Antimicrobial Stewardship and the Role of the Infection Preventionist

Zach Willis, MD, MPH

4/23/24

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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:
  - Pfizer (pediatric nirmatrelvir-ritonavir)
  - Pfizer (maternal RSV vaccine)
  - Merck (monoclonal antibody for RSV prevention)

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

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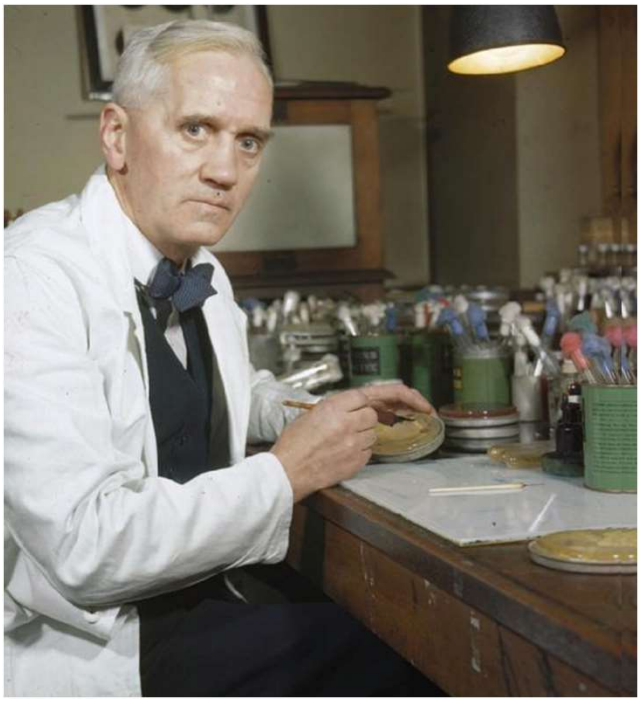

The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out.... In such cases the **thoughtless person playing with penicillin is morally responsible for the death** of the man who finally succumbs to infection with the penicillin-resistant organism.

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

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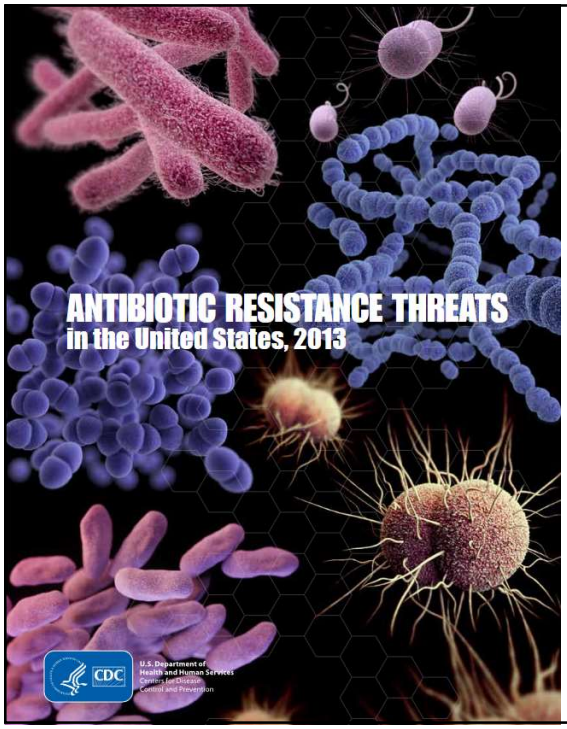

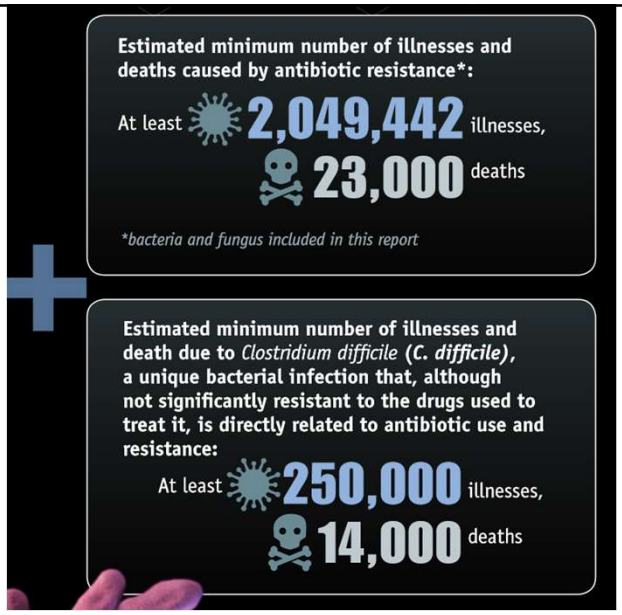

https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf

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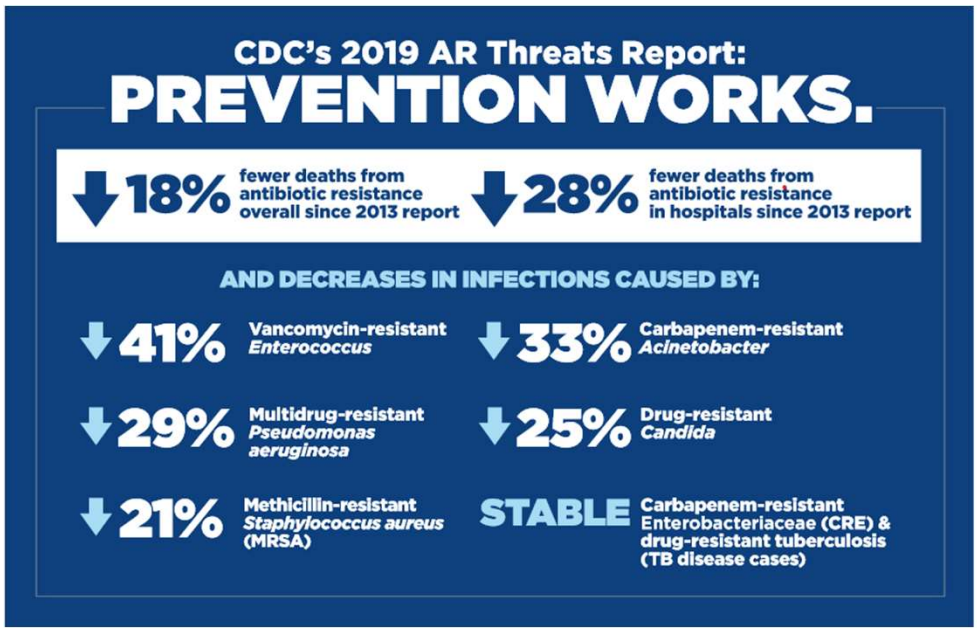

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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What Was Working?

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

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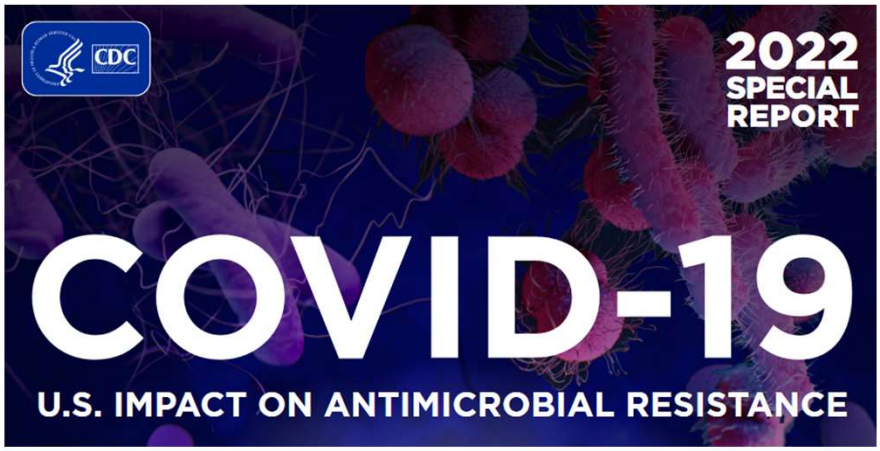

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

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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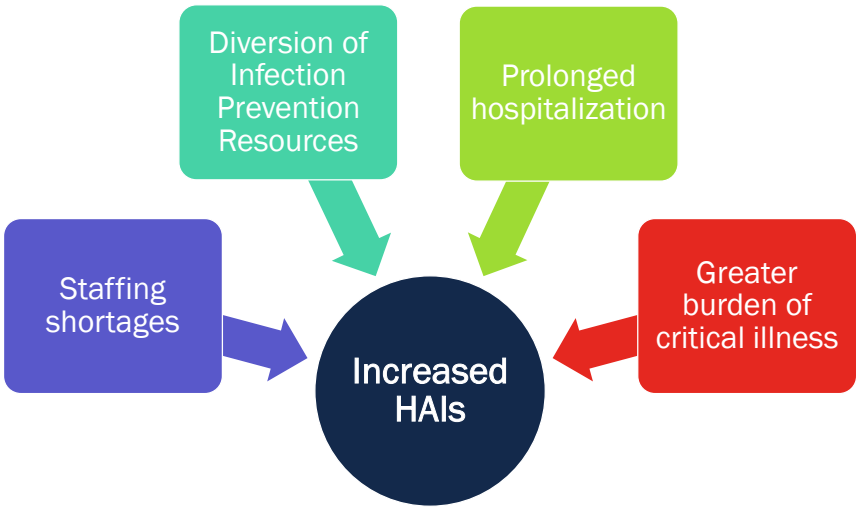

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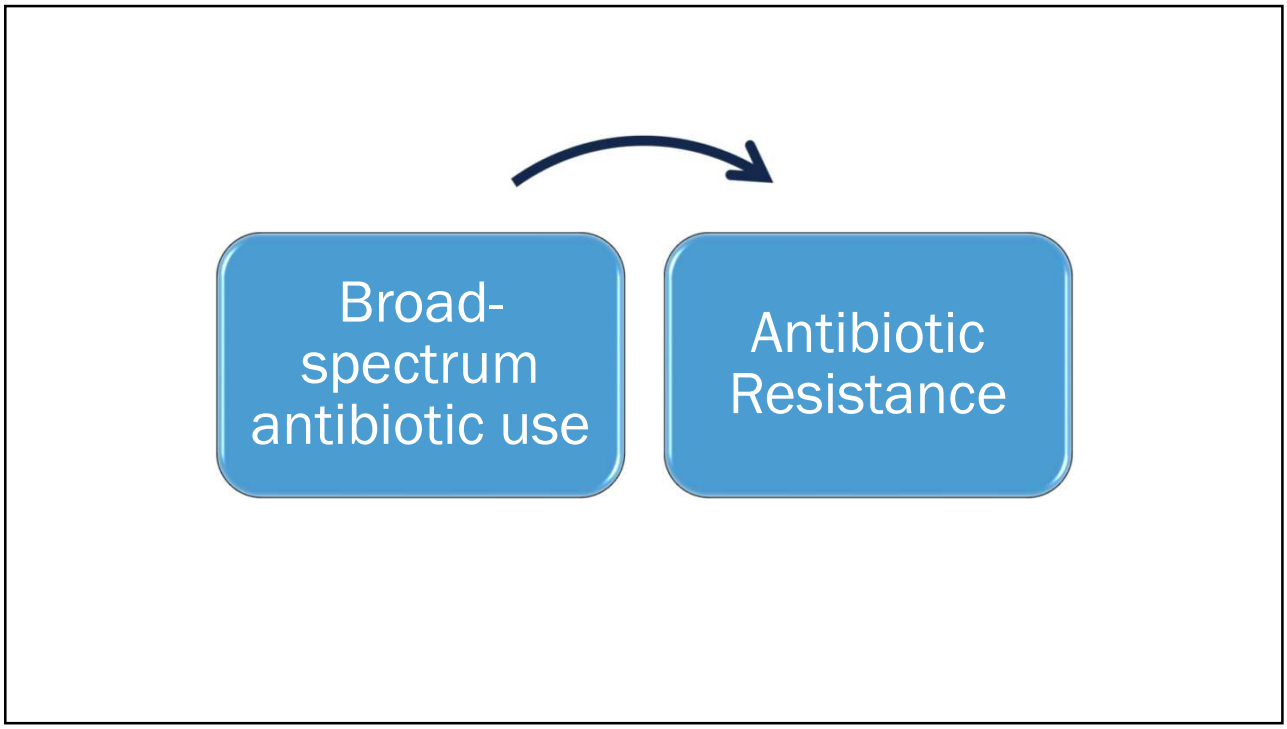
Broad-spectrum antibiotic use
Antibiotic Resistance

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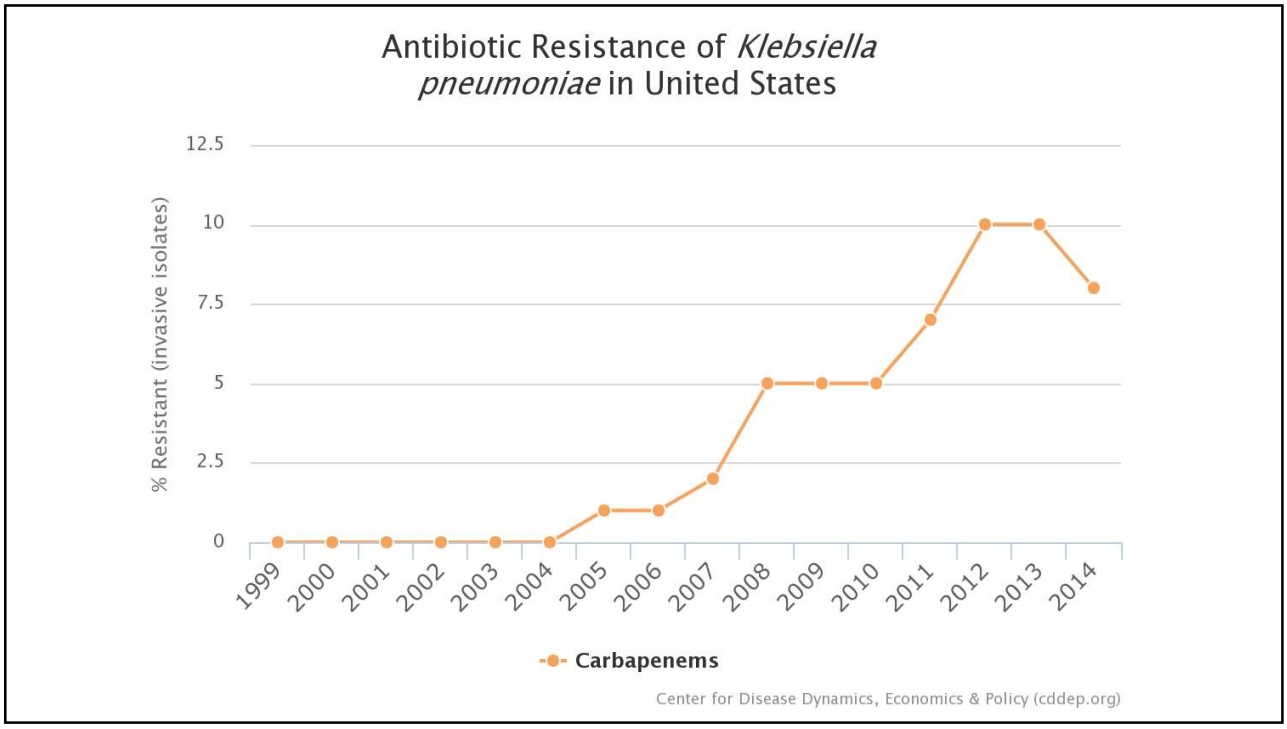
Antibiotic Resistance of *Klebsiella pneumoniae* in United States
% Resistant (invasive isolates)
12.5
10
7.5
5
2.5
0
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
Carbapenems
Center for Disease Dynamics, Economics & Policy (cddep.org)

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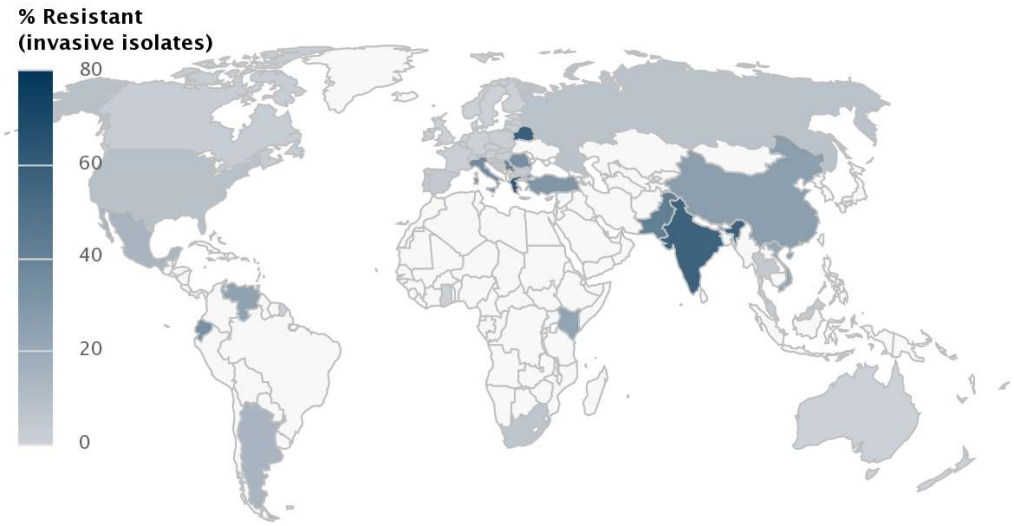
Resistance of *Klebsiella pneumoniae* to Carbapenems



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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

CDC strategies that work in healthcare:

- Preventing device- and procedure-related infections, such as from urinary catheters or central lines
- Stopping the spread of resistant germs within and between healthcare facilities
- Containing emerging threats through early detection and aggressive response
- Tracking and improving appropriate antibiotic use
- Infection prevention and control in non-hospital settings, such as long-term care facilities

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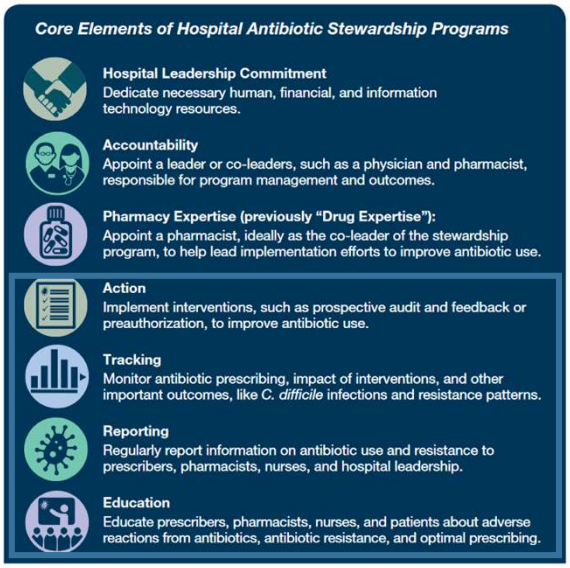
AS: Core Elements



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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Key ASP Tactics

- Prospective Audit and Feedback
  - AKA “postprescription review”
- Prior authorization/Restriction
  - Preapproval required for certain antibiotics to be released
- Clinical Pathway/Guideline development
  - Incorporates diagnosis and management guidelines; good for standardization
- 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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Stewardship: A Multidisciplinary Endeavor

Essential, "Core-Team" Personnel

- Lead Physician
- Lead Pharmacist
- Clinical Microbiologist
- Infection Preventionist
- Information Technologist

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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
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C-diff Prevention

IP	Both	ASP
• Handwashing • Surveillance • Isolation • Unit layout • Deep cleaning	• Diagnostic Stewardship!	• Avoid highest-risk CDI antibiotics • Basically everything we do

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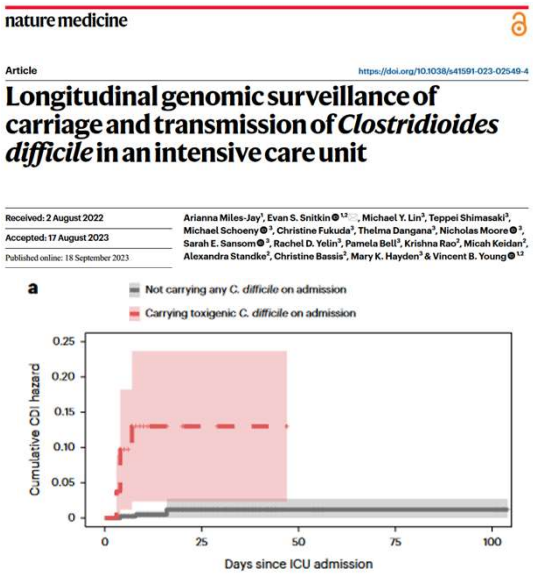
C-diff: Don't blame me!



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[3], Micah Keidan[2], Alexandra Standke[3], Christine Bassis[3], Mary K. Hayden[3] & 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**

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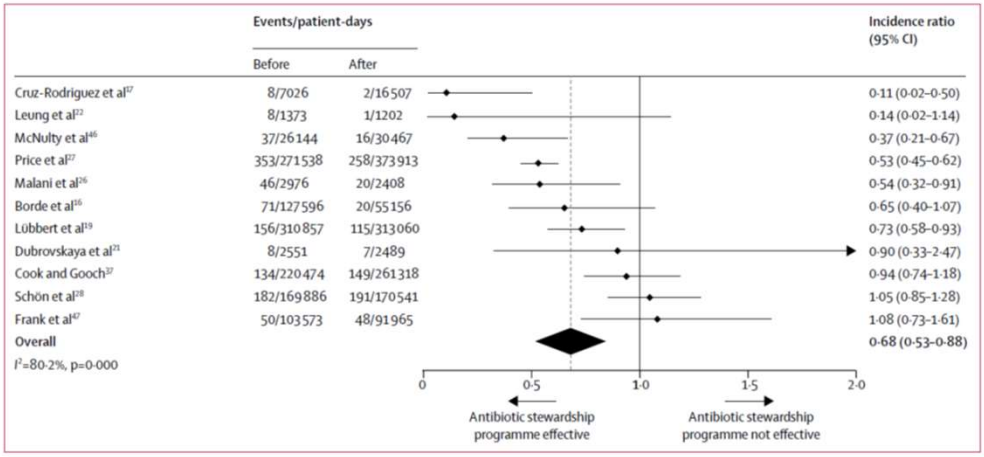
Impact of AS programs *C.difficile*



	Events/patient-days		Incidence ratio (95% CI)
	Before	After	
Cruz-Rodriguez et al[17]	8/7026	2/16507	0·11 (0·02–0·50)
Leung et al[22]	8/1373	1/1202	0·14 (0·02–1·14)
McNulty et al[46]	37/26144	16/30467	0·37 (0·21–0·67)
Price et al[27]	353/271538	258/373913	0·53 (0·45–0·62)
Malani et al[26]	46/2976	20/2408	0·54 (0·32–0·91)
Borde et al[16]	71/127596	20/55156	0·65 (0·40–1·07)
Lübbert et al[19]	156/310857	115/313060	0·73 (0·58–0·93)
Dubrovskaya et al[21]	8/2551	7/2489	0·90 (0·33–2·47)
Cook and Gooch[37]	134/220474	149/261318	0·94 (0·74–1·18)
Schön et al[28]	182/169886	191/170541	1·05 (0·85–1·28)
Frank et al[47]	50/103573	48/91965	1·08 (0·73–1·61)
Overall			0·68 (0·53–0·88)
I^2=80·2%, p=0·000			

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

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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?
- Highest-risk classes (highest to lowest):
  - Carbapenems
  - 4th-gen and 3rd-gen cephalosporins
  - Vancomycin
  - Fluoroquinolones
  - Clindamycin
  - Piperacillin-tazobactam
  - No association: narrow penicillins, 1st-gen cephalosporins, TMP-SMX, tetracyclines
- Allows ASP to prioritize high-risk

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Meropenem Use 2017-2023

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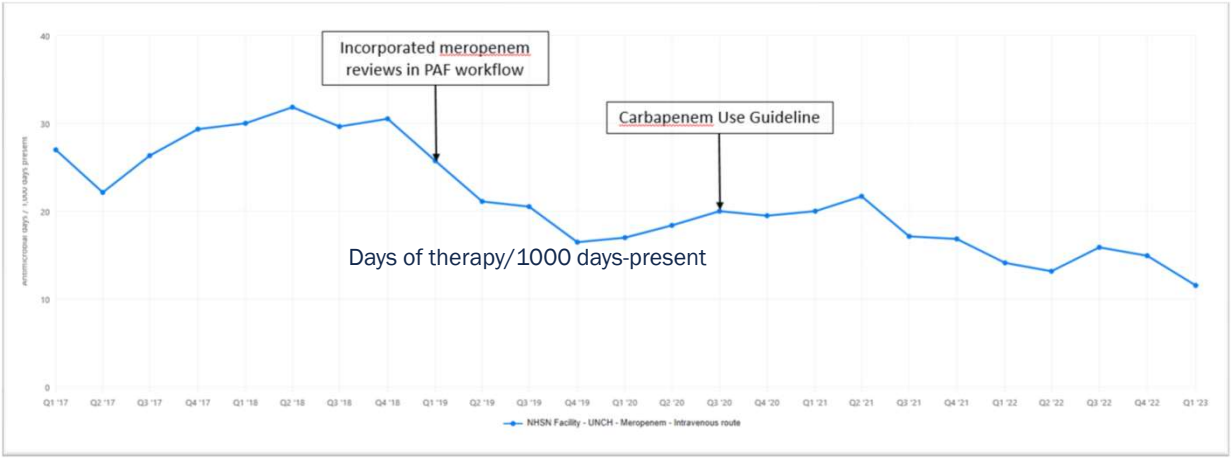

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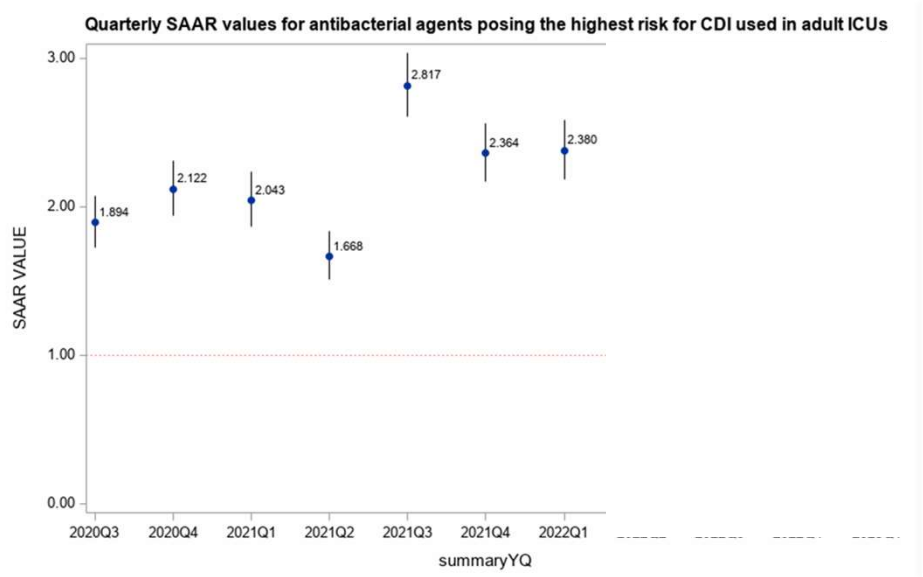
Antibiotics with high risk for CDI in SICU



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Diagnostic Stewardship: Why?

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- 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
- Not the goal: missing HAIs, saving money

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Diagnostic Stewardship Principles

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- 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

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Diagnostic Stewardship Stakeholders

Frontline staff

Obtain most samples for testing

Often suggest testing to providers

Microbiology lab

Assess sample adequacy (rejecting formed stools, rejecting "sputum" that's all spit)

Reporting algorithms:

- Urine culture with 3 organisms in low numbers vs "mixed urogenital flora"

Ordering providers and pharmacists

Order diagnostic tests and make treatment decisions

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C. difficile Diagnostic Stewardship

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- *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…
- 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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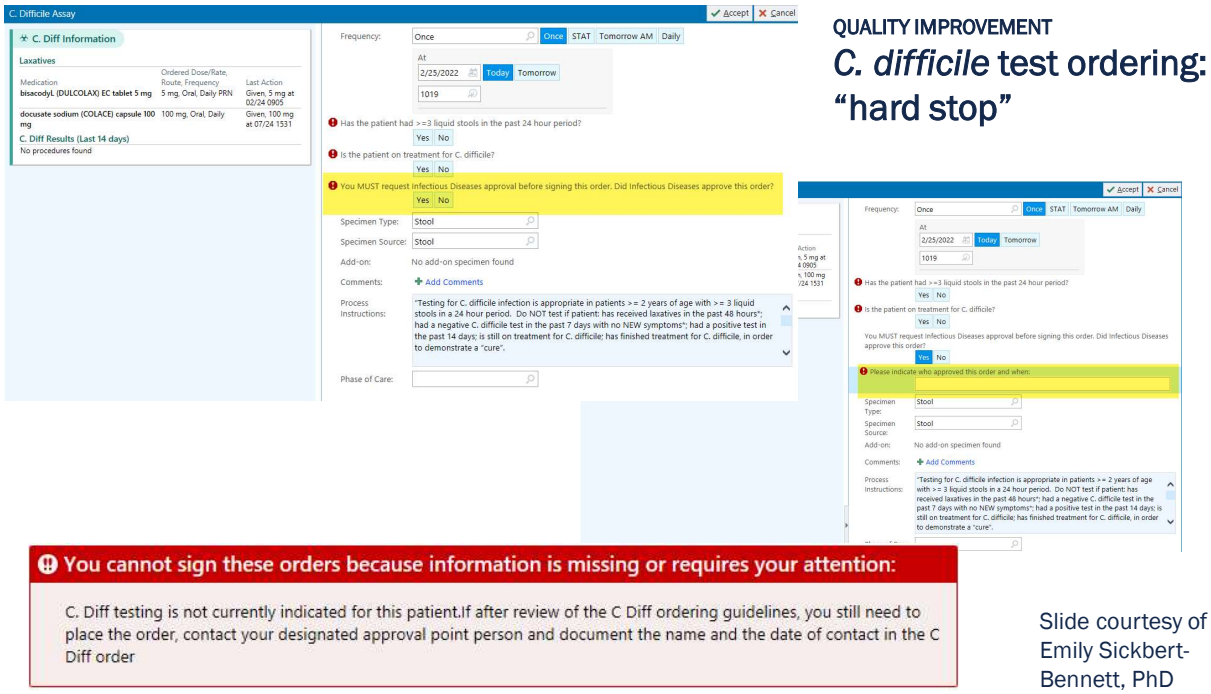

QUALITY IMPROVEMENT

C. difficile test ordering: "hard stop"

Slide courtesy of Emily Sickbert-Bennett, PhD

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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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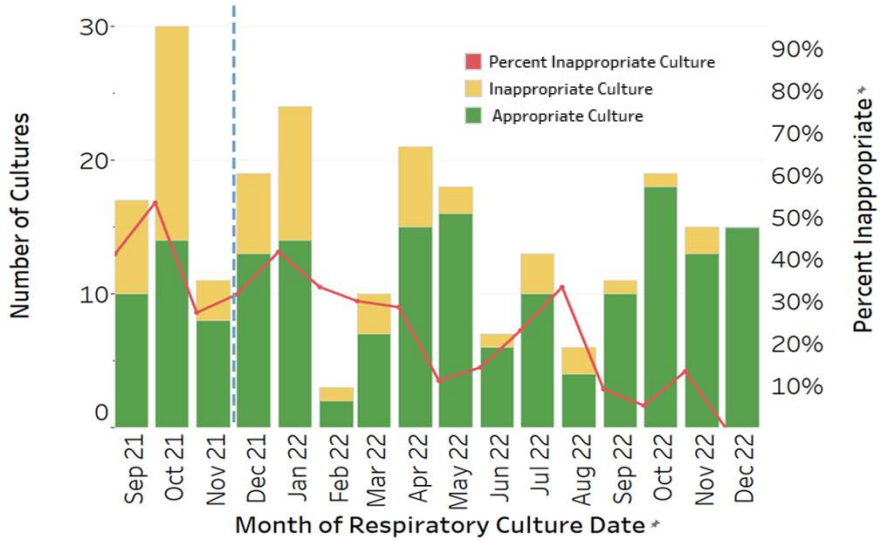
Proportion of Respiratory Cultures that were Guideline-Concordant



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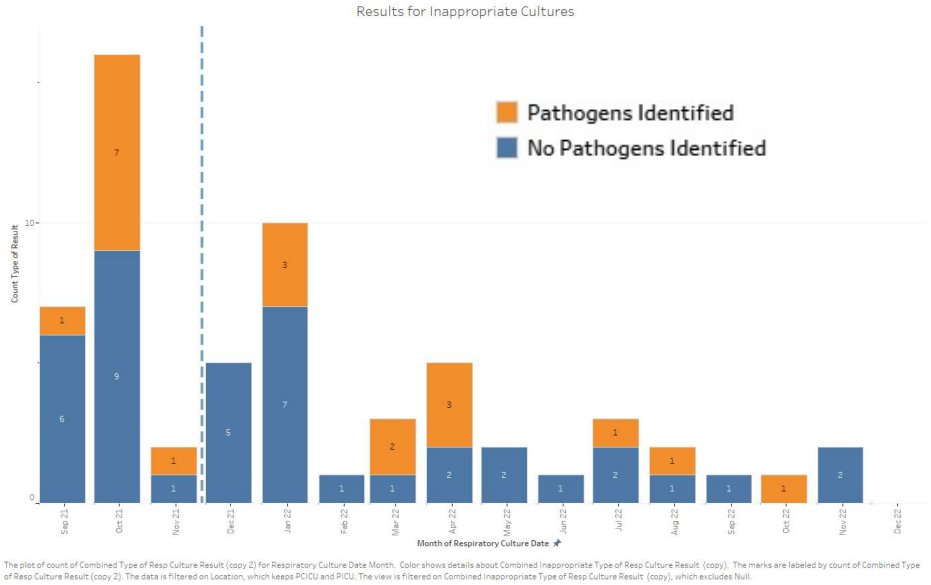
Results of Guideline-Discordant Cultures

Orange: cultures that grew pathogens

Blue: cultures that did not grow



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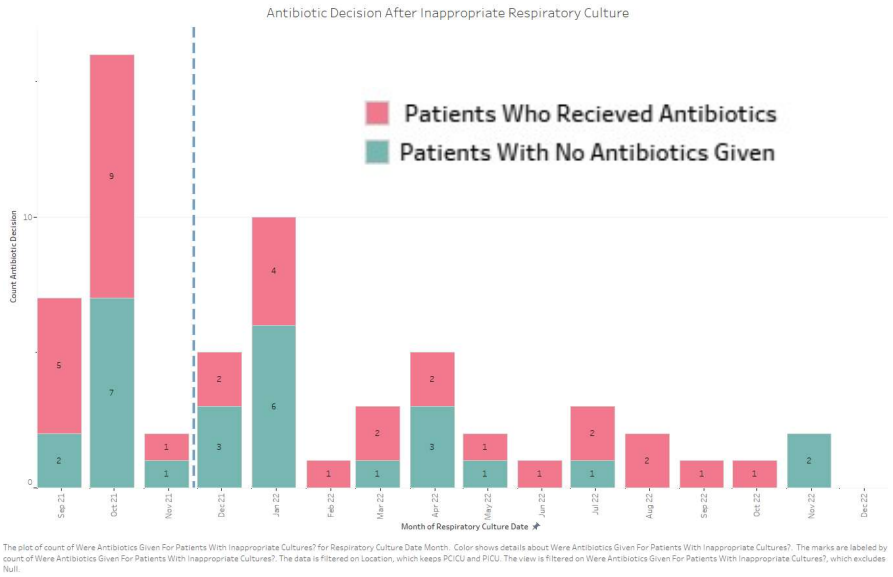
Guideline-Discordant Cultures Treated with Antibiotics

Salmon: Number of guideline-discordant cultures treated with antibiotics



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Blood Culture Diagnostic Stewardship

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?

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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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UTI Diagnostic Stewardship

- 2 major scenarios:
  - Inpatient with indwelling catheter (at risk for CAUTI)
  - Outpatients
- 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
- 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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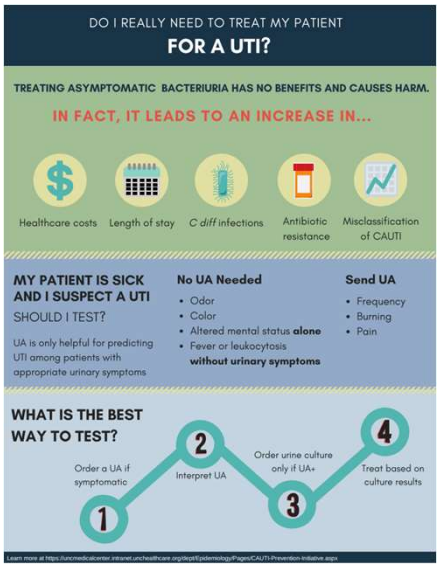
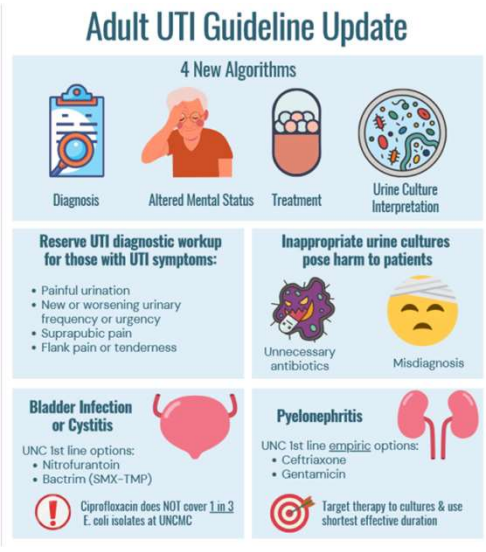
Asymptomatic bacteriuria





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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
  - Becomes mandatory by next year
  - May give us *much* more data about AR patterns, relationships between AU and AR

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Questions?

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