
بسم الله الرحمن الرحيم

ANTIBIOTIC STEWARDSHIP PROGRAM AND INFECTION CONTROL

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Tsunami of antimicrobial resistance microorganisms

- **Antimicrobial resistance results in increased Morbidity and Mortality**
- **Cost of health care.**

- **Antimicrobials account for upwards of 30% of hospital pharmacy budgets up to 50% of antimicrobial use is inappropriate, adding considerable cost to patient care**

- **Given the emergence of MDRs**
- **Pathogens and their impact on clinical care, appropriate use of antimicrobial agents has become a focus of patient safety and quality assurance along with medication errors, allergy identification, and drug-drug interactions**

- **Infection Control and Antimicrobial Stewardship: Our only two strategies to combat antimicrobial resistance**

- The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria

- **Antimicrobial stewardship includes not only limiting inappropriate use**

Antimicrobial Stewardship

- The optimal selection, dose, and duration of an antimicrobial that results in the best clinical outcome for the treatment of infection, with minimal toxicity to the patient and minimal impaction subsequent development of resistance

Primary goal

- Optimize clinical outcomes while minimizing unintended consequences of antibiotic use toxicity
- Selection of pathogenic bacteria (eg, *C difficile)*
- Emerging resistance

Secondary goal

– Reduce healthcare cost without compromising quality of care

- **The ultimate goal of antimicrobial stewardship is to improve patient care and health care outcomes.**

- **Collaboration between the antimicrobial stewardship team and the hospital infection control and pharmacy and therapeutics committees or their equivalents is essential**

Infection Control Staff and Hospital Epidemiologists

- The problem of spread of antimicrobial-resistant organisms within hospitals has long been a concern of infection control professionals

- While some resistant organisms have primarily been thought to be infection control problems and others antibiotic-use problems, an absolute distinction is artificial and both transmission and selection play important roles in the spread of antimicrobial resistance

Infection Control Staff and Hospital Epidemiologists (Cont'd)

- **Infection control staff gather highly detailed data on nosocomial infections which may assist in the antimicrobial stewardship team's evaluation of the outcomes of their strategies**

- **Hospital epidemiologists have the expertise in surveillance and study design to lend to efforts studying the effect of antimicrobial stewardship measures**

Infection Control Staff and Hospital Epidemiologists (Cont'd)

- In turn, antimicrobial stewardship programs may be able to assist in efforts to control outbreaks by focused monitoring and/or restriction of antimicrobials in the targeted units.
- Any antimicrobial stewardship program should either be fully integrated with or work closely with a hospital's infection control program
- Such collaboration has the opportunity to synergistically reduce antimicrobial resistance and improve patient outcomes

Antimicrobial prescribing facts: the 30% rule

- ~ 30% of all hospitalized inpatients at any given time receive antibiotics
- Over 30% of antibiotics are prescribed inappropriately in the community
- Up to 30% of all surgical prophylaxis is inappropriate
- ~ 30% of hospital pharmacy costs are due to antimicrobial use
- 10-30% of pharmacy costs can be saved by antimicrobial stewardship programs

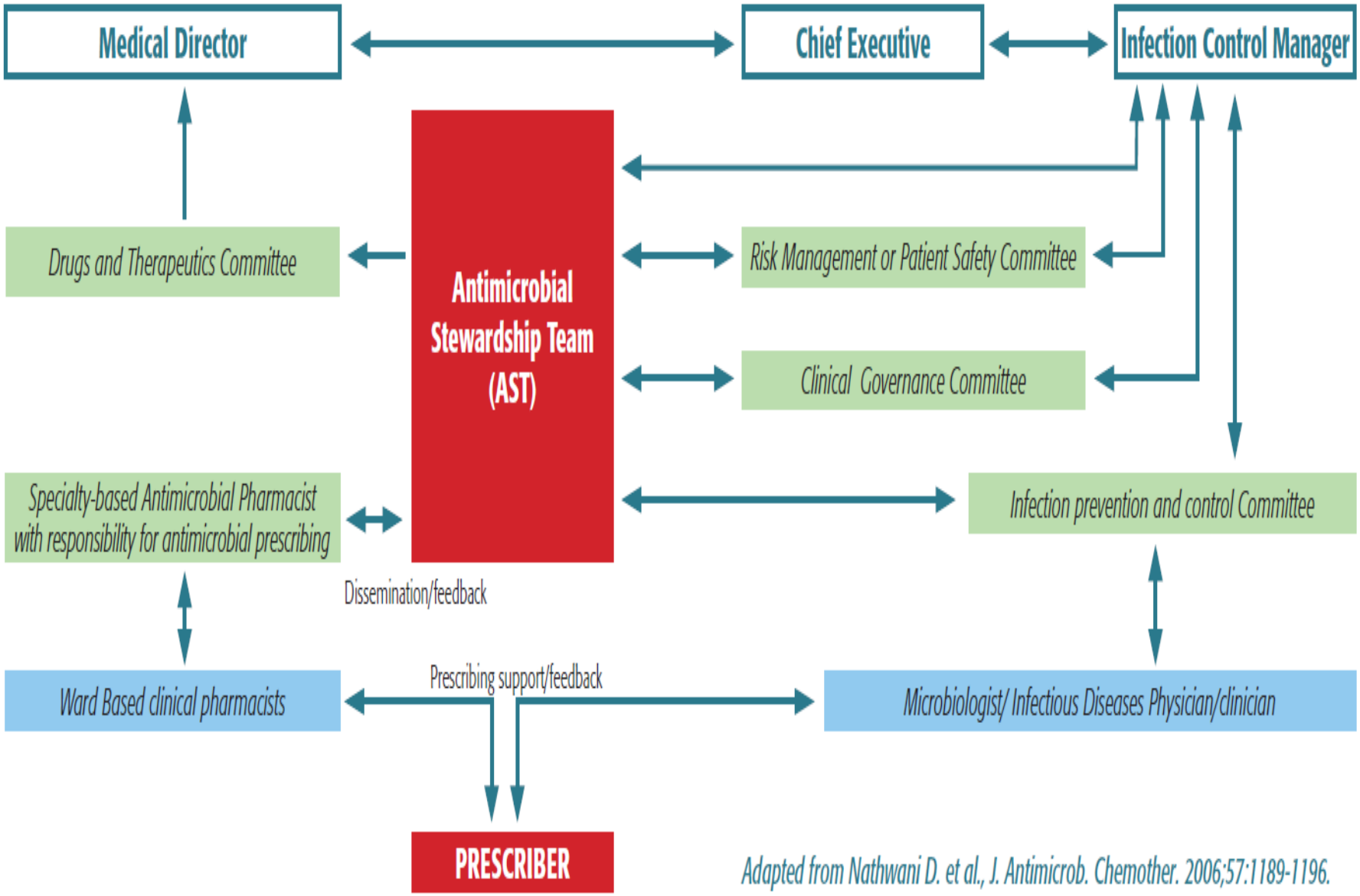
Surveillance of antimicrobial use and resistance

- Adapt empiric treatment according to local resistance trends
- Demonstrate changes in practice over time.
- Identify wards with high antimicrobial usage or use of non-policy antimicrobials and define targeted interventions required

Communicate

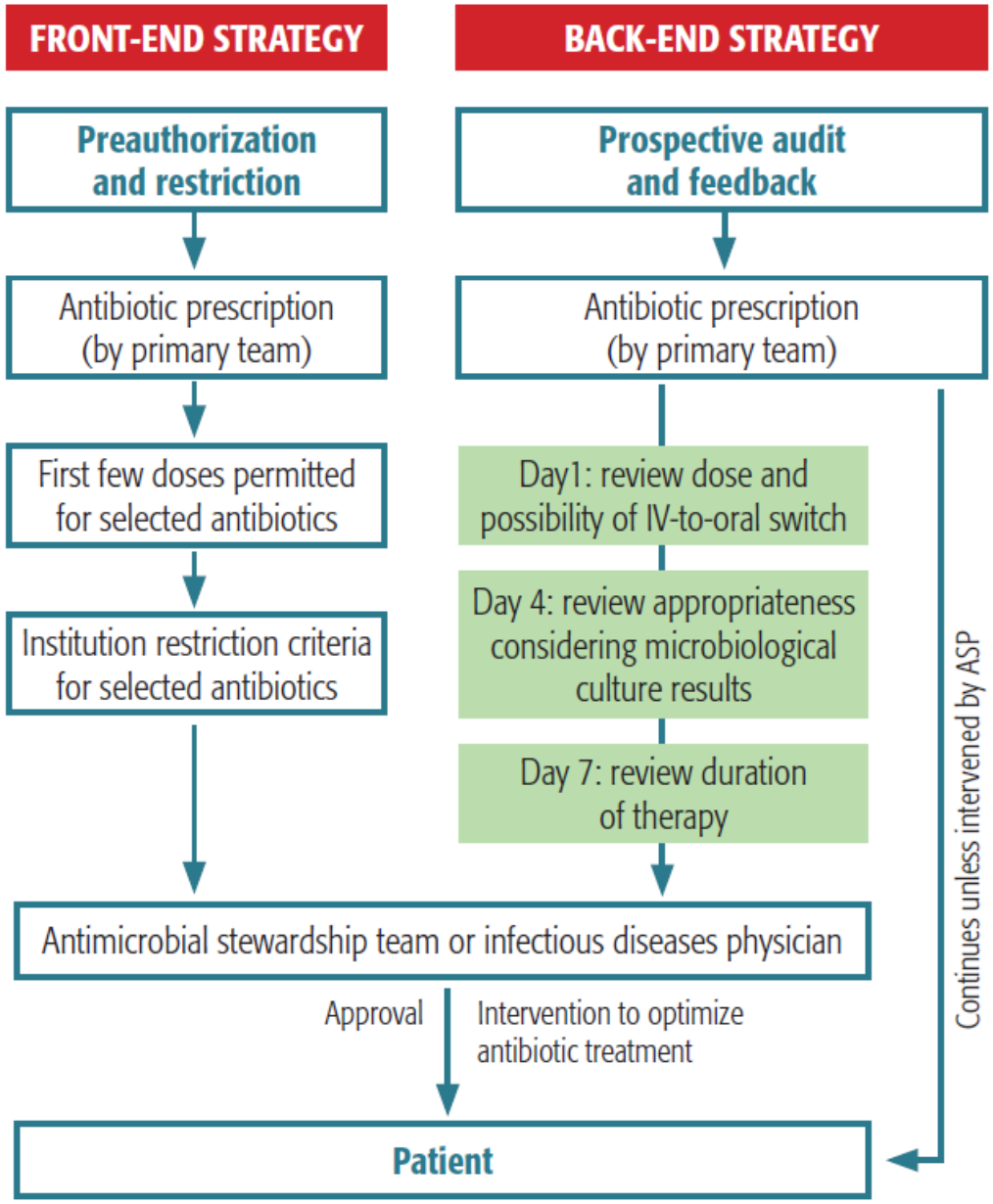
- Communication is a key component of the success of an ASP
- . clear, simple communication should show the vision and the benefits of the program, with core clinical messages.
- The “Start Smart - thenFoc us” approach in the UK is a good example of such an approach

Figure 7. Model of Antimicrobial Prescribing Pathway and Organization in Acute Hospitals in Scotland.

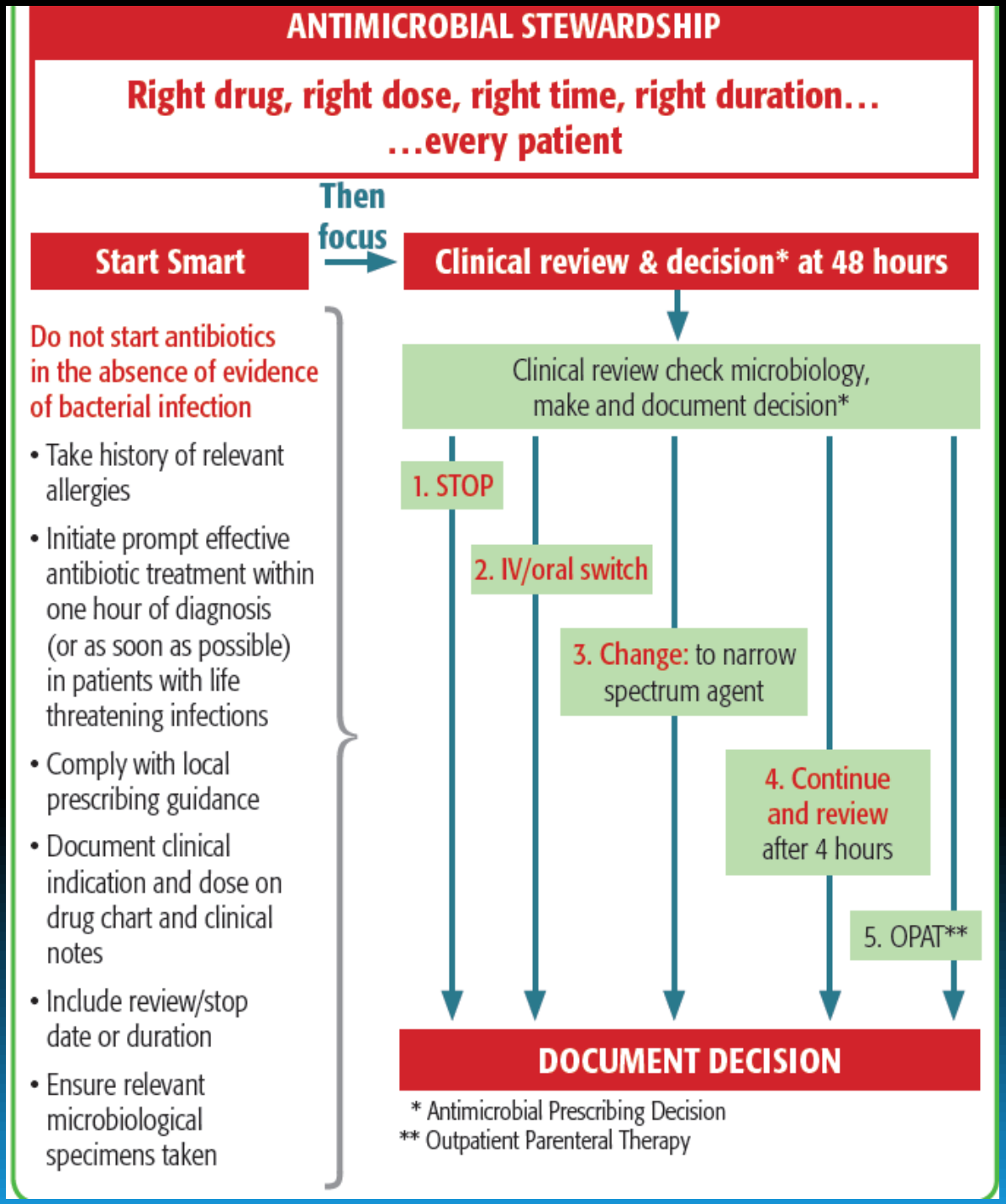


Adapted from Nathwani D. et al., J. Antimicrob. Chemother. 2006;57:1189-1196.

Figure 9. Front- and Back-end Antimicrobial Stewardship Strategy.



Adapted from Chung GW et al. Virulence 2013; 4:1-7.


ANTIMICROBIAL STEWARDSHIP
Right drug, right dose, right time, right duration…
…every patient
Then focus
Start Smart
Clinical review & decision* at 48 hours
Do not start antibiotics in the absence of evidence of bacterial infection
• Take history of relevant allergies
• Initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with life threatening infections
• Comply with local prescribing guidance
• Document clinical indication and dose on drug chart and clinical notes
• Include review/stop date or duration
• Ensure relevant microbiological specimens taken
Clinical review check microbiology, make and document decision*
1. STOP
2. IV/oral switch
3. Change: to narrow spectrum agent
4. Continue and review after 4 hours
5. OPAT**
DOCUMENT DECISION
* Antimicrobial Prescribing Decision
** Outpatient Parenteral Therapy

Shorter Is Better

- Many traditional antibiotic courses are unnecessarily long
- Durations of antibiotic therapy for most bacterial infections are based on the fact that the week has 7 days in it, resulting in traditional 7 -14 day antibiotic courses
- The modern week has 7 days in it because the Roman Emperor Constantine the Great said so in 321 CE
- Had Constantine chosen a 4-day week, providers would likely routinely prescribe 4-8 day courses of therapy

Shorter Is Better

- **Fortunately, in the last 25 years, clinical investigators have clarified necessary antibiotic durations by conducting over 40 randomized controlled trials (RCT) comparing short-course vs. traditional courses of antibiotics for a variety of bacterial infections**
- **Short-course therapy was just as effective as longer courses, and often with better point estimates of clinical success, fewer adverse events, and/or diminished emergence of resistance at the site of infection**

Shorter Is Better

- Fernandez-Lazaro et al conducted an exhaustive retrospective study of 5.6 million outpatient antibiotic courses prescribed by 10,616 Family Medicine specialists in Ontario, Canada from March 2016 to February 2017.
- Unfortunately, the authors found that the median duration of antibiotic regimens was 7-8 days (38%), under 25% of prescriptions were shorter than 7 days, and substantially more than 30% were for longer than 8 days.
- Such long durations of therapy are unlikely warranted for most routine bacterial infections treated with outpatient oral antibiotics

Shorter Is Better

- By multivariate analysis the authors found that early career physicians (<11 years since graduation from medical school) were significantly less likely to prescribe prolonged courses than mid- or late-career physicians.
- Late-career physicians (≥25 years since medical school) did the worst. Other factors associated with prolonged courses included practice in a rural setting, patients with more co-morbidities, and patients who cared for proportionately more children

Diagnosis	Short (d)	Long (d)	Result
Community Acquired Pneumonia [23-31]	3 or 5	7, 8, or 10	Equal
Hospital Acquired/Ventilator Associated Pneumonia [32, 33]	7-8	14-15	Equal
Complicated Urinary Tract Infections/Pyelonephritis [34-39]	5 or 7	10 or 14	Equal
Complicated/Post-Operative Intra-Abdominal Infections [40, 41]	4 or 8	10 or 15	Equal
Gram Negative Bacteremia [42]	7	14	Equal
Acute Exacerbation of Chronic	$\leq$5	$\geq$7	Equal

Chronic Osteomyelitis [47]	42	84	Equal
Empiric Neutropenic Fever [48]	afebrile and stable x 72 h	Afebrile and stable x 72 h and with absolute neutrophil count > 500 cells/μl	Equal

Shorter Is Better

- Yahav et al. report the first RCT comparing shorter course (7 days) versus longer course (14 days) antibiotic treatment for adult patients with Gram negative bloodstream infection.
- The investigators enrolled 604 patients with Gram negative bloodstream infection across 3 academic centers , and randomized them to either 7 or 14 days of treatment – with all other aspects of treatment left to the discretion of the clinical team.
- The results indicated that 7 day treatment was non-inferior to 14 day treatment (45.8% vs 48.3%, risk difference -2.6%, 95%CI -10.5 to +5.3%)

Outcome	Short Arm (7 d) (n = 306)	Long Arm (14 d) (n = 298)	Risk Difference (95% CI)	*P* Value
Primary outcome	140 (45.8)	144 (48.3)	–2.6 (–10.5 to 5.3)	.527
90-d all-cause mortality	36 (11.8)	32 (10.7)	1.0 (–4.0 to 6.1)	.702
Readmissions	119 (38.9)	127 (42.6)	–3.7 (–11.5 to 4.1)	.363
Extended hospitalization beyond 14 d	15 (4.9)	19 (6.4)	–1.5 (–5.1 to 2.2)	.483
Distant complications	2 (0.7)	1 (0.3)	…	1.0
Relapse of bacteremia	8 (2.6)	8 (2.7)	–0.07 (–2.6 to 2.5)	.957
Suppurative complications	16 (5.2)	10 (3.4)	1.8 (–1.4 to 5.1)	.257
14-d mortality	7 (2.3)	4 (1.3)	0.95 (–1.42 to 3.44)	.288
28-d mortality	15 (4.9)	13 (4.4)	0.54 (–2.98 to 4.06)	.753
New clinically or microbiologically documented infection	70 (22.9)	68 (22.8)	0.06 (–6.6 to 6.8)	.987
Functional capacity: needs assistance/dependent in ADL or bedridden at 30 d	150 (51.4) (n = 292)	163 (57.2) (n = 285)	–5.8 (–13.9 to 2.3)	.031
Resistance development	33 (10.8)	29 (9.7)	1.0 (–3.7 to 5.9)	.690
Time to return to baseline activity, wk (90 d)	2 (0–8.3) (n = 218)	3 (1–12) (n = 222)	…	**.010**
Total hospital days (90 d from randomization)—survivors	3 (1–9) (n = 270 alive at day 90)	3.5 (1–10) (n = 266 alive at day 90)	…	.923
Total hospital days (90 d from randomization)—all	4 (1–10)	4 (1–12)	…	.603
Duration of appropriate antibiotic therapy for bacteremia	7 (7.0–8.0)	14.0 (14.0–14.0)	…	**< .001**
Total antibiotic days from culture collection to day 90 postrandomization	10.0 (9.0–18.0) (n = 270 alive at day 90)	16.0 (15.0–22.0) (n = 266 alive at day 90)	…	**< .001**
Adverse events				
Acute kidney injury	14 (4.6)	12 (4.0)	0.5 (–2.7 to 3.8)	.842
Liver function abnormalities	16 (5.2)	20 (6.7)	–1.5 (–5.3 to 2.3)	.494
Diarrhea during hospital stay	17 (5.6)	23 (7.7)	–2.2 (–6.1 to 1.8)	.285
Diarrhea until day 90[a]	49 (16)	54 (18.1)	–2.1 (–8.1 to 3.9)	.491
Rash	2 (0.7)	4 (1.4)	…	.445
Clostridium difficile infection	3 (1.0)	1 (0.3)	…	.322

Shorter Is Better

- **The study suggests that 7 days of treatment may be sufficient for hospitalized non-critically ill patients with Gram negative bacteremia with signs of early response to treatment.**
- **Evidence-informed shortening durations of antibiotic treatment offers the best approach to a clinical cure of patients with bacteremia, while minimizing potential patient- and population-level harms of antimicrobial treatment**

Antibiotic stewardship is the effort

- To measure antibiotic prescribing
- To improve antibiotic prescribing by clinicians and use by patients so that antibiotics are only prescribed and used when needed
- To minimize misdiagnoses or delayed diagnoses leading to underuse of antibiotics
- To ensure that the right drug, dose, and duration are selected when an antibiotic is needed