article

Implemented nutritional intervention algorithm in pediatric oncology compared to standard nutritional supportive care outcomes

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SUMMARY

Aim: To implement a childhood cancer-specific nutritional algorithm adapted for the South African context for interventions at time-set intervals to evaluate differences in the nutritional status of newly diagnosed children with cancer.
Method: Children with newly diagnosed cancer were assessed for stunting, underweight, wasting, and moderate to severe malnutrition (MUAC < -2SD and < - 3 SD) between October 2018 and December 2020 in a longitudinal nutritional assessment study with monthly assessments. Two pediatric oncology units (POUs) served as the intervention group that implemented the nutritional algorithm-directed intervention and three other POUs formed the control group that implemented standard supportive nutritional care.
Results: A total of 320 patients were enrolled with a median age of 6.1 years (range three months to 15.3 years) and a male-to-female ratio of 1.1:1. The malnourished patients in the intervention group showed significant improvement at six months after diagnosis for stunting ($P = 0.028$), underweight ($P < 0.001$), and wasting until month five ($P = 0.014$). The improvements in the control group were not significant. Moderate acute malnutrition (MAM) significantly improved over the first six months of cancer treatment in the intervention group ($P < 0.001$), while MAM improvement was only significant in the control group for the children under five years of age ($P = 0.004$). The difference in mean z-scores over time for the nutritional parameters between the intervention and control groups was insignificant.

Abbreviations: BAZ, Body mass index for age; CI, Confidence interval; GHN NWG, Global Health Network Nutrition Working Group; HAZ, Height for age; LMIC, Low and middle-income country; MAM, Moderate acute malnutrition; MUAC, Mid-upper arm circumference; MUAC/A, Mid-upper arm circumference for age; NG, Nasogastric; POU, Pediatric oncology unit; SAM, Severe acute malnutrition; SD, Standard deviation; SIOP, International Society of Paediatric Oncology; WAZ, Weight for age.

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Conclusion: We established that the nutritional algorithm adapted for South Africa as an intervention tool for childhood cancer assisted in optimizing nutritional interventions and improved nutritional outcomes over the first six months of cancer treatment.
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1. Introduction

The primary goal of nutritional support for children with cancer is to ensure an optimal nutritional status [1], which is crucial in low- and middle-income countries (LMICs), as malnutrition at childhood cancer diagnosis is common and can affect the disease outcome [2]. Dietary counseling and appropriate intervention should ensure adequate macronutrient and micronutrient intake [3], to promote age-appropriate growth -and development [3,4], remediate and prevent the development of malnutrition or worsening thereof and potentially improve cancer outcomes [3,5].

The severity of treatment-related toxicity, and mortality, and treatment abandonment is higher among malnourished children than well-nourished children [6]. There is documented improved five-year overall survival for children with acute lymphoblastic leukemia whose nutritional status is improved during treatment [7].

Algorithms are developed as a tool to improve decision-making and are used in the clinical setting as a cancer-screening tool [8]. In Canada, a pediatric intensive unit a multidisciplinary-developed algorithm improved patient's nutritional support [9]. The utilization of a decision-aid algorithm or timely nutritional interventions is recommended [6]. The International Society of Paediatric Oncology (SIOP) and the Global Health Network (GHN) Nutrition Working Group (NWG) have developed such a consensus-derived nutritional intervention algorithm for LMICs in the context of the resource limitations in the LMIC setting (Supplementary Fig. 1). The goal is to harmonize care among pediatric oncology units (POUs) in an LMIC and to provide a guide for proactive nutritional care [10]. This algorithm has been validated in children with cancer in India (2019); improved nutritional status resulted from using the algorithm for a six-month period [11]. The SIOP GHN NWG algorithm was therefore adapted for the South African context, with specific nutritional guidelines based on the standard deviation (SD) of the mid-upper arm circumference (MUAC) for age (MUAC/A). Our algorithm included common nutritional interventions utilized in South Africa, such as industrialized supplements, enteral nutrition, and total parenteral nutrition in both the hospital and home settings.

This study investigated the efficacy of implementing the nutritional algorithm adapted for South Africa in newly diagnosed children with cancer to improve the nutritional status among undernourished children and maintain the nutritional status of well-nourished children undergoing treatment in South Africa. This algorithm was implemented in two POUs (intervention group) and compared to the standard nutritional supportive care provided at three other POUs (control group) during the first six months of cancer treatment.

2. Methods

2.1. Study design

This longitudinal comparative cohort study was performed between October 2018 and December 2020 at five POUs in South Africa. Two POUs (Steve Biko Academic Hospital in Gauteng and Tygerberg Hospital in the Western Cape) implemented the nutritional algorithm as the intervention group. The other three participating POUs (Chris Hani Baragwanath Hospital in Gauteng, Universitas Academic Hospital in the Free State, and Frere Hospital in the Eastern Cape) served as the control group using standard nutritional care practices. Nutritional assessments occurred monthly from diagnosis to the sixth month of treatment.

2.2. Clinical data

Prospective data collection included the clinical data (disease group and diagnosis) and demographic data (patient's sex, age, and province of residence) obtained from the medical charts and entered into the study database monthly. Children were grouped according to age; younger children were under five, years while older children were defined as five years and older.

Anthropometry (weight, height, and MUAC) was assessed within 72 h after cancer diagnosis; whilst children were barefoot and wearing light clothing. Body weight and height (older children) were measured with a calibrated column SECA weight scale with an attached height meter (the SECA 786 and SECA 220 model). Weight was recorded to the nearest 100 g and length to the nearest 0.1 cm. Children stood up straight, facing forward with their backs against the height meter. A calibrated SECA electronic baby scale with a length meter was used to assess children younger than two years (SECA 334 model). The UNICEF color band was used to measure MUAC in children under five [12], and the MUAC measuring band was used to measure MUAC in older children [13]. To measure MUAC, the child's arm was flexed toward the chest at a 90° angle. The investigator determined the midpoint of the arm, between the acromion and olecranon, the arm was relaxed, and the palm was facing towards the body; the MUAC was measured at the midpoint [14].

The WHO Anthro program was utilized to determine z-scores for height for age (HAZ), weight for age (WAZ), body mass index for age (BAZ), and MUAC/A for children younger than five years [15]. MUAC for children older than five was plotted on the Mramba et al. growth charts [16]; the absolute z-scores for MUAC/A were determined on Peditools [17] and divided into categories. Undernutrition was defined as severe if stunting was HAZ < −3 SD; underweight as WAZ < - 3 SD, wasting as BAZ < −3 SD, whilst stunting was HAZ < −2 SD, underweight as WAZ < −2 SD and wasting as BAZ < −2 SD [18]. Severe acute malnutrition (SAM) as MUAC/A < -3 SD; moderate acute malnutrition (MAM) was defined as MUAC/A < −2 SD [12].

2.3. Nutritional algorithm

Based on the SIOP GHN NWG algorithm (Supplementary Fig. 1) the South African nutritional intervention algorithm was adjusted considering the standard nutritional supportive care for children diagnosed with and treated for cancer (Fig. 1). The MUAC/A z-score was used to identify which children should receive nutritional supplements for home care with guidelines on the content and amount. The algorithm intervention depended on the MUAC/A z-score; it also included specific guidelines regarding the percentage provision of energy and/or protein requirements (in the form of the

percentage of the requirements) according to the patient's MUAC/A z-score with industrialized supplements, enteral nutrition, and/or total parenteral nutrition in the hospital.

All patients received the standardized high-energy, high-protein hospital diet according to age; additional nutritional supplementation was received if indicated. The nutritional interventions in the intervention group were implemented according to the MUAC/A z-score at the time of assessment, as follows (Fig. 1).

1. **Childre**n with MUAC for age < −3 SD were admitted to the POU, and 24-h nasogastric (NG) enteral feeds were initiated to reach the goal of feeds providing 70–100% of protein requirements. If the patient's caregivers refused an NG tube, oral supplementation was provided with a syringe.
2. Children with MUAC/A < −2 SD were admitted to the POU if medically indicated, and overnight NG enteral feeds (12–14 h feeds) were initiated to reach the goal of 40–60% of the protein requirements. Oral intake was actively encouraged, but if patients did not reach 100% of the requirements with oral intake, the enteral feeds were increased to 100% of the patient's requirements. If not admitted, patients received supplements to take home to reach 50% of the protein requirements, plus a take-home meal plan to reach 100% of the requirements.
3. Children with MUAC/A < −1 SD did not receive nutritional supplements at the POU or at home. Still, if specific criteria were applicable according to the algorithm, as seen in Fig. 1, patients did receive supplementation.

The control group's nutritional support included the existing nutritional protocol of the control POUs, including nutritional supplements and NG enteral feeds given in the hospital or at home. In both intervention group POUs, parenteral nutrition was administered if necessary (e.g., in case of neutropenic enterocolitis or pancreatitis or post-abdominal surgery).

All parents or caregivers received continuous nutritional education regarding healthy meals and food choices. The education was based on the My Plate model, which is similar to the South African paediatric food-based guidelines [19], but the food groups were explained in the form of a plate to visualize a healthy meal, which the children could understand [20] Nutritional advice sheets were given to take home. The interventions and anthropometric data were captured monthly on a REDCAP database.

2.4. Statistical analysis

All data were analyzed using STATA version 17 (STATA Corp. Texas, USA). A repeated nutritional assessment measures analysis was done monthly using a multilevel mixed-effects regression model comparing mean Z-scores in the two intervention group POUs for the first six months after diagnosis according to the classification of malnutrition based on z-scores for stunting, underweight, wasting, SAM, and MAM. Descriptive statistics such as: frequencies, percentages, means, standard deviations, and medians were calculated for each month by intervention or control group depending on the z-score at diagnosis. Chi-square tests determined the association between sex, the age groups, and disease groups at diagnosis. At the same time, a t-test was used to compare the mean age between the intervention and control groups. The severe to moderately malnourished children (<−3 and < −2 SD) were grouped together as the malnourished group for the time trend in

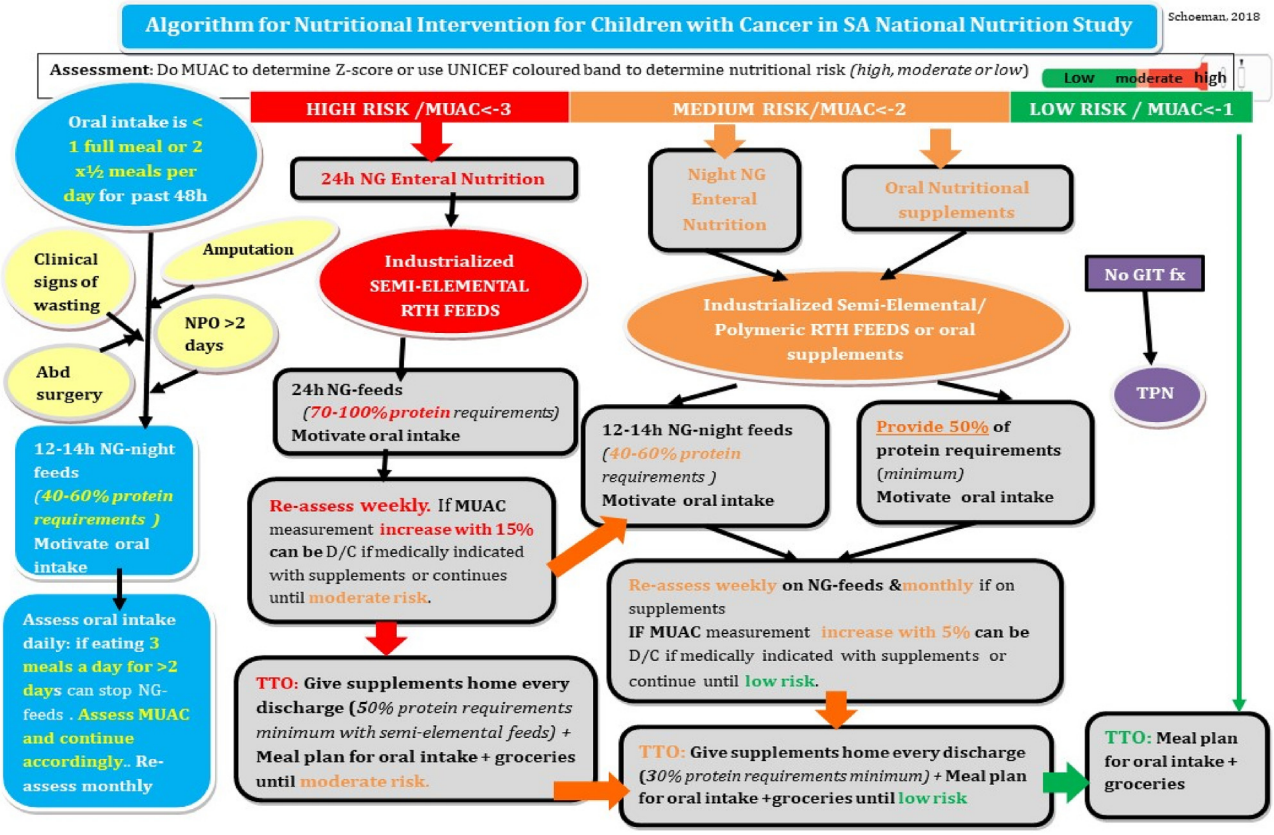


Fig. 1. The South African adopted nutritional algorithm for the intervention group according to mid-upper arm circumference for age.

the mixed-effects regression analysis. Margins plot graphs were used to visualize the improvement trend over time in the two groups if the z-score at diagnosis was < −2 SD for stunting (HAZ), underweight (WAZ), wasting (BAZ), and MAM (MUAC/A) over time. A significance level of $P < 0.05$ was applied.

2.5. Ethics approval

Parents/legal guardians provided written informed consent for each child before enrolment in the study in the language of their choice (one of the following: English, Afrikaans, Zulu, Tsonga, Tswana, Sotho, Sepedi or Xhosa). Written assent was elicited if the child was older than seven years. The following institutions provided ethics approval: Stellenbosch University (Health Research Ethics Committee, Faculty of Medicine and Health Sciences [S18/04/050]), University of Pretoria (Research Ethics Committee, [281/2018]), University of the Witwatersrand (Human Research Ethics Committee [M190485]), University of the Free State (Health Sciences Research Ethics Committee [UFS-HSD2019/0445/3007]), and Frere Hospital (Ethics Committee [CMHREC 001/19]). The national and provincial health departments approved the conduct of the study in the public sector.

3. Results

3.1. Demographics

A total of 320 children were prospectively enrolled between October 2018 and December 2020. The intervention group recruited 72% (n = 229) versus 28% in the control group (n = 91). The two groups had no significant differences in demographics or diagnosis. More than half of the children had been diagnosed with a solid tumor in both groups, 55.5% in the intervention group and 57.1% in the control group. The prevalence of hematological malignancies was 44.5% in the intervention group compared to 42.9% in the control group (Table 1).

3.2. Nutritional status at diagnosis

The children in the intervention group had a higher prevalence of undernutrition (stunting 17%, underweight 8%, and wasting 11%) compared to the control group (stunting 12%, underweight 8%, and wasting 9%), although the difference was not significant ($P = 0.266$, $P = 0.980$, and $P = 0.495$, respectively). The intervention group had more children with MAM in both age groups, namely children younger than five and those five years and older (14% and 37%) compared to the control group (14% and 23%); which was not significant (Table 1).

3.3. Nutritional interventions

During the first six months of cancer treatment, the patients in the intervention group were more likely to receive NG enteral feeds as 12% (n = 28/229) received 24-h continuous feeds compared to 1% (n = 1/91) in the control group, which was not significant ($P = 0.850$). A further 33% (n = 75/229) received 12–14 h continuous overnight feeds in the intervention group compared to 15% (n = 14/91) in the control group ($P = 0.456$). More children (125%; n = 288/229) in the intervention group received oral commercial and/or additional supplements during their hospital stay compared to the control group (65%; n = 14/91), which was significant ($P < 0.001$). A minority received parenteral nutrition over the first six months of cancer treatment, only 12% (n = 28/229) in the intervention group and 2% (n = 1/91) in the control group ($P = 0.735$).

3.4. The prevalence of severe- and moderate malnutrition during the first six months of treatment

In the intervention group, the number of children with severe stunting had decreased from 5% (n = 12) to 2% (n = 4) at six months post-diagnosis, with a similar trend observed for patients who were severely underweight and wasted. The prevalence of SAM in patients (five years and older) had decreased from 6% (n = 7) to 1% (n = 1), while the prevalence of SAM in children (under five years) had decreased from 6% (n = 6) to zero at six months post-diagnosis (Supplementary Table S1).

In contrast, in the control group, there were two children with severe stunting, which had decreased to only one after six months of treatment. Similar results were seen for patients with severe underweight and wasting. Arm anthropometry indicated only two patients with SAM, and both improved during the six months (Supplementary Table S1).

The number of patients classified as stunted in the intervention group (6%; n = 14) decreased to 1% (n = 1) at six months post-diagnosis. The number of underweight children (6%; n = 14) decreased to 1% (n = 1), as had the children with wasting, from 11% (n = 26) to 5% (n = 10). The number of children five years and older with MAM had decreased from 6% (n = 15) to 2% (n = 2), while the number of younger children with MAM had decreased from 14%

Table 1
Demographics of the total population.

Patients enrolled (n = 320)		Intervention group	Control group	*P* - value
		% (N)	% (N)	
Total		71.6 (229)	28.4 (91)	
Sex	Males	54.2 (124)	48.4 (44)	0.349
	Females	45.9 (105)	51.7 (47)	
Age in years	Median (IQR)	5.3 (2.6–10)	5.1 (2.4–8.4)	0.444
	Mean (Range)	6.3 (0.3–15.7)	5.6 (0.3–14.9)	
Age groups	<5 yr	47.6 (109)	49.5 (45)	0.765
	≥5 yr	52.4 (120)	50.5 (46)	
Disease group	Hematological malignancy	44.5 (102)	42.9 (39)	0.784
	Solid tumor	55.5 (127)	57.1 (52)	
Undernourished patients (<-2 SD)	Stunted	17.1 (39)	12.1 (11)	0.266
	Underweight (n = 248)	8.1 (14/173)	8.0 (6/75)	0.980
	Wasted	11.4 (26)	8.8 (8)	0.495
	MAM under five (n = 152)	13.8 (15/109)	14 (6/43)	0.975
	MAM five years and older (n = 162)	37 (44/119)	23.3 (10/43)	0.102

IQR: interquartile range; SD: standard deviation; MAM: moderate acute malnourished (according to MUAC for age).

(n = 15) to only 2% (n = 2) at six months post diagnosis (Supplementary Table S2).

The number of patients with stunting in the control group had decreased from 12% (n = 11) to 6% (n = 5) at six-months post-diagnosis, with a similar trend observed for the number of children who were underweight (7%; n = 6 vs. 3%; n = 2) and wasted (9%; n = 8 vs. 3%; n = 2). The number of children five years and older with MAM had decreased from 13% (n = 6) to 2% (n = 1), while the prevalence of MAM in younger children (under five years) was the same at the end of six months of treatment (Supplementary Table S2).

3.5. The difference in nutritional status of malnourished children with time trend during the first six months after diagnosis in the different groups compared to the admission diagnosis data

The intervention group showed improved nutritional status as the number of children with stunting had decreased significantly at six months post-diagnosis (HAZ coefficient 0.5; 95% CI 0.1, 0.9; $P = 0.028$). Patients' weight improved over time as the number of patients with underweight had decreased after six months of treatment (WAZ coefficient 1.3; 95% CI 0.5, 2.0; $P < 0.001$), and BMI had improved after five months of treatment (BAZ coefficient 0.9; 95% CI 0.2, 1.6; $P = 0.014$) (Table 2). MAM had also improved significantly at six months post-diagnosis for both age groups, namely for children under five years of age (MUAC coefficient 1.9; 95% CI 1.2, 2.8; $P < 0.001$) and for children five years and older (MUAC coefficient 1.1; 95% CI 0.6, 1.7; $P < 0.001$) (Table 2).

In the control group, the children's nutritional status from diagnosis to six months post-diagnosis improved, but not significantly: stunting (HAZ coefficient 0.2; 95% CI -0.2, 0.5; $P = 0.372$), underweight (WAZ coefficient 0.6; 95% CI -0.3, 1.5; $P = 0.182$), or wasting (BAZ coefficient 0.9; 95% CI -0.4, 2.1; $P = 0.182$). Children younger than five years of age with MAM had improved significantly (MUAC coefficient 1.7; 95% CI 0.6, 2.9; $P = 0.004$), while in children five years and older, improvement was not significant after six months of treatment (MUAC coefficient 1.0; 95% CI -1.3, 3.4; $P = 0.394$) (Table 2).

3.6. Predicted margins for undernourished patients (≤−2 SD) during the first six months of treatment

Figs. 2 and 3 display the difference in the time trend effect of the intervention- and control group separately according to the age groups using marginsplot graphs of the predicted margins of the mean z-scores with their 95% CI for comparison between the groups. Children from both age groups (under five and five and older) classified with MAM (MUAC/A < -2) in the intervention group showed significant improvement at six-months post-diagnosis (respectively $P < 0.001$) (Figs. 2 and 3 and Table 2). Stunting (HAZ < -2SD) for the intervention group had decreased significantly at six months post-diagnosis ($P = 0.028$) (Supplementary Fig. S2).

In the control group, children under five years of age classified with MAM (MUAC/a < −2) showed significant improvement in MUAC measurements six-months post-diagnosis ($P = 0.004$) (Fig. 2 and Table 2). The predicted margins for stunting showed a reduction that was not significant ($P = 0.356$) (Supplementary Fig. 2 and Table 2). No other significant results were reported (Figs. 2 and 3).

The multilevel mixed-effect model compared the difference between the intervention and control groups for the difference in the mean z-scores for stunting, underweight, and wasting for the two groups at six months post-diagnosis, and this was insignificant. The same was seen for MAM in both age groups (Supplementary Fig. S5).

Our study demonstrated an improved nutritional status as the severity of children with stunting, wasting, and MAM improved significantly in the intervention group but not in the control group, proving the algorithm's success as a nutrition intervention tool.

4. Discussion

Nutritional interventions during cancer treatment aim to improve nutritional status and survival.

Our study has proven that the nutritional algorithm adapted for South Africa improved nutritional status among undernourished children with cancer undergoing treatment.

4.1. Nutritional support during cancer treatment

Deterioration of children's nutritional status during cancer treatment commonly occurs in LMIC [21], and malnutrition at cancer diagnosis and during cancer treatment is a modifiable prognostic variable [22], as was seen in the intervention group in our study. Nutritional support should include a diet rich in energy and protein in the hospital and at home. In LMICs, additional foods or supplements may be needed to provide sufficient calories, protein, and micronutrients [23] to improve nutritional status [6].

Patients with Burkitt lymphoma from a Cameroon study (2011) received additional oral supplements with a protein portion despite their age for the first 28 days of treatment, which decreased MAM from 16% to 10% on day 28 of the study [24], while our intervention group received a percentage of a child's protein needs. In severely malnourished children in Guatemala receiving nutritional intervention (education, oral- or enteral supplements, or parenteral nutrition) nutritional status was improved to a well-nourished state six months after diagnosis [7]. Similar findings were seen in a retrospective study in Pretoria, South Africa (2008), with improved BMI and arm anthropometry after three months of oral nutritional supplements high in protein and/or calories [8]. Children older than 10 diagnosed with cancer in Nicaragua (2017) received a hypercaloric supplement with balanced macronutrients for a maximum of two months, decreasing severe malnutrition from 65.4% to 45.3% [2].

Algerian children who received a fortified diet for six months showed significant linear growth improvement after three months [25]. A study in Malawi gave children an energy-dense, lipid-based, ready-to-use supplement, resulting in catch-up and linear growth in wasted children [7]. The nutritional supplementation of the adapted intervention algorithm given in this study significantly improved nutritional status, as stunting, underweight, and wasting significantly decreased six months after diagnosis. The control groups' nutritional status did improve, but not significantly.

4.2. Nutritional intervention algorithm

A nutritional intervention study in India (n = 50; 2019) investigated the application of the SIOP GHN NW (previously the SIOP-PODC) nutritional algorithm for children under 12 years of age with a control group by using MUAC as an indicator. The children in the algorithm group showed significant improvement in their MUAC increments after three months ($P = 0.020$). Similar results were observed in this study, as the prevalence of MAM significantly decreased in the intervention group over the first six months of cancer treatment, highlighting the need for validated clinical nutritional intervention algorithms.

Using appropriate nutritional algorithms in LMICs for nutritional assessment and nutritional intervention aids in enhancing the clinical care of pediatric cancer patients. This study showed a decrease in the number of children with wasting, underweight, and

Table 2
The differences in nutritional status of malnourished patients (SD < -2) over time trend for the intervention and control group from admission to six months post-diagnosis.

	Intervention group			Control group		
Time period	Coefficient	95% CI	*p*-value	Coefficient	95% CI	*p*-value
Length (HAZ)						
Admission month	Ref			Ref		
Month 1	0.012	[-0.201; 0.224]	0.913	0.138	[-0.134; 0.410]	0.319
Month 2	−0.019	[-0.268; 0.229]	0.878	0.131	[-0.147; 0.408]	0.355
Month 3	0.097	[-0.182; 0.376]	0.496	0.083	[-0.230; 0.397]	0.602
Month 4	0.130	[-0.194; 0.455]	0.433	0.306	[-0.018; 0.631]	0.064
Month 5	0.369	[-0.003; 0.741]	0.052	0.272	[-0.065; 0.610]	0.114
Month 6	0.477	[0.052; 0.902]	0.028	0.172	[-0.205; 0.549]	0.372
Weight (WAZ)						
Admission month	Ref			Ref		
Month 1	0.428	[-0.030; 0.885]	0.067	−0.361	[-0.729; 0.008]	0.055
Month 2	0.289	[-0.206; 0.784]	0.252	0.137	[-0.301; 0.574]	0.541
Month 3	0.686	[0.157; 1.216]	0.011	0.367	[-0.163; 0.899]	0.174
Month 4	0.586	[0.029; 1.143]	0.039	0.431	[-0.208; 1.071]	0.186
Month 5	1.117	[0.513; 1.721]	<0.001	0.698	[-0.097; 1.492]	0.085
Month 6	1.281	[0.539; 2.024]	<0.001	0.598	[-0.280; 1.477]	0.182
Wasting (BAZ)						
Admission month	Ref			Ref		
Month 1	0.293	[-0.045; 0.631]	0.089	−0.068	[-0.800; 0.664]	0.856
Month 2	0.764	[0.349; 1.177]	<0.001	0.558	[-0.198; 1.313]	0.148
Month 3	1.099	[0.594; 1.604]	<0.001	0.841	[-0.062; 1.745]	0.068
Month 4	0.941	[0.330; 1.552]	0.003	0.938	[-0.074; 1.950]	0.069
Month 5	0.908	[0.183; 1.633]	0.014	1.225	[-0.002; 2.451]	0.050
Month 6	0.778	[-0.074; 1.663]	0.074	0.856	[-0.419; 2.132]	0.188
MAM for children under five years, according to MUAC						
Admission month	Ref			Ref		
Month 1	0.796	[0.356; 1.235]	<0.001	−0.114	[-0.818; 0.589]	0.750
Month 2	1.175	[0.690; 1.659]	<0.001	0.735	[-0.007; 1.477]	0.052
Month 3	1.448	[0.908; 1.987]	<0.001	1.167	[0.355; 1.979]	0.005
Month 4	1.848	[1.205; 2.490]	<0.001	1.175	[0.077; 2.273]	0.036
Month 5	1.904	[1.165; 2.643]	<0.001	0.845	[-0.643; 2.333]	0.266
Month 6	1.993	[1.161; 2.825]	<0.001	1.739	[0.561; 2.917]	0.004
MAM for children five years and older, according to MUAC						
Admission month	Ref			Ref		
Month 1	0.450	[0.171; 0.729]	0.002	0.567	[0.004; 1.129]	0.048
Month 2	1.093	[0.776; 1.410]	<0.001	0.375	[-0.462; 1.212]	0.380
Month 3	1.304	[0.941; 1.666]	<0.001	0.736	[-0.455; 1.927]	0.226
Month 4	1.213	[0.798; 1.628]	<0.001	0.405	[-1.256; 2.064]	0.633
Month 5	1.151	[0.676; 1.626]	<0.001	0.785	[-1.256; 2.826]	0.451
Month 6	1.115	[0.567; 1.663]	<0.001	1.031	[-1.338; 3.399]	0.394

Ref: reference data used to compare results; HAZ: height for age indicates stunting; WAZ: weight for age indicates underweight; BAZ: body mass index for age indicates wasting; MAM: moderate acute malnourished (according to MUAC for age).

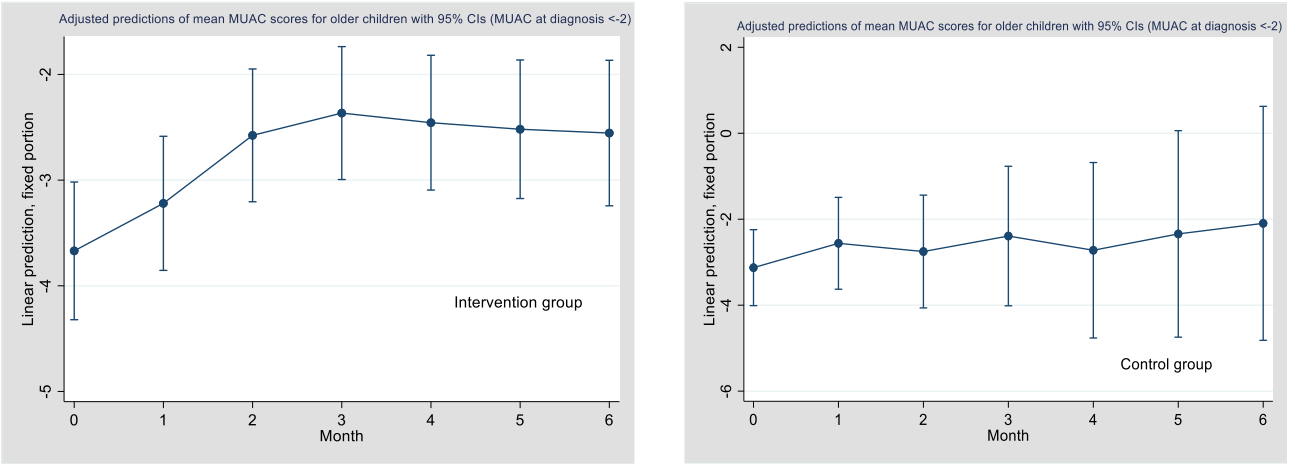


Fig. 2. Adjusted predictions of children younger than five years of age with moderate acute malnutrition (MUAC < -2) with 95% CI based on mean Z-scores during the first six months of treatment in the two groups. MUAC: mid-upper arm circumference. MUAC/A Mid-upper arm circumference for age; CI = Confidence interval.

MAM, which was significant in the intervention group. Even though some of the outcomes were not significant, all POUs participating in our study made appropriate nutritional interventions due to recognizing that malnutrition requires nutritional interventions to

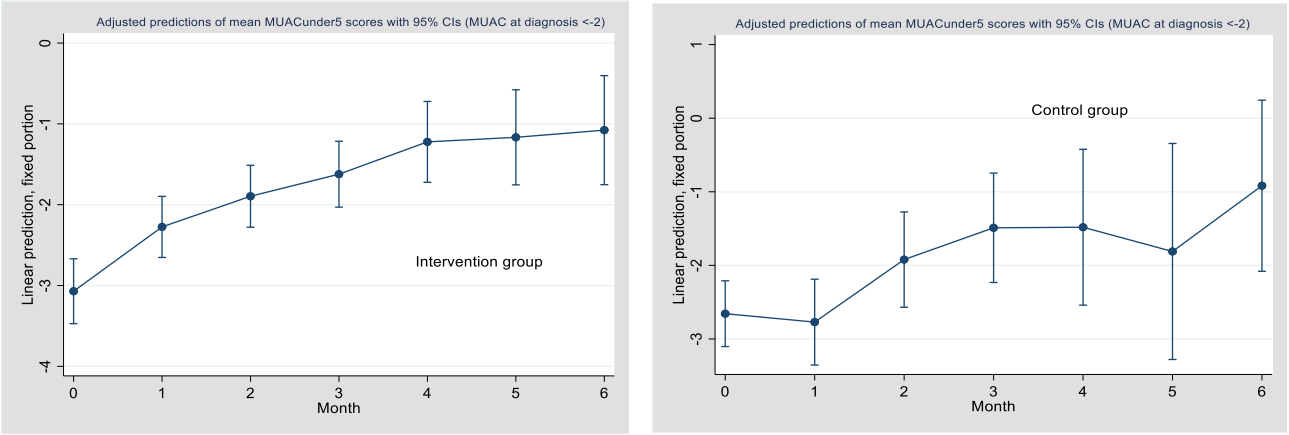


Fig. 3. Adjusted predictions of older children than five years of age with moderate acute malnutrition (MUAC < -2) with 95% CI based on mean Z-scores during the first six months of treatment in the two groups. MUAC/A = mid-upper arm circumference for age; CI = Confidence Interval.

improve outcomes. These reports all justify the importance of longitudinally assessing nutritional status and nutritional intervention when required. Using an evidence-based clinical algorithm improves decision-making and outcomes.

4.3. Strengths and limitations of the study

A notable strength of the study is the six-month anthropometric data collection period in the POUs that made the growth monitoring possible. The limitations were that intervention and control groups were not equally divided, which could have influenced the results, but the groups were similar as no significant difference in demographics or disease was observed between them. There may have been a difference between the two intervention groups' POUs' adherence to the algorithm.The two investigators part of the intervention group, followed a systematic approach in the adaptation of the nutritional algorithm to ensure adherence to the algorithm throughout the study. The enteral products used depended on the availability at the different POUs; therefore, the variability could have affected results, but the interventions depended on the percentage of protein and energy provided and were not product-specific.

5. Conclusion

Nutritional algorithms are helpful for the nutritional management [26] of children with cancer, not only for identifying malnutrition but also for optimizing nutritional intervention [11,26], improving nutritional outcomes [27], and potentially improving cancer outcomes. Nutritional support in LMICs is challenging due to low resources but is essential for children treated for cancer to improve clinical outcomes [2]. Our findings concur with those of previous studies as our intervention group's nutritional status improved significantly during the period with nutritional interventions implemented according to the developed South African nutritional algorithm. MUAC is the best indicator of malnutrition and MAM in children with cancer. The nutritional algorithm in the intervention group significantly decreased the prevalence of MAM in both age groups. The national research platform of the South African Association of Paediatric Haematology and Oncology in South Africa is under development and with much-needed funding, the platform will provide relevant resources needed. The nutritional algorithm will be implemented as the national nutritional intervention in all the POUs in South Africa. Algorithms will likely change as AI gets incorporated in the future.

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Author contributions

Judy Schoeman and Marianna Kruger conceptualized the study; Judy Schoeman, as a Ph.D. student, designed the study, adjusted the SIOP SGH NWG nutritional algorithm and REDcap database, enrolled patients, collected and managed data, transferred data to the World Health Organization Anthro plus program to calculate Z-scores and wrote the manuscript.

Mariana Kruger, Elena Ladas, and Paul Rogers supervised the study, conducted an extensive review, and contributed to and approved the manuscript.

Ilde-Marié Kellerman, Ronelle Uys, Gita Naidu, Biance Rowe, Jan du Plessis, Mariechen Herholdt, Karla Thomas, Barry Vanemmenes, Rema Mathews, Ané Büchner, Fareed E Omar and David T Reynders enrolled patients at different sites, collected data, and critically reviewed the manuscript.

Sandile Ndlovu analyzed the data statistically and critically reviewed the manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2024.08.019.

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