



Rapid-Fire Journal Club

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In Memoriam: Nirav Patel, MD

- Graduated from CSMC/VA/OVMC ID Fellowship in 2011 after completing critical care fellowship
- Chief of Staff at SSM Health Saint Louis University Hospital and University Medical Center in New Orleans
- IDSA Journal Club panelist 2013-22



The Winners This Round



- Prevalence of *Candida* endophthalmitis and role of routine eye exams
- Incidence of fever after cardiac surgery
- Improving the diagnosis of acute pulmonary coccidioidomycosis
- Yield of IR-guided biopsies for native vertebral osteomyelitis
- Deep brain stimulator infection review
- Impact of aminoglycoside breakpoint changes
- Partial oral treatment for *S. aureus* bacteremia in people who inject drugs
- Impact of time to appropriate antimicrobial treatment in bacteremia

Candidemia and Risk for Endophthalmitis

- 2016 IDSA guidelines recommend dilated eye exam by ophthalmologist in all patients with candidemia
 - Preferably within 1 wk of diagnosis
 - Delay exam for neutrophil recovery in neutropenic pts
- 2021 American Academy of Ophthalmology statement calls this a “low value” practice and only recommends ophtho consult for symptomatic patients

“The recommendation is made without participation by a body of similar stature representing ophthalmologists and is based on the presumption that such screening will prevent vision loss. It is extracted from studies that are decades old, performed before implementing appropriate definitions of ocular disease with candidemia and before the era of systemic antifungal medication. The “low-quality evidence” status has been recognized by the IDSA, whereas the guideline inflates the likelihood of sight-threatening disease and the benefits of ophthalmologic evaluation.”



h/t @okwolding on Twitter

The background...

- Lead author of statement published a systematic review (without meta-analysis) of 38 studies that made a distinction between:
 - “Concordant” endophthalmitis (frank vitreous involvement): median 0.8% incidence
 - “Discordant” endophthalmitis: median 14.9%
- Incidence higher in studies prior to 1994, when endophthalmitis classification criteria were established
- Outcomes only available for 19 cases of concordant endophthalmitis, 6 of which received invasive management
 - 3 improved; 3 did not

New systematic review/meta-analysis!

- Used same criteria of concordant vs. discordant candidal endophthalmitis (CE) as well as a broader category of ocular candidiasis (OC)
- 70 studies included in meta-analysis of OC
- 35 studies included in meta-analysis of concordant CE
- 5 studies included in meta-analysis of risk factors associated with CE

Findings

- Pooled prevalence of OC: 10.7%
- Overall pooled prevalence of CE: 3.08%
 - Concordant: 1.83%
 - Discordant: 7.37%
- Prevalence higher in studies from Asian countries (concordant CE 3.64%)
- Factors associated with CE:
 - *albicans* species (pOR 3.02)
 - TPN (pOR 6.92)

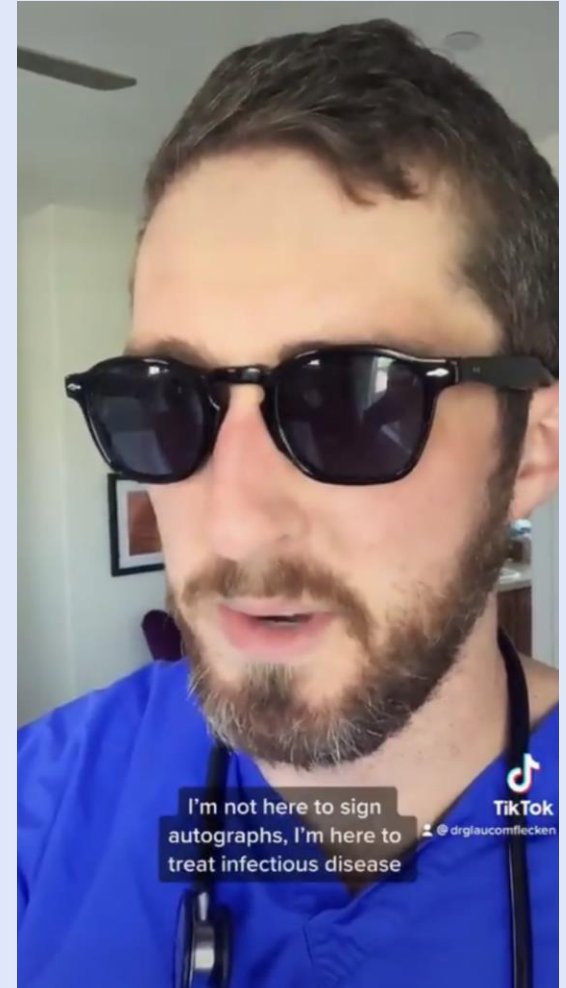
What accounted for the difference in concordant CE prevalences?

- 22 of 70 studies were published after 2018
- 10 studies published prior to 2018 were not included in Breazzano systemic review
- Analysis of pre-2018 studies yielded concordant CE prevalence of 1.3%

Take Home Points

- Last 2 sentences of paper say it the best:

“There is an urgent need for more nuanced, evidence-based screening protocols to detect Candida ocular involvement. A joint statement from both the infectious diseases and ophthalmology professional societies is called for.”

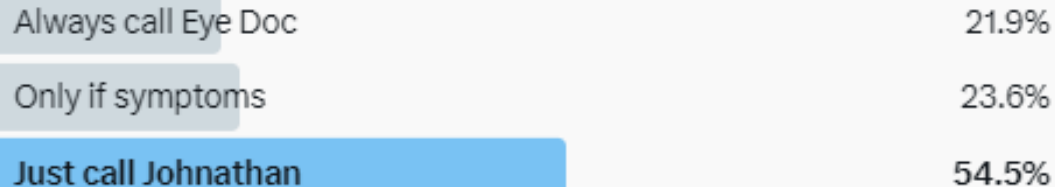


Consensus achieved?



Gabe 🐱🔵 @IdVilchez · Apr 26

[#IDTwitter](#) I am still not sure whether or not I should interrupt my ophthalmology friends golf game or sun tanning session [@DGlaucomflecken](#) to see every single patient with candidemia, should also bother them for every Bacillus cereus bacteremia? Even in asymptomatic patients



479 votes · Final results

2 1 14 34.8K



Dr. Glaucomflecken @DGlaucomflecken · Apr 26

Replying to [@IdVilchez](#)

Depends who you ask. American Academy of Ophtho says only if symptomatic. IDSA says everybody. If patient is awake and alert and is asymptomatic, I say no consult (data backs this up), but many patients with candidemia are very sick and may not be able to describe symptoms

3 1 55 32.5K



Christopher Graber @glavaidguy · Apr 26

Replying to [@DGlaucomflecken](#) and [@IdVilchez](#)
agree with this approach

Incidence of fever after cardiac surgery

- Common cause for consultation (and empiric broad-spectrum antibiotics)
- Many episodes are likely related to proinflammatory cytokine release in the context of surgery
- Does implantation of prosthetic material affect this?

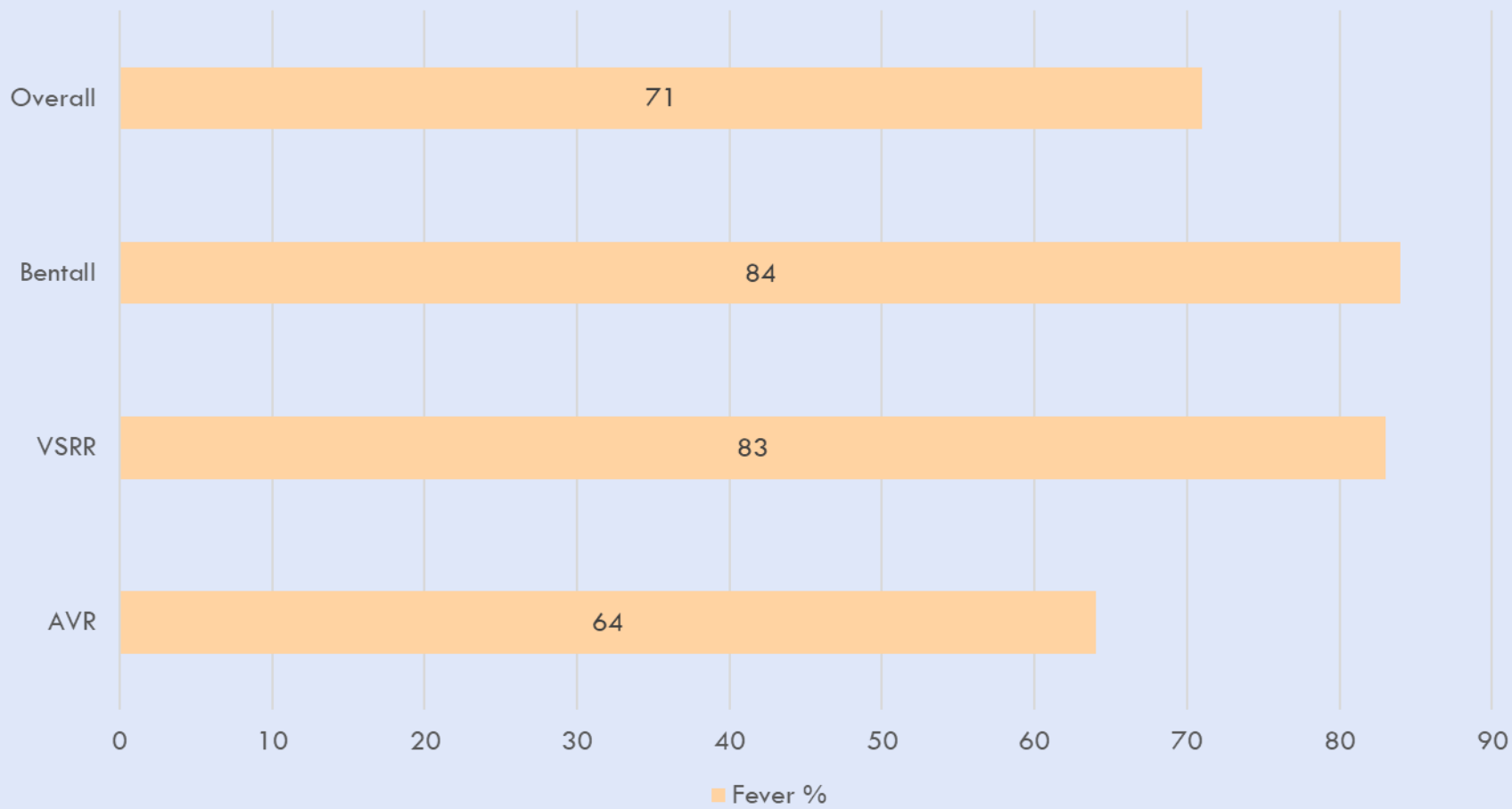
Incidence of fever after cardiac surgery

- Retrospective study of three types of cardiac surgeries performed at a university medical center in The Netherlands from 2014-21
 - Aortic root with aortic valve replacement (Bentall procedure) (n=76)
 - Valve-sparing root replacement (n=40)
 - Isolated aortic valve replacement (n=191; 2018-21)

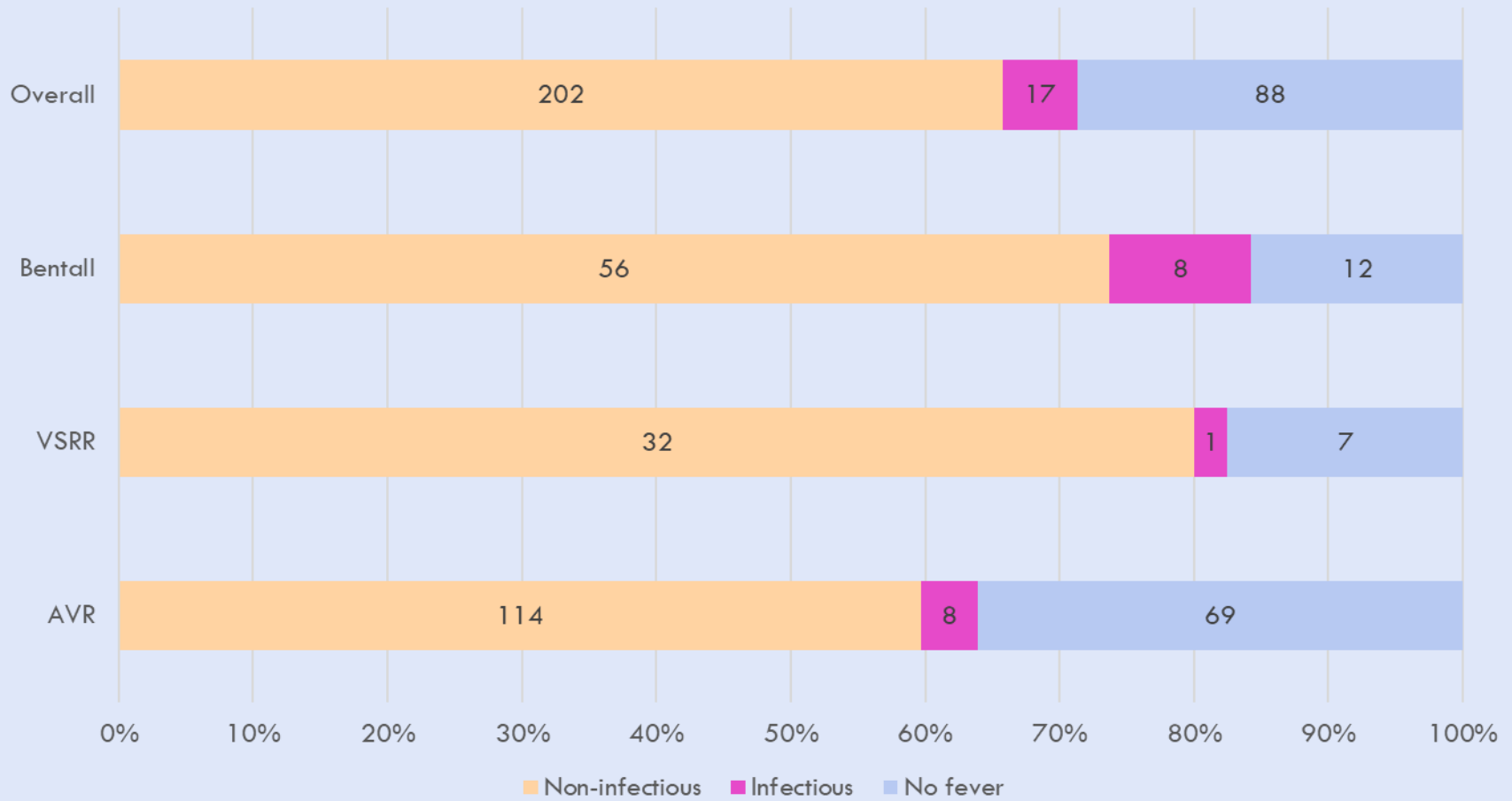
Study procedures

- Determined overall incidence of fever ($T \geq 38.0^\circ\text{C}$) during 14d post-surgery
- Exclusion criteria:
 - Reoperation
 - Pre-existing infection
 - Age $< 18\text{y}$
 - Other cardiac surgery
 - Use of deep-hypothermic circulatory arrest

Study Findings: Incidence of fever within 14d (%)



Study Findings: Non-infectious vs. infectious etiology of fever



Study Findings: Fever characteristics

- Maximum temperature 38.8°C in patients with infection; 38.4°C in patients without ($p=0.03$)
- Occurred median 1.7d after surgery in infection; 1.8 in those without
- WBC 16k in those with infection; 13.8 in those without ($p=0.03$)
- 5.8 days of fever in those with infection; 2.4 in those without ($p=0.04$)

Infection types

- UTI (n=6)
- HAP (n=6)
- Infected hematoma (n=1)
- Wound infection (n=1)
- Mediastinitis (n=1)
- Prosthetic infection (n=1)
- Fulminant colitis (n=1)

Take Home Points

- Fever after cardiac surgery is exceedingly common
- Infection associated with fever after cardiac surgery is uncommon (and rarely associated with mediastinitis/deep-seated infection)
- Watch-and-wait approach (and appropriate diagnostic workup) can likely be employed in the majority of cases

Challenges in Diagnosis of Acute Pulmonary Coccidioidomycosis

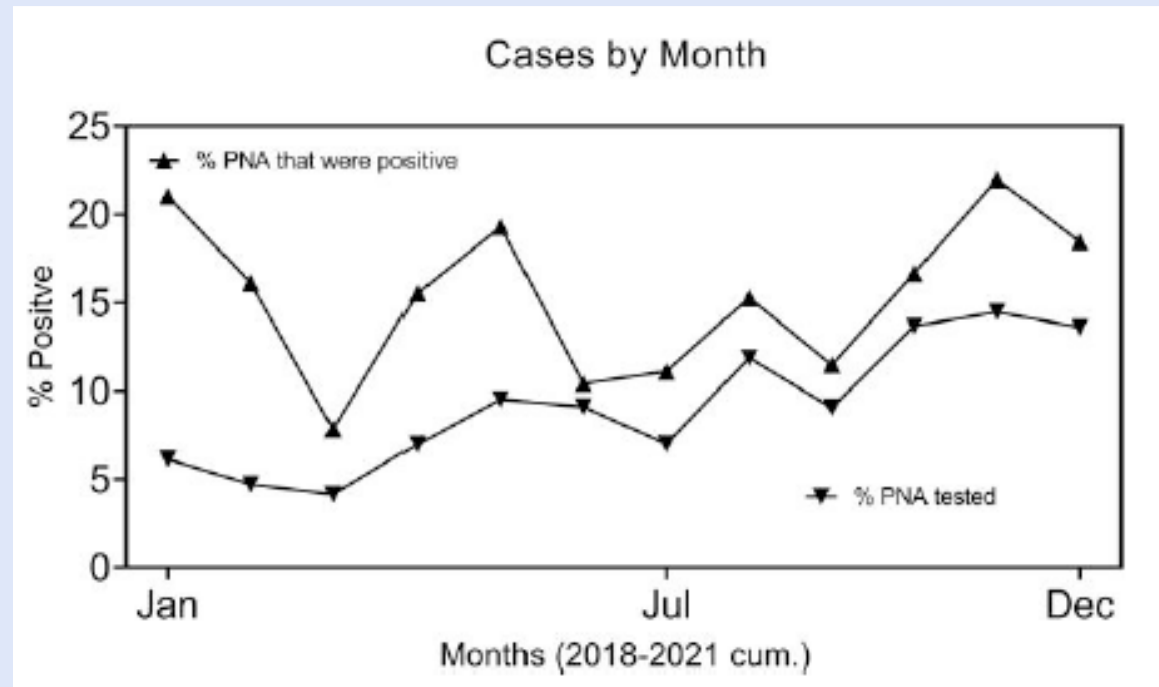
- Cognitive bias that pneumonia is a bacterial phenomenon
- Serology can be insensitive early in clinical course (and can take several days to return)
- Confusion as to the role of antifungal therapy (mild cases don't necessarily need treatment)
- As a result, acute pulmonary cocci is rarely diagnosed in urgent care clinics (~0.2%)

Banner Health Urgent Care Services intervention: February 2020

- Clinical practice guidelines to encourage sending cocci serologies included in clinical orientation lectures to newly-hired clinicians
- Cocci included as a topic in quarterly refresher lectures covering pulmonary/ENT topics
- Periodic reminders in emails and monthly provider meeting presentations

Trends in Testing Practice

- 3-fold increase in visits with cocci tests ordered in 2020-21 (21.5%) vs. 2018-19 (7.6%)
- Positivity rates highest in August, November, and December



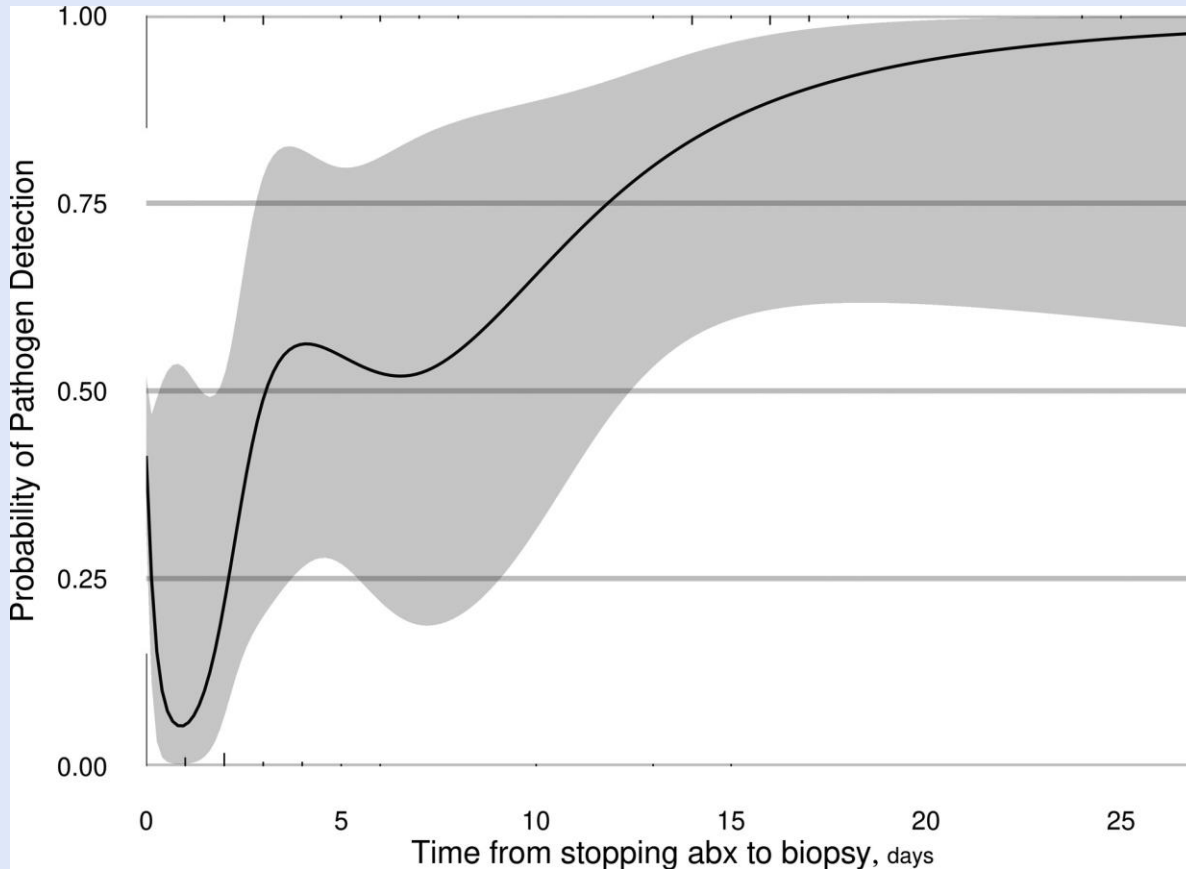
Diagnostic Challenges in Native Vertebral Osteomyelitis (NVO)

- Often subacute presentation, may not present with positive blood cultures
- Antibiotics often given prior to attempts to make a diagnosis
- Yield of open biopsy higher than image-guided, but rarely done

Mayo Experience with IR-Guided Biopsy of Suspected NVO, 2011-21

- Among 209 initial image-guided biopsies, 110 (52.6%) yielded positive microbiologic results
- Repeat biopsies were positive in 14 out of 39 (35.9%) patients
- 130 (62.2%) patients had antibiotic exposure in the prior 28d, with 87 receiving antibiotics up to the same day of biopsy

Mayo Experience with IR-Guided Biopsy of Suspected NVO, 2011-21



- Positive yield significantly higher with a longer duration of antibiotic-free period
- Microbiologic yield only improved above 50% with at least 3 antibiotic-free days prior to biopsy, increasing up to 75% around day 12.

Mayo Experience with IR-Guided Biopsy of Suspected NVO, 2011-21

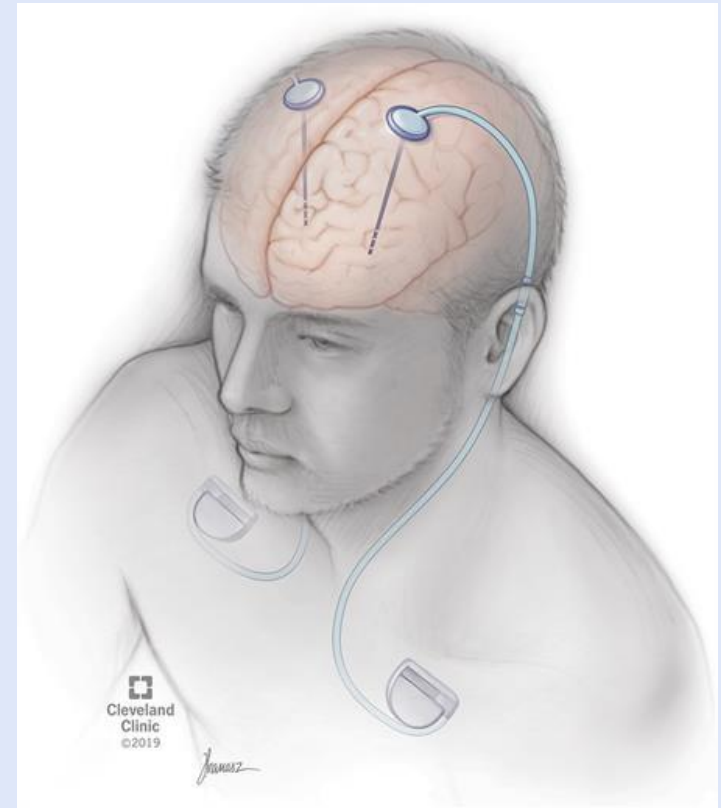
- In multivariable analysis, aspiration of fluid was associated with increased microbiologic yield (odds ratio [OR], 3.13; 95% confidence interval [CI], 1.39-7.04)
- Prior antibiotic use was associated with decreased yield (OR, 0.32; 95% CI, 0.16-0.65).

Take Home Points

- When possible, antibiotics should be held prior to biopsy, with the longer the interval between antibiotic receipt and biopsy, the better.
- Fluid collections should be aspirated wherever possible.
- Overall poor yield of biopsy suggests a need for more thorough evaluation of other diagnostic modalities (16S sequencing, Karius, etc.)
- Repeat biopsy when the initial biopsy is negative may also be of value.

Deep Brain Stimulator Infections

- Often very subacute presentation (erosion through skin)
- Favored approach is typically removal of the entire system though retention of some/all prosthetic material is often attempted
- Relatively scant data on outcomes



Mayo Experience with DBS-Related Infections, 2000-20

- 1132 primary DBS implantations and 784 revisions (all done for reasons other than infection) analyzed
- Infections classified as:
 - Superficial SSTI related to DBS
 - Deep uncomplicated DBS-related infection
 - Deep complicated DBS-related infection

Superficial SSTI related to DBS

- At least two of the following
 - Skin erythema
 - Skin swelling
 - Tenderness
 - Wound dehiscence
 - Wound drainage
- With or without positive intraop wound cultures
- No evidence of deep infection
- Infection must involve parts overlying DBS components

Deep uncomplicated DBS-related infection

- Any of the following
 - Device exposure to the outside or sinus tract communicating with the device
 - Deep purulent collection surrounding DBS parts detected intraoperatively or by ultrasound-guided needle aspiration
 - Positive growth of microorganisms in cultures from any of the following:
 - Deep intraoperative tissue or fluid surrounding DBS parts
 - DBS device parts
 - Deep fluid aspirate from IPG pocket
- No evidence of complications (see next slide)

Deep complicated DBS-related infection

- Criteria for deep uncomplicated DBS-related infection are met AND
- Evidence of at least one of the following:
 - Intracranial pus
 - Intracranial organized abscess
 - Meningitis
 - Encephalitis

Results

- 73 DBS-related infections
 - 57/1112 (5%) after primary DBS
 - 16/784 (2%) after revision DBS ($p=.0022$)
- Median 2.1 (IQR 0.9-6.9) months from time of initial surgery
- Infection associated with higher BMI, longer operative length, male sex, and diabetes mellitus

Outcomes

- 17 (23%) superficial infections
- 56 (77%) deep infections
 - 53 uncomplicated
 - 3 complicated (cerebritis, brain abscess, purulence around intracranial electrodes)
- Symptoms: localized erythema (62%), localized pain (59%), wound drainage (43%), wound dehiscence (26%), device exposure (22%), fever (15%), headache (6%), altered mentation (1%)

Microbiology

Cultures available in 62 cases, positive in 60,
114 isolates total

- 39 *Staphylococcus aureus*, 35 of which was MSSA
- 31 CONS
- 27 *Cutibacterium acnes* in 27 (23.7%)
- 2 each for *Pseudomonas aeruginosa*,
Citrobacter koseri, *Klebsiella aerogenes*

Surgical vs. Medical Management

- Complete explantation in 39/56 (70%) deep infections
- Surgical intervention with device retention in 14 (25%) deep infections
- Medical management in 3 (5%) deep infections

- Surgical intervention with device retention in 6/17 (35%) superficial infections
- Medical management in 11 (65%) superficial infections

Antimicrobial Management

- Median duration of 14-15d total, not much different for deep (15) vs. superficial (14) though deep with longer duration of IV therapy (14 vs. 3d)
- Chronic suppression in 11/73 (15%) including 3/14 cases treated with medical management and 8/20 cases treated with surgical intervention with device retention

Outcomes

- Median followup 4.2 years (IQR 1.9-6.9)
- Treatment failure in 16:
 - 4/39 (10%) with complete device explantation ($p=.015$)
 - All reinfections following reimplantation
 - 7/20 (35%) with surgical intervention with device retention
 - 5/14 (36%) with medical management
- Median time to failure 4.5mo (IQR 2.7-6.8)
- Any IV antibiotics associated with lower odds of failure
- 1 case of failure of suppressive therapy

Complications

- 13/16 treatment failures led to extraction of entire DBS system
- Only 1 complication associated with failure:
 - Initial deep infection of pocket that underwent generator removal but retained leads, got 14d abx, presented 3mo later with bacterial meningitis that resolved after lead explantation and 14d IV abx
- Take home: extraction of entire system associated with lower rates of treatment failure, but complications also quite rare with less aggressive approaches

CLSI Aminoglycoside Breakpoint Changes, 2023

- Pre-existing breakpoints based on limited clinical data but thought to be too high based on PK/PD
 - Based more on toxicity than efficacy
- Aminoglycoside-modifying enzymes (AMEs) often accompany β -lactamases on mobile genetic elements

Summary of Published Aminoglycoside Breakpoints for *Enterobacterales*

Antimicrobial	Breakpoint (Susceptible/Resistant) in mg/L				
	CLSI (2023)	CLSI (2022)	US FDA ^a	EUCAST	USCAST
Plazomicin	≤2/≥8	NA	≤2/≥8	NA	≤4/≥8
Amikacin	≤4/≥16	≤16/≥64 ^a	≤16/≥64 ^a	≤8/≥16	≤4/≥8
Gentamicin	≤2/≥8	≤4/≥16 ^a	≤4/≥16 ^a	≤2/≥4	≤2/≥4
Tobramycin	≤2/≥8	≤4/≥16 ^a	≤4/≥16 ^a	≤2/≥4	≤2/≥4

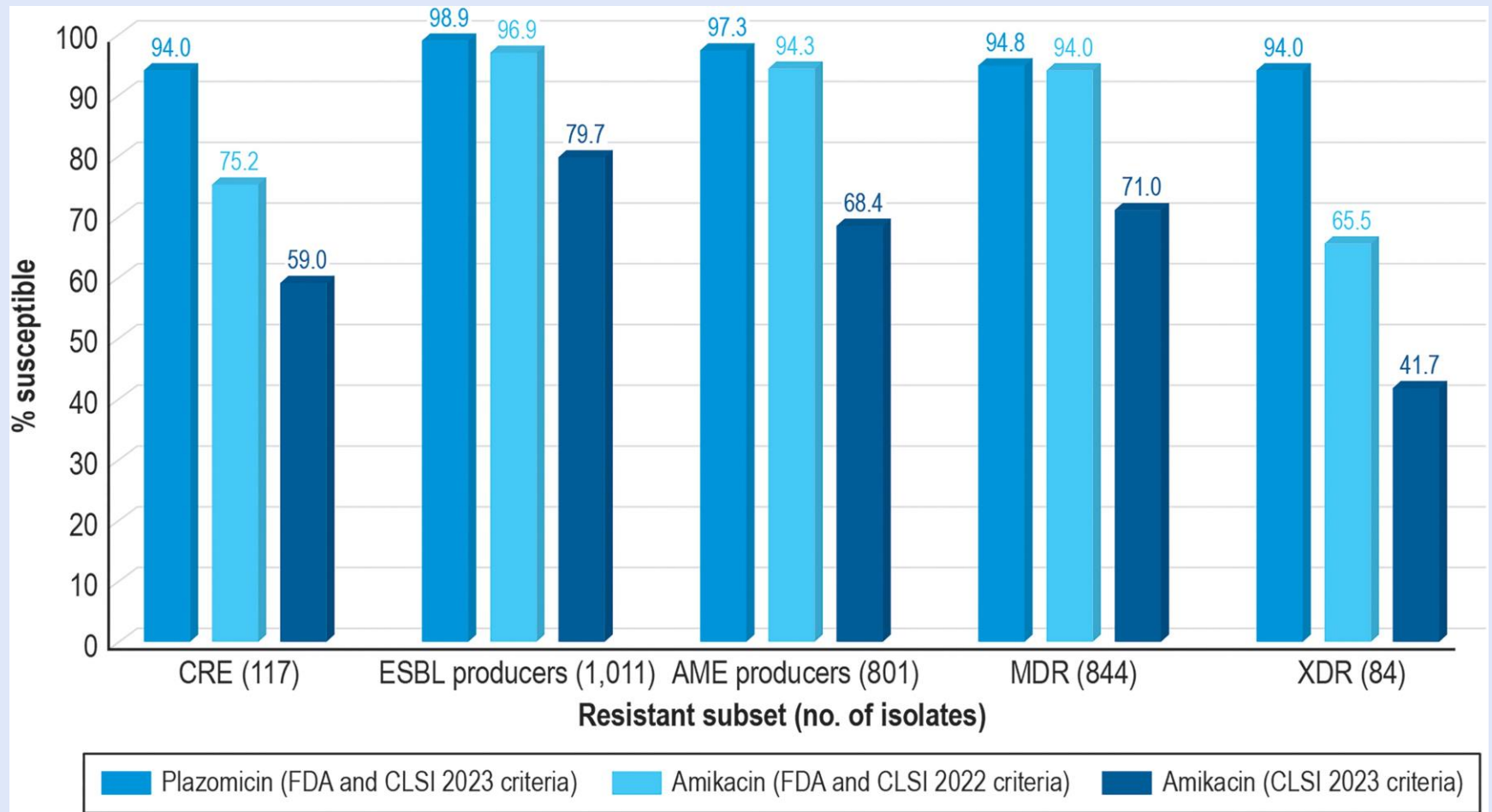
a: US FDA recognized CLSI M100 (2022) standard for amikacin, gentamicin, and tobramycin

SENTRY Surveillance, 2017-21

Amikacin

Organism(s)	N in database	Amikacin % susc (new)	Amikacin % susc (old)
<i>Enterobacterales</i>	9809	94.6	99.4
CRE	117	59.0	75.2
ESBL producers	1011	79.7	96.9
AME producers	801	68.4	94.3
MDR (nonsusc \geq 3 classes)	844	71.0	94.0
XDR (susc to \leq 2 classes)	84	41.7	65.5

Plazomicin vs. Amikacin



While We're At It...*Pseudomonas* and Aminoglycoside Breakpoints

- Amikacin breakpoint remains the same ($S \leq 16$) but specified only for urine
- Gentamicin breakpoint removed
- Tobramycin breakpoint reduced from $S \leq 4$ to $S \leq 1$

(no breakpoints for plazomicin exist, so we are really only left with tobramycin as only AG for potential use in systemic *Pseudomonas* infection)

Transitions to Oral Therapy in *S. aureus* Bacteremia

- Be careful in applying POET and OVIVA!
 - No MRSA in POET and only 5 PWID
 - OVIVA excluded bacteremia
- Likely a role for relatively early transition to oral therapy in mop up of “uncomplicated” bacteremia, but there’s a reason why I put that in quotes
- Best time to transition to oral therapy in more deep-seated/complicated bacteremia is unclear



Christopher Graber

@glavaidguy



I will know I have officially succeeded as a program director when all my fellows use air quotes when talking about any of the following:

1. “Bone penetration”
2. “Uncomplicated” *S. aureus* bact
3. “Sepsis”

1:08 PM · May 27, 2022

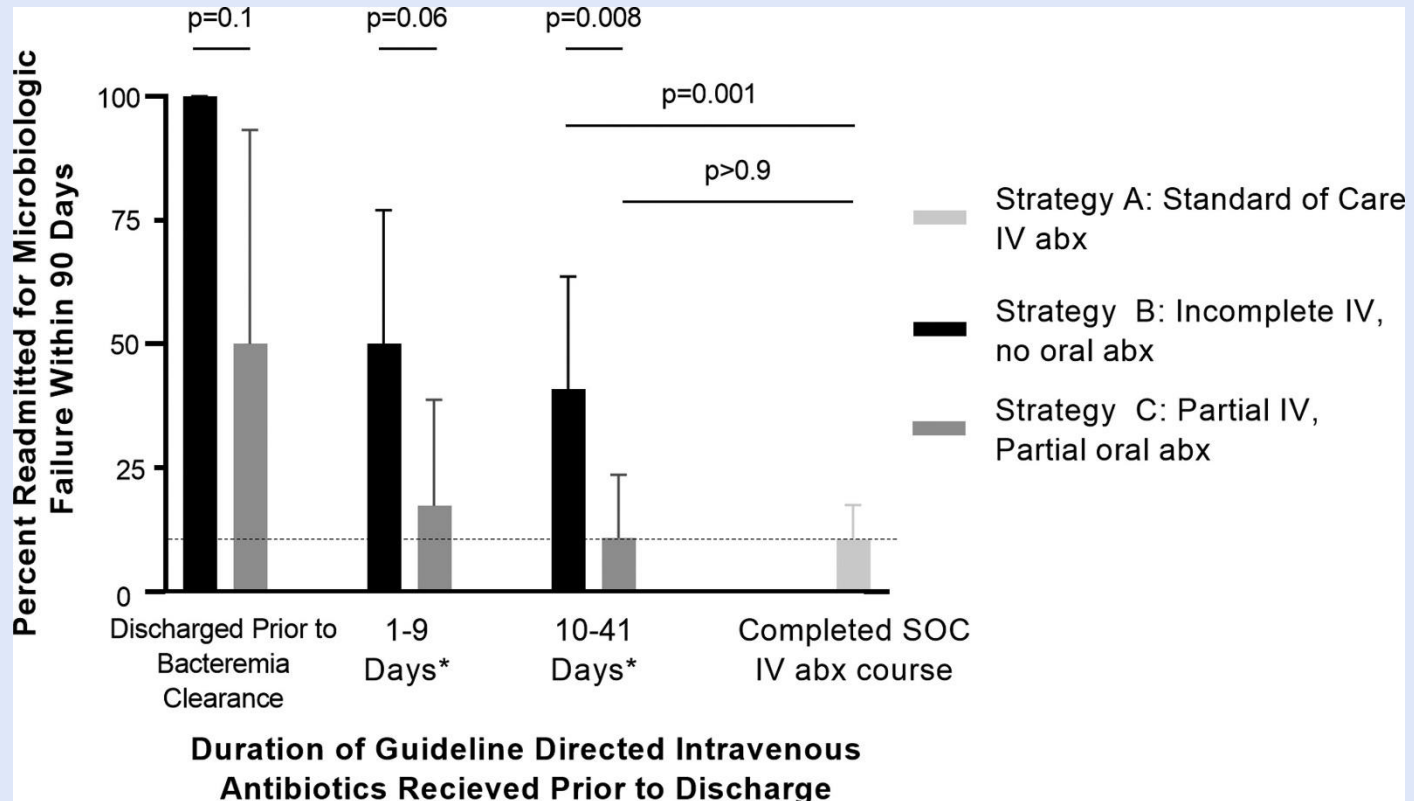
Transitions to Oral Therapy in Staphylococcal Bacteremia

- Analysis of outcomes of cSAB in people who inject drugs at Wash U focused on three categories:
 - Cat A: Completed IV therapy in-house (n=122)
 - Cat B: Partial IV course, d/c w/o po abx (n=36)
 - Cat C: Partial IV course, d/c with po abx (n=69)

Outcomes

(90d mortality/microbiologic failure)

A(IV): 10.7% B(no po): 44.4% C(po): 13.0%



Time to Appropriate Treatment for Bloodstream Infections

- Sepsis guidelines make this a big area of emphasis, which can drive initiation of overly broad-spectrum therapy in the context of suspected bacteremia
 - Lower threshold to initiate antibacterial therapy
 - Lower threshold to broaden antibacterial therapy

Time to Appropriate Treatment for Bloodstream Infections

- Difficult to study!
 - Use of time of blood culture collection imperfect measure of bacteremia onset
 - Indication bias (severity of disease)
 - Immortal time bias (have to survive long enough to be switched to appropriate treatment)

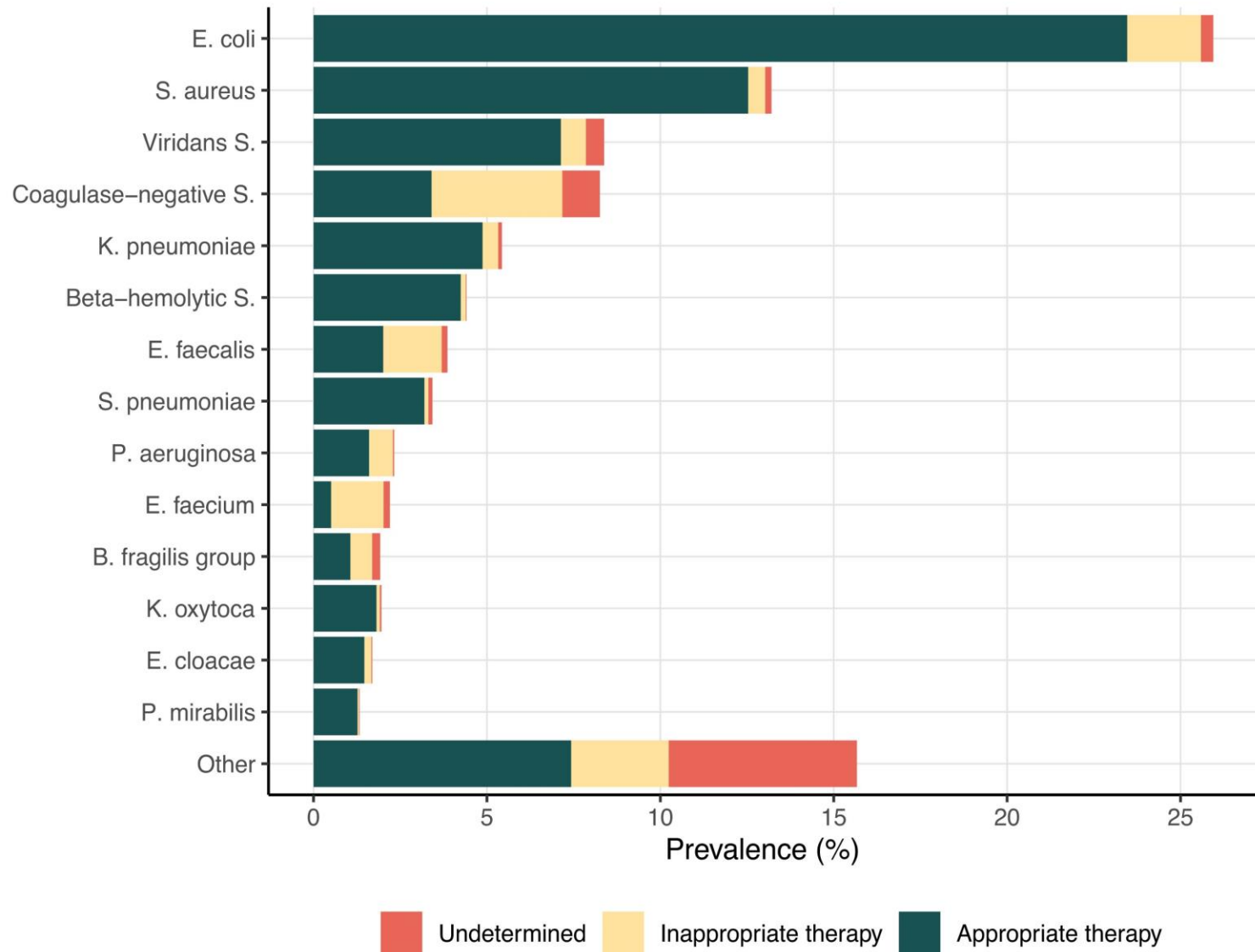
Time to Appropriate Treatment for Bloodstream Infections

- Retrospective study from Karolinska Institute in Stockholm examining 30d mortality based on time to appropriate therapy at pre-defined landmarks of:
 - 1 hour
 - 3 hours
 - 6 hours
 - 12 hours
 - 24 hours
 - 48 hours
 - 72 hours

Time to Appropriate Treatment for Bloodstream Infections

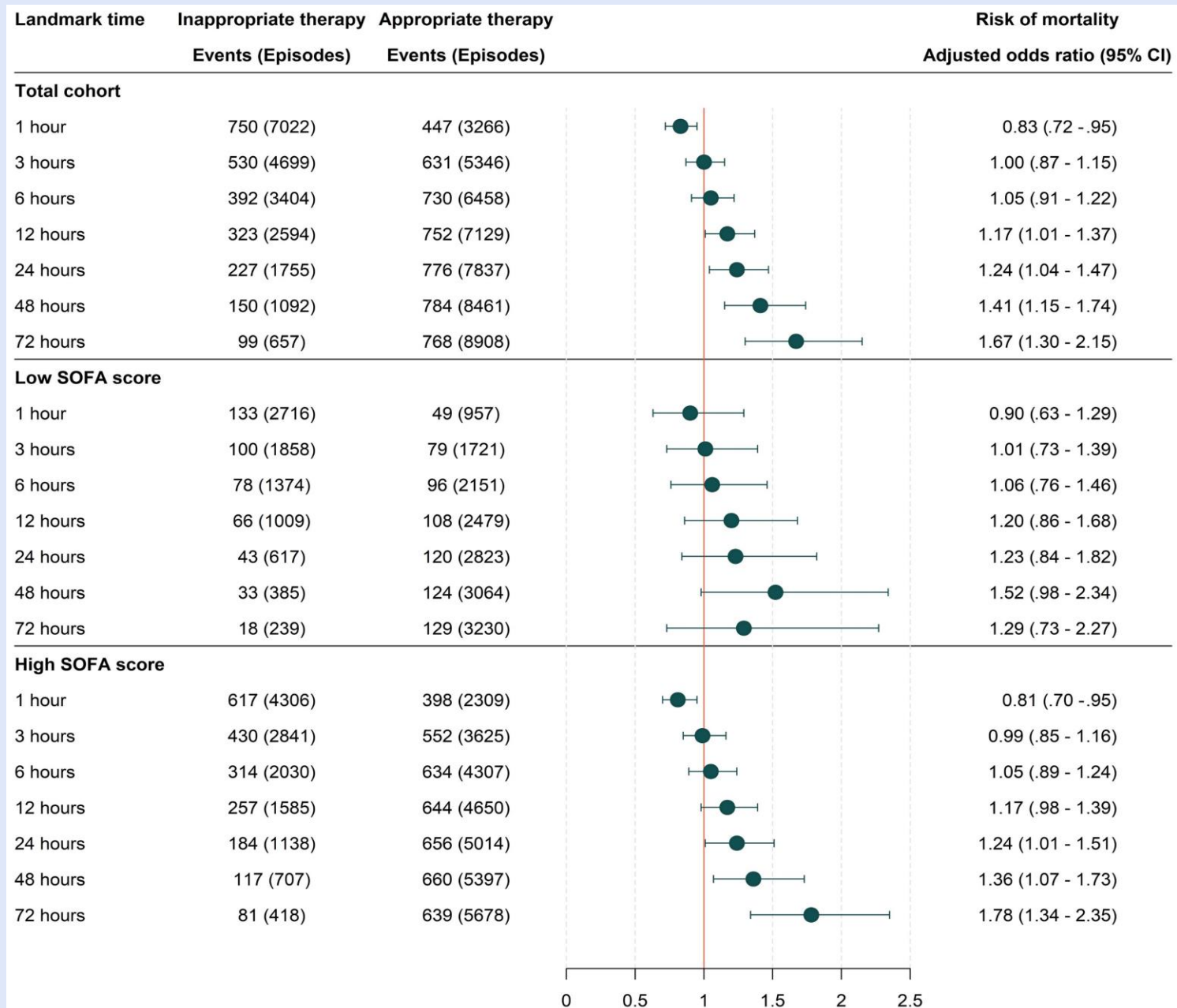
- Included 9192 adults admitted between 2012-19 for 10,628 episodes that involved starting antibiotics within 1h before and 24h after blood culture collection
- BSI onset in ICU excluded
- Adjusted for age, sex, CCI, immunosuppression, SOFA score, polymicrobial BSI, source of infection, calendar year, hospital-onset of BSI

Distribution of pathogens



Study Population

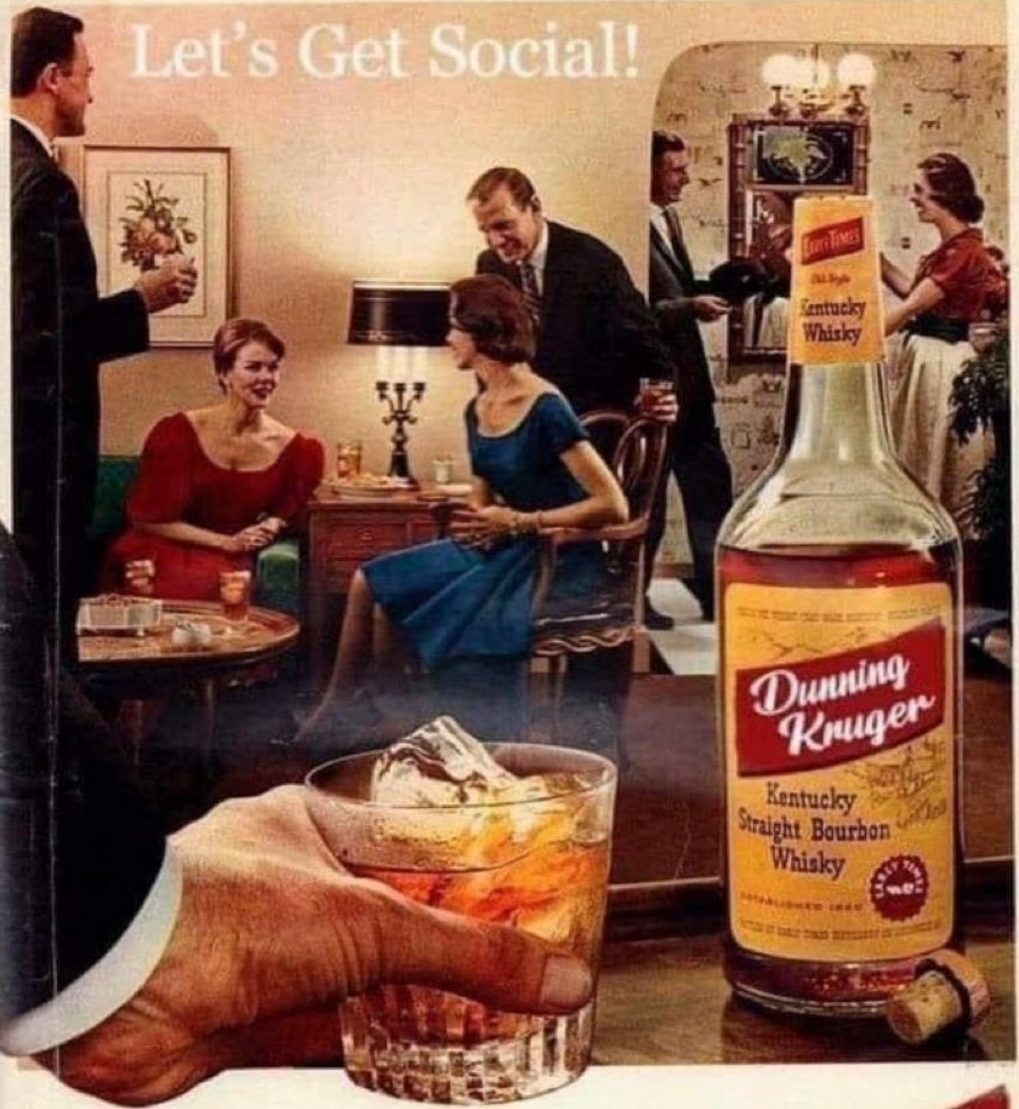
- Median age 69 years
- 56.8% female
- 85.3% community-onset BSI
- Low rates of MRSA/ESBL/VRE (4%)
- Appropriate therapy within 1h in 30.7%, 3h at 50.4%, 12.6% at 12h
- Septic shock in 5.7%
- Crude 30d mortality 11.8%



Take Home Points

- Don't apply sepsis guidelines beyond actual sepsis (numbers of actual septic shock low in this study)
- Good 12h window to explore diagnostic workup, involve rapid diagnostics, etc.
- Sweden has rather accessible health care; our mileage may vary (will patients present earlier there?)
- ICU excluded from study, so careful in applying in critically ill patients

Let's Get Social!



When you know more than the doctors who've spent their entire careers studying infectious diseases, it's time for Dunning Kruger.



Thanks to all my
IDSA Journal
Club Colleagues!

- Aldon Li, MD
- Manie Beheshti, MD
- Erica Kaufman West, MD
- Zeina Kanafani, MD

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