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ORIGINAL ARTICLE

Evaluation of an automated pediatric malnutrition screen using anthropometric measurements in the electronic health record: a quality improvement initiative

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Abstract

Purpose Malnutrition related to undernutrition in pediatric oncology patients is associated with worse outcomes including increased morbidity and mortality. At a tertiary pediatric center, traditional malnutrition screening practices were ineffective at identifying cancer patients at risk for undernutrition and needing nutrition consultation.

Methods To efficiently identify undernourished patients, an automated malnutrition screen using anthropometric data in the electronic health record (EHR) was implemented. The screen utilized pediatric malnutrition (undernutrition) indicators from the 2014 Consensus Statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition with corresponding structured EHR elements. The time periods before (January 2016–August 2017) and after (September 2017–August 2018) screen implementation were compared. Process metrics including nutrition consults, timeliness of nutrition assessments, and malnutrition diagnoses documentation were assessed using statistical process control charts. Outcome metrics including change in nutritional status at least 3 months after positive malnutrition screen were assessed with the Cochran-Armitage trend test.

Results After automated malnutrition screen implementation, all process metrics demonstrated center line shifts indicating special cause variation. For patient admissions with a positive screen for malnutrition of any severity level, no significant improvement in status of malnutrition was observed after 3 months ($P = .13$). Sub-analysis of patient admissions with screen-identified severe malnutrition noted improvement in degree of malnutrition after 3 months ($P = .02$).

Conclusions Select 2014 Consensus Statement indicators for pediatric malnutrition can be implemented as an automated screen using structured EHR data. The automated screen efficiently identifies oncology patients at risk of malnutrition and may improve clinical outcomes.

Keywords Clinical nutrition · Malnutrition · Screen · Quality improvement · Electronic health record

Introduction

Malnutrition related to undernutrition is common in pediatric cancer patients with a prevalence as high as 65% [1]. Undernutrition prevalence varies with different types of cancer as patients with solid organ malignancies are at higher risk for malnutrition than patients with hematologic malignancies [1–5]. Furthermore, recognizing malnutrition

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is critical as it negatively impacts physical and cognitive development, wound healing, immune function, mortality, and quality of life [4, 6–8].

Given the importance of nutrition support in pediatric oncology, the Children's Hospital of Philadelphia (CHOP) screens all pediatric oncology patients for malnutrition risk factors. However, the standard hospital screen, performed by nursing staff upon admission, did not adequately identify all patients in need of nutrition assessment. A multi-disciplinary team of providers including registered dietitians (RD), physicians, and nurses sought to improve screening for malnutrition through a quality improvement (QI) initiative. Timely nutrition consultation and assessment by an RD were identified as key improvement areas. Timeliness is of particular importance in an oncology population due to the dynamic nature of malnutrition with the potential to rapidly become catabolic with a malnourished state due to the interplay between iatrogenic consequences of treatment, complex interactions between energy and substrate metabolism, and hormonal and inflammatory disturbances [5]. Additionally, frequent transitions between short inpatient admissions and the outpatient setting further increase the urgency to quickly identify and intervene for patients at risk of malnutrition.

Current recommendations from the Academy of Nutrition and Dietetics are for all inpatients to be screened for nutritional status [9, 10]. Multiple validated screens exist, yet there is no universal, standardized approach to screen pediatric inpatients [10–16]. Nutrition screens assess variable combinations of dietary intake, anthropometric values, comorbid disease states, and subjective assessments of body habitus [11, 15]. These screening tools are performed manually by a nurse, dietitian, or other provider and require variable time commitments for completion [11, 15]. Nutrition screens are typically completed once upon admission and are not repeated throughout an admission [10]. Finally, the current validated nutrition screens were developed prior to publication of the indicators recommended for identification and documentation of adult and pediatric malnutrition. These were released in 2012 and 2014, respectively, by Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) [17, 18]. The pediatric publication (referred to in this paper as the Consensus Statement) includes evaluation of z-scores for anthropometrics, weight trends, and nutritional intake. Many of these data points are routinely collected in the electronic health record (EHR) and are targets for informatics-aided clinical decision support to identify patients with risk of malnutrition [10]. The Consensus Statement for malnutrition in pediatrics only addresses undernutrition [17]. While overnutrition is an important issue, in this paper the term "malnutrition" will be synonymous with "undernutrition" as this reflects the Consensus Statement.

In contrast to pediatrics, the adult malnutrition indicators incorporate overarching contexts including acute illness, chronic illness, and social circumstances [18]. Within these contexts, weight loss percentage over variable timeframes is used to identify malnutrition. For adults with a chronic illness, the shortest timeframe for weight loss is 1 month [18]. Debate exists within the nutrition community for how to best classify malnutrition for young adults as they straddle the pediatric and adult indicators.

The objectives of this quality improvement initiative were to provide timely, efficient, and equitable nutritional care to all oncology patients by decreasing time to malnutrition recognition and intervention. Iterative "plan, do study, act" cycles were performed. The primary intervention was implementation of an automated malnutrition screen based largely upon the 2014 pediatric Consensus Statement indicators with select adult indicators incorporated for young adults.

Methods

Implementation context

This work was conducted as a quality improvement initiative using an institutional quality framework based upon the Model for Improvement [19]. It was performed on an inpatient oncology unit at a single tertiary care institution with interdisciplinary participation by pediatric oncologists, nurse practitioners, nurses, dietitians, data analysts, and members of the Office of Clinical Quality Improvement. The inpatient oncology unit contains 54 beds with a patient-to-registered dietitian ratio of 20:1. Because this QI project only utilized data collected as part of standard patient care, it was exempt from review by the CHOP Institutional Review Board.

Primary intervention: an automated malnutrition screen

Core elements used in the automated malnutrition screen were structured anthropometric measurements in the EHR including serial length/height and weight values for all inpatient and outpatient encounters. This data was extracted from the EHR (Epic, Verona, Wisconsin) and body mass index (BMI) values were calculated as previously described [10]. The automated malnutrition screen was primarily based upon adapted indicators from the 2014 pediatric Consensus Statements (Table 1) and was comprised of two steps which occurred simultaneously. First, any new anthropometric measurement generated absolute z-score values for BMI and weight-for-height which were flagged as concerning if they were lower than −1. Second, the new weight measurement was compared to prior measurements to assess percent weight loss over a specified amount of time which varied by age.

Patients < 1-month-old were excluded in the pediatric Consensus Statement and this project. There was no

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Table 1 Automated malnutrition screen inclusion of Consensus Statement primary indicators [17]

Indicators	Mild malnutrition	Moderate malnutrition	Severe malnutrition	Included in automated malnutrition screen
Single data point is available				
Weight-for-height z-score	− 1 to − 1.9 z-score	− 2 to − 2.9 z-score	> − 3 z-score	Yes
Body mass index-for-age z-score	− 1 to − 1.9 z-score	− 2 to − 2.9 z-score	> − 3 z-score	Yes
Length/height-for-age z-score	No data	No data	− 3 z-score	No
Mid-upper arm circumference z-score	≥ − 1 to − 1.9 z-score	≥ − 2 to − 2.9 z-score	≥ − 3 z-score	No
Multiple data points available				
Weight gain velocity < 2 years	< 75% of the norm for expected weight gain	< 50% of the norm for expected weight gain	< 25% of the norm for expected weight gain	No[a]
Weight loss (2–20 years)	5% usual body weight	7.5% usual body weight	10% usual body weight	Yes
Deceleration in weight for length/height z-score	Decline of 1 z-score	Decline of 2 z-score	Decline of 3 z-score	No
Inadequate nutrient intake	51–75% of estimated energy/protein need	26–50% of estimated energy/protein need	≤ 25% of estimated energy/protein need	No

[a] For patients age 1–24 months, any weight loss was used in place of weight gain velocity. Patients losing weight in this age group were categorized as severely malnourished as any weight loss is, by definition, < 25% of the norm for expected weight gain

The computer-evaluable indicators of malnutrition used for this initiative are shown as they relate to the initial Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition (ASPEN) Consensus Statement indicators for pediatric malnutrition [17]. Parameters were adapted from the original Consensus Statement to allow for computer-evaluable definitions using structured height and weight data. For patients who screened positive for risk of malnutrition, the predicted malnutrition severity was assigned as shown. Patients younger than 1 month of age were excluded. Separate parameters were used to indicate malnutrition for patients between the ages of 1–24 months, 2–18 years, and ≥ 18 years. Patients from 1 to 24 months did not have time constraints for their weight measurement comparison. Patients age 2–18 and patients > 18 years had their weight measurements for evaluation by the presented screen limited to the prior 60 days and 30 days, respectively. Weights within these time constraints from both in and outpatient settings were evaluated by the presented screen. Patients > 18 years would also screen positive for risk of malnutrition if their BMI was < 18.5 in accordance with the Centers for Disease Control and World Health Organization undernutrition definitions [20, 21]. This was not part of the initial pediatric or adult Consensus Statements. The excluded portions of the pediatric Consensus Statement reflect a lack of structured EHR data for mid-upper arm circumference and nutrient intake. Length/height z-score of − 3 or worse was excluded as it would not be expected to impact a pediatric oncology population and may occur for reasons other than malnutrition

timeframe boundary for weight comparisons in patients 1–24 months of age. While weight loss is not an identified indicator of malnutrition in this age range, weight loss was used as a simplified alternative for the Consensus Statement's weight gain velocity parameters (Table 1). Weight-for-height was used in this age group in order to preserve fidelity to the Consensus Statement. The Consensus Statement does not specify a timeframe for weight loss indicators in children from the age of 2–18 years. For the purposes of the malnutrition screen, a timeframe boundary for comparison weights was limited to the past 60 days for these patients.

For patients > 18 years old, the pediatric Consensus Statement indicators were not followed as closely in favor of a hybrid approach that incorporated select adult malnutrition indicators. This was because the pediatric Consensus Statement extends until age 18 or 20 depending upon the indicator, and the adult Consensus Statement does not define a lower age boundary [17, 18]. BMI z-scores were available up to age 20 and were used as per the pediatric Consensus Statement. For patients > 18 years old, a timeframe boundary of 30 days was used for weight loss as this is consistent with the 1 month threshold for patients with chronic illness in the adult Consensus Statement [18]. Additionally for patients > 18 years old, those with a BMI < 18.5 were included as a positive screen as the Centers for Disease Control and the World Health Organization define a BMI < 18.5 as underweight for adults [20, 21].

The timeframe boundaries were included in the automated screen in an effort to reduce false positive screens while allowing flexibility based upon the patient's age. Patients with anthropometrics meeting these defined criteria were considered to be "at-risk for malnutrition" pending clinical evaluation by a registered dietitian. The positive screens were classified as concerning for mild, moderate, or severe malnutrition.

Clinical decision support simulation

To alert clinical providers including registered dietitians about inpatients who screened positive for malnutrition, a daily automated email was generated listing all inpatients meeting at least one malnutrition identifier. This email included:

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1. The computer-generated calculation of the degree of malnutrition
2. If a consult to clinical nutrition had been placed during the admission
3. The date of the most recent registered dietitian note
4. Oncology treatment team

Automated malnutrition screen assessment

The automated malnutrition screen was assessed using an uncontrolled before and after design. The baseline period of data collection was from January 2016 through August 2017 (timeline shown Table 2). The automated malnutrition screen was implemented in September 2017 and data was collected continuously. For this analysis, data was included for 1 year after implementation through August 2018. Descriptive characteristics including the number of inpatient admissions that triggered a positive malnutrition screen result were captured. The unit of assessment for the malnutrition screen was patient admissions to the inpatient oncology unit. The same patient could have been admitted multiple times during the data-collection period.

Process and outcome metrics (Table 3) were assessed with statistical process control charts with data collected continuously and grouped in monthly intervals [22]. These metrics included nutrition consults, nutrition assessments completed within three business days of the concerning measurement, Problem List documentation of malnutrition diagnoses, change in screen-defined malnutrition status, and presence of nutrition interventions such as appetite stimulants, oral, enteral, or parenteral nutrition support. All metrics were extracted from the EHR as structured data elements and tracked autonomously. The primary outcome metric was change in degree of malnutrition at least 3 months after the initial at-risk anthropometric measurement. For example, a patient with screen-defined moderate malnutrition worsening to severe malnutrition. This outcome was analyzed as a categorical variable with three possible values: worsened, unchanged, or improved. Differences before and after screen implementation were assessed using the Cochran-Armitage trend test. Any patient admission that did not have a follow up weight or length/height measurement, BMI, or weight-for-height z-score after 3 months was considered missing data and excluded from analysis. The Cochran-Armitage trend test was performed for all admissions with an at-risk anthropometric measurement and subgroup analysis was performed for patient admissions meeting automated screen criteria for each malnutrition severity level: mild, moderate, and severe. Two events of note during the study occurred in June 2017 when providers received an education session about under-referrals to clinical nutrition and in October 2018 when registered dietitians were granted permission to edit the EHR Problem List.

Analyses were conducted using R, version 3.5.1. Two-tailed P value < .05 was considered statistically significant. A statistically significant shift for statistical process control charts was considered to be six or more consecutive points above the baseline median [23]. This manuscript was written in accordance with SQUIRE Guidelines 2.0 [24].

Table 2 Timeline

Date	Event
January 2016	Start baseline data collection
June 2017	Education presentation given to oncology faculty
September 2017	Activation of automated screen with daily emails
	Start post-intervention data collection
October 2017	Registered dietitians gain ability to edit Problem List in the electronic health record
August 2018	Data collection period for analysis ends

Table 3 Process and outcome metrics

Type	Metric
	Percent of positive undernutrition screens with the following:
Process	Consult placed to clinical nutrition
Process	RD assessment completed within 3 business days
Process	Malnutrition diagnosis documented on patient Problem List
Outcome	Positive change in nutritional status three months after initial positive screen
Outcome	Interventions[a] to supplement nutritional intake

[a] Interventions to supplement oral nutritional intake were defined as a commercial oral nutritional supplement, appetite stimulant, nasogastric/gastric/jejunal/duodenal feeding tube with enteral support, and parenteral nutrition support

Results

From January 1, 2016 through August 31, 2018, 4557 patient admissions were included with 2604 occurring prior to implementation of the automated malnutrition screen and 1953 occurring afterward. During the baseline collection period from January 2016 through August 2017, the overall automated screen-reported malnutrition prevalence was 42%. Malnutrition prevalence was higher for patients with solid organ malignancies compared to patients with hematologic malignancies at 38% and 48%, respectively. For screen-identified patient admissions, the assigned malnutrition severity levels in the baseline period were as follows: 49% mild malnutrition, 24% moderate malnutrition, and 27% severe

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malnutrition. Overall, 11% of patient admissions with a positive screen were patients ≥ 18 years of age.

At baseline, 13% of patient admissions with a positive automated screen received a nutrition consult during the inpatient stay, and this increased to 45% after automated screen implementation (Fig. 1). After screen implementation, the percent of positive screens with a nutrition assessment completed within three business days increased from 57 to 76% and the percent with a malnutrition diagnosis recorded on the Problem List increased from 20 to 49%. All of these improvements were accompanied by center line shifts on the statistical process control charts (Fig. 1). The improved documentation on the Problem List started to increase in September 2017 and continued to increase after the registered dietitians gained the ability to edit the Problem List in October 2017. The percentage of patients who received interventions including appetite stimulants and nutrition support was unchanged.

For the outcome of change in screen-defined nutritional status after 3 months, the percentage of patient admissions with a decline in nutritional status decreased (11% vs. 9%) as did the percentage of patient admissions whose nutritional status remained unchanged (21% vs. 18%) (Table 4). Conversely, the percentage of patient admissions with an automated screen-defined improvement in nutritional status increased from 68 to 72%. However, this trend of change is not statistically significant ($P = .13$ from Cochran-Armitage trend test). The outcome of change in nutritional status at least 3 months later was not able to be assessed for 28% (532/1892) of patient admissions from January 2016 to August 2018. Missing data was present in all severity subgroups: mild 29% (274/931), moderate 28% (132/474), and severe 26% (126/487).

For the subgroup analysis examining the change in nutritional status after 3 months by malnutrition severity level, the percentage of patient admissions with improved nutritional status increased for all subgroups, mild (54% to 56%), moderate (77% to 81%), and severe (85% to 93%). For patient admissions with moderate malnutrition, the percentage with a decline in nutritional status decreased from 12 to 6%. Patient admissions with severe malnutrition could not worsen and the percentage that remained at severe undernutrition decreased from 15 to 7%. Overall, the Cochran-Armitage trend test was not significant for improved status of undernutrition for patient admissions with mild ($P = .65$) or moderate ($P = .18$) malnutrition but was significant for improvement in patients with severe malnutrition ($P = .02$) (Table 4).

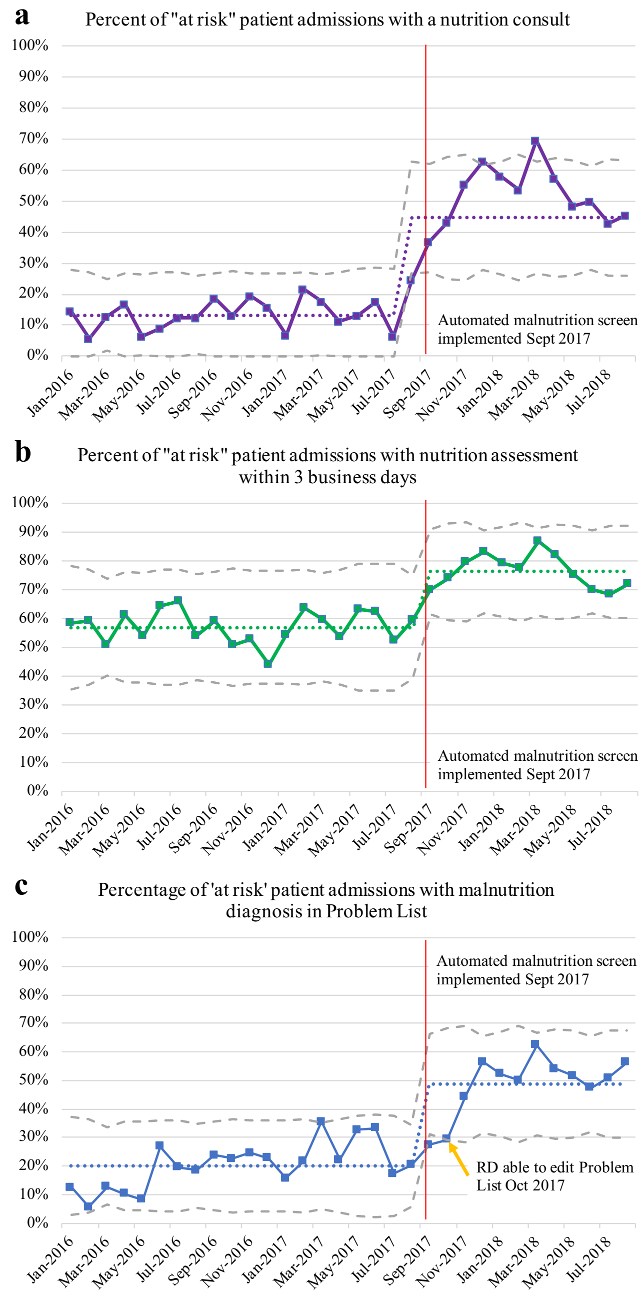

Fig. 1 Statistical process control chart for process metrics. *RD* registered dietitian. All process metrics including clinical nutrition consults (panel **a**), completion of nutrition assessment within three business days (panel **b**), and documentation of a malnutrition diagnosis on the Problem List (panel **c**), demonstrated special cause variation with center line shifts after implementation of the automated pediatric malnutrition screen in September 2017. For each panel, the dashed circle line represents the center line and the dashed gray lines represent the upper and lower control limits. The documentation on the Problem List data is confounded by the registered dietitians gaining the ability to document malnutrition on the Problem List and edit malnutrition diagnoses in October 2017

Discussion

This quality improvement initiative demonstrated that an automated pediatric malnutrition screen based upon key indicators from the 2014 Consensus Statement was associated with significant improvements in the percentage of screen-positive patient admissions with a clinical nutrition consult, timely completion of nutrition assessment, and Problem List

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Table 4 Change in nutritional status after 3 months by malnutrition severity category

Undernutrition severity category		Worsened		Unchanged		Improved		*P* value
	n	Before	After	Before	After	Before	After	
Mild	657	75 (17%)	36 (16%)	123 (28%)	62 (28%)	236 (54%)	125 (56%)	.65
Moderate	342	28 (12%)	7 (6%)	26 (11%)	13 (12%)	180 (77%)	88 (81%)	.18
Severe	361	NA	NA	37 (15%)	8 (7%)	202 (85%)	114 (93%)	.02
Combined	1360	103 (11%)	43 (9%)	186 (21%)	83 (18%)	618 (68%)	327 (72%)	.13

NA not applicable

Statistical significance was assessed using Cochran-Armitage trend test

documentation of a malnutrition diagnosis. It was also associated with a statistically significant improvement in the percentage of severely malnourished patient admissions with improved nutritional status after 3 months. It is important to note that outcomes only improved for the subset of patients with severe malnutrition. When patients who screened positive for any malnutrition severity level are grouped together, the outcome of improved nutritional status at 3 months is no longer significant. This result is not unexpected as outpatient interventions were not impacted by this study and likely serve to bias any impact of inpatient interventions to the null through a dilutional effect. It is possible that the statistically significant improvement seen for patient admissions meeting severe malnutrition status are partially due to the fact that these patients are more likely to be sick and therefore may spend more time as an inpatient. Furthermore, the study did not address treatment intensity or phase of treatment. This potentially exaggerated any dilutional effect as patients with low-intensity therapy likely would improve in the absence of any intervention. Given the likelihood of these dilutional effects, the authors believe that the automated malnutrition screen should move forward into further research validation studies and be assessed in the outpatient setting.

The greatest benefits of an automated malnutrition screen are increased efficiency of nutrition screening and ease of implementation. Because the total number of nutrition interventions were unchanged, any improvements in nutrition status are most likely attributable to treating sooner as opposed to treating with more interventions. By utilizing data collected during routine clinical care, it fits into the established care team structure. Because the screen is compatible with the z-score and weight loss definitions in the Consensus Statement, data is presented in a way that the care team readily comprehends and triggers interventions that are already considered to be the standard of care.

In addition to clinical care, implementation of an automated screen has the potential to extend to QI and process monitoring. Even though it was applied to oncology as a test case, the screen could be adapted for use in other pediatric populations. QI initiatives such as this are necessary to prevent unnecessary delays in treatment and reduce the pressure on providers to remember and document all of critical aspects of patient care. Furthermore, this work aligns well with the goals of the broader nutrition community including the Academy of Nutrition and Dietetics' Malnutrition Quality Improvement Initiative (MQii) [9, 25] by creating synergies between clinical nutrition care and the EHR. Because the malnutrition screen only includes common, structured anthropometric data from the EHR, it should be able to be implemented in most EHR platforms across academic and community settings. It could be expanded beyond oncology to other patient groups and careful validation should need to be undertaken prior to widespread use.

Future studies of the automated malnutrition screen must address the limitations present in the current analysis as these limitations preclude use of the automated screen outside of a QI or research context. This improvement initiative was designed to address inefficiencies in nutrition care, specifically delays in identifying malnutrition risk. Because the same patient potentially could require rapid identification of malnutrition multiple times, the screen permitted patients to be captured multiple times. While this method has advantages under a QI context focused on efficiency, it has obvious flaws as it was not designed to control for dependent data. In addition, the outcomes data had a high number of missing data points. This is thought to be due to patients who either died or left the institution. While the percentage of patient admissions with missing data was similar across malnutrition subgroups, the possibility that data was missing not at random cannot be excluded. Confounding is present for the process metric of malnutrition documentation on the Problem List as registered dietitians gained the ability to edit this approximately 1 month after the malnutrition screen was implemented. The improvements in malnutrition diagnosis documentation on the

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Problem List may be due to either the malnutrition screen or to expansion of providers who are able to enter this information.

The automated malnutrition screening process was built in reference to the 2014 pediatric Consensus Statements by AND/ASPEN for identification and documentation of malnutrition and was not compared to an established, validated nutrition screen. This limitation is somewhat offset by using only objective EHR data points designed to comply with the Consensus Statement. Not all components of the Consensus Statement definition were included (Table 1). Mid-upper arm circumference data is not commonly present in the EHR as a structured element. Weight gain velocities were computationally difficult to obtain in an automated way and were therefore excluded due to infeasibility. Nutrient intake estimated by diet recall is subjective in nature and therefore cannot be included in the automated screen. Future studies should examine the optimal timeframe for weight comparison for different age groups as those selected for this initial work were somewhat arbitrary. Finally, the Consensus Statement does not address the double burden of malnutrition in the setting of obesity. High values for weight and BMI z-scores could be added to future iterations of the malnutrition screen to better meet the needs for this population.

Future work should focus on the young adult population who are ≥ 18 years old. While the authors believed that all cancer patients treated during the quality improvement study should receive automated screening, ambiguity in the literature for malnutrition indicators for young adults posed dilemmas in definition and methodology. Ultimately, a combination of the pediatric Consensus Statement, adult Consensus Statement, and Centers for Disease Control (CDC)/World Health Organization (WHO) malnutrition indicators was used. The adult Consensus Statement does not lend itself well to structured data elements in the EHR beyond weight loss percentage. This makes automated surveillance more difficult and was the reason the CDC/WHO BMI threshold of 18.5 was used to indicate risk of malnutrition as BMI was very easy to implement from the available EHR data. Future work must focus on adolescent and young adult patients to better understand how screening parameters could be optimized for this population.

Finally, the automated screen is only as good as the data contained within the EHR. False positives can occur through typographical errors when weight is entered incorrectly or weight loss is detected but occurred for reasons such as diuresis, amputation, or tumor excision. It is notable that none of the process metrics were met more than 76% of the time. This is likely driven at least in part by false positive screens that do not require intervention and future work should attempt to reduce false positives. False negatives on the other hand can occur when patients have prolonged edema, ascites, or inflammation with weight or fluid gain. Fortunately, with repeated EHR anthropometric measurements, these issues should correct and minimize the impact of these spurious measurements. The clinical team can subsequently discern when to ignore measurements detected as false positives or false negative based on clinical status of the patient.

To that end, a future direction of this project is to validate the automated malnutrition screening tool as a research initiative designed to address the methodologic limitations of the current initiative. The optimal role of this quality improvement study is to demonstrate the potential of automated screening to impact supportive care in oncology and highlight the critical need for research quality validation of this work with a specific focus tailoring automated screening based upon the patient's age.

Conclusions

Key portions of the 2014 pediatric Consensus Statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition for identification and documentation malnutrition (undernutrition) can be utilized to identify pediatric cancer patients at risk for malnutrition via an automated screen using structured data within the electronic health record. This automated screen is designed to augment current nutrition screening practices. By building upon existing EHR platforms, automated screens may improve efficiency in identifying patients at risk for malnutrition and have the potential to improve nutrition-related outcomes through early identification and intervention.

Compliance with ethical standards

Conflict of interest The authors have no conflict of interest disclosures to report. Quality improvement work presented in this paper was supported by the Children's Hospital of Philadelphia. The Children's Hospital of Philadelphia retains primary control of the data presented in this manuscript. Data may be made available for external review if permission is obtained from the Children's Hospital of Philadelphia.

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