COG Cancer Control and Supportive Care Infectious Diseases Survey

The Children's Oncology Group (COG) Cancer Control and Supportive Care Committee (CCL) Infectious Diseases and Inflammation Subcommittee has created a survey that investigates the current management of a variety of infectious complications of cancer therapy. The survey is voluntary.

The goals of the survey are to define the current variability in practice across institutions to identify research opportunities that could be addressed by the COG CCL Infectious Disease Committee in the future. We think this information will be useful to the oncology community and so would plan to publish this data as a de-identified survey. The IRB of record for this study is the Vanderbilt IRB and the study is being done in support of the Children's Oncology Group (COG) Cancer Control and Supportive Care Committee (CCL) Infectious Diseases and Inflammation Subcommittee.

We are specifically reaching out to you as you are either the CCL Responsible Investigator for your site or else the COG PI if your site does not yet have a CCL Responsible Investigator (If you don't have one contact us if you would like to appoint one).

To fully understand the breadth of infection management, we hope to receive one survey response from each COG institution, and we would greatly appreciate if you would complete this survey. The survey should take approximately 15 minutes to complete. Please do your best to answer questions based on what you perceive to be the most common management practices at your institution, however, if a given question asks about a topic for which there is no consensus at your institution, then please answer based on your individual management practice.

If you believe that a different individual at your institution is better equipped to complete this survey, please feel free to delegate completion of the survey to them. This survey has been approved for distribution by COG leadership. We hope you will complete this survey and look forward to collectively learning about how infectious complications of pediatric cancer therapy are managed across the COG.

There is an option to save the survey and obtain a return code to update your responses if you need to confer with others to fully fill it out.

If there are questions about this survey please email, Adam Esbenshade adam.esbenshade@vumc.org

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Please state what COG institution you represent.

This information will be fully de-identified for analysis, however, responses will be grouped by geographic region. This is being assessed to ensure that responses from each institution are only included once.

_____

What is your role at your institution?

This survey should be preferentially completed by a site's CCL RI, or COG PI if a site does not have a CCL RI. However, the COG RI or PI can designate someone else to complete the survey if they would have more applicable expertise.

◯ COG CCL Responsible Investigator (RI)
◯ COG PI
◯ Other (Designated by the COG PI or CCL RI)

What other role do you have at your institution?

_____

How many new diagnoses of cancer does your institution treat each year?

- ◯ < 10 per year
- ◯ 10-50 per year
- ◯ 51-100 per year
- ◯ 101-200 per year
- ◯ >200 per year
- ◯ Not sure

How many oncology attendings rotate through the inpatient oncology service at your institution?

- ◯ < 5
- ◯ 5-10
- ◯ 11-20
- ◯ 20-30
- ◯ 30-40
- ◯ >40

Were you previously aware that COG has officially endorsed Clinical Practice Guidelines (CPGs) to be used in infection management?

- ◯ Yes
- ◯ No

Which of the following COG endorsed CPGs does your institution utilize? (please check all that apply)

COG CPG link:
https://childrensoncologygroup.org/cog-supportive-care-endorsed-guidelines

- ☐ Antibacterial prophylaxis
- ☐ Antifungal prophylaxis
- ☐ Clostridium (now called Clostridioides) difficile Infection
- ☐ Fever and neutropenia
- ☐ None are actively utilized
- ☐ Unsure

What ANC value does your site use as a threshold for treating febrile neutropenia?

- ◯ ANC< 1000
- ◯ ANC< 500
- ◯ ANC< 200
- ◯ ANC< 100
- ◯ Other

How does your site define severe neutropenia?

_____

The next section concerns the management of pediatric oncology patients presenting with fever, and severe neutropenia (defined as ANC < 500). Assume all patients have a central line in place.

NOTE:
-This section and general survey do not apply to patients who are have undergone hematopoietic stem cell transplant or CAR T cell therapy

For febrile neutropenia (F&N; ANC< 500) in pediatric oncology patients, how does your institution define fever?

- ◯ Temperature 38.0 sustained for at least 1 hour or at least 38.3 once
- ◯ Temperature of at least 38.5
- ◯ Temperature of at least 39.0
- ◯ Other (If other temperature cutoff or more than one of the above is used, select this option and then specify)

What is your institution's definition of fever?

_____

For F&N in oncology patients, how is count recovery for stopping antibiotics defined at your institution?

(i.e. ANC threshold when antibiotics are stopped unless another source of infection is present, this does not refer to count recovery required for bone marrow evaluation)

- ◯ We do not require any level of count recovery in order to stop antibiotics
- ◯ ANC 100 and rising
- ◯ ANC 200 and rising
- ◯ ANC 500 and rising
- ◯ No specific number but 2 days ANC rising
- ◯ APC >500
- ◯ Other (select this option if: other definition used, value varies for different patient populations , OR if more than one of the above, then specify)

How does your institution define count recovery?

_____

In order to meet the time-to-antibiotic (TTA) < 60 minutes metric, which common technique(s) are used at your site if necessary?
(Select all that apply)

- ☐ Giving empiric ceftriaxone prior to receiving CBC results
- ☐ Giving empiric anti-pseudomonal antibiotic prior to receiving CBC results
- ☐ Giving intramuscular injection if access not obtained in < 60 minutes
- ☐ Giving empiric antibiotic prior to drawing blood cultures if cultures were not obtained in < 60 minutes
- ☐ No specific technique is followed
- ☐ I do not know what the 60-minute TTA metric is
- ☐ Other

What other common techniques are used in order to try to meet the TTA metric?

_____

Does your site use a specific risk stratification tool or protocol to determine management for oncology patients presenting with F&N as opposed to giving the same management to all?

- ◯ Yes
- ◯ No

Which risk stratification tool or protocol is being used?

_____

At your institution, which of the following tests are routinely ordered at initial presentation for an oncology patient with F&N who is not ill-appearing? (This includes tests that would be ordered after a CBC proved ANC < 500)
(Please check all that apply)

- ☐ Complete blood count with differential
- ☐ Central line blood culture
- ☐ Peripheral blood culture
- ☐ Liver enzymes (AST/ALT)
- ☐ BMP (Electrolyte panel)
- ☐ Serum lactate
- ☐ Procalcitonin
- ☐ C-reactive protein
- ☐ Cytokine panel
- ☐ Respiratory viral panel (if respiratory symptoms)
- ☐ Respiratory viral panel (even if no respiratory symptoms)
- ☐ Chest xray (if respiratory symptoms)
- ☐ Chest xray (even if no respiratory symptoms)
- ☐ Urine culture (if urinary symptoms)
- ☐ Urine culture (even if no urinary symptoms)
- ☐ Cell free DNA test (such as Karius)
- ☐ Beta d glucan
- ☐ Galactomannan
- ☐ SARS-COV-2 test (if respiratory symptoms)
- ☐ SARS-COV-2 test (even if no respiratory symptoms)
- ☐ Flu test if in season (if respiratory symptoms)
- ☐ Flu test if in season (even if no respiratory symptoms)
- ☐ Other

What other tests are routinely ordered at presentation in a pediatric oncology patient with F&N?

_____

Which empiric antibiotic is most commonly used at your site for oncology patients with F&N? (Assuming the patient is not ill-appearing and has no focal source of infection.)

- ◯ Cefepime
- ◯ Piperacillin-tazobactam
- ◯ Meropenem or imipenem
- ◯ Ceftazidime
- ◯ Ceftriaxone
- ◯ Other (Select if other antibiotic is used or if antibiotic choice varies by risk stratification)

What other antibiotic is most commonly used for empiric management for pediatric oncology patients presenting with F&N?

_____

If a patient with F&N is critically ill on presentation what is the most common empiric antibiotic(s) used? (select all that apply)

- ☐ Cefepime
- ☐ Piperacillin-tazobactam (Zosyn)
- ☐ Meropenem or Imipenem
- ☐ Ceftazidime
- ☐ Ceftriaxone
- ☐ Vancomycin
- ☐ Gentamicin, Amikacin, or another aminoglycoside
- ☐ Other (Select if other antibiotic is used, or if antibiotic choice varies by risk stratification)

What other antibiotic(s) is most commonly used for empiric management for patients with F&N who are critically ill at presentation?

_____

For which of the following reasons would your site commonly add Vancomycin to empiric management? (select all that apply)

- ☐ Severely ill-appearing at presentation
- ☐ Concern for a source that could be gram positive (known abscess or pneumonia)
- ☐ Receiving high dose Cytarabine (in setting of acute myeloid leukemia)
- ☐ Severe mucositis
- ☐ Local high prevalence of resistant gram positive infections
- ☐ History of recent gram positive infection
- ☐ Persistent fever lasting over 48 hours
- ☐ Other

For what other reason would your site commonly add Vancomycin to empiric management?

_____

In what settings would your site empirically broaden antibiotics to cover anaerobic organisms ? (check any that apply)

- ☐ Mucositis
- ☐ Significant abdominal pain or concern for neutropenic colitis
- ☐ Peri-rectal pain
- ☐ Cellulitis
- ☐ Severely ill-appearing
- ☐ We don't broaden coverage since our standard empiric therapy already effectively covers anaerobic organisms
- ☐ Other

In what other settings would your site empirically broaden antibiotics to cover anaerobic organisms?

_____

At your institution is there a risk tool or protocol that identifies low-risk patients with F&N who are eligible for outpatient management?

- ◯ Yes, they can be sent home without admission after initial evaluation for febrile neutropenia on oral antibiotics
- ◯ Yes, they can be sent home without admission after initial evaluation for febrile neutropenia on IV antibiotics
- ◯ Yes patients are initially admitted, but are sent home on oral antibiotics prior to 48 hours of negative cultures
- ◯ No, we admit all of our febrile neutropenia patients for at least 48 hours
- ◯ Other

At your institution what other risk tool or protocol is used to identify low-risk patients with F&N who are eligible for outpatient management?

_____

Note: The next few questions refer to patients with or without a high-risk (HR) diagnosis for infection such as: AML, relapsed ALL during intensive phases, HR ALL.

Please select the most common management approach at your site for the following scenario:

An oncology patient (without a HR diagnosis) is admitted with F&N and has now been afebrile>24 hours, has negative cultures x48 hours, and is not ill appearing. The patient's ANC remains 0 with no signs of count recovery.

- ◯ Continue IV antibiotics until count recovery
- ◯ Stop empiric IV antibiotics with immediate hospital discharge
- ◯ Stop empiric IV antibiotics and then observe off antibiotics inpatient until count recovery
- ◯ Stop empiric IV antibiotics and then watch for short period (12-48 hours) and discharge if still not ill appearing
- ◯ Stop empiric IV antibiotics and send home on oral antibiotics until count recovery
- ◯ Other

What other management is used at your site for an oncology patient without a HR diagnosis with F&N who is now afebrile >24 hours, has negative cultures x48 hours, and is not ill appearing, but has no signs of count recovery?

_____

For a patient with a HR diagnosis who developed fever during induction, do providers at your institution ever stop empiric IV antibiotics prior to count recovery?

Note: This assumes the patient is now afebrile, has negative blood cultures >48 hours, and is well-appearing.

- ◯ No, We always continue empiric antibiotics until count recovery
- ◯ Yes, We would usually stop empiric antibiotics in this situation
- ◯ Yes, We would usually stop empiric antibiotics but after empiric antibiotics have been administered for at least 7 days
- ◯ Other

What other management is used regarding stopping IV antibiotics for a patient with a HR diagnosis that developed fever during induction and is now well-appearing and afebrile with negative cultures?

_____

When you do stop empiric IV antibiotics prior to count recovery, do you:

- ◯ Return immediately to antibacterial prophylaxis, keep in hospital until count recovery
- ◯ Return immediately to antibacterial prophylaxis consider hospital discharge prior to count recovery
- ◯ Continue to observe off antibiotics, keep in hospital until count recovery
- ◯ Continue to observe off antibiotics, consider hospital discharge prior to count recovery
- ◯ Other

What other practice is most common at your site when empiric IV antibiotics are stopped prior to count recovery in the above scenario?

_____

For patients with F&N with persistent fever >96 hours, which oncology patients (non-BMT) are standardly evaluated for potential fungal infection?

- ◯ All oncology patients with febrile neutropenia
- ◯ Oncology patients who meet a specified criteria to be at high risk of developing a fungal infection

In patients with F&N with persistent fever >96 hours for whom it has been decided needs a fungal evaluation, which of the following is done at your site?

- ◯ Start empirical antifungal therapy only without doing any fungal diagnostic evaluation at that time
- ◯ Start empirical antifungal therapy and wait until count recovery to do additional diagnostic evaluation (e.g. "count recovery scans")
- ◯ Perform fungal diagnostic evaluation at that time AND start empirical antifungal therapy regardless of diagnostic evaluation results
- ◯ Perform fungal diagnostic evaluation at that time and only start antifungal therapy if the diagnostic evaluation is concerning for a fungal infection
- ◯ Other

What other approach is used to decide on when to start antifungal therapy?

_____

Which of the following is part of your site's standard testing for an oncology patient with F&N and persistent fever >96 hours? For this question only select things done for most patients if feasible. (Please check all that apply)

- ☐ CT Scan of the Chest
- ☐ CT Scan of the Abdomen/Pelvis
- ☐ Ultrasound of the Abdomen
- ☐ MRI Abdomen/Pelvis
- ☐ CT Scan of the Sinuses
- ☐ Beta D-glucan Test
- ☐ Galactomannan Test
- ☐ Cell free DNA test (such as Karius)
- ☐ Respiratory viral panel
- ☐ Blood PCR tests (such as CMV, Adenovirus)
- ☐ Bedside nasal scope by ENT
- ☐ Other

What other testing is done as part of the standard persistent fever workup?

_____

In what scenario(s) would the infectious disease (ID) team at your site commonly be consulted? (Select all that apply)

- ☐ Prolonged fever without focal source of infection
- ☐ Confirmed fungal infection
- ☐ We do not have an infectious disease team at our site
- ☐ Confirmed central line infection
- ☐ We consult ID for all patients with F&N
- ☐ Other

In what other scenarios would the infectious disease team be consulted at your institution?

_____

This next sections deals with management of non-neutropenic fever (ANC>500) in oncology patients (not BMT patients) at your institution.
NOTE: Assume all patients have a central line in place

What is the most common management at your institution for oncology patients with fever without neutropenia (ANC >500) who are not ill-appearing? (Assuming ANC result is available in < 60 minutes of presentation)

- ◯ Deliver empiric IV antibiotics prior to CBC results being available
- ◯ Deliver empiric IV antibiotics after CBC results are available
- ◯ Deliver empiric PO antibiotics after CBC results are available
- ◯ Withhold initial empiric antibiotics if a model or risk stratification tool suggests the patients are low-risk of a bacterial infection
- ◯ Withhold initial empiric antibiotics based on the patient being well appearing
- ◯ Other strategy

What other strategy is followed for oncology patients with fever without neutropenia (ANC >500)?

_____

If an empiric antibiotic is given, what agent is used at your site for pediatric oncology patients with non-neutropenic fever?

- ◯ Ceftriaxone
- ◯ Cefepime
- ◯ Piperacillin-Tazobactam
- ◯ Meropenem or other Carbapenem
- ◯ Other

What other empiric antibiotic is most commonly given for non-neutropenic fever?

_____

This next section asks about antibacterial prophylaxis at your institution. Please select common prophylaxis approaches at your institution for different patient groups during phases of prolonged neutropenia.
This is not referring to PJP prophylaxis.

	AML	Relapsed ALL (intensive phases)	High-risk ALL during 4 drug induction	Down syndrome with leukemia (intensive phases)	Infant ALL (intensive phases)
We typically use a quinolone	☐	☐	☐	☐	☐
We typically use an agent other than a quinolone	☐	☐	☐	☐	☐
None. We don't routinely use antibacterial prophylaxis in this patient group	☐	☐	☐	☐	☐
Variable, depends on the provider or the situation	☐	☐	☐	☐	☐

What other agent does your institution routinely use for antibacterial prophylaxis in patients with AML?

_____

What other agent does your institution routinely use for antibacterial prophylaxis in patients with relapsed ALL during intensive phases?

_____

What other agent does your institution routinely use for antibacterial prophylaxis in patients with High-risk ALL during 4 drug induction?

_____

What other institution does your institution routinely use for antibacterial prophylaxis in patients with Down Syndrome and leukemia during intensive phases?

_____

What other agent does your institution routinely use for antibacterial prophylaxis in patients with infant ALL?

_____

Are there other patient groups for which your institution routinely uses antibiotic prophylaxis? If yes, please describe.

_____

When are patients with AML typically placed on antibacterial prophylaxis at your institution?

- ☐ Only during periods of neutropenia (ANC< 500) or expected neutropenia
- ☐ Only during periods of neutropenia defined as a cutoff other than ANC< 500
- ☐ Starting on Day 1 of each chemotherapy cycle through count recovery
- ☐ Throughout the entirety of treatment, including between cycles
- ☐ Other

Please describe when AML patients placed on antibacterial prophylaxis at your institution.

_____

At your site, which of the following patient populations who receive chemotherapy (not including BMT patients), but do not develop a fever, are kept in the hospital through neutrophil nadir until count recovery?

	Yes we keep them until count recovery	No, we send them home on antibacterial prophylaxis	No, we send them home off antibiotics	Not applicable
AML (specifically in Induction 1)	○	○	○	○
AML (In cycles after Induction 1)	○	○	○	○
Infant ALL	○	○	○	○
Down syndrome with leukemia (during periods of intensive therapy)	○	○	○	○
Relapsed ALL (receiving intense chemotherapy)	○	○	○	○
Infant brain tumors (receiving intense chemotherapy)	○	○	○	○

At your institution, are there any other patient groups that are kept in the hospital through neutrophil nadir until count recovery that are not listed above?

_____

Does your site currently use a standard Chlorhexidine (CHG) cleaner (wipes, liquid or foam) for pediatric oncology patients to prevent infections?

- ◯ Yes in all admitted pediatric oncology patients
- ◯ Yes but only in subset of pediatric oncology patients
- ◯ No, we do not use CHG in pediatric oncology patients
- ◯ Unsure

Did your institution previously use CHG?

- ◯ Yes, but then stopped using them
- ◯ No, CHG was never used at our institution
- ◯ Not sure

In which subset of pediatric oncology patients are CHG wipes being used?

_____

If not using a CHG based bathing strategy what strategy is used. Soap/water baths or other?

_____

What is the preferred second line therapy for Pneumocystis jirovecii prophylaxis if TMP/SMX was stopped for non-allergy reasons (ex: prolonged count suppression)?
(Please rank 1-5 with order of preference, can assign same number if all choices are at equal preference)

	1	2	3	4	5	Never use this
Rechallenge with trimethoprim/sulfamethoxazole (bactrim/septra)	◯	◯	◯	◯	◯	◯
Dapsone	◯	◯	◯	◯	◯	◯
Atovaquone	◯	◯	◯	◯	◯	◯
Inhaled pentamidine (unless patient is too young to comply)	◯	◯	◯	◯	◯	◯
Intravenous pentamidine	◯	◯	◯	◯	◯	◯

At your institution, when is PJP prophylaxis discontinued?

- ◯ 1 month after completion of chemotherapy
- ◯ 3 months after completion of chemotherapy
- ◯ 6 months after completion of chemotherapy
- ◯ Provider and/or Diagnosis dependent
- ◯ Other

When is PJP prophylaxis discontinued at your institution?

_____

Select the most accurate statement regarding G-CSF use to hasten count recovery in typical patients with hematologic malignancy and persistent F&N. (Assume the patient is in remission)

- ◯ We do not use G -CSF in patients with hematologic malignancy
- ◯ We use it commonly to expedite count recovery
- ◯ We use it occasionally in patients who have severe infection (such as in the ICU)
- ◯ We use it occasionally in higher risk patients (such as relapsed ALL)
- ◯ Other (or check here if multiple of the above apply)

Please clarify how your site uses G-CSF in patients with hematologic malignancy who have persistent febrile neutropenia. _____

This next section asks about antifungal prophylaxis:

Which agent does your center typically use for antifungal prophylaxis in the following patient groups during periods of prolonged neutropenia?
Check all that apply.

	Newly diagnosed AML	Relapsed AML	Newly diagnosed High Risk ALL	Relapsed ALL
Fluconazole	☐	☐	☐	☐
Voriconazole	☐	☐	☐	☐
Isavuconazole	☐	☐	☐	☐
Posaconazole	☐	☐	☐	☐
Micafungin or Caspofungin	☐	☐	☐	☐
Amphotericin	☐	☐	☐	☐
None	☐	☐	☐	☐
Other	☐	☐	☐	☐

What other fungal prophylaxis is used in patients with newly diagnosed AML? _____

What other fungal prophylaxis is used in patients with relapsed AML? _____

What other fungal prophylaxis is used in patients with newly diagnosed high risk ALL? _____

What other fungal prophylaxis is used in patients with relapsed ALL? _____

For which of the following subsets of ALL (non-relapsed) does your center usually give antifungal prophylaxis? Check all that apply.

	High risk B ALL	Standard risk B ALL	T ALL	Down Syndrome ALL	Infant ALL
Induction	☐	☐	☐	☐	☐
Consolidation	☐	☐	☐	☐	☐
Delayed intensification (or other intense phases)	☐	☐	☐	☐	☐
Periods of prolonged neutropenia	☐	☐	☐	☐	☐
None. We don't use antifungal prophylaxis	☐	☐	☐	☐	☐

Variable. Depends on the provider or the situation	☐	☐	☐	☐	☐

If there are other groups that your site typically uses antifungal prophylaxis for, please specify here.

_____

For patients receiving an azole (fluconazole, voriconazole, or posaconazole) for prophylaxis, does your institution hold their azole around the time of their vincristine?

- ◯ Yes, we hold azole prophylaxis for patients receiving vincristine
- ◯ No, we do not hold azole prophylaxis around the time of vincristine
- ◯ We do not use azoles for fungal prophylaxis in patients receiving vincristine
- ◯ Other, we do something else

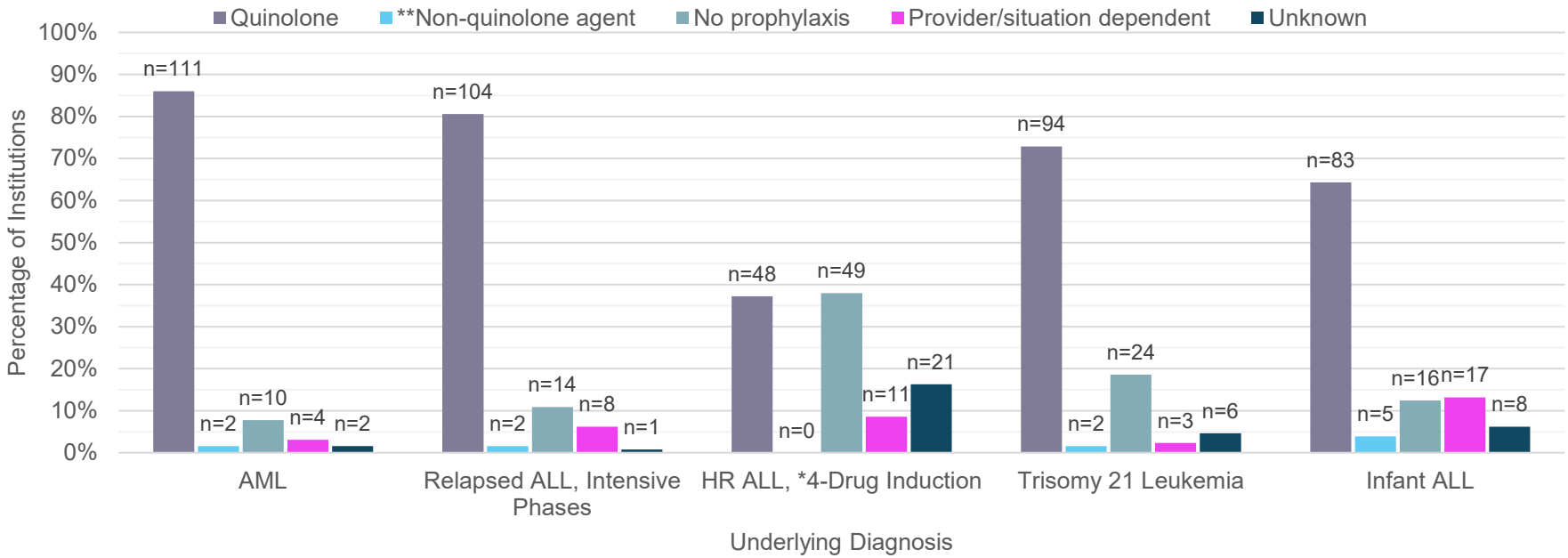
What does your institution do with azole prophylaxis around the time of vincristine and report if there has been significant toxicity with this approach?

_____

Please list what are the major research gaps for pediatric oncology infection management that still need to be answered conclusively?

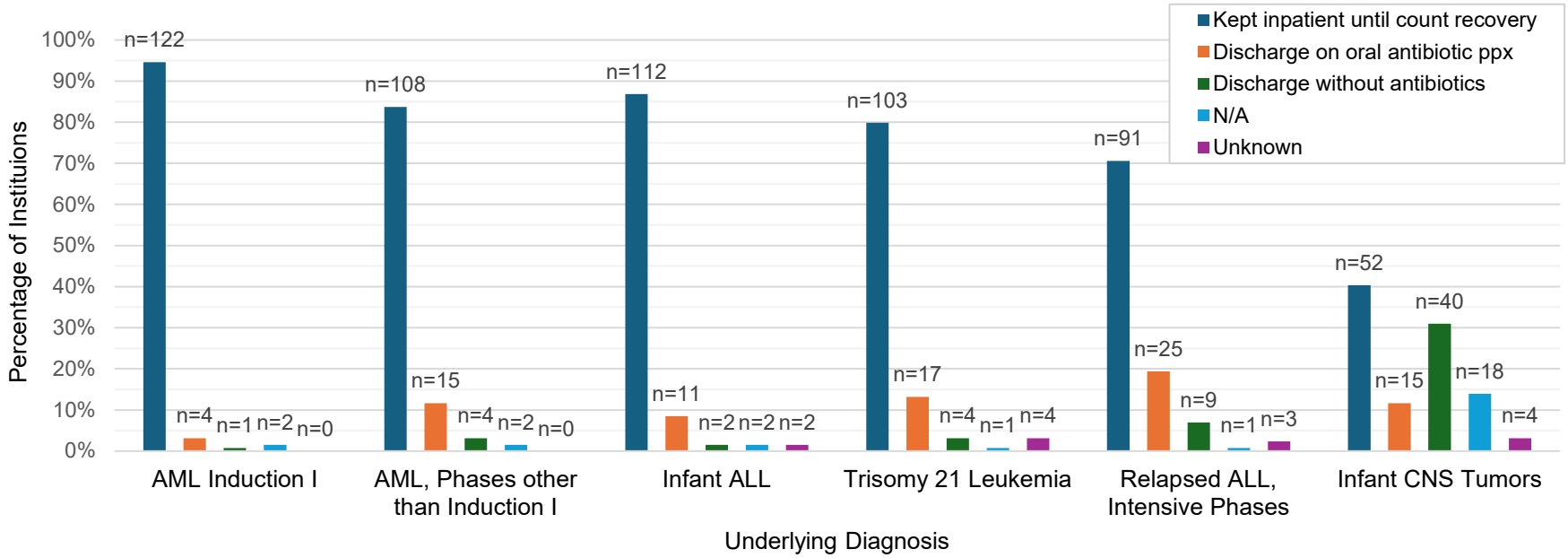
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Supplemental Figure 1: Antibacterial Prophylaxis Administration by Patient Population (n=129)



Abbreviations: AML=Acute myeloid leukemia; ALL=Acute lymphoblastic leukemia; HR=High risk
*4-drug induction includes: Corticosteroids, vincristine, asparaginase, anthracycline
**Non-quinolone agents include: AML: Cefepime (n=2); Relapsed ALL: Cefepime (n=1), Unknown (n=1); Down syndrome leukemia: Cefepime (n=2); Infant ALL: Cefepime (n=2), Unknown (n=3)

Supplemental Figure 2: Practices for Keeping Patients Admitted through Count Recovery (n=129)



Abbreviations: AML=Acute myeloid leukemia; ALL=Acute lymphoblastic leukemia; CNS=Central nervous system; ppx=Prophylaxis

Supplemental Figure 3: Next Line Alternative if Sulfamethoxazole-trimethoprim is Held for Non-allergy Reasons (n=129)

