



Original article

Different nutritional screening tools and recommended screening algorithm for pediatric oncology patients



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ARTICLE INFO

Article history:

Received 15 December 2020

Accepted 15 May 2021

Keywords:

Malnutrition
Nutritional risk screening
Risk screening tools
Pediatric cancer
Pediatric oncology

SUMMARY

Background & aims: Cancer is one of the leading causes of death for children; however, appropriate nutritional status can positively affect disease progression and outcome. The aim of this study was to present our self-developed nutritional risk screening method, relate it to another validated tool and to objective bio-impedance measures. We intended to recommend a screening algorithm which can be used in our pediatric oncology facilities.

Methods: We analysed data from 109 pediatric oncology patients (age 3–18) at the 2nd Department of Pediatrics, Semmelweis University between 2017 and 2018. The nutritional status was assessed by the Nutrition screening tool for childhood cancer (SCAN), Nutrition risk screening for pediatric cancer (NRS-PC) our own self-developed screening tool and Bio-impedance analysis (InBody 720 and S10). Classifier properties for low muscle mass measured by Bio-impedance analysis were compared for SCAN and NRS-PC in the overall sample and in the different phases of the disease.

Results: The AUC of 0.67 [95% CI:0.58,0.75] of the SCAN was significantly lower ($Z = -2.46$, $p = 0.014$) than in the case of the NRS-PC (AUC = 0.75 [95% CI:0.67,0.82]), indicating that NRS-PC has better classifier properties to identify children with lower muscle mass. No significant difference was found in the different phases of the disease.

Conclusions: Based on our results, we suggest screening high BMI patients first with NRS-PC. However, in case of low BMI bio-impedance measures provide more precise information on muscle mass and nutritional risk. Further data are needed to decide whether the NRS-PC is sensitive enough in normal BMI patients.

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1. Introduction

Cancer is one of the leading causes of death for children, with approximately 300,000 new cases diagnosed each year among children aged 0–19 years [1,2]. The aim of WHO's Global Initiative for Childhood Cancer, which was announced in 2018 September, is to reach at least 60% survival rate by 2030 [3]. In order to achieve better clinical outcome appropriate nutritional screening and therapy are required as it has been suggested in a number of

previous studies. Similarly to adult cancer patients these studies have revealed that optimising nutritional status of the patients have a positive effect on event free survival, treatment toxicity and quality of life as well [1,2,4]. Since there are no specific clinical nutrition guidelines on how to assess the nutritional state and how to provide adequate nutrition support for pediatric cancer patients, it can be challenging for professionals.

It has been long ascertained that the nutritional status in case of chronic wasting diseases, especially in case of childhood cancer, does influence the outcome of the disease, the course of the therapy, including treatment tolerance and infection risk, not to mention the quality of life and the cost of care [5,6]. It is also known that the tumour itself means a risk for malnutrition, especially in case of children. The most common categories of childhood cancers include leukaemia, brain tumors, lymphomas and solid tumours [7]. Several types of childhood cancers are associated with high

Abbreviations: SCAN, Nutrition screening tool for childhood cancer; NRS-PC, Nutrition risk screening for pediatric cancer; BIA, Bio-impedance analysis; AUC, area under the curve; ROC, receiver-operator characteristics; BMI, Body mass index; NST, Nutrition support team; LBM, Lean body mass.

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nutritional risk (e.g. AML and ALL - prevalence 33%, Brain and spinal tumors - prevalence 26%, Wilm's tumor Stage III and IV. – prevalence 5% Ewing-, and Osteosarcoma - prevalence 4%) since due to aggressive treatment protocols (surgery, stem cell transplant, chemo-, radiation therapy), which patients have to endure, nutritional status declines and thus the risk for malnutrition increases significantly.

It is already known that pediatric oncology patients tend to have lower fat free mass (FFM) at diagnosis and remains low during the treatment [8,9]. The decrease in fat free mass is often accompanied by increased fat mass, which strongly correlates with low or reduced physical activity [8,9]. Relying on BMI alone is misleading since it does not show the underlying body composition changes; therefore assessing the body composition is essential.

In the ESPEN Guideline on nutrition in cancer patients it is highlighted that weight loss and decrease in BMI negatively influence survival. The grading scheme (grades 0–4) predicts overall survival, where 0 means best, 4 means worst prognosis [10]. Another study suggested that 71.7% of the body mass loss was lean body mass (LBM) [11].

Although a number of screening tools have been developed, mainly for general pediatric patients, none of them met the specific requirements of pediatric cancer patients. Later in 2016 SCAN was published [12], the validity of which was tested against pediatric subjective global nutritional assessment (SGNA). In the present study we aimed to validate both SCAN and our self-developed screening tool (NRS-PC) to bio-impedance measures. As it was mentioned above, bio-impedance measures can assess the body composition (including fat free mass and fat mass) and it is of key importance when we decide on the nutrition therapy of children with cancer. The aim of our research was also to create a screening algorithm which would help professionals decide which screening method to use and when to use them.

2. Material and methods

In this study we analysed data from 109 pediatric oncology patients (age 3–18) at the 2nd Department of Pediatrics, Semmelweis University (Budapest, Hungary) who were inpatients between 2017 and 2018. Data were collected during the different phases of the disease: *Diagnosis* (the time between histological sampling and the initiation of cancer treatment – usually a couple of days or maximum few weeks), *Active treatment* (intensive chemotherapy until the last day of intravenous chemotherapy), *Maintenance* (oral low-dose chemotherapy mostly in leukemias and some soft tissue sarcomas) and *Post therapy* (during the follow-up period, after completing all therapies) with the approval of the Hungarian Scientific and Research Ethics Committee (number: 86,748/AOGY2/2016). During the study period, in total 156 bio-impedance measures were done, however some patients were measured more than once, but only if they proceeded to the next phase of the disease. 14 of the patients had a disease relapse, which means the reappearance of their malignancy.

Bio-impedance measures were performed by a clinical dietician who is also member of the nutrition support team. Patients were on an empty stomach; those who were physically fit enough to stand alone for 1.5 min were measured by InBody 720, and those who were not, were measured by InBody S10 in a seated position (InBody Co. Ltd. 13,850 Cerritos Corporate Drive, Unit C, Cerritos, CA 90703).

Recorded parameters were the following: name, age (date of birth), diagnosis, date of the measurement, phase of the disease, weight, height (using standardized scales and stadiometers); calculated parameters were: SCAN score and NRS-PC score. BMI

and body composition parameters including muscle mass and body fat percentage were determined by the InBody devices. BMI, muscle mass and body fat percentage were compared against normal range values. Three categories were set up regarding BMI, muscle mass and body fat mass: low, normal, and high which were also determined and provided by the InBody devices.

Three different screening tools were used to assess the nutritional status of the patients:

SCAN: nutrition screening tool for childhood cancer is a simple and quick tool to identify children with cancer who are at risk of malnutrition. It was validated and published in 2016. SCAN includes six Yes or No questions and if the total score is ≥ 3 it means being at risk of malnutrition. The patient has to be referred to a dietician for further assessment (For further details see [Appendix 1](#)).

NRS-PC: nutrition risk screening for pediatric cancer, which is our self-developed screening tool. Similarly to SCAN it is also an easy-to-use questionnaire with a score system. Apart from six questions regarding weight loss, physical activity, change in nutrition habits, stool and other gastrointestinal symptoms the BMI percentiles are also taken into consideration (For further details see [Appendix 2](#)). Scores are given according to the number of positive answers (Questions 1–6).

BIA Bioelectrical Impedance Analysis is used to measure body composition. InBody 720 and S10 are medical-grade body composition analyzers, which rely on four technological milestones (8-point tactile electrode system, direct segmental measurements, multiple frequencies, no estimations) to provide accurate and precise results that are highly correlated to gold-standard methods [13]. Our final results included three categories (low, normal or high) regarding BMI, muscle mass and body fat percentage (one by one) that has been shown to determine body composition independently of age, ethnicity or gender.

One of our primary goals was to evaluate NRS-PC to muscle mass measured by bio-impedance analysis. Based on these measures two categories were created: low muscle mass and normal or high muscle mass. The individual muscle mass values were defined by the body composition analysis, provided by InBody 720 or S10 devices. A receiver-operator characteristic curve was used to assess the relationship between muscle mass category and the different cut-off scores of the NRS-PC. The area under the curve (AUC) was calculated to measure classifier performance.

2.1. Statistical analysis

Descriptive statistics were used for the presentation of demographic data. A receiver-operator characteristic curve was used to assess the relationship between SCAN, NRS-PC and bio-impedance measures. To compare children who were at low and at high risk for malnutrition according to NRS-PC we used Chi-square test (categorical variables) and t-test (continuous variables). Significance was set at $p < 0.05$. All statistical analysis was done in R (version 3.6.1), for receiver-operator characteristic curve analysis, ROCR and epiR packages were used.

3. Results

The data of 109 patients were analyzed ($n = 64$ males). Some of the children underwent repeated assessments at different phases of their disease (see [Table 1](#)). 77 patients went through one assessment, 21 two and 11 patients three assessments. Children had a mean age of 11.3 years (range: 3–21 years, $SD = 4.8$ years). The incidence of the different tumor types can be seen in [Table 2](#). 14 of the patients had a disease relapse.

Table 1
The characteristics of the study subjects.

Phase of the disease	Number of cases (n =)	Male: Female ratio	Age (years)	Lost patients (n =)	Relapse (n =)	SCAN score	NRS-PC score
Diagnosis	44	29:15	10.5 ± 3.5	1	9	3.4 ± 2.0	1.0 ± 1.3
Active treatment	36	22:14	14.5 ± 3.5	4	1	3.4 ± 1.6	1.2 ± 1.3
Maintenance	34	19:15	9.5 ± 4.5	0	0	2.9 ± 1.7	0.5 ± 1.0
Post therapy	36	22:14	11.5 ± 2.5	1	4	1.7 ± 1.4	0.4 ± 0.9

Data are expressed as mean ± SD.

Table 2
The incidence of different tumor types.

Tumor types	Number of patients (n =)
ALL	39
AML	6
Ewing sarcoma and Osteosarcoma	23
Brain and spinal tumors (Medulloblastoma, Neuroblastoma, PNET – Central nervous system)	21
Other (Wilms-tumor, Hepatoblastoma, Melanoma, Colon cancer etc.)	20

3.1. Validation of NRS-PC to SCAN

As a first step, NRS-PC was compared to SCAN, a validated nutrition assessment tool used in pediatric oncology, to identify cut off scores for NRS-PC. According to Murphy et al. (2016), a child was classified at risk of malnutrition if the SCAN score was equal or greater than three. A receiver-operator characteristic curve was used to assess the relationship between SCAN and the different cut-off scores of the NRS-PC. The area under the curve (AUC) showed a high classifier performance (AUC = 0.9) (Fig. 1). A cut off score of one on the NRS-PC resulted in 98% [95% CI: 90, 100] sensitivity, 62% [95% CI: 51, 71] specificity, a positive predictive value of 58% [95% CI: 47, 68] and a negative predictive value of 98% [95% CI: 91, 100]. This means that in our sample one child considered malnourished by the SCAN would have been undetected with our questionnaire. A cut off score of two would decrease the sensitivity to 86% [95% CI: 77, 93], while increasing the specificity to 77% [95% CI: 65, 86]. As we aimed to identify all children at risk of malnutrition sensitivity was prioritised over specificity.

4. Evaluation of NRS-PC to bio-impedance measures

In order to evaluate NRS-PC to muscle mass measured by bio-impedance analysis low muscle mass and normal or high muscle mass categories were set up. A ROC curve was used to assess the relationship between the muscle mass category and the different cut-off scores of the NRS-PC. The area under the curve (AUC) was calculated to measure classifier performance. Sensitivity, specificity, negative and positive predictive values were calculated to each cut-off score and were reported in Table 3. Ideally, a measurement tool should have a 100% sensitivity to identify every child who has low muscle mass. A cut off score of one would give a sensitivity of 75% with 60% specificity. In our sample, this means that 13 children would have been incorrectly classified to the group of normal muscle mass, while 40 children would be incorrectly classified to the low muscle mass group.

4.1. Comparison of NRS-PC and SCAN predictive value regarding muscle mass

To evaluate whether the SCAN or the NRS-PC questionnaire was a more sensitive tool to identify patients with reduced muscle

mass, we did ROC analysis and compared the AUC values of both questionnaires with the DeLong method. The AUC of 0.67 [95% CI: 0.58, 0.75] of the SCAN was significantly lower ($Z = -2.46$, p -value = 0.014) than in the case of the NRS-PC (AUC = 0.75 [95% CI: 0.67, 0.82]), indicating that NRS-PC has better classifier properties to identify children with lower muscle mass (Fig. 2).

4.2. Evaluating the NRS-PC and SCAN at different phases of the disease

Patients were assessed at different phases of the course of their treatment. The description of the four phases and the number of participant in each case are shown in Table 4. To assess whether the classifier performance of NRS-PC differs at the different phases of the treatment, ROC analysis was performed. The AUC values at the different phases did not differ significantly from each other.

4.3. Evaluating BMI categories

Classifier performance of both questionnaires was evaluated in the three BMI categories separately. There were no significant differences in the AUC values of the two screening tools, however, in the low and normal BMI groups the result of the DeLong test approached significance. In the low BMI group, SCAN had better classifier properties, whereas in the normal BMI group, NRS-PC seemed to be better. Nevertheless, neither of the tests had sufficient sensitivity in the low BMI group (see Tables 5 and 6).

4.4. Comparing children under and over NRS-PC cut-off

Comparing children at low risk for malnutrition to those at high risk according to NRS-PC no significant differences were found in gender, the proportion of patients after relapse or age. However, there was a significant difference in the phase of the disease and the

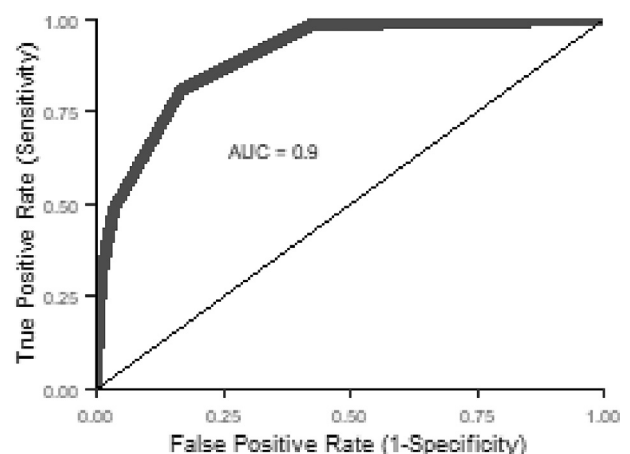


Fig. 1. ROC curve demonstrating the predictive value of NRS-PC to SCAN with a cut off score of 3.

Table 3
Validation of NRS-PC to muscle mass. 95% confidence intervals are in [].

Cut off score	Sensitivity	Specificity	Negative predictive value	Positive predictive value
1	0.75 [0.62, 0.86]	0.6 [0.49, 0.69]	0.82 [0.71, 0.9]	0.5 [0.39, 0.61]
2	0.7 [0.59, 0.79]	0.71 [0.58, 0.81]	0.64 [0.52, 0.75]	0.76 [0.65, 0.85]
3	0.62 [0.53, 0.71]	0.82 [0.65, 0.93]	0.38 [0.26, 0.5]	0.92 [0.84, 0.97]
4	0.59 [0.5, 0.68]	0.9 [0.68, 0.99]	0.25 [0.16, 0.37]	0.97 [0.91, 1]
5	0.54 [0.45, 0.62]	1 [0.29, 1]	0.04 [0.01, 0.12]	1 [0.95, 1]

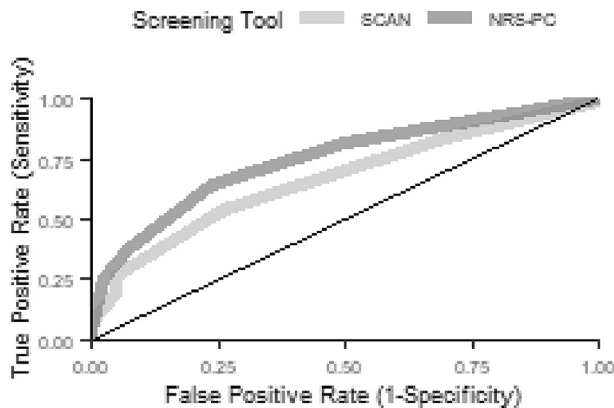


Fig. 2. ROC curve demonstrating the predictive value of the SCAN and the NRS-PC for low muscle mass. The AUC of NRS-PC (0.75) was significantly larger than the AUC (0.67) of SCAN.

BMI category of the patients. There were more high risk patients in phases 1–3, whereas less in phase 4. It is also clear that children in the low BMI category were almost all at high risk (except for 3 patients) for having low muscle mass.

5. Discussion

In the current study on pediatric cancer patients we provide a comparative analysis of the already validated SCAN, our self-developed NRS-PC score system and bio-impedance measures, the latter of which present objectively measured body composition parameters owing to a modern clinically used device.

It is known that among pediatric oncology patients the prevalence of malnutrition is high [14,15]. Therefore, screening for malnutrition risk to identify and triage patients who need further assessment and nutritional intervention may contribute to the solution of this problem. It is vital to have a nutritional screening tool which is quick, easy to use and can be performed by the nursing staff, since in busy pediatric hospitals and oncology units dieticians have limited capacity and in some centers NSTs might not be available.

There are certain validated nutrition screening tools for pediatric patients e.g. STRONGkids, Pediatric Yorkhill Malnutrition Score (PYMS), Screening Tool for Assessment of Malnutrition in Pediatrics (STAMP), Pediatric Nutrition Screening Tool (PNST), Subjective Global Nutritional Assessment (SGNA) however, these

Table 4
Comparison of SCAN and NRS-PC at different phases of the disease.

Description	Number of cases	NRS-PC AUC	SCAN-AUC	Z	p
Assessment after diagnosis	44	0.67 [0.49 0.86]	0.62 [0.45 0.8]	0.88	0.381
Active treatment	36	0.78 [0.63 0.93]	0.7 [0.53 0.86]	1.29	0.196
Maintenance	35	0.77 [0.62 0.93]	0.64 [0.46 0.81]	1.8	0.072
Assessment post therapy	37	0.82 [0.67 0.96]	0.67 [0.49 0.84]	1.57	0.115

have been designed for general patients [16–20]. STRONGkids, which is highly recommended in the EU - since it is fast, and easy to use - can also be used in case of general pediatric diseases. According to STRONGkids all cancers belong to the „medium risk” category, thus it does not distinguish malnourished cancer patients [16].

Prior to 2012 only weight loss was considered as an indicator of malnutrition risk, but there was no nutrition assessment at our hospital. In 2012 with the foundation of the nutrition support team (NST) we started to develop our own disease specific malnutrition risk screening tool in order to find a quick and simple process to identify children who are malnourished or at risk of malnutrition. This is essential in case of pediatric cancer patients to be able to decide who is in need of further assessment, dietetic counsel, oral nutritional supplementation or any other nutritional intervention. In this study we aimed to assess whether NRS-PC is suitable for these purposes and could be used at any phase of the disease. Since SCAN was already available during our study period it was possible to use both SCAN and NRS-PC on our sample. Previously, SCAN was evaluated against pediatric SGNA, in that study 32 subjects were involved, whereas in our study the data of 109 patients were analysed [12]. In Murphy's SCAN article air displacement plethysmography - Body Pod Body Composition System - was used to measure body volume, fat mass and fat free mass, whereas we used bio-impedance measures and InBody body composition devices. In a 2019 study these methods were compared to dual energy x-ray absorptiometry (DXA) and was concluded that both Body Pod and InBody 770 overestimate fat free mass and underestimate fat mass and percent body fat [21]. This however, does not influence our results. Relying on this information and the cited article, both methods are acceptable for body composition analysis.

5.1. Developing a screening algorithm for the nutritional status of pediatric oncology patients

First and foremost, we wanted to compare SCAN and our NRS-PC questionnaire in order to decide which was more sensitive to identify patients with reduced muscle mass. Although body composition studies in pediatric cancer are limited and existing literature in this area has largely focused on hematologic malignancies, it is known that the loss of muscle mass adversely affect clinical outcome and survival both in adult and pediatric cancer patients [22,23]. Our results indicated that NRS-PC has better classifier properties to identify children with lower muscle mass. However, evaluating the NRS-PC and SCAN at the different phases of the disease we found that they did not differ from each other

Table 5
Comparison of SCAN and NRS-PC at different BMI categories.

	Number of cases	NRS-PC AUC	SCAN-AUC	Z	p
Low	27	0.5 [0.22 0.78]	0.62 [0.31 0.93]	-1.86	0.063
Normal	99	0.72 [0.61 0.81]	0.64 [0.54 0.75]	1.75	0.081
High	25	0.83 [0.54 1]	0.74 [0.22 1]	0.77	0.439

Table 6
Comparison of low and high nutritional risk patients (based on bio-impedance measurements). For categorical variables, chi square tests, for age independent samples t-test were used for comparison.

		Low risk	High risk	p
Gender	Male	37	56	0.150
	Female	16	43	
Relapse	No	47	91	0.720
	Yes	6	8	
Phase	1	10	34	<0.001
	2	7	29	
	3	13	22	
	4	23	14	
BMI category	Low	3	24	0.001
	Normal	35	64	
	High	15	10	
Age		10.7	11.6	0.270

significantly. Regarding the three BMI categories (low, normal, high) there were no significant differences between them, although in the low and normal BMI groups the DeLong test approached significance.

As children in the low BMI category were almost all at high risk and as the ROC curve of NRS-PC does not show appropriate validity to identify those who have low muscle mass, we suggest bio-impedance measures in every patient with low BMI. In our sample, there were only two children who had normal muscle mass in spite of their low BMI.

In case of normal BMI, we need further studies to assess whether the NRS-PC is sensitive enough to identify approximately all patients with low muscle mass. In our sample, a first screening with NRS-PC would result in overlooking 13 children with low muscle mass. However, out of the 13 children, 3 did have normal muscle mass at the subsequent assessment, 1 had similarly low muscle mass and we did not have data from the other 9. Existing literature reinforces that during the course of cancer therapy body composition can change considerably [8,9,24,25]. Therefore, longitudinal data would be advantageous to decide whether it is safe to rely on NRS-PC without bio-impedance measures.

In the high BMI group, we suggest screening with NRS-PC first. None of the patients with low muscle mass would have been undetected in our sample with this strategy, and out of the three children who were identified being at high risk, at the subsequent assessments two had low muscle mass.

6. Conclusions

As a conclusion we can affirm that assessing the nutritional status of pediatric cancer patients by any means is proved to be very useful and can contribute to the necessary dietetic interventions. Derived from our results we suggest screening high BMI patients first with NRS-PC. In case of low BMI bio-impedance measures provide more precise information on muscle mass and nutritional risk. Further data are needed to decide whether the NRS-PC is sensitive enough in case of normal BMI patients. Using specific screening tools and following a screening algorithm facilitates the assessment and supplies more accurate information based on

which better nutritional care can be administered. The assessment of nutritional status and the implementation of nutrition therapy accordingly may contribute to better outcome and survival in pediatric cancer patients.

6.1. Limitations

In this single center study during the research period we had a limited number of patients who could be involved. In the current study we could not collect longitudinal data however, it would be beneficial to follow patients from the diagnosis until the completion of their treatment in order to further evaluate the use and accuracy of the NRS-PC.

Funding

No specific grant or funding was used for this study.

Author contribution statement

I declare that all authors approved the manuscript submitted. Individual contribution is stated below:
 Conception and design: NG, KH, ET, GK.
 Data collection: NG, KC, EF.
 Analysis and interpretation: NG, KC, ET, KH, GK.
 Drafting of the manuscript: NG, KH, GK.
 Revising the manuscript for content: NG, KC, ET, KH, EF, GK.

Conflict of interest

The authors declare that no conflict of interest exist in this study.

Acknowledgements

The authors would like to thank the members of the nutrition support team and all the employees of the 2nd Department of Pediatrics, Semmelweis University for their active participation in this study.

Appendix A

Appendix 1

Nutrition screening tool for childhood cancer (SCAN).

Does the patient have a high risk cancer?	1
Is the patient currently undergoing intensive treatment?	1
Does the patient have any symptoms relating to the GI tract?	2
Has the patient had poor intake over the past week?	2
Has the patient had any weight loss over the past month?	2
Does the patient show signs of under nutrition?	2
Total:	

Score indication.

≥3 At risk of malnutrition – Refer to dietician for further assessment.

Appendix 2

NRS-PC (Nutrition Risk Screening for Pediatric Cancer) Questionnaire

- New or returning patient:
- Name:
- Date of birth:
- Department (ward):
- Weight (kg)
- Height (cm)
- Age:
- Diagnosis:
- Does the patient receive any nutritional supplement? Yes or No
- Does the patient have a feeding tube upon admission? Yes or No
- BMI percentile <10? Yes or No
- BMI percentile <5? Yes or No

Questions	YES	NO
1. More than 1 kg weight loss since tumor associated complaints and symptoms		
2. Change in nutrition habits: reduced amount of food consumed		
3. Change in nutrition habits: fewer occasions (compared to previous number of meals)		
4. Stool is more frequent than usual or change in consistency		
5. Increased vomiting compared to earlier		
6. Reduced physical activity compared to earlier (before diagnosis)		
NRS-PC score (number of positive responses from Questions 1–6)		

Date.

Screening done by (name of the person).

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