COG Supportive Care Endorsed Guidelines

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The Children's Oncology Group (COG) Supportive Care Endorsed Guidelines are comprised of evidence-based guidelines which have been developed by other organizations and endorsed by the COG. The COG guideline endorsement process is available on the COG Supportive Care Guidelines webpage. The endorsed guideline developers' assessment of the strength of each recommendation and the quality of the evidence to support the recommendation is provided whenever possible (see Appendix 1). When the endorsed guideline developers used another method to communicate the strength of each recommendation and the quality of the evidence to support the recommendation, the method is provided in the guideline summary.

To discuss any aspect of the COG Supportive Care Guidelines please contact a member of the COG Supportive Care Guideline Task Force.

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1. Guideline for Antibacterial Prophylaxis Administration in Pediatric Cancer and Hematopoietic Stem Cell Transplantation

The "Guideline for Antibacterial Prophylaxis Administration in Pediatric Cancer and Hematopoietic Stem Cell Transplantation" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG Supportive Care Guideline Committee in June 2020.

The source clinical practice guideline is published (Lehrnbecher T, Fisher BT, Phillips B, et al. Guideline for antibacterial prophylaxis administration in pediatric cancer and hematopoietic stem cell transplantation. *Clinical Infectious Diseases* 2020; 71 (1): 226-36.) and is available at: https://doi.org/10.1093/cid/ciz1082.

The purpose of the source clinical practice guideline is to provide recommendations for systemic antibacterial prophylaxis administration in pediatric patients with cancer and recipients of hematopoietic stem cell transplant. These recommendations are presented in the table below.

Summary of Recommendations for Antibacterial Prophylaxis Administration in Pediatric Cancer and Hematopoietic Stem Cell Transplantation

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Which pediatric patients with cancer and HSCT recipients (if any) should routinely receive systemic antibacterial prophylaxis?	
1. Consider systemic antibacterial prophylaxis administration in children with AML and relapsed ALL receiving intensive chemotherapy expected to result in severe neutropenia (absolute neutrophil count <500/µL) for at least 7 days. *Remarks*: This is a weak recommendation because the benefits of prophylaxis were closely balanced against its known and potential impacts on resistance. The panel valued what is known about efficacy and resistance outcomes of prophylaxis administered within the finite time frame of a clinical trial among enrolled participants but also considered the less certain impacts of a universal prophylaxis strategy at both the patient and institutional level. Limiting prophylaxis to patient populations at highest risk of fever and neutropenia, bacteremia, and infection-related mortality could limit antibiotic utilization to those most likely to benefit from prophylaxis. Careful discussion with patients and families about the potential risks and benefits of prophylaxis is important. Understanding local resistance epidemiology is critical to the decision of whether to implement prophylaxis.	Weak recommendation High-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2. We suggest that systemic antibacterial prophylaxis not be used routinely for children receiving induction chemotherapy for newly diagnosed ALL. *Remarks:* The panel acknowledged the paucity of direct contemporary randomized data applicable to children living in high-income countries. A recommendation to provide universal systemic prophylaxis to this group could have a substantial impact on institutions, given that ALL is the most common cancer diagnosis in children. There is great variability in duration of neutropenia and risk of bacteremia based on treatment protocol and patient-level characteristics. Further data are required to identify subgroups of pediatric patients with ALL who might particularly benefit from prophylaxis.	Weak recommendation Low-quality evidence
3. Do not use systemic antibacterial prophylaxis for children whose therapy is not expected to result in severe neutropenia (absolute neutrophil count severe neutropenia (absolute neutrophil count <500/µL) for at least 7 days. *Remarks*: This strong recommendation was based on reduced chance of benefit combined with continued risk of harm associated with systemic antibacterial prophylaxis.	Strong recommendation Moderate-quality evidence
4. We suggest that systemic antibacterial prophylaxis not be used routinely for children undergoing autologous HSCT. *Remarks:* This weak recommendation against routine use of antibacterial prophylaxis in autologous HSCT recipients acknowledged the risk reduction of bacteremia among this cohort. However, the panel believed that the lower baseline risk of bacteremia resulted in the impact on resistance (known and potential) outweighing the benefits. The moderate quality of evidence reflected the lack of granular data specifically in autologous HSCT recipients rather than HSCT patients as a group.	Weak recommendation Moderate-quality evidence
5. We suggest that systemic antibacterial prophylaxis not be used routinely for children undergoing allogeneic HSCT. *Remarks*: The panel acknowledged that the granularity of available data did not allow a different recommendation for allogeneic compared with autologous HSCT recipients. However, the panel noted that allogeneic HSCT recipients often have preceding conditions that could be associated with prophylaxis (eg, AML or relapsed ALL) and have prolonged neutropenia during the HSCT process, which could influence the effectiveness and adverse effects associated with prophylaxis.	Weak recommendation Moderate-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Which agents should be used for systemic antibacterial prophylaxis in children with cancer and HSCT recipients?	
6.Levofloxacin is the preferred agent if systemic antibacterial prophylaxis is planned. *Remarks:* The strong recommendation to use levofloxacin is related to direct contemporary data in children and its microbiological spectrum of activity. If levofloxacin is not available or not able to be used, ciprofloxacin is an alternative, although lack of activity against gram-positive bacteria including viridans group streptococci may reduce the benefits of prophylaxis. Patients and families should be informed about potential short- and long-term fluoroquinolone-related adverse effects. Understanding local resistance epidemiology is critical to the decision of whether to implement fluoroquinolone prophylaxis. If fluoroquinolones are not available or cannot be used, providing no systemic antibacterial prophylaxis is an important option to consider.	Strong recommendation Moderate-quality evidence
When should systemic antibacterial prophylaxis be started and stopped?	
7.If systemic antibacterial prophylaxis is planned, we suggest that administration be restricted to the expected period of severe neutropenia (absolute neutrophil count <500/µL). *Remarks*: This is a weak recommendation based on low-quality evidence because there are no trials that compared different start and stop criteria. In general, trials administered prophylaxis during severe neutropenia and thus this recommendation reflects the available evidence and the panel's desire to minimize duration of prophylaxis administration.	Weak recommendation Low-quality evidence

*see Appendix 1

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2. Clinical Practice Guideline for Systemic Antifungal Prophylaxis in Pediatric Patients with Cancer and Hematopoietic Stem-Cell Transplantation Recipients

The "Clinical Practice Guideline for Systemic Antifungal Prophylaxis in Pediatric Patients with Cancer and Hematopoietic Stem-Cell Transplantation Recipients" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG Supportive Care Guideline Committee in August 2020.

The source clinical practice guideline is published (Lehrnbecher T, Fisher BT, Phillips B, et al. Clinical practice guideline for systemic antifungal prophylaxis in pediatric patients with cancer and hematopoietic stem-cell transplantation recipients. JCO 2020; [ePub May 27, 2020]) and is available at: https://ascopubs.org/doi/full/10.1200/JCO.20.00158

The purpose of the source clinical practice guideline is to provide recommendations for systemic antifungal prophylaxis administration in pediatric patients with cancer and hematopoietic stem cell transplant recipients. These recommendations are presented in the table below.

Summary of Recommendations for Systemic Antifungal Prophylaxis in Pediatric Patients with Cancer and Hematopoietic Stem-Cell Transplantation Recipients

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Which pediatric patients with cancer and HSCT recipients should routinely receive systemic antifungal prophylaxis?	
Acute myeloid leukemia	
1. Administer systemic antifungal prophylaxis to children and adolescents receiving treatment of acute myeloid leukemia that is expected to result in profound and prolonged neutropenia. *Remarks*: This strong recommendation is based on the increasing benefit of systemic antifungal prophylaxis versus no prophylaxis to reduce proven or probable invasive fungal disease (IFD) as the risk for IFD increases. Although this recommendation advocates for a universal prophylaxis approach, future research should identify patient and treatment factors that may allow tailoring of prophylaxis to those at the highest risk for IFD.	Strong recommendation High-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Acute lymphoblastic leukemia	
2. Consider administering systemic antifungal prophylaxis to children and adolescents with newly diagnosed and relapsed acute lymphoblastic leukemia at high risk for IFD. *Remarks:* Children and adolescents with acute lymphoblastic leukemia encompass a group with wide variability in IFD risk that is not solely accounted for by relapse status. Those with relapsed acute lymphoblastic leukemia receiving intensive myelosuppressive chemotherapy are most likely to warrant systemic antifungal prophylaxis, whereas greater uncertainty is present for those with newly diagnosed acute lymphoblastic leukemia. Given the heterogeneity in IFD risk across protocols overall and by phase of treatment, adaptation will be required for each protocol to recommend whether and when systemic antifungal prophylaxis should be administered.	Weak recommendation Low-quality evidence
3. Do not routinely administer systemic antifungal prophylaxis to children and adolescents with acute lymphoblastic leukemia at low risk for IFD. *Remarks*: A low risk for IFD can be inferred based on absence of risk factors such as prolonged neutropenia and corticosteroid administration and observed IFD rates across different protocols. This group includes, for example, pediatric patients receiving maintenance chemotherapy for acute lymphoblastic leukemia.	Strong recommendation Low-quality evidence
Other malignancies including most patients with lymphomas and solid tumors	
4. Do not routinely administer systemic antifungal prophylaxis to children and adolescents with cancer at low risk for IFD, such as most pediatric patients with lymphomas and solid tumors. *Remarks:* In pediatric patients at low risk for IFD, the benefit of systemic antifungal prophylaxis is likely to be small and outweighed by the risk for adverse effects, costs, and inconvenience. Thus, systemic antifungal prophylaxis should not routinely be administered in this setting.	Strong recommendation Moderate-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
HSCT	
5. Administer systemic antifungal prophylaxis to children and adolescents undergoing allogeneic HSCT pre-engraftment and to those receiving systemic immunosuppression for the treatment of graft-versus host disease. *Remarks*: The panel recognized that these two phases of therapy are associated with different epidemiology of IFD. However, the nature of the trials included in the systematic review precluded the ability to make separate recommendations for them. This strong recommendation was influenced by the finding in the systemic prophylaxis versus no systemic prophylaxis stratified analysis that HSCT recipients experienced greater benefit in IFD reduction compared with chemotherapy recipients. In addition, the subgroup analysis showed that among the HSCT stratum, prophylaxis significantly reduced fungal infection–related mortality.	Strong recommendation Moderate-quality evidence
6. We suggest that systemic antifungal prophylaxis not be used routinely in children and adolescents undergoing autologous HSCT. *Remarks*: This weak recommendation was based on the lower risk for IFD associated with autologous HSCT. There is less certainty in the setting of tandem transplantations where the cumulative duration of neutropenia may be longer.	Weak recommendation Low-quality evidence
If systemic antifungal prophylaxis is planned, which agents should be used?	
7. If systemic antifungal prophylaxis is warranted, administer a mold-active agent. *Remarks:* This strong recommendation was based on the comparison of different systemic antifungal prophylaxis agents where mold-active agent versus fluconazole significantly reduced proven or probable IFD, mold infection, and invasive aspergillosis (IA), and reduced fungal infection–related mortality. Direct pediatric data were available, increasing quality of the evidence.	Strong recommendation High-quality evidence
8. In choosing a mold-active agent, administer an echinocandin or a mold-active azole. *Remarks*: The choice of specific mold-active agent is influenced by multiple factors including local epidemiology, adverse effect profile, potential for drug interactions, costs, and jurisdictional availability. For children younger than 13 years of age, an echinocandin, voriconazole, or itraconazole is suggested based on efficacy and adverse effects. In those 13 years of age and older, posaconazole also is an option.	Strong recommendation Moderate-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
9. Do not use amphotericin routinely as systemic antifungal prophylaxis. *Remarks*: This strong recommendation was based on the finding that both conventional and lipid formulations of amphotericin were not more effective than fluconazole in reducing IFD. It is important to note that liposomal amphotericin was not included in studies comparing amphotericin versus fluconazole and, thus, there is less certainty about the benefits and risks of this formulation.	Strong recommendation Low-quality evidence
When should systemic antifungal prophylaxis be started and stopped?	
10. If systemic antifungal prophylaxis is warranted, consider administration during periods of observed or expected severe neutropenia. For allogeneic HSCT recipients, consider administration during systemic immunosuppression for graft-versus-host disease treatment. *Remarks*: There are limited data that inform the decision of when to initiate and discontinue systemic antifungal prophylaxis. This recommendation was based on the criteria used in the included randomized trials and the anticipated highest risk period.	Weak recommendation Low-quality evidence

*see Appendix 1

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3. Detection of Bronchiolitis Obliterans Syndrome after Pediatric Hematopoietic Stem Cell Transplantation

"Detection of Bronchiolitis Obliterans Syndrome after Pediatric Hematopoietic Stem Cell Transplantation", developed by the American Thoracic Society, was endorsed by the COG Supportive Care Guidelines sub-Committee in June 2025.

The source guideline is published (Shanthikumar S, Gower WA, Srinivasan S, et al. Detection of bronchiolitis obliterans syndrome after pediatric hematopoietic stem cell transplantation: an official American Thoracic Society clinical practice guideline. Amer J Resp Critical Care Medicine. 2024; 210(3):262-80.) and is available at: https://doi.org/10.1164/rccm.202406-1117ST

The purpose of the source guideline is to provide an evidence-based approach to detection of post-HSCT BOS in children. The recommendations from the endorsed clinical practice guideline are presented in the table below.

Summary of Recommendations for Detection of Bronchiolitis Obliterans Syndrome (BOS) after Pediatric Hematopoietic Stem Cell Transplantation (HSCT)

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. We recommend pre-HSCT spirometry, static lung volumes, and Diffusing Capacity of the Lungs for Carbon Monoxide (D_{LCO}) for children who can perform them.	Strong recommendation Moderate certainty of evidence
2a. We suggest active surveillance rather than testing only symptomatic patients using spirometry and, where feasible, static lung volumes and D_{LCO} beginning at 3 months post-HSCT.	Conditional recommendation Low certainty of evidence
2b. We suggest that spirometry and, where feasible, static lung volumes and D_{LCO}, be performed every 3 months in the first year post-HSCT and every 3 to 6 months in the second year post-HSCT in patients who are not at high risk of BOS.	Conditional recommendation Low certainty of evidence
2c. For long-term follow-up in asymptomatic patients, we suggest surveillance using spirometry and, where feasible, static lung volumes and D_{LCO} every 6 months, between 2 and 3 years post-HSCT and yearly after 3 years, lasting until10 years post-HSCT.	Conditional recommendation Low certainty of evidence
3a. At centers with adequate technical expertise to perform multiple breath washout (MBW), we suggest including MBW and spirometry as part of a pre-HSCT assessment of pulmonary function, or MBW alone if spirometry is not feasible.	Conditional recommendation Low certainty of evidence
3b. At centers with adequate technical expertise to perform MBW, we suggest the use of post-HSCT MBW as part of the diagnostic evaluation of suspected BOS, either as a complementary tool to spirometry or alone if spirometry is not feasible.	Conditional recommendation Very low certainty of evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
4a. We suggest performing a chest computerized tomography (CT) scan, with inspiratory and expiratory views, in all children before allogeneic HSCT.	Conditional recommendation Low certainty of evidence
4b. We suggest performing a chest CT scan with inspiratory and expiratory views in all children post–allogeneic HSCT who develop obstructive lung function or in those children with clinical suspicion of BOS.	Conditional recommendation Low certainty of evidence
5. We suggest that bronchoscopy with bronchoalveolar lavage (BAL) be performed to assess for infection as part of the BOS evaluation.	Conditional recommendation Very low certainty of evidence
6. We suggest surgical lung biopsy in pediatric post-HSCT patients in cases where BOS is suspected but uncertainty regarding the diagnosis exists and the risks of biopsy are smaller than the risks of the uncertainty.	Conditional recommendation Low certainty of evidence

*see Appendix 1

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4. Guidelines on Chemotherapy-induced Nausea and Vomiting in Pediatric Cancer Patients

This document summarizes four clinical practice guidelines on the topic of chemotherapy-induced nausea and vomiting:
I. The "Classification of the Acute Emetogenicity of Chemotherapy in Pediatric Patients: A Clinical Practice Guideline" developed by the Pediatric Oncology Group of Ontario (endorsed by the COG Supportive Care Guideline Task Force in August 2019).
II. The "Antiemetics: ASCO Guideline Update" developed by the American Society of Clinical Oncology (endorsed by the COG Supportive Care Guideline Task Force in December 2020)
III. The "Prevention of acute and delayed chemotherapy-induced nausea and vomiting in pediatric cancer patients: A clinical practice guideline" developed by the Pediatric Oncology Group of Ontario (endorsed by the COG Supportive Care Guideline Task Force in February 2023) and
IV. The "Prevention and treatment of anticipatory chemotherapy-induced nausea and vomiting in pediatric cancer patients and hematopoietic stem cell recipients: Clinical practice guideline update" developed by the Pediatric Oncology Group of Ontario (endorsed by the COG Supportive Care Guideline Task Force in July 2021).
V. The "Treatment of breakthrough and prevention of refractory chemotherapy-induced nausea and vomiting in pediatric cancer patients: Clinical practice guideline update" developed by the Pediatric Oncology Group of Ontario (endorsed by the COG Supportive Care Guideline Task Force in December 2023).

4.1 **Classification of Chemotherapy Emetogenicity**

The "Classification of the Acute Emetogenicity of Chemotherapy in Pediatric Patients: A Clinical Practice Guideline" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG Supportive Care Guideline Committee in August 2019.

The source guideline is published (Paw Cho Sing E, Robinson PD, Flank J et al. Pediatr Blood Cancer. 2019; 66: e27646.) and is available at https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.27646. It is an update of an earlier guideline that was published in 2011.

The purpose of this guideline is to provide evidence-based recommendations regarding the acute emetic potential of chemotherapy in pediatric oncology patients aged 1 month to 18 years. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Classification of Chemotherapy Emetogenicity

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. Which chemotherapy regimens are highly emetogenic?	
Single-agent regimens: Asparaginase (*Erwinia*) IV ≥ 20,000 IU/m^2/dose Busulfan IV ≥ 0.8mg/kg/dose Busulfan PO ≥ 1mg/kg/dose Carboplatin IV ≥ 175 mg/m^2/dose Cisplatin IV ≥ 12 mg/m^2/dose Cyclophosphamide IV ≥ 1,200 mg/m^2/dose Cytarabine IV ≥ 3g/m^2/day Dactinomycin IV ≥ 1.35 mg/m^2/dose Doxorubicin IV ≥ 30 mg/m^2/dose Idarubicin PO ≥ 30 mg/m^2/dose Melphalan IV Methotrexate IV ≥ 12 g/m^2/dose	Strong recommendation Very low to high quality of evidence
Multiple-agent regimens: Cyclophosphamide ≥ 600 mg/m^2/dose + dactinomycin ≥ 1 mg/m^2/dose Cyclophosphamide ≥ 400 mg/m^2/dose + doxorubicin ≥ 40 mg/m^2/dose Cytarabine IV ≥ 90 mg/m^2/dose + methotrexate IV ≥ 150 mg/m^2/dose Cytarabine IV + teniposide IV Dacarbazine IV ≥ 250 mg/m^2/dose + doxorubicin IV ≥ 60 mg/m^2/dose Dactinomycin IV ≥ 900 µg/m^2/dose + ifosfamide IV ≥ 3 g/m^2/dose Etoposide IV ≥ 60 mg/m^2/dose + ifosfamide IV ≥ 1.2 g/m^2/dose Etoposide IV ≥ 250 mg/m^2/dose + thiotepa IV ≥ 300 mg/m^2/dose	

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2. Which single-agent and multiple-agent chemotherapy regimens are moderately emetogenic?	
Single-agent regimens: Cyclophosphamide IV 1000 mg/m^2/dose Cytarabine IV 75 mg/m^2/dose Dactinomycin IV 10 µg/kg/dose Doxorubicin IV 25 mg/m^2/dose Gemtuzumab IV 3–9mg/m^2/dose Imatinib PO > 260 mg/m^2/day Interferon alpha IV 15–30 million U/m^2/day Ixabepilone IV 3–10 mg/m^2/dose Methotrexate IV 5 g/m^2/dose Methotrexate IT Topotecan PO 0.4–2.3 mg/m^2/day Multiple-agent regimens: Cytarabine IV 100 mg/m^2/dose + daunorubicin IV 45 mg/m^2/dose + etoposide IV 100 mg/m^2/dose + prednisolone PO + thioguanine PO 80mg/m^2/dose Cytarabine 60 or 90 mg/m^2/dose + methotrexate 120 mg/m^2/dose Liposomal doxorubicin IV 20–50 mg/m^2/dose + topotecan PO 0.6mg/m^2/day	Strong recommendation Very low to high quality of evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
3. Which single-agent and multiple-agent chemotherapy regimens are of low emetogenicity?	
Single-agent regimens: Cyclophosphamide IV 500 mg/m^2/dose Cyclophosphamide PO2–3 mg/kg/dose Dasatinib PO 60–120 mg/m^2/dose Erlotinib PO 35–150 mg/m^2/day Everolimus PO 0.8–9mg/m^2/day Gefitinib PO 150–500 mg/m^2/day Imatinib PO 260 mg/m^2/day Mafosfamide IT 1–6.5 mg/dose Melphalan PO 0.2 mg/kg/dose Mercaptopurine PO ≤ 4.2mg/kg/dose Methotrexate 38–83 mg/m^2/dose IV Mitoxantrone IV ≤ 33 mg/m^2/dose Procarbazine PO 50–100 mg/m^2/day Ruxolitinib PO 15–21 mg/m^2/dose Selumetinib PO 20–30 mg/m^2/dose Sorafenib PO 150–325 mg/m^2/dose Temozolomide PO 200 mg/m^2/dose Multiple-agent regimens: Cytarabine IV 60 mg/m^2/dose + methotrexate IV 90 mg/m^2/dose	Strong recommendation Very low to moderate quality of evidence
4. Which single-agent and multiple-agent chemotherapy regimens are minimally emetogenic?	
Single-agent regimens: Asparaginase (*E. coli*) IM ≤ 6000 IU/m^2/dose Asparaginase (*Erwinia*) IM ≤ 25 000 IU/m^2/dose Chlorambucil ≤ 0.2mg/kg/day PO Doxorubicin IV 10 mg/m^2/dose Liposomal doxorubicin IV ≤ 50 mg/m^2/dose Mercaptopurine PO ≤ 4.2mg/kg/dose Methotrexate PO/SC ≤ 10 mg/m^2/dose Pracinostat PO 25–45 mg/m^2/dose Vincristine IV ≤ 1.5mg/m^2/dose Multiple-agent regimens: Cisplatin ≤ 60 mg/m^2/dose intra-arterially + doxorubicin ≤ 30 mg/m^2/dose intra-arterially Cisplatin ≤ 60 mg/m^2/dose intra-arterially + pirarubicin ≤ 30 mg/m^2/dose intra-arterially Mercaptopurine PO ≤ 2.5mg/kg/dose + methotrexate PO ≤ 0.1mg/kg/day	Strong recommendation Very low to low quality of evidence

*see Appendix 1

4.2 **Prevention of Acute Chemotherapy-induced Nausea and Vomiting**

The "Antiemetics: ASCO Update" developed by the American Society of Clinical Oncology was endorsed by the COG in December 2020.

The source guideline is published (Hesketh P, Kris MG, Basch E et al. JCO 2020; 38 (24): 2782-97.) and is available at: https://ascopubs.org/doi/10.1200/JCO.20.01296

The "Prevention of acute and delayed chemotherapy-induced nausea and vomiting in pediatric cancer patients: A clinical practice guideline" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG in February 2023.

The source guideline is published (Patel P, Robinson PD, Cohen M, et al. Prevention of acute and delayed chemotherapy-induced nausea and vomiting in pediatric cancer patients: A clinical practice guideline. Pediatr Blood Cancer. 2022 Dec;69(12):e30001) and is available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.30001

The purpose of these guidelines is to provide evidence-based recommendations for the prevention of acute chemotherapy-induced nausea and vomiting in children. The recommendations of the endorsed guidelines are presented below.

Summary of Recommendations for the Prevention of Acute Chemotherapy-induced Nausea and Vomiting (CINV)

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. In pediatric patients receiving highly emetogenic chemotherapy (HEC), what strategies are recommended to prevent acute CINV?	
• Use a 5HT3RA + dexamethasone + (fos)aprepitant	Strong recommendation High quality evidence
• Use palonosetron + dexamethasone in patients unable to receive (fos)aprepitant	Strong recommendation Moderate quality evidence
• Use palonosetron + (fos)aprepitant in patients unable to receive dexamethasone	Strong recommendation Low quality evidence
• Use palonosetron in patients unable to receive dexamethasone + (fos)aprepitant	Strong recommendation Moderate quality evidence
• Consider adding olanzapine to other CPG-consistent antiemetics	Conditional recommendation Moderate quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
2. In pediatric patients receiving moderately emetogenic chemotherapy (MEC), what strategies are recommended to prevent acute CINV?	
a. Use a 5HT3RA + dexamethasone	Strong recommendation Moderate quality evidence
b. Use a 5HT3RA + (fos)aprepitant in patients unable to receive dexamethasone	Strong recommendation Low quality evidence
c. Use a 5HT3RA in patients unable to receive dexamethasone + (fos)aprepitant	Strong recommendation Low quality evidence
d. Consider using palonosetron as the preferred 5HT3RA in patients unable to receive dexamethasone + (fos)aprepitant	Conditional recommendation Low quality evidence
e. Consider adding olanzapine to other CPG-consistent antiemetics in patients unable to receive dexamethasone + (fos)aprepitant	Conditional recommendation Low quality evidence
3. In pediatric patients receiving low emetogenic chemotherapy (LEC), what strategies are recommended to prevent acute CINV?	
a. Use a 5HT3RA	Strong recommendation Low quality evidence
4. In pediatric patients receiving minimally emetogenic chemotherapy (minEC), what strategies are recommended to prevent acute CINV?	
a. Do not use prophylaxis routinely	Strong recommendation Very low quality evidence

CINV, chemotherapy-induced nausea and vomiting; 5HT3RA, serotonin-3 receptor antagonist; (fos)aprepitant, IV fosaprepitant or oral aprepitant
*see Appendix 1

4.3 **Prevention and Treatment of Delayed Chemotherapy-Induced Nausea and Vomiting**

The "Prevention of acute and delayed chemotherapy-induced nausea and vomiting in pediatric cancer patients: A clinical practice guideline" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG in February 2023.

The source guideline is published (Patel P, Robinson PD, Cohen M, et al. Prevention of acute and delayed chemotherapy-induced nausea and vomiting in pediatric cancer patients: A clinical practice guideline. Pediatr Blood Cancer. 2022 Dec;69(12):e30001) and is available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.30001

The purpose of this guideline is to provide evidence-based guidance on strategies for delayed chemotherapy-induced nausea and vomiting prevention. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Prevention of Delayed Chemotherapy-induced Nausea and Vomiting (CINV)

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. In pediatric patients receiving highly emetogenic chemotherapy (HEC), what strategies are recommended to prevent delayed CINV?	
a. Use palonosetron in the acute phase as the preferred 5HT3RA in patients at high risk of delayed phase CINV	Strong recommendation Moderate quality evidence
b. Use oral aprepitant in the delayed phase, if (fos)aprepitant started in the acute phase	Strong recommendation High quality evidence
c. Add dexamethasone in the delayed phase in patients who received granisetron or ondansetron in the acute phase	Strong recommendation Moderate quality evidence
d. Consider adding dexamethasone in the delayed phase in patients who received palonosetron in the acute phase	Conditional recommendation Moderate quality evidence
e. Use dexamethasone in the delayed phase in patients unable to receive oral aprepitant	Strong recommendation Moderate quality evidence
f. Continue olanzapine in the delayed phase, if started in the acute phase	Strong recommendation Moderate quality evidence
g. Do not use 5HT3RAs in the delayed phase	Strong recommendation Low quality evidence
2. In pediatric patients receiving moderately emetogenic chemotherapy (MEC), what strategies are recommended to prevent delayed CINV?	
a. Consider using dexamethasone in the delayed phase	Conditional recommendation Low quality evidence
b. Continue oral aprepitant in the delayed phase in patients receiving single-day chemotherapy who received (fos)aprepitant in the acute phase	Strong recommendation Moderate quality evidence
c. Consider not using oral aprepitant in the delayed phase in patients receiving multi-day chemotherapy (≥ 3 days) who received (fos)aprepitant in the acute phase	Conditional recommendation Low quality evidence
d. Continue olanzapine in the delayed phase, if started in the acute phase	Strong recommendation Low quality evidence
3. In pediatric patients receiving low emetogenic chemotherapy (LEC), what strategies are recommended to prevent delayed CINV?	
a. Do not use prophylaxis routinely in the delayed phase	Strong recommendation Very low quality evidence
4. In pediatric patients receiving minimally emetogenic chemotherapy (minEC), what strategies are recommended to prevent delayed CINV?	
a. Do not use prophylaxis routinely in the delayed phase	Strong recommendation Very low quality evidence

CINV, chemotherapy-induced nausea and vomiting; 5HT3RA, serotonin-3 receptor antagonist; (fos)aprepitant, IV fosaprepitant or oral aprepitant

*See Appendix 1

4.4 **Prevention and Treatment of Anticipatory Chemotherapy-Induced Nausea and Vomiting**

The "Prevention and treatment of anticipatory chemotherapy-induced nausea and vomiting in pediatric cancer patients and hematopoietic stem cell recipients: Clinical practice guideline update" was endorsed by the COG in July 2021.

The source guideline is published (Patel P, Robinson PD, Devine KA, et al. Pediatr Blood Cancer 2021; e28947.) and is available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.28947

The purpose of this guideline is to provide those caring for pediatric oncology or hematopoietic stem cell recipients up to 18 years of age with updated recommendations for the prevention of anticipatory CINV. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Prevention and Treatment of Anticipatory Chemotherapy-induced Nausea and Vomiting (CINV)

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. What strategies are recommended for primary prevention of anticipatory CINV in pediatric patients?	
1.1 Optimize acute and delayed CINV control to minimize the risk of anticipatory CINV *Remarks:* This recommendation places high value on the consistent evidence that a history of acute or delayed CINV is a risk factor for anticipatory CINV. This recommendation also considers the other benefits of optimized acute or delayed CINV control including improved quality of life and the low risk of toxicities anticipated with CPG-consistent antiemetics.	Strong recommendation Moderate-quality evidence
2. What strategies are recommended for secondary prevention of anticipatory CINV in pediatric patients?	
2.1: Consider offering cooperative patients one or more of the following nonpharmacological interventions for secondary prevention of anticipatory CINV: hypnosis, systematic desensitization, or relaxation techniques. *Remarks*: This recommendation places a high value on the minimal risks associated with these interventions. A conditional recommendation was made as the supporting evidence was limited to a small number of studies, the direct pediatric experience is scant and reports of the benefits of these interventions are inconsistent.	Conditional recommendation Low-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2.2 Consider using lorazepam for secondary prevention of anticipatory CINV. *Remarks*: This recommendation remained unchanged from the 2014 CPG. It places a high value on the limited data demonstrating improved anticipatory CINV control in adults given benzodiazepines. It is a conditional recommendation because there is no direct pediatric evidence among included studies describing the use of benzodiazepines for this purpose.	Conditional recommendation Very low-quality evidence
2.3 We suggest that ginger not be used routinely for secondary prevention of anticipatory CINV. *Remarks:* The panel made a conditional recommendation against the routine use of ginger given inconsistent study results in adult patients and the absence of pediatric data to support the use of ginger for this purpose. The panel also appreciated that the ginger formulations evaluated in included studies may not be comparable because doses of the components thought to be medically active are not uniformly reported.	Conditional recommendation Low-quality evidence
2.4 Do not use clonidine for secondary prevention of anticipatory CINV. *Remarks*: The panel made a strong recommendation against the use of clonidine given its poor safety profile, lack of clear benefit, and lack of direct data for its use in pediatric patients for anticipatory CINV prevention.	Strong recommendation Low-quality evidence
3. What strategies are recommended for acute treatment of anticipatory CINV in pediatric patients?	
No recommendation can be made. *Remarks:* No identified study directly evaluated an intervention aimed at the treatment of anticipatory CINV. The evidence describing primary and secondary anticipatory CINV prevention could not be extrapolated to make a recommendation.	

*See Appendix 1.

4.5 **Treatment of Breakthrough and Prevention of Refractory Chemotherapy-induced Nausea and Vomiting**

The "Treatment of breakthrough and prevention of refractory chemotherapy-induced nausea and vomiting in pediatric cancer patients: Clinical practice guideline update", developed by the Pediatric Oncology Group of Ontario, was endorsed by the COG in December 2023.

The source guideline is published (Patel P, Robinson PD, Phillips R, et al. Pediatr Blood Cancer 2023; 70:e30395.) and is available at: https://doi.org/10.1002/pbc.30395

The purpose of this guideline is to provide those caring for pediatric oncology or hematopoietic stem cell recipients up to 18 years of age with updated recommendations for the treatment of breakthrough CINV and the prevention of refractory CINV. Breakthrough CINV is defined as nausea and/or vomiting that occurs during the acute or delayed phase of chemotherapy despite receipt of CINV prophylaxis. Refractory CINV occurs in patients who have experienced breakthrough CINV in previous chemotherapy blocks. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Treatment of Breakthrough Chemotherapy-induced Nausea and Vomiting (CINV) and Prevention of Refractory CINV

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. What strategies are recommended to treat breakthrough CINV in pediatric patients?	
1.1 Escalate the antiemetic agents provided in the current chemotherapy block to those recommended for CINV prophylaxis for chemotherapy of the next higher level of emetogenic risk in pediatric patients with breakthrough CINV receiving acute and delayed CINV prophylaxis recommended for minEC, LEC or MEC.	Strong recommendation Low-quality evidence
1.2 In pediatric patients receiving acute or delayed CINV prophylaxis recommended for HEC who are not already receiving palonosetron, consider giving palonosetron instead of ondansetron/granisetron at the next scheduled ondansetron/granisetron administration time during the acute phase of the current chemotherapy block	Conditional recommendation Low-quality evidence
1.3 In pediatric patients receiving acute or delayed CINV prophylaxis recommended for HEC, consider adding one or more of the following antiemetic agents in the current chemotherapy block in patients who are not already receiving them: • dexamethasone • (fos)aprepitant[†] • olanzapine	Conditional recommendation Moderate-quality evidence
1.4 In pediatric patients receiving acute or delayed CINV prophylaxis recommended for HEC, consider adding metoclopramide in the current chemotherapy block in pediatric patients unable to receive olanzapine	Conditional recommendation Low-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2. What strategies are recommended to prevent refractory CINV in pediatric patients who have experienced breakthrough CINV?	
2.1 Use CPG-consistent antiemetic agents that controlled breakthrough CINV in previous chemotherapy blocks	Strong recommendation Low-quality evidence
2.2 Use the antiemetic agents recommended for CINV prophylaxis for chemotherapy of the next higher level of emetogenic risk in patients who did not experience control of breakthrough CINV in previous chemotherapy blocks and are receiving minEC or LEC	Strong recommendation Moderate-quality evidence
2.3 Consider adding one or more of the following, if not already receiving them, in patients who did not experience control of breakthrough CINV in previous chemotherapy blocks and are receiving MEC or HEC: • dexamethasone • (fos)aprepitant† • olanzapine	Conditional recommendation Moderate-quality evidence
2.4 Consider offering one or more of the following to patients who experience refractory CINV despite receipt of all suitable CPG-consistent antiemetic agents: • CINV-focused dietary counselling • yoga	Conditional recommendation Low-quality evidence

HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; LEC, low emetogenic chemotherapy; minEC, minimally emetogenic chemotherapy.

*See Appendix 1

†IV fosaprepitant or oral aprepitant

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5. Management of Chronic Pain in Children

The "Guidelines on the management of chronic pain in children" developed by the World Health Organization was endorsed by the COG Supportive Care Guideline Committee in July 2021.

The source clinical practice guideline is published (Guidelines on the management of chronic pain in children. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.) and is available at: https://www.who.int/publications/i/item/9789240017870

The purpose of the source clinical practice guideline is to assist World Health Organization Member States and their partners in developing and implementing national and local policies, regulations, pain management protocol and best practices. The source clinical practice guidelines focus on physical, psychological and pharmacological interventions for the management of primary and secondary chronic pain in children 0 to 19 years old. The guiding principles, recommendations and best principles of the source clinical practice guideline are presented in the tables below.

Table 1. Guiding Principles for Guidelines on the Management of Chronic Pain in Children

GUIDING PRINCIPLES
1. Access to pain management is a fundamental human right.
2. Children have the right to enjoyment of the highest attainable standard of health.
3. Member States and healthcare providers should ensure that children, and their families and caregivers, know their rights to self-determination, non-discrimination, accessible and appropriate health services, and confidentiality.

Table 2. Summary of Recommendations on the Management of Chronic Pain in Children

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. In children with chronic pain, physical therapies may be used, either alone or in combination with other treatments.	Conditional recommendation Very low certainty evidence
2.a) In children with chronic pain, psychological management through cognitive behavioural therapy and related interventions (acceptance and commitment therapy, behavioural therapy and relaxation therapy) may be used.	Conditional recommendation Moderate certainty evidence
b) Psychological therapy may be delivered either face-to-face or remotely, or using a combined approach.	Conditional recommendation Moderate certainty evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
3. In children with chronic pain, appropriate pharmacological management tailored to specific indications and conditions may be used.	Conditional recommendation Low certainty evidence
4.a) Appropriate pharmacological management tailored to specific indications may include the use of morphine under the principles of opioid stewardship, for end-of-life-care. b) In children with chronic pain associated with life-limiting conditions, morphine may be given by appropriately trained healthcare providers, under the principles of opioid stewardship.	Conditional recommendation Very low certainty evidence Conditional recommendation Very low certainty evidence

*see Appendix 1

Table 3. Summary of Best Practices on the Management of Chronic Pain in Children

BEST PRACTICES FOR THE CLINICAL MANAGEMENT OF CHRONIC PAIN IN CHILDREN
1. Children with chronic pain and their families and caregivers must be cared for from a biopsychological perspective; pain should not be treated simply as a biomedical problem.
2. A comprehensive biopsychosocial assessment is essential to inform pain management and planning. As a component of this assessment, healthcare providers should use age-, context- and culturally appropriate tools to screen for, and monitor, pain intensity and its impact on the quality of life of the child and family.
3. Children with chronic pain must have a thorough evaluation of any underlying conditions and access to appropriate treatment for those conditions, in addition to appropriate interventions for the management of pain. Chronic pain in childhood often exists with comorbid conditions affecting the child's health, and social and emotional well-being, which require concurrent management.
4. Children presenting with chronic pain should be assessed by healthcare providers who are skilled and experienced in the evaluation, diagnosis and management of chronic pain.
5. Management, whether with physical therapies, psychological or pharmacological interventions, or combinations thereof, should be tailored to the child's health; underlying condition; developmental age; physical, language and cognitive abilities; and social and emotional needs.
6. Care of children with chronic pain should be child- and family-centred. That is, the child's care should: i. focus on, and be organized around, the health needs, preferences and expectations of the child, and their families and communities; ii. be tailored to the family's values, culture, preferences and resources; and iii. promote engagement and support children and their families to play an active role in care through informed and shared decision-making.
7. Families and caregivers must receive timely and accurate information. Shared decision-making and clear communication are essential to good clinical care. Communication with patients should correspond to their cognitive, development and language abilities. There must be adequate time in a comfortable space for discussions and questions regarding care management plans and progress.

BEST PRACTICES FOR THE CLINICAL MANAGEMENT OF CHRONIC PAIN IN CHILDREN
8. The child and their family and caregivers should be treated in a comprehensive and integrated manner: all aspects of the child's development and well-being must be attended to, including their cognitive, emotional and physical health. Moreover, the child's educational, cultural and social needs and goals must be addressed as part of the care management plan.
9. In children with chronic pain, an interdisciplinary, multimodal approach should be adopted which is tailored to the needs and desires of the child, family and caregivers, and to available resources. The biopsychosocial model of pain supports the use of multiple modalities to address the management of chronic pain.
10. Policy-makers, programme managers and healthcare providers, as well as families and caregivers must attend to opioid stewardship to ensure the rational and cautious use of opioids. The essential practices of opioid stewardship in children include: i. Opioids must only be used for appropriate indications and prescribed by trained providers, with careful assessments of the benefits and risks. The use of opioids by individuals, their impact on pain and their adverse effects must be continuously monitored and evaluated by trained providers. ii. The prescribing provider must have a clear plan for the continuation, tapering or discontinuation of opioids according to the child's condition. The child and family must be apprised of the plan and its rationale. iii. There must be due attention to procurement, storage and the disposal of unused opioids.

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6. Prevention of cisplatin-induced ototoxicity in children and adolescents with cancer

The clinical practice guideline "Prevention of cisplatin-induced ototoxicity in children and adolescents with cancer" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG Supportive Care Guideline Committee in August 2020.

The source clinical practice guideline is published (Freyer DR, Brock PR, Chang KW, et al. Prevention of cisplatin-induced ototoxicity in children and adolescents with cancer: a clinical practice guideline. Lancet Child Adolescent Health 2020; 4(2): 141-50.) and is available open access at: https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(19)30336-0/fulltext.

The purpose of the source clinical practice guideline is to address the clinical question: what adjuvant interventions should be offered in conjunction with cisplatin to prevent ototoxicity in children and adolescents with cancer?

Summary of Recommendations for Prevention of Cisplatin-induced Ototoxicity in Children and Adolescents with Cancer

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. Do not use amifostine for the prevention of cisplatin-induced ototoxicity in children and adolescents with cancer	Strong recommendation High quality evidence
2. Do not use sodium diethyldithiocarbamate for the prevention of cisplatin-induced ototoxicity in children and adolescents with cancer	Strong recommendation Low quality evidence
3. Use sodium thiosulfate for the prevention of cisplatin-induced ototoxicity in children and adolescents with non-metastatic hepatoblastoma	Strong recommendation High quality evidence
4. Consider sodium thiosulfate for the prevention of cisplatin-induced ototoxicity in children and adolescents with non-metastatic cancers other than hepatoblastoma	Weak recommendation Low quality evidence
5. We suggest sodium thiosulfate not be used routinely for the prevention of cisplatin-induced ototoxicity for children and adolescents with metastatic cancers	Weak recommendation Low quality evidence
6. Do not use intratympanic middle ear therapy for the prevention of cisplatin-induced ototoxicity in children and adolescents with cancer	Strong recommendation Low quality evidence
7. Do not alter cisplatin infusion duration, as a means in itself, to reduce ototoxicity in children and adolescents with cancer	Strong recommendation Low quality evidence

*see Appendix 1

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7. Guideline for the Management of Clostridioides difficile Infection in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation Recipients

The "Guideline for the Management of *Clostridioides difficile* Infection in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation Recipients: 2024 Update" developed by the Pediatric Oncology Group of Ontario (POGO) was endorsed by the COG Supportive Care Guideline Committee in August 2024.

The source guideline is published (Patel P, Robinson PD, Fisher BT, et al. Guideline for the management of *Clostridioides difficile* Infection in pediatric patients with cancer and hematopoietic cell transplantation recipients: 2024 Update. eClinMed 2024.) and is available at: https://doi.org/10.1016/j.eclinm.2024.102604

The purpose of the source guideline is to update the previously created clinical practice guideline for the management of *Clostridioides difficile* in pediatric patients with cancer and pediatric hematopoietic cell transplantation recipients. Recommendations and good practice statements from the endorsed clinical practice guideline are presented in the tables below.

Summary of Recommendations for the Management of *Clostridioides difficile* Infection (CDI) in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation (HCT) Recipients

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
What interventions should be used for the prevention of CDI in pediatric patients with cancer and HCT recipients?	
1. We suggest that probiotics not be used routinely for the prevention of CDI in pediatric patients with cancer and HCT recipients	Conditional recommendation Low quality evidence
What interventions should be used for the treatment of CDI in pediatric patients with cancer and HCT recipients?	
2. Use either oral metronidazole or oral vancomycin for the treatment of non-severe CDI in pediatric patients with cancer and HCT recipients	Strong recommendation Low quality evidence
3. Use either oral vancomycin or oral fidaxomicin for the treatment of severe CDI in pediatric patients with cancer or HCT recipients	Strong recommendation Low quality evidence
4. Consider fidaxomicin for the treatment of recurrent CDI in pediatric patients with cancer and HCT recipients	Conditional recommendation Low quality evidence
5. Do not use fecal microbiota transplantation routinely for the treatment of CDI in pediatric patients with cancer and HCT recipients	Strong recommendation Low quality evidence
6. We suggest that monoclonal antibodies not be used routinely for the treatment of CDI in pediatric patients with cancer and HCT recipients	Conditional recommendation Low quality evidence
7. We suggest that probiotics not be used routinely for the treatment of CDI in pediatric patients with cancer and HCT recipients	Conditional recommendation Low quality evidence

*see Appendix 1

Summary of Good Practice Statements for the Management of *Clostridioides Difficile* Infection (CDI) in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation (HCT) Recipients

GOOD PRACTICE STATEMENTS
1. In pediatric patients with cancer and HCT recipients experiencing CDI, follow infection control practices including isolation according to jurisdictional policies
2. In pediatric patients with cancer and HCT recipients, especially those who have experienced CDI, minimize systemic antibacterial administration where feasible

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8. Less restrictions in daily life: a clinical practice guideline for children with cancer

"Less restrictions in daily life: a clinical practice guideline for children with cancer", developed by the Dutch Children's Oncology Group, was endorsed by the COG Supportive Care Guideline Committee in March 2025.

The source guideline is published (Stavleu DC, Mulder RL, Kruimer DM, et al. Less restrictions in daily life: a clinical practice guideline for children with cancer. Supportive Care in Cancer. 2024;32(7):419.) and is available at: https://doi.org/10.1007/s00520-024-08537-9

The purpose of the source guideline is to develop a clinical practice guideline for clinicians, children, and their parents regarding social restrictions in children with cancer. The good practice statement and clinical practice guideline-derived recommendations from the endorsed clinical practice guideline are presented in the table below. The source guideline also includes expert opinion statements. Those who are reviewing the clinical practice guideline-derived recommendations for implementation may consider reviewing the expert opinion statements for added context.

Summary of Recommendations for Less Restrictions in Daily Life: a Clinical Practice Guideline for Children with Cancer

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. We recommend against the use of bath toys that have a reservoir (in which water can be retained) or bath toys that cannot be dried thoroughly.	Strong recommendation Very low quality evidence
2.1 We suggest not to use warm publicly accessible bubble baths.	Weak recommendation Very low quality evidence
3. We suggest not to use chlorhexidine bathing or other bath wipes as it does not have an added value to basic hygiene measures.	Weak recommendation Very low quality evidence
9.1 We suggest allowing to keep domestic pets in the households of children with cancer.	Weak recommendation Very low quality evidence
11 We recommend allowing children with cancer to attend school or kindergarten irrespective of neutropenia (unless someone in their class or group has a contagious disease with potential severe consequences, e.g. varicella zoster).	Strong recommendation Very low quality evidence
13.1 We suggest allowing children with cancer to swim (irrespective of neutropenia).	Weak recommendation Very low quality evidence

*see Appendix 1

Good Practice Statement for Less Restrictions in Daily Life: a Clinical Practice Guideline for Children with Cancer

GOOD PRACTICE STATEMENT
Proper hand hygiene should be performed by parents, caregivers and medical personnel.

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9. Management of Fatigue in Children and Adolescents with Cancer and in Pediatric Hematopoietic Cell Transplant Recipients

The "Guideline for the management of fatigue in children and adolescents with cancer or pediatric hematopoietic cell transplant recipients: 2023 update" was endorsed by the COG Supportive Care Guideline Task Force in January 2024.

The source guideline is published (Patel P, Robinson PD, van der Torre P, et al. Guideline for the management of fatigue in children and adolescents with cancer or pediatric hematopoietic cell transplant recipients: 2023 update. eClinicalMedicine 2023; 63: 102147.) and is available at: https://doi.org/10.1016/j.eclinm.2023.102147

The purpose of this guideline is to provide guidance for management of fatigue in children and adolescents with cancer and paediatric recipients of hematopoietic stem cell transplantation recipients.

The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Management of Fatigue in Children and Adolescents with Cancer or Pediatric Hematopoietic Cell Transplant (HCT) Recipients

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
What are effective interventions for the management of fatigue in children and adolescents with cancer or pediatric HCT recipients?	
• Use physical activity interventions to manage fatigue in children and adolescents with cancer or paediatric HCT recipients	Strong recommendation High quality evidence
• Do not routinely use pharmacological approaches to manage fatigue in children and adolescents with cancer or pediatric HCT recipients	Strong recommendation Moderate quality evidence
• Offer relaxation, mindfulness, or both to manage fatigue in children and adolescents with cancer or pediatric HCT recipients	Strong recommendation Moderate quality evidence
• In settings where strongly recommended approaches are not feasible or were not successful, consider offering cognitive or cognitive behavioural therapies to manage fatigue in children and adolescents with cancer or pediatric HCT recipients	Conditional recommendation Moderate quality evidence
Routinely assess for fatigue, ideally using a validated scale, in children and adolescents with cancer or pediatric HCT recipients	Good practice statement

*see Appendix 1

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10. Fertility Preservation for Patients with Cancer

The "Fertility Preservation in People with Cancer: ASCO Clinical Practice Guideline Update" guideline was endorsed by the COG Supportive Care Guidelines sub-Committee in June 2025. It is an update to the 2018 clinical practice guideline that was also endorsed by the COG and is now archived. The 2025 clinical practice guideline is published (Su HI, Lacchetti C, Letourneau J, et al. Fertility preservation in people with cancer: ASCO guideline update. J Clin Onc 2025; 43, 1488-1515.) and is available here: https://ascopubs.org/doi/10.1200/JCO-24-02782

This guideline provides a comprehensive approach to assessing, discussing and offering fertility preservation options to people with cancer. The good practice statements and recommendations of the source clinical practice guideline are presented below.

Good Practice Statements for Fertility Preservation for People with Cancer

GOOD PRACTICE STATEMENTS
Role of clinicians
6.2. All clinicians should encourage patients to participate in registries and clinical studies, as available, to define further the gonadotoxic risks of cancer-directed therapies as well as the safety and efficacy of fertility preservation interventions and strategies.
6.3. All clinicians should refer patients who express an interest in fertility, as well as those who are ambivalent or uncertain, to reproductive specialists as soon as possible.
6.4. Oncology teams should identify and ensure prompt access to a multidisciplinary fertility preservation team including fertility specialists, trained mental-health professionals for emotional support and guidance on family building decision-making, social workers, financial counseling and insurance navigation, and genetic counselors. Effective, timely, and regular communication among team members is essential to provide coordinated, comprehensive care for patients.
6.5. Health insurance benefit mandates and benefits for fertility preservation should specify comprehensive coverage of guideline-based fertility preservation services and long-term storage, parity with other insurance benefits, and elimination of prior authorization. Clinicians should advocate for comprehensive insurance coverage of fertility preservation services for their patients with cancer with legislators, insurance regulators, and health plans, as well as for clinic-based resources to help patients access insurance benefits.

Summary of Recommendations for Fertility Preservation for People with Cancer

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Discussing risk of infertility with patient	
1.1 Clinicians caring for adult and pediatric patients with cancer should discuss the possibility of infertility as early as possible before treatment starts to preserve the full range of options.	Strong Moderate quality evidence
1.2 Clinicians should refer patients who express an interest in fertility preservation, and those who are uncertain, to reproductive specialists.	Strong Very low quality evidence
1.3 Clinicians should initiate the discussion regarding infertility with the knowledge that it can ultimately reduce distress and improve quality of life, even if the patient does not undergo fertility preservation.	Strong Moderate quality evidence
1.4 Additional discussions and/or referrals may be offered yearly when the patient returns for follow-up after completion of cancer-directed therapy or when treatment plans change or evolve, as well as if pregnancy is being considered. The discussions should be ongoing throughout survivorship and documented in the medical record.	Strong Low quality evidence
Qualifying Statement for Recommendations 1.3 and 1.4*: It is essential that these discussions take place with all patients, irrespective of their reproductive risk profile, current family size, cancer prognosis, sexual orientation or identity, religious beliefs, financial or insurance resources, access to care, or other potential considerations, including disparities.*	
Risks of infertility from cancer treatment	
2.1 Clinicians should offer an evaluation and counseling regarding the risk of reproductive function impairment and infertility to ensure that all patients are appropriately informed and supported in managing the potential reproductive impacts of their cancer treatment. This assessment should consider specific patient groups known to be at increased risk due to the gonadotoxic nature of the therapies they receive or could receive in the future, and those on longer-term treatments that delay or preclude the ability to conceive. It should also consider those for whom the risk remains uncertain due to the unknown reproductive toxicity of many cancer-directed therapies. The effect of chronologic age should also be taken into account for females due to increased infertility risk with concomitant aging.	Strong Moderate quality evidence
Fertility preservation in males	
3.1 Sperm cryopreservation: Cryopreservation of ejaculated sperm (sperm banking) should be offered prior to initiating cancer-directed therapy. Health care clinicians should discuss sperm banking with all pubertal and postpubertal males prior to receiving cancer treatment.	Strong High quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Qualifying Statement for Recommendation 3.1*: More sperm samples will provide greater flexibility in future fertility treatments, ie, inseminations versus IVF. While fertility clinicians empirically recommend a minimum of three ejaculates of sufficient quality, achieving this may not be feasible for all patients. Clinicians should adopt a flexible approach and collect as many ejaculates as possible before the start of gonadotoxic therapy. Importantly, any cryopreserved sperm can offer a chance for biological parenthood.*	
3.2 Testicular sperm extraction (TESE): TESE with sperm cryopreservation should be offered to pubertal and postpubertal males who cannot produce a semen sample, before cancer treatment begins.	Strong High quality evidence
3.3 Hormonal gonadoprotection: Hormonal suppression therapy should not be offered to males as an approach for preserving fertility. It is not effective and therefore not recommended.	Strong High quality evidence
3.4 Other methods to preserve male fertility: Other methods, such as testicular tissue cryopreservation in pre-pubertal males and reimplantation or grafting of human testicular tissue, should be performed only as part of clinical trials or approved experimental protocols.	Strong Very low quality evidence
3.5 Post-treatment setting: Males should be advised of a potentially higher risk of genetic damage in sperm collected soon after initiation and completion of antineoplastic and/or radiation therapy. It is strongly recommended that sperm be collected before initiation of treatment because the quality of the sample and sperm DNA integrity may be compromised after single treatment. Although sperm counts and quality of sperm may be diminished even before initiation of therapy, and even if there may be a need to initiate chemotherapy quickly such that there may be limited time to obtain optimal numbers of ejaculate specimens, these concerns should not dissuade patients from banking sperm. Intracytoplasmic sperm injection allows the future use of a very limited amount of sperm; thus, even in these compromised scenarios, fertility may still be preserved.	Strong Low quality evidence
Fertility preservation in females	
4.1 Embryo cryopreservation: Embryo cryopreservation should be offered as it is an established fertility preservation method, and it has routinely been used for storing embryos after in vitro fertilization.	Strong High quality evidence
4.2 Mature oocyte cryopreservation: Cryopreservation of unfertilized oocytes should be offered as it is an established fertility preservation method and may be especially well suited to females who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing. Oocyte cryopreservation should be performed in centers with the necessary expertise.	Strong High quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Qualifying Statements for Recommendations 4.1 and 4.2*: Embryo and oocyte cryopreservation are both recommended options for fertility preservation in female patients with cancer undergoing gonadotoxic therapy. The choice between embryo and oocyte cryopreservation should be guided by patient preferences, clinical considerations, and individual circumstances including future flexibility, success rates, and legal considerations. The Expert Panel emphasizes shared decision-making among the primary oncology team, the reproductive endocrinology team, and the patient to determine safety and appropriateness of ovarian stimulation and to tailor protocols. Flexible ovarian stimulation protocols for oocyte collection are available. Timing of this procedure no longer depends on the menstrual cycle in most cases, and stimulation can be initiated with less delay compared with older protocols. Thus, oocyte harvesting for the purpose of oocyte or embryo cryopreservation is now possible on a cycle day–independent schedule. Of special concern in estrogen-sensitive breast and gynecologic malignancies is the possibility that these fertility preservation interventions (eg, ovarian stimulation regimens that increase estrogen levels) may increase the risk of cancer progression or recurrence. Aromatase inhibitor– based stimulation protocols are now well established and may alleviate these concerns. In particular, there is no increased cancer recurrence risk as a result of aromatase inhibitor–supplemented ovarian stimulation.*	
4.3 Post-treatment setting: Embryo and oocyte cryopreservation for fertility preservation may be offered in the post-treatment setting to patients who did not undergo fertility preservation before their cancer treatment but are at risk of primary ovarian insufficiency or infertility. They may also be offered to survivors who previously underwent fertility preservation but may not have enough cryopreserved tissue to meet their desired family size, as well as for those who want or need to delay childbearing and consequently face the risk of age-related fertility decline, which may be accelerated in cancer survivors.	Strong Moderate quality evidence
Qualifying Statement for Recommendation 4.3*: In the post-treatment setting, the efficacy of oocyte retrieval and embryo creation is contingent upon the presence of a viable ovarian reserve, which can be assessed through markers such as anti-Mullerian hormone (AMH) levels and antral follicle count (AFC). It is important to acknowledge that the reproductive potential of gametes may be affected by the proximity to cancer treatment. Due to timelines of oocyte development, there may be no oocyte yield within 3 months of last chemotherapy dose. Patients should be counseled on the unknown reproductive potential and offspring health of gametes obtained proximal to gonadotoxic therapy.*	
4.4. In vitro maturation (IVM): IVM of oocytes may be offered as an emerging FP method.	Conditional Low quality evidence
Qualifying Statement for Recommendation 4.4*: IVM has lower pregnancy and live birth rates compared to IVF in females without cancer. The pregnancy and live birth rates of IVM in cancer survivors is unknown.*	

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
4.5. Ovarian transposition: Ovarian transposition (oophoropexy) may be offered to reproductive-aged patients when pelvic irradiation is required. However, because of radiation scatter, ovaries are not always protected, and patients should be aware that this technique is not always successful. Because of the risk of remigration of the ovaries, this procedure should be performed as close to the time of radiation treatment as possible.	Strong Moderate quality evidence
Qualifying Statement for Recommendation 4.5*: Ovarian transposition is not suitable for patients with a moderate or high risk of ovarian metastasis, or those receiving concomitant gonadotoxic chemotherapy.*	
4.6. Uterine transposition: Uterine transposition in reproductive-aged patients remains experimental and should be offered only as part of a clinical trial or approved experimental protocols.	Conditional Low quality evidence
4.7. Conservative gynecologic surgery: a. For patients with stage IA2 to IB1 cervical cancer, radical trachelectomy may be offered to preserve fertility if the tumor diameter is <2 cm and invasion depth is < 10mm. b. For patients with well-differentiated (grade1) endometrial tumors with minimal myometrial invasion, as confirmed by magnetic resonance imaging, fertility-sparing surgery may be offered. Hormonal therapy using progestins, either orally or via an intrauterine device, is the primary fertility-preserving option for early-stage endometrial cancer. c. Patients with stage IA grade1 epithelial ovarian cancer after thorough staging may be offered fertility-sparing surgery. Uterine preservation may be considered in other stages and grades to enable future use of assisted reproductive technologies. d. In other gynecologic malignancies, less radical surgeries may be offered to spare reproductive organs when clinically appropriate.	Strong Moderate quality evidence
Qualifying Statement for Recommendation 4.7*: Each surgical decision should balance optimal oncologic care with the patient's fertility goals, involving a multidisciplinary team for comprehensive treatment planning and follow-up care.*	
4.8. Ovarian suppression: Gonadotropin-releasing hormone agonists (GnRHa) should not be used in place of established fertility preservation methods such as oocyte, embryo, or ovarian tissue cryopreservation. GnRHa may be offered as an adjunct to females with breast cancer. Beyond breast cancer, the potential benefits and risks of GnRHa warrant further investigation, and trials are encouraged.	Conditional Moderate quality evidence
4.9. Ovarian suppression: For patients with oncologic emergencies requiring urgent chemotherapy, GnRHa may be offered and can provide benefits such as menstrual suppression.	Conditional Low quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
4.10. Ovarian tissue cryopreservation and transplantation: Ovarian tissue cryopreservation (OTC) for the purpose of future transplantation may be offered to patients with cancer as an established fertility preservation method. As it does not require ovarian stimulation, it can be performed immediately in those unable to delay chemotherapy. In addition, it does not require sexual maturity and hence may be the only method available in prepubertal patients. This method may also be offered as an emerging method to restore global ovarian function. While this option may be offered as an alternative to embryo or oocyte cryopreservation, it may also serve as an adjunct option. Proceeding with OTC should be guided by patient preferences, clinical considerations, and individual circumstances including future flexibility, success rates, and legal considerations.	Strong Moderate quality evidence
Qualifying Statement for Recommendation 4.10*: Evaluating cancer survivors for residual neoplastic cells before ovarian tissue transplantation is essential to mitigate disease transmission risks and to prioritize patient safety. There is a theoretical risk of reintroducing malignant cells but the clinical significance of this is unknown. To reduce this risk, OTC may be deferred until posttreatment MRD negativity is achieved.*	
Fertility preservation in children	
5.1 Clinicians should offer established methods of fertility preservation (eg, semen or oocyte cryopreservation) in children and adolescents who have initiated puberty, with patient assent and parent or guardian consent. For prepubertal children, the only fertility preservation options are ovarian and testicular cryopreservation, the latter of which is currently investigational.	Strong Moderate quality evidence
Role of clinicians	
6.1 All clinicians should be prepared to discuss infertility as a potential risk of therapy. This discussion should take place as soon as possible once a cancer diagnosis is made and can occur simultaneously with staging and the formulation of a treatment plan. There are benefits for patients in discussing fertility information with clinicians at every step of the cancer journey.	Strong Very low quality evidence

*see Appendix 1

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11. Guideline for the Management of Fever and Neutropenia in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation Recipients

The "Guideline for the Management of Fever and Neutropenia in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation Recipients: 2023 Update" was endorsed by the COG Supportive Care Guideline Committee in May 2023.

The source guideline is published in the Journal of Clinical Oncology 2023 41:9, 1774-1785: https://ascopubs.org/doi/abs/10.1200/JCO.22.02224

The purpose of this guideline is to provide evidence-based recommendations for the empiric management of fever and neutropenia in pediatric patients with cancer and hematopoietic cell transplant patients. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Empiric Management of Fever and Neutropenia

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
A. Initial Management	
Risk Stratification	
A1. Adopt a validated risk stratification strategy and incorporate it into routine clinical management	Strong recommendation Low quality evidence
Evaluation	
A2. Obtain blood cultures at onset of fever and neutropenia from all lumens of central venous catheters	Strong recommendation Low quality evidence
A3. Consider obtaining peripheral blood cultures concurrent with central venous catheter cultures	Conditional recommendation Moderate quality evidence
A4. Consider urinalysis and urine culture in patients where a clean-catch, mid-stream specimen is readily available	Conditional recommendation Low quality evidence
A5. Obtain chest radiography only in patients with respiratory signs or symptoms	Strong recommendation Moderate quality evidence
Treatment	
A6. In high-risk fever and neutropenia:	
A6a. Use monotherapy with an antipseudomonal β-lactam, a fourth generation cephalosporin or a carbapenem as empiric antibacterial therapy in pediatric high-risk fever and neutropenia	Strong recommendation High quality evidence
A6b. Reserve addition of a second anti-Gram-negative agent or a glycopeptide for patients who are clinically unstable, when a resistant infection is suspected or for centers with a high rate of resistant pathogens	Strong recommendation Moderate quality evidence
A7. In low-risk fever and neutropenia:	
A7a. Consider initial or step-down outpatient management if the infrastructure is in place to ensure careful monitoring and follow-up	Conditional recommendation Moderate quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
A7b. Consider oral antibacterial therapy administration if the patient is able to tolerate this route of administration reliably	Conditional recommendation Moderate quality evidence
B. Ongoing Management	
Modification of Treatment	
B1. In patients who are responding to initial empiric antibacterial therapy, discontinue double coverage for Gram-negative infection or empiric glycopeptide (if initiated) after 24 to 72 hours if there is no specific microbiologic indication to continue combination therapy	Strong recommendation Moderate quality evidence
B2. Do not broaden the initial empiric antibacterial regimen based solely on persistent fever in patients who are clinically stable	Strong recommendation Low quality evidence
B3. In patients with persistent fever who become clinically unstable, escalate the initial empiric antibacterial regimen to include coverage for resistant Gram-negative, Gram-positive, and anaerobic bacteria	Strong recommendation Very low-quality evidence
Cessation of Treatment	
B4. In both high-risk and low-risk fever and neutropenia patients who have been clinically well and afebrile for at least 24 hours, discontinue empiric antibacterial therapy if blood cultures remain negative at 48 hours, if there is evidence of marrow recovery	Strong recommendation Low quality evidence
B5. In patients with low-risk fever and neutropenia who have been clinically well and afebrile for at least 24 hours, consider discontinuation of empiric antibacterial therapy if blood cultures remain negative at 48 hours despite no evidence of marrow recovery	Conditional recommendation Moderate quality evidence
C. Empiric Antifungal Treatment	
Risk Stratification	
C1. Invasive fungal disease high-risk patients are those with AML, high-risk acute lymphoblastic leukemia, or relapsed acute leukemia; those with prolonged neutropenia; those receiving high-dose steroids; and those undergoing allogeneic HCT in the first year after HCT without evidence of T-cell reconstitution, or receiving steroids or multiple immune suppressive agents to prevent or treat graft-versus-host disease. Those not meeting these criteria are categorized as invasive fungal disease low-risk patients.	Strong recommendation Low quality evidence
Evaluation	
C2. In terms of biomarkers to guide empiric antifungal management for prolonged (≥ 96 hours) fever with neutropenia in invasive fungal disease high-risk patients:	
C2a. Consider not using serum galactomannan	Conditional recommendation Moderate quality evidence
C2b. Do not use β-D-glucan.	Strong recommendation Low quality evidence
C2c. Do not use fungal polymerase chain reaction testing in blood	Strong recommendation Moderate quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
C3. In terms of imaging for the evaluation of prolonged (≥ 96 hours) fever with neutropenia in invasive fungal disease high-risk patients:	
C3a. Perform CT of the lungs.	Strong recommendation Low quality evidence
C3b. Consider imaging of abdomen such as ultrasound	Conditional recommendation Low quality evidence
C3c. Consider not routinely performing CT of sinuses in patients without localizing signs or symptoms	Conditional recommendation Low quality evidence
Treatment	
C4. In invasive fungal disease high-risk patients with prolonged (≥ 96 hours) fever with neutropenia unresponsive to broad-spectrum antibacterial therapy, initiate caspofungin or liposomal amphotericin B for empirical antifungal therapy unless a pre-emptive antifungal therapy approach is chosen	Strong recommendation High quality evidence
C5. In non-HCT invasive fungal disease high-risk patients not receiving antimold prophylaxis with prolonged (≥ 96 hours) fever with neutropenia, consider a pre-emptive antifungal therapy approach by deferring empiric antifungal therapy and initiating antifungal therapy only if evaluation suggests of indicates invasive fungal disease	Conditional recommendation Moderate quality evidence
C6. In invasive fungal disease low-risk patients with prolonged (≥ 96 hours) fever with neutropenia, consider withholding empiric antifungal therapy	Conditional recommendation Low quality evidence

HCT, hematopoietic cell transplant

*see Appendix 1

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12. Guideline on Use of Food Restrictions to Prevent Infections

"Use of food restrictions to prevent infections in paediatric patients with cancer and haematopoietic cell transplantation recipients: a systematic review and clinical practice guideline", developed by the Pediatric Oncology Group of Ontario, was endorsed by the COG Supportive Care Guidelines sub-Committee in June 2025.

The source guideline is published (Phillips R, Fisher BT, Ladas E, et al. Use of food restrictions to prevent infections in paediatric patients with cancer and haematopoietic cell transplantation recipients: a systematic review and clinical practice guideline. eClinical Med 2025; 81:103093.) and is available at: https://doi.org/10.1016/j.eclinm.2025.103093

The purpose of the source guideline is to provide to develop evidence-based recommendations on the use of food restrictions to prevent infections in pediatric patients being treated for cancer or undergoing hematopoietic cell transplant (HCT). The good practice statement and recommendations from the endorsed clinical practice guideline are presented in the tables below.

Good Practice Statement on the Use of Food Restrictions to Prevent Infections in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation (HCT) Recipients

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

Summary of Recommendations on the Use of Food Restrictions to Prevent Infections in Pediatric Patients with Cancer and Hematopoietic Cell Transplantation (HCT) Recipients

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. Should food restrictions be used to prevent infections in pediatric 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
2. 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

*see Appendix 1

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13. Guideline for the Prevention of Oral and Oropharyngeal Mucositis

The "Clinical practice guideline for the prevention of oral and oropharyngeal mucositis in pediatric cancer and hematopoietic stem cell transplant patients: 2021 update" developed by the Pediatric Oncology Group of Ontario (POGO) was endorsed by the COG Supportive Care Guideline Committee in December 2021.

The source clinical practice guideline is published (Patel P, et al. Clinical practice guideline for the prevention of oral and oropharyngeal mucositis in pediatric cancer and hematopoietic stem cell transplant patients: 2021 update. Eur J Cancer 2021; 154: 92-101.) and is available at: https://www.sciencedirect.com/science/article/pii/S095980492100321X

The purpose of the source clinical practice guideline was to update the 2015 clinical practice guideline for mucositis prevention in pediatric cancer and HSCT patients. The recommendations of the source clinical practice guideline are presented below.

Summary of Recommendations for the Prevention of Oral and Oropharyngeal Mucositis

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
What prophylactic interventions are effective at preventing or reducing the severity of oral and oropharyngeal mucositis in pediatric patients (0 to 18 years) receiving treatment for cancer or undergoing HSCT?	
1. Use cryotherapy for older, cooperative pediatric patients receiving treatment for cancer or undergoing HSCT who will receive short infusions of melphalan or 5-fluorouracil. ***Remarks:*** The panel valued the absence of documented adverse effects, low costs and consistent benefits associated with cryotherapy. The duration of melphalan and 5-fluorouracil administration in the included trials was 30 min or less where infusion duration was described. The panel did not believe that cryotherapy would be feasible for chemotherapy administrations longer than 1 h.	Strong recommendation High-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2. Consider using cryotherapy for older, cooperative pediatric patients receiving treatment for cancer or undergoing HSCT who will receive short infusions of chemotherapy associated with mucositis other than melphalan or 5-fluorouracil. ***Remarks:*** The panel hypothesized that the efficacy of cryotherapy is likely generalizable to chemotherapy other than melphalan and 5-fluorouracil. However, the indirectness of the data lowered the panel's certainty and resulted in a conditional recommendation. It is important to counsel families and patients that mucositis may develop even with diligent cryotherapy use, and the efficacy of cryotherapy may vary depending on the chemotherapy regimen administered.	Conditional recommendation Moderate-quality evidence
3. Do not administer palifermin routinely to pediatric patients with cancer receiving treatment for cancer or undergoing HSCT. ***Remarks:*** While the panel acknowledged the significant reduction in severe mucositis associated with palifermin, the observed effect size was relatively modest. Based on its known short-term adverse effects, its potential for long-term negative effects on cancer outcomes, high costs and restricted availability, the panel made a strong recommendation against its routine use.	Strong recommendation High-quality evidence
4. Use intraoral photobiomodulation therapy in the red light spectrum (620–750 nm) for pediatric patients undergoing autologous or allogeneic HSCT and for pediatric patients who will receive radiotherapy for head and neck carcinoma. ***Remarks:*** The panel valued the consistent benefits of photobiomodulation therapy and data regarding feasibility in pediatric patients. The ability to deliver photobiomodulation therapy requires specialized equipment, training and protective eyewear for the patient and those in attendance. The panel believed these requirements to be acceptable given the magnitude of benefit and the restricted patient populations included in the recommendation based on direct data. The ability to deliver photobiomodulation therapy to very young children requires assistance and support from family members and may not always be successful.	Strong recommendation High-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
5. Consider using intraoral photobiomodulation therapy in the red light spectrum (620–750 nm) for pediatric patients who will receive radiotherapy for head and neck cancers other than carcinoma. ***Remarks:*** Although direct data were not available, the panel hypothesized that the efficacy of photobiomodulation therapy for head and neck carcinoma patients receiving radiotherapy is likely generalizable to pediatric patients who will receive radiotherapy for other head and neck cancers such as rhabdomyosarcoma. However, the indirectness of the data lowered the panel's certainty and resulted in a conditional recommendation.	Conditional recommendation Moderate-quality evidence
6. Do not administer GCSFs to pediatric patients receiving treatment for cancer or undergoing HSCT for the purpose of mucositis prevention. ***Remarks***: While the panel recognized that patients receive GCSFs for other indications including shortening the duration of neutropenia, the absence of benefit, adverse effects and costs led the panel to make a strong recommendation against its use for the purpose of mucositis prevention.	Strong recommendation High-quality evidence

HSCT: hematopoietic stem cell transplant; GCSFs: granulocyte colony-stimulating factors
*see Appendix 1

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14. Platelet Transfusion Guideline

The "Platelet Transfusion 2025 AABB and ICTMG International Clinical Practice Guidelines" were endorsed by the COG Supportive Care Guidelines sub-Committee in February 2026. This clinical practice guideline is published (Metcalf RA, Nahirniak S, Guyatt G, et al. Platelet transfusion: 2025 AABB and ICTMG international clinical practice guidelines. JAMA. 2025 Aug 19;334(7).) and is available here: https://jamanetwork.com/journals/jama/article-abstract/2834703

This guideline provides recommendations for adult and pediatric populations in whom platelet transfusions are commonly performed. The good practice statements and recommendations of the source clinical practice guideline are presented below.

Good Practice Statement for Platelet Transfusion

GOOD PRACTICE STATEMENT
Consider symptoms, signs, other laboratory parameters, bleeding history, medications, patients' values and preferences, alternative therapies, and overall clinical context when deciding to perform a platelet transfusion on a particular patient.

Summary of Recommendations for Platelet Transfusion

Note that only recommendations applicable to pediatric patients are summarized below.

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
1.1 Nonbleeding patients with hypoproliferative thrombocytopenia actively receiving chemotherapy or undergoing allogeneic stem cell transplant (SCT): Platelet transfusion should be administered when the platelet count is <10 × 10^3/µL	Strong / Moderate
Summary Justification: The data support no benefit with liberal strategies and a platelet count threshold <10 × 10^3/µL is practical for implementation.	
1.2 Preterm neonates without major bleeding: Platelet transfusion should be administered when the platelet count is <25 × 10^3/µL	Strong / High
Summary Justification: The data support no benefits with liberal policies of <50 × 10^3/µL and the possibility of harm.	
1.3 Patients undergoing lumbar puncture: Platelet transfusion should be administered when the platelet count is <20 × 10^3/µL	Strong / Moderate
Summary Justification: A platelet count threshold <20 × 10^3/µL is practical for implementation, and minimizes need for platelet transfusion, while recognizing the extremely low event rate estimate	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
1.4 Patients with Dengue-related consumptive thrombocytopenia in the absence of major bleeding: No platelet transfusion	Strong / Moderate
Summary Justification: The data support no benefits with use of platelets as prophylaxis and possibility of harm.	
2.6 Nonthrombocytopenic patients undergoing cardiovascular surgery in the absence of major hemorrhage, including those receiving cardiopulmonary bypass: No platelet transfusion	Conditional / Very low
Summary Justification: The limited data available support no benefit with use of platelets.	

*see Appendix 1

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15. Treatment of Pediatric Venous Thromboembolism

The "American Society of Hematology/International Society on Thrombosis and Haemostasis 2024 updated guidelines for treatment of venous thromboembolism" were endorsed by the COG Supportive Care Guidelines Working Group in May 2026. This clinical practice guideline is published (Monagle P, Azzam M, Bercovitz R, et al. American Society of Hematology/International Society on Thrombosis and Haemostasis 2024 updated guidelines for treatment of venous thromboembolism in pediatric patients. Blood advances. 2025; 9(10): 2587-636.) and is available here: https://doi.org/10.1182/bloodadvances.2024015328

The purpose of these guidelines is to provide evidence-based recommendations on the treatment of venous thromboembolism in pediatric patients. The good practice statements and recommendations of the source clinical practice guideline are presented below.

Good Practice Statements for Venous Thromboembolism Treatment

GOOD PRACTICE STATEMENTS
A pediatric hematologist or a pediatrician in consultation with a hematologist will be best suited to implement these recommendations given the complexity of the care involved in children with VTE.
For pediatric patients who are at high risk of bleeding (eg, CSVT and associated hemorrhage secondary to venous congestion, immediate after or anticipated invasive procedures), consider the use of a short half-life agent such as UFH rather than LMWH or DOACs if anticoagulation is required, to decrease the risk of worsening hemorrhage or bleeds.

VTE, venous thromboembolism; CSVT, cerebral simus venous thrombosis; UFH, unfractionated heparin; LMWH, low molecular weight heparin; DOAC, direct oral anticoagulants.

Summary of Recommendations for Venous Thromboembolism Treatment (VTE)

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
1. For pediatric patients with symptomatic deep vein thrombosis (DVT) or pulmonary embolism (PE), the ASH/ISTH guideline panel suggests using anticoagulation rather than no anticoagulation	Conditional / Very low
Remarks: Although there remains limited direct evidence in pediatric patients, there is strong indirect evidence in adults that symptomatic VTE requires treatment. However, based on recently published observational studies in pediatric patients, there may be specific clinical scenarios such as neonatal central venous catheter–associated VTE or trauma-associated VTE in which anticoagulation may result in either no significant benefit or potentially an increased risk of harm. Outside of these specific clinical scenarios, the panel agrees that in most pediatric patients with symptomatic DVT and PE, anticoagulation is warranted. Therefore, the panel made a conditional recommendation with very low certainty in the evidence.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
2. For pediatric patients with clinically unsuspected (previously termed asymptomatic) DVT or PE, the ASH/ISTH guideline panel suggests either using anticoagulation or no anticoagulation	Conditional / Very low
Remarks: The natural history of clinically unsuspected DVT or PE in pediatric patients appears to carry a lower risk (compared with symptomatic DVT or PE) of acute and long-term sequelae, especially in certain pediatric subpopulations. The recommendation is based on studies that report outcomes for pediatric patients with clinically unsuspected DVT or PE. Single institution, observational, and retrospective studies in select subpopulations of pediatric patients suggest that not using anticoagulation for clinically unsuspected DVT or PE does not lead to severe outcomes. The benefits or harms of anticoagulation or no anticoagulation vary for different populations including neonates, pediatric patients who are critically ill, patients with cardiac disease, or patients who have experienced trauma. However, if clinically unsuspected DVT or PE is detected, the decision to treat or not treat should be individualized. Research to better understand the natural history of clinically unsuspected DVT or PE, benefits, and harms of treatment in a variety of subgroups and clinical settings in pediatrics is a high priority.	
3. For select pediatric patients with provoked VTE, the ASH/ISTH guideline panel suggests 6 weeks rather than 3 months of anticoagulation. Exclusions to this recommendation include (1) PE, (2) recurrent VTE, (3) persistent occlusive thrombus at 6 weeks, (4) cancer-associated thrombosis, (5) patients with persistent antiphospholipid antibodies (APAs) or major thrombophilia, and (6) ongoing VTE risk factors	Conditional / Very low
Remarks: This recommendation is based mainly on the Kids-DOTT randomized clinical trial (RCT) that evaluated the duration of anticoagulation therapy in pediatric patients with provoked VTE. Importantly, the criteria for inclusion and randomization were stringent, and many pediatric patients with provoked VTE were excluded. The recommendation reflects the population that was studied and cannot be extrapolated to all patients with provoked VTE. For patients with provoked VTE not meeting these low-risk criteria, the panel suggests the use of anticoagulation therapy for 3 months, and for those with persistent provoking VTE risk factors, longer duration of anticoagulation may be considered.	
4. For pediatric patients with unprovoked DVT or PE, the ASH/ISTH guideline panel suggests using anticoagulation for 6 to 12 months rather than indefinite anticoagulation	Conditional / Very low
Remarks: Unprovoked VTE is rare in pediatrics. Although studies suggest that rates of recurrent VTE in children and adolescents with age of >1 year with unprovoked VTE are relatively high (21%-36% at 3.5 years follow up), there are no pediatric studies evaluating duration of therapy in this cohort. Although extrapolation of adult data might favor prolonged treatment in terms of VTE recurrence, in the absence of pediatric data, the panel felt that the impact of indefinite anticoagulation on bleeding risk and quality of life (QOL) would more negatively affect pediatric patients compared with adults. Patient values and preferences should be considered when making this decision.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
5. For pediatric patients with cerebral sinus venous thrombosis (CSVT) with and without hemorrhage secondary to venous congestion, the ASH/ISTH guideline panel suggests using anticoagulation rather than no anticoagulation	Conditional / Very low
Remarks: Observational studies suggest lower mortality and improved neurologic outcomes in patients with CSVT treated with anticoagulation. However, the panel recognized different populations of patients with CSVT (eg, neonates, and those with infection-associated CSVT, who have experienced trauma, have had surgery, and have cancer) may have different risks for bleeding and neurologic outcomes that should be considered in the decision to use anticoagulation. Evidence of venous congestion secondary to thrombus obstruction with or without hemorrhage should be managed with anticoagulation. The panel notes that when anticoagulation is prescribed, it is important that appropriate therapy for additional associated conditions (eg, surgical interventions for infection-associated CSVT) be used.	
6. For pediatric patients with CSVT, the ASH/ ISTH guideline panel suggests using anticoagulation alone rather than thrombolysis followed by anticoagulation	Conditional / Very low
Remarks: The evidence is sparse for the balance of benefits and harms of thrombolysis compared with anticoagulation in pediatric patients with CSVT. Based on the experience of the panel members, the panel suggests use of anticoagulation rather than thrombolysis for children with CSVT who have no evidence of ischemia. However, thrombolysis may be considered when there is neurologic deterioration despite anticoagulation and, in such or similar instances, reperfusion therapies may be considered depending on local resources or experiences.	
7a. For neonates and pediatric patients with right atrial thrombosis (RAT), the ASH/ISTH guideline panel suggests anticoagulation rather than no anticoagulation for patients with high-risk features and low perceived risk of bleeding	Conditional / Very low
Remarks: Insufficient data are available for formal risk stratification of RAT and bleeding from anticoagulation. Based on available literature and experience of panel members, high-risk features of RAT to consider include large size, shape (snake-shaped or pedunculated), mobility, location (eg, involvement of tricuspid valve or restricting blood flow), presence of intracardiac right-to-left shunt, presence of a central venous catheter, or associated with symptoms (arrhythmias, hemodynamic compromise, etc). The decision to start anticoagulation should be individualized based on the risk of thrombotic complications and the perceived risk of bleeding from anticoagulation.	
7b. For neonates and pediatric patients with RAT and the absence of high-risk features or with unacceptable perceived risk of bleeding, the ASH/ISTH guideline panel suggests no anticoagulation over anticoagulation	Conditional / Very low
Remarks: Studies in patients without high-risk features treated with anticoagulation do not demonstrate clinical benefits compared with patients not treated with anticoagulation. The studies are not randomized, are small, and are subject to significant bias. Study participants treated with anticoagulation had an increased risk of bleeding.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
8. For neonates and pediatric patients with RAT requiring anti-thrombotic treatment, the ASH/ISTH guideline panel suggests using anticoagulation alone over thrombolysis followed by anticoagulation	Conditional / Very low
Remarks: In most cases, anticoagulation alone is adequate. However, there are individual cases in which the hemodynamic status, size, and mobility of the thrombus might dictate more aggressive therapy. The choice to use thrombolysis will depend on feasibility or the intervention and patient and family acceptability of the anticipated risks and benefits of thrombolysis.	
9. For neonates with renal vein thrombosis (RVT), the ASH/ISTH guideline panel suggests using anticoagulation rather than no anticoagulation	Conditional / Very low
Remarks: The panel considers the intervention to have a potential beneficial effect if the long-term outcomes of avoiding hypertension, chronic kidney disease, and renal failure are considered. Anticoagulation is likely more important with bilateral renal vein involvement compared with unilateral involvement with or without extension to the inferior vena cava (IVC). Severity of disease, gestational age, presence of intraventricular hemorrhage, underlying comorbidities, and degree of thrombocytopenia may affect bleeding risk with treatment.	
10a. For neonates with non–life-threatening RVT, the ASH/ISTH guideline panel recommends anticoagulation alone vs thrombolysis followed by anticoagulation	Strong / Very low
Remarks: Available evidence is derived from observational studies in which patients treated with thrombolysis were critically ill, and because the studies did not adjust for this bias, causation is difficult to ascertain. The panel placed a high value on avoiding the potential bleeding risks of thrombolysis, especially in neonates, and therefore, made this recommendation for cases with low mortality risk (ie, unilateral RVT or unilateral RVT with IVC extension). The panel made a strong recommendation, considering high-quality evidence for harm and high costs, despite very low quality evidence for benefit.	
10b. For neonates with life-threatening RVT, the ASH/ISTH guideline panel suggests using thrombolysis followed by anticoagulation, rather than anticoagulation alone	Conditional / Very low
Remarks: When RVT is life threatening (ie, bilateral thrombosis), the panel considered that the beneficial effects of thrombolysis may outweigh the undesirable consequences of the intervention. Gestational age, presence of intraventricular hemorrhage, underlying comorbidities, and degree of thrombocytopenia may affect bleeding risk with thrombolysis.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
11a. For neonates and children with occlusive portal vein thrombosis (PVT) and for children with nonocclusive PVT, post–liver transplant PVT, or unprovoked PVT, the ASH/ISTH guideline panel suggests using anticoagulation rather than no anticoagulation	Conditional / Very low
11b. For neonates with nonocclusive PVT, and for children who have already developed portal hypertension (PHTN) secondary to PVT, the ASH/ISTH guideline panel suggests no anticoagulation rather than using anticoagulation	Conditional / Very low
Remarks: For recommendations 11a and 11b: neonates and pediatric patients who did not receive anticoagulation warrant follow-up monitoring, because extension of thrombus or organ dysfunction may require reconsideration of treatment options. Evidence from the available observational studies describes (complete or partial) PVT resolution in patients who did receive anticoagulation, as well as those who did not receive anticoagulation, and therefore, does not allow for assessment of the degree of benefit from anticoagulation. However, the panel placed value on avoiding the potential increased risk of long-term complications associated with persistent occlusive thrombus, and therefore, favored treatment in this setting. The panel also recognized the potential increased risk of bleeding in pediatric patients with PHTN and development of esophageal varices, and therefore, did not recommend anticoagulation in that setting.	
12a. For pediatric patients with superficial vein thrombosis (SVT) secondary to IV cannulation in the upper limb, the ASH/ISTH guideline panel suggests no anticoagulation rather than using anticoagulation	Conditional / Very low
12b. For pediatric patients with SVT in the upper limb, which is not cannula related, or in the lower limbs associated with cancer or varicose veins, the ASH/ISTH guideline panel suggests anticoagulation rather than no anticoagulation	Conditional / Very low
Remarks: There were no direct and only limited indirect data upon which to base this recommendation. The panel members experience suggested that, in most instances (eg, peripheral IV [PIV]– or CVAD-related events in the upper extremity), no anticoagulation may be required. However, anticoagulation could be considered in select patients with symptomatic SVT (eg, non–PIV-/PICC (peripherally inserted central catheter)-related, cancer, varicose vein, and lower limb events) or scenarios (eg, PIV/long-term PICC and/or symptom progression). The panel notes that when anticoagulation is prescribed, there is uncertainty about the optimal intensity (eg, prophylactic vs full dose) and duration of therapy.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
13. For pediatric patients with proximal DVT, the ASH/ISTH guideline panel suggests using anticoagulation alone rather than thrombolysis followed by anticoagulation	Conditional / Very low
Remarks: The panel considered characteristics such as the extent and clinical impact of VTE, as important in determining the risk to benefit ratio of thrombolysis. In most cases, the risks seem higher than the potential benefit; however, there may be individuals for whom the opposite is true. In this clinical scenario, extrapolation from adult data was difficult. There are insufficient data to address the risk to benefit ratio of local thrombolysis via interventional radiology compared with systemic thrombolysis, and the panel noted that the centers with access to pediatric interventional radiology were often stronger advocates of thrombolysis.	
14. For pediatric patients with PE and echocardiographic or biochemical evidence of right ventricular dysfunction but without hemodynamic compromise, the ASH/ISTH guideline panel suggests using anticoagulation alone rather than thrombolysis followed by anticoagulation	Conditional / Very low
Remarks: The panel considered submassive PE to represent pediatric patients with PE who do not have hemodynamic compromise (ie, systemic hypotension or other signs of shock) but who do have echocardiographic (eg, right ventricular dilation or intraventricular septal bowing into the left ventricle, etc) or biochemical (eg, elevated troponin or brain natriuretic peptide, etc) evidence of right ventricular dysfunction. There were minimal pediatric data, and recent international adult guideline panels have recommended anticoagulation alone rather than thrombolysis followed by anticoagulation in this situation (based on low certainty in the evidence of effects). These same adult guidelines, however, have suggested that thrombolysis may be reasonable to consider for younger patients with submassive PE at low risk of bleeding and those who have evidence of both echocardiographic and biochemical evidence of right ventricular dysfunction, which may be extrapolated to select pediatric patients. Patients with submassive PE should be monitored closely for the development of hemodynamic compromise. The panel concluded that the risks of thrombolysis outweighed the benefits in most cases, hence the conditional recommendation for anticoagulation alone.	
15. For pediatric patients with PE and hemodynamic compromise the ASH/ISTH guideline panel suggests using thrombolysis followed by anticoagulation rather than anticoagulation alone	Conditional / Very low
Remarks: The panel considered massive PE to represent pediatric patients with PE who do have hemodynamic compromise that may be life threatening, with limited time to respond to standard anticoagulation, and therefore, conditionally recommended thrombolysis followed by anticoagulation, based predominantly on extrapolation from recent adult guidelines and 3 small pediatric studies that suggested a trend toward decreased mortality with thrombolysis.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
16. For pediatric patients with symptomatic CVAD-related thrombosis who no longer require venous access or whose CVAD is nonfunctioning, the ASH/ISTH guideline panel suggests either immediate removal or delayed removal of the CVAD	Conditional / Low
Remarks: Recent observational studies provided data that >48 hours of anticoagulation before CVAD removal vs immediate CVAD removal are comparable in terms of potential risk of emboli leading to PE or paradoxical stroke. The panel recognized that some clinical scenarios, such as children with a large thrombotic burden or those with right-to-left cardiac shunts, may benefit from a few days of anticoagulation before CVAD removal to decrease the risk of embolism.	
17. For pediatric patients with VTE, the ASH/ISTH guideline panel suggests using DOACs (rivaroxaban/dabigatran) over standard-of-care anticoagulants (low molecular weight heparin [LMWH], unfractionated heparin [UFH], vitamin K antagonists [VKAs], and fondaparinux)	Conditional / Low
Remarks: The panel concluded that there was a small benefit of DOACs over SOC, in relation to reduced thrombus recurrence rate and increased rate of thrombus resolution. The undesirable effects of DOACs vs SOC were felt to be small, with a reduction in major bleeding albeit with an increase in clinically relevant non major bleeding (CRNMB). The panel acknowledged the limitations of these data when evaluating the outcomes of mortality, recurrence, postthrombotic syndrome (PTS), and major/CRNMB due to the small number of events reported. Given the natural history of PTS and thrombus recurrence, evaluation at 3 to 6 months was considered to be too soon to provide accurate representation of these outcomes. The monitoring of drug level and dose adjustment of dabigatran during the DIVERSITY trial raised concern about the potential effect on efficacy and safety of routine use according to current approvals, which do not require such monitoring. Although data on QOL, cost-effectiveness, and acceptability of an oral agent that does not require monitoring were lacking, the panel felt that these were important factors when making this recommendation.	
18. For pediatric patients with VTE the ASH/ISTH guideline panel suggests using rivaroxaban over SOC anticoagulants (LMWH, UFH, VKA, and fondaparinux)	Conditional / Very low
Remarks: The panel concluded that there was a small benefit of rivaroxaban over SOC, in relation to reduced thrombus recurrence and improved thrombus resolution. The undesirable effects of rivaroxaban vs SOC were felt to be small, with a reduction in major bleeding countered by an increase in CRNMB. These data were limited by the small number of important outcomes that were reported, that is mortality, recurrence, PTS, and major bleeding/ CRNMB. The panel noted that some individuals were excluded from the EINSTEIN-Junior trial, including those aged <6 months with low birth weight and those with severe liver or renal impairment. The panel also noted reports of heavier menstrual bleeding while on rivaroxaban and felt that this was an important consideration when choosing an anticoagulant.	

RECOMMENDATIONS	Strength of Recommendation / Certainty of Evidence
19. For pediatric patients with VTE, the ASH/ISTH guideline panel suggests using dabigatran over SOC anticoagulants (LMWH, UFH, VKA, and fondaparinux)	Conditional / Very low
Remarks: The panel concluded that there was a small benefit of dabigatran over SOC, in relation to reduced thrombus recurrence and improved thrombus resolution. The undesirable effects were felt to be trivial, with major bleeding reported in fewer patients treated with dabigatran and an equivalent frequency of CRNMB. The panel noted that some individuals were excluded from the DIVERSITY trial, including those aged <2 years with low body weight, and those with severe liver or renal impairment. The monitoring and dose adjustment of dabigatran during the DIVERSITY trial raised concern about the potential effect on efficacy and safety of routine use according to current approvals, which do not require such monitoring. The panel also noted reports of gastrointestinal side effects while on dabigatran and felt that this was an important consideration when choosing an anticoagulant.	
20. For pediatric patients with VTE, the ASH/ISTH guideline panel suggests using either rivaroxaban or dabigatran, although there may be individual populations or jurisdictional availability that would lead clinicians to choose 1 agent over the other	Conditional / Very low
Remarks: The panel undertook an exercise to review the evidence-to-decisions (EtDs) for rivaroxaban vs SOC and dabigatran vs SOC to examine if 1 of these agents (given the available data) would be a preferred agent to use in treatment of pediatric VTE. To accomplish this, the panel first assigned weights to the summary of judgments. Balance of effects, certainty in the evidence, and acceptability and feasibility of implementation were given the highest weighting, with resources required given moderate weighting, and cost-effectiveness and equity given the lowest weighting.	

*see Appendix 1

Appendix 1: Systems for Classifying Recommendations and Evidence used by the Source Clinical Practice Guidelines

I. GRADE

Strength of Recommendations:

Strong Recommendation	When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak or Conditional Recommendation	Weak or conditional recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendations Determinants:

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

Quality of Evidence or Certainty in Evidence

High Quality/Certainty	Further research is very unlikely to change our confidence in the estimate of effect
Moderate Quality/Certainty	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low Quality/Certainty	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low Quality/Certainty	Any estimate of effect is very uncertain

Guyatt, G.H., et al., *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.* BMJ, 2008; 336: 924-926.
Guyatt, G.H., et al., *GRADE: going from evidence to recommendations.* BMJ, 2008; 336: 1049-1051.