Use of food restrictions to prevent infections in paediatric patients with cancer and haematopoietic cell transplantation recipients: a systematic review and clinical practice guideline

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Summary

Background Food restrictions during periods of neutropenia have been widely used in oncology settings to prevent infections. As there is a lack of clearly demonstrated effectiveness, this strategy is being increasingly questioned.

Methods A multi-national panel of 23 individuals was convened to develop a clinical practice guideline (CPG) on the use of food restrictions to prevent infections in paediatric patients with cancer and haematopoietic cell transplantation (HCT) recipients. It included representation from persons with lived experience and physicians, dieticians, nurses,

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pharmacists and guideline methodologists working in paediatric oncology/HCT or infectious diseases. Panel members (female n = 15; 65%) were from North America (12, 52%), Europe (8, 35%), South America (2, 9%) and Australia (1, 4%). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to formulate the CPG recommendations based on a systematic review of randomised controlled trials (RCTs). MEDLINE, MEDLINE in-Process and Embase databases were searched from January 1, 1980, to May 7, 2024, with a broad strategy which combined subject headings and text words relating to neutropenia, infection and diet.

Findings The systematic review, which provided the evidence base for the CPG recommendations, identified 4312 unique citations, of which 52 were retrieved for full-text evaluation. Eight RCTs met the eligibility criteria and informed panel deliberations. Although there was clinical heterogeneity in the food restrictions evaluated, data were consistent in suggesting that food restrictions lack clinically significant benefit in preventing infections. The panel made two conditional recommendations against the use of food restrictions in a) paediatric patients with cancer receiving chemotherapy and b) in the setting of allogeneic and autologous HCT. The panel developed a good practice statement to emphasise the importance of health care organisations and families adhering to local food safety practices.

Interpretation This CPG provides the first evidence-based recommendations on use of food restrictions to prevent infections in children and adolescents undergoing chemotherapy and paediatric haematopoietic cell transplant recipients.

Funding This CPG was funded and developed through the POGO Guidelines Program.

Keywords: Practice guideline; Food restrictions; Neutropenic diet; Paediatric oncology

Research in context

Evidence before this study

Food restrictions during periods of neutropenia have been widely used in both paediatric and adult oncology settings to prevent infections. Despite several commentaries and expert opinion position statements, no paediatric clinical practice guideline (CPG) addressed this topic and provided evidence-based recommendations despite food restrictions being used frequently in the clinical care of children and adolescents with cancer or paediatric haematopoietic cell transplant recipients.

Added value of this study

This CPG provides the first evidence-based recommendations addressing the use of the food restrictions ('neutropenic diet') in children and adolescents undergoing chemotherapy and paediatric haematopoietic cell transplant recipients.

Implications of all the available evidence

Based on the systematic literature review, the CPG recommendations suggest food restrictions not be used to prevent infections in this population. The CPG panel emphasized the importance of ensuring local/regional food safety policies in children and adolescents undergoing chemotherapy and paediatric haematopoietic cell transplant recipients.

Introduction

Infectious complications remain an important cause of morbidity and mortality in patients receiving therapy for cancer or undergoing haematopoietic cell transplantation (HCT).[1,2] To decrease the risk of infection in these patients, various strategies have been suggested, such as prophylactic antimicrobials, protective isolation, and the restriction of certain food items (often termed a neutropenic diet). The rationale for food restrictions is to limit the introduction of potentially harmful bacteria, parasites and fungi, which could migrate from the gastrointestinal tract to the bloodstream, by avoiding foods that might harbour these organisms.[3] Although there is no uniform definition of a neutropenic diet, consumption of raw vegetables and fruits is usually restricted.[4] Food restrictions during periods of neutropenia have been widely used in both paediatric and adult oncology settings, despite a lack of clearly demonstrated effectiveness of this strategy. Since dietary restrictions can impair the intake, enjoyment of food, and lower quality of life during treatment they are being increasingly questioned.[3,5–7]

Clinical practice guidelines (CPGs) facilitate evidence-based care by describing the risks and benefits

of different management options based on a systematic review of the literature. A recent CPG by the American Society of Clinical Oncology (ASCO) addressed the use of the food restrictions in adult oncology patients and made a weak recommendation to not use a neutropenic diet during active treatment.[8] Although several commentaries and editorials regarding the restriction of certain food items have been published,[5,9] no CPG for paediatric patients with cancer or those undergoing HCT have been developed to date. Therefore, the Pediatric Oncology Group of Ontario (POGO) Supportive Care and Guidelines Program brought together a multinational and multidisciplinary panel to develop a CPG on the use of food restrictions to prevent infections in paediatric patients being treated for cancer or undergoing HCT. The CPG recommendations are intended for children and adolescents 1–18 years old with cancer or HCT recipients. The CPG recommendations may be most useful to paediatric oncology and HCT health care professionals, patients and their caregivers, policy makers and quality improvement leaders.

Methods

Panel constitution

A multi-national and multidisciplinary panel was convened specifically for this CPG to provide representation from persons with lived experience and physicians, dieticians, nurses, pharmacists and guideline methodologists working in paediatric oncology/HCT (n = 13) or infectious diseases (n = 8). Panel members (female n = 15, 65%) were selected then invited through existing supportive care research networks based on relevant clinical and research professional expertise or lived experience and were drawn from North America (12, 52%), Europe (8, 35%), South America (2, 9%) and Australia (1, 4%); see Appendix 1 for further detail. Clinical specialist physicians made up the largest proportion of the panel (14, 61%). No member had a conflict that precluded their participation in the development of any of the CPG recommendations (Appendix 2).

General CPG development process

This CPG was developed through the POGO Supportive Care and Guidelines Program. Widely accepted CPG development procedures were followed.[10] The procedure requires the compilation of a relevant panel of stakeholders, including experts and those with lived experience. The panel members set the scope of the CPG, propose the main health questions to be answered, rank the importance of relevant outcomes of interest, and participate in the systematic review process to answer specific questions. The panel then interprets the systematic review results and develops recommendations based on those results. The panel votes on agreement or disagreement with the recommendations, with subsequent modification, until at least 80% of the panel agrees with the draft recommendation.

Two key health questions were addressed:

1. Should food restrictions be used to prevent infections in paediatric patients with cancer?
2. Should food restrictions be used to prevent infections in paediatric HCT recipients?

The panel identified a potential for different CPG user perspectives regarding the use of food restrictions in patients with cancer versus those undergoing HCT and believed that answering the health questions separately was important. The panel identified key outcomes and rated their importance by consensus. The following outcomes were considered critical or important for panel decision making: bloodstream infections, febrile neutropenia, major infection (defined as per study authors or a documented infection in the absence of a study author definition), mortality, diet acceptability, diet adherence, nutritional status and quality of life.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to formulate recommendations.[11] The level of evidence was rated as high, moderate, low or very low. The rating is based on study design, and influenced by risk of study bias, and the consistency, precision and the directness of the evidence to the target population. Risk of bias was assessed using the Cochrane Collaboration's tool.[12] Consistency and precision were evaluated qualitatively by the CPG panel. Directness was considered in terms of the age range of population studied, and the proportion of patients who had undergone HCT or conventional chemotherapy. GRADE recommendations can be either strong or conditional. Strong recommendations are made when the benefit of an intervention clearly outweighs the harms or vice versa, and generally should be adopted as a matter of policy. Conditional recommendations are made when the potential benefits of an intervention versus its downsides are more closely matched or if there is uncertainty regarding the benefits or risks of an intervention. In cases of a conditional recommendation, the decision to implement the recommendation may take into consideration other values, preferences or available resources. The panel also considered making good practice statements. GRADE good practice statements are made in situations where there is indirect evidence that strongly supports the benefit of an intervention.[13] The GRADE approach suggests asking whether the alternative is absurd or clearly inconsistent with ethical norms when making a good practice statement.

Search strategy and selection criteria

With the assistance of a library scientist, we performed searches of Ovid MEDLINE, MEDLINE in-Process and

Embase indexed up to May 7, 2024, to identify randomised controlled trials (RCTs) evaluating the use of a food restriction intervention to prevent infection in patients with cancer or undergoing HCT. The full search strategy is provided in Appendix 3. Eligibility criteria were determined *a priori*. Studies were included if they were a parallel group RCT fully published in 1980 or later, compared the use of a food restriction intervention to prevent infection to an alternative strategy, and where at least 90% of patients of any age received chemotherapy for cancer treatment or HCT for any indication. As the CPG panel anticipated that there would be a limited number of randomised trials evaluating the use of food restrictions to prevent infections specifically in the paediatric cancer/HCT setting, the CPG panel made the *a priori* decision to include randomised trials conducted in the cancer/HCT setting regardless of age of the study participants. The CPG panel made this decision as data from the adult cancer/HCT setting, while more indirect, were thought to be generalizable to the paediatric cancer/HCT setting. There was no restriction by language.

Two reviewers (PP, PDR, TL or SC) independently evaluated the titles and abstracts of publications identified by the search strategy and potentially relevant publications were retrieved in full. Two reviewers (PP, PDR or TL) independently assessed the full-text papers for eligibility. Disagreements were resolved by consensus. We described agreement with study inclusion between the two reviewers using the kappa statistic and agreement was defined as slight (0–20%), fair (21–40%), moderate (41–60%), substantial (61–80%) or almost perfect (81–100%).[14]

The following data elements were abstracted by one reviewer (PP or PDR) and double-checked by a second reviewer (PP or PDR): study-level characteristics (population, country of enrolment, age, infection prophylaxis given, hospital and treatment setting), details of the intervention and control groups, and the *a priori* determined critical and important outcomes (bloodstream infections, febrile neutropenia, major infection, mortality, diet acceptability, adherence, nutritional status and quality of life) along with the risk of bias characteristics. Discrepancies were resolved by consensus.

Statistics

We planned to combine data at the study level through a random effects meta-analysis. Synthesis was to be conducted when there were at least three studies that reported the same outcome. Given the heterogeneity of the intervention group food restrictions between included studies, meta-analysis was not performed but forest plots were created to visualise results of key outcomes. Forest plots were created using Review Manager 5.4 (Cochrane Collaboration, Nordic Cochrane Centre).[15]

Formulating recommendations

During three virtual calls, panel members reviewed the evidence tables and formulated draft recommendations and a good practice statement. Each draft recommendation or good practice statement was voted upon, and acceptance was determined by at least 80% agreement. Notes on the discussion leading to the recommendation were made. Following the panel calls, a draft version of the manuscript was circulated to panel members and revised until approved by all authors. The final CPG was not circulated externally for further review. Instead, the peer review process during manuscript submission was considered to be a suitably rigorous and pragmatic approach to external review. This CPG will be updated in five years or sooner in the event of publication of important new information.

Ethics

Ethical approval was not required for this study as it used only secondary data from existing published studies.

Role of funding source

This work was supported by POGO. The funder did not have any influence over the content of this manuscript or the decision to submit for publication.

Results

Table 1 presents the CPG recommendations and panel remarks based on the GRADE system. The systematic review, which provided the evidence base for the CPG recommendations, identified 4312 unique citations, of which 52 were retrieved for full-text evaluation. Eight RCTs met the eligibility criteria and informed the deliberations of the panel. The PRISMA flow diagram is provided in Appendix 4. The characteristics of the included studies are summarised in Table 2, and further study details and outcomes are included in Table 3 and Appendices 5-9 provides a summary of the risk of bias results.

The included studies showed clinical heterogeneity and limitations in their reporting. Most of the studies (6/8 RCTs) were conducted in high-income countries. All studies included inpatients, whereas only three also included outpatients. Half (4/8) included paediatric patients; the panel considered that there was high relevance in using indirect data from adult cancer and HCT populations. Studies lacked details on air-handling procedures applied (2/8 studies reported patients being in rooms that had high-efficiency particulate air filters) and antimicrobial prophylaxis (6/8 studies had at least partial reporting). The food restrictions intervention varied, but all studies stated that the avoidance of raw fruits (unless thick-skinned or peeled) and vegetables were a component of the food restriction intervention. Some

Good practice statement	Panel remarks
Follow practices for safe food handling, storing, preparation and consumption outlined by applicable health authorities.	This good practice statement reflects the importance of food safety practices for the prevention of infection.
Health questions and recommendations	**Panel remarks**
Should food restrictions be used to prevent infections in paediatric patients with cancer?	
We suggest that food restrictions not be routinely used for the prevention of infections in paediatric patients with cancer (*conditional recommendation, moderate quality evidence*)	The six RCTs conducted in cancer patients receiving chemotherapy failed to show any consistent improvement in infection outcomes with the use of food restrictions. The panel also considered the potential harms and impact on quality of life of strict food restrictions. The panel made a conditional rather than strong recommendation against the use of food restrictions in recognition of the heterogeneity of the food restrictions evaluated.
Should food restrictions be used to prevent infections in paediatric HCT recipients?	
We suggest that food restrictions not be routinely used for the prevention of infections in paediatric autologous HCT and allogeneic HCT recipients (*conditional recommendation, low quality evidence*)	The two RCTs conducted in the HCT setting did not show a significant benefit of using food restrictions during periods of neutropenia. The panel also considered the more indirect but generalizable evidence from the cancer chemotherapy setting. The panel made a conditional rather than strong recommendation against the use of food restrictions based on both the lack of direct paediatric data and the heterogeneity in the food restrictions evaluated.

HCT, haematopoietic cell transplantation; RCT, randomized controlled trial.

Table 1: **Summary of recommendations and good practice statement.**

studies restricted various cheese products and yogurt. The food restrictions intervention was compared to control groups with unrestricted diets. In two studies,[17,19] the control groups were encouraged to have at least one well-washed raw fruit or vegetable a day. In most studies (5/8), food safety guidance was explicitly provided to both the food restrictions group and the control group. Additional details on the study comparisons are provided in Appendices 7 and 8. Knowledge gaps uncovered through CPG development are shown in Table 4.

Characteristic and strata	No. studies (%)[a]
Study population characteristics	
Treatment	
Cancer patients receiving chemotherapy only	6 (75%)
Haematopoietic cell transplantation only	2 (25%)
Age of participants[b]	
Adult	4 (50%)
Paediatric	2 (25%)
Both	2 (25%)
Hospitalization status	
In-patient	5 (63%)
Out-patient	0 (0%)
Both	3 (38%)
Country	
India	2 (25%)
Italy	1 (13%)
Netherlands	1 (13%)
United States	4 (50%)
Risk of bias	
Adequate sequence generation	6 (75%)
Adequate allocation concealment	5 (63%)
Participants and personnel blinded	0 (0%)
Outcome assessors blinded	2 (25%)
Lack of attrition bias	8 (100%)
Free of selective reporting	7 (88%)

[a]May not add to 100 due to rounding. [b]Adult: all patients >15 years; Paediatric: all patients <25 years; Both: Patients ≤ 15 and ≥25 years or all patients 15–25 years.

Table 2: **Characteristics of included studies (N = 8).**

Good practice statement

Follow practices for safe food handling, storing, preparation and consumption outlined by applicable health authorities.

This Good Practice Statement was made by the panel to emphasise that safe handling, storing, preparation and consumption of food is important to prevent infection. The panel also noted that while individual health care institutions may have these practices mandated for hospitalised patients, it is important that patients and their families also receive education on following food safety practices at home. Health authorities vary on their specific recommendations on the basis of local food practices; consequently, it is important that institutions and families follow local or regional applicable guidance.

For example, food safety practices may draw from the five core steps outlined by the World Health Organization as follows[24]: keep food clean; separate raw and cooked items; cook thoroughly; keep food at safe temperatures; and use safe water. Regionally, the Food and Drug Administration in the United States uses "clean, separate, cook and chill"[25] as the core elements of food safety, as water safety is considered to be already assured. The United Kingdom's Food Standards Agency similarly provides advice on cooking, cleaning, chilling

Author	Year	No.	Age range	Cancer or HCT type	Neutropenic status	Bloodstream infection		Febrile neutropenia		Major infection[c]		Overall mortality	
						Food restriction group	Control group	Food restriction group	Control group	Food restriction group	Control group	Food restriction group	Control group
Cancer													
Gupta[16]	2022	42	3–13	Acute leukaemia, lymphoma, solid tumors	NR	NR	NR	12/21 (57%)	9/21 (43%)	10/21 (48%)	3/21 (14%)	3/21 (14%)	0/21 (0%)
Radhakrishnan[17]	2022	200	1–60	Acute leukaemia (induction phase)	NR	9/102 (9%)	6/98 (6%)	33/102 (32%)	37/98 (38%)	26/102 (25%)	32/98 (33%)	4/102 (4%)	9/98 (9%)
Moody[18]	2018	150	1–28	Acute leukaemia, lymphoma, solid tumors	ANC < 0.5: 57/77 (74%); 52/73 (71%) Median no. Days ANC < 0.5: 10.5; 9.6	7/77 (9%)	5/73 (7%)	27/77 (35%)	24/73 (33%)	8/77 (10%)	6/73 (8%)	NR	NR
Gardner[19]	2008	153	17–88	AML or high-risk myelodysplastic syndrome	Median no. Days ANC < 0.5: 20, 21	11/78 (14%)	22/75 (29%)	NR	NR	23/78 (29%)	26/75 (35%)	unclear	unclear
van Tiel[20,a]	2007	20	30–69	Acute leukaemia (induction phase)	ANC <1: all patients	NR	NR	NR	NR	NR	NR	NR	NR
Moody[21]	2006	19	1–8	ALL, osteosarcoma, Ewing's sarcoma, medulloblastoma	ANC < 1.5: 8/9 (89%); 9/10 (90%) Mean no. Days ANC < 0.5: 5.9; 9.2	1/9 (11%)	0/10 (0%)	4/9 (44%)	4/10 (40%)	2/9 (22%)	0/10 (0%)	NR	NR
HCT													
Stella[22,b]	2023	222	22–72	Allogeneic or autologous HCT	ANC < 0.5: all patients Median no. Days ANC < 0.5: 6; 6	16/111 (14%)	22/111 (20%)	48/111 (43%)	37/111 (33%)	NR	NR	0/111 (0%)	1/111 (1%)
Lassiter[23]	2015	47	23–62	Allogeneic HCT	NR (Given setting, assume all patients)	6/20 (30%)	7/25 (28%)	NR	NR	NR	NR	NR	NR

No., number of participants; NR, not reported; AML, acute myeloid leukaemia; ALL, acute lymphoblastic leukaemia; ANC, absolute neutrophil count; HCT, haematopoietic cell transplantation. [a]Cycle-level data only presented by authors (i.e., not patient-level); data not shown. [b]216/222 patients received allogeneic or autologous HCT; 6/222 received high dose chemotherapy. [c]Defined as per study authors or a documented infection in the absence of a study author definition.

Table 3: **Infection outcomes and overall mortality reported in the included randomized controlled trials.**

Impact of food restrictions on quality of life and nutritional status in children and adolescents receiving chemotherapy or undergoing HCT
Uncertainty of safety of particular foods (e.g., unpasteurized teas, some cured meats)
Effectiveness of different regional/local advice regarding food safety
Application to low resource settings

HCT, haematopoietic cell transplantation.

Table 4: **Identified knowledge gaps.**

and avoiding cross-contamination.[26] In addition, avoidance of raw egg, undercooked meats, unpasteurised milk and cheeses, food with visible or introduced mould, and potentially contaminated drinking water seem reasonable in all patients, since each of these is an important risk factor for life-threatening disease in immunocompromised children.

Recommendation 1

We suggest that food restrictions not be routinely used for the prevention of infections in paediatric patients with cancer (conditional recommendation, moderate quality evidence).

Literature review and analysis

Six RCTs evaluating food restrictions in patients receiving chemotherapy for cancer and reporting key infection related outcomes informed this recommendation (Table 3 and Fig. 1). Additional outcome details are provided in Appendices 8 and 9. Two of the RCTs were conducted exclusively in paediatric patients, and two RCTs included both paediatric and adult patients. A single RCT conducted in 153 patients (median age: 64 years) with acute myeloblastic leukaemia or high-risk myelodysplastic syndrome reported rates of bloodstream infections were lower in the food restriction group compared with the control group (14% versus 29%, p-value: 0.022).[19] The panel noted that these patients were older and had different diagnoses than many paediatric patients would have, limiting the directness of this evidence. No RCT enrolling at least one patient 16 years age or younger demonstrated a significant clinical

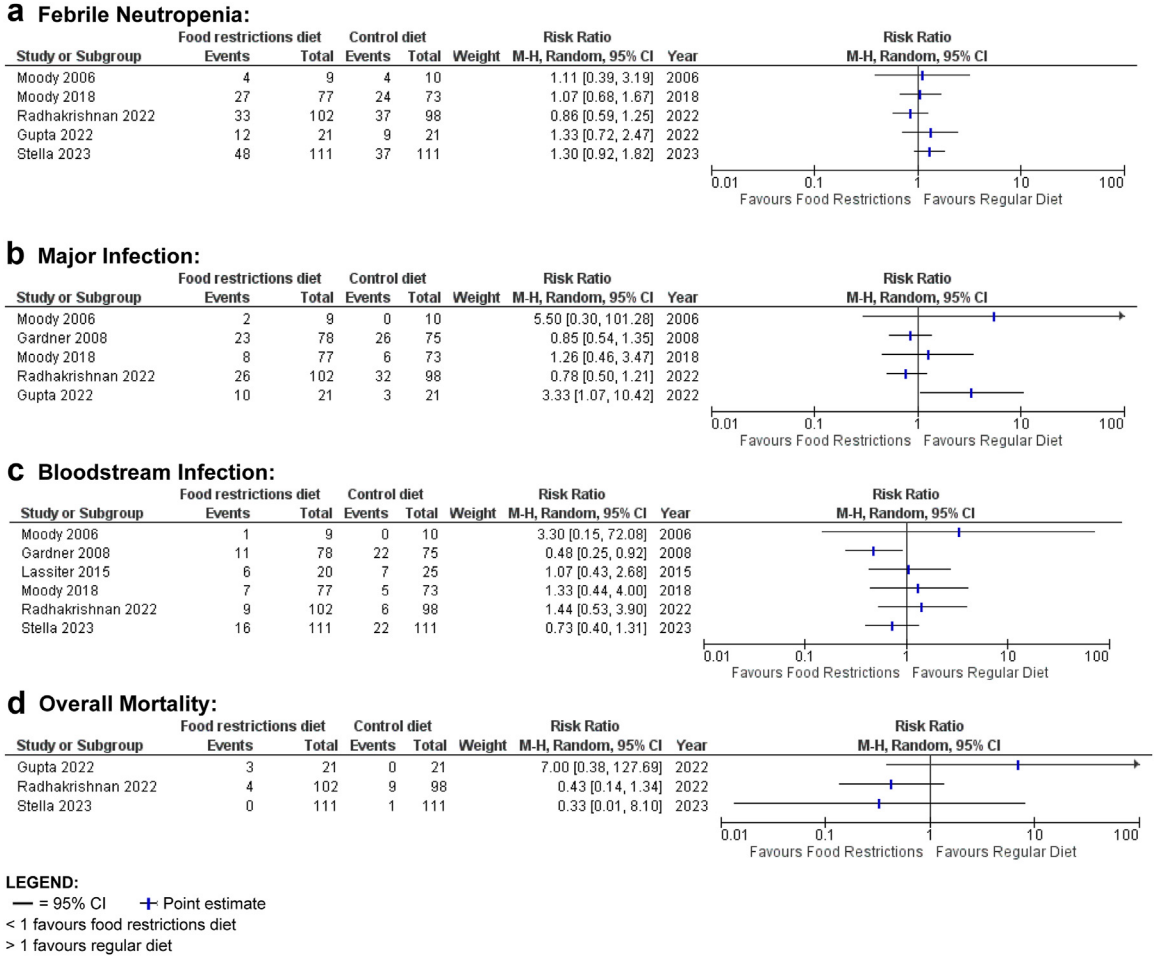

Fig. 1: Forest plots of efficacy outcomes for food restrictions versus regular diet. Outcomes: (a) febrile neutropenia; (b) major infection; (c) bloodstream infection; and (d) overall mortality.

benefit of food restrictions on preventing infections or mortality (Table 3).[16–18,21] The panel also considered the potential negative impacts of implementing food restrictions on paediatric patients' quality of life and nutritional status with no conclusive evidence for either outcome (Appendix 7).

The panel made a conditional recommendation against the use of food restrictions in paediatric patients with cancer receiving chemotherapy as the evidence suggests a lack of clinically significant benefit in preventing infections. The conditional rather than strong recommendation was made as the panel noted the clinical heterogeneity in the food restrictions evaluated.

Recommendation 2

We suggest that food restrictions not be routinely used for the prevention of infections in paediatric autologous HCT and allogeneic HCT recipients (conditional recommendation, low quality evidence).

Literature review and analysis

Two RCTs were identified evaluating food restrictions in patients prior to engraftment who had received HCT.[22,23] Both RCTs were conducted in high-income countries (Italy and USA) in adult patients undergoing allogeneic HCT, one of which also included patients undergoing autologous HCT. Neither showed a significant difference with respect to infection outcomes between study arms (Table 3 and Fig. 1). Additional outcome details are provided in Appendices 8 and 9. In both studies, the food restriction interventions were in place during the neutropenic period and the use of antimicrobial prophylaxis was permitted.

The panel made a conditional recommendation given the limited data in the HCT setting and lack of direct paediatric data. The panel drew from the study data in cancer patients receiving chemotherapy. The potential effect of food restrictions having a negative impact on quality of life, especially considering HCT recipients' additional burden of gastrointestinal toxicity, was also considered. As the studies reported data regarding allogeneic HCT and autologous HCT together, these were grouped under this recommendation. The panel recognised that the infection risk during the neutropenic period (i.e., the start of conditioning to engraftment) would be similar in both settings and unanimously agreed a combined recommendation was valid, but that keeping the HCT and chemotherapy recommendations separate would be clinically more meaningful. The panel recognised that more data in this area could change the recommendation in the future.

Discussion

This is the first CPG on the use of food restrictions in paediatric patients with cancer or HCT recipients. A multi-national panel composed of interprofessional experts and persons with lived experience deliberated on the eight RCTs identified by the systematic review of the literature and their clinical implications.

The panel made conditional recommendations against the routine use of food restrictions, often referred to as the neutropenic diet, in paediatric patients with cancer receiving chemotherapy and in the setting of allogeneic and autologous HCT. Although the included trials did not report enjoyment of eating or nutritional status outcomes, it has been demonstrated[27] that food restrictions have a negative impact on the nutritional status in the paediatric setting. Cooking processes, consumption of processed foods, and limited intake of fresh fruit and vegetables may reduce the quantity and quality of nutrients consumed, reduce nutrients and also diminish nutritional quality.[27,28] Food restrictions may also alter the gut microbial composition particularly through the reduction of high-fibre containing foods and preference of highly-processed foods.[29] As the microbiome is an important factor of the host defence, diet-driven dysbiosis may conversely increase risk for bloodstream infections[30,31] and antibiotic-resistant pathogens.[32,33]

The panel sought to emphasise the importance of adherence to food safety practices with the creation of the good practice statement. Foodborne illness such as those caused by *Salmonella* spp., *Campylobacter* spp., and norovirus may result in severe disease in this immunologically vulnerable population.[6] In the Good Practice Statement the choice to refer to 'applicable' health authorities' food safety practices was made to align with ease of local implementation as well as if specific nuances related to local contexts and regulations were to be found.

Implementation of the CPG's recommendations may face challenges due to the heterogeneity of the interventional diets examined and established beliefs in different cultural, economic, and geographical contexts. In addition, we recognize the limitations of the identified randomised studies we included in our analysis, as these studies often had small numbers of patients, administered prophylactic broad-spectrum antibiotics and antifungal compounds, or evaluated the neutropenic diet only in an inpatient setting. However, consistent areas across studies show the lack of obvious harm by allowing patients to consume well-washed raw fruit or vegetables, pasteurised dairy products and thoroughly cooked meats, fish and poultry. Items with fewer data include cured meats, nuts, seeds, teas, and chutneys. This variability is in keeping with a lack of agreement over the definition of the neutropenic diet in the included studies and in practice.[34] The recommendations made in this CPG are consistent with those from the American Society of Clinical Oncology's CPG[8] for adult patients undergoing standard chemotherapy for cancer. Our recommendations also align with the core message of the guidance paper from the European

Society for Bone and Marrow Transplantation[35] which focused on paediatric patients in the setting of HCT, and used an expert opinion working group approach for its development.

Providing food and nutrition to patients undergoing paediatric cancer treatment or HCT, where taste alteration and damage to the gastrointestinal tract (e.g., mucositis) is frequent and significant,[36] is a constant physical and emotional challenge to the majority of patients and families.[37,38] Providing food is a form of loving care held important to many caregivers.[39] The body of evidence supports the CPG recommendations to encourage a pragmatic approach to food safety rather than imposing the additional food restrictions of a neutropenic diet, and therefore, our CPG recommendations against the routine use of food restrictions will have a huge clinical impact. The decision to advise banning certain food items should be based on the possible adverse consequences of ingestion (i.e., likelihood of microbial burden and severity of resultant infection) weighed against not just nutritional value, but the potential joy the food could bring. For some food items, safe food handling guidance should be consistent across jurisdictions, such as avoidance of unpasteurised milks and cheeses, undercooked eggs and meats, food with visible or introduced mould, and potentially contaminated drinking water. For other foods, such as sushi, an approach which respects the cultural and geographic context should be used. In addition, our data are in line with data of non-randomised studies, which, however are of limited value and were not included in our analysis.

Although the analysis of the randomised studies uniformly do not demonstrate a benefit of food restriction during neutropenia, there remain important knowledge gaps. For example, there is still uncertainty of safety regarding particular foods (e.g., unpasteurised teas, some cured meats), or how food restrictions impact on quality of life and nutritional status in children and adolescents receiving chemotherapy or undergoing HCT (Table 4).

In summary, we present a CPG underscoring the importance of local food safety practices and suggest against the routine use of food restrictions for the prevention of infection in children and adolescents treated for cancer and paediatric HCT recipients. The provision of safe foods which promote nutrition and enjoyment is emphasised.

Contributors

Study concepts and design: RP, BTF, EJL, PP, PDR, LLD, RAA, MPB, FC, EC, BLD, KE, CWE, AHG, GMH, CK, AM, MES, DS, WJET, JW, LS, TL.

Data acquisition and verification: PP, PDR.

Data analysis: PP, PDR, RP, TL.

Data interpretation: RP, BTF, EJL, PP, PDR, LLD, RAA, MPB, FC, EC, BLD, KE, CWE, AHG, GMH, CK, AM, MES, DS, WJET, JW, LS, TL.

Drafting the manuscript or revising it critically for important intellectual content: RP, BTF, EJL, PP, PDR, LLD, RAA, MPB, FC, EC, BLD, KE, CWE, AHG, GMH, CK, AM, MES, DS, WJET, JW, LS, TL.

Final approval of version to be published: RP, BTF, EJL, PP, PDR, LLD, RAA, MPB, FC, EC, BLD, KE, CWE, AHG, GMH, CK, AM, MES, DS, WJET, JW, LS, TL.

Agreement to be accountable for all aspects of the work: RP, BTF, EJL, PP, PDR, LLD, RAA, MPB, FC, EC, BLD, KE, CWE, AHG, GMH, CK, AM, MES, DS, WJET, JW, LS, TL.

RP, BTF, EJL, PP, PDR, LLD, RAA, MPB, FC, EC, BLD, KE, CWE, AHG, GMH, CK, AM, MES, DS, WJET, JW, LS, TL have read and approved the final version of the manuscript.

Data sharing statement

The authors declare that all of the results of the systematic review used to inform the recommendations in this clinical practice guideline are presented within the article and appendices. No original study data are presented.

Declaration of interests

FC has: 1) received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Pfizer, Knight, Sandoz; 2) received support for attending meetings and/or travel from Pfizer and Mundipharma; 3) participated on a Data Safety Monitoring Board or Advisory Board for Pfizer and Sandoz.

JW's institution has received grants from Merck, Pfizer and National Institutes of Health for his work as a co-investigator and participant in industry sponsored research and JW's institution holds a patent for use of metagenomic sequencing to predict infection. JW has also been a speaker for Cook Children's Hospital and American Association of Pediatrics.

No other authors declared a conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103093.

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