Children's Cancer & Blood Disorders

Guideline for Platelet Transfusion Thresholds for Pediatric Hematology / Oncology Patients

Complete Reference Guide

The C17 Guidelines Committee

www.C17.ca

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C^{17} supportive care guidelines are developed by Canadian health professional specialists using evidence-based or best practice references at the time of their creation. Format and content of the guidelines will change as they are reviewed and revised on a periodic basis. Care has been taken to ensure accuracy of the information. However, any physician or health professional using these guidelines will be responsible for administering transfusions and care according to their own institutional policies and standards of care.

Glossary

Prophylactic platelet transfusion – given to prevent bleeding.

Therapeutic platelet transfusion – given to treat clinically significant bleeding

Trigger or threshold for platelet transfusion – a particular value for platelet count or clinical sign that prompts a platelet transfusion, based on adverse consequences to the patient if transfusion is not performed (Abrams-Ogg, 2003).

Oncology (cancer) – inclusive of solid cancers and leukemia / lymphoma as well as disorders such as myelodysplastic disorders, myeloproliferative disorders and histiocytic disorders.

Overview of Material

Guideline release date: June, 2010; Literature search last updated March 2011 (no new studies identified)

Status: Adapted, revised and updated

Sources: Print copies available through:

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Adapters: C[17] Guidelines Committee

Source Guidelines

This guideline has been broadly adapted with permission from "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" (Schiffer et al, 2001). The American Society of Clinical Oncology is not responsible in any way for the adaption. This guideline was updated with information from sources obtained through a Medline search of "platelet transfusion", "guideline", "pediatric" [published in English language], as well as secondary references from the literature reviewed (Appendix A). Preference was given to information obtained from randomized controlled trials where available; where not, best practice information was used to determine the recommendations for intervention contained in this guideline.

Abstract/ Summary

For the recommendations that follow, there is insufficient evidence to definitively support a particular threshold for transfusion. The recommendations that follow are adapted from guidelines developed for adult patients. They are based on expert clinical opinion and the deliberations of the C[17] Guidelines Committee.

	Recommendation	Evidence*
Prophylactic approach	Prophylactic platelet transfusions at the threshold levels indicated below, rather than therapeutic transfusions at the time of clinically significant bleeding are recommended for pediatric oncology patients.	1C
Threshold for patients with leukemia / lymphoma	Platelet threshold of 10 x10^9/L is recommended for clinically stable pediatric patients receiving chemotherapy for leukemia. Transfusions at a higher level (given the absence of research evidence, as determined by clinical circumstances, generally at threshold of 40 x 10^9/L) **may** be required for patients with signs of bleeding, high fever, hyperleucocytosis, rapid fall in platelet count, acute promyelocytic leukemia (APL), concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced). Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below).	1C
Threshold for patients post stem cell transplantation	Threshold for stable patients post stem cell transplantation to receive prophylactic platelet transfusions is 10 x10^9/L. Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced). Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below).	1C

**Using American College of Chest Physicians "GRADE" criteria (Guyatt et al, 2008)*

	Recommendation	Evidence*
Threshold for patients with solid tumors	Threshold for stable patients with solid tumors to receive prophylactic platelet transfusions is 10 x10^9/L. Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced). Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below). Transfusions at a higher level may be required for patients with bladder tumors or necrotic tumors.	1C
Threshold for patients with CNS tumors	Note that these recommendations are based on a survey of neuro-oncologists (66.7%), neurosurgeons (11.1%) and others (22.2%) from the C[17] centers across Canada who treat pediatric neuro-oncology patients. **The numbers provided are based on a minimum 75% acceptance of those responding to the survey.** Therefore all evidence for this category would be classified as 2C (weak; recommendations with poor quality evidence; observation only) 1. Child has a CNS tumor with: ▪ VP shunt or Ommaya reservoir – 30 x 10^9/L ▪ Past history of ICH – 50 x 10^9/L ▪ An infant receiving intensive chemotherapy – 30 x 10^9/L ▪ Child to undergo a neurosurgical procedure – 100 x10^9/L 2. Child has a **gross total resection** and is receiving chemo and/or radiation – 30 x10^9/L 3. Child has **residual tumor** (subtotal resection or biopsy only) and is receiving chemo and/or radiation – 30 x 10^9/L 4. Child is receiving an antiangiogenesis agent – 50 x 10^9/L (Note – 72% of respondents accepted 30,000 as threshold in this circumstance) 5. Child to undergo LP with past history of CNS tumor – 50 x 10^9/L	2C
Thresholds for patients with chronic thromboctyopenia	Stable patients with chronic, stable, severe thrombocytopenia due to alloimmunization should be observed without prophylactic platelet transfusions. These patients should receive platelet transfusions with clinically significant bleeding only.	1C

**Using American College of Chest Physicians "GRADE" criteria (Guyatt et al, 2008)*

	Recommendation	Evidence*
Threshold for patients requiring a lumbar puncture	Threshold for stable patients requiring a lumbar puncture to receive prophylactic platelet transfusions is 20 $x10^9$/L. **It is also recognized that some may be uncomfortable with a threshold of 20 $x10^9$/L because of the potentially devastating consequences of an intraspinal bleed.** Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced). Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below). **Transfusions at a higher level (>50 x 10^9) are recommended for diagnostic LP for newly diagnosed patients with leukemia to minimize the risk of a traumatic LP.**	2B
Threshold for patients requiring a major invasive procedure	Threshold for stable patients requiring a major invasive surgical procedure to receive prophylactic platelet transfusions is 40-50 $x10^9$/L. Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, hyperleucocytosis , APL , concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced). Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below). Transfusions at a higher level may be required for newly diagnosed patients with leukemia or neurosurgical procedures or other invasive procedure with an intrinsic high risk of significant bleeding.	1C

**Using American College of Chest Physicians "GRADE" criteria (Guyatt et al, 2008)*

The purpose of these guidelines is to provide clinical institutions and other organizations with a framework on which to build their own institutional protocols and to encourage standardization of protocols across regions to enhance consistency of care for patients and families.

The C^{17} Guidelines Committee recommends, based on the absence of sufficient available data, that C^{17} and other institutions develop trials that can supply evidence to inform future decision-making on thresholds for platelet transfusions.

The goal of platelet transfusion therapy is not to eliminate all bleeding but to prevent or arrest major or critical bleeding. Such bleeding includes epistaxis, other mucosal or soft tissue bleeding resulting in red blood cell transfusion; hemoptysis, hematemesis, melena and gross hematuria; and retinal or CNS bleeding (Abrams-Ogg, 2003).

Introduction

The ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" (Schiffer et al, 2001) mainly addresses the indications for adult patients. It is recognized that extrapolation of adult recommendations to the pediatric population is not always appropriate considering the differences in clinical disease and generally more aggressive treatment. When available, additional information was obtained specifically for pediatric patients and is highlighted in the section "Supporting evidence and information for recommendations".

Scope and Purpose

The overall objective of this guideline is to provide healthcare professionals with an approach to the routine assessment **of pediatric oncology (cancer) patients** for the requirement of platelet transfusions. The recommendations of this guideline are intended to apply to clinical practice in the context of all patients aged 1 month to 19 years with cancer or hematologic disorder requiring platelet transfusions. The scope of this guideline is limited to the assessment of the *platelet transfusion thresholds* within the context of the patient's current clinical status and does not directly address issues related to other medical diagnoses. Although it was recognized there *may be* an impact on platelet transfusion thresholds, this guideline did not consider other aspects of platelet transfusion such as dose of platelet transfusions, ABO matching, presence of immature platelets, use of irradiated or CMV negative blood products, or apheresis versus single unit versus buffy coat procured platelet transfusions. The issue of platelet transfusion in the face of alloimmunization / platelet refractoriness is not addressed.

Although this guideline has been developed within the context of pediatric oncology, it is acknowledged that thresholds may be affected by more than the experience reflected in this guideline and may also be impacted by issues surrounding other existing co-morbidities. It is also acknowledged that the recommendations presented here are only the "best enough" recommendations based on the available evidence. Readers are reminded that implementation of these recommendations will depend on their "fit" with patient needs and preferences, clinician knowledge, skill and practice scope, available resources and organizational policies and standards.

This guideline has been developed based on the assumption that the assessment process to determine an individual patient's requirement for platelet transfusion is the foundation for appropriate supportive transfusion interventions. Assessment for the requirement for platelet transfusion will allow the clinician and individual/ family to identify a tailored and cost-effective approach.

Finally, just as assessment is only the first step in providing platelet transfusion care, this guideline represents only the beginning of a proposed series of guidelines to support clinical practice as it relates to blood and blood product transfusions. Guidelines specific to needs identified in the assessment process should be used to ensure more focused assessment and management of particular needs. In the meantime, readers are encouraged to refer to the reference list at the back of this document for other guidelines and resources related to interventions.

The objectives of this guideline are:

1. To facilitate the care of pediatric oncology patients at risk for bleeding from thrombocytopenia.

2. To provide recommendations on thresholds for platelet transfusion which balance the risk of bleeding versus the risk of platelet transfusion, inclusive of consideration of costs in quality of life and financial cost as well as consideration of appropriate utilization of limited resources with available blood products.

3. To reduce the impact on patients, families and staff of inconsistent practice, especially with transitions of care between centres.

Target Audience of the Guideline

The intended users of this guideline are all health professionals within Canada caring for children and youth with cancer and at risk for bleeding that may be ameliorated by platelet transfusion. The guideline is particularly addressed to physicians, blood bank personnel, nurse practitioners and nurses working in hospitals and satellite clinics where pediatric oncology patients receive care.

The guideline will also be relevant to the administrators, educators and researchers, including those at Canadian Blood Services and Hema-Quebec, who must ensure sufficient resources are available to address platelet transfusion needs.

Health Questions

The following clinical questions guided the development of this guideline:

1. Who are the pediatric oncology patients at highest risk of bleeding with thrombocytopenia?

2. What platelet transfusion thresholds are recommended for particular clinical circumstances?

3. What complications of platelet transfusions are considered in determining the thresholds?

Levels of Evidence

**Source: Australian Guideline (as utilized in the ASCO guideline from which this guideline is adapted)*

Level I Evidence obtained from meta-analysis of multiple, well-designed, controlled studies. Randomized trials with low false-positive and low false-negative errors (high power).

Level II Evidence obtained from at least one well-designed experimental study. Randomized trials with high false-positive and/or negative errors (low power).

Level III Evidence obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled single-group, pre-post, cohort, time, or matched case-control series.

Level IV Evidence from well-designed, nonexperimental studies such as comparative and correlational descriptive and case studies.

Level V Evidence obtained from case reports and clinical examples.

Grades for Recommendations

(as utilized in the ASCO guideline from which this guideline is adapted)

Grade A There is evidence of level I or consistent findings from multiple studies of types II, III or IV.

Grade B There is evidence of level II, III or IV, and findings are generally consistent.

Grade C There is evidence of level II, III or IV, but findings are inconsistent.

Grade D There is little or no systematic empirical evidence.

Grades for Recommendations (Guyatt et al, 2008)* *(as utilized for this guideline)*

Grade of Recommendation	Benefit vs Risk and Burdens	Methodology	Implications
1A Strong recommendation, high-quality evidence	Desirable effects clearly outweigh undesirable effects or *vice versa*	Evidence from well done RCTs or Exceptional observational studies	Apply to most patients in most circumstances Further research unlikely to change recommendation
1B Strong recommendation, moderate quality evidence	Desirable effects clearly outweigh undesirable effects or *vice versa*	Evidence from RCTs with some flaws in study or Very strong evidence from observational studies	Apply to most patients in most circumstances Further research might be helpful

** (American College of Chest Physicians [ACCP] criteria)*

Grades for Recommendations (continued) (Guyatt et al, 2008)* *(as utilized for this guideline)*

Grade of Recommendation	Benefit vs Risk and Burdens	Methodology	Implications
1C Strong recommendation, poor quality evidence	Desirable effects clearly outweigh undesirable effects or *vice versa*	Evidence of at least one critical outcome from observational studies, case series or RCTs with flaws	Apply to most patients in many circumstances Further research would be helpful
2A Weak recommendation, high quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important flaws or Exceptionally strong evidence from observational studies	Best action may depend on circumstances or patient or society values Further research unlikely to change recommendation
2B Weak recommendation, moderate quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important flaws or Very strong evidence from observational studies	Best action dependent on patient circumstances or patient or society values Further research may change recommendation
2C Weak recommendation with poor quality evidence	Desirable effects closely balanced with undesirable effects	Evidence of at least one critical outcome from observational studies, case series or RCTs with serious flaws	Other alternatives may be equally reasonable Further research very likely to change recommendation

** (American College of Chest Physicians [ACCP] criteria)*

This system provides a clear separation between the quality of the evidence and the strength of the recommendation as influenced by outcome criteria important to patients (Guyatt et al, 2008) (see also Brozek et al, 2009). Implicit important patient outcomes for the evaluation within this guideline include, besides mortality and morbidity (short and long-term), quality-of-life/life-style issues and consideration of fear associated with bleeding manifestations.

Note that the grading of evidence given for each recommendation was determined by consensus of the C^{17} Guidelines Committee based on the literature reviewed.

Background

Two major considerations related to platelet transfusion thresholds are the risks of platelet transfusions and an evaluation of degree of bleeding. Current risks of transfusion are given in the table below, followed by scales used to describe bleeding manifestations. In addition, evidence correlating bleeding risk and platelet counts is provided.

Risks Associated with Platelet Transfusions in Canada*

Complication	Risk
Bacterial infection	1 in 50,000 or 1 in 10,000 per pooled units
HBV	1 in 153,000
HCV	1 in 2,300,000
HIV	1 in 7,800,000
HTLV	1 in 4,300,000
Malaria	1 in 4,000,000
Transfusion related acute lung injury	1 in 5,000
Febrile reactions	1 in 10
Allergic reactions	1 in 100
Anaphylaxis	1 in 40,000
Hemolysis – acute	1 in 40,000
Hemolysis – delayed	1 in 7,000
Volume overload	1 in 700
Immunomodulation/ multi-organ failure	n/a

**Data for all blood components derived from Kleinman S et al. 2003. Risks associated with transfusion of cellular blood components in Canada. Trans Med Rev 17:120-162; O'Brien et al. 2007. Current incidence and estimated residual risk of transfusion-transmitted infections in donations made to CBS. Transfusion 47:316-325.*

Bleeding Score

WHO Bleeding Score

Grade 0 No bleeding

Grade 1 Petechiae, ecchymosis, occult blood in body secretions, mild vaginal spotting

Grade 2 Evidence of gross hemorrhage not requiring red cell transfusion over routine transfusion

Grade 3 Hemorrhage requiring transfusion of one or more units of PRBC

Grade 4 Life-threatening hemorrhage, defined as either massive bleeding causing hemodynamic compromise or bleeding into a vital organ

(Slichter, 2004)

GEMIMA Bleeding Score

Grade 0 No bleeding

Grade 1 Petechial, mucosal, microscopic

Grade 2a Melena or hematemesis not requiring transfusion

Grade 2b Gross hematuria

Grade 3 Bleeding requiring PRBC

Grade 4 Retinal bleeding with visual impairment

Grade 5 Nonfatal cerebral bleeding

Grade 6 Fatal cerebral bleeding

Grade 7 Fatal non-cerebral bleeding

(Zumberg et al, 2002)

Correlation of Bleeding and Platelet Count

In practice, the threshold for platelet transfusion for a particular patient may be modified by the clinician for fever, rapid decline in platelet count, immediate or future availability of platelets for transfusion or inpatient versus outpatient status, for example. The vast majority of studies have been conducted with adult patients. Information about the correlation of bleeding and platelet count may influence the decision to transfuse. It is unknown if age-related physiologic characteristics would alter correlation of bleeding and platelet count. Neonates and the elderly are felt to have increased vascular and integument fragility. Activity and risk may vary with pediatric patients compared with adult patients.

Table 1: Summary of Studies that Describe Relationship Between Platelet Count and Bleeding

Study	Results
Webert et al, 2006 (no pediatric patients)	• Historical data – clinically significant bleeding in 20-32% of thrombocytopenic AML (non-APL) patients, 34-58% of patients undergoing allogeneic SCT. • Study considered 15 variables with respect to correlation with bleeding on following day: antibiotics, antifibrinolytic, antifungal, antiviral, corticosteroids, chemotherapy, platelet transfusion, PRBC transfusion, hemoglobin concentration, platelet count, positive blood culture, temperature, presence of clinical infection, bleeding status. • 255 adults with AML undergoing induction therapy (re-analysis of data from study by Rebulla et al, 1997).

Table 1: Summary of Studies that Describe Relationship Between Platelet Count and Bleeding (continued)

Study	Results
Webert et al, 2006 (no pediatric patients) - continued	• Randomized control trial of prophylactic platelet transfusion at 10 x10^9/L versus 20 x10^9/L. • Significant predictors of bleeding included platelet count, temperature, clinical infection, antifungal medication, administration of platelet transfusion. • Grade 1 and 2 bleeding was associated with antifungal medication (decrease in risk), increased temperature, platelet count, platelet transfusion. • Grade 3 and 4 bleeding was associated with platelet count (each 1 x 10^9/L increase associated with a 4% reduction in bleeding), increased temperature, presence of infection, mild bleeding on the previous day; increased hemoglobin level decreased/delayed bleeding. • The majority of major bleeds were predicted by the presence of prior mild bleeding.
Stanworth et al, 2006 (no pediatric patients)	• Nineteen adult patients with hematologic malignancies studied prospectively with self assessment bleeding instrument compared with health professional assessment • No association between morning platelet count and WHO bleeding score • 86% agreement on bleeding assessment between patient and health professional; discrepancies mostly related to microscopic hematuria; validity of giving platelet transfusion for microscopic hematuria questioned • 26% of prophylactic platelet transfusions not in compliance with local guidelines
Slichter, 2004 (no pediatric patients)	• Platelet loss through senescence and to maintain endothelium • In a 1963-1965 study, 30 leukemic patients who were autopsied after death and who did not receive platelet transfusions were compared with 27 who did; of the non-transfused, 63% died with major hemorrhage (50% intracranial bleeds), of the transfused 15% died with major hemorrhage • Retrospective review of 103 patients who died with acute leukemia – 48% had minor bleeding (WHO Grade 1) when platelet count less than 50 x10^9/L, 12% had severe bleeding (WHO grade 2 or greater) • Transfusion with platelet free plasma did not prevent bleeding in a double blind study comparing platelet concentrate with plasma
Cook et al, 2004 (no pediatric patients)	• Risk of bleeding 8x greater when count less than 5 x10^9/L, 2x greater when 5-15 x10^9/L compared with count of 20-29 x10^9/L

Table 1: Summary of Studies that Describe Relationship Between Platelet Count and Bleeding (continued)

Study	Results
Friedmann et al, 2002 (no pediatric patients)	• Retrospective review of all adult thrombocytopenic 2942 inpatients (1988-1997)(79,546 patient days of platelet count less than 50 $x10^9$/L) who were prospectively evaluated daily using the WHO bleeding score • Patients had leukemia, solid tumors, bone marrow transplantation • 11.63% patients had Grade 2 bleeding; 1.15% had Grade 3 bleeding; 0.12% had Grade 4 bleeding; 0.03% had missing data • In multi-variant analysis, there was no correlation between morning platelet count and severe bleeding. However, lack of information on temporal relationship between platelet counts, bleeds and transfusions • Bleeding risk was increased in patients with recent BMT, recent hemorrhage, hypoalbuminemia, uremia • Did not find an increased risk with bacteremia • Leucopenia reduced the risk of bleeding
Goldberg et al, 1994 (in Avvisati et al, 2003) (no pediatric patients)	• Retrospective analysis of 182 patients with gynaecologic cancer with platelet count less than 100 $x10^9$/L • 76% had no bleeding; 18.7% had minor bleeding; 4.9% had major bleeding • Half of the major bleeds were in patients with platelet counts between 0-10 $x10^9$/L; 3 of the 9 episodes occurred at platelet count between 11-20 $x10^9$/L, but were associated with instrumentation or trauma; one occurred at a count greater than 20 $x10^9$/L and was associated with a necrotic lesion
Dutcher et al, 1984 (in Avvisati et al, 2003) (no pediatric patients)	• Of 301 patients with solid tumors with thrombocytopenia less than 50 $x10^9$/L, there were 44 episodes of serious bleeding of 5063 days of thrombocytopenia, 37 episodes were at a platelet count between 20-50 $x10^9$/L • Of 12 patients who died of bleeding, 7 had normal platelet counts

In summary, there appear to be many factors that influence bleeding risk other than the level of the platelet count. However, the risk of bleeding appears to increase markedly at counts less than 5-10 X 109/L. These findings stress that decisions to give platelet transfusions must be based on both platelet count and clinical context.

Supporting Evidence and Information for Recommendations

1. Prophylactic Versus Therapeutic Platelet Transfusion

Guideline:
Prophylactic platelet transfusions, rather than therapeutic transfusions at the time of clinically significant bleeding are recommended for stable pediatric oncology patients without proposed intervention.

Level of Evidence (American College of Chest Physicians [ACCP] Criteria)*:
Desirable effects likely outweigh undesirable effects (see Risks of Platelet Transfusions). Study findings suggest prophylactic transfusions are prudent.

Grade of Recommendation (ACCP Criteria):
1C

**Note: the authors of the ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" assigned a level of evidence of IV ('expert consensus' – approximately 80% of clinicians follow a prophylactic rather than therapeutic approach to transfusion of platelets) and a grade of recommendation of B to this guideline.*

Evidence:

Table 2: Summary of Studies Used to Inform Recommendation #1

Study	Results
Stanworth et al, 2009	• Review of 3 studies (Higby et al, 1974; Solomon et al, 1978; Murphy et al, 1982) • Felt the three studies should be considered as hypothesis testing rather than equivalence testing.
Wandt et al, 2006 (no pediatric patients) (included in ASCO guideline review)	• Prospective study of 50 consecutive patients receiving 60 PBSCT, 2001-2005 – therapeutic platelet transfusion strategy • Compared to retrospective analysis of 54 patients receiving 60 PBSCT, prior to therapeutic platelet transfusion strategy (transfused if morning platelet count less than 10 $x10^9$/L) • Clinically stable patients – platelet transfusion given for WHO bleeding Grade 2 or greater • In clinically unstable patients, prophylactic platelet transfusions if platelet count less than 10 $x10^9$/L; for surgery used platelet count less than 20 $x10^9$/L • For 81% of PBSCT, there were no clinically relevant bleeding episodes, no episodes of Grade 3 or 4 bleeding • Grade 2 bleeding mainly epistaxis or mucositis • Therapeutic group – fewer platelet transfusions (@ ½), no difference in bleeding • However, 16% of transfusion did not follow protocol (mainly given for mucositis without bleeding)

Table 2: Summary of Studies Used to Inform Recommendation #1 (continued)

Study	Results
Friedmann et al, 2002 (no pediatric patients)	• Retrospective review of all adult thrombocytopenic 2942 inpatients (1988-1997)(79,546 patient days of platelet count less than 50 x10^9/L) who were prospectively evaluated daily using the WHO bleeding score • Patients had leukemia, solid tumors, bone marrow transplantation • 11.63% patients had Grade 2 bleeding; 1.15% had Grade 3 bleeding; 0.12% had Grade 4 bleeding; 0.03% had missing data • In multi-variant analysis, there was no correlation between morning platelet count and severe bleeding. However, lack of information on temporal relationship between platelet counts, bleeds and transfusions • Recommended a therapeutic rather than prophylactic approach
Murphy et al, 1982 (pediatric patients) (included in ASCO guideline review)	• Randomized prospective study of 56 children with leukemia – prophylactic group transfused when platelet count less than 20 x10^9/L, therapeutic transfusions, given when child had significant bleeding (@WHO grade 2 or greater)(1972-1976) • 1.9 bleeds per 100 patient months in prophylactic group versus 7.9 in therapeutic group • Prophylactic group received twice as many platelet transfusions as the therapeutic group • No difference in survival rates
Ilett et al, 1979 (in Slichter, 2004) (pediatric patients)	• Non-randomized study of 70 children with ALL • Platelet transfusions given when platelet count less than 20 x10^9/L and clinically significant bleeding • No deaths caused by hemorrhage • 84% of patients did not receive any platelet transfusions during induction
Solomon et al, 1978 (in Ancliff, Machin, 1998; Slichter, 2004) (no pediatric patients)	• Randomized study of 39 adult AML patients • Prophylactic transfusion for counts less than 20 x10^9/L; therapeutic transfusion if bleeding or had a platelet count less than 20 x10^9/L and their count had fallen by 50% in the prior 24 hours • Prophylactic group received twice as many platelet transfusions as the therapeutic group • No difference in survival rates or rate of red cell transfusions • Two deaths from hemorrhage were in prophylactic group
Higby et al, 1974 (no pediatric patients) (included in ASCO guideline review)	• Randomized study of 24 adult AML patients • Prophylactic platelet transfusion for counts less than 30 x10^9/L compared with transfusion of plasma; platelets given if septic shock or clinical bleeding • Plasma group – 3/12 had serious bleeding events

Discussion:
The studies of Gaydos (1962), Higby et al (1974) and Murphy et al (1982) were all conducted in an era of the use of aspirin when the effect of non-steroidal anti-inflammatory agents such as aspirin on platelet function was not appreciated and when cancer treatment protocols were far less aggressive than those currently utilized. In addition, the studies included limited numbers of participants, were unblinded and varied in follow-up duration. Thus these studies may not be directly applicable to present circumstances where the use of drugs altering platelet function is less common and the treatment protocols utilized may increase the risk of bleeding more than those used in these studies. In a review of case reports of intracranial bleeds in thrombocytopenic oncology patients receiving prophylactic platelet transfusion, there was no demonstrated association between platelet count and risk of intracranial bleed (Stanworth et al, 2005). Newer drugs such as Gleevac present an increased risk of intracranial bleeding.

It is recognized that the need for prophylactic transfusions has not been conclusively proven (Brecher, 2007). The correlation between platelet count and bleeding, and clinical experience favouring an impression of improved quality of life with prophylactic transfusions were factors in recommending prophylactic transfusions at this time. This must be balanced against risks of transfusions, costs to the family and to the healthcare system, scarcity of platelet units and difficulties of managing hemorrhage following alloimmunization (Heddle et al, 2003). In the analyses by Stanworth et al, 2009, mortality from bleeding, incidence of major or severe bleeding episodes and number of platelet and red cell transfusions received were fewer with prophylactic platelet transfusions. Further research is urgently required; the results of current or recently completed studies (German study, TOPPS study) may help to clarify (Blajchman et al, 2008).

2. Platelet Count Threshold for Prophylactic Platelet Transfusion – Acute Leukemia

Guideline:
Platelet threshold of 10 $x10^9$/L is recommended for clinically stable pediatric patients receiving chemotherapy for leukemia.

Transfusions at a higher level (given the absence of research evidence, as determined by clinical circumstances, generally at threshold of 40 x 10^9) **may** be required for patients with signs of bleeding, high fever, hyperleucocytosis, rapid fall in platelet count, APL, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced).

Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below).

Level of Evidence (ACCP Criteria):
Desirable effects likely outweigh undesirable effects.

Grade of Recommendation (ACCP Criteria):
1C

**Note: the authors of the ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" assigned a level of evidence of I and a grade of recommendation of A to this recommendation.*

Evidence:

Table 3: Summary of Evidence Used to Inform Recommendation #2

Study	Results
Oka et al, 2007 (no pediatric patients)	• Years 1994-2006 retrospectively analysed; 56 adult patients with AML (APL excluded) • Single institution study following established Japanese transfusion guidelines – changed in 1994 to between 10-20 $x10^9$/L • Cohort A – 33 patients treated between 1994-1999; 23 patients treated between 2004-2006 • Mean transfusion trigger in Group A – 27 $x10^9$/L and in Group B 17.9 $x10^9$/L • Group B patients received more aggressive chemotherapy but had no significant bleeding episodes compared with 5 Grade 2 bleeds in Group A
Callow et al, 2002 (no pediatric patients)	• Non-randomized, prospectively analysed study of 98 adult patients with hematologic malignancies • Platelet threshold less than 10 $x10^9$/L in all cases, 10-20 $x10^9$/L if fever, coagulation disorder, major bleeding marrow biopsy; 20-50 $x10^9$/L if major bleeding, bleeding requiring PRBC, fresh retinal hemorrhage impairing vision, DIC, hemorrhagic cystitis; 50 $x10^9$/L prior to surgical intervention (including LP) • Major bleeding 1.3% of study days where count less than 10 $x10^9$/L; 2.3% when platelet count between 10-20 $x10^9$/L; 5.45% of study days when count greater than 20 $x10^9$/L (most associated with hemorrhagic cystitis or DIC) • Major bleeding occurred on 0.51% of study days when platelet count less than 10 $x10^9$/L and there were no risk factors present
Lawrence et al, 2001 (no pediatric patients)	• Non-randomized, single institute study, prospectively analysed • Years 1992-1993, threshold less than 20 $x10^9$/L (64 adult patients with leukemia, transplant or lymphoma); 1993 less than 10 $x10^9$/L (77 patients) • For patients with counts between 10-20 $x10^9$/L, there was a reduction in the number of platelet transfusion by 51% in the lower threshold group • Multivariate analysis of clinical variables associated with minor bleeding included platelet count, Ampho B therapy, fever, splenomegaly, transplant, semi-synthetic penicillin therapy and sepsis; for major bleeding associations were transplant, platelet count and Ampho B • 94% compliance with lower threshold • 97% of patients with minor bleeding developed major bleeding, only 1.7% without developed major bleeding

Table 3: Summary of Evidence Used to Inform Recommendation #2 (continued)

Study	Results
Navarro et al, 1998 (no pediatric patients)	• Single institution, non-randomized study of 48 adult AML patients (1989-1998); retrospective analysis • In the years 1989-1993, prophylactic transfusions when platelet count less than 20 $x10^9$/L (27 patients); years 1994-1998, prophylactic transfusions when count less than 10 $x10^9$/L, or 10-20 $x10^9$/L when fever, active infection or coagulopathy • Patients with APL excluded • No difference in WHO Grade 2 or greater bleeding – 11 of 27 versus 13 of 21 patients • No deaths due to hemorrhage
Heckman et al, 1997 (no pediatric patients) (included in ASCO Guideline review)	• Randomized control trial comparing threshold of 10 versus 20 $x10^9$/L • Adult patients (78patients) during induction treatment for leukemia • Equivalence for bleeding outcome and mortality • Transfusion permitted for significant bleeding (not defined) • Platelet transfusion reactions considered • Inadequate allocation concealment • Clinicians unblinded (detection of bleeding bias; performance {discretionary use} bias) • Low study power/ wide confidence intervals for severe bleeding
Rebulla et al, 1997 (no pediatric patients) (included in ASCO Guideline review)	• Randomized multi-institutional controlled trial • Adult newly diagnosed AML patients – 225 patients (1994-1996) • Standard care – platelet transfusion if count less than 20 $x10^9$/L or bleeding versus low threshold care – platelet transfusion if count less than 10 $x10^9$/L or 10-20 $x10^9$/L if temperature greater than 38^0C, or if bleeding • No significant difference between groups for frequency of severe bleeding or deaths during induction; however, g.i. bleeding twice as common in low threshold group • Overall deaths in low threshold group – 13.3% versus 7.5% in the higher threshold group (thought to be due to infectious complications) • Adverse events from platelet transfusions not reported • Clinicians unblinded (detection of bleeding bias; performance {discretionary use} bias) • Adequate allocation concealment • Low study power / wide confidence intervals for severe bleeding • Protocol deviation of 5% in low threshold arm and 2% in high threshold arm

Table 3: Summary of Evidence Used to Inform Recommendation #2 (continued)

Study	Results
Gmur et al, 1991 (in Ancliff, Machin, 1998; Benjamin et al, 2002) (no pediatric patients) (included in ASCO Guideline review)	• Prospective study of restrictive platelet transfusions in 102 adult leukemia patients • Patients were examined daily including fundoscopic exam • Transfusion if count less than 20 $x10^9$/L in the presence of major bleeding or minor surgery; at 11-20 $x10^9$/L in the presence of coagulation disorders, heparin therapy or minor procedure; 6-10 $x10^9$/L if fever or fresh minor bleeding; less than 5 $x10^9$/L in all cases • The majority of major bleeds occurred when the platelet count was less than 10 $x10^9$/L • Three of the 31 major bleeds were fatal, two were associated with DIC, one was associated with a platelet count less than 1 $x10^9$/L and refractoriness to platelet transfusions
Aderka et al, 1986 (in Benjamin et al, 2002) (no pediatric patients)	• Retrospective, single center, single arm study of 64 adults with acute leukemia • Threshold less than 10 $x10^9$/L • 67 episodes of bleeding, 15% major; one death secondary to bleeding (platelet count less than 5 $x10^9$/L) • When the thrombocytopenia was caused by the leukemia rather than chemotherapy, the bleeding tendency was higher

Discussion:

Reasons for lowering the threshold for platelet transfusion have included a belief in the safety of this measure, shortages of platelet concentrates, costs of platelet transfusions, risk of infection from platelet transfusions and risk of alloimmunization (Benjamin et al, 2002).

In a 2002-2003 survey of 52 Canadian hospitals with pediatric care services, 80% of hospitals used a prophylactic platelet transfusion threshold of 10-20 $x10^9$/L for non-bleeding, stable patients that included children with leukemia/ lymphoma (Luke, Rock, Berger, 2008).

Stanworth et al, 2005, argue that perhaps the evidence for lowering the platelet transfusion threshold may not sufficiently support the safety of the lower threshold of 10 $x10^9$/L as the confidence interval for relative risk of severe bleeds for the combined studies of Zumberg et al (below) and Rebulla et al above is 0.99 (0.66-1.48), indicating the true risk could lie between 10 per 100 more severe bleeds to 6 per 100 fewer severe bleeds in the higher threshold arm. Stanworth et al, 2005, also question adherence with guidelines/ protocols and accuracy of automatic platelet counts at lower count levels where count tends to be over-estimated (Hong et al, 2009). They suggest that efforts to decrease platelet thresholds in clinically stable patients to less than 5 $x10^9$/L have been insufficiently studied to date to warrant inclusion in guidelines. Corash, 2003 cautions that the randomized studies of Rebulla et al and Heckman et al were not sufficiently powered for equivalence studies for the prevention of bleeding and that all studies fail to address the dilemma that observations within patients are not independent. Heddle et al, 2003, emphasize the need for validated, objective bleeding assessment tools, the danger of observational bias and that the choice of analytic methods influences the results and their interpretation.

The AFSSAPS (French Health Products Safety Agency) guidelines recommend based on experience that in the presence of bleeding risk factors, in general the threshold for transfusion be increased by 10 $x10^9$/L. For example in the presence of fever greater than 38.5 C^0, mucositis of greater than grade 2, potential hemorrhagic lesion, hypertension or infection, a threshold of 20 $x10^9$/L should be used; coagulopathy, a threshold of 50 $x10^9$/L (Andreu et al, 2009).

3. Platelet Count Threshold for Prophylactic Platelet Transfusion – Stem Cell Transplantation

Guideline:

Threshold for stable patients post stem cell transplantation to receive prophylactic platelet transfusions is 10 $x10^9$/L.

Transfusions at a higher level may be required for patients with signs of bleeding, high fever, rapid fall in platelet count, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced).
Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below).

Level of Evidence (ACCP Criteria):

Desirable effects likely outweigh undesirable effects.

Grade of Recommendation (ACCP Criteria):

1C

**Note: the authors of the ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" assigned a level of evidence of III and a grade of recommendation of B to this recommendation.*

Evidence:

Table 4: Summary of Evidence Used to Inform Recommendation #3

Study	Results
Nevo et al, 2007 Nevo et al, 2001 (no pediatric patients)	• Non-randomized retrospective analysis • Study period 1997-1998, platelet transfusions given if morning count less than 20 $x10^9$/L (170 adult patients); study period 1999-2001 (211 patients) given if count less than 10 $x10^9$/L if without fever, urea greater than 70 mg/dL, veno-occlusive disease, CNS disease, low-dose anticoagulant therapy or repeated minor bleeding. These patients were transfused at less than 20 $x10^9$/L • Patients with active bleeding or invasive procedures, less than 50 $x10^9$/L trigger

Table 4: Summary of Evidence Used to Inform Recommendation #3 (continued)

Study	Results
Nevo et al, 2007 Nevo et al, 2001 (no pediatric patients) - continued	• In these non-bleeding patients, a platelet count less than 10 x10^9/L for greater than 4 consecutive days was associated with an overall risk of dying (not secondary to bleeding) 4x greater than patients with 3 or fewer days with a platelet count less than 10 x10^9/L (OR 3.99; 95% CI 1.69-9.40). This finding remained significant after adjustment for risk status, marrow source and study period (OR 3.18; 95% CI 1.25-8.07) • In an earlier report (2001), bleeding patients (321), on the first day of bleeding, 13.5% had a platelet count less than 10 x10^9/L; 20.4% had a platelet count between 10-20 x10^9/L, and 66.1% had a count greater than 20 x10^9/L
Diedrich et al, 2005 (included pediatric patients)	• Randomized trial of 166 pediatric and adult allogeneic SCT patients to threshold of 10 x10^9/L versus 30 x10^9/L (1996-2001) • Transfused if platelet count less than 50 x10^9/L for procedures • Excluded patients with coagulopathy • Daily physical examination and bleeding score using WHO criteria • No differences in clinical outcomes; no deaths secondary to bleeding • Number of platelet transfusions were significantly decreased in the lower threshold group ($p<0.001$)
Zumberg et al, 2002 (included pediatric patients) (included in ASCO Guideline review)	• Randomized control trial • Children and adults undergoing SCT (159 patients) • Equivalence for bleeding outcome and mortality; no deaths attributed to bleeding • Used platelet transfusion indication algorithm based on post-transfusion platelet counts • Used modified GIMEMA bleeding criteria • Transfusion permitted for significant bleeding (not defined) • Adverse events from platelet transfusions not reported • Inadequate allocation concealment • Clinicians unblinded (detection of bleeding bias; performance {discretionary use} bias) • Low study power/ wide confidence intervals for severe bleeding
Gil-Fernandez et al, 1996 (in Lozano et al, 2007) (no pediatric patients) (included in ASCO Guideline review)	• Retrospective analysis of 190 adult patients undergoing bone marrow transplantation • 87 patients transfusion threshold less than 20 x10^9/L; 103 at less than 10 x10^9/L • In the lower threshold group, 12 patients had major bleeding and 4 died, in the higher threshold group, 12 patients had major bleeding and 3 died • All but 3 episodes of major bleeding involved patients with other bleeding risk factors

Discussion:
Many of the issues discussed above apply to this recommendation. Survey results of centres treating adult patients showed the majority used a threshold of less than 20 x10^9/L, particularly for allogeneic transplant patients (Bernstein et al, 1998). The two randomized controlled trials, both of which included pediatric patients, detected no adverse consequences of the lower threshold. Data on longer term adverse events of platelet transfusions were not obtained. Overall, the evidence supports the safety of the lower threshold when the guideline carried out according to clinician judgement.

4. Platelet Count Threshold for Prophylactic Platelet Transfusion – Solid Tumors

Guideline:
Threshold for stable patients with solid tumors to receive prophylactic platelet transfusions is 10 x10^9/L.

Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced).

Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below).

Transfusions at a higher level may be required for patients with bladder tumors, brain tumors or necrotic tumors.

Level of Evidence:
Desirable effects likely outweigh undesirable effects.

Grade of Recommendation:
1C

**Note: the authors of the ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" assigned a level of evidence of III and a grade of recommendation of B to this recommendation.*

Evidence:
Table 5: Summary of Evidence Used to Inform Recommendation #4

Study	Results
Belt et al, 1978 (no pediatric patients) (included in ASCO Guideline review)	• Single institution review of 718 patients with solid tumors • 10.4% had hemorrhagic episode • In 33%, bleeding secondary to tumor invasion, 9% due to DIC and unrelated to tumor or treatment in 8% • In 49% of those with bleeding episodes, associated with thrombocytopenia • Major bleeding unusual with platelet count greater than 10 x10^9/L (5 episodes nadir 20-50 x10^9/L; 1 episode at 10-20 x10^9/L)

Table 5: Summary of Evidence Used to Inform Recommendation #4 (continued)

Study	Results
Dutcher et al, 1984 (no pediatric patients) (included in ASCO Guideline review)	• Single institution review of 1274 adult patients with solid tumors (1972-1980) • 5063 days of thrombocytopenia (less than 50 $x10^9$/L); 670 days less than 20 $x10^9$/L • 44 episodes of serious bleeding • 15 associated with other coagulopathies; 24 with serious infection; 12 within the tumor • 86 patients with CNS tumors did not display evidence of CNS bleed associated with thrombocytopenia • Of 12 patients dying from hemorrhage, 7 had normal platelet counts
Goldberg et al, 1994 (no pediatric patients) (included in ASCO Guideline review)	• Single institution review of 501 patients with gynaecologic tumors (1985-1993) • Platelet transfusions given to bleeding patients and to some with a platelet count less than 20 $x10^9$/L • 10% of patients with platelet count less than 10 $x10^9$/L had major bleeding; 3% between 10-20 $x10^9$/L; and one each at 20-30 $x10^9$/L, 50-75 $x10^9$/L; no CNS bleeds
Fanning et al, 1995 (no pediatric patients) (included in ASCO Guideline review)	• 46 patients entered in chemotherapeutic gynaecologic cancer trials • Retrospective review • No patient with platelet count greater than 20 $x10^9$/L received a prophylactic platelet transfusion • Prophylactic platelet transfusions were given for 30 of 100 episodes of platelet count less than 20 $x10^9$/L; half of episodes of counts 5-10 $x10^9$/L were not transfused • Episodes where the platelet count was less than 5 $x10^9$/L (11 episodes) were excluded (all received prophylactic transfusion and none bled) • 10% of thrombocytopenic episodes were associated with minor bleeding • No difference between bleeding episodes of those transfused versus those not (counts between 5-20 $x10^9$/L)
Etling et al, 2001 (no pediatric patients) (included in ASCO Guideline review)	• Single institution review of 609 patients (1994-1995) with solid tumor or lymphoma • 1262 cycles with thrombocytopenia • Bleeding occurred in 111 cycles – major bleeding occurred in 43 cycles (nasal, g.i., bladder, vaginal, pulmonary); multiple sites were involved in six episodes • Bleeding more common when fever present

Table 5: Summary of Evidence Used to Inform Recommendation #4 (continued)

Study	Results
Etling et al, 2001 (no pediatric patients) (included in ASCO Guideline review) - continued	• In 129 cycles, CNS tumor or metastases present; in 77 cycles, CNS radiation, one CNS bleed (patient recovered) • Four deaths attributed to hemorrhage • In general, outcomes poorer for those with bleeding (consequence or cause?) • Bleeding increased in patients with poor performance status and multiple co-morbidities

Discussion:
The evidence for this recommendation is based on five retrospective studies in adult patients. No life threatening bleeding was seen when the platelet count was greater than 10 $x10^9$/L except for patients with necrotic tumors where the risk of bleeding did not correlate with the platelet count (Schiffer et al, 2001).

5. Platelet Count Threshold for Prophylactic Platelet Transfusion – Brain Tumors

No specific data found. No guideline was able to be formulated. This is an area for which research is strongly recommended.

The general practice appears to be maintenance of the platelet count greater than 10-20 $x10^9$/L during chemotherapy. Local practice dictates platelet threshold for patients receiving radiation.

Note that these recommendations in the summary table are based on a survey of neuro-oncologists (66.7%), neurosurgeons (11.1%) and others (22.2%) from the C^{17} centers across Canada who treat pediatric neuro-oncology patients. **The numbers provided are based on a minimum 75% acceptance of those responding to the survey.**

6. Platelet Count Threshold for Prophylactic Platelet Transfusion – Surgical or Invasive Procedures

6.1 Guideline for Lumbar Puncture

Threshold for stable patients requiring a lumbar puncture to receive prophylactic platelet transfusions is 20 $x10^9$/L.

Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, APL, hyperleucocytosis, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced). Transfusions at a higher level may be required for patients undergoing invasive procedures (see sections below).

Transfusions at a higher level are recommended for newly diagnosed patients with leukemia.

Level of Evidence:
Desirable effects likely outweigh or balance undesirable effects.

Grade of Recommendation:
2B

**Note: the authors of the ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" assigned a level of evidence of IV ('expert consensus') and a grade of recommendation of B to this recommendation.*

Evidence:

Table 6: Summary of Evidence Used to Inform Recommendation #6.1

Study	Results
Howard et al, 2000	• Retrospective study 956 consecutive pediatric patients in a single institution with acute lymphoblastic leukemia (total of 5223 LPs). • Prophylactic platelet transfusion was not routinely given • Patients all had their LP performed under conscious sedation or general anesthetic • No neurologic complications related to bleeding in any of the patients • Traumatic LPs (>500 RBCs/mL) occurred in 10.5% of patients • Although the likelihood of a traumatic or bloody LP (10-500 RBCs/mL) was increased if the platelet count was <100 $x10^9$/L, there was no correlation between bleeding and platelet count below 100 $x10^9$/L • The confidence interval for patients with a platelet count of 1-5 $x10^9$/L was 0-40 and that for patients with a platelet count of 6-10 $x10^9$/L was 0-13 for probability serious bleeding complications (subdural etc). The confidence interval for all patients was 0-0.07.
Howard et al, 2002	• Risk factors for bloody or traumatic LPs in pediatric patients with acute leukemia – age < 1 year, experience of the practitioner with the procedure, platelet count <100 $x10^9$/L, previous traumatic or bloody LP and time since last LP. • Bloody or traumatic LPs carry a theoretical risk of meningitis if the patient is bacteremic

Discussion:
Others have found that the patient's platelet count does not correlate with serious bleeding complications (epidural, subdural or subarchnoid bleeds)(for example, Lee et al, 2007). Of concern, patients with high risk acute lymphoblastic leukemia with an initial bloody or traumatic LP and had the instillation of intrathecal medication delayed by 24-48 hours had a higher relapse rate (odds ratio 21) versus 1.5 for those with high risk and immediate instillation of intrathecal medication when compared with 58 patients without bloody or traumatic LPs (Rech et al, 2005). Other studies have reported that the risk of recurrence in patient with a traumatic LP with blasts present is 1.5 – 3.5 times greater than for those without traumatic LPs (Burger et al, 2003; Gajjar et al, 2000; te Loo et al, 2006). It is also recognized that some may be uncomfortable with a threshold of 20 $x10^9$/L because of the potentially devastating consequences of an intraspinal bleed.

6.2 Guideline for Minor Invasive Procedure

Procedures such as bone marrow aspirate and biopsy can be performed without risk at a platelet count of 10 $x10^9$/L.

A higher threshold for intramuscular injections is the general practice (usually 20-30 $x10^9$/L).

6.3 Guideline for Major Invasive Procedure

Threshold for stable patients requiring a major invasive surgical procedure to receive prophylactic platelet transfusions is 40-50 $x10^9$/L. For the purpose of this guideline, major surgery includes insertion of a central venous access device, tissue biopsy of internal organs or sites, endoscopy and tumor removal.

Transfusions at a higher level **may** be required for patients with signs of bleeding, high fever, rapid fall in platelet count, APL, hyperleucocytosis, concomitant coagulation abnormality, critically ill patients, and those with impaired platelet function (including drug induced).

Transfusions at a higher level may be required for newly diagnosed patients with leukemia or patients undergoing removal of necrotic or vascular tumors.

Level of Evidence:
Desirable effects likely outweigh undesirable effects.

Grade of Recommendation:
1C

**Note: the authors of the ASCO guideline "Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology" assigned a level of evidence of IV ('expert consensus') and a grade of recommendation of C to this recommendation.*

Evidence:

Table 7: Summary of Evidence Used to Inform Recommendation #6.3

Study	Results
Foster et al, 1992	• 40 adult liver allograft recipients, had percutaneous insertion of 259 central lines (1988) • 160 patients had category I coagulopathy (one abnormality), 40 had category II (two abnormalities), 2 category III (three or more) • No corrective treatments given • No bleeding complications were observed in any of the patients
DeLoughery et al, 1996	• Retrospective chart review of adult 490 intensive care patients • 41% had coagulation abnormality prior to line insertion; 27% with severe abnormalities • 37% received corrective interventions for the coagulopathy • 16 of 490 patients had bleeding complications, two were life-threatening, none fatal • Recommend that blood components are not necessary prior to line insertion except for those with severe abnormalities • Complications related to experience of surgeon
Doerfler et al, 1996	• Retrospective review of adult patients receiving percutaneously inserted lines • 30 patients had platelet counts of 20-50 $x10^9$/L; 11 had platelet counts less than 20 $x10^9$/L • Patients were not transfused prior to line insertion • Seven patients had bleeding complications, all stopped with direct pressure; median platelet count 21 $x10^9$/L at the time of insertion
Ray et al, 1997	• Retrospective 112 catheters in 105 adult patients • 37 patients had platelet counts less than 50 $x10^9$/L (median 30 $x10^9$/L); these patients received 1 unit of single-donor platelets prior to surgery (median count post transfusion 40 $x10^9$/L); 8 of these patients had a port inserted; no patients had bleeding complications • 35 patients had platelet counts of 50-100 $x10^9$/L, 6 had a port; one patient had a bleeding complication (also had factor VIII deficiency)
Van Os et al, 1999	• Retrospective review • Risk of bleeding with polypectomy (@0.4-1.6%) is not increased in adult patients receiving ASA, suggest no increased risk in patients with platelet count of 20 x 10^9/L or greater • Liver biopsy (risk <1% baseline); not increased if platelet count 50 x 10^9/L or greater

Table 7: Summary of Evidence Used to Inform Recommendation #6.3 (continued)

Study	Results
Van Os et al, 1999 - continued	• Recommend transfusion with platelets if count is less than 20 x 10^9/L for low risk procedures (endoscopy with mucosal biopsy) and if count is less than 50 x 10^9/L for high risk procedures (liver biopsy)
Mumtaz et al, 2001	• 2010 catheters placed in 1875 adult patients (1997-1999) • Retrospective review • 88 patients had abnormal hemostasis uncorrected prior to surgery • Four patients had bleeding complications; one with platelet count of 12 x10^9/L; one with septic shock and platelet count of 31, INR of 1.5; one with renal failure and platelet count of 46 x10^9/L; one with platelet count of 154 x10^9/L and INR 1.1
Samama et al, 2006	• Pre-operative guidelines of the AFSSAPS • Threshold of 50 x10^9/L for procedures such as liver biopsy, transbronchial endoscopic biopsy, placement of catheter (grade C recommendation) • Most surgeries, threshold of 50 x10^9/L (grade C recommendation) • Neurosurgery and ophthalmologic surgery, threshold of 100 x10^9/L (grade C recommendation) • Spinal anesthesia, threshold of 50 x10^9/L; epidural anesthesia, threshold of 80 x10^9/L (grade C recommendation)
Loh, Chui, 2007 (pediatric patients)	• Single institution retrospective review of insertion of a port-a-cath in 80 pediatric patients with acute lymphoblastic leukemia (2002-2004) • Usually performed during the first week of diagnosis • Performed by 5 senior surgeons using a standardized surgical approach and post-op care • Threshold for transfusion 50 x 10^9/L • However, 22 children had surgery with platelet count less than 50 x 10^9/L (10-49, median 35) • The outcomes of these children were no different than those whose surgery was performed at platelet counts of 50 x 10^9/L or greater; two bleeding episodes occurred in children with a pre-operative platelet count of greater than 50 x 10^9/Land none in the children with pre-operative platelet counts of less than 50 x 10^9/L

Table 7: Summary of Evidence Used to Inform Recommendation #6.3 (continued)

Study	Results
Weigand et al, 2009 (no pediatric patients)	• Review of 196 adult intensive care patients with coagulopathies who required insertion of central venous catheters (2005-2007) • Open prospective trial • Exclusion criteria included bleeding from causes other than coagulopathy, patients receiving chemotherapy, patients undergoing systemic lysis therapy • Lines were placed by surgical residents • 55 patients had an INR of greater than 1.5 and/or a platelet count of less than 50 $x10^9$/L • No significant difference in bleeding complication between patients with normal coagulation profiles and those with elevated INR/decreased platelets

Discussion:
The ASCO Expert panel determined the threshold of 40-50 x 10^9/L based on accumulated experience of multiple surgeons. Requirements for platelet transfusions should be negotiated with the involved surgeon and anesthetist. Removal of necrotic and/or vascular tumors may require transfusion at a higher threshold.

External Review and Consultation Process

The guideline was first reviewed by a panel of seven experts in pediatric hematology / oncology and / or transfusion medicine. They were asked to complete a questionnaire as summarized below.

Question	Response
Role in care of children with cancer?	Oncologist – 20% Hematologist – 60% Transfusion Medicine – 20%
Currently following a guideline on platelet transfusion thresholds?	No – 40% Yes – 60%
If using a guideline, is it consistent with this guideline?	No – 33% Yes – 66%
Rationale for guideline clear?	100% agree or strongly agree
Is there a need for this Canadian guideline?	80 % strongly agree 20% neutral
Literature search complete?	100% agree or strongly agree
Evidence described relevant?	100% agree or strongly agree

Question	Response
Methods used to summarize effective?	100% agree or strongly agree
Results interpreted in accordance with your own interpretation?	100% agree or strongly agree
Draft recommendations are clear?	100% agree or strongly agree
Agree with draft recommendations as stated?	80% agree or strongly agree 20% neutral
Comfortable recommending use of the guideline in own institution?	100% agree or strongly agree
Likely to adopt for own practice?	40% agree or strongly agree 20% neutral 40% not applicable

Comments:

Comment	Response
Objective #2 on page 7 – unsure how the guideline is providing this information. The guideline helps health care providers balance risks and benefits of platelet transfusion by providing recommendations on their use.	Statement modified as per suggestion.
The literature search did not include studies of platelet dose (comment of two reviewers).	As amended in the introduction, this was outside of the scope of the guideline.
Uncomfortable with the recommendation of a platelet transfusion threshold of <20 for lumbar puncture. Even with limited data, the magnitude of risk must be considered. Even one small bleed would be devastating if it were potentially avoidable with platelet transfusions. Seems incongruent with recommendations about other invasive procedures.	Modifying statement added.
Would avoid using the < sign with reference to the recommended threshold; state platelet transfusions are recommended for counts less than 10 or that the threshold is 10.	This was rectified throughout the document.
Recommendation for alloimmunization; meaning of alloimmunization needs clarification. Also the practice is widely varied across centres, most would state to try specialized products such as HLA matched platelets. Should this topic be omitted from the guideline?	Recommendations regarding alloimmunization have been deleted.
Other areas for consideration are apheresed platelets, irradiation, CMV negative products.	These were not in the purview of the guideline; clarified in the introduction.
Should mention Hema-Quebec along with Canadian Blood Services.	This was added.

Comment	Response
More critical appraisal would be useful (as given under recommendation #2).	Some additional appraisal added.
More detail required for solid tumor studies quoted.	Table inserted.
Section 7.2 needs revision to provide the results as in other sections.	Corrected.
Why are some of the grades of recommendations different from the ASCO guidelines?	The ASCO guideline used a different grading system than used for this guideline (as expanded on under the grading section).
No clear recommendation on brain tumor patients. It is important to provide guidance (even if no guidelines are available). Important to provide guidelines for surgical procedures.	A statement of common practice inserted re brain tumors. Pre-operative guidelines added.

Plan for Scheduled Review and Update

The Committee will review this guideline bi-annually and at any time if significant information becomes available.

Implementation Considerations

The guideline will have been circulated to the seventeen Canadian centres providing tertiary pediatric hematology / oncology care for feedback prior to finalization of the guideline. The aspect most likely to provide difficulty is the threshold for lumbar puncture. Some centres will modify the recommended thresholds to accommodate patients living in more remote areas.

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Panel Members

The Guideline development group included:

- Dorothy Barnard, pediatric hematologist/oncologist/hematopathologist
- Carol Portwine, pediatric hematologist/oncologist
- Lillian Sung, pediatric hematologist/oncologist
- Lee Dupuis, pharmacist
- Marcel Romanick, pharmacist
- Gwen Erdmann, nurse
- Anne McDermid, nurse practitioner
- Anne Choquette, nurse
- Maureen McCory, social worker

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Appendix A: Guideline Adaptation/Development Process

ADAPTE Methodology

The initial stages of this project were informed by the guideline adaptation methodology developed by the ADAPTE Collaboration. The ADAPTE process is a systematic approach to considering the use and/or modification of existing guidelines developed in one context for application in a different context, so as to enhance the efficient production and use of high-quality adapted guidelines (ADAPTE Collaboration,). The ADAPTE process is currently under evaluation for usability, acceptability, relevance and benefits to different user groups. Its use in this project was in the context of this evaluation. A summary of the ADAPTE process is provided in Figure 1. More detailed information on the ADAPTE process is available on www.adapte.org.

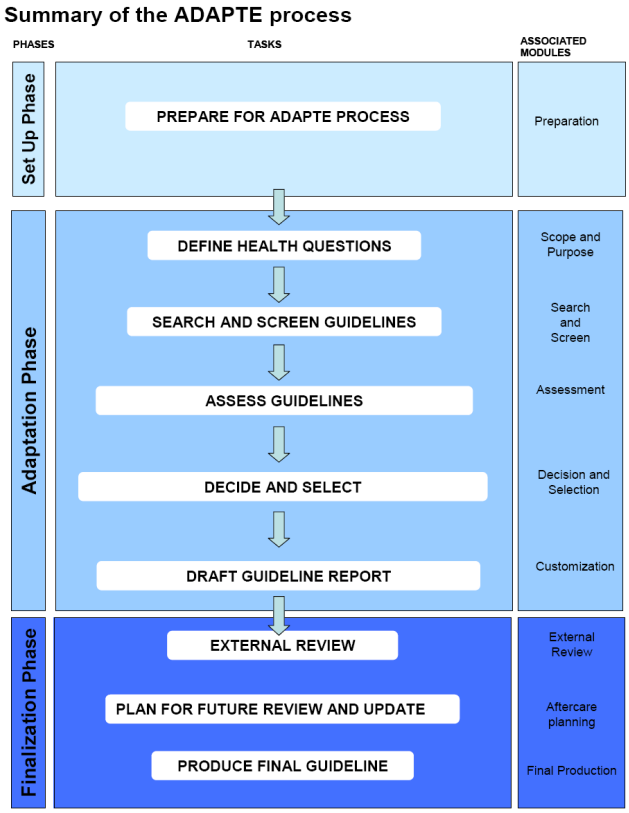

Figure 1: Summary of the ADAPTE Process

Guideline Search

Search Strategy

In March 2007, the Guidelines Committee of C[17] conducted a comprehensive literature review and environmental scan to identify Guidelines and Standards specific to prophylactic platelet transfusions for children and youth with cancer or serious hematologic disorders. To ensure the currency of this list, a Research Consultant and Research Assistant used the following search strategy to identify guidelines and standards published between 2000 and 2008. The following processes were used to search for guidelines and standards:

1. Review of scientific literature sources using empirical databases - HealthStar, Medline, CINHAL, Embase and PsycINFO databases were systematically searched by a Research Consultant using the following search terms:

    - HealthStar Search terms: platelet transfusion threshold combined with terms of neoplasms, guideline or practice guideline
    - Medline Search Terms: platelet transfusion threshold combined with terms of neoplasms, guideline or practice guideline
    - CINHAL Search Terms: platelet transfusion threshold combined with terms of neoplasms or cancer and practice guidelines or standards
    - EMBASE Search Terms: platelet transfusion threshold cancer patient or cancer combined with terms of practice guideline
    - PsycINFO Search Terms: platelet transfusion threshold combined with terms of neoplasms, treatment guidelines or professional standards

2. Review of grey literature sources such as annual reports or publications of organizations as identified on the world-wide web – The internet search engine utilized was Google Scholar. Search terms included: platelet transfusion threshold paired with terms of cancer, guidelines and standards.

3. Review of local, provincial, national and international databases -

    a) All oncology professional associations and organizations for platelet transfusion threshold.

    b) All Canadian Provincial Cancer Care Organizations within provinces websites were searched (except Quebec: no provincial source found) including the *"site map"* to reveal any guideline or standard embedded under another topic inclusive of provincial cancer organizations, regional and local cancer organizations within provinces and specific guideline development organizations in cancer care at the provincial level such as the Program in Evidence-Based Medicine, which is under the auspices of Cancer Care Ontario.

    c) International organizations or agencies or associations whose mandate is focused on systematic reviews or guideline development.

    The organizations and agency's sites that were searched are included in Appendix B.

Inclusion/Exclusion Criteria

Inclusion:

1. Guidelines focused on clinical practice of practitioners relevant to **pediatric platelet transfusion need assessment** for pediatric hematology / oncology patients and their families**.**
    a. Clinical practice guidelines: those specific to situations in which clinicians are making decisions about direct patient care.
    b. Best practice guidelines: those that identify the best choice from a range of appropriate health care options, as defined by a consensus of experts following review of relevant literature using systematic review methods.
2. Published between 2000-2008.

Exclusion*:

1. Guidelines for which it was not clear that the guideline statements or recommendations were based on a review of evidence from the literature and / or were not based on a source that used evidence to support the guideline development process (included as topic areas in appendices only).
2. Guidelines focused strictly on assessment.

**Excluded guidelines may have still been considered by the panel during the guideline development process, but were not considered for the basis of guideline adaptation.*

**Note: Preference was given to guidelines and guides to practice that based the development of substantive statements/recommendations on a review of evidence from the literature and/or were based on a source that used evidence to support the guideline development process.*

Included Guidelines

Guideline Assessments

Each guideline was independently reviewed and scored by 6 panel members, using the Appraisal of Guidelines for Research & Evaluation (AGREE) instrument (AGREE Collaboration, 2001). The AGREE instrument provides a framework for the evaluation of guideline quality on the basis of 6 domains: scope and purpose; stakeholder involvement; rigour of involvement; clarity and presentation; applicability; and editorial independence. Domain scores and overall assessments from each reviewer were compiled for each guideline, and results were presented for discussion at an in-person panel meeting. Panel members were provided copies of all guidelines to facilitate discussion of the results and reach consensus on the suitability of each guideline for guideline adaptation via the ADAPTE process. Each guideline was discussed as to why they were or were not recommended. Particular attention was paid to rigor scores and guideline scope.

Decision Process Followed by Panel

Decisions were established through panel discussions, whereby any differences of opinion were resolved with consensus. If consensus was unable to be reached, a vote was cast.

Results

Overall Impressions:

Based on the overall assessment of the guidelines and the number of recommendations received it was a unanimous group decision to use the **ASCO Clinical Practice Guideline for Platelet Transfusion for Patients with Cancer** as the basis for guideline adaptation. The British *Transfusion guidelines for neonates and older children* and *Guidelines for the use of platelet transfusions* as well as Slichter's *Evidence-based platelet transfusion guidelines* were identified as having strengths that would be used to influence the development of the present guideline.

Despite the number of guidelines to guide platelet transfusions, it was found that there was a lack of evidence-based guidelines that were specifically within the scope of platelet thresholds for pediatric patients. Although the *Transfusion guidelines for neonates and older children* and *Guidelines for the use of platelet transfusions* as well as Slichter's *Evidence-based platelet transfusion guidelines* address specific aspects of the assessment process, it was found that the recommendations provided in these guidelines were largely included in the ASCO guidelines which were felt to be more complete and formatted in a manner that would suit the purposes of this guideline. However, the ASCO guidelines are largely based on adult patient data. As a result, it was acknowledged that a separate literature search for empirical studies would be necessary to supplement the recommendations that address the health questions of interest in the present guideline.

Literature Search for Guidelines

Search Strategies for Paediatric Oncology Group

Database: Ovid MEDLINE(R) <1996 to April Week 1 2008>
Search Strategy:

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1 Platelet Transfusion/ (1801)
2 exp Neoplasms/ (790623)
3 1 and 2 (286)
4 limit 3 to (yr="1999 - 2008" and (English or French)) (186)
5 limit 4 to practice guideline (2)
6 "recommendation*".m_titl (8437)
7 "standard*".m_titl (20202)
8 "guideline*".m_titl (19906)
9 6 or 7 or 8 (47389)
10 4 and 9 (4)
11 5 or 10 (4)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to April Week 2 2008>
Search Strategy:

---

1 Platelet Transfusion/ (253)
2 exp neoplasms/ (84980)
3 1 and 2 (20)
4 limit 3 to (yr="1999 - 2008" and (English or French)) (16)
5 limit 4 to practice guidelines (0)
6 “recommendation*”.m_titl (3750)
7 “standard*”.m_titl (10801)
8 “guideline*”.m_titl (11648)
9 6 or 7 or 8 (25577)
10 4 and 9 (0)

Database: EMBASE <1996 to 2008 Week 16>
Search Strategy:

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1 thrombocyte transfusion/ (3573)
2 exp neoplasm/ (857060)
3 1 and 2 (1032)
4 limit 3 to ((English or French) and yr="1999 - 2008") (852)
5 Practice Guideline/ (92027)
6 4 and 5 (26)
7 guideline$.m_titl. (17944)
8 recommendation$.m_titl. (8257)
9 standard$.m_titl. (18413)
10 4 and (7 or 8 or 9) (9)
11 6 or 10 (30)

Database: PsycINFO <1967 to April Week 4 2008>
Search Strategy:

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1 blood transfusion/ (74)
2 exp neoplasms/ (17881)
3 1 and 2 (5)
4 limit 3 to ((English or French) and yr="1999 - 2008") (1)
5 guideline$.m_titl. (3408)
6 recommendation$.m_titl. (2320)
7 standard$.m_titl. (7277)
8 4 and (5 or 6 or 7) (0)

Guidelines Reviewed

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Not applicable, no guidelines re platelet thresholds given, adult disease.

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Not applicable, guidelines are related to patients with heparin-induced thrombocytopenia.

Guidelines for the diagnosis and therapy of adult myelodysplastic syndromes. Retrieved 4/25/2008, 2008, from http://www.guideline.gov/summary/summary.aspx?doc_id=9575&nbr=005107&string=platelet+AND+transfusions

Not applicable, refers to Platelet Transfusion Guideline published by the Royal College of Physicians of Edinburgh.

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Not applicable, no guideline provided for platelet transfusion.

Thrombocytopenia. Retrieved 4/25/2008, 2008, from http://www.guideline.gov/summary/summary.aspx?doc_id=11048&nbr=005827&string=platelet+AND+transfusions

Applicable for guidance.

Practice guideline for the performance of therapy with unsealed radiopharmaceutical sources. Retrieved 4/25/2008, 2008, from http://www.guideline.gov/summary/summary.aspx?doc_id=9434&nbr=005055&string=platelet+AND+transfusions

Not applicable, refers only to polycythemia vera patients receiving phosphate 32.

Treatment for anemia with erythropoietic agents in patients with non-myeloid hematological malignancies: A clinical prac. Retrieved 4/25/2008, 2008, from http://www.guideline.gov/summary/summary.aspx?doc_id=10583&nbr=005525&string=platelet+AND+transfusions

Not applicable, refers to red cell transfusion only.

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Not applicable, refers to methods of making platelet concentrates only.

Guidance for industry - for platelet testing and evaluation of platelet substitute products. Retrieved 4/28/2008, 2008, from http://www.fda.gov/cber/gdlns/platelet.htm
Not applicable, related to platelet concentrate quality only.

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Not applicable.

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Not applicable, not a guideline refers only to number of platelet transfusion required with one treatment versus another.

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Not applicable, not a guideline, no specific advice re transfusion thresholds.

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Applicable for guidance, not evidence-based.

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Not a guideline.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

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Not a guideline.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

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Not a guideline.

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Applicable for guidance, no evidence-based.

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Not a guideline, for use in empiric literature search.

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Not a guideline, for use in empiric literature search.

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Applicable.

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Applicable.

Slichter, S., Raife, T., Davis, K., Rheinschmidt, M., Buchholz, D., Corash, L., et al. (2006). Platelets photochemically treated with amotosalen HCl and ultraviolet A light correct prolonged bleeding times in patients with thrombocytopenia. *Transfusion, 46*(5), 731-740.
Not applicable, not a guideline, no specific advice re platelet thresholds.

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Not a guideline, for use in empiric literature search.

Stasi, R., & Provan, D. (2004). Management of immune thrombocytopenic purpura in adults. *Mayo Clinic Proceedings, 79*(4), 504-522.
Not applicable, not a guideline, no specific advice re platelet thresholds, not applicable disorder.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

Stolarska, M., Mlynarski, W., Zalewska-Szewczyk, B., & Bodalski, J. (2006). Cytoprotective effect of amifostine in the treatment of childhood neoplastic diseases: A clinical study including the pharmacoeconomic analysis. *Pharmacological Reports, 58*(1), 30.
Not applicable, not a guideline, no specific advice re platelet thresholds.

Stroncek, D., & Rebulla, P. (2007). Platelet transfusions. *Lancet, 370*(9585), 427-438.
Applicable for guidance.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

Tinmouth, A. T., & Freedman, J. (2003). Prophylactic platelet transfusions: Which dose is the best dose? A review of the literature. *Transfusion Medicine Reviews, 17*(3), 181-193.
Not applicable.

Transfusion Task Force. (2007). Amendments and corrections to the 'transfusion guidelines for neonates and older children' (BCSH, 2004a); and to the 'guidelines for the use of fresh frozen plasma, cryoprecipitate and cryosupernatant' (BCSH, 2004b). *British Journal of Haematology, 136*(3), 514-516.
Applicable.

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Not applicable.

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Not applicable, not a guideline, no specific advice re platelet thresholds.

Van Veen, J. J., Vora, A. J., Welch, J. C., Boulton, F., Gibson, B., & Murphy, M. (2004). Lumbar puncture in thrombocytopenic children (multiple letters) [4]. *British Journal of Haematology, 127*(2), 233-235.
Not guideline, for use in empiric literature review.

von Stackelberg, A., Karatchunsky, A., Kudrjashova, J., Miakova, N., Belikova, L., Rumiantzev, A., et al. (1999). Toxicity, supportive care and costs of two chemotherapy protocols for treatment of childhood ALL in Russia: BFM 90m and MB 91. *European Journal of Cancer, 35*(9), 1349-1355.
Not applicable, not a guideline, no specific advice re platelet thresholds.

Wong, E. C. C., Perez-Albuerne, E., Moscow, J. A., & Luban, N. L. C. (2005). Transfusion management strategies: A survey of practicing pediatric hematology/oncology specialists. *Pediatric Blood and Cancer, 44*(2), 119-127.
Not guideline.

Literature Search for Empirical Studies to Supplement Guidelines

Sources of Evidence

- ASCO guideline which included a review of the literature up until mid-1999;
- Searches of CINAHL, EMBASE, HealthSTAR, MEDLINE, PsycINFO, CDSR (Cochrane Database of Systematic Reviews), DARE (Database of Abstracts of Reviews of Effects), HTA (Health Technology Assessments) in May 2008 for systematic reviews published after 2000;
- Randomized trials cited in relevant systematic reviews found by the search described above
- Search of CINAHL, EMBASE, HealthSTAR, MEDLINE, PsycINFO, CCTR (Cochrane Central Register of Controlled Trials) in June 2008 for randomized trials published after 2000; a literature search update for new randomized trials was conducted in March 2011;
- Randomized trials cited by guidelines published between 2000 and May 2008. These guidelines were either listed in the *Literature Review and Environmental Scan* - or were found by a comprehensive update search for guidelines conducted in May 2008.

Inclusion/Exclusion Criteria

- The population of interest was: children and youth (age 1 month to 19 years) with cancer or serious hematologic disorder (and their families).
- A broad set of interventions and outcomes were considered eligible for the evidence review.

Interventions

- Assessment of platelet transfusion needs of patient including one or more of:
- Physical (freedom from bleeding, needs for physical comfort and freedom from pain)
- Informational (to inform patient and family decision making)
- Psychological (needs related to risk of bleeding)
- Practical (bleeding risks)

Specific attributes of assessment programs may also reflect sensitivity to the social and cultural context of the patient and special needs arising from social environment or general health issues.

Outcomes

Quality of life
Symptom severity
Early identification of bleeding risk
Reduced uncertainty
Functional status

Results

Additional information gleaned from the literature review was incorporated as appropriate into the recommendations and outlined under the *Supporting Evidence and Information for Recommendations*.

Appendix B: Websites Searched for Guidelines and Standards

Web sites checked:

National Guidelines Clearinghouse

Ontario Guidelines Advisory Committee (GAC) Recommended Clinical Practice Guidelines

TRIP

Institute for Clinical Systems Improvement

National Institute for Clinical Evidence

New Zealand Guidelines Group

Scottish Intercollegiate Guidelines Network (SIGN)

Canadian Agency for Drugs and Technology in Health

CMA Infobase

Food and Drug Administration

Haute Authorite de Sante (HAS) (French)

CHU de Rouen - Catalogue & index des Sites Medicaux Francophones (CISMef) (French)

Bibliothèque medicale AF Lemanissier (French)

Direction de la lutte contre le cancer - Ministere de la sante et des services sociaux du Quebec (French)

SOR: Standards, Options et Recommandations (French)

Registered Nurses Association of Ontario

Agency for Quality in Medicine (German, guidelines in English)

Finnish Medical Society Duodecim (Finnish, guidelines in English)

American Society of Clinical Oncology

BC Cancer Agency

Cancer Care Ontario Practice Guideline Initiative

National Cancer Institute

National Comprehensive Cancer Network

Cancer Backup (UK)

Agence Francaise de Securite Sanitaire des Produits de Sante (AFSSAPS) (French)

National Library of Guidelines (UK)

Alberta Cancer Board

Saskatchewan Cancer Agency

Cancer Care Nova Scotia

Canadian Cancer Academic Centers
Alberta Cancer Board: www.cancerboard.ab.ca British Columbia Cancer Agency: www.bc.cancer.ca Cancer Care Nova Scotia: www.cancercare.ns.ca Cancer Care Ontario: www.cancercare.on.ca Saskatchewan Cancer Agency: www.scf.sk.ca
International Cancer Academic Centers
www.library.nhs.uk* St. Jude's Children's: www.stjude.org*

Professional Associations and Agencies
Association of Pediatric Oncology Nurses: www.apon.org
American Society of Clinical Oncology: www.asco.org
POGO: www.pogo.on.ca*
Children's Oncology Group: www.childrensoncologygroup.org*
RNAO: www.rnao.org
Canadian Association of Provincial Cancer Agencies: www.capa.ca*
Associations of Community Cancer Centres: www.accc-cancer.org*
International Society of Pediatric Oncology: www.siop.nl*
Academic and Government Associated Websites
NCCN: www.nccn.org
NCI: www.nci.nih.gov/cancertopics
New Zealand Guidelines Group: www.qualityhealth.org.nz
SIGN: www.sign.ac.uk
National Institute for Health and Clinical Excellence: www.nice.org.ul (guidance.nice.org.uk)
Cancer Resource Websites
Crisis, Grief and Healing: www.webhealing.com
Lance Armstrong Foundation: www.laf.org
The National Coalition for Cancer Survivorship: www.canceradvocacy.org
Vanderbilt Children's: www.vanderbeltchildrens.org
Guideline Specific Websites
www.guideline.gov
www.cancerindex.org
Directory of Clinical Practice Guidelines
National Guideline Clearing House
National Quality Measures Clearinghouse
National Library for Health Care (NICE)
The Medical Outcomes & Guidelines Sourcebook
National Comprehensive Cancer Network
Scottish Intercollegiate Guideline Network (SIGN)
Cochrane Collaboration

Appendix C: C[17] Survey Results for Patients with CNS Tumors

1. **If a child with a CNS tumor had the following characteristics I would transfuse the patient with platelets if their platelet count dropped below:**

	10,000 plts/µl	20,000 plts/µl	30,000 plts/µl	40,000 plts/µl	50,000 plts/µl	75,000 plts/µl	100,000 plts/µl	Other	No.
Child has a VP shunt or Ommaya reservoir	5.6% (1)	61.1% (11)	16.7% (3)	0.0% (0)	16.7% (3)	0.0% (0)	0.0% (0)	0.0% (0)	18
Child has a past history of ICH	0.0% (0)	16.7% (3)	11.2% (2)	0.0% (0)	61.1% (11)	5.6% (1)	5.6% (1)	0.0% (0)	18
Infant on intensive chemo regimen	5.6% (1)	55.6% (10)	27.8% (5)	0.0% (0)	5.6% (1)	0.0% (0)	5.6% (1)	0.0% (0)	18
Child who will have neurosurgical procedure	0.0% (0)	5.6% (1)	0.0% (0)	0.0% (0)	16.7% (3)	0.0% (0)	72.2% (13)	5.6% (1)	18

Comments:

- If there is a large residual tumor I would transfuse at a level <30,000
- Depends on invasiveness of procedure; between 50 – 100,000

2. **If a child has a gross total resection of a CNS tumor and is on treatment (chemotherapy and/or radiation) I would transfuse the child with platelets if the platelet count dropped below:**

	Percent	Count (TOTAL 18)
10,000 plts/µl	11.10%	2
20,000 plts/µl	61.10%	11
30,000 plts/µl	16.70%	3
40,000 plts/µl	0.00%	0
50,000 plts/µl	11.10%	2
75,000 plts/µl	0.00%	0
100,000 plts/µl	0.00%	0
OTHER	0.00%	0

Comments:

- Depending how close from the previous surgery and how fast platelets are dropping

3. **If a child has a residual tumor (subtotal resection or biopsy only) and is on treatment (chemotherapy and/or radiation) I would transfuse the child with platelets if the platelet count dropped below:**

	Percent	Count (TOTAL 18)
10,000 plts/µl	5.60%	1
20,000 plts/µl	44.40%	8
30,000 plts/µl	27.80%	5
40,000 plts/µl	0.00%	0
50,000 plts/µl	11.10%	2
75,000 plts/µl	5.60%	1
100,000 plts/µl	0.00%	0
OTHER	5.60%	1

Comments:

- Depending on how close from the previous surgery and how fast the platelets are dropping.
- Significant residual (less than partial resection) or very hemorrhagic tumor (choroid plexus, ATRT) would increase threshold to 50,000; but for STR and "benign histological subtype" (LGG) a level of 20,000 seems acceptable to me.

4. **If a child is treated with one of the antiangiogenesis agents (eg: bevacizumab), I would transfuse the child with platelets if the platelet count dropped below:**

	Percent	Count (TOTAL 18)
10,000 plts/µl	0.00%	0
20,000 plts/µl	55.60%	10
30,000 plts/µl	16.70%	3
40,000 plts/µl	0.00%	0
50,000 plts/µl	27.80%	5
75,000 plts/µl	0.00%	0
100,000 plts/µl	0.00%	0
OTHER	0.00%	0

5. **If a child with a past history of a CNS tumor is to have a lumbar puncture, I would transfuse with platelets to maintain a count above:**

	Percent	Count (TOTAL 18)
10,000 plts/µl	0.00%	0
20,000 plts/µl	5.60%	1
30,000 plts/µl	16.70%	3
40,000 plts/µl	0.00%	0
50,000 plts/µl	72.20%	13
75,000 plts/µl	5.60%	1
100,000 plts/µl	0.00%	0
OTHER	0.00%	0

6. **Are there any other situations where you would use a particular transfusion threshold (eg: a child receiving cranial radiation; a child with infection)?**

Responses:

- At least 20,000 with infection
- 20,000 for sepsis in febrile neutropenic patients
- In a child with neutropenia, severe sepsis
- For a child on anticoagulation I would keep the number > 50,000
- Sepsis / DIC I would keep the number > 50,000

Appendix D: Tools for Application

Appropriate information and support will be provided to families so as to facilitate decision-making regarding the risks and benefits of platelet transfusion when the guideline has been approved.

Appendix E: Organizational Barriers and Cost Implications

Potential organizational barriers / cost implications to applying the recommendations found in this guideline include:

- Inability to obtain timely access to platelets

Patient / family preferences:

- Religious or other objection to platelet transfusion

Appendix F: Key Review Criteria for Monitoring and/or Audit Purposes

Key review criteria for monitoring / audit include:

- Use of platelet transfusion only for appropriate indications
- Number of children requiring platelet transfusion
- Number of children with clinically significant bleeding as a consequence of major invasive procedure