NACMID 2022: Antimicrobial Stewardship Panel: From Culture to Bedside– Practices that Work

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Disclosures

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- Gilead Sciences, Inc. – research funding
- Merck & Co. – ad-hoc consultant

Objectives

- Explain how to leverage antimicrobial stewardship principles to communicate microbiology results to key stakeholders at the bedside.
- Demonstrate the utility of reflex testing in the clinical microbiology laboratory as a means to guide appropriate clinical decisions and patient care.
- Discuss how to integrate laboratory stewardship to reduce inappropriate management of common clinical syndromes including hospital acquired infections (HAIs).

The million dollar question..

Explain how to leverage antimicrobial stewardship principles to communicate microbiology results to key stakeholders at the bedside.

What is ‘nudging’?

Nudging in the context of clinical microbiology reports can be:

1. Presenting 1 or more default options that are more desirable than other options (and masking non-desirable options)
2. Framing recommendations by adding comments or context to guide decision making
3. Presenting desired options at eye level by keeping desired choices at the top, or, emphasizing the text of desired agents

Langford BJ et al. Infect Control Hosp Epidemiol 2019;40:1400-1406.

Susceptibility Cascading or Suppression

What is cascading & suppression

Cascading:

- "…a strategy of reporting antimicrobial susceptibility test results in which secondary (e.g. broader-spectrum, costlier) agents may only be reported if an organism is resistant to primary agents within a particular drug class"
- Customizable based on institutional needs, antibiogram, antibiotic formulary
- Oftentimes are reflexive rules set in place for microbiology to follow

Suppression:

- Selectively displaying certain antibiotics
- Can be customizable:
  - *Ex:* hiding all daptomycin and linezolid results for all Gram-positive results; released upon request
  - *Ex:* hiding all 3rd generation cephalosporins for AmpC harboring organisms
- Oftentimes require a request from a clinician to release suppressed results

Combining ≥ 1 testing modalities: *C.difficile*

- Clinical context for *C.difficil*e testing
  - PCR (+) and Toxin EIA (+): CDI likely
  - PCR (+) and Toxin EIA (-): CDI unlikely (colonization vs. early infection)

- Pre-Intervention:
  - (PCR+/EIA−) reported as "*Clostridium difficile* cytotoxin B gene detected"
  - Treatment recommendations included

- Post-intervention:
  - (PCR+/EIA−) reported as "*Clostridium difficile* organism present but toxin not detected by EIA. Consider *C. difficile* colonization or early infection."
  - Treatment recommendations removed for any toxin-negative test

Herman DJ et al. Open Forum Infect Dis 2020;8:ofaa605.

Optimization of CDI cases

- 199 pre-intervention vs. 165 post-intervention
- Total days of therapy (mean):
  - Pre- 13.6 vs. Post- 7.9 (-5.8 days; 95% CI:-3.9 to -7.6)
- Proportion of patients receiving no antibiotic therapy
  - Pre- 6.5% vs. Post- 23.6% (OR, 4.5; 95% CI, 2.3–8.7)

Herman DJ et al. Open Forum Infect Dis 2020;8:ofaa605.

	Pre-intervention	Post-intervention
Subsequently developed toxin positive disease	9%	6.7%
Colectomy	0%	0.6%
Mortality	7.5%	12.1%
Hospital length-of-stay	19 days	16 days

No significant statistical differences detected

Cascading rules: Enterobacterales

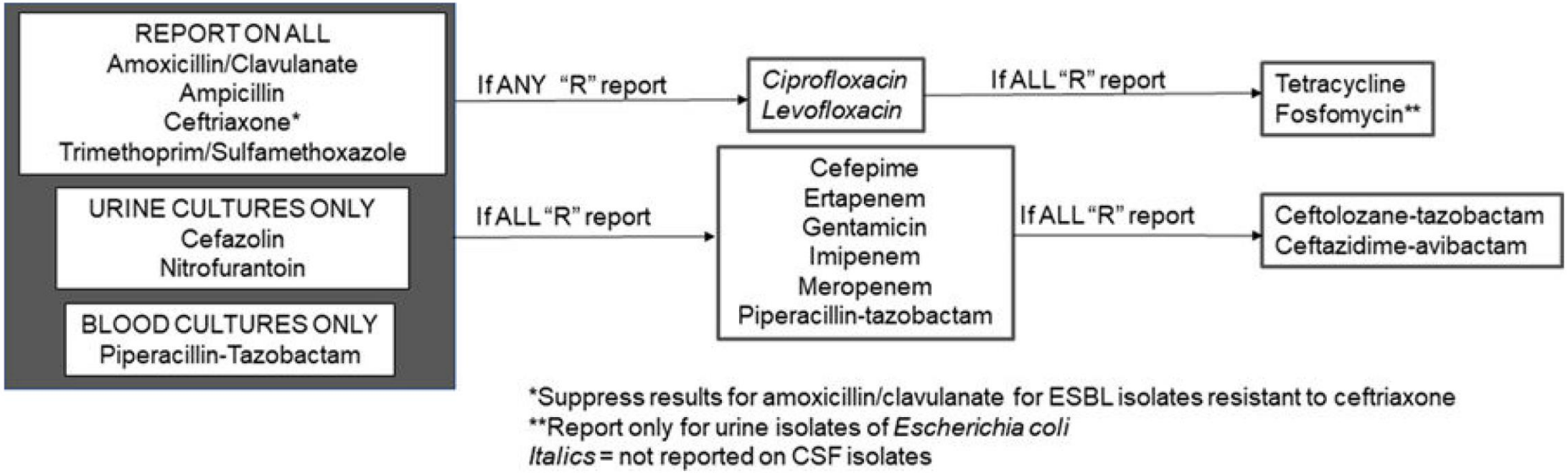

Fig. 1 A.
Cascade reporting algorithm for antimicrobial susceptibility reporting for *Enterobacteriaceae.*

Vissichelli NC et al. Infect Control Hosp Epidemiol 2022;43:199-204.

Cascading rules: *P.aeruginosa*

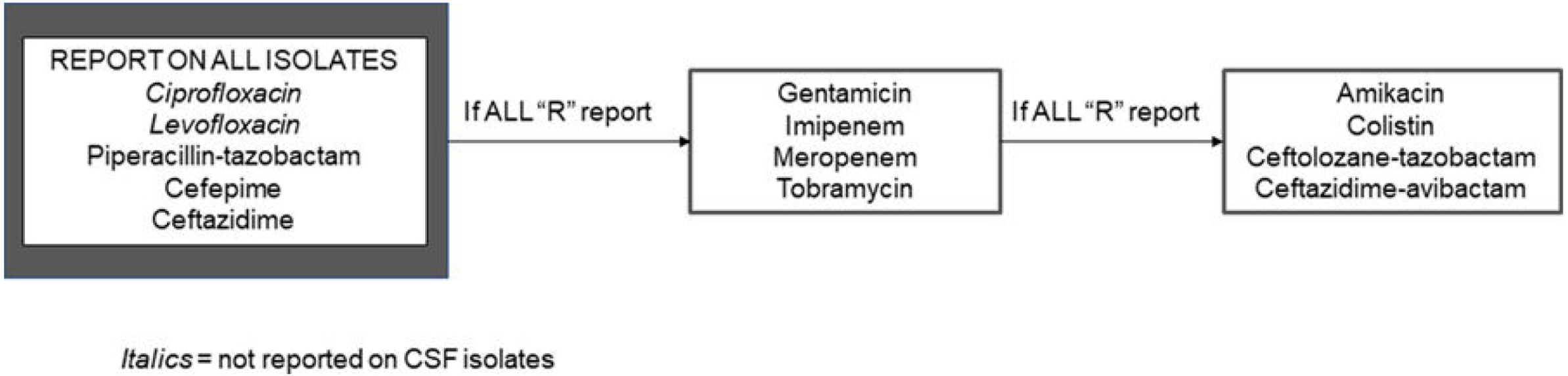

Fig. 1 B.
Cascade reporting algorithm for antimicrobial susceptibility reporting for *Pseudomonas aeruginosa.*

Vissichelli NC et al. Infect Control Hosp Epidemiol 2022;43:199-204.

Impact of cascade reporting at VA

Consumption of Antimicrobials Before and After the Cascade Reporting Intervention

Outcome	Mean (SD) DOTs/1,000 DP During the Period Before the Intervention	Mean (SD) DOTs/1,000 DP During the Period After the Intervention	*P* Value
Amoxicillin/Clavulanate	13.86 (12.06)	20.23 (16.37)	.001
Cefpodoxime[a]	0.00 (0.00–0.00)	0.00 (0.00–0.00)	.065
Cephalexin	7.76 (9.08)	8.29 (10.18)	.702
Ciprofloxacin	18.38 (15.59)	16.53 (14.72)	.325
Levofloxacin	39.50 (26.64)	36.35 (24.75)	.362
Moxifloxacin[a]	0.00 (0.00–0.00)	0.00 (0.00–1.33)	.184
Trimethoprim/Sulfamethoxazole	10.15 (10.74)	10.76 (10.84)	.654
Ceftriaxone	30.41 (22.90)	28.27 (21.54)	.390
Cefepime	6.98 (10.12)	19.01 (20.09)	<.001
Meropenem	52.96 (43.83)	40.42 (32.97)	.005
Piperacillin/Tazobactam	132.56 (73.70)	113.80 (67.28)	.002

Note. SD, standard deviation; DOT, days of therapy, DP, days present.

[a]Median (interquartile range). The Wilcoxon signed-rank test was used due to low utilization.

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Experience from OH Community Hospital

Antimicrobial Agents Reported Without Cascade

Ampicillin

Ampicillin/sulbactam

Piperacillin/tazobactam

Cefazolin

Ciprofloxacin

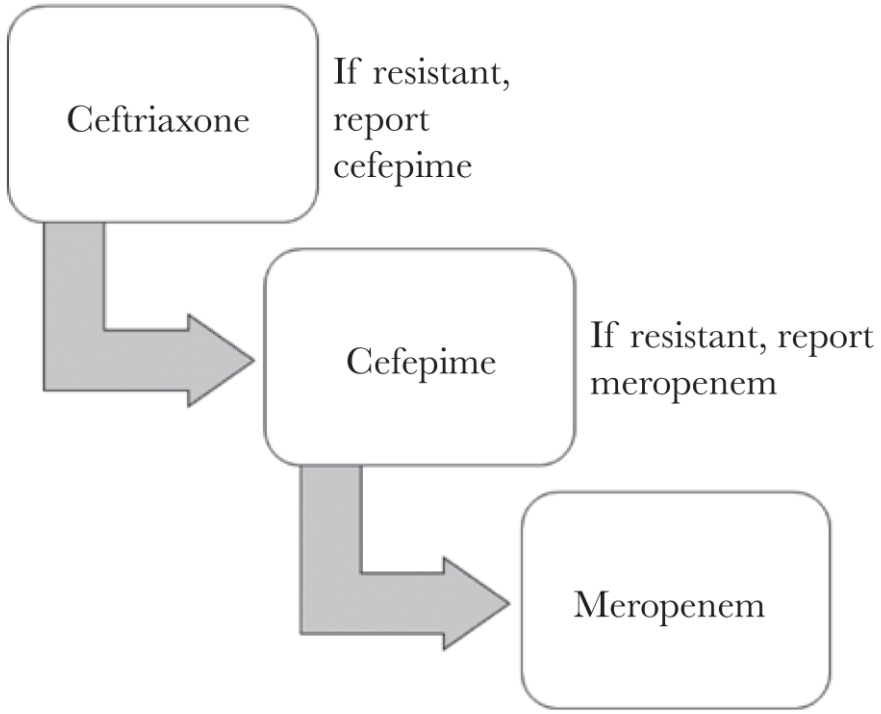
Tobramycin

Gentamicin

Trimethoprim/sulfamethoxazole

Nitrofurantoin

Antimicrobial Agents Reported Through Cascade



Liao S et al. Open Forum Infect Dis 2020;7:ofaa002.

Effect of Cascade Reporting

- Antibiotic treatment vs. *E.coli* and *Klebsiella* spp.
- Reviewed 852 episodes pre-CR vs. 1049 post-CR
- Overall, ↓ in cefepime use measured as mean days-of-therapy
  - Pre-CR 1.229 days vs. post-CR 0.813 days
- Very minimal use of meropenem across both study time periods
  - Two pre-CR vs. two post-CR
- Length of stay impact (↓): 14.1 ± 0.46 vs. 10.9 ± 0.34

Liao S et al. Open Forum Infect Dis 2020;7:ofaa002.

Additional Comments in Microbiology Report

Meaningful microbiology report interventions

- Number of blood culture bottles (+) in a set

- Preliminary tests
  - Coagulase test (Latex test) → differentiates between *S.aureus* vs. non-*S.aureus* cases
  - Germ tube test → allows clinician to consider appropriate antifungal treatment options
  - Optochin test → *S.pneumoniae* vs. non-*S.pneumoniae*

- Including antibiotic options based on local (or regional/national) susceptibility results

- Culture-specific add-ons:
  - Sputum cultures (e.g. normal flora → add layer stating “lack of MRSA and Pseudomonas”)

Tweaks to Respiratory Culture Report

- Modified comment for all respiratory cultures that previously would be reported “commensal respiratory flora” to:
  - “Commensal respiratory flora only: No *S. aureus*/MRSA or *P. aeruginosa*”
- Clinician education provided at the time of report comment change
- De-escalation occurred in 39% (41/105) pre- vs. 73% (77/105) post-
  - MRSA de-escalation 37% pre- vs. 71% post-
  - Anti-pseudomonal de-escalation 32% pre- vs. 70% post-
- Less co-morbidities and severely ill 5.5 times more likely to be de-escalated

Musgrove MA et al. Open Forum Infect Dis 2018;5:ofy162.
McBride J et al. Open Forum Infect Dis 2015;2(Suppl 1):1500.

Rapid Diagnostics Experience at Maine Medical Center (MMC)

Partnership with NorDx

A focus on optimizing communication

Fall 2015

- Agreement to a 6-month pilot to implement molecular on GP (Nanosphere®)

Spring/Summer 2016

- Expanded molecular platform to GNRs
- Now performed (reflex) on all (+) BCx

Jan 2020

- Transitioned all GNR from molecular to phenotypical platform (Accelerate Diagnostics®)
- GPs remained on molecular

GP: Gram-positive

GNR: Gram-negative rods

Note: NorDx utilizes BD Phoenix for automated identification and antimicrobial susceptibility testing

Rapid Identification at MMC

Simple and straight forward interpretation

Component	
Rapid Blood Culture Identification	Staphylococcus aureus (Mec A positive)-detected by molecular testing. **MRSA** (methicillin-resistant S. aureus) Susceptibility, and phenotypical confirmation to follow. Refer to NorDx test Catalogue for a listing of all targets tested. (http://testcat.nordx.mmc.org/) RAPID ORGANISM IDENTIFICATION CALLED TO: S S - P ON: 08/31/2022 AT: 13:46 BY CG06;RB.

Translate technical info to clinical info for bedside clinician

mecA → methicillin-resistance → MRSA

VERIGENE Gram-positive Panel

Gram-Positive Blood Culture Test (BC-GP)

Species

Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus lugdunensis
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes
Enterococcus faecalis
Enterococcus faecium

Group

Streptococcus anginosus

Genus

Staphylococcus spp.
Streptococcus spp.
Micrococcus spp.[+]
Listeria spp.

Resistance

mecA (methicillin)
vanA (vancomycin)
vanB (vancomycin)

VERIGENE Gram-positive Panel

Gram-Positive Blood Culture Test (BC-GP)

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~~*Staphylococcus epidermidis*~~
~~*Staphylococcus lugdunensis*~~
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes
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Genus

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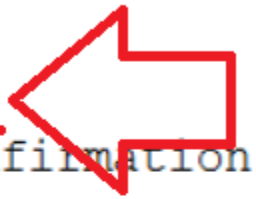
Listeria spp.

Resistance

mecA (methicillin)
vanA (vancomycin)
vanB (vancomycin)

Rapid Blood Culture Identification

Staphylococcus spp-detected by molecular testing.
Coagulase-negative staphylococcus,
NOT S.epidermidis or S. lugdunensis
Susceptibility and phenotypical confirmation to follow.
-
Refer to NorDx test Catalogue for a listing of all targets tested. (http://testcat.nordx.mmc.org/)
Aerococcus and Listeria species may also give a positive result.
RAPID ORGANISM IDENTIFICATION CALLED TO:R C ON: 08/18/2022 AT: 04:15 BY;BS RB.



"On menu" – genus only

Final identification: *Staphylococcus hominis*

Rapid Blood Culture Identification	Streptococcus pyogenes, Beta-Hemolytic Group A detected by molecular testing Susceptibility and phenotypical confirmation to follow. - Refer to NorDx test Catalogue for a listing of all targets tested. (http://testcat.nordx.mmc.org/) RAPID ORGANISM IDENTIFICATION CALLED TO: M M ON: 07/25/2022 AT: 20:09 BY:KW;RB.

"On menu" – genus & species

Final identification: *Streptococcus pyogenes*

Rapid Blood Culture Identification	Streptococcus spp- detected by molecular testing. This is not S. anginosus group, S. pneumoniae, S.pyogenes or S. agalactiae Susceptibility and phenotypical confirmation to follow. - Refer to NorDx test Catalogue for a listing of all targets tested. (http://testcat.nordx.mmc.org/) Lactococcus species may also give a positive result. CALLED TO:BROGAN OXFORD RN ON:07/10/2022 AT:0652 BY:ALG01 ;RB.

"On menu" – genus only

Final identification: Group G streptococcus

Lessons Learned at MMC/MaineHealth

Gram-Positive Blood Culture Test (BC-GP)

Species

Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus lugdunensis
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes
Enterococcus faecalis
Enterococcus faecium

Group

Streptococcus anginosus

Genus

Staphylococcus spp.
Streptococcus spp.
Micrococcus spp.+
Listeria spp.

Resistance

mecA (methicillin)
vanA (vancomycin)
vanB (vancomycin)

- Hands down, the rapid technologies are great!
- Collaborate with specialists (e.g. stewardship team) and bed-side clinicians (hospitalist team) to maximize the clinical impact and outcome of each result
- Consider useful verbiage/comments to promote understand and use of the results from rapid platforms

Future Plans at Maine Medical Center

- Group A and B streptococci
  - Add comment suggesting pan-susceptibility to penicillins and cephalosporins
  - **Goal:** ↓ duration of broad-spectrum antibiotics and vancomycin

- Urine culture with E.coli, K.pneumoniae, P.mirabilus
  - Add comment on ability to use oral cephalosporins for uncomplicated UTIs if cefazolin MIC ≤ 16
  - **Goal:** ↓ use of fluoroquinolones, ↑awareness of PO cephalosporins as option

- *E. faecalis*
  - Add comment (based on local antibiogram data) stating universal susceptibility to ampicillin
  - **Goal:** ↓ duration of empiric vancomycin

- Micrococcus luteus
  - Add comment describing this organism as a common contaminant. Use clinical judgement when determining need to p
  - **Goal:** ↓ duration of empiric vancomycin

Future Plans at Maine Medical Center

AmpC harboring organisms

- *Enterobacter cloacae*
- *Klebsiella aerogenes*
- *Citrobacter freundii*

In discussion with microbiology, clinicians, and antibiotic stewardship to consider adding ‘nudge’ language to suggest use of cefepime.

Take Home Points

- Nudging and cascading has shown to be highly effective antibiotic stewardship tools
  - Multi-disciplinary efforts will result in more effective and measurable outcomes
  - ↑ understanding and use of the information by bedside clinician

- Do not reinvent the wheel
  - Existing protocols exist in the literature
  - Adapt them and fit your institution, stewardship program, and patient population

- When implementing rapid diagnostic technologies, look for ways to squeeze as much juice as possible

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