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Abstract

This narrative synthesis aims to examine the dietary intake, diet quality, and dietary preferences of pediatric cancer patients during cancer treatment. Thirteen studies were eligible for review. Studies mostly investigated nutrient intake, with 7 reporting on children's food intake. There was consensus among studies, which reported suboptimal fruit and vegetable intake and a preference for savory, carbohydrate-based foods. Results suggest that pediatric cancer patients consume a limited variety of foods, with a high intake of noncore foods. Future research should aim to examine dietary food data against dietary guidelines to assess adequacy and variety within core food groups.

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Dietary intake and diet quality in children receiving treatment for cancer: a systematic narrative synthesis

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Abstract: This systematic narrative synthesis aimed to examine dietary intake, diet quality and dietary preferences of childhood cancer patients during cancer treatment. Thirteen studies were eligible for review. Studies mostly investigated nutrient intake,

with seven reporting on children’s food intake. There was consensus among studies, reporting suboptimal fruit and vegetable intake, and a preference for savoury, carbohydrate based foods. Results suggest that childhood cancer patients are consuming a limited variety of foods, with high intake of non-core foods. Future research should aim to examine dietary food data against dietary guidelines, for adequacy and an assessment of variety within core food groups.

Key Words: childhood cancer patients, diet, diet quality, intake, nutrition

Introduction

Improvements in medical therapy for paediatric cancer patients has led to an increase in overall childhood cancer survival rates.[1] Adult survivors of childhood cancer are at an increased risk of developing chronic long term health conditions such as obesity, cardiovascular disease, metabolic syndrome and osteoporosis.[2-4] Health-related research has recently commenced, to address the late effects of anti-cancer treatment on survival quality in both adult and child survivors of childhood cancer.[2, 3, 5] In the non-cancer population, a healthy diet has been shown to reduce the prevalence of the metabolic syndrome.[6] These chronic conditions seen in adult survivors of childhood cancer, all have the potential to be reduced and managed through healthy dietary behaviours similar to that seen in the general adult population.[7]

Prospective studies identify that up to 70% of adult childhood cancer survivors with metabolic syndrome do not consume a heart healthy diet.[2] Exploration into the dietary habits of adult survivors of childhood cancer has revealed inadequate intakes of fruit and vegetables and an excessive intake of saturated fat.[2, 8] Female and male adult survivors of childhood cancer with a poor diet are 2.4 and 2.2 times, respectively, more likely to be diagnosed with metabolic syndrome than those who meet recommended dietary guidelines.[2] It appears these poor dietary habits prevalent in survivorship are manifesting early after treatment completion.[9, 10] Young survivors of childhood cancer have been shown to have inadequate intake of calcium and folate.[9] Parents of young survivors of childhood cancer report their children have a suboptimal intake of fruit and vegetables, and an excessive intake of discretionary

foods.[10] They also identify that the dietary habits of their children have changed compared with their dietary habits prior to diagnosis.[10]

Adequate nutrition for children is essential to ensure their optimal growth and development, with good dietary habits enabling them to build sufficient muscle and bone mass. The aetiology of the development of poor dietary intake and habits in both young and older survivors of childhood cancer remains unknown. Reasons for these changing dietary habits may include long term changes in taste and smell function[11] or alterations in appetite regulation.[12] Negative side effects of cancer treatment can also impact on nutrition, including nausea, vomiting, mucositis and altered taste sensation. These side effects cause a reduction in oral intake,[13] causing childhood cancer patients' motivation to eat to be low.[10, 14-16] Alterations in dietary patterns as a consequence may become longer-term dietary habits potentially due to a lack of exposure to good dietary practices on-treatment.

To prevent treatment-related weight loss and malnutrition it is common for health professionals to encourage a high energy diet during treatment for childhood cancer.[17] Parents may also alter their strategies towards managing their child's dietary intake.[10, 16] Parents may start using more negative feeding practices such as reducing levels of discipline during meal times and introducing unhealthy foods to increase their child's intake.[18] Parents and carers commonly reward intake of any kind during treatment for their child's cancer, rather than focusing on habits likely to be healthy in the longer term. A prior experience, will affect how likely a person will select a food for a second time.[19] Development of cancer treatment related food aversions secondary to taste and smell changes, or gastrointestinal related

symptoms may also result in negative feeding experiences.[20] Most childhood cancer patients are undergoing anti-cancer treatment at a time when lifelong dietary habits are likely to be established.[21, 22] Very young childhood cancer patients are most at risk, as lifelong dietary habits are often created through food experiences during the first three years of life.[23]

While there is literature highlighting areas of concern in relation to diet.[24-26] To further explore the aetiology of the development of poor dietary habits among childhood cancer patients, and guide future nutrition interventions, on-treatment dietary intake must be explored. This systematic narrative synthesis aimed to examine the literature which assesses dietary intake, including diet quality and dietary preferences of childhood cancer patients during cancer treatment, we also aimed to compare this intake with country-specific recommended dietary guidelines.

Method

This systematic narrative synthesis was conducted using framework from the "Guidance on the conduct of narrative synthesis in systematic reviews: A product from the Economic and Social Research Council Methods Programme"[27] to explore the dietary intake and dietary preferences of childhood cancer patients during treatment.

Search strategy

MEDLINE, Scopus, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Cochrane Library databases were electronically searched in January 2018 to identify studies published in the English language prior to, and

including studies to date. Each database was searched with the following keywords and Booleans: '(child* OR pediat* OR paediat* OR adolescen*) AND (cancer OR oncol* OR tumor OR tumour OR leuk* OR neoplasms) AND (diet* OR intake OR food OR nutr*) AND (treatment OR chemotherapy)'. A secondary search was conducted by hand searching research abstracts presented at the Congress of the International Society of Paediatric Oncology (2011-2015). Reference lists of identified full text articles were searched for further eligible articles.

Eligibility criteria

Primary research studies were eligible if they investigated the dietary intake, quality, or preferences of children and adolescents aged one to 17 years of age during active treatment for cancer. There were no restrictions on cancer type or treatment regimen (radiotherapy or chemotherapy of all types). Studies were excluded if they assessed dietary intake during maintenance therapy only. Studies were required to report detail of food intake at a minimum, with studies reporting only energy intake as a measure of intake excluded. Studies were also excluded if they were case studies.

Titles and abstracts of studies identified through the combined database searches were screened for inclusion by one researcher (E.G.). The remaining studies were retrieved in full text and assessed for eligibility by two independent researchers (E.G. and L.B.). For cases of uncertainty regarding study eligibility (n=2) two independent advisors (J.C. and E.B.) were consulted and a final decision on inclusion of studies was made by consensus.

Data collection

Data extracted from eligible studies included: publication authors, year and country; population characteristics, including number of participants, age, diagnosis and treatment; dietary data collection methods; and food and/or nutrient intake results. We deemed a child's nutrient intake to be adequate if their intake was greater than or equal to 90% of recommended intake for that child's country of origin.

Data management

Studies were critically appraised and graded according to the National Health and Medical Research Council's (NHMRC)[28] level of evidence hierarchy, and were quality rated as either 'positive', 'neutral' or 'negative' according to the Academy of Nutrition and Dietetics (AND)[29] quality rating of primary studies checklist. A positive rating indicates that most aspects of the study meet validity criteria questions for sound scientific research, neutral indicates that the study is not exceptionally strong, and negative indicates that the majority of the aspects of the study do not meet validity criteria.

Results

Characteristics of studies

After removal of duplicates, 1729 articles were initially screened. The majority of articles were excluded based on title and abstract with 41 articles undergoing further review (Figure 1). Thirteen studies[10, 15, 16, 30-38] were eligible for critical appraisal. Of these, three were case-control studies,[38-40] six were case series studies,[30, 31, 34-37] and four were of cross-sectional design.[10, 15, 16, 32] All studies reported on participants who were receiving chemotherapy. Four studies[30, 31, 37, 39] also reported some study participants receiving radiotherapy, with one study[39] reporting on two participants

receiving both chemotherapy and radiotherapy and one[37] reporting on four participants receiving radiotherapy only. Two studies[30, 31] did not specify participant treatment regimen.

Two studies[37, 39] quantitatively reported children's food intake, (Table 1) and five[10, 15, 16, 32, 34] reported children's food preferences during treatment (Table 2). Nine[30, 31, 34-39] reported intake in the form of nutrients (Tables 3 and 4). Of those reporting nutrient intake, five[30, 31, 34, 37, 38] reported on micronutrients and protein, one[39] reported macronutrients and calcium and three[35, 36, 40] reported on macronutrients only.

Quality of the evidence

Quality assessment guided by the AND quality rating checklist resulted in nine[10, 15, 16, 30, 32, 36-38, 40] studies rated 'positive', three[34, 35, 39] 'neutral' and one[31] 'negative' (Table 5). The majority of studies (n=9/13)[10, 15, 16, 30-32, 34, 36, 37] were graded as the lowest level of evidence (level IV) according to the NHMRC's level of evidence hierarchy, though three[38-40] were graded as level III-2, and one[35] as level III-3. All studies, irrespective of their reported intakes, quality rating and level of evidence were reviewed in order to provide general descriptions of outcomes and recommendations for future research.

Dietary data collection methods

Four studies[10, 15, 16, 32] assessed dietary intake through semi-structured interviews. Two[15, 16] of these studies employed reflective interviewing techniques to determine the effects of treatment on oral dietary intake. One study[10] conducted telephone

interviews with parents of childhood cancer survivors, whilst the other utilised photographs, drawings and writing to prompt answers from children and their parents.[32] Two studies[15, 16] used face-to-face interviews with parents of children at various stages of treatment, with one[16] interviewing both the child and their parent/s.

The remaining studies collected data using either 24 hour dietary recalls (n=4)[30, 34, 37, 40] or daily food records (n=5),[31, 35, 36, 38, 39] with days of food recording ranging from two to 21 days. Dietary data collection time points varied greatly between studies. Four studies[30, 34, 38, 40] collected dietary data at unspecified time points during treatment. Specified time points of dietary data collection included the first 21 days of chemotherapy[35, 36] and at three months,[37] six months,[31] and one year post diagnosis.[39]

Food intake and food preferences

Food groups assessed by studies varied, however there was a general consensus among studies reporting suboptimal intake of fruit and vegetables.[37, 39] Fuemmeler et al.[39] reported children's food intake as number of serves consumed compared to Dietary Guidelines for Americans. Foods were grouped as fruit, vegetables, fried potatoes and snack chips, soft drinks, sweet beverages, milk, yoghurt and cheese. Comparisons to recommended serves per day of three of the five core food groups (fruits, vegetables and dairy products) were made in some papers, whilst grains and meat/alternatives were not reported. This revealed that children were not meeting recommended intakes for the three core food groups assessed. Overall low fruit, vegetable and dairy consumption were reported by Soliman Baghat et al.[37] with 30% of children consuming foods from these food groups. Considering other core foods,

only limited studies reported meat intake during treatment (n=2). Results were conflicting, with one study reporting participant meat intake to have decreased significantly when compared to pre-treatment[37] and another reported an increased desire to eat meat.[34]

Studies describing the dietary preferences of patients during treatment reported an increased preference for savoury and carbohydrate based foods specifically, bread, pasta, rice and potato dishes (n=5).[10, 15, 16, 32, 34] Takeaway foods, junk foods and salty foods were also reportedly purchased by parents for their child with cancer more regularly than usual (n=4).[10, 15, 16, 32] Two studies[16, 32] reported that children on-treatment for cancer had an increased preference for foods with strong flavours, including spicy and sour foods, with one study[16] reporting an avoidance of sweet foods. One study[10] described a reduction in fruit and vegetable intake.

Nutrient intake

The micro and macronutrients assessed differed greatly between studies (Table 3). Seven studies reported mean nutrient intake as a percentage of recommended dietary intakes.[16, 30, 31, 34, 36-40] Most studies found that childhood cancer patients were meeting micronutrient intake recommendations, with only one study reporting inadequate intakes for the majority of micronutrients assessed.[30] Calcium intake was deemed to be inadequate across all studies assessing this nutrient.[30, 31, 38, 39] Macronutrient intake results were inconsistent with two studies reporting intake of all macronutrients to be adequate[39, 40] and two reporting an inadequate intake for all macronutrients.[35, 36] Except for protein and fat, when focusing on adequacy of dietary intake at home.[36]

Two studies reported nutrient intake as a total percentage of children meeting the recommended intakes (Table 4), therefore, comparison to individual adequacy of recommended intakes could not be made. The studies did compare treatment intake to pre-treatment intake however results between the two studies were conflicting. Micronutrients assessed in the studies differed and protein intake was assessed in both. One reported an increased[34] intake of nutrients during treatment and the other reported a decreased intake.[37] Protein was the only nutrient assessed by all studies. Protein intake recommendations were met in six of the nine studies.

Discussion

This narrative synthesis is the first to systematically evaluate dietary intake and diet quality in children receiving active treatment for cancer through describing on-treatment diet intake and food preferences and comparing intake to recommended dietary guidelines. Measurement and reporting of dietary intake were highly variable among studies. Altered dietary intakes and food preferences of childhood cancer patients after commencing treatment were noted by all studies. The studies in this review suggest that childhood cancer patients' dietary changes often involved an increased preference for unhealthy foods. The changed dietary habits also included an increased preference for carbohydrate based savoury foods and salty foods, and a decreased intake of fruit and vegetables with subsequent impact on intake of micro and macronutrients.

This narrative synthesis shows that the poor dietary habits of childhood cancer patients are occurring during the intensive treatment period. This is concerning as

food preferences and habits of children established during childhood can persist later in life.[21] A previously published review reporting on the dietary intake of survivors of childhood cancer found that few consume diets that provide adequate nutrition.[41] Specifically, an insufficient intake of fruits, vegetables and calcium containing foods suggesting that the dietary quality of survivors of childhood cancer is poor.[41]

Poor diet quality combined with an increased risk of chronic health conditions within this population[2, 42, 43] is concerning. Dietary intake may be reduced due to treatment side effects resulting in nausea, vomiting, taste changes or oral mucositis.[44] Furthermore, food preferences during treatment may be significantly influenced by both the treatment-related side effects combined with treatment drugs, specifically steroids, which were recognised to impact on oral intake. Children receiving treatment for cancer will often require nutrition support when their food intake alone fails to provide sufficient energy and nutrients for growth.

Although this review attempted to assess nutrient adequacy within studies, overall nutrient adequacy could not be determined as the nutrients assessed differed greatly between studies and results were often confounding. Overall the dietary intake of childhood cancer patients who are undergoing cancer therapy without enteral or parenteral nutrition support (excluded here) are meeting the majority of their recommended micronutrient intakes. Calcium was the only micronutrient that was reported consistently as inadequate across all studies assessing nutrient intake. Macronutrient intake results were less definitive, with inconsistencies reported among studies assessing the adequacy of carbohydrate and fat intake as a percentage of total energy. Protein adequacy may be at risk in some cases.[45] It is

possible that nutrient intake is not a sensitive marker of dietary adequacy and quality alone.[46] Simultaneous reporting of total energy intake may contribute to confirmation of dietary adequacy from a perspective of meeting estimated requirements, however total energy intake was not a focus of this review. Intake of nutrients including sugar, saturated fat and sodium which when consumed in excessive amounts may contribute to chronic disease burden and impact dietary quality[47] were not reported by studies included in this review, yet they may be most relevant to investigate where changes to practice may be required.

A thorough assessment of diet quality involves an investigation into food quantity, variety and choice, and comparison of these measures to age appropriate dietary recommendations and guidelines.[46, 48] This review provides evidence that there are limited quality studies investigating the dietary intake of childhood cancer patients during treatment. The literature suggests that their micronutrient intake may be adequate but there is limited literature on their diet quality and variety. The limited studies do suggest that cancer patients are consuming poor food variety with a high intake of non-core foods but further work is need to confirm this. Dietary intake requires analysis at both a nutrient and a food level to allow comparison of dietary intake to recommended guidelines and subsequent development of practice recommendations for dietary therapy during treatment.

Due to the lack of literature, this systematic narrative synthesis investigated dietary intake and quality through the subgroups of food intake, food preferences and nutrient intake. If any participant in a study was receiving maintenance chemotherapy the study was excluded from this review as intake results were not

able to be separated by type of chemotherapy received. This exclusion may have resulted in otherwise suitable articles being excluded. Intervention and comparison studies are not required when describing a specified population's dietary intake and quality, so it was expected that most of the studies included in this review were of an observational design which rank as level IV according to the NHMRC's level of evidence hierarchy. All studies, regardless of their geographical origin were included which may reduce the applicability of results to single countries. Additionally, the variability of results found and difficulties describing diet quality may be explained by the varying medical systems and food provision available to children during treatment.

Although the findings of this narrative synthesis are limited by the small number of relevant studies, our review highlights the need for further advances in the field. There is a need for current research to investigate dietary intake patterns of children during their anti-cancer treatment to form an evidence base to guide appropriate and relevant recommendations for this population. Future research should aim to examine dietary food data against dietary guidelines, specific to the country of study, for adequacy and variety assessment of core food groups. Additionally, confounding factors to oral intake should be accounted for and described in detail, such as stage of treatment, treatment side effects which may impact on nutrition and treatment drugs which may stimulate or depress appetite. Nutrient intake assessment should support examinations of dietary food intake data to dietary guidelines and include both macronutrients and a variety of micronutrients, including sugar, saturated fat and sodium.

Conclusion

This systematic investigation of dietary intake and quality in children receiving treatment for cancer has revealed some evidence that dietary intake often meets minimum recommendations for daily intake of micro and macronutrients. There is fair evidence that children's dietary intake alters during treatment and some evidence to suggest that this intake is of a poor quality, with fruits, vegetables and calcium containing foods perhaps areas to be targeted for review. Comprehensive conclusions cannot be made due to conflicting results and a lack of dietary data describing food intake both qualitatively and quantitatively. Although lacking in numbers, studies reporting food intake did describe similar unhealthy food preferences. Longitudinal cohort or interrupted time series studies that take into consideration the recommendations presented by this review are warranted in order to strengthen this evidence base and assist with the development of appropriate interventions. Ongoing review is necessary when more research is available on this topic.

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Declaration of interest

The authors declare no conflicts of interest.

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441 **Figure Legends**

442 Figure 1: Methodological process of systematic narrative synthesis.

443 **Tables**

TABLE 1 Studies reporting food intake during treatment

Reference, country	No. and age (y) of population	Diagnosis (*n*)	Tx	Method (M) and time (T) of dietary data collection	Dietary intake during treatment		NHMRC level of evidence
Fuemmeler et al. (2013)[39] USA	n=8 Mean: 10.3	ALL or Lymphoma (15)	CT RT	M: 2-day food diary (1 x weekday, 1 x weekend day) T: 12 months post diagnosis	Mean serves consumed/day: *1 serve = 0.5 cup* Fruit: 2.1 (SD±2.5), vegetables: 2.7 (SD±1.6), fried potatoes and snack chips: 1 (SD±1.1) *1 serve = 1 cup* Soda/soft drinks: 0.0 (SD±0.0), sweet beverages: 0.6 (SD±0.7), milk: 0.6 (SD±0.9), yoghurt: 0.04 (SD±0.12) *1 serve = ~40g* Cheese: 0.9 (SD±1.2)	USDA recommended serves/day of core food groups assessed: Fruit = 4 Vegetables = 3-4 Dairy products = 2-3 - Mean intakes did not meet recommended serves for all core food groups	III-2
Soliman Bahgat et al. (2013)[37] Egypt	n=60 Mean (±SD): 9.5 (±3.4)	Leukaemia (28), lymphoma (14), bone tumour (7), CNS tumour (7), soft tissue tumour (4)	CT RT	M: 24 hour dietary recall T: 3 months post diagnosis	% of children consuming: Fruit, vegetable, beans and milk/cheese products = ~30 Meat = 22 Bread products = 47 Juice = 70 Sweets = 57 Comparison to pre-treatment: - Sig. ↑ in snacking (*p*=0.001) and meals (*p*=0.000) offered† to children/day - Sig. ↓ in meat consumption		IV

Abbreviations: *ALL* acute lymphoblastic leukaemia; *CNS* central nervous system; *CT* chemotherapy; *n* number; *NHMRC* National Health and Medical Research Council; *RT* radiotherapy; *Sig.* significant; *Tx* treatment; *USDA* United States recommended dietary allowance; *wks* weeks; *y* years
† Intake was not specified

TABLE 2 Studies reporting food preferences developed during treatment

Reference, country	Population (*n*) and age (y) at time of dietary ax	Diagnosis (*n*)	Tx	Method (M) and time (T) of dietary data collection	Food preferences during treatment	NHMRC level of evidence
Studies comparing preferences to pre-treatment						
Cohen et al. (2015)[10] Australia	n=18 Mean (±SD): 8.50 (±2.71)	ALL (8), Neuroblastoma (3), WT (3), BT (1) Rhabdomyosarcoma (1), Lymphoma (2)	CT	M: semi-structured telephone interviews with parents reporting retrospectively on their child's dietary habits during tx T: 2.29±1.56SD y post tx completion	- 100% reported their child had an ↑preference for savoury and junk foods - 61% reported an ↑preference for carbohydrate-based foods e.g. bread, pasta, savoury biscuits - 72% reported a ↓fruit and vegetable intake	IV
Gibson et al. (2011)[32] UK	n=13 Median (range): NS (4-12)	ALL (1), relapsed ALL (2), NHL (2), HL (1), WT (2), relapsed WT (1), BT (1), relapsed AML (1), PNT (1)	CT	M: 'auto driven' interviewing using photographs, drawings and writing as prompts T: children at various stages of tx, start (n=6), middle (n=5), end (n=2)	- Pasta based dishes craved - ↑preference for savoury foods - ↑preference for foods with strong flavours (e.g. cheese sandwich too bland) - Parents report an ↑ in purchasing of takeaway foods	IV
Sgarbieri et al. (2006)[34] Brazil	n=45 Median age: 5 years	ALL (45)	CT	M: 24 hour dietary recall T: induction and reinduction CT	- ↑desire to eat rice, beans, meat, bread and pasta	IV
Studies reporting current food preferences						
Skolin et al. (2006)[16] Sweden	n=21 Median (range) at start of CT: 8 (2-17)	Leukaemia (9), Solid tumour (6), Lymphoma (5), CNS tumour (2)	CT	M: semi-structured face-to-face interviews T: median (range) from start of CT to interview: 4 (1–12) months	Patient reported food preferences: - Pancakes, pasta, potato dishes, taco shells, rice, salty snacks Parent reported preferences: - Salty foods (3/21), Spicy and sour foods (3/21) Foods avoided by patients: - Red meat, hot dogs and chicken (total 8/21), sweets (6/21), chocolate (2/21)	IV

TABLE 2 *(continued)*

Reference, country	Population (*n*) and age (y) at time of dietary ax	Diagnosis (*n*)	Tx	Method (M) and time (T) of dietary data collection	Food preferences during treatment	NHMRC level of evidence
Skolin et al. (2001b)[15] Sweden	n=11 Median (range): 7 (2-15)	CNS tumour (4), ALL (4), LCH (1), HL (2)	CT	M: semi-structured face-to-face retrospective interviews with parents reporting their child's dietary habits at the start of tx T: since initiation CT, 3wks (n=3), 4wks (n=2), 5wks (n=1), 1y (n=5)	CHO based dishes, macaroni, fried chicken, fast food, broccoli and the avoidance of meat	IV

Abbreviations: *ALL* acute lymphoblastic leukaemia; *AML* acute myeloid leukaemia; *ax* assessment, *BT* brain tumour; *CNS* central nervous system; *CT* chemotherapy; *HL* Hodgkin Lymphoma; *LCH* Langerhans cell histiocytosis; *n* number; *NHMRC* National Health and Medical Research Council; *NHL* Non-Hodgkin Lymphoma; *NS* not specified; *PNT* primitive neuroectodermal tumour; *Tx* treatment; *wks* weeks; *WT* Wilms tumour; *y* years

TABLE 3 Studies reporting nutrient intake during treatment as a percentage of country specific recommended intakes

Reference, country	No. and age (y) of population	Diagnosis (n)	Tx	Method (M) and time (T) of dietary data collection	Nutrients assessed		Results		NHMRC level of evidence
					Micronutrients	Macronutrients	Diagnosis	Adequate intake (≥ 90% of recommended)	
Abdel-Kadar et al. (1995)[30] Egypt	n=70 Age range: 4-10	Lymphoma (33), leukaemia (30), rhabdomyosarcoma (7)	CT RT	M: 24 hour dietary recall T: > 3 unspecified time points over the 6 month study period	Calcium Iron Niacin Phosphorus Thiamine Vitamin A Vitamin C	Protein	Lymphoma or leukaemia Rhabdomyosarcoma	Thiamine Iron Thiamine	IV
Carter et al. (1983)[31] USA	n=99 Median (range): 7 (0.5-17)	Solid tumour (18), Haematopoietic cancer (25)	CT RT	M: 4-day food record (2 week days and 2 weekend days) T: 6 months after diagnosis	Calcium Iron Niacin Phosphorus Riboflavin Thiamine Vitamin A Vitamin C	Protein	Solid tumour Haematopoietic group	All nutrients Protein and all micronutrients except calcium	IV
Fuemmeler et al. (2013)[39] USA	n=8 Mean: 10.3	ALL or lymphoma (15)	CT RT	M: 2-day food diary (1 x weekday, 1 x weekend day) T: 12 months after diagnosis	Calcium	Carbohydrate Fat Protein	All	All macronutrients	III-2

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TABLE 3 *(continued)*

Reference, country	No. and age (y) of population	Diagnosis (n)	Tx	Method (M) and time (T) of dietary data collection	Nutrients assessed		Results		NHMRC level of evidence
					Micronutrients	Macronutrients	Diagnosis	Adequate intake (≥ 90% of recommended)	
Delbecque-Boussard et al. (1997)[40] France	n=15 Mean age: 6.2 years	ALL (15)	CT	M: 24 hour dietary recall T: 22, 36 and 71 of CT	Nil	Carbohydrate Fat Protein	ALL	Day 22: protein Day 36: protein and carbohydrate Day 71: all macronutrients	III-2
Skolin et al. (1997)[35] Sweden	n=14 Median (range) :10 (5-16)	ALL (3), CNS tumour (4), Sarcoma (3), Lymphoma (3), WT tumour (1)	CT	M: 21-day dietary food record T: Day -1 of CT		Carbohydrate Fat Protein	All	Nil	IV
Skolin et al. (2001a)[36] Sweden	n=11 Median age: 7 Range: 2-15	CNS tumour (4), ALL (4), LCH (1), HL(2)	CT	M: 21-day dietary food record T: Day 0 of CT		Carbohydrate Fat Protein	All	Entire recording period: nil Hospital days: nil Home days: protein and fat Mixed† days: nil	IV
Tan et al. (2013)[38] Malaysia	n=53 Age range: 3-12	ALL (43), AML (10)	CT	M: 3-day food records T: during induction or consolidation CT	Calcium Iron Niacin Riboflavin Thiamine Vitamin A Vitamin C	Protein	All	Protein and all micronutrients except calcium	III-2

Abbreviations: *ALL* acute lymphoblastic leukaemia; *AML* acute myeloid leukaemia; *CNS* central nervous system; *CT* chemotherapy; *HL* Hodgkin Lymphoma*; LCH* Langerhans cell histiocytosis; *Tx* treatment; *RT* radiotherapy; *NHMRC* National Health and Medical Research Council; *wks* weeks; *WT* Wilms tumour; *Y* year

† Days spent at home and hospital

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TABLE 4 Studies comparing nutrient intake during treatment to baseline intake

Reference, country	No. and age (y) of population	Diagnosis (n)	Tx	Method (M) and time (T) of dietary data collection	Nutrients assessed		Results	NHMRC level of evidence
					Micronutrients	Macronutrients		
Sgarbieri et al. (2006)[34] Brazil	n=45 Median age: 5 years	ALL (45)	CT	M: 24 hour dietary recall T: during induction and reinduction CT	Copper Zinc	Protein	% of children meeting recommended intakes at baseline: Protein = 91 Zinc = 76 Copper = 98 Children ↑ their intake of all nutrients during induction and reinduction CT	IV
Soliman Bahgat et al. (2013)[37] Egypt	n=60 Mean (±SD): 9.5 (±3.4)	Leukaemia (28), lymphoma (14), bone tumour (7), CNS tumour (7), soft tissue tumour (4)	CT RT	M: 24 hour dietary recall T: 3 months after diagnosis	Calcium Iron Vitamin A Vitamin C	Protein	% of children meeting recommended intake at 3 months: Calcium = 25% Iron = 18% Protein = 0% Vitamin A = 17% Vitamin C = 10% Children ↓ their intake of all nutrients during treatment	IV

Abbreviations: *ALL* acute lymphoblastic leukaemia; *CNS* central nervous system; *CT* chemotherapy; *Tx* treatment; *RT* radiotherapy; *NHMRC* National Health and Medical Research Council; wks weeks

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TABLE 5 Quality appraisal of studies included in this systematic literature review based on the AND's quality rating system[29]

Reference	Research question clearly stated	Selection of study subjects free from bias†	Study groups comparable†	Method of handling withdrawals described	Blinding of assessors	Procedure, comparisons and intervening factors described in detail†	Outcomes and measures defined, valid and reliable†	Appropriate statistical analysis	Conclusions supported by results with biases and limitations taken into consideration	Bias due to study's funding/ sponsorship unlikely?	Quality Rating
Abdel-Kadar et al. (1995)[30]	Yes	Yes	N/A	No	Yes	Yes	Yes	Yes	Yes	Unclear	Positive
Carter et al. (1983)[31]	No	Yes	N/A	No	Yes	No	No	No	No	Yes	Negative
Cohen et al. (2015)[10]	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Positive
Delbecque-Boussard et al. (1997)[40]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Positive
Fuemmeler et al. (2013)[39]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Neutral
Gibson et al. (2012)[32]	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Positive
Sgarbieri et al. (2006)[34]	Yes	Yes	N/A	No	Yes	Yes	No	Unclear	No	Unclear	Neutral
Skolin et al. (1997)[35]	Yes	Yes	N/A	No	Yes	Yes	No	Yes	Yes	Unclear	Neutral
Skolin et al. (2001a)[36]	Yes	Yes	N/A	Yes	Yes	Yes	No	Yes	Yes	Yes	Positive
Skolin et al. (2001b)[15]	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Positive
Skolin et al. (2006)[16]	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Positive
Soliman Bahgat et al. (2013)[37]	Yes	Yes	N/A	No	Yes	Yes	Yes	Yes	No	Unclear	Positive
Tan et al. (2013)[38]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Positive

Abbreviations: *N/A* not applicable

† If the answers the questions marked with 'a' do not indicate that the study is exceptionally strong the quality rating is designated as 'neutral', if the majority of the answers to the questions marked with 'a' are 'yes' plus one additional 'yes' the quality rating is designated as 'positive. If six or more answers are 'no' the quality rating is designated as 'negative'.

Legends

Figure 1: Methodological process of systematic narrative synthesis.