



Memorial Sloan Kettering
Cancer Alliance



Management of Non-Neutropenic Fever in Pediatric Oncology Patients

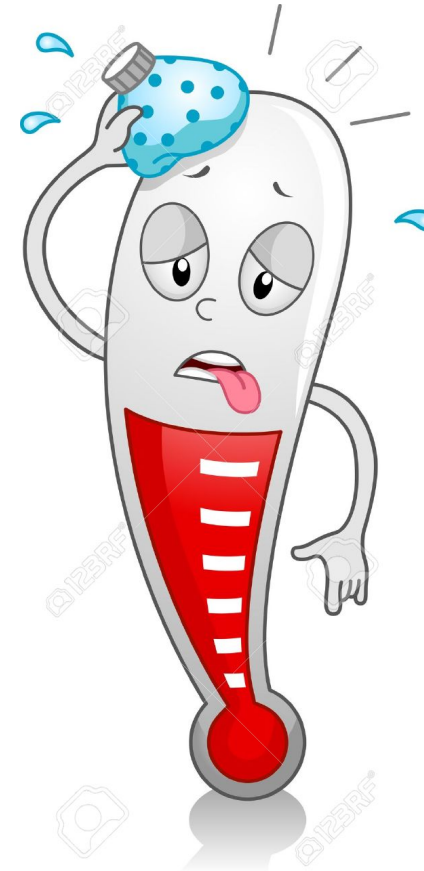
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No conflicts of interest to disclose

Fever is a common complication in pediatric oncology patients, but is not consistently defined

- Temperature $\geq 38.0^{\circ}\text{C}$
OR
- Temperature $\geq 38.0^{\circ}\text{C}$ for over an hour or $\geq 38.3^{\circ}\text{C}$
OR
- Temperature $\geq 38.0^{\circ}\text{C}$ for over an hour or $\geq 38.5^{\circ}\text{C}$



Paganini *et al.*, 2000
Esbenshade *et al.*, 2015
Wu *et al.*, 2019
Freifeld *et al.*, 2011

Fever may be caused by many etiologies, the most common of which is infection

- Infection
 - Bacterial
 - Viral
 - Fungal
- Inflammation
- Transfusion reaction
- Hemophagocytic lymphohistiocytosis (HLH)
- Medication-induced: antibiotics, chemotherapy
- Underlying malignancy
- Dysautonomia

Serious bacterial infection occurs more commonly in pediatric oncology patients, and can lead to increased morbidity and mortality

Pediatric oncology patients are at high risk for serious bacterial infections due to **underlying diagnosis** and **treatment-related side effects**

Rates of bacteremia in pediatric oncology patients presenting with fever estimated at:

- Neutropenic fever: 10 – 16.1%
- Non-neutropenic fever: 3.1 – 10.9%

Risk factors for serious bacterial infections:

- Presence of indwelling central catheter
- Quantitative or functional neutropenia
- Immune suppression
- Mucosal barrier breakdown due to mucositis

Considerations in the evaluation of pediatric oncology patients with fever

- Does the patient have an indwelling central venous catheter?
- Is patient likely to be severely neutropenic?
 - What treatment regimen is patient receiving
 - What day of cycle are they today?
 - What was their last ANC?
 - What was their ANC at this time in their last cycle?
- Does patient have other risk factors for bacteremia?
- Is there another likely explanation for etiology of fever?

While management of fever with severe neutropenia is fairly standardized, management of non-neutropenic fever varies widely

- No consensus recommendations for management of fever in patients with central venous catheters (CVC) who are not severely neutropenic
- ASPHO survey (2003): 55-69% of providers reported administering antibiotics empirically to patients with non-neutropenic fever
- Small single institution studies suggest safety of withholding empiric antibiotics:
 - Stanford: 2.5% received empiric antibiotics (all admitted due to ill appearance) – 6.1% rate of bacteremia
 - Northwestern: 17.3% empiric antibiotics – 3.4% bacteremia

Ali *et al.*, 2015
Salzer *et al.*, 2003
Wu *et al.*, 2019

Clinical risk-prediction models are being developed to predict risk of serious bacterial infection in patients with non-neutropenic fever

Clinical risk-prediction model (EsVan) –

- Patient location at presentation
- Type of CVC
- Presence of hypotension
- Presence of shaking chills
- Diagnosis of ALL vs. other
- History of HSCT
- Presence of URI symptoms
- Exposure to medication(s) known to cause fever within prior 24h
 - Cytarabine, anti-GD2 Ab, ATG
- Age
- Maximum fever
- ANC
- Absolute monocyte count (AMC)

Clinical risk-prediction models are being developed to predict risk of serious bacterial infection in patients with non-neutropenic fever

← → ↻ 🏠 cqs.app.vumc.org/shiny/RiskPrediction/



🏠 OneMSK Home - O...

Risk prediction model for the diagnosis of blood stream infection in febrile pediatric oncology patients without severe neutropenia

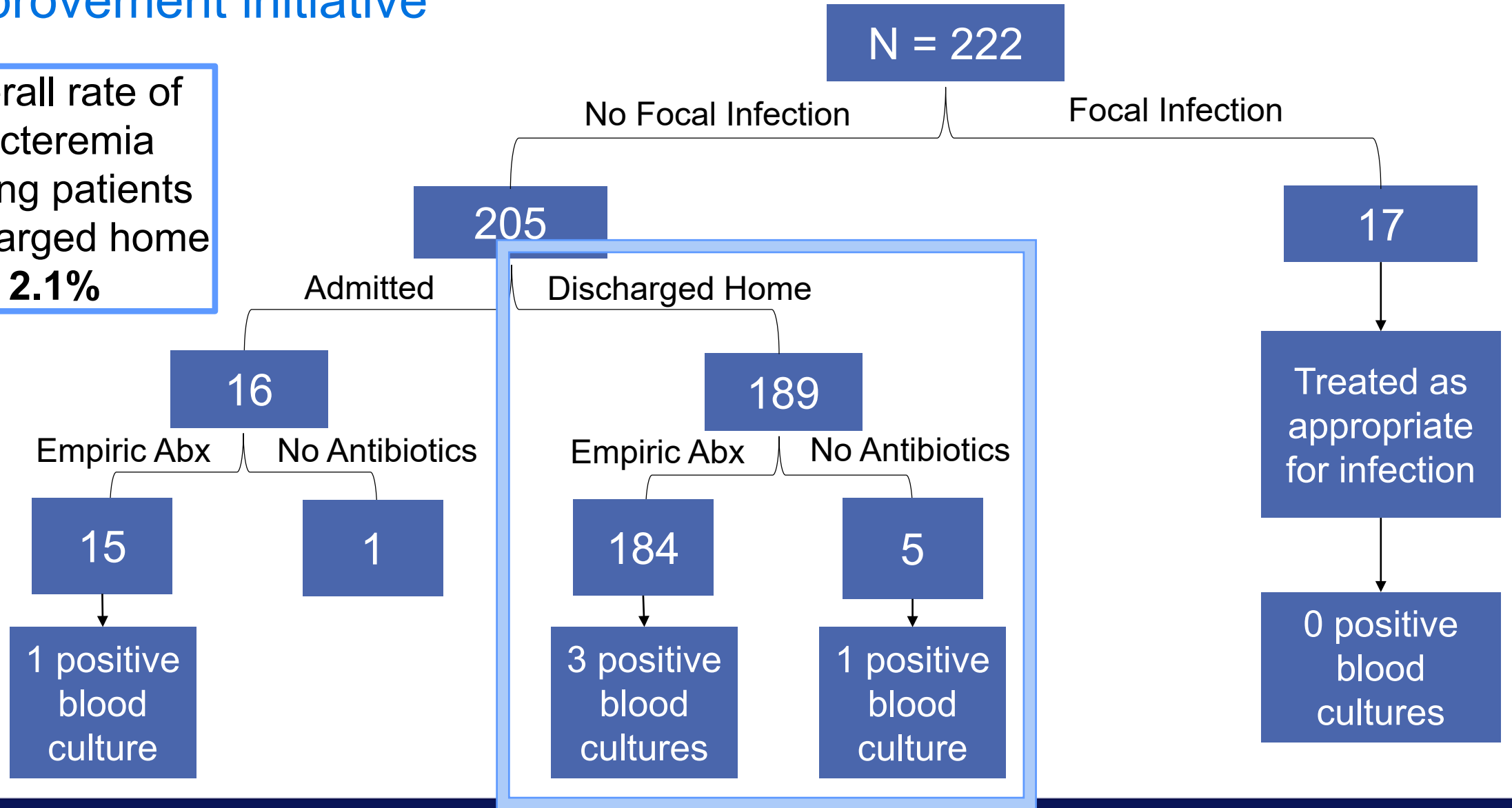
Where was the patient located at presentation? <input type="radio"/> In patient <input type="radio"/> Out patient	Did the patient have Acute lymphoblastic leukemia? <input type="radio"/> Yes <input type="radio"/> No	What is the patient's age in years? [0 - 25] <input type="text"/>
What type of central line did the subject have at presentation? <input type="radio"/> Port-A-Cath <input type="radio"/> PICC line <input type="radio"/> Hickman line	Did the patient have a history of stem cell transplant? <input type="radio"/> Yes <input type="radio"/> No	Body temperature unit <input type="text" value="Please select"/>
Was Hypotension present? <input type="radio"/> Yes <input type="radio"/> No	Did the patient have upper respiratory symptoms? <input type="radio"/> Yes <input type="radio"/> No	What was the Absolute Neutrophil Count (ANC)? [cells/uL, 500 - 45000] <input type="text"/>
Did the patient have shaking chills or rigors? <input type="radio"/> Yes <input type="radio"/> No	Did the patient have drug exposure to cytarabine, ATG, or Anti-GD2 within 24 hours of presentation? <input type="radio"/> Yes <input type="radio"/> No	Was the absolute monocyte count available at the time of presentation? <input type="radio"/> Yes <input type="radio"/> No
		<input type="button" value="Generate Prediction based on ESVAN2"/> <input type="button" value="Reset"/>

→ Predicted risk of bloodstream infection

Esbenshade *et al.*, 2020

Decreasing empiric antibiotic administration: a single center quality improvement initiative

Overall rate of bacteremia among patients discharged home **2.1%**



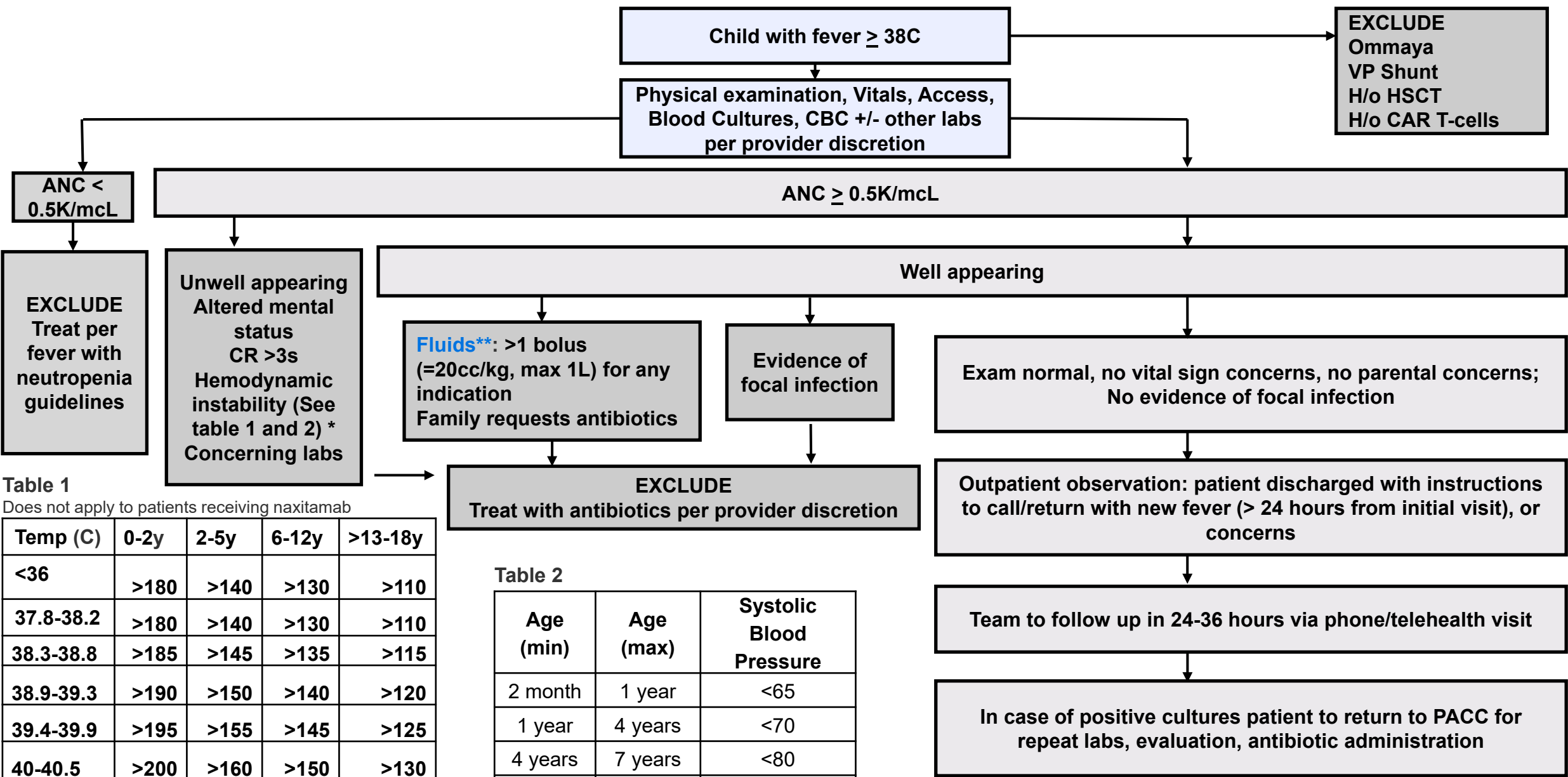


Table 1
Does not apply to patients receiving naxitamab

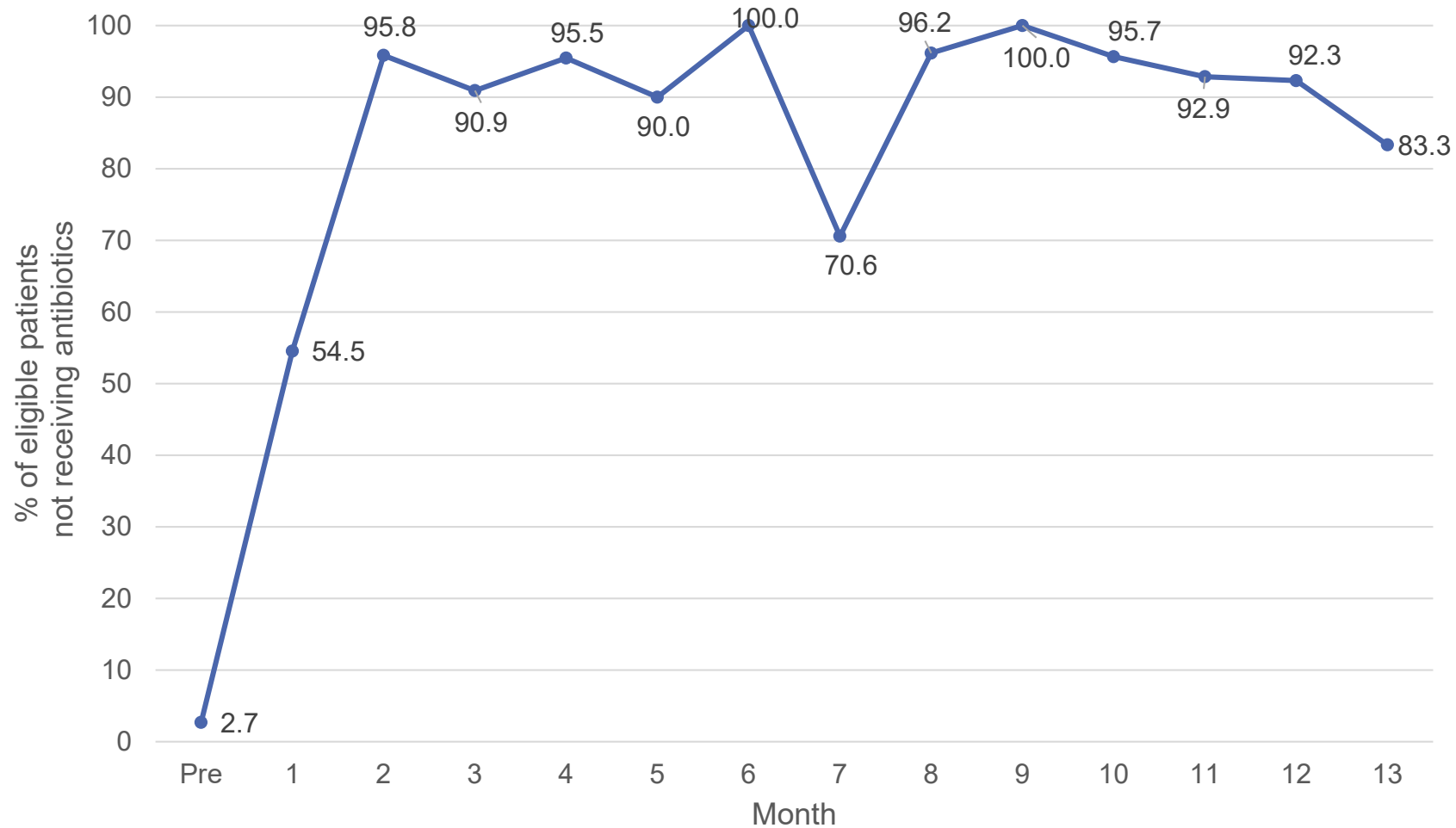
Temp (C)	0-2y	2-5y	6-12y	>13-18y
<36	>180	>140	>130	>110
37.8-38.2	>180	>140	>130	>110
38.3-38.8	>185	>145	>135	>115
38.9-39.3	>190	>150	>140	>120
39.4-39.9	>195	>155	>145	>125
40-40.5	>200	>160	>150	>130
40.6-41	>205	>165	>155	>135
>41.1	>210	>170	>160	>140

Table 2

Age (min)	Age (max)	Systolic Blood Pressure
2 month	1 year	<65
1 year	4 years	<70
4 years	7 years	<80
7 years	13 years	<85
13 years	18 years	<85

**This does NOT include patients who are well-appearing and receive ≤1 bolus (≤20cc/kg, maximum 1L) for treatment of dehydration

Decreasing empiric antibiotic administration: a single center quality improvement initiative



Decreasing empiric antibiotic administration: a single center quality improvement initiative

Bacteremia: Pre-intervention
2.1%

Event: **5.1% (11/217)**

Serious adverse event: **0% (0/217)**

Conclusions

- (1) Fever is a common complication in pediatric oncology
- (2) Pediatric oncology patients have many risk factors for serious bacterial infections
- (3) Empiric antibiotics may be safely withheld in selected patients with non-neutropenic fever assessed to be at low risk of bacteremia

Thank you!

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MSK Kids MDs, APPs,
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Patients and families