UWTASP tele-antimicrobial stewardship program | echo

October 31, 2023

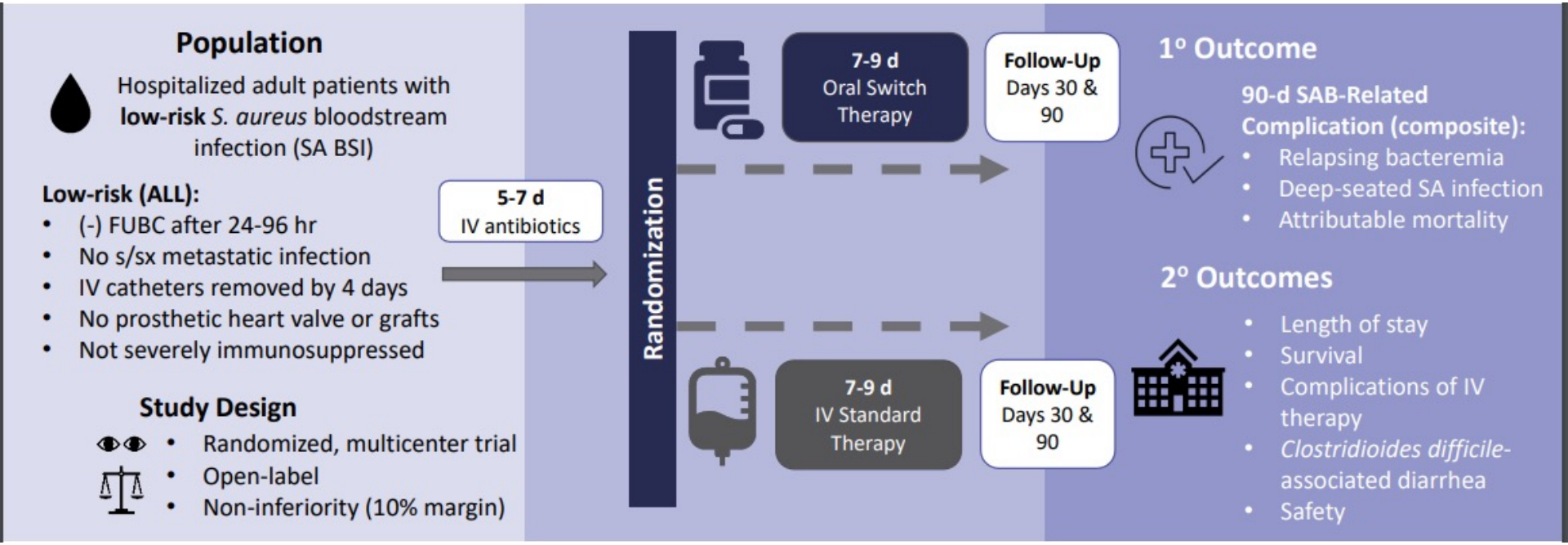
ID Week 2023 Highlights: Part 2

- Darra Drucker, PharmD
- Paul Pottinger, MD
- Hayato Mitaka, MD

Project ECHO

Oral Antibiotics for Staphylococcal Infections – SABATO Trial

Staphylococcus aureus Bacteremia Antibiotic Treatment Options (SABATO) Trial



Kaasch A, et al. ECCMID. 2022 April 25.

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ClinicalTrials.gov.NCT01792804. https://clinicaltrials.gov/ct2/show/NCT01792804

IDWeek 2023. *Slide credit*: Julie Justo, PharmD, MS, FIDSA, BCPS.

Oral Antibiotics for Staphylococcal Infections – SABATO Trial

Staphylococcus aureus Bacteremia Antibiotic Treatment Options (SABATO) Trial

Population

5063 patients screened
→ 213 enrolled (ITT)
→ 165 enrolled (CE)

- Only 16/213 (7.5%) MRSA
- Sources primarily venous catheters & SSTIs

Oral Switch Therapy Options

Oral Switch Therapy	First-line	Alternative
MSSA	TMP/SMX 1 DS PO Q12h	Clindamycin 600mg PO Q8h
MRSA	TMP/SMX 1 DS PO Q12h	Linezolid 600mg PO Q12h

CE = Clinically Evaluable Population; ITT = Intention-to-Treat Population

1º Outcome

90-day SAB-Related Complication (ITT)

13.0% (14/108)

12.4% (13/105)

Difference 0.7% (95% CI: -7.8 to **9.1%**)

Oral switch **non-inferior** to IV standard therapy

2º Outcomes

- ↔ **Length of stay** mean -3.1 days (95% CI -7.5 to 1.4)
- ↔ **90-day survival** 83.6% vs. 89.0%, diff. -5.4% (95% CI -14.8 to 4.0%)
- ↔ **IV complications** 9.3% vs. 17.0%, diff. -7.9% (95% CI -17.6 to 1.9%)
- ↔ *C. difficile* associated diarrhea 2% vs. 2%
- ↔ **Serious adverse events** 33.6% vs. 26.2%, p=0.292

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Oral Antibiotics for Staphylococcal Infections – SABATO Trial

Staphylococcus aureus Bacteremia Antibiotic Treatment Options (SABATO) Trial

Arm	Analysis	Age group and sex	Admission diagnosis	CCI	Initial focus of SAB	Days to complication	Reported complication	Death	Microbiologically documented	Interpretation
OST	CE mITT ITT	60-69, f	Oedema of lower limbs	5	Central venous catheter	1	Readmission on day 2 of study medication due to clinically suspected complicated infection with pulmonary focus on chest CT	No	No	Early deep-seated infection
OST	CE mITT ITT	70-79, m	Hepatic lobectomy due to colorectal cancer metastasis	7	Central venous catheter	19	Septic knee arthritis and SAB followed by aortic dissection (Gram-positive cocci in pathology specimen)	Yes	Yes	Late complication (deep-seated focus, bacteremia, attributable death)
OST	CE mITT ITT	60-69, m	Cardiac failure	4	Peripheral venous catheter	28	Participant had a second episode of SAB with *S. aureus* cultured from blood and a tibial ulcer	No	Yes	Late complication (bacteremia, deep-seated focus)
OST	mITT ITT	80-89, m	Cellulitis	4	Skin and soft tissue infection	4	Participant with diabetic foot ulcer, a CT was performed on day 5 of study medication and showed osteomyelitis at the site of the ulcer	No	No	Early deep-seated infection
OST	mITT ITT	80-89, f	Hypertensive crisis	2	Peripheral venous catheter	15	Participant felt weak 3d after EOT but declined readmission. On day 8 after EOT, participant was found unconscious at home and was readmitted. Recurrent SAB due to suppurative thrombophlebitis at exit site of previous catheter. TEE unremarkable. Death one week later.	Yes	Yes	Late complication (extension of focus, bacteremia, attributable death)
OST	ITT	50-59, f	Repeated falls	5	Skin and soft tissue infection (subcutaneous abscess)	3	On day 3 of study medication, an extension of the original focus occurred from the gluteal region to proximal inner thigh. Resolved with drainage and prolongation of oral antimicrobial therapy.	No	No	Early deep-seated infection (extension of focus)

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Oral Antibiotics for Staphylococcal Infections – SABATO Trial

Conclusion

- Promising results, helpful strategy for transitions of care
- Possible increased serious adverse events requires further evaluation
- Limitations:
  - Still awaiting peer-reviewed publication
  - Uncomplicated cases are minority of *staphylococcus aureus* cases overall
  - Few MRSA cases (7.5%) in trial
  - Limited PO regimens (mostly TMP/SMX)
  - Trial terminated early due to slow enrollment rate

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Oral Antibiotics for Staphylococcal Infections – PK/PD

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Review

Clinical pharmacological considerations in an early intravenous to oral antibiotic switch: are barriers real or simply perceived?

Cornelia B. Landersdorfer [1,*], Amanda Gwee [2,3,4], Roger L. Nation [1]

[1] Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia
[2] Department of Pediatrics, The University of Melbourne, Parkville, Australia
[3] Infectious Diseases Unit, The Royal Children's Hospital, Melbourne, Parkville, Australia
[4] Infectious Diseases Research Group, Murdoch Children's Research Institute, Parkville, Australia

Objective: to examine rationale for early IV to PO antibiotic switch in the context of clinical PK/PD principles

→Not just bioavailability, but considering other factors

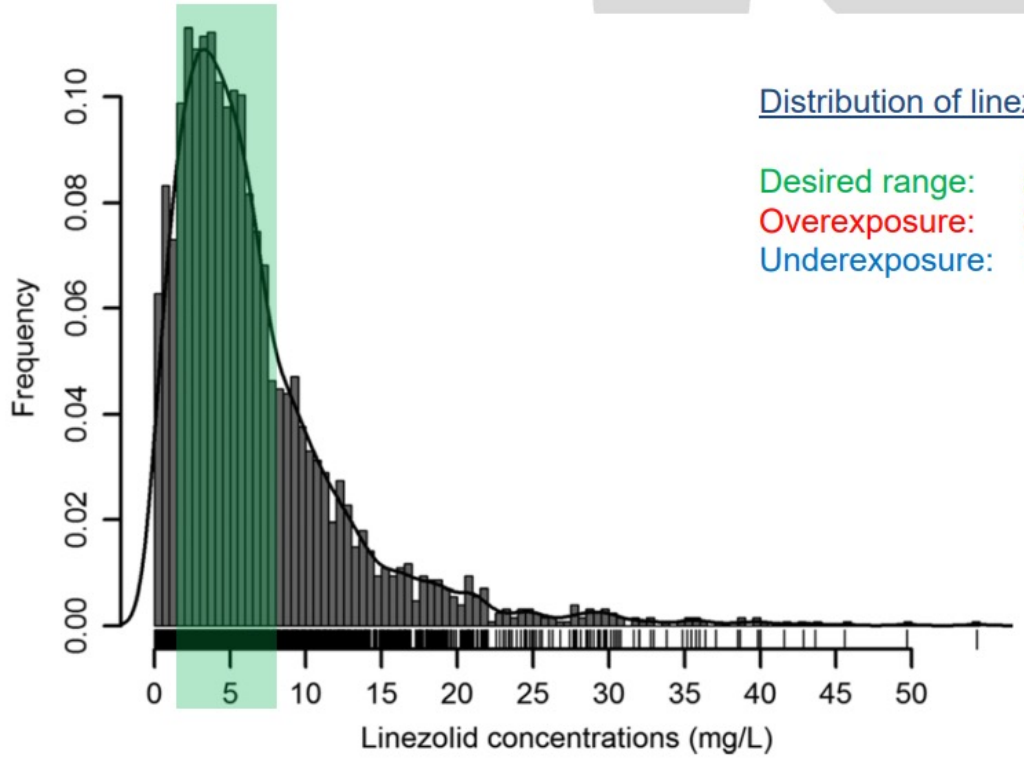
→Focus on probability of Target Attainment

IDWeek 2023.
Landersdorfer CB, et al. Clin Microbiol Infect. 2023;29:1120. doi: 10.1016/j.cmi.2023.04.009.

Linezolid Dosing and TDM

A 10-Year Experience of Therapeutic Drug Monitoring (TDM) of Linezolid in a Hospital-wide Population of Patients Receiving Conventional Dosing: Is there Enough Evidence for Suggesting TDM in the Majority of Patients?

Pea F, Cojutti P, Baraldo M. *Basic Clin Pharmacol Toxicol.* 2017;121(4):303-308



Distribution of linezolid Cmin

Desired range: 50.8% (1262/ 2484)
Overexposure: 33% (821/2484)
Underexposure: 16.2% (401/2484)

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IDWeek 2023. *Slide credit*: Pier Giorgio Cojutti, MD, PhD.

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Linezolid Dosing and TDM

Proactive therapeutic drug monitoring (TDM) may be helpful in managing long-term treatment with linezolid safely: findings from a monocentric, prospective, open-label, interventional study
Cojutti P, Merelli M, Bassetti M and Pea F. *J Antimicrob Chemother.*2019:74(12):3588-95

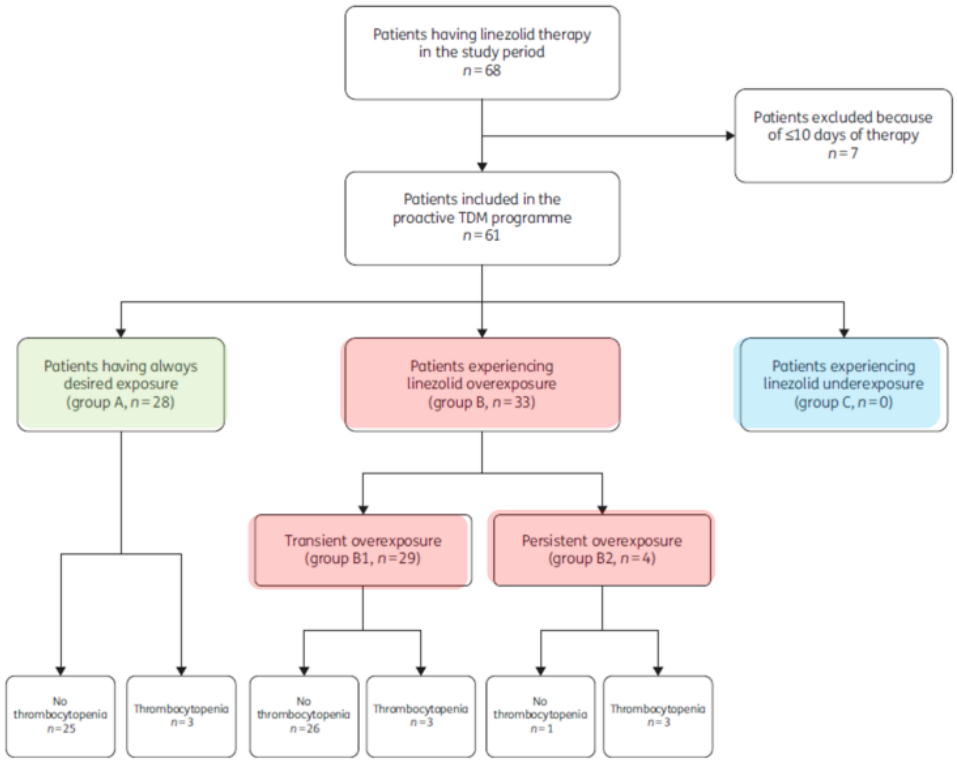

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Table 3. Univariate and multivariate regression analysis of variables associated with the occurrence of thrombocytopenia (n=61 patients)

	Univariate analysis		Multivariate analysis	
Variable	unstandardized β coefficient (95% CI)	*P*	unstandardized β coefficient (95% CI)[a]	*P*
Age	0.002 (−0.003 to 0.007)	0.459		
Gender	0.006 (−0.214 to 0.226)	0.956		
Weight	0.003 (−0.003 to 0.009)	0.374		
Mean CL_{CR}	0.000 (−0.002 to 0.002)	0.923		
Baseline platelet count	**−0.001 (−0.002 to 0.000)**	**0.001**	**−0.001 (−0.002 to 0.000)**	**0.007**
Length of therapy	−0.001 (−0.003 to 0.001)	0.418		
Median linezolid C_{min}	**0.048 (0.020 to 0.076)**	**0.001**	**0.038 (0.005 to 0.070)**	**0.023**
Duration of overexposure	0.012 (0.000 to 0.023)	0.042	0.002 (−0.011 to 0.014)	0.797

IDWeek 2023. *Slide credit*: Pier Giorgio Cojutti, MD, PhD.

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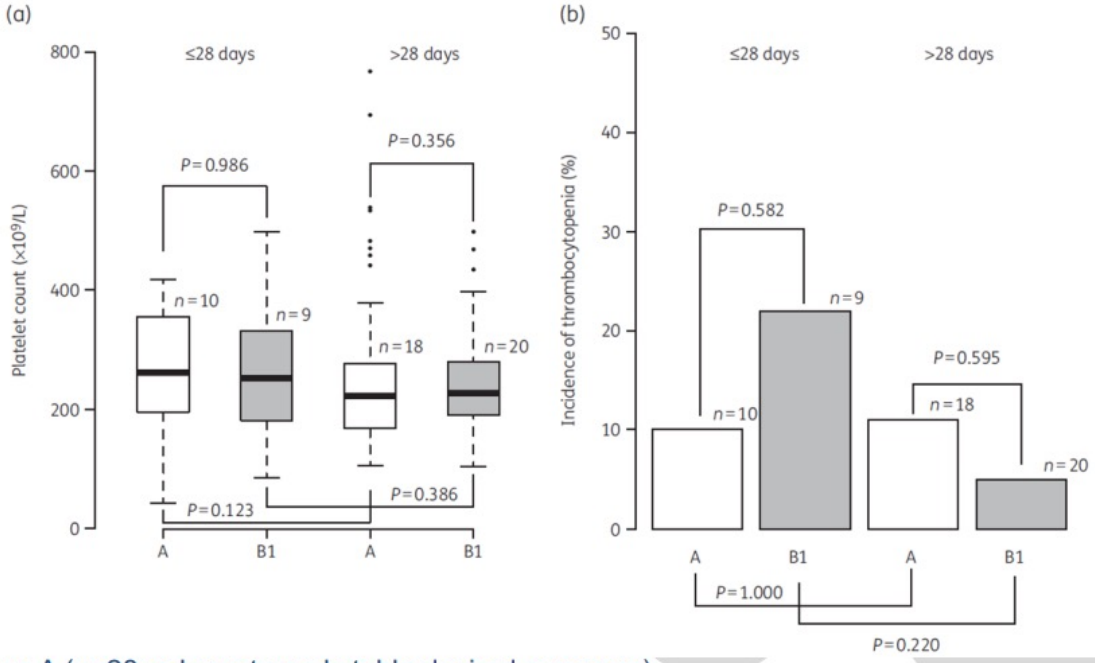

Group A (n=28; adequate and stable desired exposure)

Group B1 (n=29; transient overexposure with subsequent attainment of stable desired exposure)

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Building ID Resiliency: Beyond Cookies in the Break Room

What We Should Measure: Strategies for Understanding Burnout and Other Drivers of Workforce Challenges

Ronda L. Cochran, MPH

Healthcare Worker Burnout

An Analogy…
To a Microbiologic Disease Process

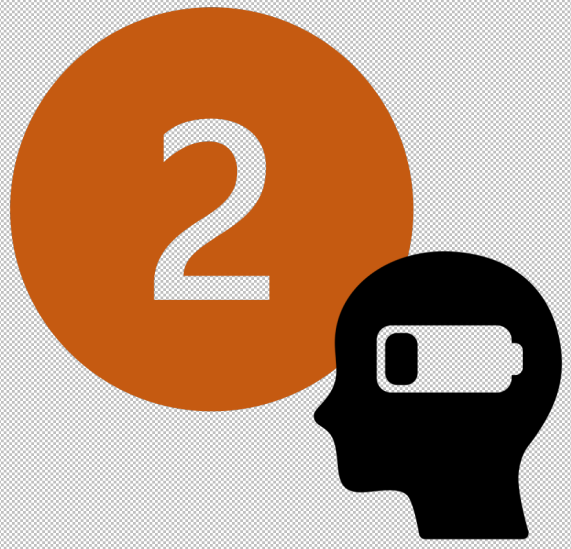
"An individual who works in a particularly toxic work environment (aggressive pathogen) is at risk of getting sick independent of their resilience, whereas an individual with poor resilience (immunosuppressed) may be at risk for burnout even in supportive environments"

Ref: Rehder Arch Pathol Lab Med (2021)
Amoeba Sisters: Immune System https://www.youtube.com/watch?v=fSEFXl2XQpc

Physical Signs of Burnout

- Headaches
- Fatigue
- Insomnia
- Muscle pains
- Sadness, anger or irritability
- Restlessness
- Nervous tics
- Loss/gain in weight
- Vulnerability to illnesses:
  - Heart disease
  - High blood pressure

Mayo Clinic and https://www.helpguide.org/articles/stress/burnout-prevention-and-recovery.htm



Psychological Signs of Burnout

- Feeling helpless, detached, and defeated
- Sense of failure and self-doubt
- Decreased satisfaction and sense of accomplishment
- Increasingly cynical and negative outlook

Mayo Clinic and https://www.helpguide.org/articles/stress/burnout-prevention-and-recovery.htm

Behavioral Signs of Burnout

- Withdrawing from responsibilities
- Isolating oneself from others
- Procrastinating, taking longer to get things done
  - Increased sick leave
  - Skipping work
  - Coming in late and leaving early
- Overindulging
  - Using food, drugs, or alcohol to cope

Mayo Clinic and https://www.helpguide.org/articles/stress/burnout-prevention-and-recovery.htm

Convergent Themes

Convergent Themes Expressed by Participants Across Focus Groups
Theme 1: Mental & Physical Toll of the Job
Theme 2: Staffing
Theme 3: Support from Facility Leadership
Theme 4: Respect, Recognition, and Value
Theme 5: Pay & Incentives

Burnout - In the Words of Healthcare Workers

"It just got unbearable. I was emotional, tired, anxious about what I was going to go into. And just not having support. It was over and over with no end in sight. There was no thanks." - RN

"For me, burnout involved moral injury. I was at a place where we didn't have receptive administration to listen to our concerns as we worked on the frontline. It was moral injury but also fatigue. When I take care of a patient, I give my heart and soul. I was burnt out, I wasn't taking care of myself." - MD

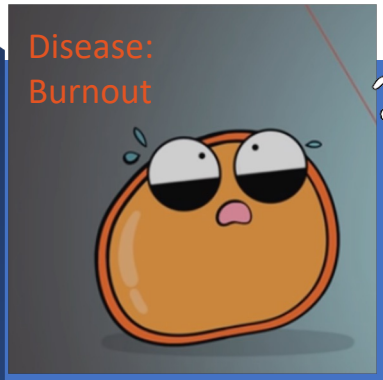
"I got so stressed and burned out and anxious that I wasn't sleeping. I wasn't eating. I wasn't taking care of myself. And if I wasn't taking care of myself, then I couldn't take care of my patients."- CNA

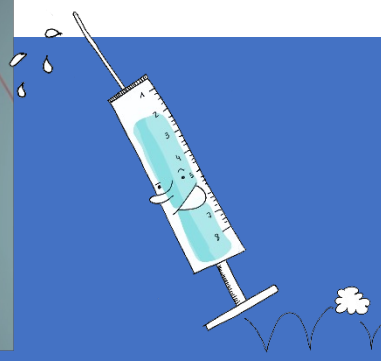
Evaluation of Burnout

- Maslach Burnout Inventory – By far the most widely used in the literature, but proprietary and costs associated with use; 22 questions covering emotional exhaustion, depersonalization, and low sense of personal accomplishment based on frequency (Never-Every day)

How often:	Never	A few times a year	Once a month or less	A few times a month	Once a week	A few times a week	Every day
	0	1	2	3	4	5	6
1) I deal very effectively with the problems of my patients.							
2) I feel I treat some patients as if they were impersonal objects.							
3) I feel emotionally drained from my work.							
4) I feel fatigued when I get up in the morning and have to face another day on the job.							
5) I've become more callous towards people since I took this job.							
6) I feel I'm positively influencing other people's lives through my work.							
7) Working with people all day is really a strain for me.							
8) I don't really care what happens to some patients.							
9) I feel exhilarated after working closely with my patients.							

An Analogy…
To a Microbiologic Disease Process





"Some features of work environments bolster our resilience, in the same manner as a live attenuated vaccine prepares the immune system against future assaults… these work environments may be characterized by meaningful work with:

- Recognition from Leaders
- Opportunities for Personal Growth
- Considerate & Supportive Colleagues
- Leaders who promote Autonomy, Psychologic Safety, & Adaptability"

Ref: Rehder Arch Pathol Lab Med (2021)
Amoeba Sisters: Immune System https://www.youtube.com/watch?v=fSEFXl2XQpc

Smells Like Team Spirit: Lessons for Sustainable ID Practice- A Soccer Enthusiast's Perspective

Lessons learned from a lifetime of playing and watching soccer…

Gonzalo Bearman MD, MPH, FACP, FSHEA, FIDSA
Richard P. Wenzel Professor of Medicine
Chair- Division of Infectious Diseases
Virginia Commonwealth University

VCU Medical Center

Win, lose or draw there is (almost) always another match- Setbacks Abound, Burnout is a Threat

On Team Players….

"Jamie, I think that you might be so sure that you're one in a million, that sometimes you forget that out there, you're just 1 of 11. And if you just figure out some way to turn that 'me' into 'us'…the sky's the limit for you."

– -Ted Lasso

Leadership Goal: Recognize the Unique Talents of the Physicians on the Team

Evidence suggests that physician's who spent at least 20% of the professional effort focused on the dimension of work they find most meaningful are significant at a lower risk for burn out

Shanafelt TD et al *Mayo Clin Proc.* 2017;92(1):129-146

Google: Project Aristotle

- 180 teams studies across organization
  - The 'who' of the team equation not impactful
  - Team behavioral norms (dynamic) most important
    - Psychologically safe environments (norm) leading to team bonding- most critical for high functioning teams
      - Leaders encourage and promote honest and compassionate conversations about ideas, challenges, frictions, everyday annoyances- *to address needs*
- Teams are most effective when work is purposeful, personally integrated and not just focused on efficiency

https://www.nytimes.com/2016/02/28/magazine/what-google-learned-from-its-quest-to-build-the-perfect-team.html

Infection Control & Hospital Epidemiology

Infection Control & Hospital Epidemiology (2022), 1–4
doi:10.1017/ice.2022.221

SHEA

Commentary

Leadership in healthcare epidemiology, antimicrobial stewardship, and medicine: A soccer enthusiast's perspective

Gonzalo Bearman MD, MPH, FACP, FHSEA, FIDSA
Division of Infectious Diseases, Virginia Commonwealth University, Richmond, Virginia

Soccer is the world's most popular game, enjoyed by billions. In the book *How Soccer Explains the World*, by Franklin Foerr, the greater cultural meaning and resonance of the sport is neatly explored.[1] Although soccer is neither Bach nor Buddhism, it is often more deeply felt than religion and just as much a part of a community's fabric as a repository of traditions.[1]

I was born in Argentina, where soccer is an institution, as deeply revered as Catholicism and Eva Peron. Although I neither played professionally nor coached, I played competitively in my youth and as an NCAA Division I collegiate athlete. I continue to compete as an adult and watch as many matches as feasible. As an academic infectious disease specialist, healthcare epidemiologist, and division chair, many of the lessons learned from a lifetime of watching and playing soccer parallel my experiences and challenges on the job. Herein, I highlight leadership insights learned as a soccer enthusiast.

Successful individuals are gritty and resilient yet underpinned by a supportive organization

"I start early and I stay late, day after day, year after year. It took me 17 years and 114 days to become an overnight success." —Lionel Messi, FIFA World Footballer of the Year 2009–2012, 2015, Argentina

"To excel you have to learn to be comfortable being uncomfortable and be willing to respond to adversity" —Rose Lavelle, 2019 FIFA World Cup Champion, USA

"It is hard to beat somebody that never gives up" —Megan Rapinoe, 2019 FIFA World Cup Champion, USA

It is impossible to perform flawlessly. Even the most successful players and teams lose matches and fail to achieve goals. The success of a career is largely a driven by grit, resilience, and organizational culture. In *Grit*, Angela Duckworth defines the single most important predictor of success and achievement: a steadfast passion and perseverance for long-term goals.[2] Grit is about having an "ultimate concern"—a goal you care about so much that it organizes and gives meaning to almost everything you do, even when progress toward that goal is halting or slow.[2] Resilience, or the ability to recover quickly from difficulties, stems from grit and from positive, deliberate coping mechanisms cultivating compassion, compartmentalizing work, serial monotasking, taking on site detachment breaks, exercising mindfulness for emotional stability, cognitive flexibility, and mental agility.[3]

Grit and resilience mitigate burnout. Burnout is a threat in athletics and other high-intensity professions. In the field of infectious diseases, only 45% of respondents to a recent survey were happy and fulfilled in their profession,[4] and overall physician burnout is nearly 50%.[5] Studies to understand the prevalence and drivers of burnout in healthcare epidemiology and antimicrobial stewardship are urgently needed.

Successful organizations promote both individual- and system-level strategies to mitigate burnout. These include individual and organization interventions such as mindfulness training, stress management guidance, and small group discussions. Duty-hour reductions and workload reductions in combination reduced physician burnout by 10%.[6] Shanafelt et al[5] highlighted the key organizational strategies that significantly decreased burnout to two-thirds the national rate. These included acknowledging the issue, harnessing the power of leadership, implementing targeted work-unit interventions, cultivating community at work, using rewards and incentives, aligning values, strengthening culture, promoting flexibility and work-life integration, providing resources to promote resilience and self-care, and funding organizational science on mitigating burnout.[5]

Highly accomplished soccer players, such as Rose Lavelle, Megan Rapinoe, and Lionel Messi, are individually gritty and resilient yet are supported by high-quality national teams and professional clubs with top-tier coaches, athletic trainers, management, and a relentless culture of excellence.[7] Healthcare is no different; individual factors such as grit and resilience should be nurtured by leaders while they relentlessly demand a supportive organizational culture with a sustained commitment to wellness that will minimize burnout and maximize career development, mastery, and purpose in work.

Sometimes agendas are discordant, even in the same organization

"Part of the manager's job is to act as a scapegoat, shielding the club owners from blame." —Simon Kuper in *Soccernomics*

Professional soccer is a business with the aim of making money through ticket sales, player transfer fees, merchandising, advertising, and television contracts. Although not always discordant, the role of the professional soccer coach is team preparation and winning games, whereas management prioritizes profitability. However, the pursuit of profit does not guarantee victories on the field, yet successful sporting performance rarely has a negative impact on club profitability and organizational health.[8]

Author for correspondence: Gonzalo Bearman, E-mail: gonzalo.bearman@vcuhealth.org

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VCU Medical Center

Spoiler Alert! Preview of Clinical Practice Guideline Updates

Catheter-related Bloodstream Infection Management Guideline Update

Nasia Safdar, MD, PhD University of Wisconsin

CSiM

CQ 2: In the assessment of multi-lumen IV catheter and suspected CRBSI, what is the impact of BCx from one versus all lumens on patient important outcomes?

How important is it to collect blood cultures from all lumens?

Old (2009, archived)

- If a blood sample cannot be drawn from a peripheral vein, it is recommended that ≥2 blood samples should be drawn through different catheter lumens (B-III).
- **It is unclear whether blood cultures should be drawn through all catheter lumens** in such circumstances (C-III)."

New

- In adult patients suspected of CRBSI with a multi-lumen catheter, **obtain blood cultures from all lumens** rather than a single lumen (strong recommendation, low quality evidence).

CQ 2: In the assessment of multi-lumen IV catheter and suspected CRBSI, what is the impact of BCx from one versus all lumens on patient important outcomes?

Outcomes	Study	Findings		
Microbial colonization		Lumen 1	Lumen 2	Lumen 3
	Dobbins 2003	40%	40%	20%
Discordant cultures	Rider 2022 (pediatric cancer)	34% discordant results (pathogen from one lumen and no growth from another)		
	Planes 2016	41% of total episodes, QBCs for at least one of the IVC lumens tested negative		
Percentage of CRBSI episodes picked up	Guembe 2010 (how many episodes are picked up)	keep 1 lumen	keep 2 lumens	Keep 3 lumens
		62%	84.2%	100%
	Planes 2016	2/3^{rds} of confirmed CRBSI picked up		

Dobbins BM et al. Crit Care Med. 2003 Jun;31(6):1688-90.
Guembe M et al. Clin Infect Dis. 2010 Jun 15;50(12):1575-9.

Is guidewire exchange an option?

- Patient with suspected CRBSI. BCx both from CVC and peripheral draw grew Coag-negative Staph.
- IV vancomycin was started.
- Patient has very few vascular re-siting options and suppose that the catheter has not been removed. IR would like to know if guidewire exchange can be an option. What should we do?

    A. guidewire exchange
    B. no guidewire exchange

CQ 7: What is the impact of guidewire exchange at the existing IVC site versus removal and replacement at a new site? Does the impact differ for patients with hemodialysis catheters or short-term catheters?

Draft Recommendation:

- In situations where there are limited alternatives to secure vascular access, **we suggest using guidewire exchange**, for antimicrobial-impregnated catheter if available, with activity against the infecting organism (weak recommendation, very low quality of evidence).
- The recommendation is the same **regardless of device type (e.g., HD cath vs short-term CVC)**.

CQ 7: What is the impact of guidewire exchange at the existing IVC site versus removal and replacement at a new site? Does the impact differ for patients with hemodialysis catheters or short-term catheters?

Outcome	Studies	Number of patients	Risk ratio (GE vs CR)
Mortality	Saleh 2017 (RCT in HD patients)	678	0.67 [0.19, 2.34]
	Voiculescu 2021 (Fibrin sheath disruption, retrospective, no adjustment)	55	0.06 [0.00, 1.15]
	Chaftari 2011 (retrospective cohort, cancer patients, AMC)	120	0.21 [0.01, 3.88]
In-hospital mortality	2 studies: Parbat 2013, Chaftari 2011	428	0.75 [0.37, 1.52]
ICU mortality	Parbat 2013 (AST catheters)	308	0.69 [0.41, 1.17]
Recurrent infection	Chaftari 2011	120	0.18 [0.01, 3.12]
	Saleh 2017	678	1.20 [0.37, 3.89]
	Erbay 2006	73	1.25 [0.64, 2.42]
	Voiculescu 2021	55	0.24 [0.07, 0.86]
Persistent bacteremia	Chaftari 2011	120	1.33 [0.23, 7.66]
New infection	Voiculescu 2021	55	1.43 [0.30, 6.81]
Local site infection	Hou 2006 (retrospective, HD catheters)	36	1.44 [0.13, 15.34]

CQ 8: In patients with CRBSI who have had their IVC removed and are on appropriate antibiotic therapy, what is the impact of inserting a catheter before versus after blood cultures are negative on patient important outcomes?

Guidewire exchange failed - new catheter needed. Timing of a new catheter insertion?

Draft Recommendation:

- In patients with CRBSI who have had their IVC removed and who are on antibiotic therapy, **we suggest delaying IVC reinsertion until after blood cultures are confirmed to be sterile** rather than reinsertion before blood cultures is confirmed to be sterile (weak recommendation, low quality evidence).

Timing of reinsertion of a new CVC

HOWEVER,

- In patients with CRBSI who have had their IVC removed and who are on antibiotic therapy and **clinically responding**, and causative **pathogen is not Candida spp**, IVC **reinsertion can be done if and when clinically indicated with close observation** of the clinical status of the patient (**weak recommendation, low quality evidence**).

Timing of reinsertion of a new CVC

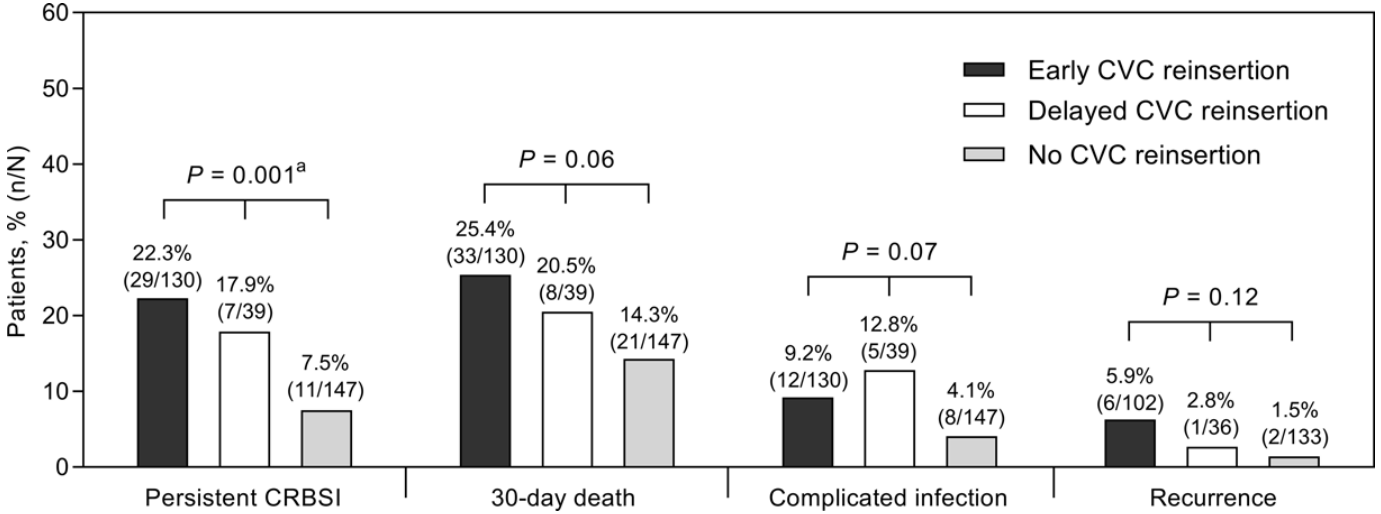


Fig. 2. The clinical outcomes of 316 patients with CRBSI who underwent early, delayed, or no CVC reinsertion. [a]*Post hoc* analysis with Bonferroni correction failed to show a significant difference between the early and delayed reinsertion groups (adjusted $P > .99$) but revealed a significant difference between the early and no reinsertion groups (adjusted $P = .002$).

- Retrospective cohort study of 316 adult patients with confirmed CRBSI who underwent CVC removal, comparing Early (< 3 days) vs delayed (> 3 days) reinsertion
- After controlling for several confounding factors, early CVC reinsertion was not associated with persistent CRBSI or 30-day mortality compared with delayed reinsertion

Lee YM et al., Infect Control Hosp Epidemiol. 2021 Feb;42(2):162-168.

Follow-up Blood Culture in Gram-negative Bacteremia

Duke University School of Medicine

Clinical impact of follow-up blood cultures in gram-negative bloodstream infections: A validation cohort

Joshua T. Thaden, Felicia Ruffin, Larry Park, Joshua B. Parsons,
Vance G. Fowler Jr., and Stacey A. Maskarinec

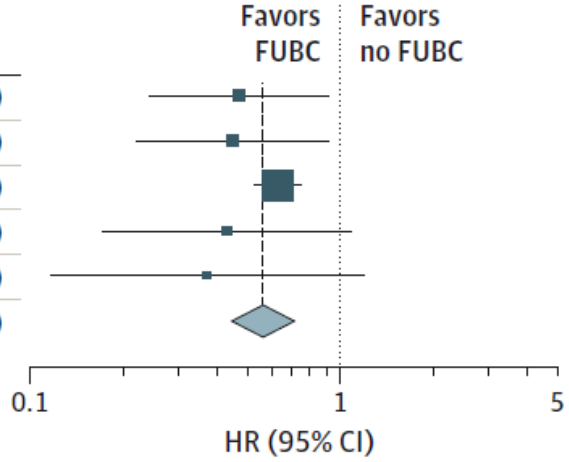
Follow-up Blood Cultures (FUBC) in Gram-negative Bacteremia are Controversial

PROS	CONS
Document clearance	Contaminants
Identify source control issues	Increased work/cost
Identify antibiotic issues	Extend hospital stay

FUBC may be associated with better mortality

Figure 2. Association of Obtaining Follow-up Blood Cultures (FUBCs) With Mortality in Patients With Gram-Negative Bloodstream Infection

Source	HR (95% CI)
Amipara et al,[9] 2021	0.47 (0.24-0.91)
Giannella et al,[7] 2020	0.45 (0.22-0.92)
Maskarinec et al,[5] 2020	0.63 (0.53-0.75)
Green et al,[21] 2021	0.43 (0.17-1.08)
Mitaka et al,[22] 2021	0.37 (0.12-1.19)
Total	0.56 (0.45-0.71)
Heterogeneity: $\chi^2_4 = 2.57$ ($P = .63$); $I^2 = 0\%$	



- **However,**

Studies accounted for **selection bias** and **immortal time bias**

Thaden JT, et al. JAMA Netw Open 2022

Methods: Prospective cohort study at Duke

Clinical data from patients enrolled into the Duke Bloodstream Infection Biorepository (BSIB)

Prospectively-enrolled cohort of adult inpatients with monomicrobial gram-negative bloodstream infection at Duke

2015 - 2021

Exclusion criteria:

- Hospice
- Death w/in 24h of initial Bcx
- Neutropenia

Selection bias: → Propensity score-based outcome comparison (IPTW)

Immortal time bias: → Exclusion criteria; Sensitivity analysis
(Exclude patients died <48h and <72h from index Cx)

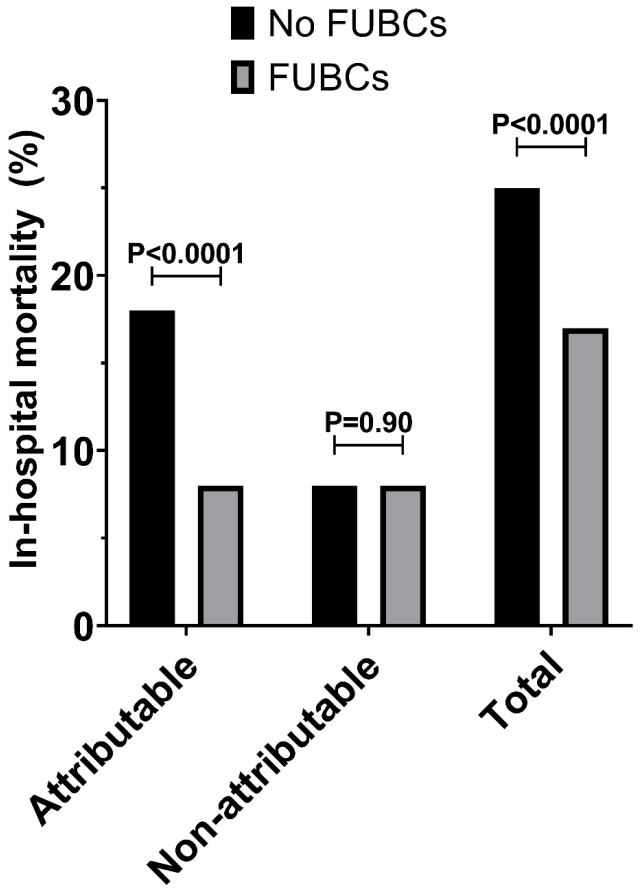
FUBCs were associated with lower mortality

Patient cohort

N=1291 patients

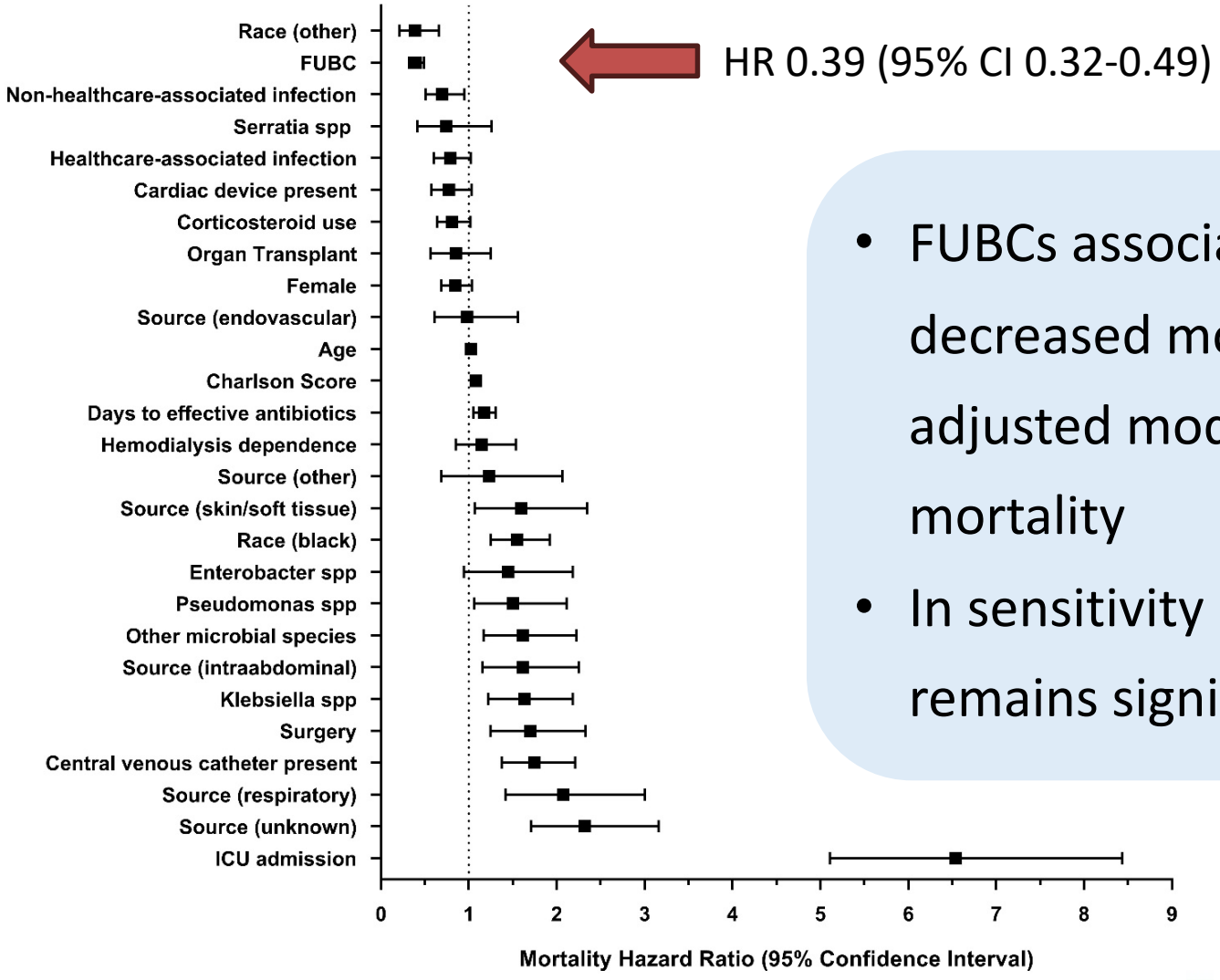
n=279 (22%) No FUBCs

n=1012 (78%) FUBCs



Unadjusted attributable and total mortality higher in patients without FUBCs

FUBCs were associated with lower mortality

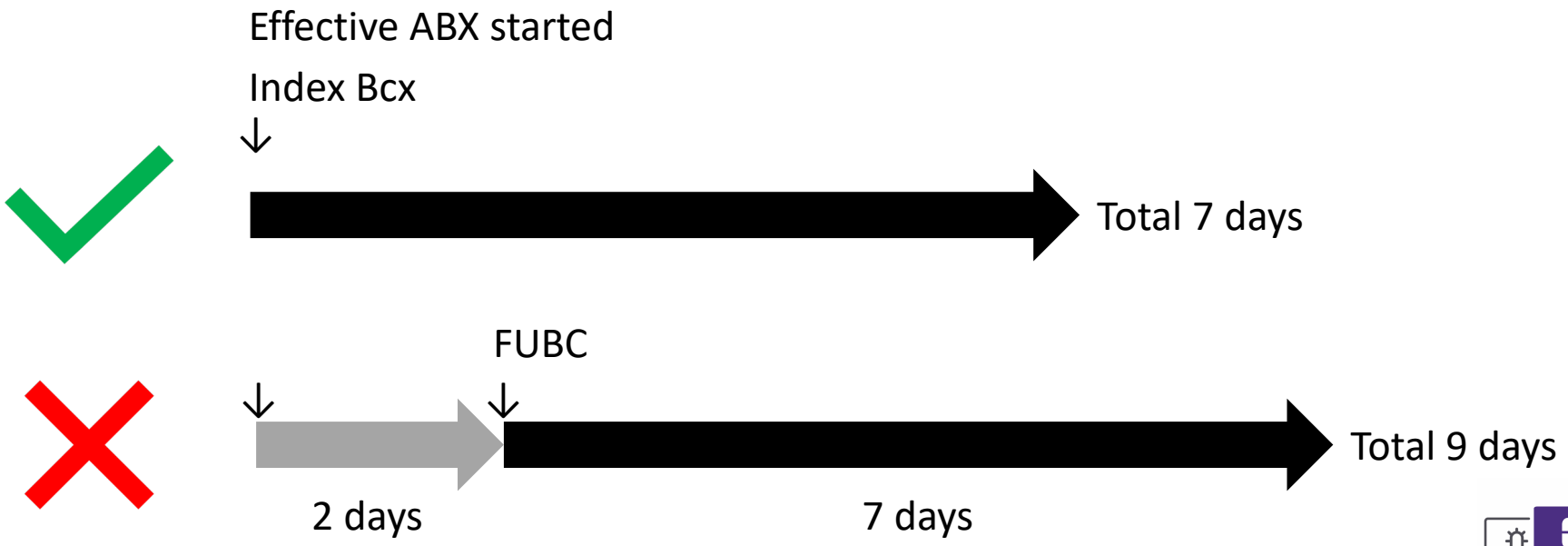


HR 0.39 (95% CI 0.32-0.49)

- FUBCs associated with decreased mortality in adjusted model of attributable mortality
- In sensitivity analysis, there remains significant difference

Reminder: Duration of ABX therapy for bacteremic UTI = 7 days

Per new cUTI guidelines panel member, **Day 1 should be the 1st day of effective abx therapy**, **NOT the day of 1st negative Bcx**



Questions?