UWTASP

tele-antimicrobial stewardship program

August 18, 2020

Agenda

- Antibiotic IV to PO Conversion
- Case Discussions

When are oral antibiotics safe and effective as step-down?

Agenda:

1.) What type of infections

2.) When can you consider orals

3.) Which oral antibiotic as step-down

What type of infections can we use oral antibiotics as step-down therapy?

A. Bacteremia

B. Pneumonia

C. Bone and Joint

D. Endocarditis

E. None of the above

F. All of the above

Gram-Negative Bacteremia

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]

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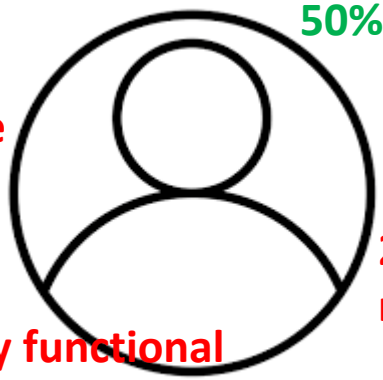
Patient population

PATIENTS

71 years old
50% female

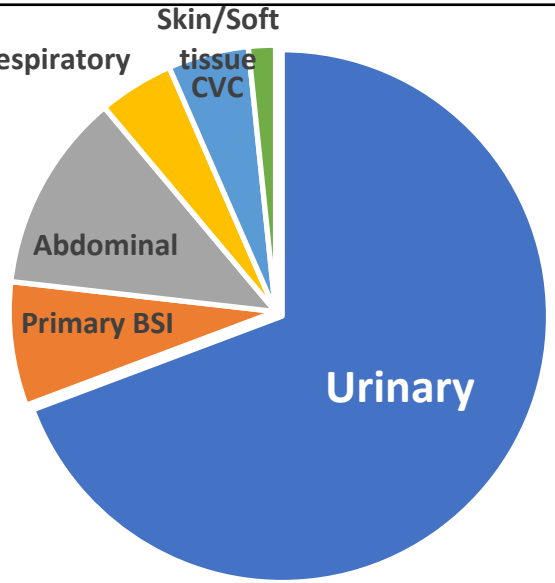
20-25%
urinary device



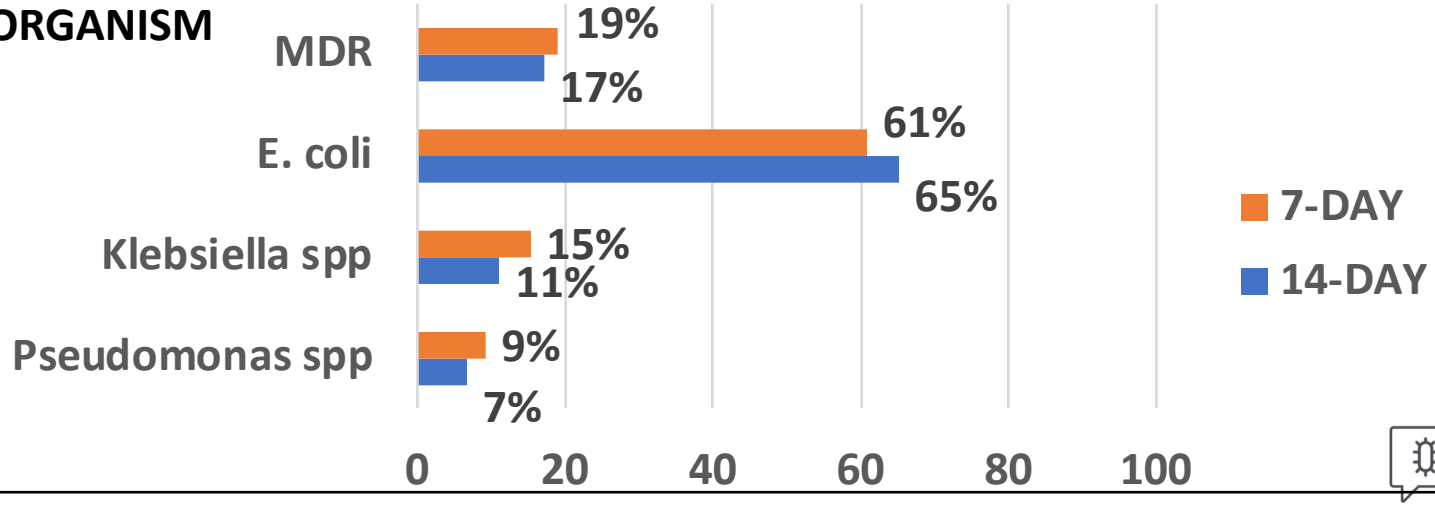
25%
malignancy

60%
independently functional

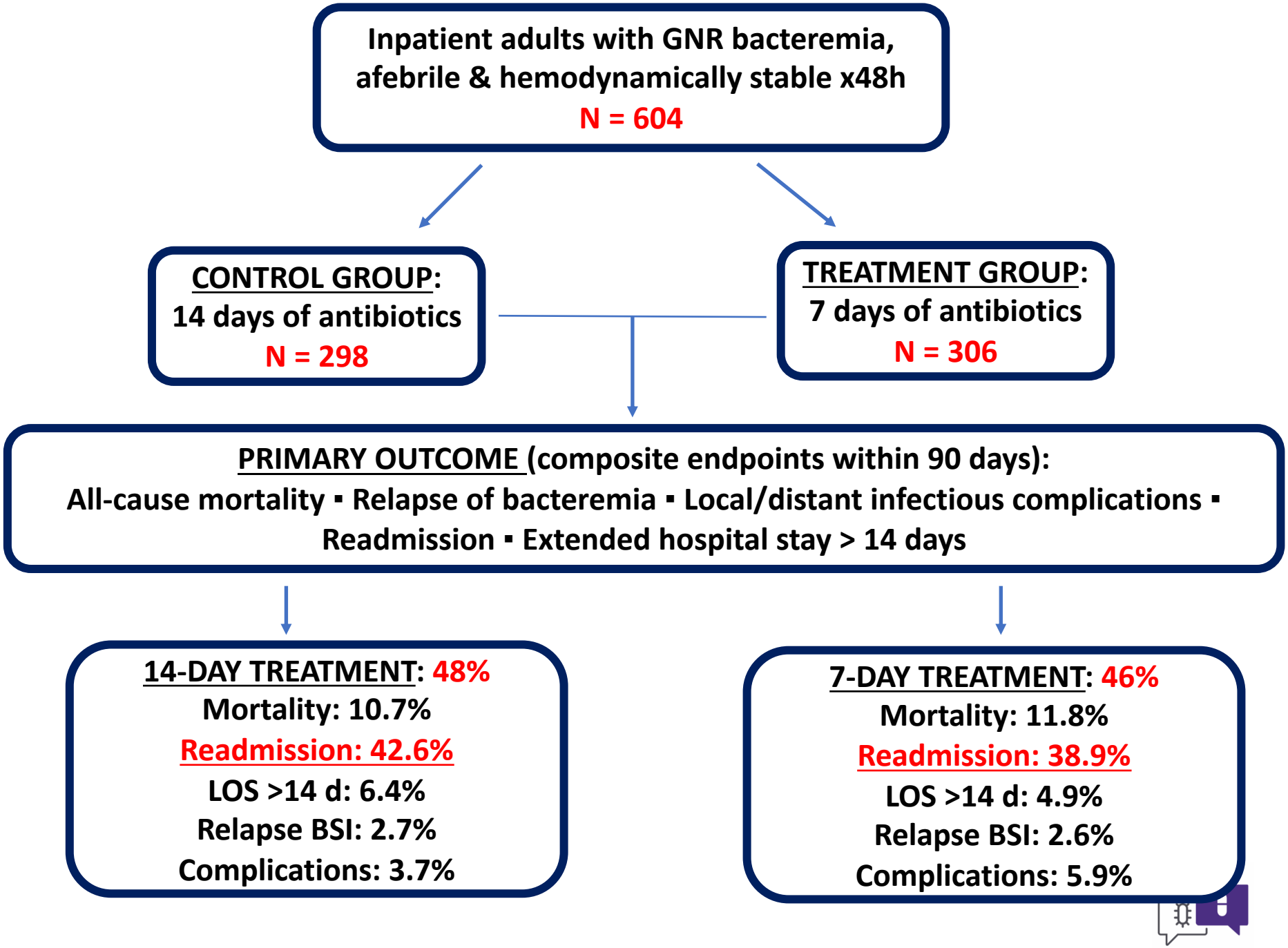
SOURCE



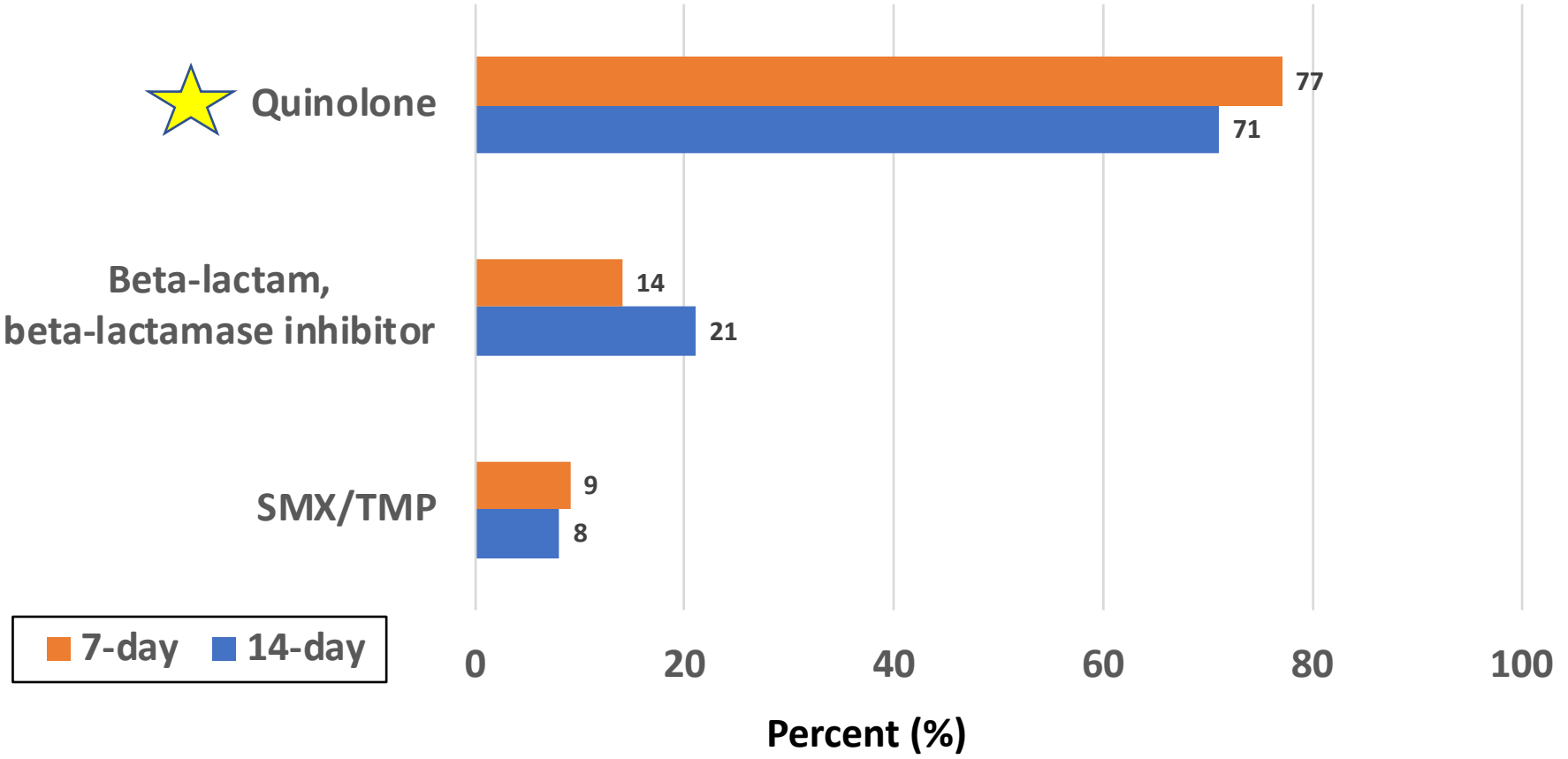
BACTERIAL ORGANISM



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


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 (composite endpoints within 90 days):
All-cause mortality ▪ Relapse of bacteremia ▪ Local/distant infectious complications ▪ Readmission ▪ Extended hospital stay > 14 days
14-DAY TREATMENT: 48%
Mortality: 10.7%
Readmission: 42.6%
LOS >14 d: 6.4%
Relapse BSI: 2.7%
Complications: 3.7%
7-DAY TREATMENT: 46%
Mortality: 11.8%
Readmission: 38.9%
LOS >14 d: 4.9%
Relapse BSI: 2.6%
Complications: 5.9%

Oral antibiotic step-down



64% (7-d) and 81%(14-d) groups received oral antibiotics

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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

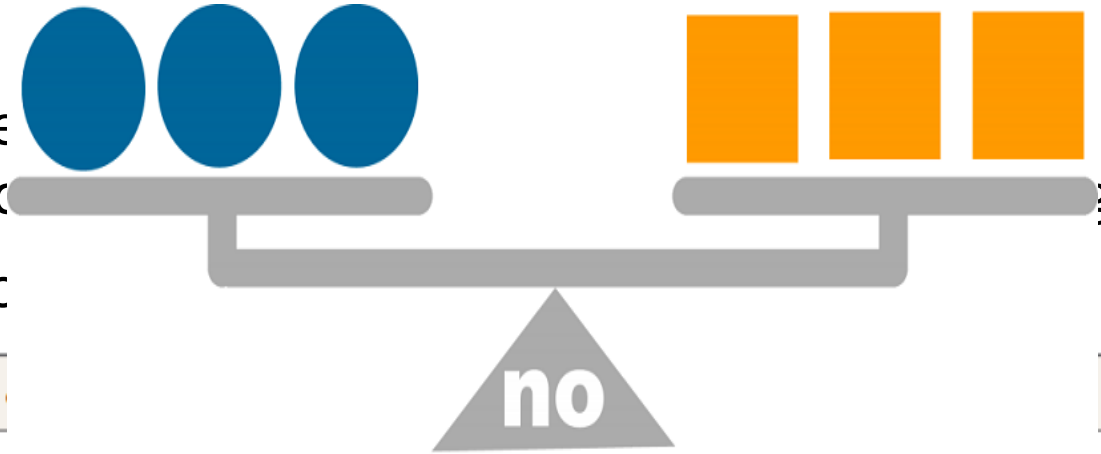
- 1054 patients with osteomyelitis/septic joint infections at 26 UK centers
- 7d IV (with or w/o surgery), randomized to PO vs IV x ≥ 6 wks

Outcome	IV (n=527)	PO (n=527)	
Failure	74 (14%)	67 (13%)	Non-inferior
Catheter complication	9%	1%	P<0.001
Discontinuation of therapy	19%	13%	P=0.006
Length of stay	14 days	11 days	P<0.001

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment



- 400 patie
  streptocc gative *Staph*
- At least c

Table 2. Distribution

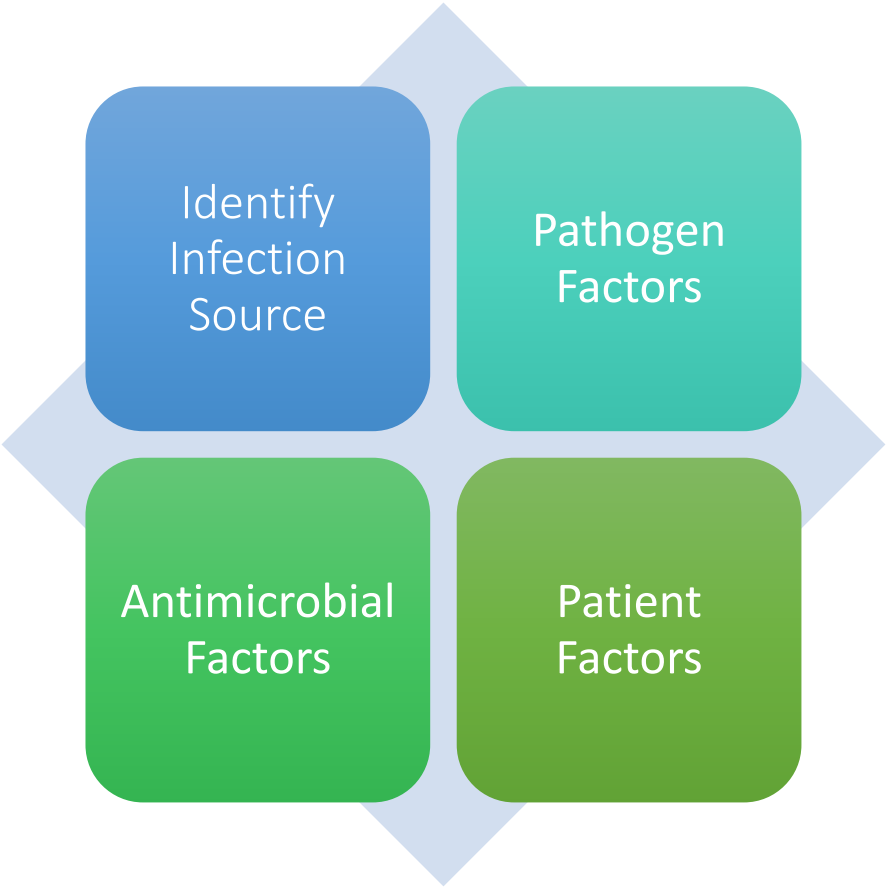
Component			Hazard Ratio (95% CI)
	number (percent)	*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (–1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (–3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (–2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (–3.1 to 3.1)	0.97 (0.28 to 3.33)

Benefits of oral antibiotic

- Reduce hospital length of stay
- Improve quality of life
  - Discomfort of IV catheter
  - Improve mobility
  - Perception of health and functional capacity
- Decrease risk of infectious and non-infectious catheter associated complications
- Supported by Choosing Wisely Initiatives and CDC
  - Preference for oral antibiotics whenever possible

Tamma PD, et al. JAMA Internal Medicine 2019;179:316-323

Check List



- **Identify Source**
  - Source control
- **Bacterial Factors**
  - Susceptibility profile
- **Antibiotic Factors**
  - Bioavailability
  - Tolerability
  - Safety profile
  - Drug interactions
- **Patient Factors**
  - Clinical improvement
  - Absorption
  - Dietary consideration
  - Adherence
  - Follow up

Hale AJ, et al. Journal of Hospital Medicine 2018

Tissue Penetration and Bioavailability

TABLE 1. Penetration of Select Oral Antimicrobials to Tissue Sites[7,44]

Antimicrobial	Bloodstream Bioavailability	Lung	Liver	Urinary Tract	Prostate	Bone	GI	Skin	Bile	CSF	Synovial
Ciprofloxacin	70%	++	+++	+++	+++	+++	+++	+++	+++	+	+++
Levofloxacin	99%	+++	+++	+++	+++	+++	+++	+++	+++	+	+++
Moxifloxacin	90%	+++	+++	+++	+++	+++	+++	+++	+++	+	+++
Trimethoprim-Sulfamethoxazole	90%	++	++	+++	++	++	++	+++	++	+	++
Doxycycline	95%	++	++	++	++	++	++	++	++	+	++
Minocycline	95%	++	++	++	++	++	++	++	++	+	++
Linezolid	99%	+++	++	+++	++	++	++	+++	++	++	++
Metronidazole	90%	++	+++	++	++	++	++	++	++	++	++
Clindamycin	90%	++	++	++	++	++	++	++	++	+	++
Ampicillin	50%	+	++	++	+	++	++	++	++	++	+
Penicillin V	50%	++	++	++	+	++	++	++	++	++	+
Amoxicillin	85%	+	++	++	+	++	++	++	++	++	+
Cephalexin	60%	++	++	++	++	++	++	++	++	+	++

Hale AJ, et al. Journal of Hospital Medicine 2018

Which oral antibiotics?

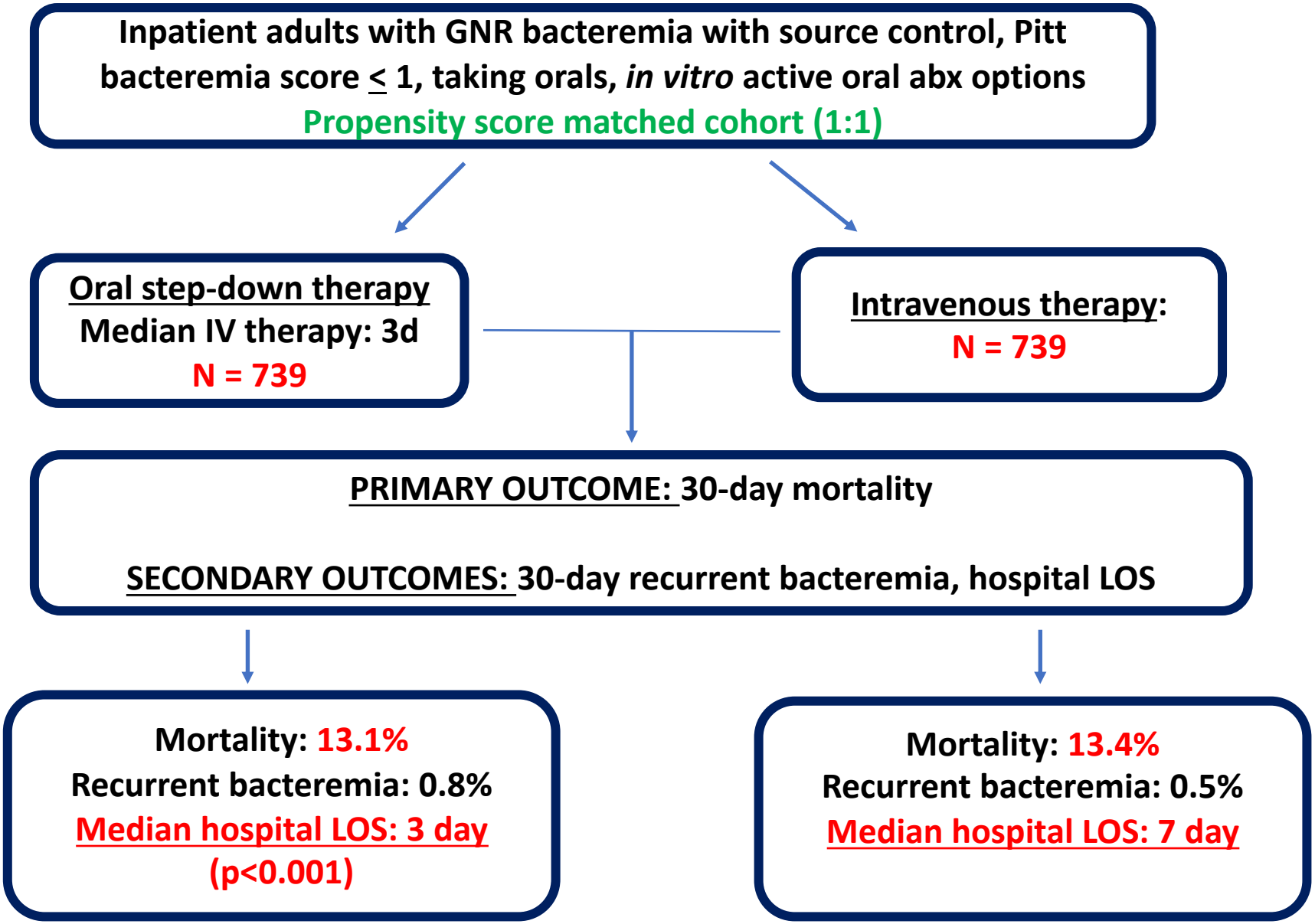
49 yo female with *E. coli* bacteremia secondary to pyelonephritis. She received 3 days of Ceftriaxone and is ready to be discharged home with oral antibiotics. She has no allergy to any medication. *E. coli* is susceptible to all of the following antibiotics.

A) Levofloxacin

B) Cefpodoxime

C) Amoxicillin/clavulanate acid

D) Trimethoprim/sulfamethoxazole



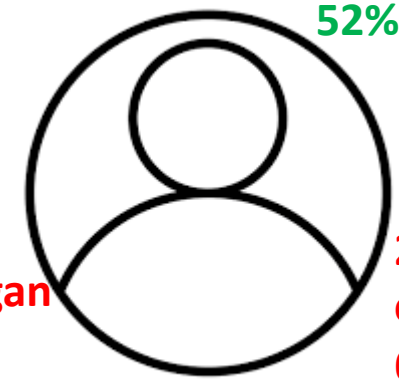
Tamma PD, et al. JAMA Internal Medicine 2019;179:316-323

Patient population

PATIENTS

59 years old
52% male

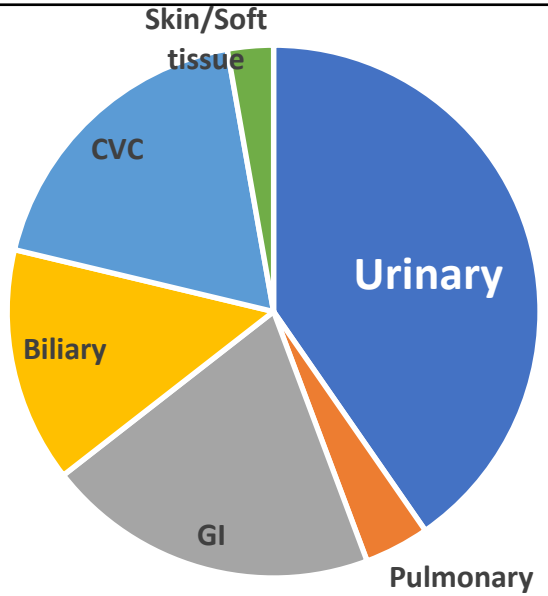
Median abx:
14 days



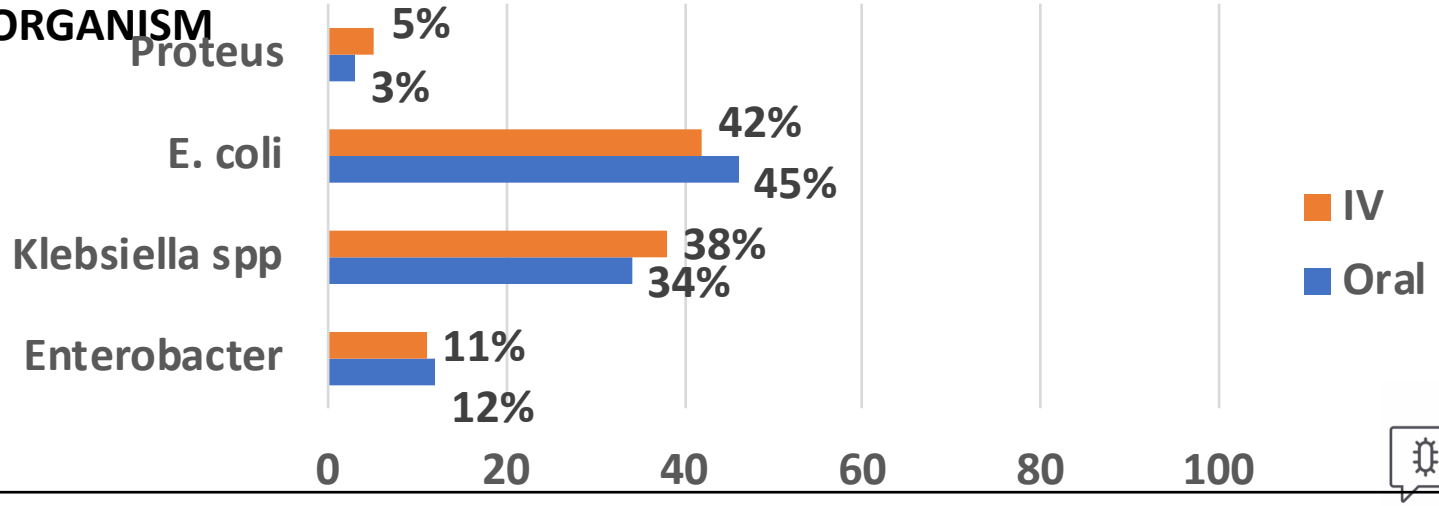
11% solid organ transplant

28% rec'vd chemo (past 6 mos)

SOURCE



BACTERIAL ORGANISM



Tamma PD, et al. JAMA Internal Medicine 2019;179:316-323

From: **Association of 30-Day Mortality With Oral Step-Down vs Continued Intravenous Therapy in Patients Hospitalized With Enterobacteriaceae Bacteremia**

JAMA Intern Med. 2019;179(3):316-323. doi:10.1001/jamainternmed.2018.6226

Table 2. Antibiotic Therapy Administered to Patients Transitioned to Oral Antibiotic Therapy for Enterobacteriaceae Bacteremia

Antibiotic	Common Regimen	Bioavailability	Patients Receiving Treatment, No. (%) (n = 739)
Amoxicillin-clavulanate	500-1000 mg orally every 8-12 h	Low	38 (5.1)
Cefdinir	300 mg orally every 12 h	Low	30 (4.1)
Cefixime	200-400 mg orally every 12-24 h	Low	21 (2.8)
Cephalexin hydrochloride	500 mg orally every 6 h	Low	16 (2.2)
Cefpodoxime proxetil	200-400 mg orally every 12 h	Low	17 (2.3)
Ciprofloxacin hydrochloride	500-750 mg orally every 12 h	High	337 (45.6)
Levofloxacin	500-750 mg orally every 24 h	High	171 (23.1)
Moxifloxacin hydrochloride	400 mg orally every 24 h	High	10 (1.3)
Trimethoprim-sulfamethoxazole	160-320 mg orally every 6-12 h	High	99 (13.4)

70% FQ

	High Bioavailability N = 617 (%)	Low Bioavailability N = 122 (%)
30-day mortality	68 (11)	15 (12)
Recurrent bacteremia	4 (0.6)	0 (0)

Open Forum Infectious Diseases

MAJOR ARTICLE

Oral Fluoroquinolone or Trimethoprim-Sulfamethoxazole vs ß-Lactams as Step-Down Therapy for Enterobacteriaceae Bacteremia: Systematic Review and Meta-analysis

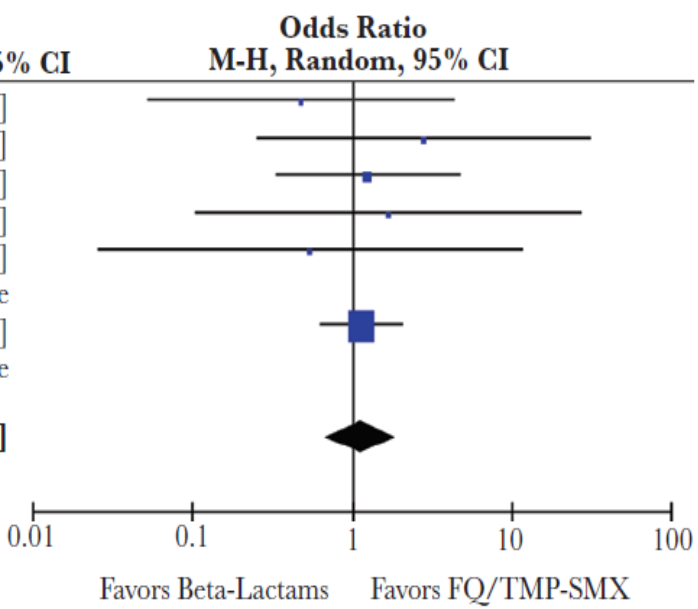
Chitra Punjabi,[1] Vivian Tien,[1] Lina Meng,[2] Stan Deresinski,[1] and Marisa Holubar[1]

[1]Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California; [2]Department of Pharmacy, Stanford Health Care, Stanford, California

	Beta-Lactams		FQ/TMP-SMX			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Fong 2018	1	59	4	114	5.1%	0.47 [0.05, 4.34]
Gumbleton 2018	2	86	1	119	4.3%	2.81 [0.25, 31.49]
Kutob 2016	3	77	9	285	14.1%	1.24 [0.33, 4.71]
Mercuro 2018	1	84	1	140	3.2%	1.67 [0.10, 27.13]
Rieger 2018	0	30	2	84	2.7%	0.54 [0.03, 11.59]
Sessa 2018	0	151	0	57		Not estimable
Tamma 2019	15	122	68	617	70.5%	1.13 [0.62, 205]
Thurber 2019	0	14	0	250		Not estimable
Total (95% CI)		**623**		**1666**	**100.0%**	**1.13 [0.69, 1.87]**
Total events	22		85			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.46$, df = 5 ($P = 0.92$); $I^2 = 0\%$

Test for overall effect: Z = 0.49 ($P = 0.63$)



Oral antibiotics

- Safe are effective as step-down therapy

- Which one?
  - FQ, most data and experience
  - Consider SMX/TMP, 90% bioavailable
  - β-lactam if no other options

- Once source control is achieved, and bacterial inoculum burden lessened, bioavailability may be less important

When to consider oral antibiotics?

Clinical Improvement

- Afebrile, improved WBC, hemodynamically stable, source control

Absorption

- Regular diet
- Taking other oral meds

Duration (IV + PO)

- Less is more
- Longer courses are associated with adverse effects, CDI, emergence of resistance, and longer hospital stay