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ORIGINAL RESEARCH

Malnutrition identification and management variability: An administrative database study of children with solid tumors

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Abstract

Background: Malnutrition during cancer treatment increases treatment-related morbidity and mortality. Our study better characterizes variability in malnutrition identification and treatment by examining nutrition-related diagnoses and support for children with central nervous system (CNS) and non-CNS solid tumors during therapy. We examined diagnosis of malnutrition, use of tube feeding or parenteral nutrition (PN), and appetite stimulants.

Methods: We retrospectively reviewed 0 to 21-year-old patients in the Pediatric Health Information System from 2015 to 2019. Patients were classified as having (1) billed malnutrition diagnosis, (2) malnutrition diagnosis or using PN and enteral nutrition ("functional malnutrition"), and (3) any previous criteria or prescribed appetite stimulants ("possible malnutrition"), as well as associated risk factors.

Results: Among 13,375 unique patients, CNS tumors were most common (24.4%). Overall, 26.5% of patients had malnutrition diagnoses, 45.4% met functional malnutrition criteria, and 56.0% had possible malnutrition. Patients with adrenal tumors had highest billed, functional, and possible malnutrition (36.6%, 64.1%, and 69.4%, respectively) followed by CNS tumors (29.1%, 52.4%, and 64.1%). Patients with adrenal tumors had highest rates of PN use (47.4%) and those with CNS tumors had the highest tube feeding use (26.8%). Hospital admissions with malnutrition had a longer hospital length of stay (LOS) (6 vs 3 days, $P < 0.0001$), more emergency department admissions (24.4% vs 21.8%, $P < 0.0001$), and more opioid use (58.6% vs 41.4%, $P < 0.0001$).

Conclusions: Variability in malnutrition diagnoses hinders clinical care and nutrition research in pediatric oncology. Improving disease-specific recognition and treatment of malnutrition can target nutrition support, ensure appropriate reimbursement, and potentially improve outcomes for children with solid tumors.

KEYWORDS

cancer cachexia, malnutrition, pediatric, weight loss

CLINICAL RELEVANCY STATEMENT

Proper nutrition is vital to pediatric development. This article describes a unique approach to identifying malnutrition in children during cancer treatment. Using a large pediatric hospital database, we examined the variability in malnutrition diagnoses among children with solid tumors in addition to the use of parenteral nutrition, enteral nutrition and supplies, and appetite stimulants. Understanding disease-specific patterns of malnutrition diagnosis and support will allow for targeted screening and intervention in prospective studies.

INTRODUCTION

Malnutrition during cancer treatment affects up to 90% of children and dramatically increases the risk for febrile neutropenia, infection, and death.[1,2] Malnutrition can be diagnosed using standardized *z* scores, changes in growth velocity, and insufficient oral intake; however, only absolute changes in weight are used to adjust cancer-directed therapy in the clinical setting.[3,4] This approach results in consistent underdiagnosis of malnutrition, as has been published in hospitalized children with nononcologic acute or chronic medical conditions.[5,6] Few studies have specifically examined malnutrition in pediatric oncology patients, resulting in a lack of broadly accepted screening tools in the field.[7,8] Additionally, overlooking inadequate protein or energy consumption to diagnose malnutrition in addition to weight loss and impaired growth velocity leads to under recognition in pediatric oncology patients.[9] To date, no studies have independently utilized parenteral nutrition (PN), feeding tube placement or supplies, or use of appetite stimulants as indicators of pediatric malnutrition in patients undergoing cancer treatment. Failure to appropriately identify malnutrition, even when implementing nutrition support strategies, leads to inadequate recognition and financial reimbursement, resulting in further strain on already scarcely available nutrition support services.[10] Evaluating these components as surrogates for a billed diagnosis of malnutrition in a large, national pediatric database will help to better identify the prevalence of patients needing nutrition support during cancer therapy.

Patients with solid tumors, including neuroblastoma, sarcomas, and brain tumors, are at particularly high risk for malnutrition during treatment due to highly emetogenic chemotherapy, radiation therapy regimens, and direct toxic damage to the musculoskeletal and nervous systems.[8,11] Small studies have demonstrated nutrition toxicities with specific cancer treatment, but fail to provide a comprehensive assessment of malnutrition and specifically undernutrition.[12] Adult oncologists have more completely characterized "cancer cachexia" as a phenotype including standardized diagnostic, therapeutic, and research criteria, which has led to improved outcomes and quality of life for adult cancer patients.[13] Beyond the terms "weight loss" or "malnutrition," cancer cachexia includes a comprehensive evaluation of a patient's overall nutrition status. It involves both the cancer and subsequent treatment contributing to loss of appetite, weight, or muscle mass (sarcopenia), and increased fatigue, functional impairment, and treatment-related toxicity.[13] Appetite stimulants as well as enteral nutrition and PN supplements are frequently used during childhood cancer treatment but may or may not correspond to a coded diagnosis of malnutrition or appropriate classification (mild, moderate, or severe), impairing both clinical care and research in the field.[10] Although professional societies have stressed the importance of prioritizing research into body composition, nutrition support, and exercise interventions in children with cancer, the lack of standardized definitions prevents the application of this study into improving clinical practice.[8,11,14]

Children treated for cancer often experience other nutrition-related side effects regardless of being appropriately diagnosed or classified. Patients with central nervous system (CNS) tumors may experience feeding difficulty due to swallowing dysfunction from tumor location in addition to mucositis, inflammation, or damage from radiation directed towards the head and neck.[15,16] Children treated with intense chemotherapy and radiation regimens for non–Hodgkin lymphoma or rhabdomyosarcoma have been shown to face different challenges including severe chemotherapy induced nausea and vomiting and anorexia.[17,18] Additionally, neuroblastoma, one of the most common extracranial solid tumors, occurs most commonly in the abdomen and involves surgery and radiation therapy directly affecting the viscera and gastrointestinal (GI) tract. Despite these disease-specific issues, we continue to lack universal evidence-based, guided screening for nutrition complications and risk-directed interventions. No studies have explored this variability of malnutrition diagnoses nor examined nutrition support treatment in the context of malnutrition diagnoses. The purpose of this study is to utilize a national database to better understand the prevalence of malnutrition diagnoses in children being treated for solid tumors and understand utilization of nutrition support in these patients. We also explore variable use of nutrition resources for children diagnosed with different cancers through this database.

METHODS

Data source

The Pediatric Hospital Information System (PHIS) database was utilized to obtain data for this study with methods similar to those used in previously published work.[19] Managed by the Children's Hospital Association (CHA) (Overland Park, Kansas), the PHIS database includes detailed information reported from 48 of the largest freestanding children's hospitals across the United States (US) regarding hospital-based billing and discharge information. Participating institutions include all US census geographic regions and most US tertiary care pediatric hospitals. Data quality assessments are continually performed to ensure validity and reliability of the data by both CHA and participating institutions. Patient data are deidentified, given a unique patient identification number, and followed over the course of their illness. This study was reviewed and approved

through the PHIS External Data Release and was covered by institutional review board approval because of all the data being aggregated and deidentified.

Study population

This study included patients, aged 0–21 years old, who were admitted to a participating PHIS hospital between October 2015 and December 2019. Patients were included if they had a diagnosis of a solid cancer (CNS or non-CNS) and had one of the following: documentation of central line placement (via billing supply codes), a chemotherapy medication or administration billing code, or an encounter for chemotherapy using the International Classification of Diseases, 10th Revision, Clinical Modification (*ICD-10-CM*) at any time during the study period. Solid tumors of interest were organized into clinically relevant groups around organ system involvement and hypothesized treatment modalities. The groups included CNS tumors, bone, liver/biliary, kidney, retinal, abdominal or pelvic tumors not otherwise classified, and adrenal tumors. All remaining diagnoses were reviewed by two separate individuals to ensure they were appropriate to be classified as solid tumors not otherwise classified. Any disagreement between two evaluators was sent to a third reviewer. Hodgkin and non-Hodgkin lymphomas were also included. Patients with diagnosis codes from multiple cancer groups were excluded from the study. Demographic information, such as patient age, sex, race, and geographic region, was also extracted from the PHIS database.

Study definitions

Relevant *ICD-10-CM* codes were examined for any nutrition-related diagnoses. These were reviewed by two separate reviewers to determine the clinically relevant codes to include in the study and statistical analysis. A billed diagnosis of malnutrition included patients found to have *ICD-10-CM* codes for protein-energy malnutrition (E43, E44.0, E44.1, E46). Additional nutrition-related diagnoses were identified, including those for overweight or obesity (E66), abnormal weight loss (R63.4), and Kwashiorkor or Marasmus malnutrition (E4142). When defining functional malnutrition, we included any patient who had a billed diagnosis code of malnutrition, any procedure or supply code for feeding tubes, or a billed code for PN. Possible malnutrition expanded on the definition of functional malnutrition with the inclusion of pharmacy billing code for any of appetite stimulant available in PHIS (metoclopramide, megestrol, or cyproheptadine). GI conditions were defined using methods from a similar study in patients with pediatric leukemia.[19] Finally, hospital admissions with or without malnutrition were examined with descriptive statistics reported for patient-specific risk factors of interest. Hospitalizations were also examined for characteristics of interest among patients with malnutrition diagnosed, functional malnutrition, or possible malnutrition. Functional malnutrition admissions were compared with those without functional malnutrition for statistical analysis.

Statistical analysis

All data were summarized using descriptive statistics. Medians and interquartile ranges were used to describe quantitative variables and frequency with percentage used for qualitative variables. The prevalence of malnutrition (billed diagnosis, functional, or possible) was calculated as a percentage with corresponding exact 95% binomial confidence interval. The management of malnutrition was summarized descriptively. Statistical significance was determined by P value < 0.05. All analyses were performed using Statistical Analysis System software, version 9.4 (SAS Institute).

RESULTS

Demographics

We identified 13,375 unique patients with solid tumor cancers and 79,530 inpatient admissions during the study period (Table 1). Most patients were male (55.8%) and White (63.9%). The most common underlying solid tumor diagnoses included CNS tumors ($n = 3264$, 24.4%), non-Hodgkin lymphoma ($n = 1925$, 14.4%), and bone tumors ($n = 1730$, 12.9%), followed by kidney tumors ($n = 1111$, 8.3%), abdominal and pelvic tumors ($n = 910$, 6.8%), and adrenal tumors ($n = 896$, 6.7%).

Malnutrition diagnoses

In total, 26.5% ($n = 3546$) of patients were diagnosed with malnutrition, 45.4% ($n = 6076$) met functional malnutrition criteria, and 56% of patients ($n = 7484$) had possible malnutrition after receiving at least one appetite stimulant (Table 2). Among cancer groups, the prevalence of billed malnutrition diagnosis ranged from 14.1%–36.6% (Table 3). With the expanded definition of functional malnutrition, the prevalence nearly doubled in each cancer group, ranging from 24.8%–64.1% (Figure 1). Prevalence of possible malnutrition ranged from 34.7%–69.1% of patients among cancer groups (Table 3). Additional nutrition-related diagnoses demonstrated a higher prevalence of feeding difficulties among patients with CNS cancers (18.3%) and adrenal tumors (15.1%) compared with diagnoses of anorexia, abnormal weight loss, or underweight. The prevalence of diagnosed feeding difficulties was lower among children with other types of cancers.

Management of malnutrition

PN usage was highest among children with adrenal tumors (Table 3). Almost 50% of patients with adrenal tumors received PN ($n = 425$, 47.4%), followed by abdominal/pelvic cancers ($n = 244$, 26.8%), CNS tumors ($n = 817$, 25.0%), kidney ($n = 269$, 24.2%), and bone cancer ($n = 343$, 19.8%). Feeding tubes were most commonly utilized in CNS cancers

TABLE 1 Patient demographics

Characteristic	N (%)
Unique patients	13,375
Unique admissions	79,530
Male sex	7465 (55.8)
Race[a]	
White	8550 (63.9)
Black	1757 (13.1)
Asian	605 (4.5)
Other[b]/unknown	2463 (18.4)
Age at last encounter (age range), years	9.9 (infant−21)
Solid cancers	
CNS	3264 (24.4)
Bone	1730 (12.9)
Liver/biliary	686 (5.1)
Kidney	1111 (8.3)
Retinal	378 (2.8)
Abdominal/pelvic NOS	910 (6.8)
Adrenal tumors NOS	896 (6.7)
Other solid tumors[c]	1110 (8.3)
Lymphoma	
Hodgkin	1365 (10.2)
Non-Hodgkin	1925 (14.4)

Abbreviation: NOS, not otherwise specified.

[a]Race was patient or family self-reported and utilized the United States Census Bureau racial categories.

[b]Other includes: Native Hawaiian or Pacific Islander, Alaskan Native or American Indian, and Multiracial categories.

[c]Includes other solid tumors/masses of other organ systems not listed.

TABLE 2 Prevalence among patients of malnutrition diagnoses and study classifications with 95% CI

Malnutrition diagnosis	N (%)	95% CI
Billed diagnosis of malnutrition	3546 (26.5)	25.8%–27.3%
Functional malnutrition[a]	6076 (45.4)	44.6%–46.3%
Possible malnutrition[b]	7484 (56.0)	55.1%–56.8%

[a]Presence of a malnutrition diagnosis, parenteral nutrition, or feeding tube supply code.

[b]Presence of malnutrition diagnosis, feeding tube or supplies, parenteral nutrition, or appetite stimulant.

(n = 875, 26.8%) and adrenal tumors (n = 180, 20.1%). Patients with CNS tumors, bone cancers, and adrenal tumors most frequently utilized appetite stimulants. Metoclopramide was the most frequently used appetite stimulant in CNS cancers (n = 747, 22.9%), bone tumors (n = 392, 22.7%), and adrenal tumors (n = 190, 21.2%), and cyproheptadine was the most common in patients with kidney tumors (16.7%).

Associated factors with malnutrition admissions

Younger patients were more likely to have hospital admissions with a malnutrition diagnosis (Figure 2). Patients admitted with malnutrition diagnoses had a lower median age (7.8 years) compared with those without a malnutrition diagnosis (10.9 years, $P < 0.0001$). Patients with functional malnutrition were more likely to be even younger (<4 years of age) (Table 4). Hospital admissions with functional malnutrition were more prevalent in patients with public insurance compared with private (49.0% vs 45.1% of admissions, respectively; $P < 0.0001$). Admissions with functional malnutrition also had higher rates of chronic GI conditions (23.6% vs 6.6%, $P < 0.0001$), nausea and vomiting (24.0% vs 20.2%, $P < 0.0001$), and were more likely to have been admitted through the emergency department (24.4% vs 21.8%, $P < 0.0001$). Use of opioid medication was also different between hospitalizations with functional constipation compared with those without (58.6% vs 41.4%, $P < 0.0001$).

Median length of stay (LOS) was longer for admissions with functional malnutrition compared with admissions without functional malnutrition (6 vs 3 days, $P < 0.0001$). Of the 6076 patients with functional malnutrition, 1287 (21.2%) patients were observed to have malnutrition in 100% of their hospital admissions (ie, every recorded hospitalization in the data set had a malnutrition diagnosis, PN, or a feeding tube). Most of these patients had 1–4 admissions, but 133 had ≥5 admissions and still met the definition for functional malnutrition for every admission. Hospitalizations with functional malnutrition were also more likely to use appetite stimulants than hospitalizations without (28.5% vs 13.9%, $P < 0.0001$). The highest number of admissions for a single patient was 20 and all of them met criteria for functional malnutrition.

Nutrition interventions

We investigated the combination of malnutrition diagnosis in association with multiple interventions. Among 25,914 admissions with possible malnutrition, 50.8% were treated with a single intervention. Of those unique admissions, 33.3% were treated with an appetite stimulant (n = 8644), 10% received PN only (n = 2598), and 7.4% received only tube feeds (n = 1911) (Figure 3). Of patients with a malnutrition diagnosis code, the most common intervention was use of an appetite stimulant (8.3%, n = 2174), followed by PN use (n = 890), and least common use of a feeding tube (n = 570).

DISCUSSION

This study demonstrates a novel approach to investigating malnutrition diagnoses and nutrition support interventions in children with solid tumors. Although large pediatric databases have been used to examine

TABLE 3 Cancer specific prevalence of nutrition diagnoses and nutrition support therapies among patients

Diagnosis	CNS cancers *N* (%)	Bone cancers *N* (%)	Kidney *N* (%)	Abdm/pelvic *N* (%)	Adrenal tumors *N* (%)	Hodgkin lymph *N* (%)	Non-Hodgkin *N* (%)
Total patients	3264	1730	1111	910	896	1365	1925
Billed dx malnutrition only	949 (29.1)	524 (30.3)	265 (23.9)	211 (23.2)	328 (36.6)	193 (14.1)	505 (26.2)
Functional malnutrition	1709 (52.4)	733 (42.4)	452 (40.7)	374 (41.1)	574 (64.1)	338 (24.8)	886 (46.0)
Possible malnutrition	2092 (64.1)	1027 (59.4)	559 (50.3)	469 (51.5)	622 (69.4)	474 (34.7)	1024 (53.2)
Other nutrition/weight diagnoses							
Marasmus	5 (0.2)	3 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0)	3 (0.2)
Obese/overweight	231 (7.1)	176 (10.2)	19 (1.7)	74 (8.1)	20 (2.2)	119 (8.7)	189 (9.8)
Anorexia	225 (6.9)	124 (7.2)	44 (4.0)	40 (4.4)	72 (8.0)	47 (3.4)	85 (4.4)
Abnormal weight loss	205 (6.3)	191 (11.0)	47 (4.2)	60 (6.6)	42 (4.7)	96 (7.0)	120 (6.2)
Feeding difficulties	596 (18.3)	90 (5.2)	68 (6.1)	41 (4.5)	135 (15.1)	17 (1.3)	96 (5.0)
Underweight	27 (0.8)	15 (0.9)	1 (0.1)	5 (0.6)	11 (1.2)	4 (0.3)	8 (0.4)
Treatments							
PN	817 (25.0)	343 (19.8)	269 (24.2)	244 (26.8)	425 (47.4)	202 (14.8)	603 (31.3)
Feeding tube	875 (26.8)	170 (9.8)	122 (11.0)	93 (10.2)	180 (20.1)	42 (3.1)	215 (11.2)
Appetite stimulants	1302 (39.9)	690 (39.9)	329 (29.6)	247 (27.1)	346 (38.6)	259 (19.0)	532 (27.6)
Metoclopramide	747 (22.9)	392 (22.7)	126 (11.3)	146 (16.0)	190 (21.2)	187 (13.7)	292 (15.2)
Megestrol	242 (7.4)	118 (6.8)	63 (5.7)	44 (4.8)	61 (6.8)	37 (2.7)	76 (3.9)
Cyproheptadine	597 (18.3)	286 (16.5)	185 (16.7)	78 (8.6)	178 (19.9)	60 (4.4)	234 (12.2)
Other diagnoses							
UTI	278 (8.5)	119 (6.9)	75 (6.8)	85 (9.3)	60 (6.7)	24 (1.8)	90 (4.7)
Fever/neutropenia	1264 (38.7)	1090 (63.0)	475 (42.8)	245 (26.9)	488 (54.5)	604 (44.3)	1152 (59.8)

Note: Patients with retinoblastoma or other solid tumor not included in the table.

Abbreviations: Abdm, abdominal; CNS, central nervous system; dx, diagnosed; PN, parenteral nutrition; UTI, urinary tract infection.

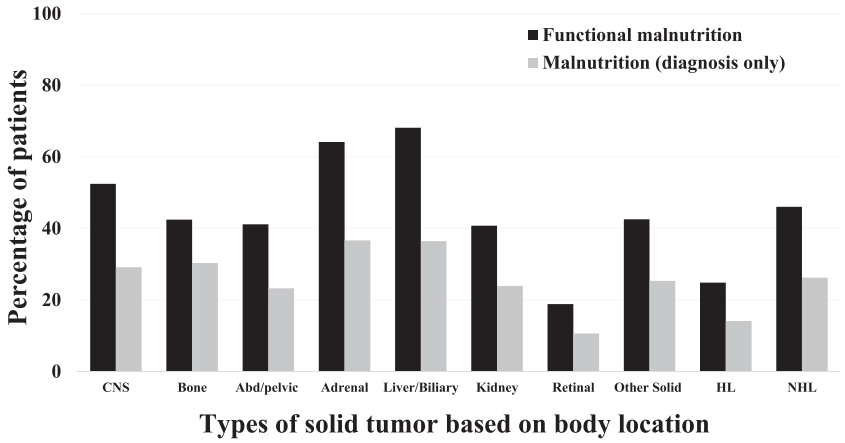

FIGURE 1 Comparison of patients with billed malnutrition diagnosis to functional malnutrition by cancer type. Abd, abdominal; CNS, central nervous system; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma

long-term outcome data in survivors of pediatric cancers, PHIS can specifically examine treatment and hospital characteristics surrounding nutrition and nutrition-related toxicities. In this study of children treated for solid malignancies, we identified 3546 patients with a billed diagnosis code of malnutrition, 6076 with functional malnutrition, and 7484 children with possible malnutrition. The prevalence and interventions varied among different types of solid cancers. Our data demonstrate fewer patients were diagnosed with malnutrition in this

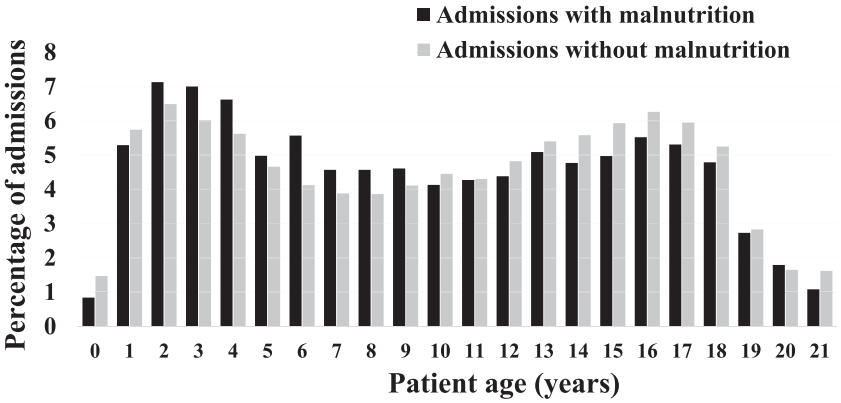

FIGURE 2 Percentage of evaluated hospital admissions occurring with or without malnutrition diagnosis broken down by age

TABLE 4 Factors associated with hospital admission with or without functional malnutrition

Characteristics	Functional malnutrition admissions[a] *N* = 17,270	Malnutrition diagnosis[b] *N* = 10,547	Possible malnutrition[c] *N* = 25,914	No functional malnutrition *N* = 62,260	*P* value[d]
Median age (IQR), years	7.8 (3.4–14.0)	9.3 (4.2–14.8)	8.5 (3.8–14.2)	10.9 (4.8–15.4)	<0.0001
Male sex	9704 (56.2)	5945 (56.4)	14,412 (55.6)	35,045 (56.3)	0.82
Race[e]					
White	10,843 (62.8)	6606 (62.6)	16,289 (62.9)	40,218 (64.6)	
Black	2178 (12.6)	1352 (12.8)	3200 (12.3)	7680 (12.3)	
Asian	832 (4.8)	514 (4.9)	1281 (4.9)	2960 (4.8)	
Other	3417 (19.8)	2075 (19.7)	5144 (19.9)	11,402 (18.3)	
Ethnicity					<0.0001
Hispanic/Latino	3919 (22.7)	2309 (21.9)	5643 (21.8)	12,848 (20.6)	
Non-Hispanic/Latino	12,432 (72.0)	7702 (73.0)	18,874 (72.8)	46,106 (74.1)	
Unknown/Not reported	919 (5.3)	536 (5.1)	1397 (5.4)	3306 (5.3)	
Median LOS (IQR), days	6 (3–17)	5 (3–9)	5 (3–11)	3 (2–5)	<0.0001
Insurance type					<0.0001
Public	8469 (49.0)	5076 (48.1)	12,509 (48.3)	28,055 (45.1)	
Private	7698 (44.6)	4788 (45.4)	11,807 (45.6)	30,379 (48.8)	
Other	763 (4.4)	459 (4.4)	1068 (4.1)	2412 (3.9)	
Unknown	340 (2.0)	224 (2.1)	530 (2.0)	1414 (2.3)	
Use of opioid	10,113 (58.6)	5290 (50.2)	13,580 (52.4)	25,790 (41.4)	<0.0001
Use of appetite stimulant	4291 (28.5)	3208 (30.4)	13,565 (52.3)	8644 (13.9)	<0.0001
GI chronic condition	4077 (23.6)	2002 (19.0)	4872 (18.8)	4120 (6.6)	<0.0001
Nausea/vomiting	4301 (24.0)	2815 (26.7)	6281 (24.2)	12,594 (20.2)	<0.0001
Admitted via ED	4207 (24.4)	2331 (22.1)	5915 (22.8)	13,551 (21.8)	<0.0001

Abbreviations: ED, emergency department; GI, gastrointestinal; IQR, interquartile range; LOS, length of stay.

[a]Functional malnutrition is defined as diagnosis code, parenteral nutrition, or feeding tube in this table.

[b]Includes admissions in which an *ICD-10-CM* code for malnutrition was documented.

[c]Includes admissions with a diagnosis code of malnutrition, parenteral nutrition, feeding tube, or use of an appetite stimulant.

[d]*P* value is comparing functional malnutrition and admission without functional malnutrition admissions.

[e]Race was patient or family self-reported and utilized the United States Census Bureau racial categories. Other includes: Native Hawaiian or Pacific Islander, Alaskan Native or American Indian, and Multiracial categories.

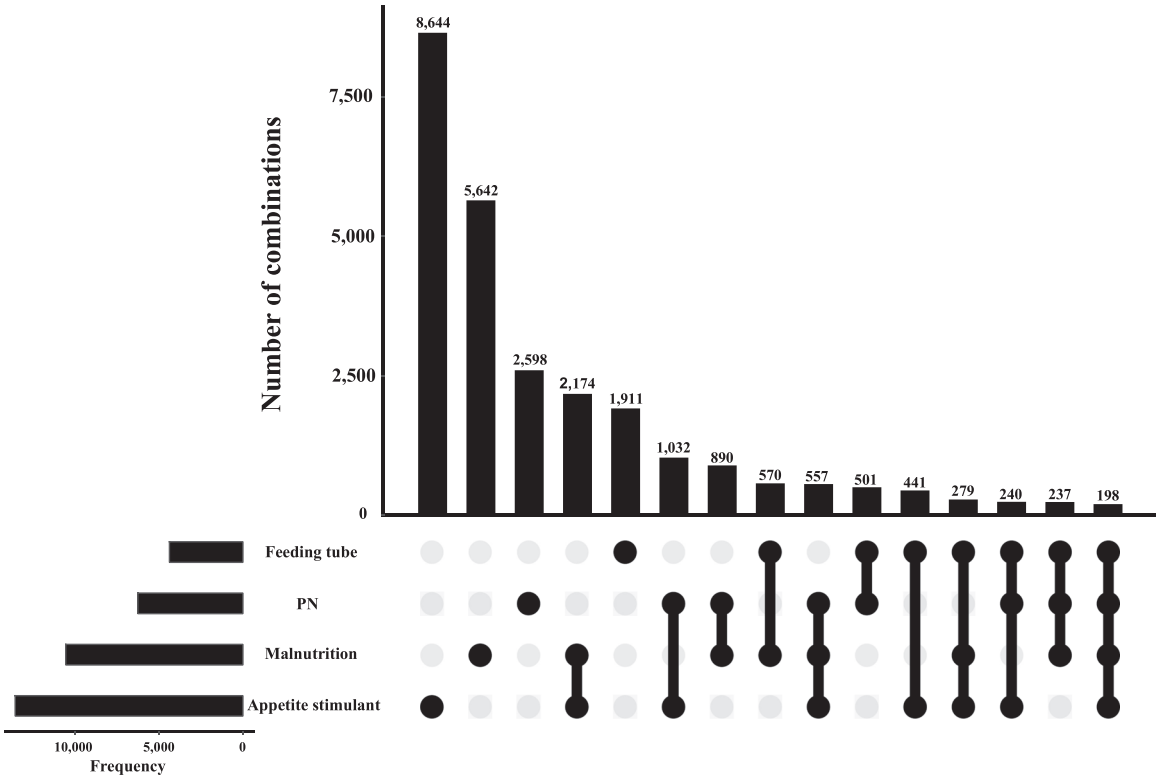

FIGURE 3 Common nutrition support interventions occurring with a billed malnutrition diagnosis. PN, parenteral nutrition

administrative database than has been previously reported in the literature.[2] This discrepancy reinforces the need to better define malnutrition in the pediatric oncology population. We included patients receiving enteral or parenteral supplements, which better captures the extent of children needing nutrition support. It is imperative to gain an accurate understanding of the scope of malnutrition, as a lack of appropriate recognition further complicates the ability to provide appropriate nutrition support for children undergoing cancer treatment.[20–22]

We found, independent of treatment, that tumor type can predispose to nutrition difficulties. CNS and adrenal tumors demonstrated the highest rates of malnutrition, both in terms of billed, functional, and possible malnutrition diagnoses. These two groups also demonstrated higher rates of feeding difficulties, which further supports the need for risk-based screening and intervention.[12,17,23] Patients with adrenal tumors had the highest use of PN, which likely reflects the intense treatment directed towards the abdomen including surgery, chemotherapy, radiation, immunotherapy, and stem cell transplantation. Feeding tubes and feeding dysfunction were commonly coded among patients with CNS tumors, which may indicate unique needs in patients who may have neurologic impairment from their tumor or treatment. Recognizing these disease-specific differences is critical in understanding the nutrition impact on cancer-directed therapies and guiding future clinical trials.[24,25]

Admissions with malnutrition diagnoses required a longer LOS, consistent with existing literature.[26–29] We also found that malnutrition inpatient encounters were more likely to be admitted through the emergency department and were associated with an increase in opioid prescription. Early identification and treatment of at-risk patients for malnutrition could lead decreased LOS and emergency department visits. Hospital admissions with malnutrition resulting in a longer LOS, and higher rates of opioid prescriptions may result in higher financial burden to the family as well potentially worse quality of life. Existing literature supports that proper nutrition during cancer treatment may avoid delays or dose reductions in cancer-directed therapy.[14,30] Additionally, it may support the need for increased nutrition support among patients with more complicated illnesses (those more highly affected use the emergency department and opioids). Regardless, proper nutrition may play a role in decreasing hospital LOS and emergency department utilization which has been suggested to contribute to avoiding delays or dose reductions in treatment.[23–26] Although adult studies have demonstrated worsened overall survival with cancer cachexia, it has only been postulated that pediatric survival is directly impacted by nutrition status and this will need to be examined in future studies.[30]

The imbalance of nutrition needs in conjunction with inadequate financial reimbursement contributes to an unsustainable model of providing critically needed nutrition support and professional dietetic services in pediatric oncology. We found that administration of PN, enteral tube feeds, or appetite stimulants were frequently used without a diagnosis code of malnutrition, further emphasizing the potential loss of diagnostic information and appropriate revenue reimbursement. Of the patients with functional malnutrition, 21% of

them met criteria for functional malnutrition on 100% of their admissions. It is unclear whether the remaining patients improved their nutrition status through interventions or treatment or if this is further evidence of the lack of consistent identification of nutrition needs. Regardless, this study demonstrates the importance of incorporating prospective nutrition outcomes into pediatric clinical trials and treatment. These inconsistencies demonstrated in our study also reflect the lack of consensus definition of cachexia and impairs research that can be performed in pediatric nutrition and the impact of muscle breakdown on cancer treatment for children.[31] Although adult cancer cachexia researchers are developing new targeted agents to prevent and treat cancer cachexia, particularly in pancreatic, colon, and lung cancers, pediatric oncologists are unable to implement treatments in children. A standardized definition and approach to malnutrition would allow for a uniform approach to research and clinical care in pediatric cancer cachexia.

There are limitations that are important to recognize in this study. First, as a retrospective study using an administrative database, we rely on the accuracy of billing codes and are unable to study any causal relationships. Additionally, utilizing aggregate, institutional data also rely on information reported and stored. One piece of information that is not readily accessible is the number of days or hours patients are not allowed to take anything by mouth. This would impact the ability to take in food, but unfortunately cannot be examined in the retrospective database. Second, we used billable codes to identify patients who received PN or had a feeding tube procedure or supplies. Although this is a useful surrogate for those receiving enteral nutrition support, it is likely to include patients who used feeding tubes for medication administration only. We utilized feeding tube supplies (such as pumps, flushes, bags, etc) to try to minimize the patients using enteral tubes for something other than nutrition support. Next, we acknowledge that the use of appetite stimulants alone does not necessarily constitute a diagnosis of malnutrition. Some medications utilized for appetite stimulation can be used as promotility agents or for other purposes and should not themselves be misconstrued with weight loss or malnutrition. However, accounting for this is meant to highlight the prevalence of use and to propose the importance of focusing on this population to prevent undernutrition. Finally, this is a very broad examination of solid tumors in general, but more direct and disease-specific study should be conducted to identify patient, disease, and treatment-related complications that impact nutrition support. Several assumptions must be made when using a deidentified, multi-institutional database, but evaluation by anatomic location aims to consider the tumor location, as well as chemotherapy, radiation, and/or surgery directed towards that specific site would impact gastrointestinal symptoms and nutrition needs. Prospectively, directed study towards specific disease entities will better elucidate the individual impact of certain chemotherapy drugs, doses administered, and other modalities of treatment on nutrition. Although the assessment of overall and progression-free survival is also limited by the use of a large, multicenter database, future study should focus directly on the impact of proper nutrition on these factors in specific cancer types.

CONCLUSIONS

Children with solid tumors have low rates of billed malnutrition diagnoses that do not necessarily correspond to the use of feeding tubes, PN, or appetite stimulants. Classification and treatment of malnutrition varies by tumor type and can be used to develop disease-specific guidelines on nutrition screening and interventions for children with the highest risk of developing malnutrition. Future studies will involve early malnutrition screening and prophylactic nutrition support to prevent malnutrition to determine the impact on hospital LOS, quality of life, and other treatment-related outcomes.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Daniel V. Runco and Jennifer A. Belsky equally contributed to the conception of this study. Daniel V. Runco, Jennifer A. Belsky, Joseph R. Stanek, and Nicholas D. Yeager contributed to the design of the study. Data acquisition and analysis was primarily performed by Joseph R. Stanek with review and interpretation by all authors. The manuscript was drafted by Daniel V. Runco and Jennifer A. Belsky and was additionally critically reviewed by Joseph R. Stanek and Nicholas D. Yeager. All authors gave final approval of the manuscript and agree to be fully accountable for ensuring the integrity and accuracy of the work.

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