UWTASP

tele-antimicrobial stewardship program

Gram Negative Blood Stream Infections

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March 19, 2019

Agenda

Goal: Determine optimal treatment and duration once GNR BSI has been identified

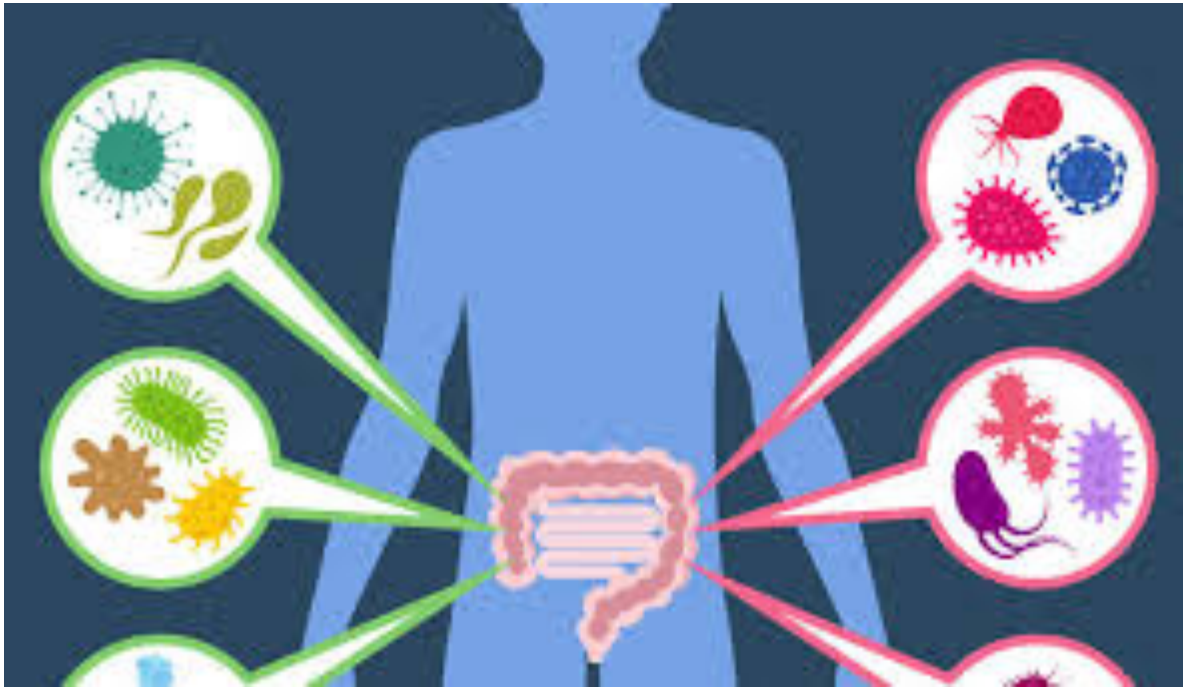
1.) How long to treat

2.) What antibiotic agent to treat with

3.) Repeat blood cultures

Gram Negatives

- ***E. coli***
- ***Klebsiella* spp.**
- ***Proteus* spp.**
- ***± P. aeruginosa***



A 62 yo female presents to your hospital with sepsis. Urine and blood cultures grow *E. coli*

On Day 3, the patient is stabilized. What duration of therapy would you recommend to complete a course.

a. **5 days**
b. **7 days**
c. **10 days**
d. **14 days**

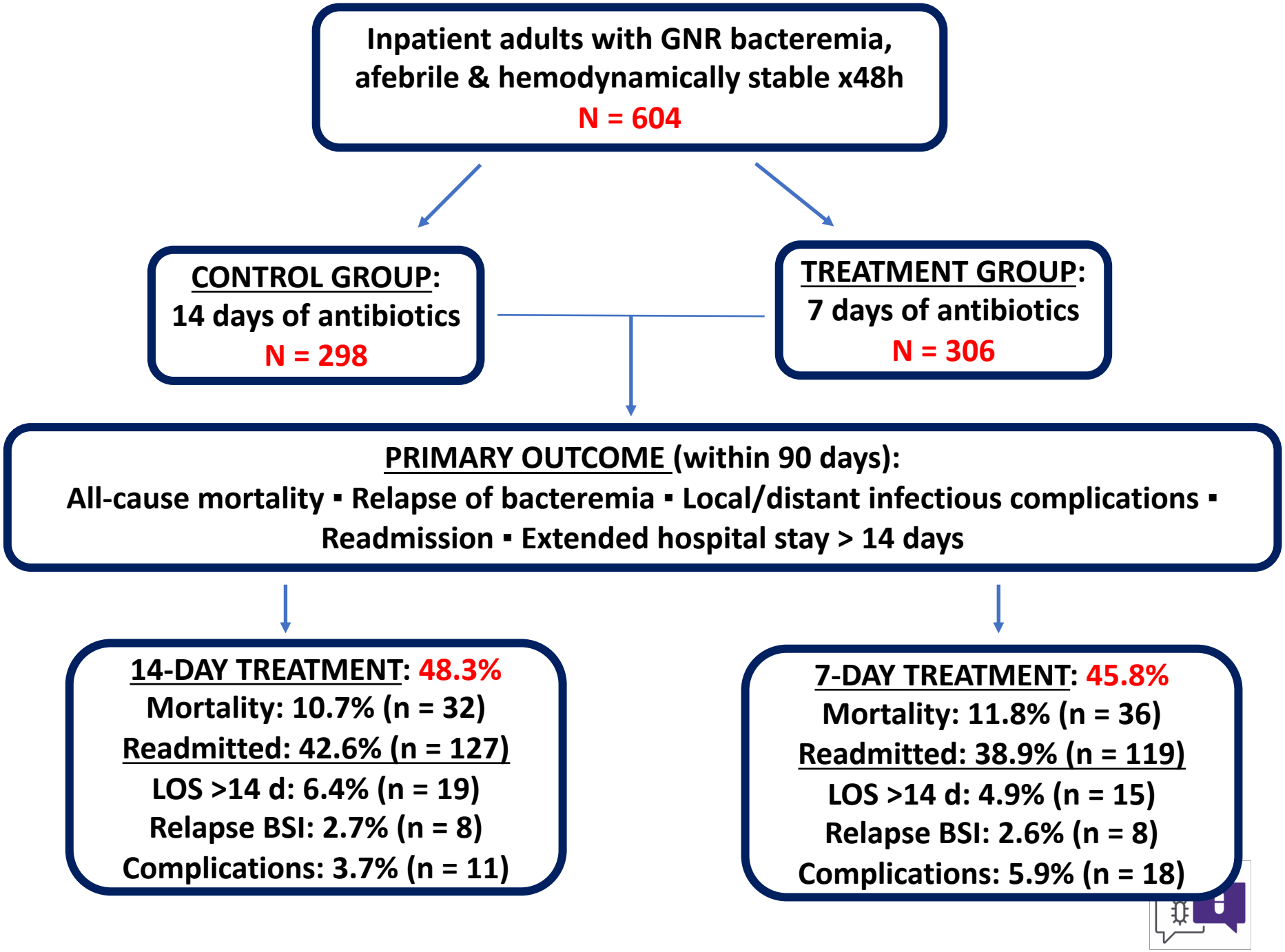
Clinical Infectious Diseases

MAJOR ARTICLE

Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

Dafna Yahav,[1,2] Erica Franceschini,[3] Fidi Koppel,[4] Adi Turjeman,[2,5] Tanya Babich,[2,5] Roni Bitterman,[4] Ami Neuberger,[4,6] Nesrin Ghanem-Zoubi,[4] Antonella Santoro,[3] Noa Eliakim-Raz,[1,2] Barak Pertzov,[5] Tali Steinmetz,[5] Anat Stern,[4] Yaakov Dickstein,[4] Elias Maroun,[4] Hiba Zayyad,[4] Jihad Bishara,[1,2] Danny Alon,[7] Yonatan Edel,[2,8] Elad Goldberg,[9] Claudia Venturelli,[3] Cristina Mussini,[3] Leonard Leibovici,[2,5] Mical Paul[4,6]; for the Bacteremia Duration Study Group[a]

[1]Infectious Diseases Unit, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, and [2]Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel; [3]Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Italy; [4]Infectious Diseases Institute, Rambam Health Care Campus, Haifa, [5]Department of Medicine E, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, [6]The Ruth and Bruce Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, and [7]Department of Medicine B, [8]Department of Medicine C, and [9]Department of Medicine F, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel

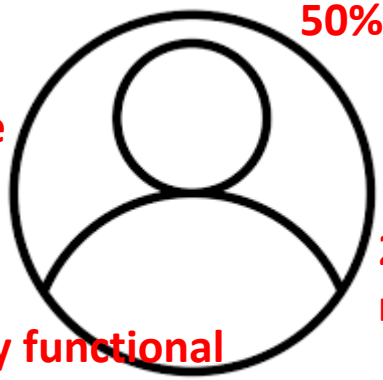

Inpatient adults with GNR bacteremia, afebrile & hemodynamically stable x48h
N = 604
CONTROL GROUP:
14 days of antibiotics
N = 298
TREATMENT GROUP:
7 days of antibiotics
N = 306
PRIMARY OUTCOME (within 90 days):
All-cause mortality ▪ Relapse of bacteremia ▪ Local/distant infectious complications ▪ Readmission ▪ Extended hospital stay > 14 days
14-DAY TREATMENT: 48.3%
Mortality: 10.7% (n = 32)
Readmitted: 42.6% (n = 127)
LOS >14 d: 6.4% (n = 19)
Relapse BSI: 2.7% (n = 8)
Complications: 3.7% (n = 11)
7-DAY TREATMENT: 45.8%
Mortality: 11.8% (n = 36)
Readmitted: 38.9% (n = 119)
LOS >14 d: 4.9% (n = 15)
Relapse BSI: 2.6% (n = 8)
Complications: 5.9% (n = 18)

Patient population

PATIENTS

71 years old
50% female

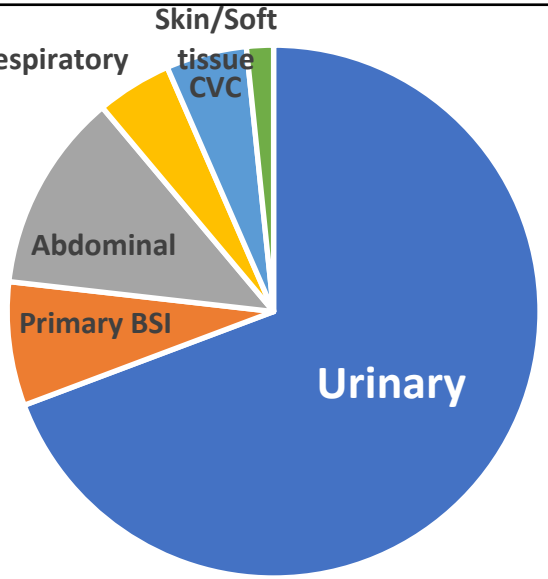
20-25%
urinary device



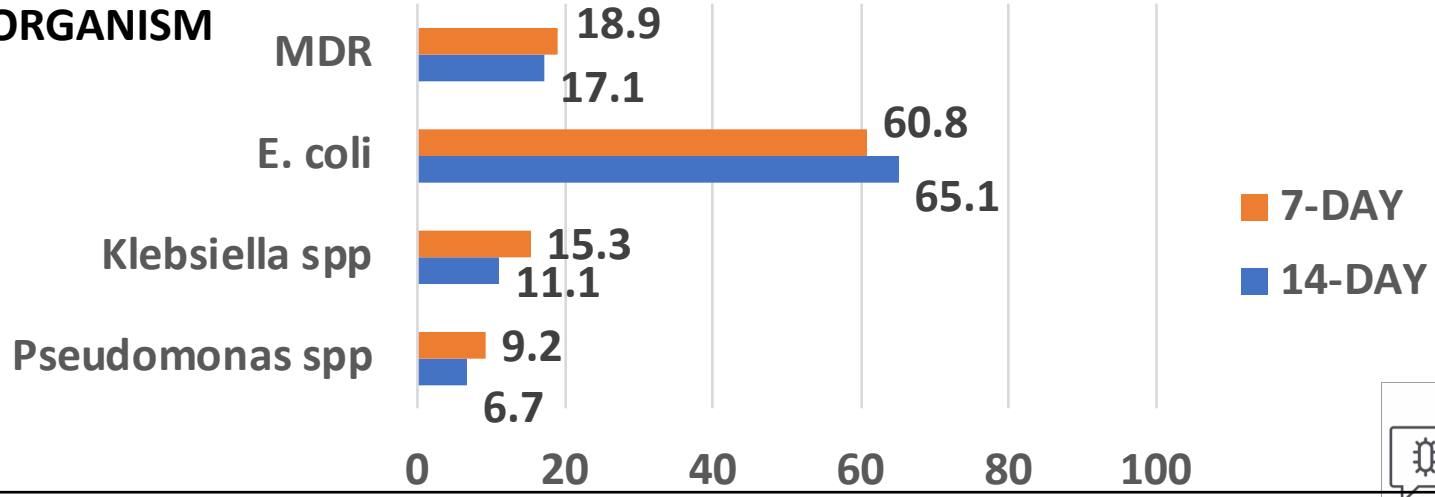
25%
malignancy

60%
independently functional

SOURCE

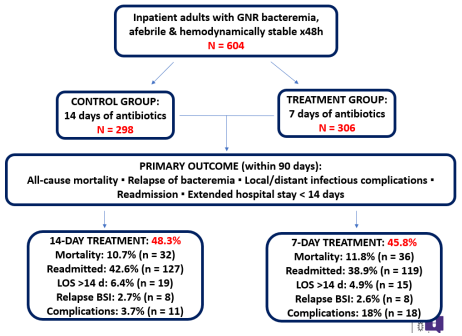


BACTERIAL ORGANISM

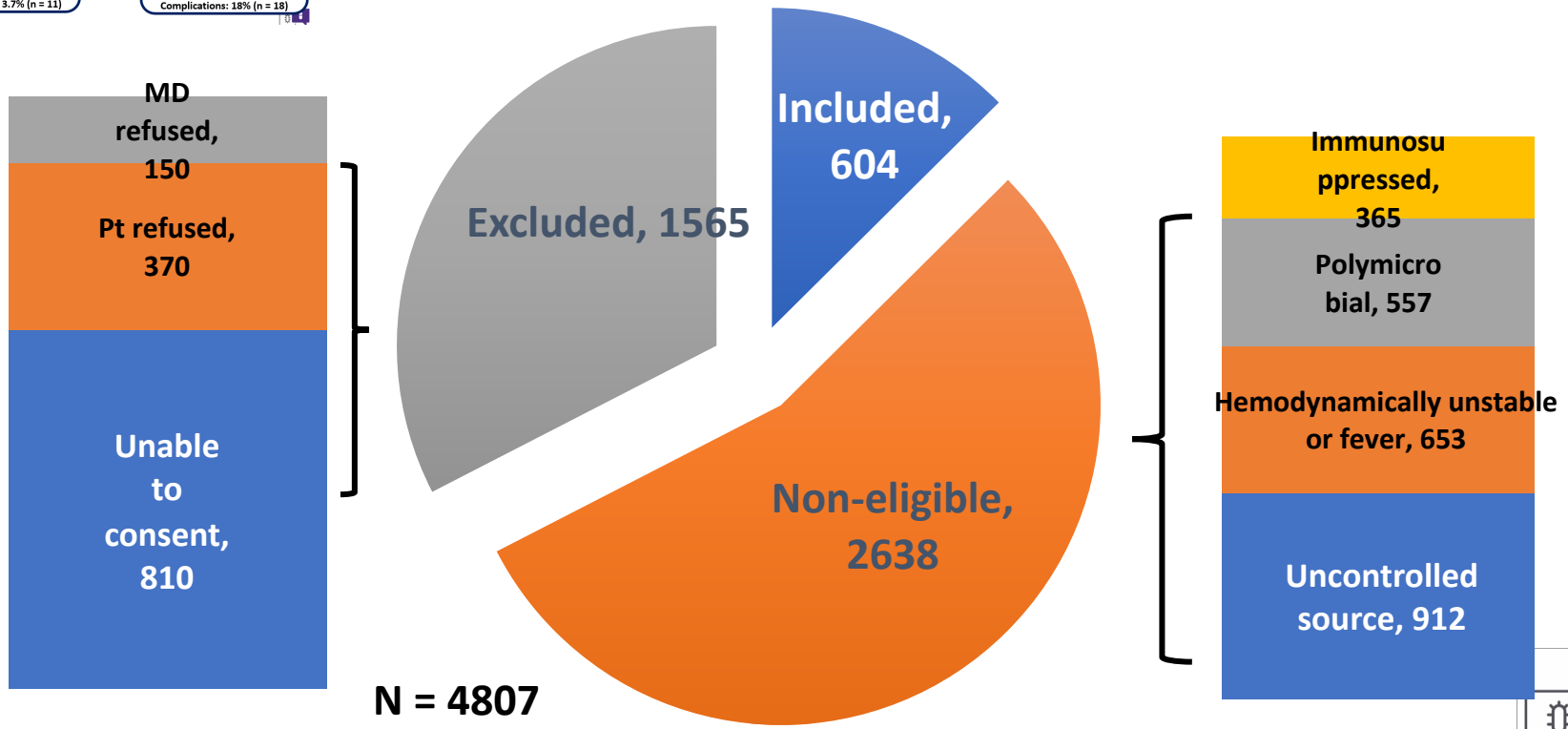


Yahav et al. Clin Infect Dis. 2018 Dec 11.

Does this trial apply to *my* patients?



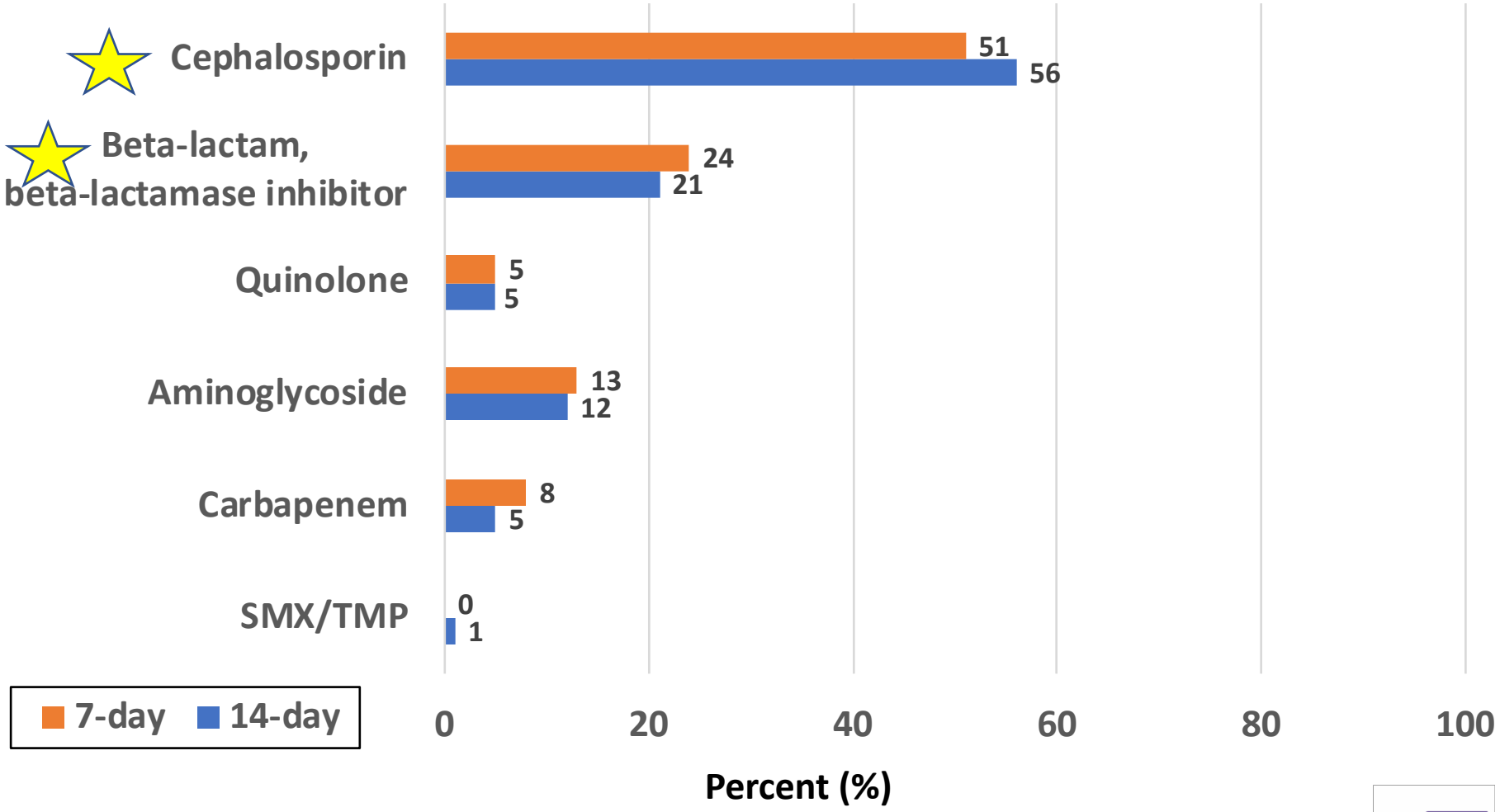
Inpatient adults with GNR bacteremia, afebrile & hemodynamically stable x48h
N = 604



N = 4807
Patients with GN bacteremia screened for trial

Yahav et al. Clin Infect Dis. 2018 Dec 11.

Antibiotic selection, IV



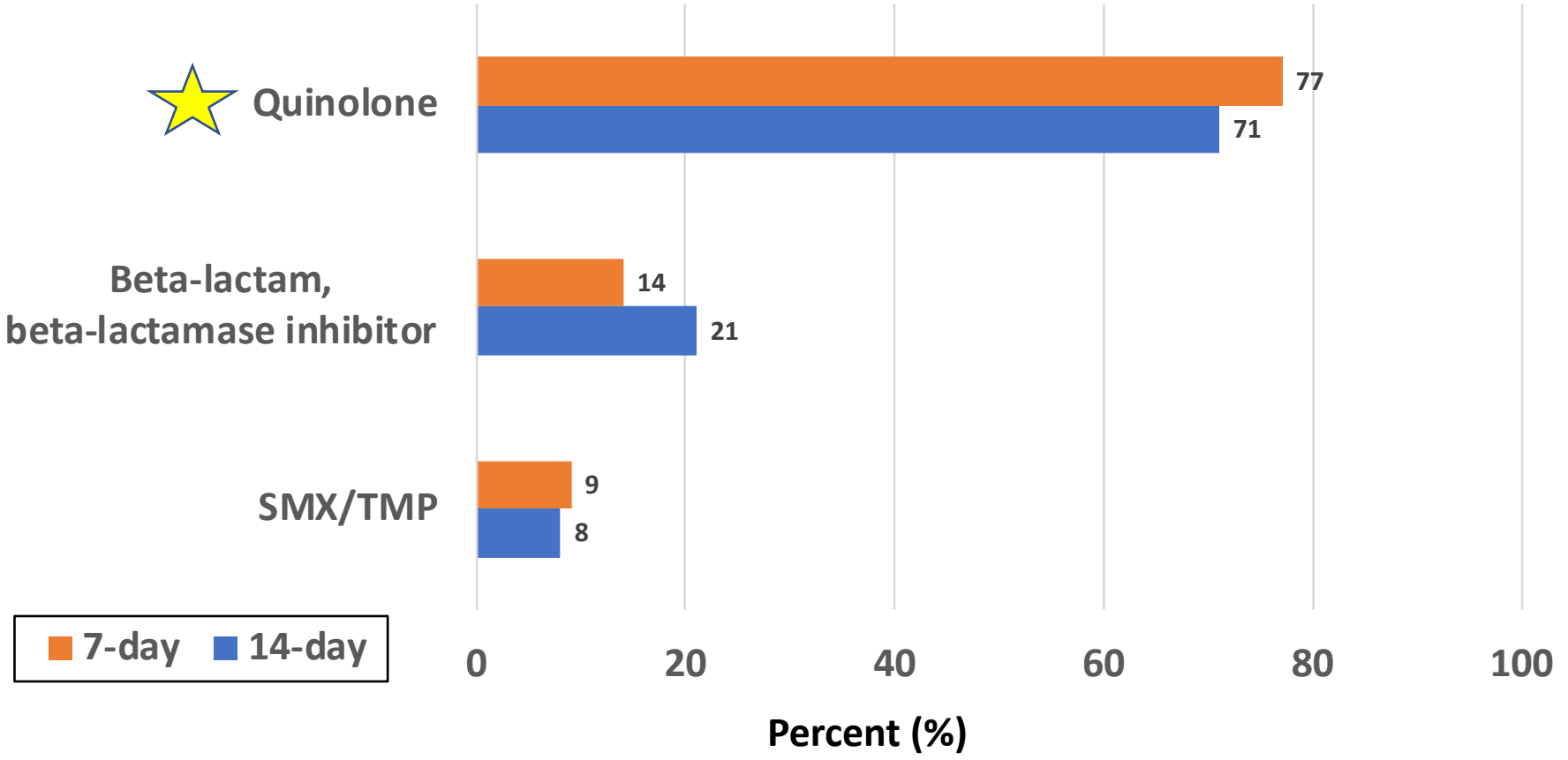
Yahav et al. Clin Infect Dis. 2018 Dec 11.

The patient is ready for discharge but has 4 days on antibiotic therapy remaining.

What oral agent would you recommend?

a. **Amoxicillin/clavulanate**
b. **Cefpodoxime**
c. **Levofloxacin**
d. **Sulfamethoxazole/trimethoprim**

Antibiotic selection, PO



36% (7-day) and 19%(14-day) groups received only IV antibiotics

Yahav et al. Clin Infect Dis. 2018 Dec 11.

International Journal of Antimicrobial Agents 48 (2016) 498–503

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

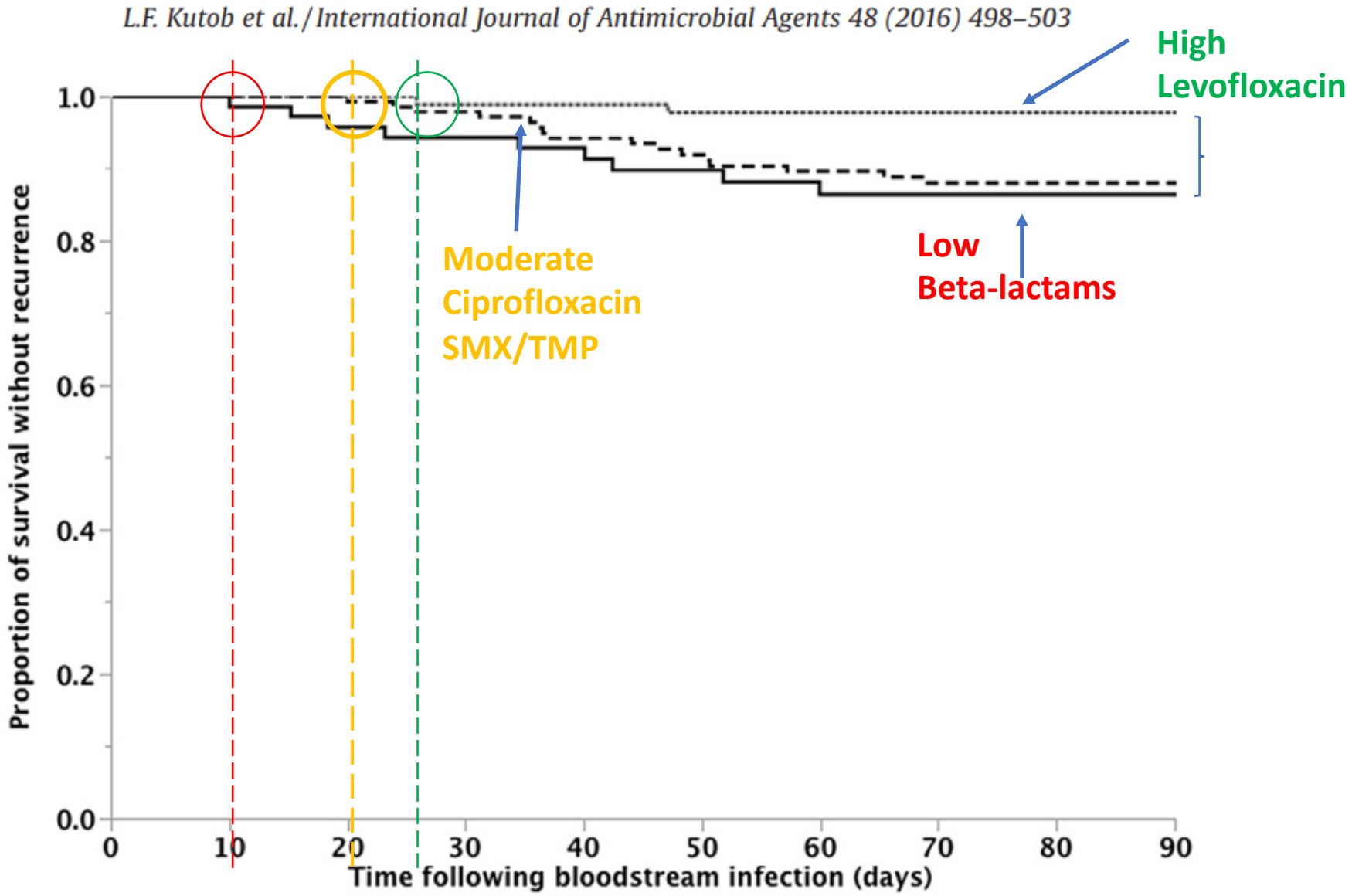
Effectiveness of oral antibiotics for definitive therapy of Gram-negative bloodstream infections *

Leila F. Kutob [a], Julie Ann Justo [b,c], P. Brandon Bookstaver [b], Joseph Kohn [c], Helmut Albrecht [d], Majdi N. Al-Hasan [d,*]

[a] University of South Carolina School of Medicine, Columbia, SC, USA
[b] Department of Clinical Pharmacy and Outcomes Science, South Carolina College of Pharmacy, University of South Carolina, Columbia, SC, USA
[c] Department of Pharmacy, Palmetto Health Richland, Columbia, SC, USA
[d] Department of Medicine, Division of Infectious Diseases, University of South Carolina School of Medicine, Columbia, SC, USA

Highly Bioavailable N = 106	Moderately Bioavailable N = 179	Low Bioavailable N = 77
Levofloxacin	Ciprofloxacin SMX/TMP	Beta-lactams

Time to Failure: Faster with low bioavailable abx



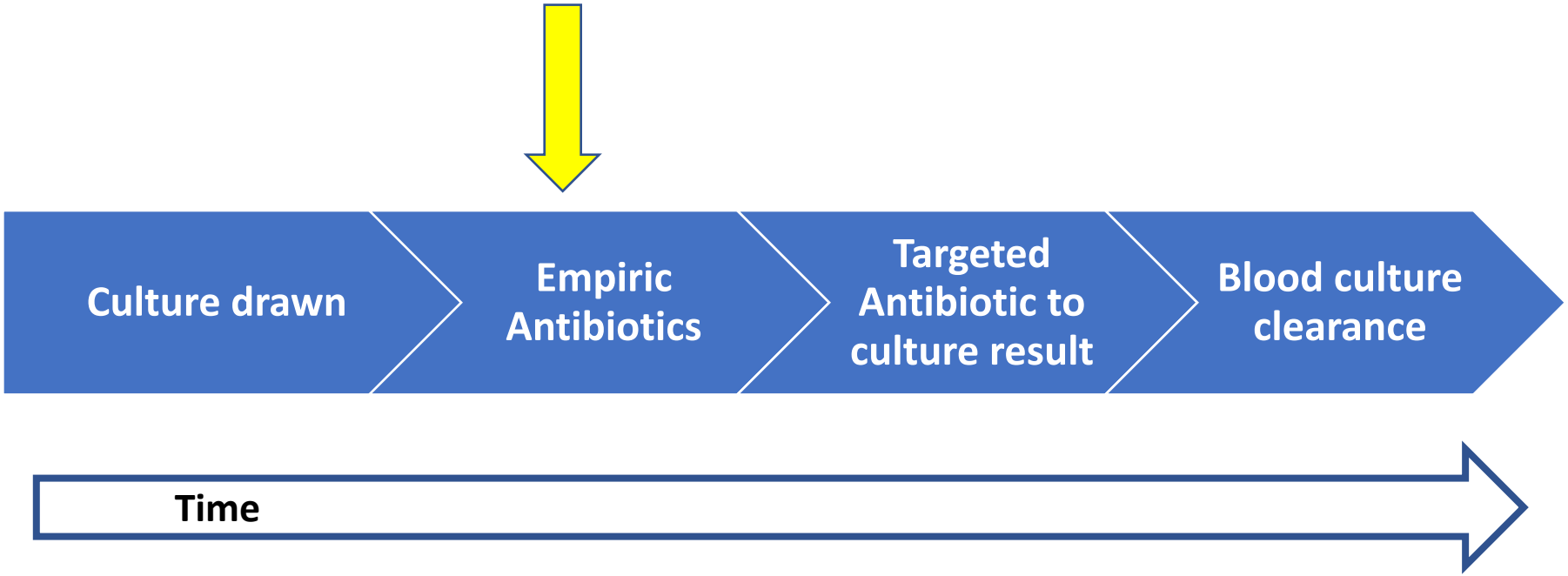
MD is writing a script for the antibiotic you recommended, she calls and asks: Remind me, when was day 1?

Day 1

a. **When empiric antibiotic started**
b. **When targeted antibiotic started**
c. **When the blood culture first cleared**
d. **Not sure**

Duration of therapy: When Is Day 1?

As long as active antimicrobial agent



Yahav et al. Clin Infect Dis. 2018 Dec 11.

Repeat cultures after 48 hours are low yield for most Gram-negative bacteremias

Wiggers *et al. BMC Infectious Diseases* (2016) 16:286
DOI 10.1186/s12879-016-1622-z

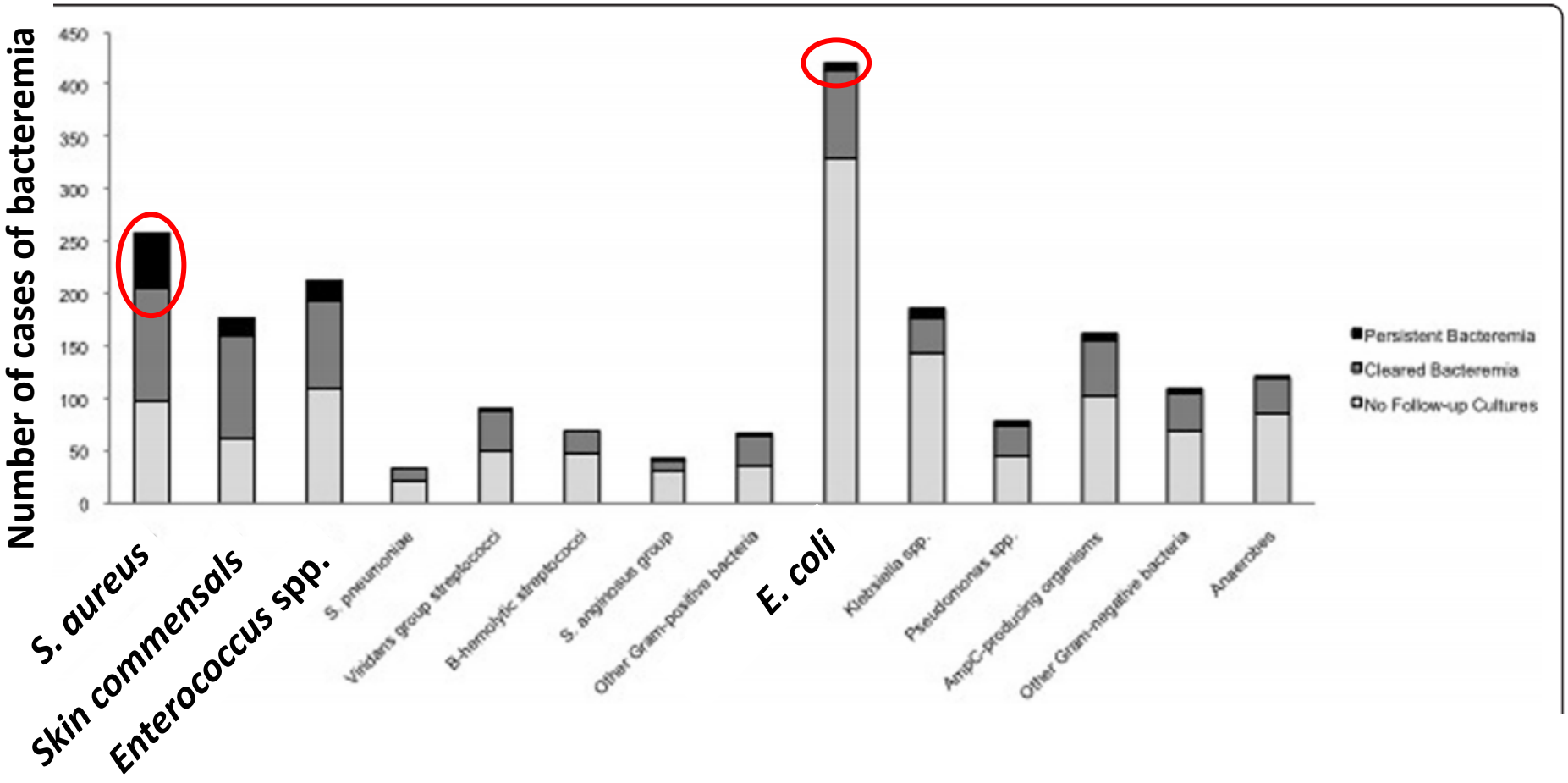
BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Sending repeat cultures: is there a role in the management of bacteremic episodes? (SCRIBE study)

J. Brad Wiggers[1], Wei Xiong[2] and Nick Daneman[1,3,4,5*]

Duration of therapy: Accounting for Blood Culture Clearance



Wiggers et al. 2016 BMC Infect Dis. 16:286

Summary

- Treat Gram negative bacteremia for 7 days
  - Patient must show signs of clinical improvement
  - Source must be controlled
- Antibiotic selection
  - Based on organism susceptibility
  - IV: Cephalosporin
  - PO: Fluoroquinolones
- No need to repeat blood cultures for clearance
  - Unless:
  - Uncontrolled source
  - Ongoing infection (e.g. endovascular)