Identification and management of children with cancer and low-risk febrile neutropenia

1. Background

In children with cancer and fever and neutropenia (FN) an infection or serious medical complication is documented in less than half of all episodes. The risk of infection or complication may be assessed using the 'Swiss Paediatric Oncology Group (SPOG) risk index that has been validated at the Royal Children's Hospital, Melbourne and nationally during the Australian Predicting Infectious Complications in Children with Cancer (PICNICC) study. Children with low-risk FN may be managed safely at home with oral or intravenous antibiotics. This has been shown to improve quality of life and reduce healthcare expenditures.

2. Risk stratification

The following criteria below need to be fulfilled to be suitable for assessment with the SPOG risk index.

Table 1. Suitability for risk stratification

Criteria	Eligible	Not eligible
Neutropenia ANC of < 1.0 X 10^9/L	☐ Yes	☐ No
Fever of ≥ 38.0^{o}C	☐ Yes	☐ No
Cancer or haematological malignancy	☐ Yes	☐ No
All criteria needs to be fulfilled to continue with risk stratification		

2.1 SPOG clinical decision rule

All children admitted to hospital with fever (≥ 38.0^{o}C) and neutropenia (ANC < 1.0 x 10^9 cells/L) should be risk stratified using the SPOG clinical decision rule (CDR) (Table 2). The risk score must be documented in the medical record. This includes patients who may already be admitted and who develop FN while an inpatient and who are not already on any antimicrobials (excluding prophylactic antimicrobials). The SPOG score is based on the FBE blood results at the time of the initial onset of fever.

The SPOG rule is applied after an overnight period of observation. Total score less than 9 indicates the patient is at low risk of adverse event (AE). An AE is defined as a serious medical complication (death, complication requiring ICU and potentially life-threatening complication as judged by the treating physician) as a result of infection, microbiologically defined infection (positive bacterial or fungal culture from a normally sterile site and detection of a viral antigen by PCR) or radiologically confirmed pneumonia.

Table 2. SPOG clinical decision rule

SPOG Variables	Yes	No
Preceding chemotherapy more intensive than ALL maintenance	☐ 4	☐ 0
Admission haemoglobin ≥ 90 g/L	☐ 5	☐ 0
Admission total white cell count < 0.3 x10^9/L	☐ 3	☐ 0
Admission platelet <50 x10^9/L	☐ 3	☐ 0
TOTAL SCORE		

3. Eligibility for early transfer to Hospital-In-The-Home (HITH)

Patients with FN and identified as low risk using the SPOG rule (i.e. score <9) may be suitable for transfer to HITH within 24 hours of admission provided all the criteria are fulfilled in Table 3. The patient will require outpatient monitoring and antibiotics (Table 4), via HITH, until resolution of fever and evidence of marrow recovery (see 5.2).

In some instances, children classified as high risk (ie. SPOG score of 9 or above) may also be suitable for the low-risk program. This decision should be made by the oncology consultant and prior to transfer home, patients should have at least 24 hours of in-hospital observation and fulfil all criteria in Table 3.

Table 3: Eligibility criteria for early transfer to HITH (must be YES to all to proceed to HITH):

Criteria	**Eligible**	**Not eligible**
Disease status. Leukaemia/lymphoma in remission (as per last BMA) or solid tumour stable/responding (as per oncologist)	☐ Yes	☐ No
Disease group. Not any of: ALL induction, infant ALL, AML, post HSCT, congenital immunodeficiency, aplastic anaemia	☐ Yes	☐ No
Expected duration of neutropenia < 7 days	☐ Yes	☐ No
No confirmed focus of infection requiring inpatient care*	☐ Yes	☐ No
No medical complication requiring inpatient care**	☐ Yes	☐ No
No severe sepsis on FN presentation***	☐ Yes	☐ No
No active infection with multi-drug resistant bacteria (ie, MRSA, VRE, MDRGN)	☐ Yes	☐ No
Availability of a 24 hour caregiver	☐ Yes	☐ No
Good education of patient and carer on reportable symptoms	☐ Yes	☐ No
Availability of a telephone (with credit)	☐ Yes	☐ No
Availability of 24 hour phone advice/emergency department review from treating hospital	☐ Yes	☐ No
Within 1-hour of an emergency department or treating hospital	☐ Yes	☐ No
Treating team preference	☐ Yes	☐ No
No previous history of non-compliance with medical care	☐ Yes	☐ No

*including, *but not limited to*, CVAD site infection, cellulitis, perianal cellulitis or pain, pneumonia, colitis.
**including, *but not limited to*, pain requiring intravenous analgesia, poor oral intake or excessive loss requiring intravenous hydration; respiratory distress or oxygen requirement; pulmonary infiltrates on CXR.
***severe sepsis includes any of (i) altered conscious state, (ii) inotrope requirement, (iii) fluid bolus requirement >40ml/kg or (iv) respiratory report requirement

Table 4a. Antibiotic options for HITH

No beta-lactam allergy:
Piperacillin-tazobactam 400mg/kg/day (maximum16,000mg of piperacillin every 24 hours) intravenous continuous infusion.
Pharmacy must be notified by 10am the morning of discharge to make up infusion the same day

For patients who are well (inc. no mucositis, vomiting or diarrhoea) oral Augmentin and Ciprofloxacin can be considered instead of intravenous antibiotics. The patient should have a dose of both antibiotics prior to transfer home.
Non-life threatening beta-lactam allergy (rash): Cefepime . For patients who are well (inc. no mucositis, vomiting or diarrhoea) oral Clindamycin and Ciprofloxacin can be considered instead of intravenous antibiotics. The patient should have a dose of both antibiotics prior to transfer home. ***Life-threatening beta-lactam allergy (anaphylaxis):*** Manage as inpatient

5. HITH schedule, key responsibilities and patient point of contact

Once patient is assessed as low risk (as per the clinical decision rule) and has met all criteria for early transfer, they are referred to HITH. Transfer to HITH is recommended after a minimum of overnight observation in hospital. See Table 5 for HITH schedule.

5.1 HITH schedule and key responsibilities

The following is a recommended schedule for HITH visits and interventions (see Table 5).

- Daily visits (Day 0 is day of transfer to HITH) until suitable for discharge (see 5.2)
- Interventions to be undertaken during home visit;
    - Administer intravenous antibiotic (if applicable)
    - Blood specimens taken - FBE (all) and U&E, LFTs (as required)
    - Home assessment chart reviewed / discussed (refer to home assessment chart), including temperature, oral intake / hydration, bowel patterns
- Patients' blood results monitored daily by the HITH nurse who will liaise with the oncology treating team. The oncology inpatient registrar/resident team should also check the HITH bloods and handover any pending results to the evening/night medical team.
- Patient/family contacted by telephone by paediatric Oncology Registrar or Fellow at least once during the HITH admission for a phone review and discussion of results
- If absolute neutrophil count (ANC) remains $<0.2 \times 10^9$/L on Day 4, the patient must have medical review on Day 5 and decision made for readmission or ongoing HITH follow up.

5.2 HITH discharge criteria

Patients can be discharged from HITH when all of the following are fulfilled:

- clinically well
- no documented infection requiring ongoing antibiotics
- afebrile for >24 hours
- evidence of marrow recovery (as judged by the treating clinician), including a post nadir ANC of at least $>0.2 \times 10^9$ cells/L and platelet recovery

Table 5: HITH schedule

Day	Appointments / interventions	Responsibility
0 (day of transfer	Bloods reviewed prior to hospital discharge HITH appointments arranged Order Baxter bottles x 3 (x1 for ward, x2 for HITH)	Treating team *and* HITH nurse

	Educational material / self-assessments (temperature monitoring) provided to patient Readmission letter provided to patient	
1	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests HITH nurse to update treating team	HITH nurse
	Review of blood results and action as required	HITH nurse *and* Treating team
2	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests HITH nurse to update treating team	HITH nurse
	Review of blood results and action as required Contact pharmacy to order additional Baxters if required	HITH nurse *and* Treating team
3	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests HITH nurse to update treating team	HITH nurse
	Review of blood results	HITH nurse *and* Treating team
	Telephone follow up Blood results discussed	Treating team (O*ncology registrar or fellow)*
4	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests HITH nurse to update treating team *NB. If ANC < 0.2 x 10^9 /L and still on program, patient must have medical review on Day 5 and decision made for readmission or ongoing HITH follow up.*	HITH nurse
	Review of blood results	HITH nurse *and* Treating team
	Telephone follow up Blood results discussed	Treating team (O*ncology registrar or fellow)*
5-7	If ANC remains < 0.2 X 10^9 cells/L patient to attend hospital for medical review and decision made for readmission or ongoing HITH follow up.	HITH nurse *and* Treating team

5.3 Patient point of contact

The hospital contact number for all patients admitted to HITH on the low-risk FN program is the:

- **Business hours** (Monday to Friday from 8am to 6pm) – Children's Cancer Centre on 8572 3450
- **After hours and weekends –** 1st on call for Paediatric Oncology via hospital switchboard on 9594 6666

6. Patient resources

Patient resources should include:

- HITH brochure
- Pathology requests
- Educational material:
    - home observation and assessment chart with instructions for use
    - when to call the hospital and when to re-present to hospital
    - hospital contact numbers
    - letter for presentation to an emergency department including description of medical history, recent treatment received and current situation
- Ensure patient has a thermometer

7. Medical reviews and re-admission

A medical review and/or re-admission for in hospital care may be required for some patients on the low-risk FN program. All patients/families should receive education on symptoms and signs for review or readmission, prior to transfer to HITH.

Patients with the following criteria will require a medical review and/or readmission for inpatient care:

- Recurrent or persistent fever **(>** 48hrs from **presentation)** or new fever after being afebrile for 24 hours
- Feeling unwell / new signs and symptoms
- Significant decrease in oral intake (i.e. < 50% baseline) or significantly increased losses (vomiting or diarrhoea)
- Positive blood culture result (reported after patient hospital discharge) or other infection requiring inpatient care
- Pain: severe or persistent
- Inability to continue with oral antibiotics if applicable (i.e. allergy, vomiting, severe diarrhoea or patient refusal)
- Chills/rigors/shaking

Patients requiring review for readmission are required to present to the Children's Cancer Centre in normal business hours (Monday-Friday 8am to 4pm), or the Emergency Department (ED) after hours and on weekends. The HITH nurse and CCC AUM (during business hours) and the 1st on call for Oncology (after hours) is responsible for notifying the ED of the patient expect. The patient will be initially managed by ED according to triage category. The Paediatric Oncology team should be contacted after the patient is stabilised to discuss the plan . Patients on IV antibiotics with signs of sepsis should receive a stat dose of an Amikacin +/- Vancomycin as per the Victorian **'Fever and suspected or confirmed neutropenia' clinical practice guideline** accessed via www.rch.org.au/clinicalguideline/