Antimicrobial Stewardship and the Role of the Infection Preventionist

Zach Willis, MD, MPH

4/28/26

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Disclosures

I have the following financial relationships with the manufacturer(s) and/or provider(s) of commercial services discussed in this activity:

- Contracted research with:
  - Merck (monoclonal antibody for RSV prevention)
- Consultation for:
  - Scanogen, Inc. (microbiology diagnostics company)

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

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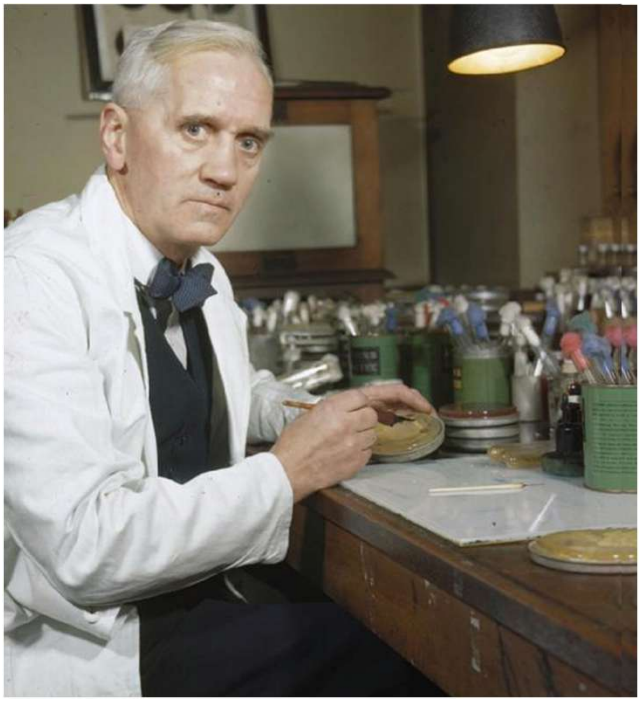

The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out.... In such cases the **thoughtless person playing with penicillin is morally responsible for the death** of the man who finally succumbs to infection with the penicillin-resistant organism.

Sir Alexander Fleming, 6/14/1945, *New York Times*

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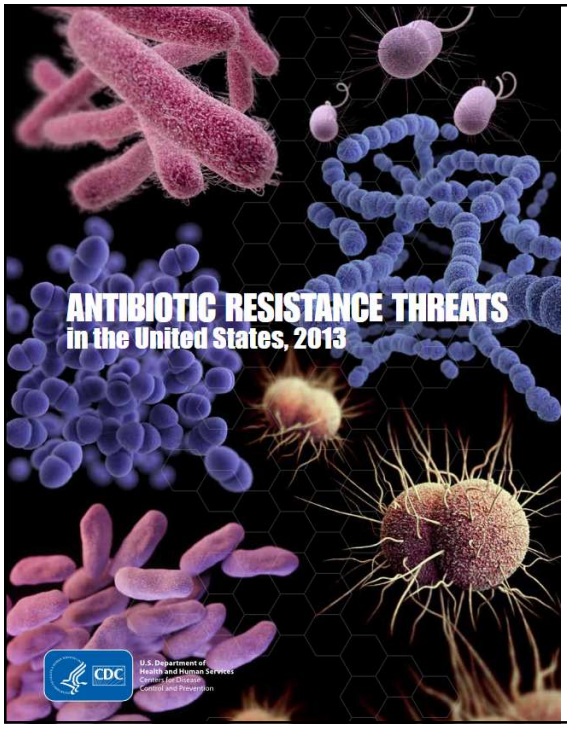

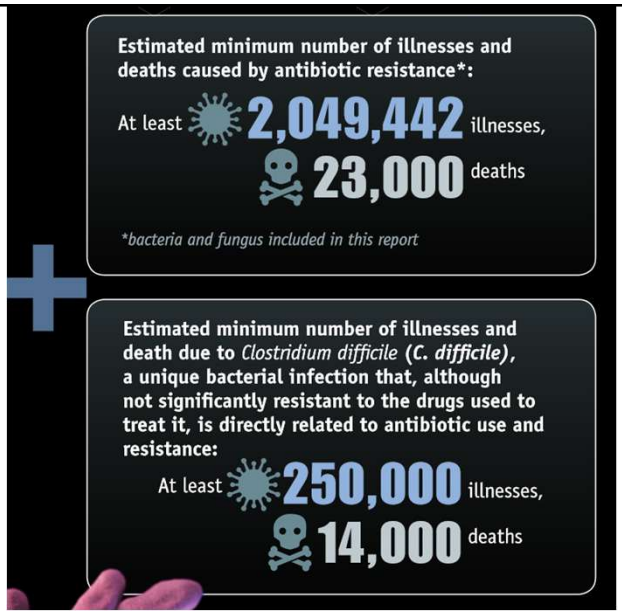

https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf

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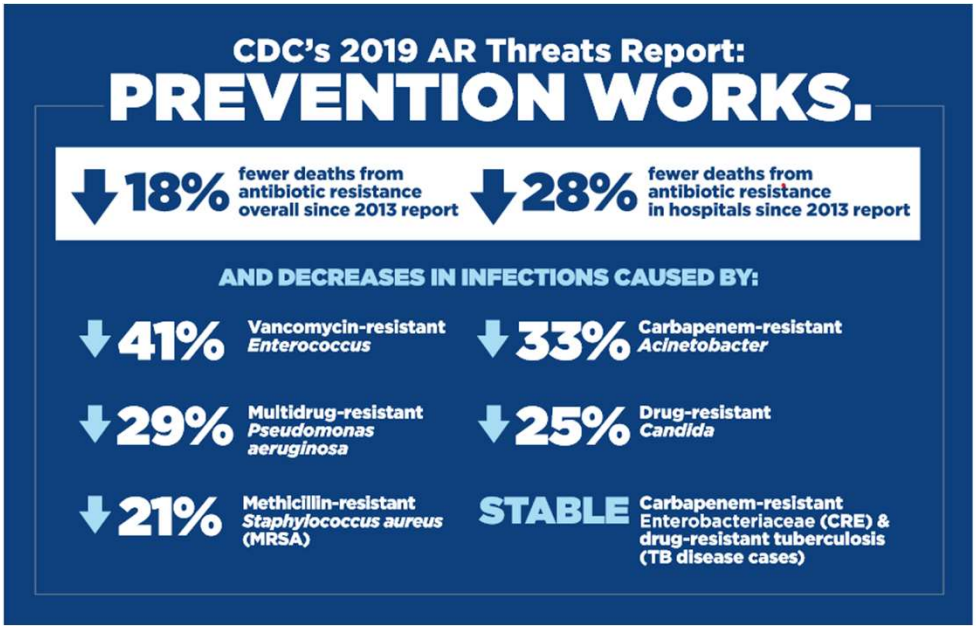

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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What Was Working?

1. Infection Prevention
   - Known MDRO infections:
     - Screening, isolation
     - Information sharing between facilities
     - Surveillance
   - Reduction in Hospital-Acquired Infections
     - CLABSI, VAP, CAUTI
2. Antimicrobial Stewardship

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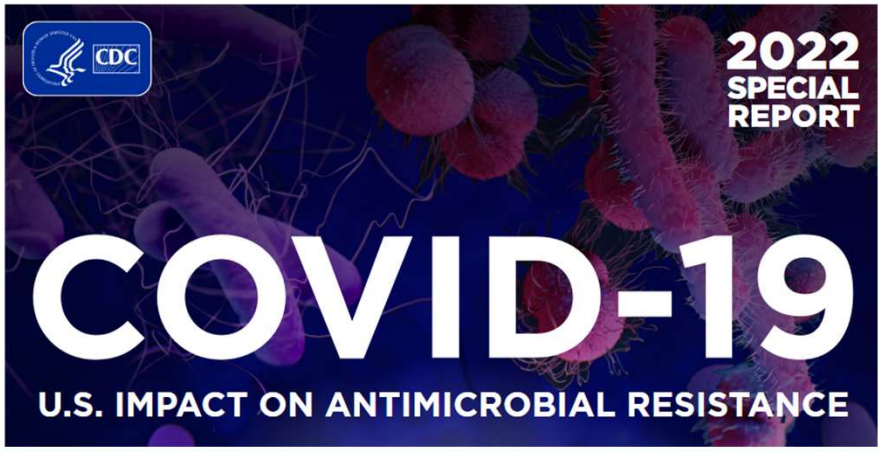

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

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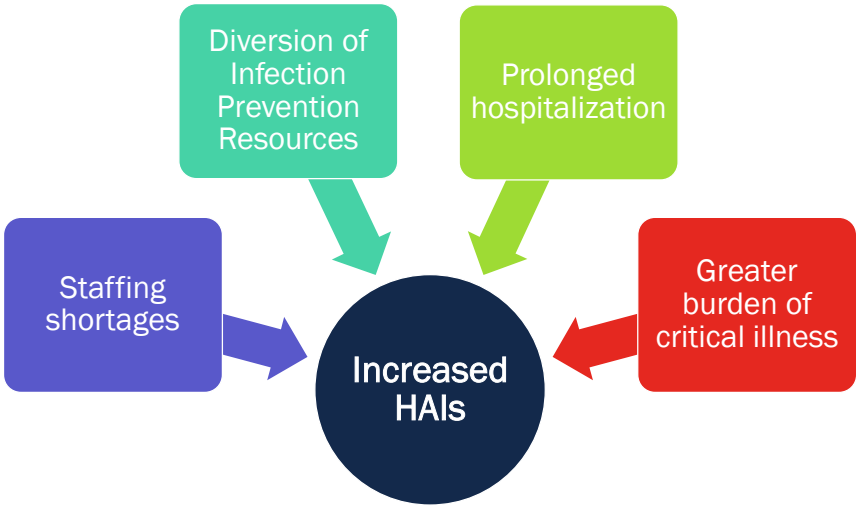
Why Did Antimicrobial Resistance Get Worse in the Pandemic?



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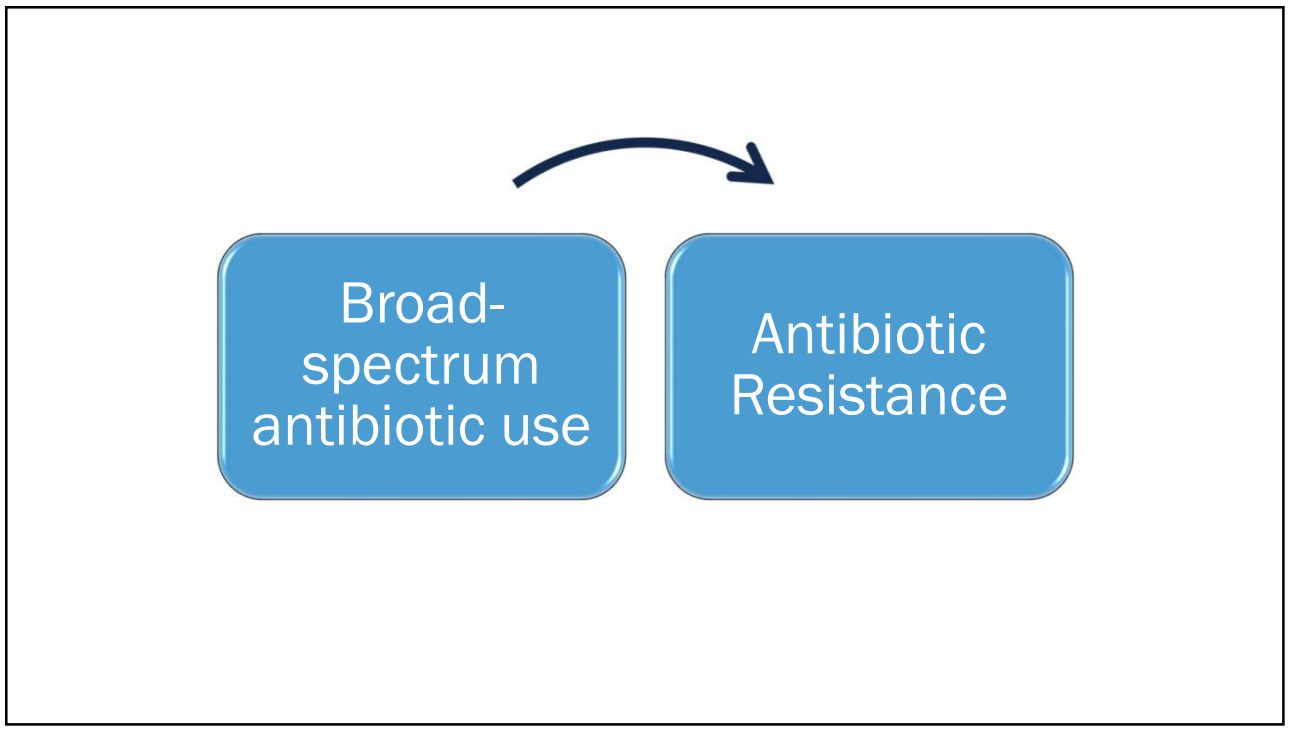

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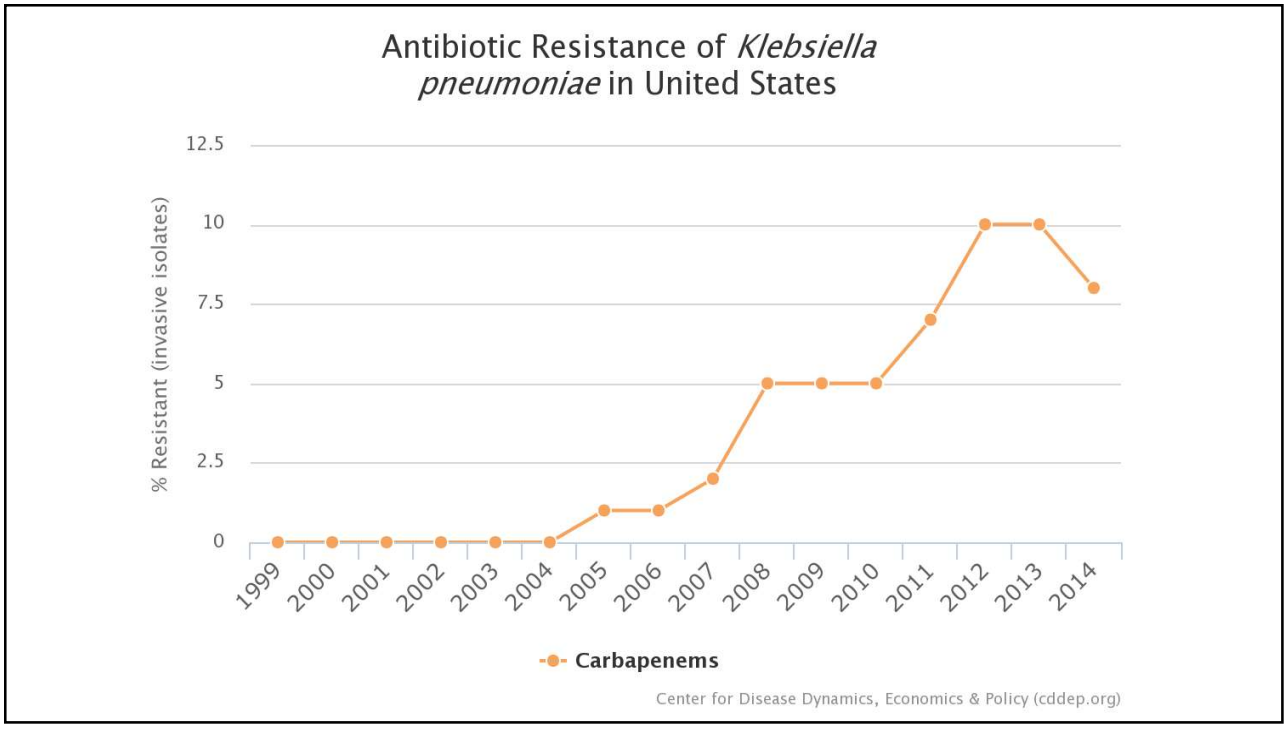
Antibiotic Resistance of *Klebsiella pneumoniae* in United States
% Resistant (invasive isolates)
12.5
10
7.5
5
2.5
0
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
Carbapenems
Center for Disease Dynamics, Economics & Policy (cddep.org)

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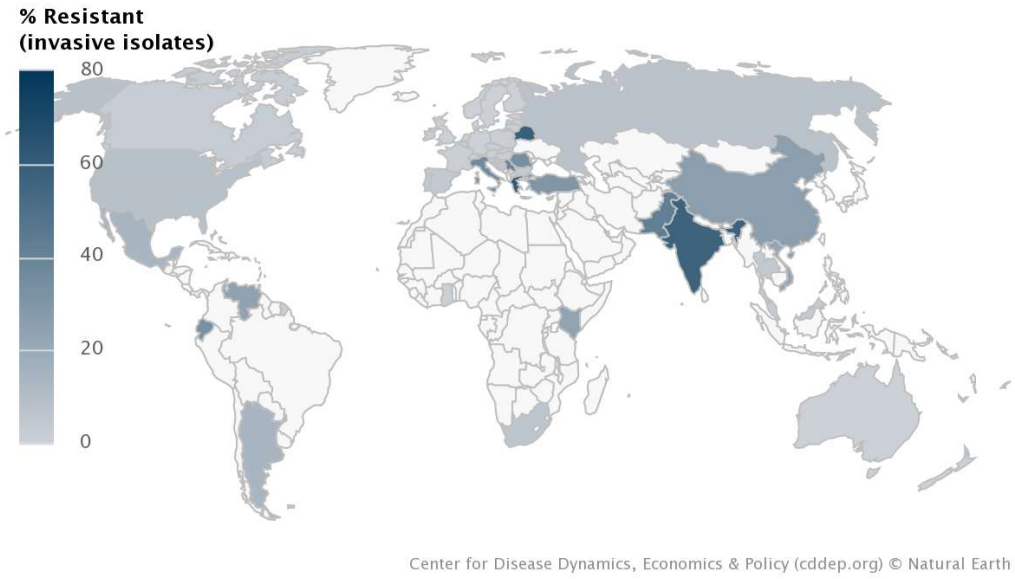
Resistance of *Klebsiella pneumoniae* to Carbapenems



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IP and AS Goal

Prevent antimicrobial resistant infections and C-diff

Antibiotic Resistance Threats in the United States, 2019 (cdc.gov)

Slide courtesy of Emily Sickbert-Bennett, PhD

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AS: Core Elements

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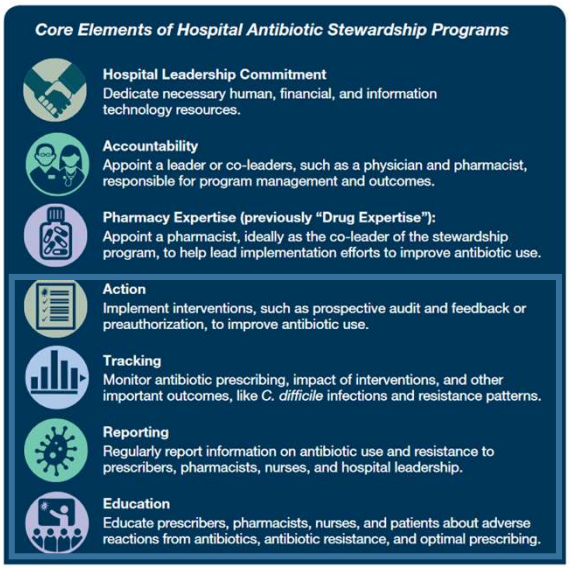

4 of 7 have direct link to IP

https://www.cdc.gov/antibiotic-use/healthcare/pdfs/hospital-core-elements-H.pdf

Slide courtesy of Emily Sickbert-Bennett, PhD

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AS/IP Strategy Alignment

- MDRO epidemiology
- *C. difficile* prevention
- Diagnostic stewardship
  - CLABSI
  - HAP and VAP
  - CAUTI
  - *C. difficile*

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Stewardship: A Multidisciplinary Endeavor

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Essential, "Core-Team" Personnel

- Physician (usually ID)
- Lead Pharmacist (usually ID)
- Clinical Microbiologist
- Infection Preventionist
- Information Technologist

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Core AS Strategies

Restriction (“prior authorization”)	Requires expert approval before drug is dispensed (or to continue past 48-72 hours)
Prospective audit and feedback	Monitoring positive cultures, targeted antibiotics
Guideline Development	Implement evidence-based practices in diagnosis and management of infections
Quality Improvement	Continuous improvement to reduce variance and unnecessary care
Provider Education	

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Additional ASP Tactics

- 48-hour antibiotic time-outs
- Handshake stewardship
  - ASP rounds
- Patient education
- Antimicrobial formulary management
- Medication use evaluations (MUE) and targeted education

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ASP: Tracking Data

- Antibiotic use in days of therapy/1000 patient-days (DOT/1000)
  - Can look at individual antibiotics, groups of antibiotics
  - Hospital-wide, specific units, groups of units…
- NHSN Antimicrobial Use (AU data)
  - Adds: reasonable(ish) antibiotic groupings
  - Benchmarks with similar(ish) units at other hospitals
  - SAAR ≈ SIR
- Major limitation:
  - Don't know if the patient *should* be on antibiotics
  - Don't know if the antibiotic choices were optimal

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IP vs AS

	Infection Prevention	Antimicrobial Stewardship
#1 audience	Bedside staff esp. nursing	Ordering providers and pharmacists

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Case

A surgical ICU has noticed an increase in the incidence of HA-CDI over the past six months, from 5 cases in the prior 4 quarters to 7 in the past 2 quarters. They have had no significant changes in staffing or patient population. What should they look at first?

- Adherence to isolation precautions
- Post-operative antibiotic prophylaxis
- Post-discharge deep cleaning
- Empiric antibiotic selection
- Handwashing practices

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- Empiric antibiotic selection
- Handwashing practices

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C-diff Prevention

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IP	Both	ASP
• Handwashing • Surveillance • Isolation • Unit layout • Deep cleaning	• Diagnostic Stewardship!	• Avoid highest-risk CDI antibiotics • Minimize antibiotic durations • Prevent unnecessary antibiotic initiation

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C-diff: Don't blame me!

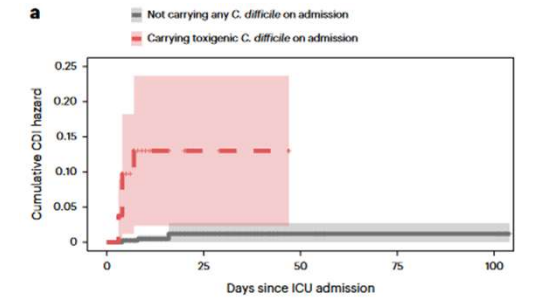
nature medicine

Article https://doi.org/10.1038/s41591-023-02549-4

Longitudinal genomic surveillance of carriage and transmission of *Clostridioides difficile* in an intensive care unit

Received: 2 August 2022
Accepted: 17 August 2023
Published online: 18 September 2023

Arianna Miles-Jay[1], Evan S. Snitkin[1,2], Michael Y. Lin[3], Teppei Shimasaki[3], Michael Schoeny[3], Christine Fukuda[3], Thelma Dangana[3], Nicholas Moore[3], Sarah E. Sansom[3], Rachel D. Yelin[3], Pamela Bell[3], Krishna Rao[2], Micah Keidan[2], Alexandra Standke[2], Christine Bassis[2], Mary K. Hayden[2] & Vincent B. Young[1,2]



- Cultured almost 4,000 stools and rectal swabs from 1,289 ICU admissions
- Only 1% of eligible patients had acquisition of toxigenic *C. difficile* via cross-transmission
- Colonized with toxigenic *C. difficile* on admission: **24x greater risk of CDI**

Impact of AS programs on *C.difficile*

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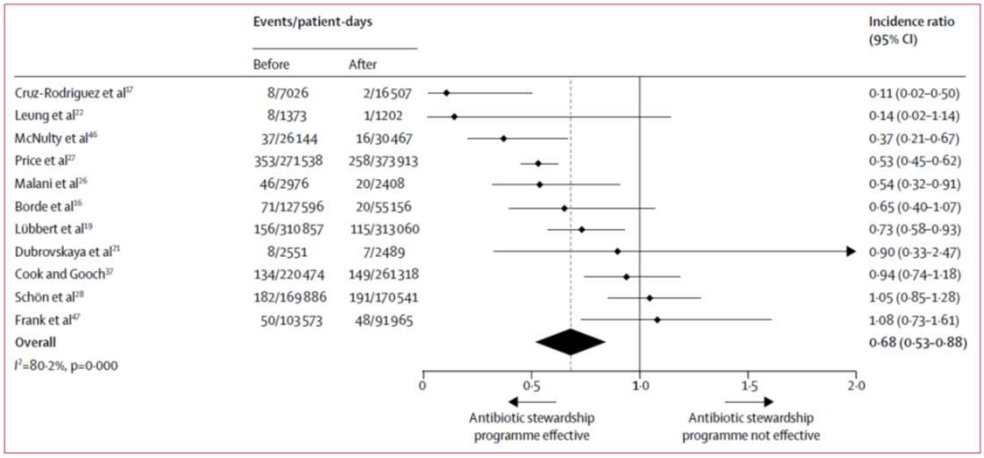


Figure 4: Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of *Clostridium difficile* infections

Baur, Gladstone, Burkert, et al. Lancet Infectious Diseases; 17:9:990-1001, 2017

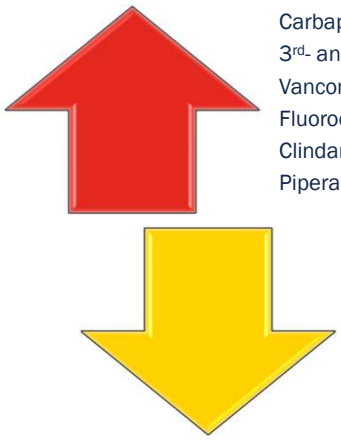
J Antimicrob Chemother 2021; 76: 1676–1688
doi:10.1093/jac/dkab091 Advance Access publication 31 March 2021

Journal of Antimicrobial Chemotherapy

Antibiotics and healthcare facility-associated *Clostridioides difficile* infection: systematic review and meta-analysis 2020 update

Claudia Slimings [1]* and Thomas V. Riley[2,3]

Which antibiotics are most likely to cause CDI?



Carbapenems
3rd- and 4th-gen cephalosporins
Vancomycin
Fluoroquinolones
Clindamycin
Piperacillin-tazobactam

Narrow penicillins
1st-gen cepalosporins
TMP-SMX
Tetracyclines

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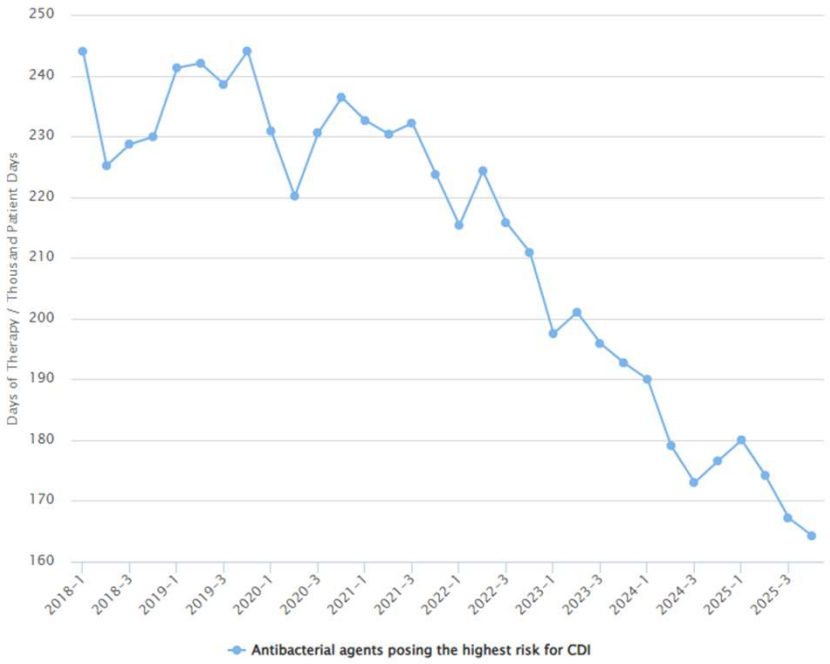
Antibiotics with High Risk of CDI

UNC Medical Center



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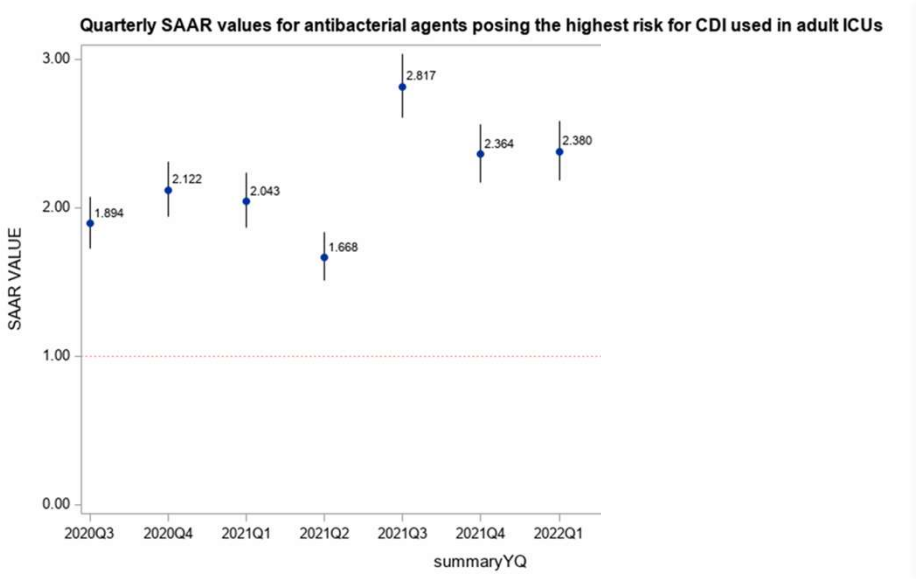
Antibiotics with high risk for CDI in SICU



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Diagnostic Stewardship: Why?

- Most infectious diseases diagnostics have imperfect specificity and positive predictive value
  - Patients can have C-diff colonization, urinary tract colonization, ET tube or trach colonization, Group A Strep colonization, CVC colonization…
- False-positives:
  - Mask the patient's true problem
  - Cause unnecessary antibiotic exposure
  - Overcount HAIs
- Very difficult for clinicians to ignore a positive culture
- Not the goal: missing HAIs, saving money

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Diagnostic Stewardship Principles

- Perform infectious diseases diagnostic testing *appropriately*
  - Examples:
    - Adequate blood culture volumes sent from fresh peripheral sticks
    - Reject formed stools sent for C-diff testing
- Only send testing when infection reasonably suspected
  - Avoid false-positives
  - Especially nonsterile sites (respiratory tract, urinary tract, wounds)

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Diagnostic Stewardship Partnership between IP and AS

Complementary skill sets:

- IP: expertise in bedside/nursing care and QI
- AS: experience working with/educating ordering providers

Shared goals:

- Overdiagnosis of HAI → overuse of antibiotics

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Diagnostic Stewardship Stakeholders

Frontline staff	Obtain most samples for testing Often suggest testing to providers
Microbiology lab	Assess sample adequacy (e.g., rejecting formed stools) Reporting algorithms
Ordering providers and pharmacists	Order diagnostic tests and make treatment decisions

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C. difficile Diagnostic Stewardship

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Problem

- *C. difficile* colonization is common
  - Nontoxigenic strains
  - Toxigenic strains not causing symptoms
- Diarrhea is common in the hospital
  - Laxatives, enteral feeds, withdrawal symptoms, most drugs, etc…

Strategies

- Use high-specificity test algorithms
  - Avoid PCR-only CDI testing
- Avoid *C. difficile* testing if:
  - Not true diarrhea (<3 episodes/24 hours, formed stool)
  - Recent laxative exposure
  - Recent negative test

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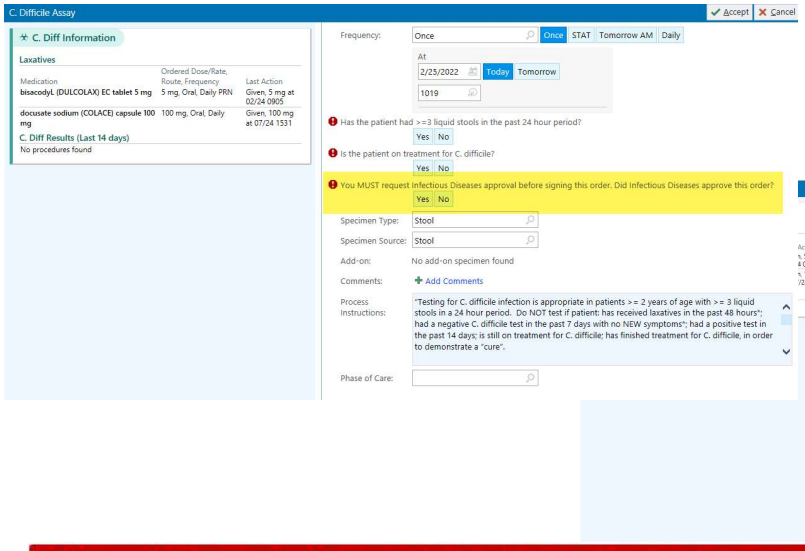

QUALITY IMPROVEMENT

C. difficile test ordering: "hard stop"

Slide courtesy of Emily Sickbert-Bennett, PhD

ASP Role in CDI Diagnostic Stewardship

- Hard stop design
- Provider education
- Clinical review of C-diff tests that violated hard stop
  - Physicians and pharmacists on staff already doing clinical reviews daily
  - Approvals when clinically indicated

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HAP/VAP Diagnostic Stewardship

- Surveillance definition ≠ Clinical definition
- Respiratory cultures from airway devices have very poor specificity and PPV
- False-positive cultures → treatment courses
  - Often repetitively in one patient
  - Usually broad-spectrum

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Diagnostic Stewardship Project

- Education provided to PICU before launch
- Audited every respiratory culture sent from patients in PICU
  - 9/1/21-12/31/22 (15 months)
    - 3 months pre- and 12 months post-intervention.
  - Cultures assessed as guideline-concordant or –discordant
    - Systemic signs of illness (fever, leukocytosis, etc) PLUS respiratory symptoms (persistently increased PEEP/FiO2, CXR changes, purulent ETT output)
- Periodic feedback to PICU providers

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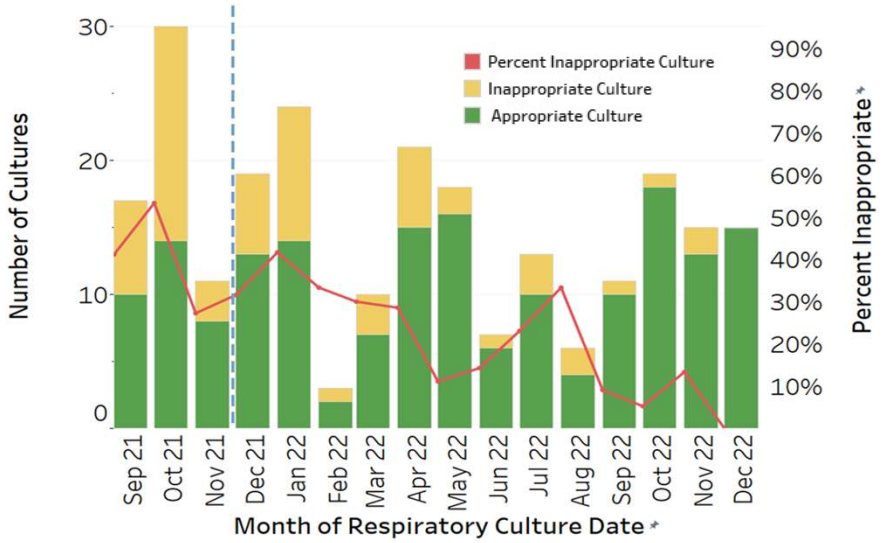
Proportion of Respiratory Cultures that were Guideline-Concordant



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Results of Guideline-Discordant Cultures

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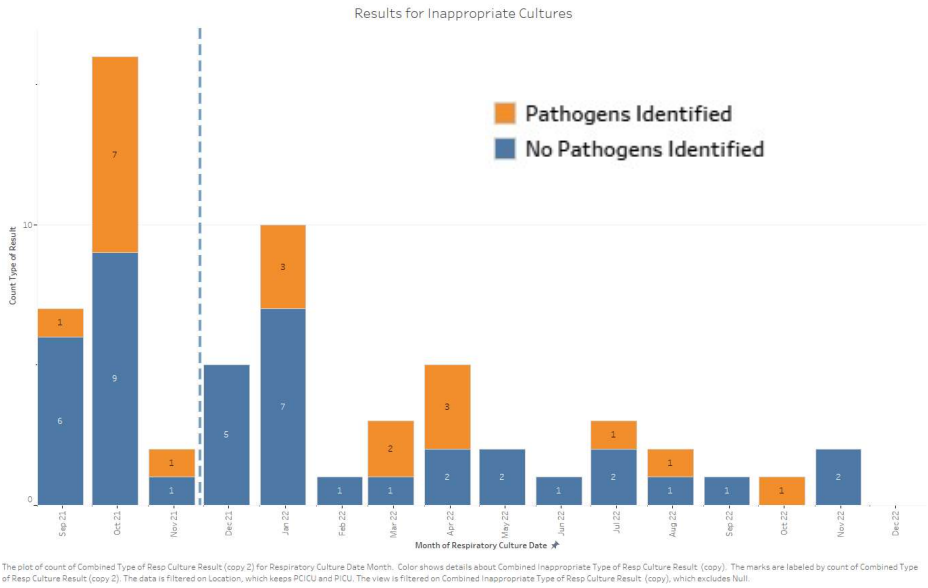
Orange: cultures that grew pathogens

Blue: cultures that did not grow



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Guideline-Discordant Cultures Treated with Antibiotics

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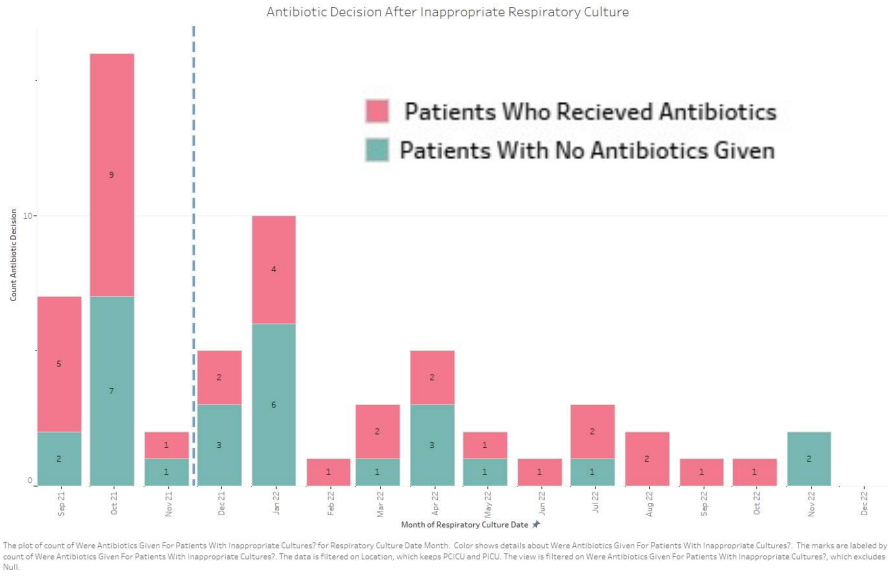
Salmon: Number of guideline-discordant cultures treated with antibiotics



The plot of count of Were Antibiotics Given For Patients With Inappropriate Cultures? for Respiratory Culture Date Month. Color shows details about Were Antibiotics Given For Patients With Inappropriate Cultures?. The marks are labeled by count of Were Antibiotics Given For Patients With Inappropriate Cultures?. The data is filtered on Location, which keeps PCICU and PICU. The view is filtered on Were Antibiotics Given For Patients With Inappropriate Cultures?, which excludes Null.

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UTI Diagnostic Stewardship

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- Asymptomatic bacteriuria is common
  - Older adults
  - Patients with indwelling catheters
- Overdiagnosis leads to:
  - Missed diagnoses
  - Antibiotic exposure (often repeatedly)
  - False-positive CAUTIs

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CAUTI Diagnosis Pitfalls

- Pyuria and asymptomatic bacteriuria are very common with long-dwelling urinary catheters
  - You can have ASB with or without pyuria, and pyuria may be sterile
  - You can NOT have a UTI without pyuria
    - Exception: neutropenia
- UTIs are symptomatic, but ICU patients often unable to report symptoms
- Always get a UA BEFORE or at least with the urine culture
  - Use fresh catheter for culture whenever possible
- "Pan-culture" for febrile patients with an ETT and a Foley is likely to turn up a positive culture
  - Avoid this approach

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Protocolized Urine Sampling is Associated with Reduced Catheter-associated Urinary Tract Infections: A Pre- and Postintervention Study

Jennifer A. Frontera,[1,a] Erwin Wang,[2] Michael Phillips,[2] Martha Radford,[2] Stephanie Sterling,[2] Karen Delorenzo,[3] Archana Saxena,[2] Shadi Yaghi,[1] Ting Zhou,[1] D. Ethan Kahn,[1] Aaron S. Lord,[1] and Joseph Weisstuch[2]

- Intervention:
  - Catheter removal required before sending urinary testing
  - Urine culture sent only after UA
- Urinary catheter days reduced by 37%
- 63% reduction in CAUTI
  - 5.9 → 2.2 CAUTI/1000 catheter days

Clinical Infectious Diseases, 2020

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Blood Culture Diagnostic Stewardship

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Blood Culture Diagnostic Stewardship

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JAMA Pediatrics | Original Investigation

Association of Diagnostic Stewardship for Blood Cultures in Critically Ill Children With Culture Rates, Antibiotic Use, and Patient Outcomes
Results of the Bright STAR Collaborative

Charlotte Z. Woods-Hill, MD, MSHP; Elizabeth A. Colantuoni, PhD; Danielle W. Koontz, MA, MS; Annie Voskertchian, MPH; Anping Xie, PhD; Cary Thurm, PhD; Marlene R. Miller, MD, MSc; James C. Fackler, MD; Aaron M. Milstone, MD, MHS; and the Bright STAR Authorship Group

- Can we steward *blood cultures*? Should we?
- Logic: Fever → blood cultures → empiric antibiotics
- Would *CLABSIs go down*?? Would septic shock go up?

Blood Culture Diagnostic Stewardship

- 14 PICUs independently developed blood culture best practices
  - Reduce variability in blood culture decision, source, frequency of repeats
  - Studied 24 months pre- and 18 months post-implementation
- Results:
  - Blood cultures fell 33% (49 blood cultures/1000 patient-days fewer)
  - Broad-spectrum antibiotics use fell 13%
  - Unchanged: PICU mortality, LOS, readmission, sepsis, severe sepsis
  - **CLABSIs fell 36%** (1.79 → 1.14 CLABSI/1000 line-days)

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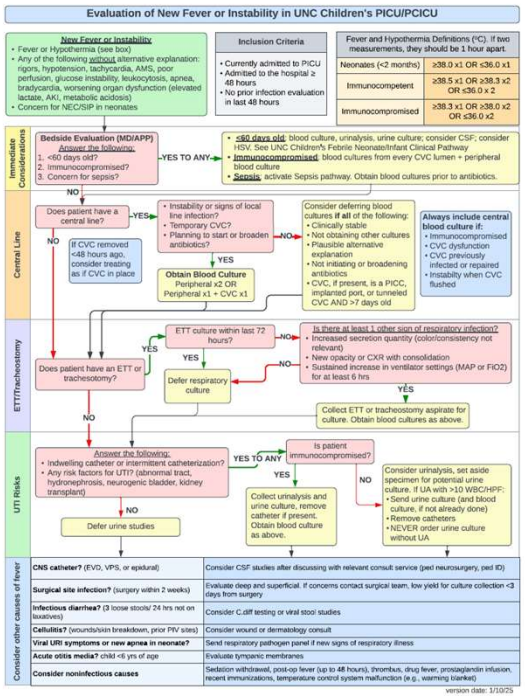
Unified ICU Diagnostic Stewardship

- No more automatic “pan-culture”!
- Fever is common in the ICU and has many non-infectious causes
- Poor specificity of cultures (frequent false-positives)
- Considered approach to cultures
  - Illness severity
  - Pre-test probability



Asymptomatic bacteriuria

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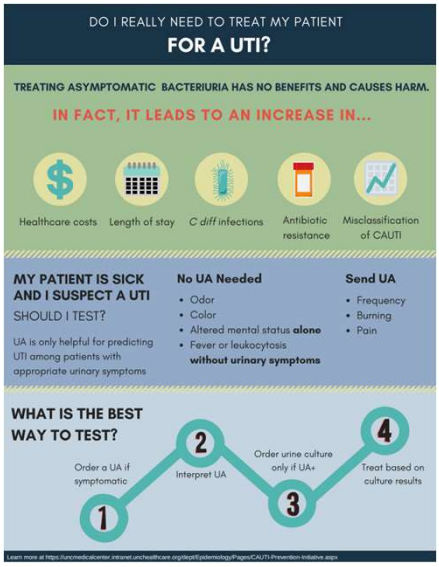

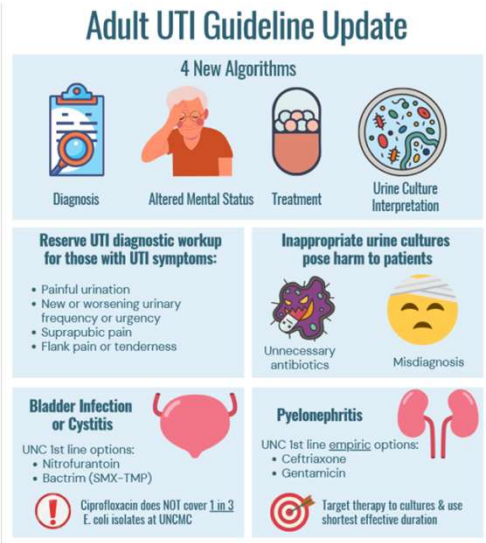

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Case

The neonatal ICU has had three CLABSIs in the past four months with a similar pattern. The infections have occurred during the time period of days of life 3-7. The infants have all had umbilical venous catheters; all had had negative blood cultures at birth and received 48 hours of empiric antibiotics.

A NICU clinician notes that at their previous employer, it was common to continue the birth antibiotics until day of life 7, regardless of birth culture results.

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AS/IP: Are we ever at odds?

- Head in the sand approaches
  - No culture → No HAI!
- Antibiotic prophylaxis example:
  - Reduced incidence of VAP in neuro ICU patients who received a single dose of ceftriaxone

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Future Directions

- Diagnostic stewardship
  - Only scratched the surface
  - Requires IP/ASP collaboration and *many* stakeholders
- NHSN AR data
  - Now mandatory
  - But not yet useful
    - Hopefully will provide more data about AR patterns.

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References

CDC. The biggest antibiotic-resistant threats in the U.S. [Internet]. Centers for Disease Control and Prevention. 2022 [cited 2024 Mar 25]. Available from: https://www.cdc.gov/drugresistance/biggest-threats.html

Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013 [Internet]. 2013 p. 1–114. Available from: http://www.cdc.gov/drugresistance/threat-report-2013/index.html

Core Elements of Hospital Antibiotic Stewardship Programs | Antibiotic Use | CDC [Internet]. 2021 [cited 2021 Apr 28]. Available from: https://www.cdc.gov/antibiotic-use/core-elements/hospital.html

Miles-Jay A, Snitkin ES, Lin MY, Shimasaki T, Schoeny M, Fukuda C, Dangana T, Moore N, Sansom SE, Yelin RD, Bell P, Rao K, Keidan M, Standke A, Bassis C, Hayden MK, Young VB. Longitudinal genomic surveillance of carriage and transmission of Clostridioides difficile in an intensive care unit. Nat Med. Nature Publishing Group; 2023 Oct;29(10):2526–2534.

Slimings C, Riley TV. Antibiotics and healthcare facility-associated Clostridioides difficile infection: systematic review and meta-analysis 2020 update. Journal of Antimicrobial Chemotherapy. 2021 Jul 1;76(7):1676–1688.

Woods-Hill CZ, Colantuoni EA, Koontz DW, Voskertchian A, Xie A, Thurm C, Miller MR, Fackler JC, Milstone AM, Bright STAR Authorship Group. Association of Diagnostic Stewardship for Blood Cultures in Critically Ill Children With Culture Rates, Antibiotic Use, and Patient Outcomes: Results of the Bright STAR Collaborative. JAMA Pediatrics [Internet]. 2022 May 2 [cited 2022 Jun 7]; Available from: https://doi.org/10.1001/jamapediatrics.2022.1024

Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, Tacconelli E. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infect Dis. 2017 Sep;17(9):990–1001. PMID: 28629876