Fred Hutch Cancer Center

Follow Up Blood Cultures: When are They Needed?

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Disclosures

I have no financial relationships relevant to this presentation to disclose.

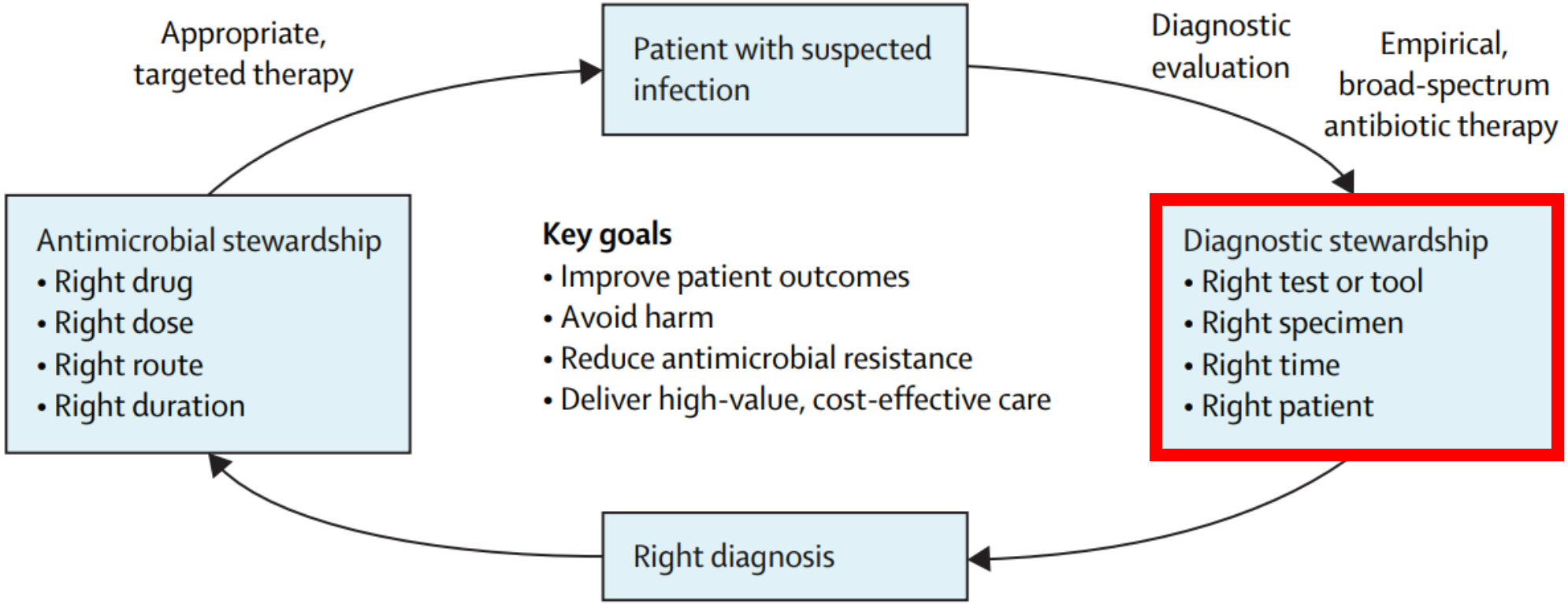
Outline

1. Brief overview of blood culture diagnostic stewardship

2. Review common indications for follow-up blood cultures… and areas of controversy

3. Blood culture stewardship in patients who are immunocompromised

Diagnostic stewardship advances antimicrobial stewardship



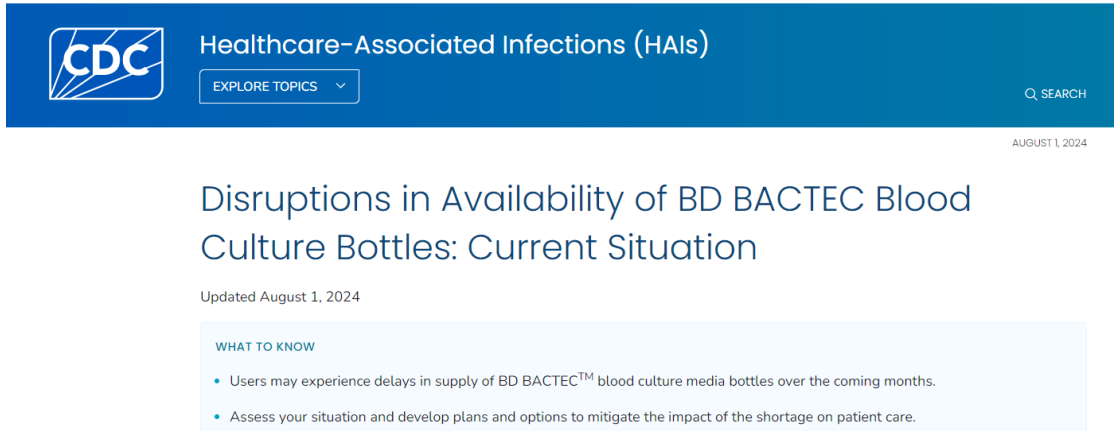
Liu *Lancet Infect Dis* 2025.

Importance of blood culture stewardship

Unnecessary blood cultures may lead to:

- Contaminant detection → excess antibiotics
- Misclassification of central line-associated infections (CLABSI)
- Iatrogenic anemia
- Increased length of hospital stay
- Increased healthcare costs

Image credit cdc.gov



Fabre *J Clin Microbiol* 2022; Singh *ICHE* 2024; Morgan *JAMA* 2023.

Definitions for this talk

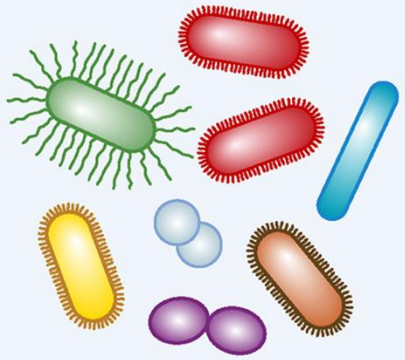
Initial blood cultures – ordered for a new clinical event

Repeat blood cultures* – ordered following negative blood cultures when there is on-going concern for infection

Follow-up blood cultures* – ordered following positive blood cultures to document clearance

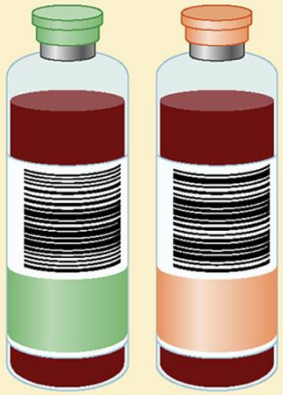
*These terms are often used interchangeably in the literature.

Key considerations when ordering blood cultures



1) Is there an infection that requires blood cultures?

- Yes for severe sepsis/septic shock and syndromes with high or moderate risk of bacteremia
- If the above not present and the triggering event is fever; what are the other clinical findings? What other tests/cultures could be more useful?



Follow-up

2) Are ~~repeat~~ blood cultures needed? Consider:

- Source control and response to therapy
- Causative pathogen (always yes for *S. aureus*, usually not for Enterobacterales or *S. pneumoniae* if source control and clinical response)
- Type of infection (always yes for endovascular infection)

Fabre *Journal of Clin Microbiol* 2022.

Staph aureus bacteremia: evidence supporting follow-up blood cultures

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Defining the Breakpoint Duration of *Staphylococcus aureus* Bacteremia Predictive of Poor Outcomes

Emi Minejima,[1,2] Nikki Mai,[1] Nancy Bui,[1] Melissa Mert,[3] Wendy J. Mack,[4] Rosemary C. She,[5] Paul Nieberg,[6] Brad Spellberg,[2,7] and Annie Wong-Beringer[1,8]

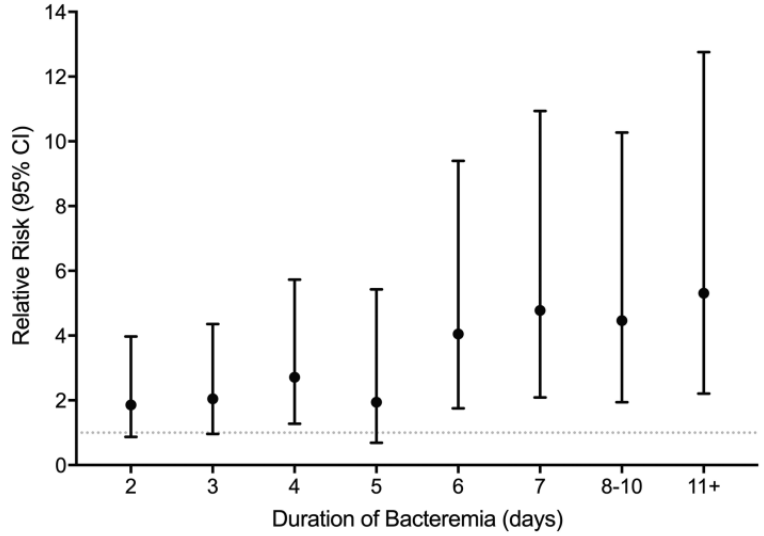
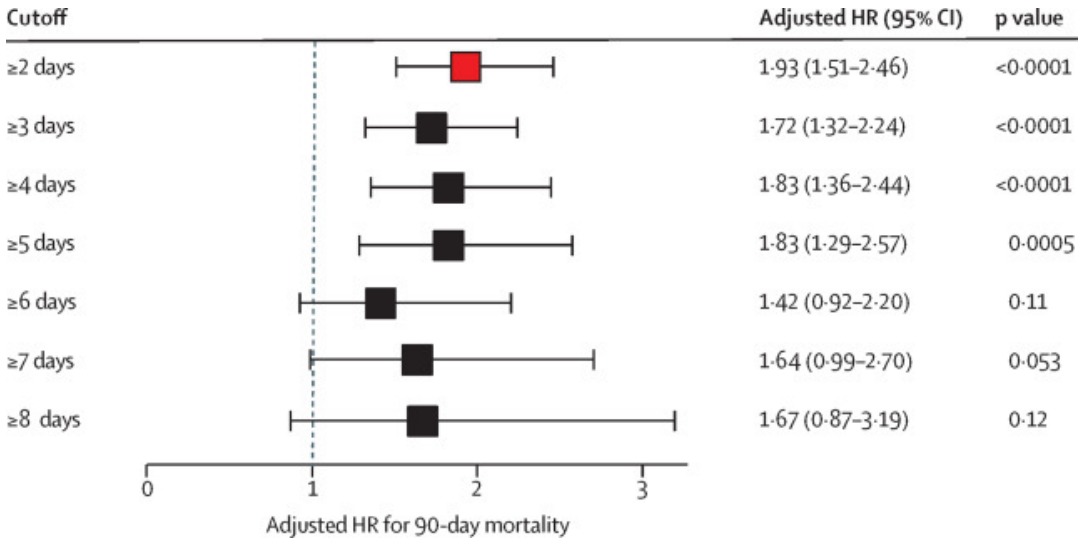


Figure 1. Relative risk (95% confidence interval) of mortality by duration of bacteremia (N = 884). The numbers of days of infection at 8–10 and 11+ were collapsed to account for the observed sample sizes.

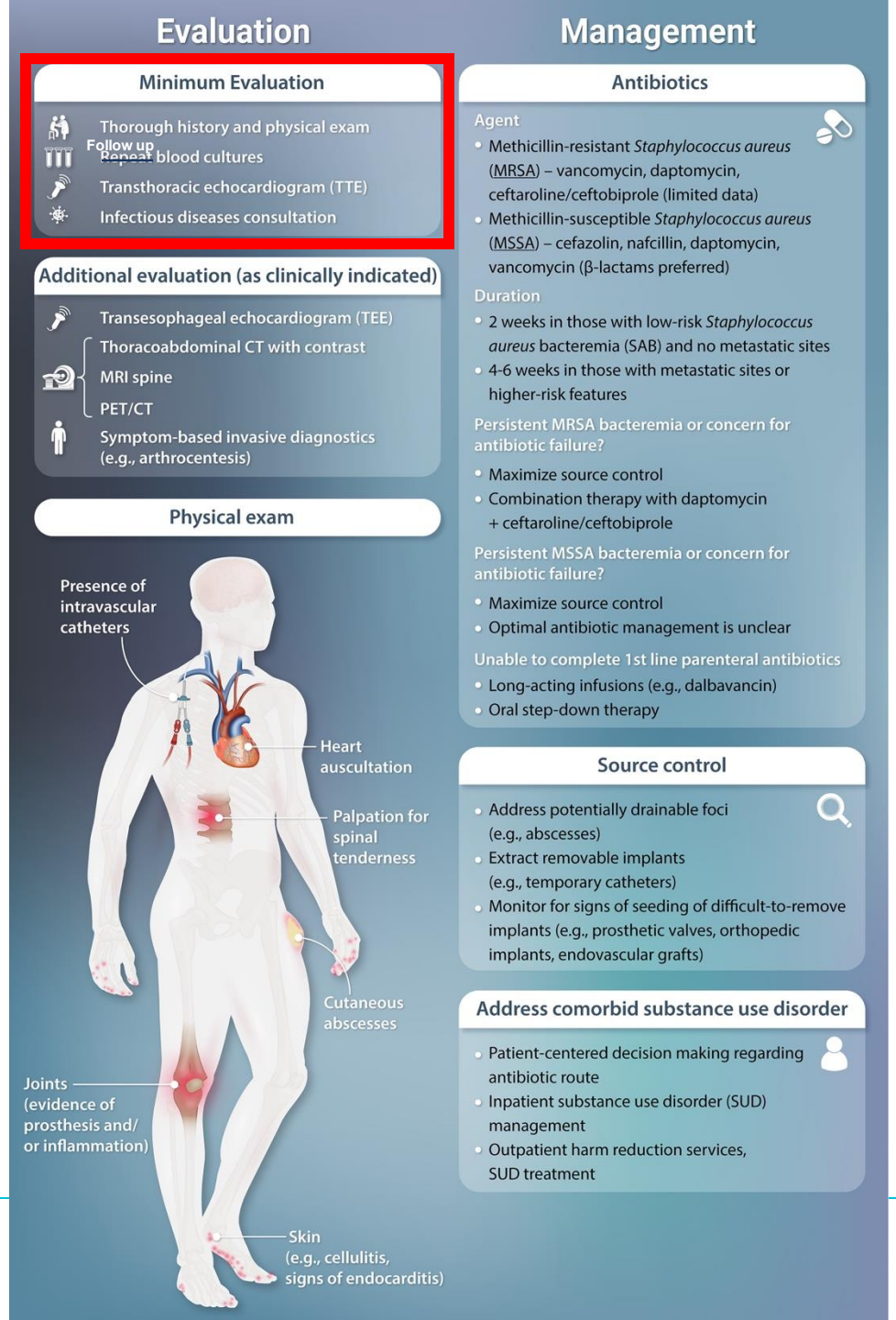
Defining persistent *Staphylococcus aureus* bacteraemia: secondary analysis of a prospective cohort study

*Richard Kuehl, Laura Morata, Christian Boeing, Isaac Subirana, Harald Seifert, Siegbert Rieg, Winfried V Kern, Hong Bin Kim, Eu Suk Kim, Chun-Hsing Liao, Robert Tilley, Luis Eduardo Lopez-Cortés, Martin J Llewelyn, Vance G Fowler, Guy Thwaites, José Miguel Cisneros, Matt Scarborough, Emmanuel Nsutebu, Mercedes Gurgui Ferrer, José L Pérez, Gavin Barlow, Susan Hopkins, Hugo Guillermo Ternavasio-de la Vega, M Estée Török, Peter Wilson, Achim J Kaasch, Alex Soriano, on behalf of the International Staphylococcus aureus collaboration study group and the ESCMID Study Group for Bloodstream Infections, Endocarditis and Sepsis**



Minejima *Clin Infect Dis* 2020; Kuehl *Lancet Infect Dis* 2020.

Follow-up blood cultures are always indicated for *Staph aureus* bacteremia



Minter *Clin Infect Dis* 2023.

Follow-up blood cultures are recommended for Candidemia

IDSA PRACTICE GUIDELINES · CURRENT

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by IDSA

Published December 16, 2015 **Last Updated** August 16, 2018

11. Follow-up blood cultures should be performed every day or every other day to establish the time point at which candidemia has been cleared *(strong recommendation; low-quality evidence)*.

12. Recommended duration of therapy for candidemia without obvious metastatic complications is for 2 weeks after documented clearance of *Candida* species from the bloodstream and resolution of symptoms attributable to candidemia *(strong recommendation; moderate-quality evidence)*.

Pappas *Clin Infect Dis* 2016.

Follow-up blood cultures for other gram-positives (i.e. not *Staph aureus*)

- Data is less robust than for *Staph aureus*
- Follow-up blood cultures are indicated for:
  - *Staph lugdunensis* bacteremia (behaves like *Staph aureus*!)
  - Suspected or confirmed endocarditis / other endovascular infection (e.g. line infection)
  - High risk for endovascular infection (e.g. prosthetic valve, ICD, vascular graft)
  - Inadequate source control and/or lack of clinical improvement
  - Distinguishing blood culture contamination vs infection (sometimes)

Fabre *Clin Infect Dis* 2020; Fabre *Journal of Clin Microbiol* 2022.

Open Forum Infectious Diseases

MAJOR ARTICLE

Limited Clinical Utility of Follow-up Blood Cultures in Patients With Streptococcal Bacteremia: An Opportunity for Blood Culture Stewardship

Emily A. Siegrist,[1,2] Minkey Wungwattana,[1] Leyla Azis,[3] Patricia Stogsdill,[3] Wendy Y. Craig,[4] and Kristina E. Rokas[1]

- Retrospective cohort study; patients with *Strep* bacteremia
  - viridans (33%), pneumoniae (17%), group B (21%), group A (12%), groups C/G (13%)
- 10 / 304 (3.2%) patients had *Strep* in a follow-up blood culture

Table 2. Presumed Source of Bacteremia, Overall and After Stratification by Follow-Up Blood Culture Result[a]

	Follow-up Blood Culture Result for *Streptococcus* spp		
Source of Infection	Overall (n = 314)	Negative (n = 304)	Positive (n = 10)
None identified	86 (27.4)	85 (28.0)	1 (10.0)
Skin and skin structure	64 (20.4)	64 (21.1)	0 (0)
Respiratory	48 (15.3)	48 (15.8)	0 (0)
Endocarditis	40 (12.7)	35 (11.5)	5 (50.0)
Discitis/vertebral osteomyelitis	17 (5.4)	14 (4.6)	3 (30.0)
Gastrointestinal	11 (3.5)	11 (3.6)	0 (0)
Meningitis	10 (3.2)	10 (3.3)	0 (0)
Nonvertebral osteomyelitis	9 (2.9)	9 (3.0)	0 (0)
Septic arthritis	8 (2.5)	8 (2.6)	0 (0)
Dental	7 (2.2)	6 (2.0)	1 (10.0)
Epidural abscess	6 (1.9)	4 (1.3)	2 (20.0)
Diabetic foot infection	6 (1.9)	6 (2.0)	0 (0)
UTI	6 (1.9)	6 (2.0)	0 (0)
Prosthetic joint	4 (1.3)	4 (1.3)	0 (0)
Catheter-associated	2 (0.6)	2 (0.7)	0 (0)
Intravascular device	2 (0.6)	2 (0.7)	0 (0)
Other	38 (12.1)	35 (11.5)	3 (30.0)

Abbreviations: UTI, urinary tract infection.

[a]Patients could have multiple sources identified. All data are n (%).

Siegrist *OFID* 2020.

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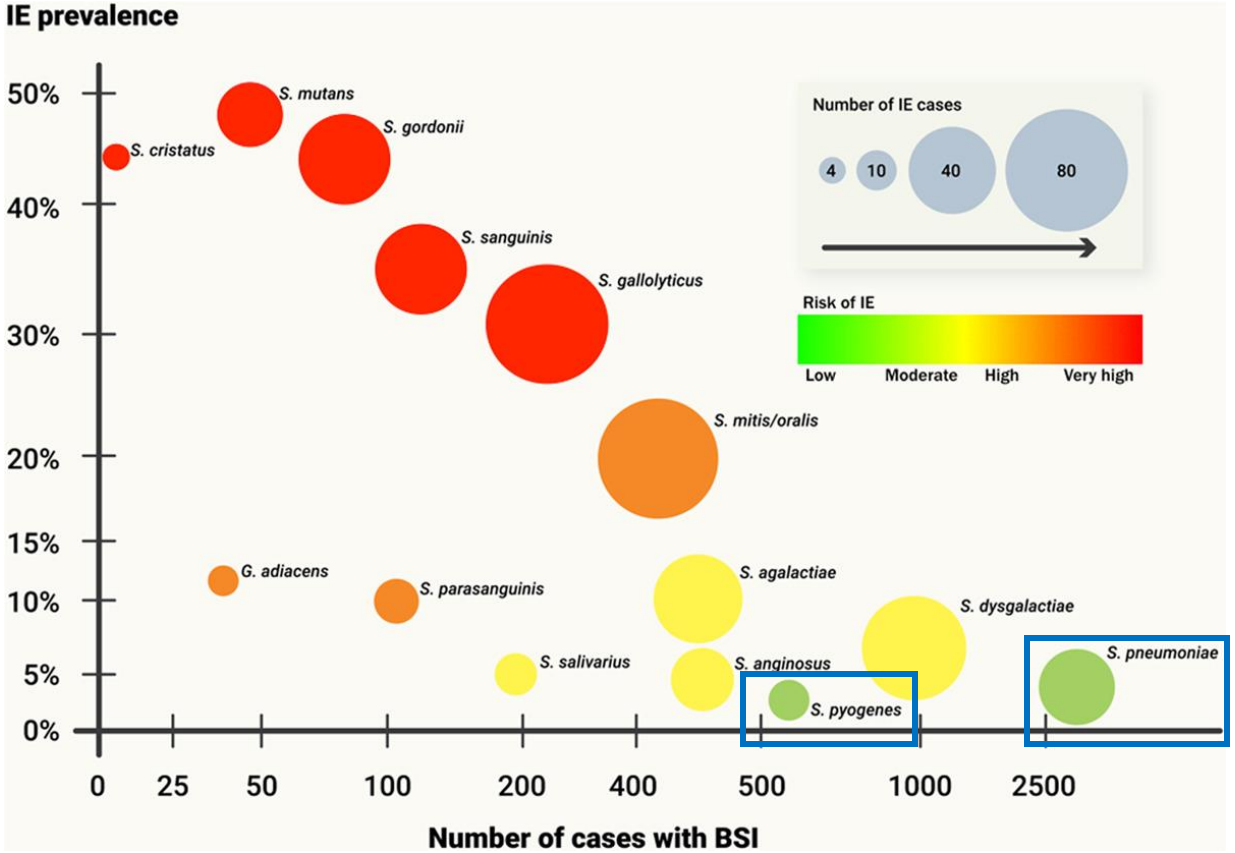
Siegrist *OFID* 2020.

Follow-up blood cultures in *Strep* bacteremia

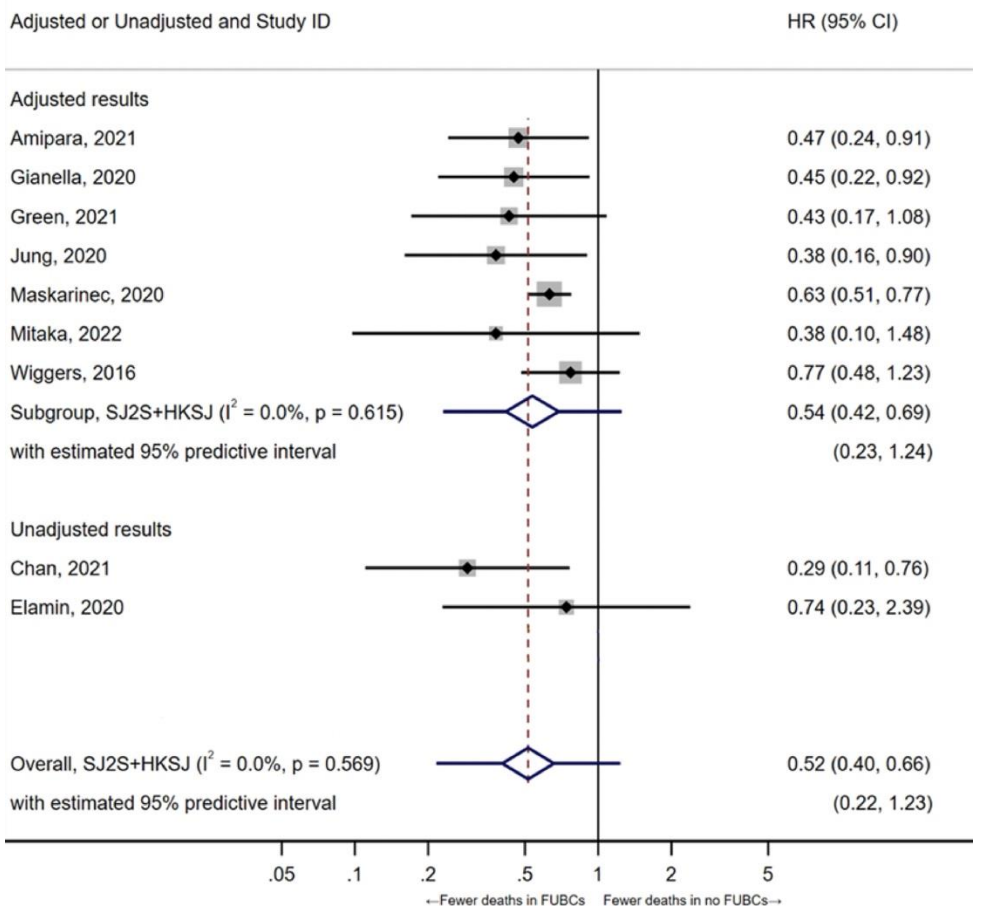
- Data are scarce
- Yield of follow-up blood cultures varies by type of infection and *Strep* species



Chamat-Hedemand *Circulation* 2020.

Utility of follow-up blood cultures in gram-negative rod (GNR) bacteremia is unclear

- Meta-analysis of 9 retrospective studies: follow-up blood cultures associated with lower mortality…but study had significant limitations
- Overall uncertain benefit of follow-up blood cultures for GNR bacteremia
- Need for prospective studies



Shinohara *OFID* 2022.

Follow-up blood cultures for GNR bacteremia associated with ↑ LOS and ↑ antibiotic duration

Infection Control & Hospital Epidemiology (2023), **44**, 474–479
doi:10.1017/ice.2022.110

SHEA

Original Article

Association between follow-up blood cultures for gram-negative bacilli bacteremia and length of hospital stay and duration of antibiotic treatment: A propensity score-matched cohort study

Hayato Mitaka MD[1,2], Shigeki Fujitani MD, PhD[2], Toshiki Kuno MD, PhD[3] and David C. Perlman MD[4]

Table 3. Outcomes of Patients with Gram-Negative Bacilli Bacteremia With and Without Follow-up Blood Cultures (FUBCs) Performed

	Propensity Score-Matched Cohort			
Outcome	With FUBC (N = 87)	Without FUBC (N = 87)	OR (95% CI)	*P* Value
Length of stay, median d (IQR)	9 (6–14)	7 (4.5–10.5)	. . .	**.02**
Duration of inpatient antibiotic treatment, median d (IQR)	8 (5.5–13)	6 (4–10)	. . .	**.01**
In-hospital mortality (%)	4.6	11.5	0.36 (0.12–1.14)	0.16

Note. OR, odds ratio; CI, confidence interval; IQR, interquartile range.

Mitaka *ICHE* 2023.

Which patients are more likely to benefit from follow-up blood cultures for GNR bacteremia?

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MAJOR ARTICLE

Risk Factors for Positive Follow-Up Blood Cultures in Gram-Negative Bacilli Bacteremia: Implications for Selecting Who Needs Follow-Up Blood Cultures

Hayato Mitaka,[1] Tessa Gomez,[2] Young Im Lee,[3] and David C. Perlman[2]

Table 2. Factors Independently Associated With Positive Follow-Up Blood Culture for Gram-Negative Bacilli Bacteremia[a]

Variable	Adjusted OR (95% CI)	*P* Value
ESRD on hemodialysis	2.95 (1.14–7.61)	**.025**
Intravascular device	2.52 (1.02–6.28)	**.046**
ESBL or carbapenemase-producing organism	3.07 (1.22–7.76)	**.018**

Table 3. The Yield of Follow-Up Blood Cultures[a]

	Total	Positive FUBC	The Yield of FUBC (%) (95% CI)	*P* Value
All patients with FUBC	306	28	9.2 (6.2–13.0)	–
Patients with ≥1 risk factors	155	23	14.8 (9.7–21.4)	–
Patients with no risk factors	151	5	3.3 (1.1–7.6)	**.001**

Mitaka *OFID* 2020.

Follow-up blood cultures for GNR bacteremia

- Area of controversy; no universal consensus

- Definitely obtain follow-up blood cultures for GNR bacteremia if:
  - Suspected or confirmed endocarditis/endovascular infection
  - Inadequate source control
  - Lack of clinical improvement

- Need additional studies to define which patients are most likely to benefit from follow-up blood cultures and if specific GN organisms should prompt follow-up blood cultures

Fabre *Clin Infect Dis* 2020; Fabre *Journal of Clin Microbiol* 2022.

Follow-up & repeat blood cultures for patients who are immunocompromised

- Data are limited
- Clinical practice is variable
- Diagnostic + antimicrobial stewardship is increasingly important for these patients

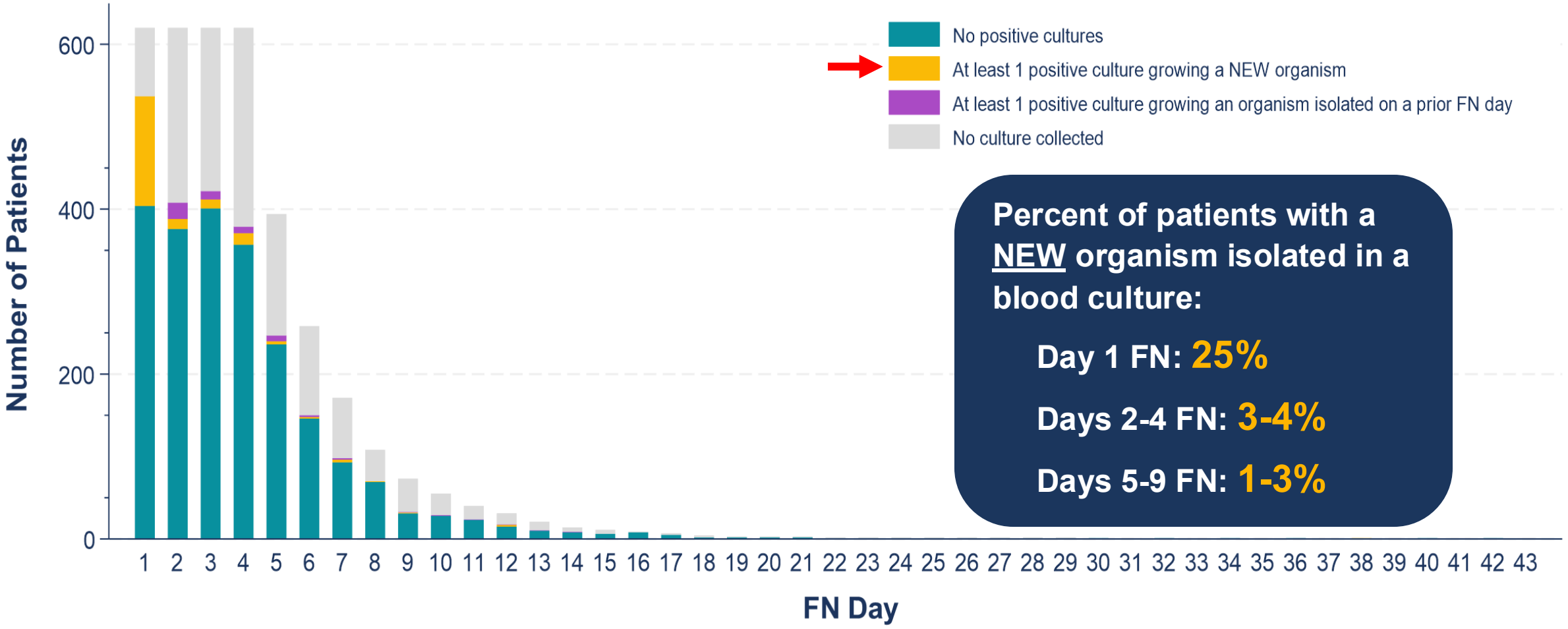
Febrile neutropenia (FN) is associated with high blood culture utilization

- Most common in patients with hematologic malignancies or those receiving chemotherapy
- Bloodstream infection identified in only 10-25% of FN episodes
- IDSA guidelines and retrospective studies note low yield of repeat blood cultures beyond FN day 3 in clinically stable patients

Freifeld *Clin Infec Dis* 2011; Robinson *OFID* 2022; Kimura *Infect Dis (London)* 2017; Sheu *Transpl Infect Dis* 2024; Haeusler *JPIDS* 2021; Serody *Bone Marrow Transpl* 2000.

Timing of Positive Blood Cultures in Persistent FN

N= 620 patients with persistent FN (>3 days) from March 2021 – June 2024



Percent of patients with a NEW organism isolated in a blood culture:

- **Day 1 FN: 25%**
- **Days 2-4 FN: 3-4%**
- **Days 5-9 FN: 1-3%**

Median FN duration: 5 days (IQR 4-7)
Median blood culture bottles per FN episode: 12 (IQR 8-18)

Rosen, manuscript under review.

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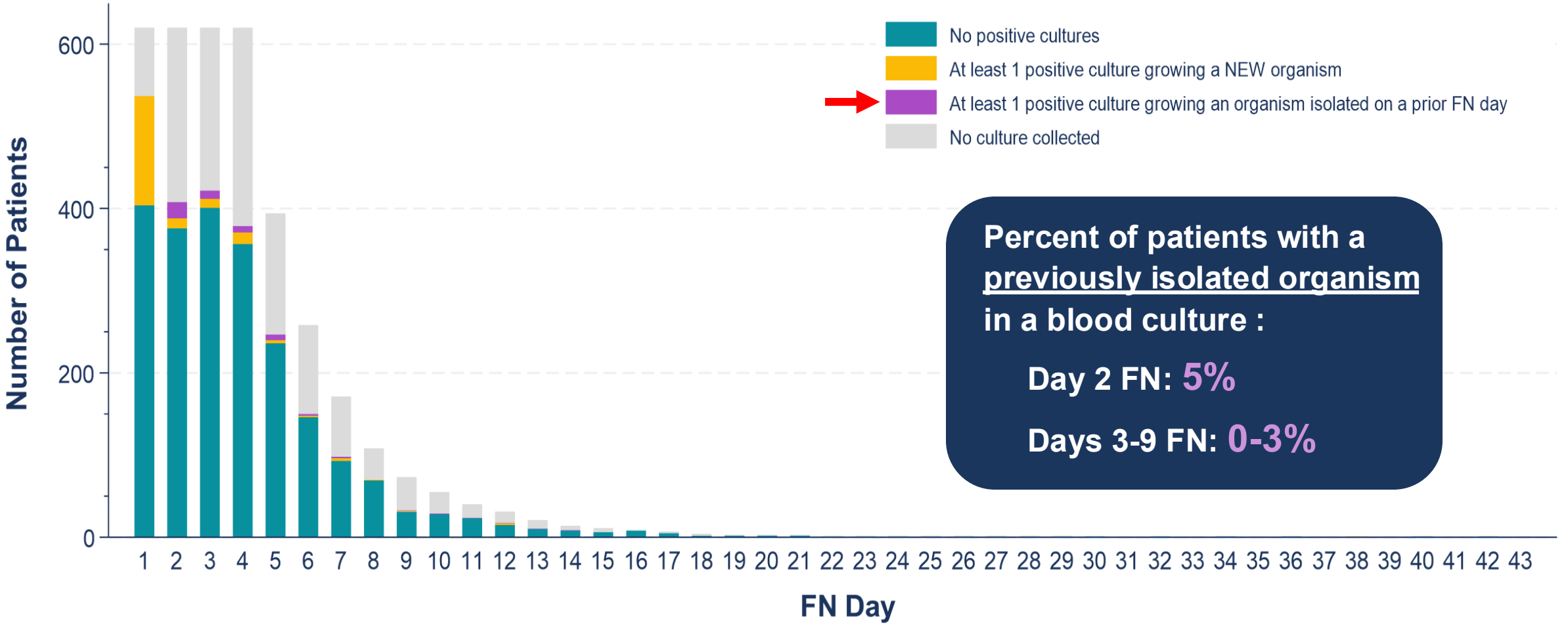

Percent of patients with a <u>previously isolated organism</u> in a blood culture :

Day 2 FN: 5%

Days 3-9 FN: 0-3%

Median FN duration: 5 days (IQR 4-7)
Median blood culture bottles per FN episode: 12 (IQR 8-18)

Rosen, manuscript under review.

Summary and Take-Home Points

- Follow-up blood cultures are high-yield / recommended for:
  - *Staph aureus* & *Staph lugdunensis* bacteremia
  - Candidemia
  - Suspected or confirmed endocarditis or endovascular infection
  - Lack of clinical improvement and/or poor source control
- Yield of follow-up blood cultures in *Strep* bacteremia is variable
- Role of follow-up blood cultures for GNR bacteremia is not well defined
- Opportunities for blood culture stewardship also exist for patients who are immunocompromised
- Clinical judgement is important in deciding when to send follow-up blood cultures

Teaching Peer Evaluation for
Dr. Emily Rosen

Thank You!