Hot Topics in Antimicrobial Stewardship

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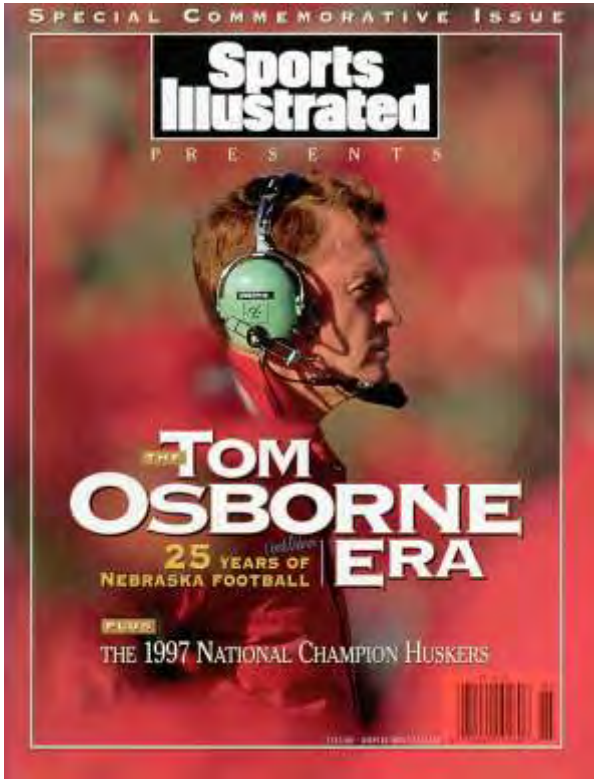
Disclosures

I have no relevant financial conflicts of interest to report related to this presentation.

Overview – Hot Topics in Antimicrobial Stewardship

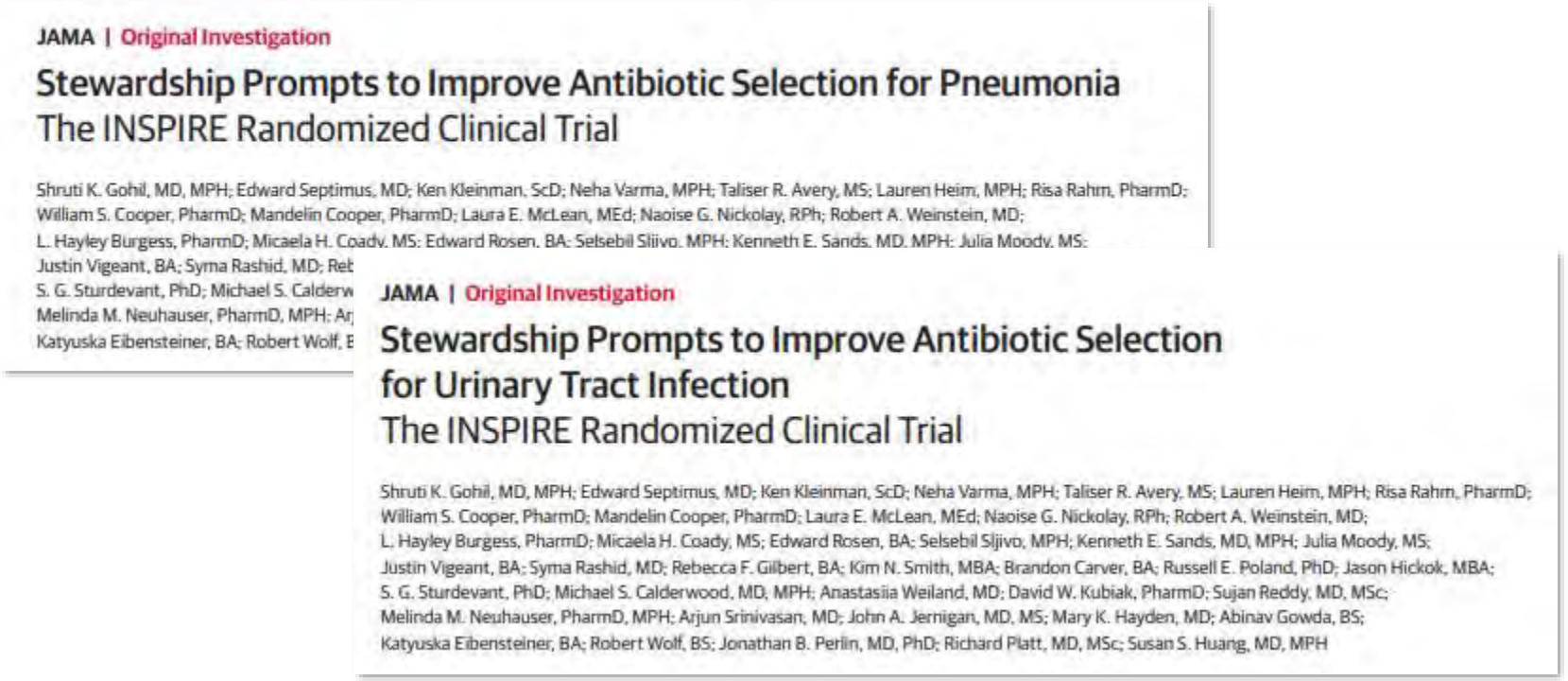
Precision Medicine	Inspire – ASP Pneumonia, UTI, IAI, and SSTI
Next-Level Stewardship	Opt-out electronic antimicrobial stewardship
Next-Level Beta-Lactam Allergy Management	PEN-FAST, CEPH-FAST, nurse documentation
Another Thing	To be revealed later

The real Hot Topics, though amirite?



Precision Medicine to Improve Empiric Therapy Selection

INSPIRE Pneumonia and UTI



JAMA | Original Investigation

Stewardship Prompts to Improve Antibiotic Selection for Pneumonia
The INSPIRE Randomized Clinical Trial

Shruti K. Gohil, MD, MPH; Edward Septimus, MD; Ken Kleinman, ScD; Neha Varma, MPH; Taliser R. Avery, MS; Lauren Heim, MPH; Risa Rahm, PharmD; William S. Cooper, PharmD; Mandelin Cooper, PharmD; Laura E. McLean, MEd; Naoise G. Nickolay, RPh; Robert A. Weinstein, MD; L. Hayley Burgess, PharmD; Micaela H. Coady, MS; Edward Rosen, BA; Selsebil Sljivo, MPH; Kenneth E. Sands, MD, MPH; Julia Moody, MS; Justin Vigeant, BA; Syma Rashid, MD; Reb
S. G. Sturdevant, PhD; Michael S. Calderw
Melinda M. Neuhauser, PharmD, MPH; Ar
Katyuska Eibensteiner, BA; Robert Wolf, B

JAMA | Original Investigation

Stewardship Prompts to Improve Antibiotic Selection for Urinary Tract Infection
The INSPIRE Randomized Clinical Trial

Shruti K. Gohil, MD, MPH; Edward Septimus, MD; Ken Kleinman, ScD; Neha Varma, MPH; Taliser R. Avery, MS; Lauren Heim, MPH; Risa Rahm, PharmD; William S. Cooper, PharmD; Mandelin Cooper, PharmD; Laura E. McLean, MEd; Naoise G. Nickolay, RPh; Robert A. Weinstein, MD; L. Hayley Burgess, PharmD; Micaela H. Coady, MS; Edward Rosen, BA; Selsebil Sljivo, MPH; Kenneth E. Sands, MD, MPH; Julia Moody, MS; Justin Vigeant, BA; Syma Rashid, MD; Rebecca F. Gilbert, BA; Kim N. Smith, MBA; Brandon Carver, BA; Russell E. Poland, PhD; Jason Hickok, MBA; S. G. Sturdevant, PhD; Michael S. Calderwood, MD, MPH; Anastasiia Weiland, MD; David W. Kubiak, PharmD; Sujan Reddy, MD, MSc; Melinda M. Neuhauser, PharmD, MPH; Arjun Srinivasan, MD; John A. Jernigan, MD, MS; Mary K. Hayden, MD; Abinav Gowda, BS; Katyuska Eibensteiner, BA; Robert Wolf, BS; Jonathan B. Perlin, MD, PhD; Richard Platt, MD, MSc; Susan S. Huang, MD, MPH

INtelligent Stewardship Prompts to Improve Real-time Empiric Antibiotic Selection for Patients

Gohil SK, Septimus E, Kleinman K, et al. JAMA 2024;331(23):2007-17
Gohil SK, Septimus E, Kleinman K, et al. JAMA 2024;331(23):2018-28

INSPIRE Pneumonia and UTI

- Goal – compare two strategies to determine best practices for empiric antibiotic selection
- Rationale
  - Uncertainty about risk drives overuse of broad-spectrum antibiotics
  - Most hospitalized patients for PNA or UTI are low risk for multidrug-resistant organisms (MDROs)
  - Providing real-time estimates of a patient's risk will allow more informed antibiotic choices
- Arm 1 – Routine Care: regular antibiotic stewardship strategies
- Arm 2 – Smart Prompt Alert Intervention: precision medicine smart prompt using a computerized physician order entry (CPOE) alert
  - Provides patient-specific probability of MDRO infection
    - Tailored to each patient, type of infection, and type of MDRO
  - Recommends a standard-spectrum antibiotic choice if risk is low (< 10%)

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INSPIRE Pneumonia and UTI

POPULATION

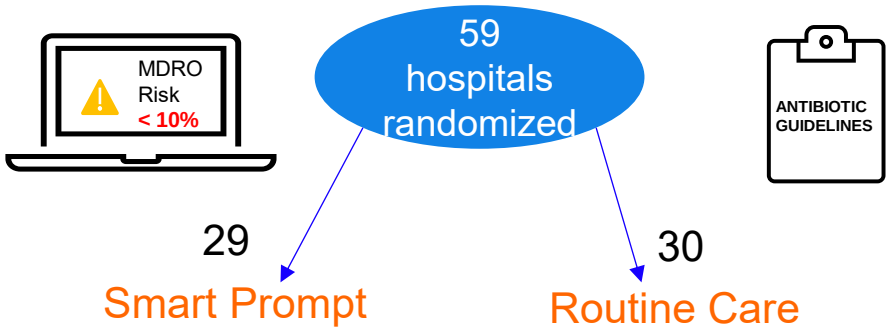
Non-critically ill adults hospitalized with:

Pneumonia	UTI
49,963 Women	88,249 Women
46,232 Men	38,729 Men

LOCATION

59 community hospitals in the U.S.

INTERVENTION



PRIMARY OUTCOME

Extended-spectrum antibiotic days of therapy (first 3 days of admission)

Secondary: Use of vancomycin and antipseudomonals

Safety: Antibiotic escalation, ICU transfer, and length of stay

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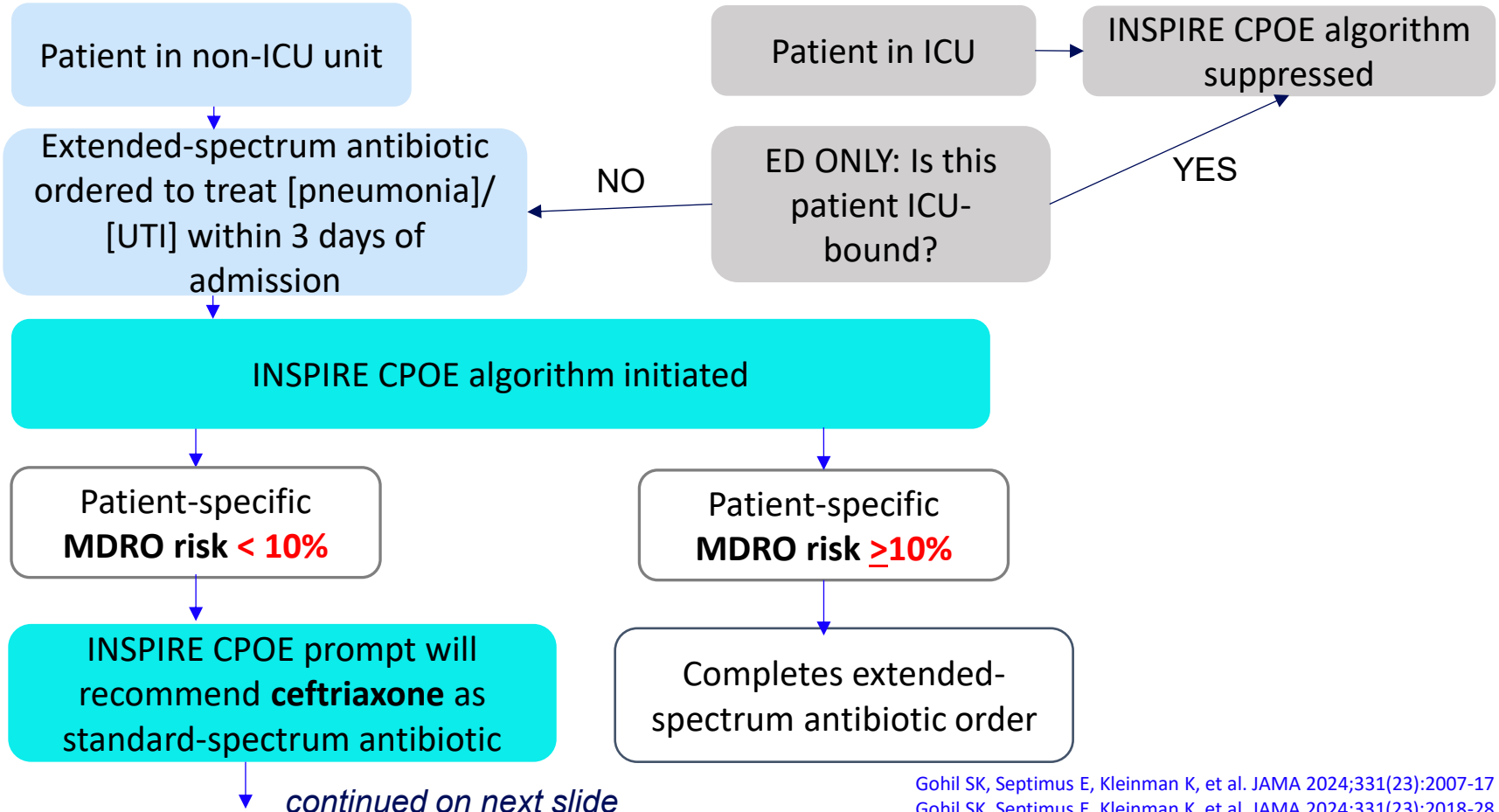
INSPIRE Pneumonia and UTI Workflow



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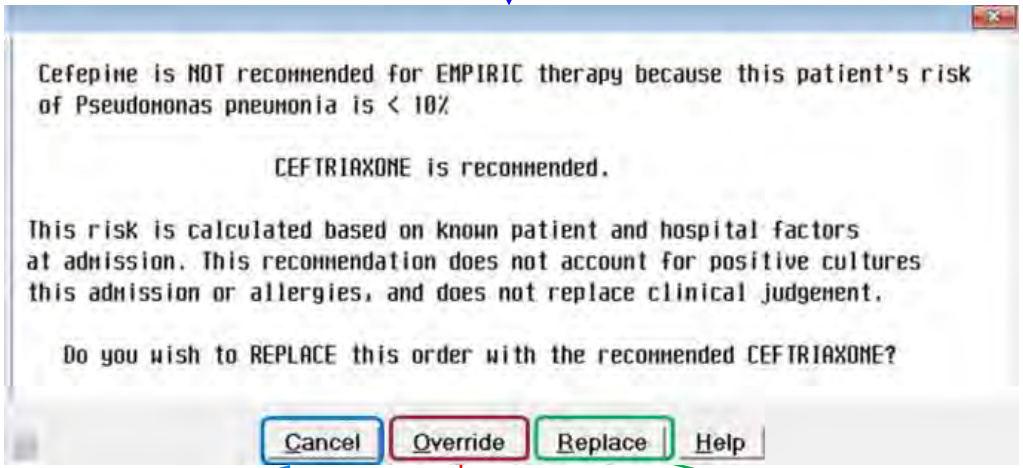
INSPIRE Pneumonia and UTI Workflow (continued)



Returns to order screen

Must enter reason to keep cefepime

1. Allergy
2. Patient requires ICU care for infection
3. Positive MDRO culture this admission or outside hospital
4. Neutropenia
5. Other:

Taken to **ceftriaxone** order screen

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INSPIRE Pneumonia and UTI Results

Pneumonia

Primary outcome

Smart prompts had a **28.4% reduction in empiric extended-spectrum DOTs** (95% CI, 22.2% to 34.1%); P < .001).

UTI

Primary outcome

Smart prompts had a **17.4% reduction in empiric extended-spectrum DOTs** (95% CI, 11.2% to 23.2%); P < .001)

Safety Outcomes	No differences in length of stay, days to ICU transfer, or days to antibiotic escalation

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INSPIRE Pneumonia

- > 96% classified as low risk in both groups
- < 2% of patients classified as low risk (< 10%) for pneumonia due to an MDRO eventually grew an MDRO from blood or respiratory source

Supplemental eTable 8: Group Comparisons of Multidrug-Resistant Organism (MDRO) Growth Among Patients in the INSPIRE Pneumonia Trial Classified as Low Absolute Risk (<10%) for MDRO Pneumonia

	CPOE Bundle[a] N = 22,782[b]		Routine Stewardship N = 21,998[c]	
MDRO Risk Estimate Model[d]	**Classified Low Risk N (%)**	**Classified Low Risk and Grew MDRO[e] N (%)**	**Classified Low Risk N (%)**	**Classified Low Risk and Grew MDRO[e] N (%)**
Methicillin-Resistant *Staphylococcus aureus* (MRSA)	22,465 (98.6)	229 (1.0)	21,720 (98.7)	253 (1.2)
Pseudomonas	22,011 (96.6)	245 (1.1)	21,291 (96.8)	276 (1.3)
ESBL and MDR-*Acinetobacter* (Pathogen susceptible to ertapenem)[f]	22,782 (100)	118 (0.5)	21,998 (100)	138 (0.6)
ESBL, MDR-*Acinetobacter*, and MDR-*Pseudomonas* (Pathogen susceptible to meropenem, imipenem)[g]	22,782 (100)	149 (0.7)	21,998 (100)	167 (0.8)
Carbapenem-Resistant Enterobacterales[h]	22,782 (100)	33 (0.1)	21,998 (100)	43 (0.2)

Gohil SK, Septimus E, Kleinman K, et al. JAMA 2024;331(23):2007-17

INSPIRE UTI

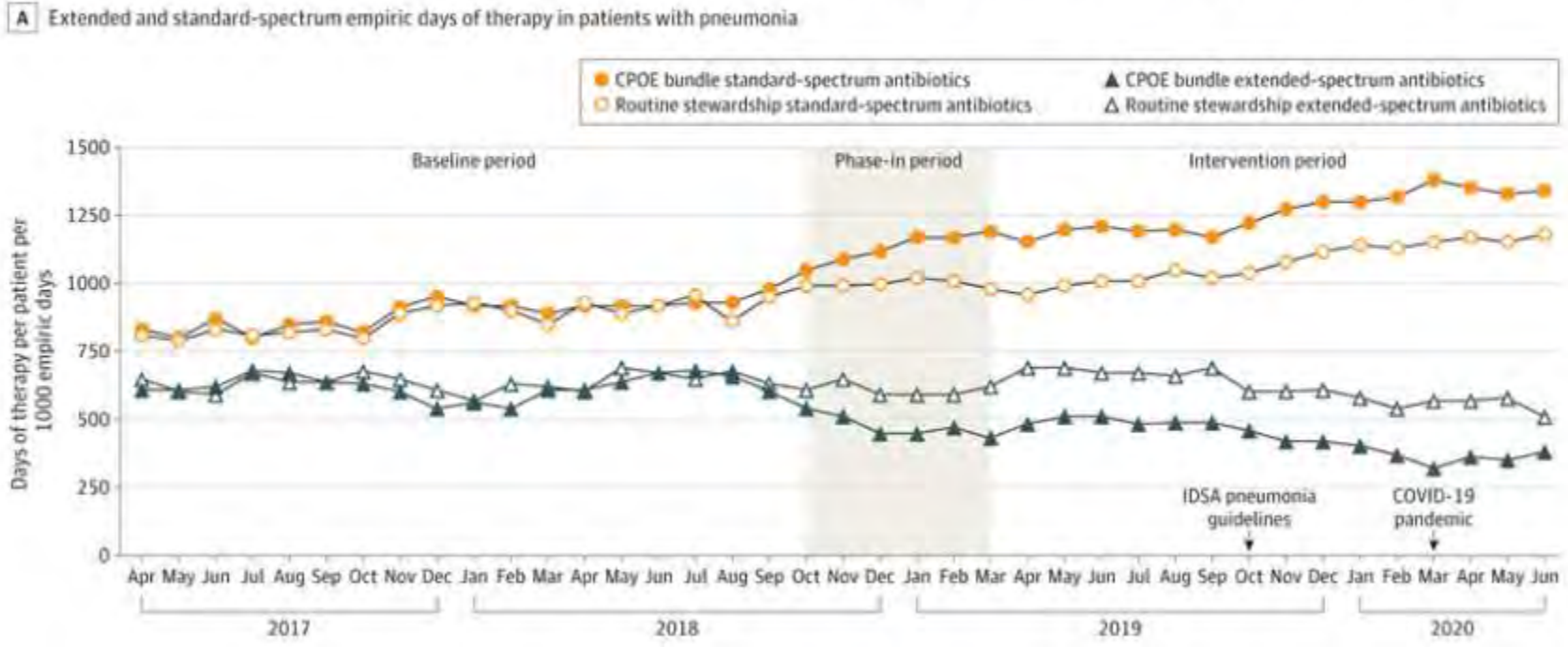
- > 94% classified as low risk in both groups
- < 6% of patients classified as low risk (< 10%) for UTI due to an MDRO eventually grew an MDRO from blood or urinary source

Supplemental eTable 8: Group Comparisons of Multidrug-Resistant Organism (MDRO) Growth Among Patients in INSPIRE Urinary Tract Infection (UTI) Trial Classified as Low Absolute Risk (<10%) for MDRO UTI

	CPOE Bundle[a] N = 27,907[b]		Routine Stewardship N = 27,505[c]	
MDRO Risk Estimate Model[d]	**Classified Low Risk N (%)**	**Classified Low Risk and Grew MDRO[e] N (%)**	**Classified Low Risk N (%)**	**Classified Low Risk and Grew MDRO[e] N (%)**
Methicillin-Resistant *Staphylococcus aureus* (MRSA)	27,551 (98.7)	260 (0.9)	27,074 (98.4)	228 (0.8)
MRSA or Vancomycin-Resistant *Enterococci* (Pathogen susceptible to daptomycin, linezolid)	27,073 (97.0)	352 (1.3)	26,759 (97.3)	342 (1.3)
Pseudomonas	26,757 (95.9)	645 (2.4)	26,462 (96.2)	622 (2.4)
ESBL and MDR-*Acinetobacter* (Pathogen susceptible to ertapenem)[f]	26,364 (94.5)	1,305 (4.9)	25,995 (94.5)	1,435 (5.5)
ESBL, MDR-*Acinetobacter*, and MDR *Pseudomonas* (Pathogen susceptible to meropenem, imipenem)[g]	26,385 (94.5)	1,354 (5.1)	26,019 (94.6)	1,489 (5.7)
Carbapenem-Resistant Enterobacterales[h]	27,907 (100)	84 (0.3)	27,505 (100)	111 (0.4)

INSPIRE Pneumonia DOTs

Figure 2. Monthly Empiric Extended- and Standard-Spectrum Antibiotic Days of Therapy in the Computerized Provider Order Entry (CPOE) Bundle vs Routine Stewardship Across the Baseline and Intervention Periods



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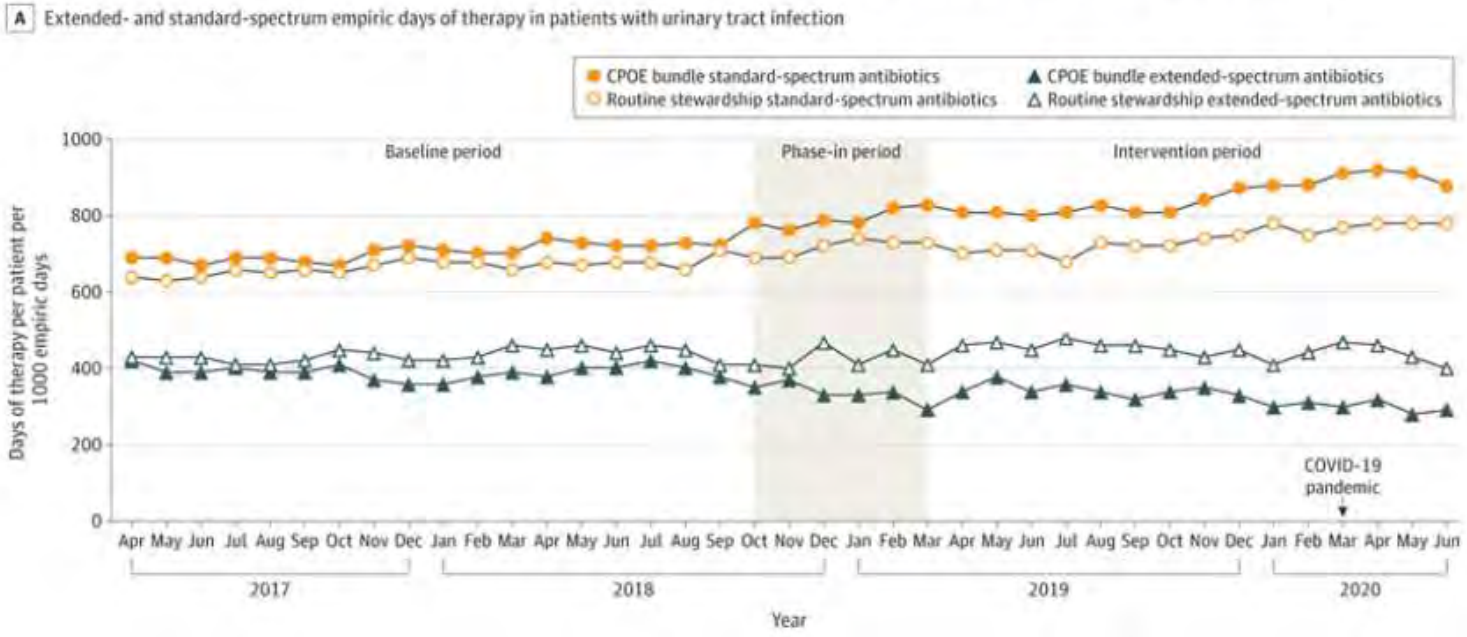
INSPIRE UTI DOTs

Figure 2. Monthly Empiric Extended- and Standard-Spectrum Antibiotic Days of Therapy in the Computerized Provider Order Entry (CPOE) Bundle vs Routine Stewardship Across the Baseline and Intervention Periods



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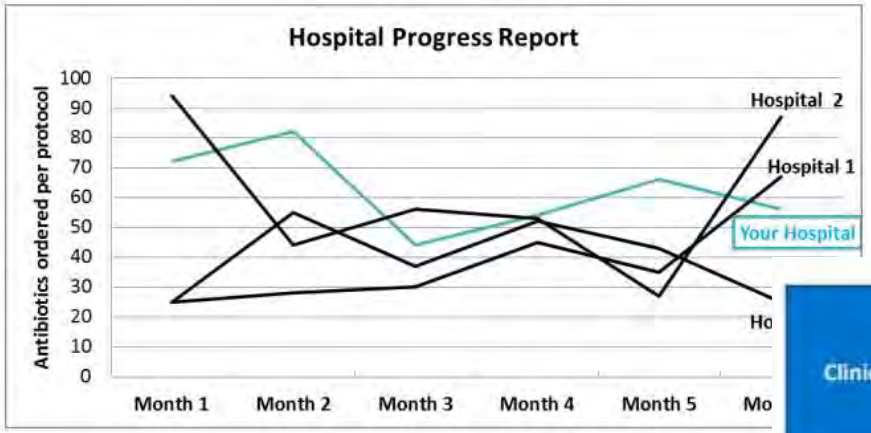
Quarterly Hospital and Clinician Progress Reports



Clinician	Total PNA Non-ICU Admissions N	Empiric Antibiotics Ordered Per Protocol N (%)	Smart Prompts Triggered N (%)	Smart Prompt Declined/ Overridden N (%)	Acceptance of Smart Prompt Recommendation N (%)
You	12	8 (67)	4 (33)	3 (75)	9 (75)
MD 1	10	5 (50)	5 (50)	2 (40)	8 (80)
MD 2	9	3 (33)	6 (67)	4 (67)	5 (56)
MD 3	7	4 (57)	3 (43)	1 (33)	6 (86)
MD 4	3	2 (67)	1 (33)	1 (100)	2 (67)
All Clinicians This Hospital	41	22 (54)	19 (46)	11 (58)	30 (73)
All Clinicians Arm 2 Trial	1189	638 (54)	551 (46)	319 (58)	870 (73)

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What makes the prompt smart?

Table 1: Extended-Spectrum Antibiotics and Pathogen Included in the CPOE Alert

Antibiotic Ordered	Pathogen Included in Risk Estimate	
	PNEUMONIA	UTI
Daptomycin	Not Recommended for PNA	MRSA, VRE
Linezolid[1]	MRSA	
Vancomycin (IV only)	MRSA	
Ceftaroline		
Aztreonam	*Pseudomonas*	
Cefepime		
Ceftazidime		
Piperacillin/Tazobactam		
Ertapenem	ESBL, GNR Resistant to cephalosporins and penicillins	
Doripenem	ESBL, GNR+*Pseudomonas* Resistant to cephalosporins and penicillins	
Imipenem		
Meropenem		
Ceftolozane/Tazobactam		
Ceftazidime/Avibactam	No Screen - Requires ID Approval[2]	
Tigecycline		
Colistin		
Polymyxin B		

1. Both oral and intravenous formulations of drugs in this category are included.
2. For anti-CRE medications, all models show <10% patient risk for having a highly drug resistant pathogen warranting the use of these drugs. Therefore, patient specific risk estimate will not be calculated and a static CPOE screen will be developed that will recommend avoiding empiric use without consultation with antibiotic stewardship team or infectious diseases.
3. Newly released ES medications require ID approval and will be considered for inclusion in the CPOE prompts on a case by case basis

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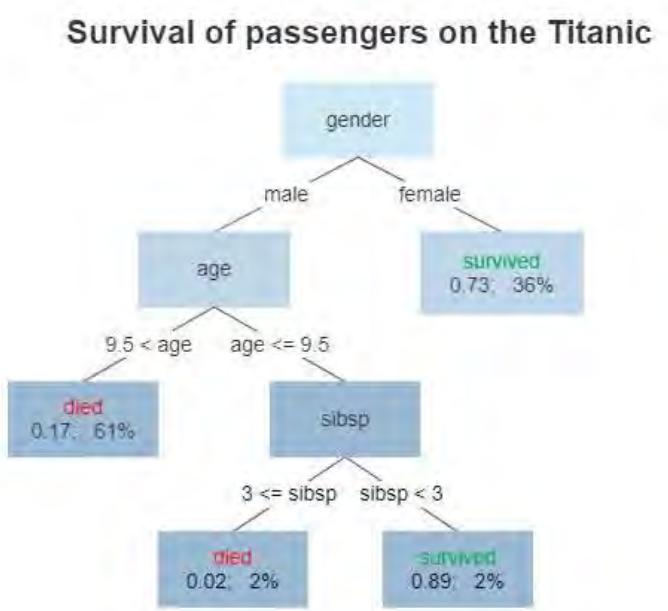
- If vancomycin ordered for pneumonia, returns risk for MRSA pneumonia
- If cefepime ordered for UTI, returns risk for Pseudomonas UTI
- If meropenem ordered for pneumonia, returns risk for pneumonia due to ESBL or resistant GNR/*Pseudomonas*

How did they determine the risk factors?

- 536,000 hospitalized patients over 3 years
- Hospital antibiogram for pneumonia and UTI patients
- Risk factors of MDRO or *Pseudomonas* infection
  - Age, gender, race, ethnicity, insurance status
  - Comorbidities, history of MDRO
  - History of prior hospitalization, ED, or nursing home visit
  - Prior antibiotics
  - Labs
- Decision tree learning to identify most common risk factors in patients with PNA or UTI with an MDRO



Odds of survival good if female or male, <9.5, and < 3 siblings

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What are those risk factors?

Pneumonia

Supplemental eTable 2: Risk Factors Predicting ≥10% Absolute Risk for Multidrug-Resistant Organism (MDRO) Pneumonia

MDRO Pneumonia Risk Estimate Model[a]	Elements Predictive of Absolute Risk ≥10%
Methicillin-Resistant *Staphylococcus aureus* (MRSA)	Patient history of MRSA Facility % MRSA of all pneumonia ≥2.5%
Pseudomonas	Patient history of Pseudomonas Facility % Pseudomonas of all pneumonia ≥2.0%
ESBL and MDR-*Acinetobacter* (Pathogen susceptible to ertapenem)[b]	No risk factors predicted ≥10% risk
ESBL, MDR-*Acinetobacter*, and MDR *Pseudomonas* (Pathogen susceptible to meropenem, imipenem, ceftolozane/tazobactam)[c]	No risk factors predicted ≥10% risk
Carbapenem-Resistant Enterobacterales[d]	No risk factors predicted ≥10% risk

[a]MDRO risk estimate models categorized according to extended-spectrum antibiotic group used to treat each MDRO pneumonia.
[b]Extended-Spectrum Beta-Lactamase Producing Enterobacterales (ESBLs) and multidrug-resistant *Acinetobacter* susceptible to ertapenem; the following risk factors were predictive of risk ≥5% but lower than <10%: Patient history of ESBL and Facility %ESBL of pneumonia ≥1.0%.
[c]ESBLs and *Acinetobacter* and *Pseudomonas* species with multidrug-resistance to antipseudomonal antibiotics but can be treated with a carbapenem or ceftolozane/tazobactam; the following risk factors were predictive of risk ≥5% but lower than <10%: Patient history of ESBL and Facility %ESBL of pneumonia ≥0.8%.
[d]Carbapenem-Resistant Enterobacterales including Carbapenem-Resistant *Acinetobacter* and *Pseudomonas* species; patients with CRE-pneumonia too few, model did not converge.

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What are those risk factors?

UTI

Supplemental eTable 2: Risk Factors Predicting ≥10% Absolute Risk for Multidrug-Resistant Organism (MDRO) Urinary Tract Infection

MDRO Urinary Tract Infection (UTI) Risk Estimate Model[a]	Elements Predictive of Absolute Risk ≥10%
Methicillin-Resistant *Staphylococcus aureus* (MRSA)	History of MRSA, Facility %MRSA of all UTI ≥2.5%, Male sex, Medicaid
MRSA or Vancomycin-Resistant *Enterococci* (Pathogen susceptible to linezolid or daptomycin)	History of MRSA/VRE/*Pseudomonas*, Facility %VRE of all UTI ≥2.5%, Male sex
Pseudomonas	History of *Pseudomonas*/ESBL, Male sex
ESBL and MDR-Acinetobacter (Pathogen susceptible to ertapenem)[b]	History of ESBL/*Pseudomonas*/CRE/VRE/MRSA, Facility %ESBL of all UTI ≥9.5%, age ≥65, Medicaid
ESBL, MDR-Acinetobacter, and MDR *Pseudomonas* (Pathogen susceptible to meropenem, imipenem, ceftolozane/tazobactam)[c]	History of ESBL/*Pseudomonas*/CRE/VRE, Facility %ESBL of all UTI ≥5.0%, Medicaid, Male sex, BUN ≥20
CRE[d]	No risk factors predicted ≥10% risk

[a]MDRO risk estimate models categorized according to extended-spectrum antibiotic group used to treat each MDRO UTI.
[b]Extended-Spectrum Beta-Lactamase Producing Enterobacterales (ESBLs) and multidrug-resistant *Acinetobacter* susceptible to ertapenem; the following risk factors were predictive of risk ≥5% but lower than <10%: Patient history of MRSA
[c]ESBLs and *Acinetobacter* and *Pseudomonas* species with multidrug-resistance to antipseudomonal antibiotics but can be treated with a carbapenem or ceftolozane/tazobactam; no additional risk factors were predictive of risk ≥5% but lower than <10%
[d]Carbapenem-Resistant Enterobacterales including Carbapenem-Resistant *Acinetobacter* and *Pseudomonas* species; patients with CRE-UTI too few, model did not converge.

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INSPIRE 3 Skin and Soft Tissue Infections (SSTI)
INSPIRE 4 Intra-Abdominal Infections (IAI)

SSTI

Primary Outcome

Smart prompts had a **27.5% reduction in empiric extended-spectrum DOTs** (95% CI, 21.2% to 33.1%); P < .001)

IAI

Primary Outcome

Smart prompts had a **35% reduction in empiric extended-spectrum DOTs** (rate ratio, 0.65; 95% CI, 0.60-0.71; *P* < .001)

Safety Outcomes	No differences in length of stay or days to ICU transfer

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Gohil SK, Septimus E, Kleinman K, et al. JAMA Intern Med 2025;doi:10.1001/jamainternmed.2025.0887
Gohil SK, Septimus E, Kleinman K, et al. JAMA Intern Med 2025;doi:10.1001/jamasurg.2025.1108

INSPIRE ASP Takeaways

- Patient-specific risk info at the point of care can be a game changer
- Showed results within 3 months
- CPOE build is sustainable during times of disruption
- Risk factors are not transferrable between facilities
- Determining risk levels is complex and requires IT programming
- EHRs need to integrate models

Next-Level Stewardship

Opt-Out Electronic Antimicrobial Stewardship

Large community health system – 4 adult hospitals, >1600 beds total

Problem:

- Prospective audit & feedback (PAF) (review current antimicrobials, contact prescriber, recommend optimizations)
  - High resource demands, inconsistency
  - Delays in communication
  - Lack of provider participation

Solution:

- Electronic antimicrobial stewardship program (E-ASP)
- Opt-out antimicrobial stewardship approach

Wilde AM, Song M, Moore SE, et al. American Journal of Health-System Pharmacy 2023;80(2):75-82

Patient List

- EHR populated with all patients with active orders for systemic antimicrobials
- Columns for broad spectrum antibiotics, duplicate coverage, restricted, complicated, bug-drug mismatch

Figure 1. Patient list display for the antimicrobial stewardship program (ASP) in the electronic medical record. BPA indicates best-practice advisory.

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Antimicrobial Stewardship Report

Summarizes current antimicrobial orders, cultures, labs, vital signs, imaging, respiratory charting

Pharmacist documentation embedded – adds checkmark in “ASP reviewed” column

Figure 2. Report displaying in the electronic medical record when a patient is selected from the patient list. BPA indicates best-practice advisory; ID, infectious diseases.

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Create custom recommendation

- After completion, the pharmacist pends the updated orders as saved work
- Saved orders are reviewable and ready to sign for the provider at order entry

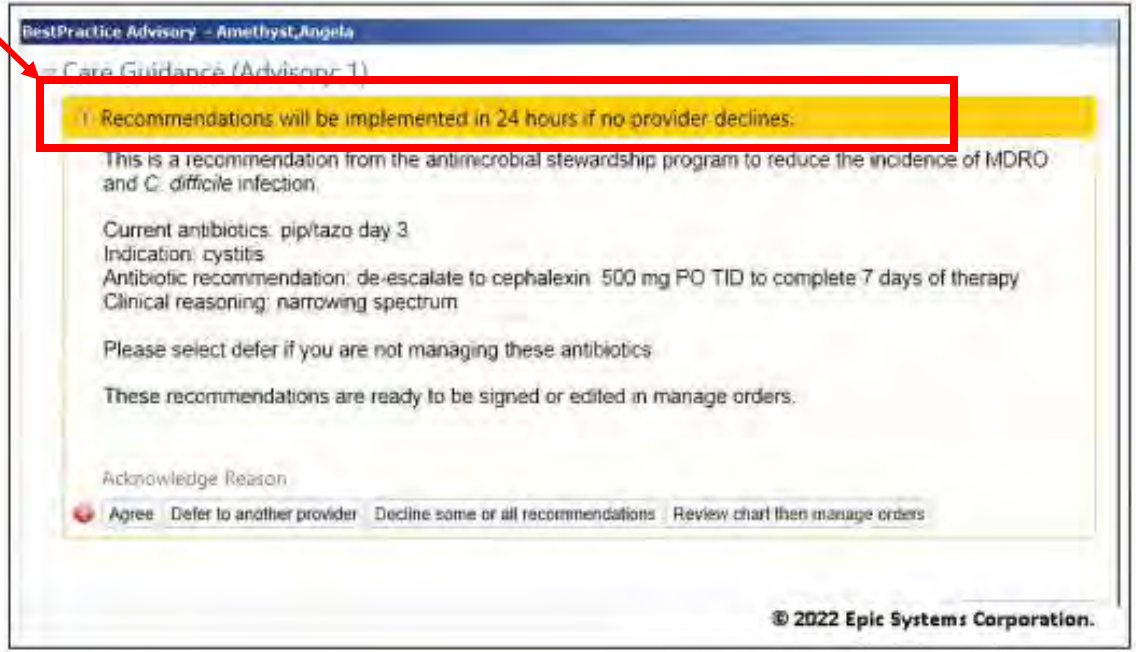
Figure 3. Flowsheet in the patient chart for documentation of customized antimicrobial recommendations.

Wilde AM, Song M, Moore SE, et al. American Journal of Health-System Pharmacy 2023;80(2):75-82

Recommendation delivered to provider in an alert

- "Implemented in 24 hours if not declined" *[not actually automatic (described later)*]
- Options
  - ❑ Agree
  - ❑ Defer to another provider
  - ❑ Decline some or all recs
  - ❑ Review chart then manage orders
- Only recs to discontinue, de-escalate, or set stop dates
- Escalations or nuanced discussions require direct contact

Figure 4. Best-practice advisory displaying in the patient's medical chart.



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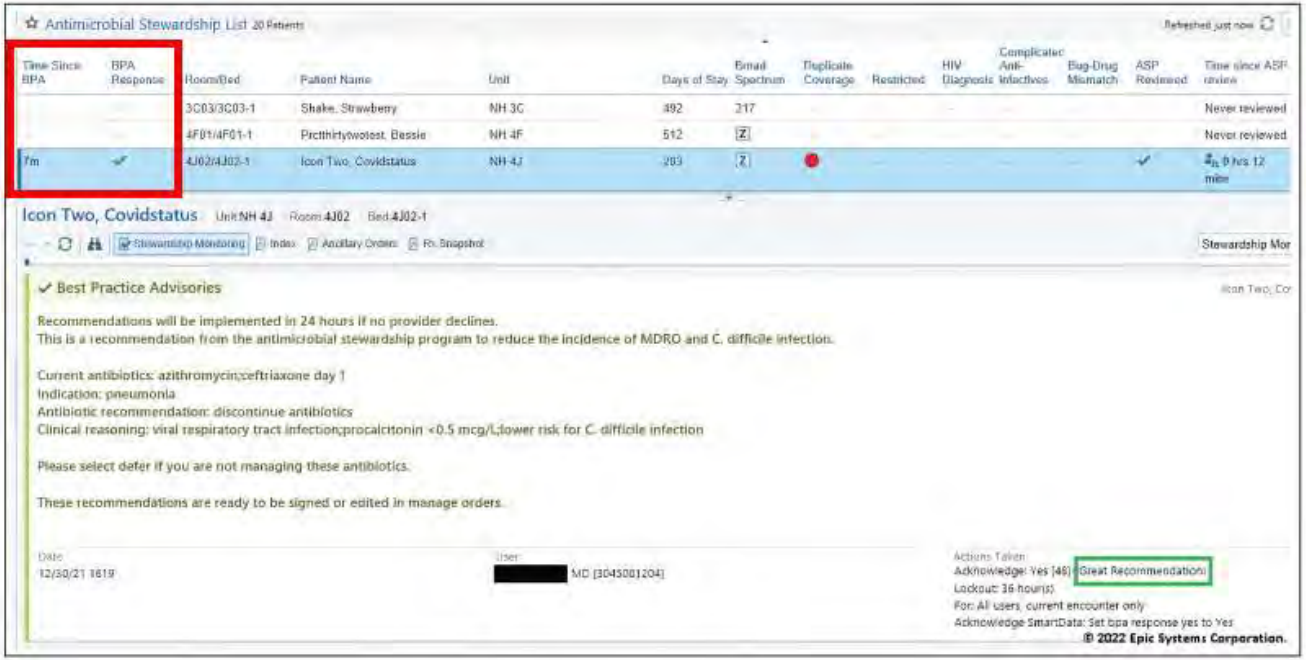
Time since alert and response are documented on patient list

- If rejected, displays a red “X”
- If no declination after 24 hrs, ID pharm reviews chart again, confirms rec still appropriate and verifies all providers have acknowledged the alert
- If any changes in clinical status or new info, the rec is removed

Figure 5. Display of provider acknowledgement reason and comments in the report below the antimicrobial stewardship program patient list.



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E-ASP Pilot

- Created comprehensive clinical guidelines for common disease states
  - Empiric recommendations
  - Discontinuation/de-escalation strategies
- Engaged stakeholders for approval of pilot
  - Medical director, Medical Executive Committee chair
- Full program approved by Medical Executive Committee
- Education – providers, pharmacists
- Pilot results
  - 432 beds over 3-month period
  - 1,170 recommendations made, with 69% acceptance rate (discontinue 631, de-escalate 524)
  - 113 (14%) implemented after not being rejected for 24 hours

Justified hiring 3 more full-time pharmacists so available onsite at each hospital

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E-ASP Impact

Type of recommendation n (% accepted)			
Discontinue	De-escalate	Set stop date	Total
1891 (49%)	2932 (60%)	38 (50%)	4860 (56%)

DOTs decreased by **25%** over 5 years

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Discussion

Strengths	Limitations

• Alert eliminates wait on return calls
• Aids with providers switching service
• Beneficial in setting without provider-led rounds
• E-ASP may be beneficial to lower-resourced hospitals in health systems
• Residency-trained ID pharmacists can focus on more complex situations (IV to PO, dose adjustments and education provided by clinical generalist pharmacists)
• Enables review in < 48 hours
• Anecdotal positive feedback from medical staff – streamlined technology and actionable alerts
• Some providers appreciate minimally intrusive nature
	• No impact on one-time orders
	• May contribute to alert fatigue
	• Alert at chart opening may not be optimal trigger point if haven't reviewed chart/seen patient yet
	• May not be feasible at other institutions
	  o Medical leadership support and ongoing provider participation
	  o EHR, IT support limitations
	• Lack of full ID pharmacist support on weekends
	• Some providers may prefer face-to-face conversations

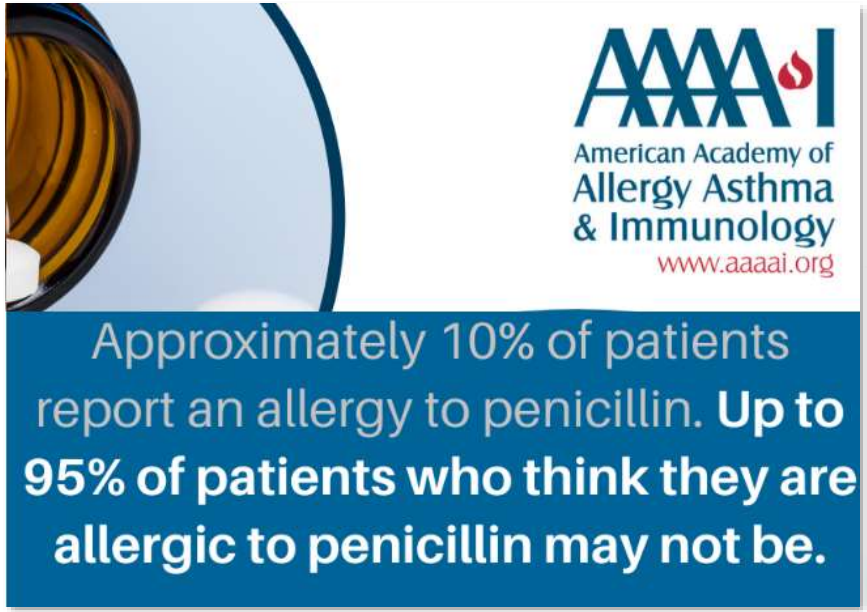
Wilde AM, Song M, Moore SE, et al. American Journal of Health-System Pharmacy 2023;80(2):75-82

E-ASP/Opt-Out Stewardship Takeaways

- E-ASP as a foundation can improve efficiency of PAF by addressing practical barriers
- Can consider broader-reaching telestewardship and electronic recommendations for other clinical pharmacy specialties
- Progressive approach, but may be difficult to replicate

Next-Level Beta-Lactam Allergy Management

Facts About Penicillin Allergy



Penicillin Allergy Label Badness

Exposed to more second-line, broad-spectrum antibiotics

Outcomes	• 14% increase in all-cause mortality • MSSA Bacteremia: 6% more treatment failures, 16% more deaths • Gram-negative bacteremia: 10% more treatment failures • >3-fold increased adverse events • Prolonged hospital stays
Hospital-Acquired Infections (HAIs) and Antibiotic Resistance	• Surgical patients: 50% increased surgical site infections • Inpatients: 23% increased *C. diff*, 14% increased MRSA, 30% increased VRE • Outpatients: 26% increased *C. diff*, 69% increased MRSA
Costs	• Increased readmissions • Increased number/duration of antibiotics and toxicities • Increased HAIs

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Blumenthal *CID* 2015; Jeffres *JACI* 2015; MacFadden *CID* 2016; Blumenthal *CID* 2017; Macy *JACI* 2013; Blumenthal *BMJ* 2018;Blumenthal J Gen Intern Med 2019

Delabeling PCN Allergies

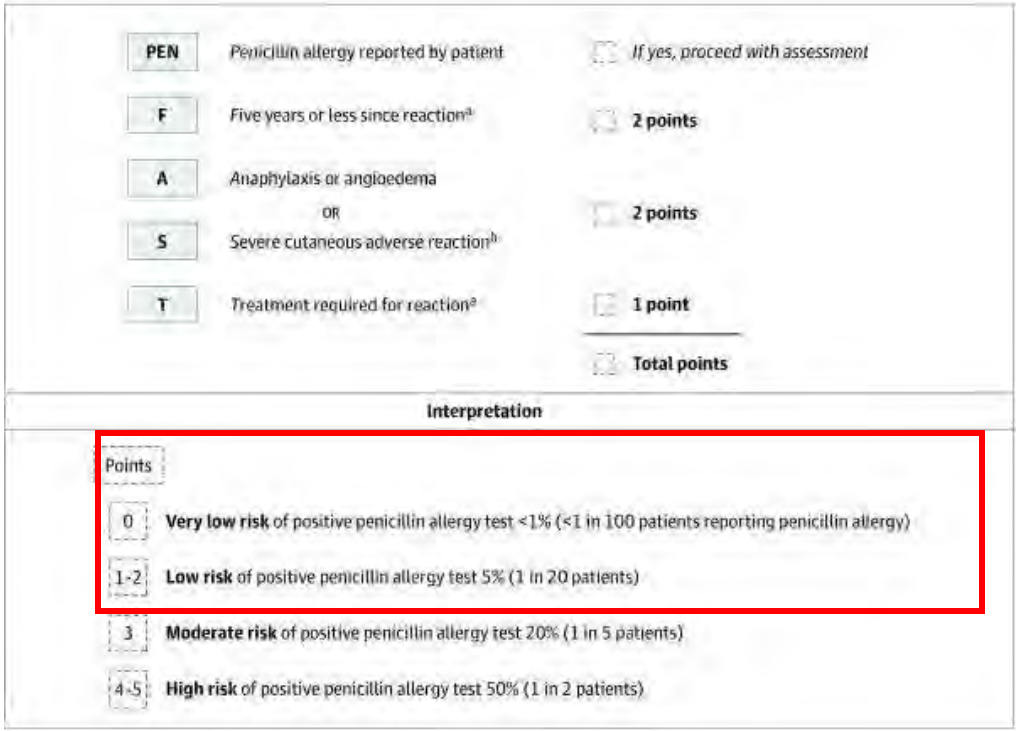
History	Family history of penicillin allergy or side effect (e.g., headache or nausea)
Direct oral challenge*	low-risk patients (PEN-FAST clinical decision rule)
Skin testing*	reserved for higher risk (e.g., history of anaphylaxis, recent IgE-mediated reaction, pregnant, etc)

*Contraindicated with history of severe cutaneous adverse reactions to beta-lactams (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, or drug reaction with eosinophilia and systemic symptoms, or drug-induced organ damage, concurrent treatment with etc)

www.aaaai.org 2023

Khan DA et al. JJ Allergy Clin Immunol 2022; 16;S0091-6749(22)01186-1

PEN-FAST – a penicillin allergy clinical decision rule to determine risk



PEN	Penicillin allergy reported by patient	☐ If yes, proceed with assessment
F	Five years or less since reaction[a]	☐ 2 points
A	Anaphylaxis or angioedema	☐ 2 points
OR		
S	Severe cutaneous adverse reaction[b]	
T	Treatment required for reaction[c]	☐ 1 point
		☐ Total points

Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

Demonstrated that patients with low risk(< 3) can safely receive direct oral penicillin challenge

Can be safely used without allergist expertise

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Trubiano JA, Vogrin S, Chua KY, et al; JAMA Intern Med 2020;180(5):745-752
Copaescu AM, Vogrin S, James F, et al; JAMA Intern Med 2023;183(9):944-952

“Penicillin Allergy Evaluation Should Be Performed Proactively in Patients with a Penicillin Allergy Label”

“Efforts to delabel can and should be performed by all clinicians, especially for patients with low-risk histories”

Position Statement

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PEN-FAST Nursing Validation

Goal: evaluate performance of RN assessments of PEN-FAST compared to ASP pharmacists

Population	4 hospitals in large health system in Houston, TX, 338 patients included
Intervention	• Implemented modified* PEN-FAST rule questions into the EHR for RNs to perform. • Patients randomly selected prospectively • RN scores hidden and compared to ASP pharm scores to evaluate for consistency

*modified to reduce chance of reported reactions being miscategorized as low risk

Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

Modified PEN-FAST

- Increased score for anaphylaxis or angioedema to 3 points (from 2 points)
- Assigned 1 point for “unknown” responses to the questions:
  - “Did the reaction happen in the past 5 years?”
  - “Was the reaction characterized as anaphylaxis or angioedema?”
- Assigned 4 points for severe non-IgE mediated reactions (Stevens Johnson, etc)
  - To ensure these patients would not be challenged

Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

Workflow

- Alert to RN upon admission if penicillin allergy documented
- PEN-FAST documented in admission workflow
- Total score auto-calculated and saved in allergies section of EHR

Assessment

- Report for admitted patients w/ documented allergy and PEN-FAST score
- Patient's PEN-FAST scores were concealed
- Assessors interviewed patient and scored PEN-FAST
- Asked if ever tolerated amoxicillin or amoxicillin/clavulanate

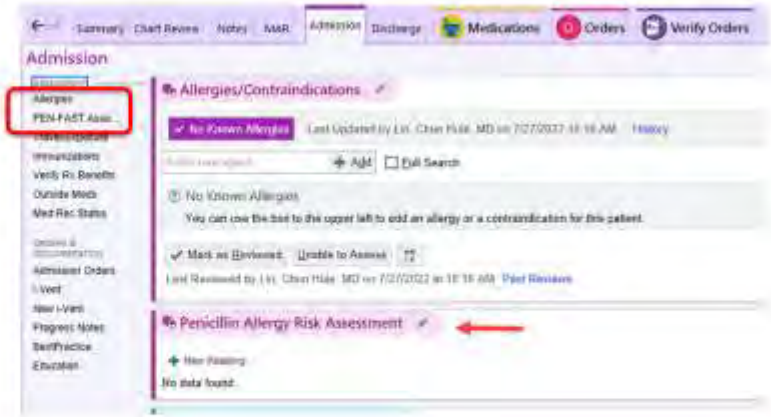
Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

PEN-FAST Nursing Validation

How to Get to PenFAST Assessment – Admission Navigator Route

HOUSTON Methodist LEADING MEDICINE

Next in line after allergies in the admission navigator



Complete the Penicillin Allergy Risk assessment by clicking on the pencil icon or + new reading link

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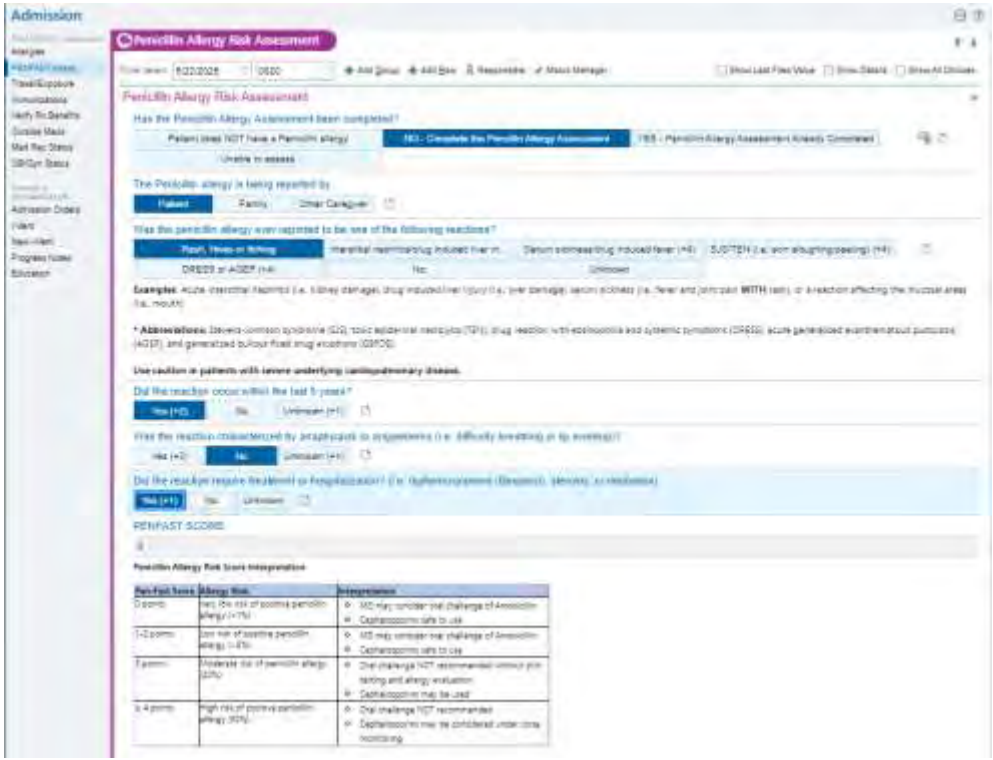
Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

PEN-FAST Nursing Validation



Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

PEN-FAST Nursing Validation

Results	• Agreement of high-risk and low-risk between RNs and ASP Pharmacists was **84.3%** • **116/344 (34.4%)** of patients reported tolerating amoxicillin and/or amoxicillin/clavulanate after their initial reaction to penicillin. **69 (59%)** of these patients had reported anaphylaxis • **72 (7.8%)** high risk falsely classified as low risk • **26 (7.6%)** low risk falsely classified as high risk

Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

Discussion

Strengths	Limitations
• Nurses are well-equipped to perform standardized penicillin allergy assessment • Usually part of routine hospital admission workflow • Standardized questions such as PEN-FAST can provider more accurate assessment compared to open-ended patient reporting • Can identify candidates for delabeling or antibiotic challenges • Critical info available at point of prescribing • Scalable	• Additional time to complete may be burdensome • Small but notable discrepancies • Workload/other urgent responsibilities may contribute to errors • Does not eliminate need for clinician reassessment before antibiotic challenges

Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

PEN-FAST Nursing Validation Takeaways

- Effective approach for categorizing patient allergy risk
- Strong concordance with ID pharmacists specialized in penicillin allergy management
- Feasibility may vary among hospitals
- Ongoing education needed
- Future research could explore antibiotic prescribing patterns

Hoffmann WJ, Patel S, Lee EJ, et al; (Accepted manuscript) Antimicrobial Stewardship & Healthcare Epidemiology 2025

CEPH-FAST – a cephalosporin allergy clinical decision rule to determine risk

Rationale

- Validated clinical decision rules have been identified for penicillin allergy for low-risk patients
- Generalizability to low-risk cephalosporin allergy remains uncertain

Goal

- Validate a clinical decision rule for cephalosporin allergies

Trubiano JA, Mitri E, Cox F, et al; J Allergy Clin Immunol 2025;155(2) Supplement, AB 429

CEPH-FAST Validation


JACI The Journal of Allergy and Clinical Immunology

ABSTRACT ONLY

Development and Validation of a Cephalosporin Allergy Clinical Decision Rule – CEPH-FAST

Population	3 hospitals in Australia, 228 patients with self-reported cephalosporin allergy
Intervention	Either skin testing or oral challenge. CEPH-FAST score was calculated and compared
Results	• The 4 clinical features associated with a positive penicillin allergy from PEN-FAST showed similar associations with a positive cephalosporin test • CEPH-FAST score < 3, 5.7% had positive results of allergy testing, negative predictive value 93% (95% CI, 88.0, 97.9), sensitivity 93.4%, (86.2, 97.5) and specificity 72.3% (64.0, 79.6). • External validation in North American cohort (n=167) resulted in similar findings.

Trubiano JA, Mitri E, Cox F, et al; J Allergy Clin Immunol 2025;155(2) Supplement, AB 429

CEPH-FAST Takeaways

- Abstract is the only available data so far
- Promising expansion of PEN-FAST to assess risk for direct oral challenge or utilization of cross-reactive cephalosporins

Another Thing

(trigger warning, I’m sorry)

Is it time to re-evaluate remdesivir use?

- Limited data to support routine remdesivir use in the modern era
- Widespread SARS-CoV-2 seropositivity now
- RCTs evaluating remdesivir are from 2020-2021
  - Limited or no prior SARS-CoV-2 infection or vaccination.
- Societal guidelines: “< 7 days of symptom onset, oxygen requirement”
  - Conditional recs w/very low-moderate certainty of evidence
  - Last updated early 2022
- Most hospitals have not implemented restrictions beyond those set in early COVID-19 era

Bhimraj A, Falck-Ytter Y, Kim AY, et al. Clinical Infectious Diseases 2022;78(7);e250-e349

Practical Remdesivir Restriction

Hypothesis: possible benefit seen during periods with minimal seropositivity may not be true in highly vaccinated populations

Clinical Infectious Diseases

MAJOR ARTICLE

Into the Unknown: Practical Remdesivir Restriction in the Era of Widespread SARS-cov-2 Seropositivity

Alyssa Christensen, PharmD, BCIDP[1]; Zachary Nelson, PharmD, MPH, BCIDP[1]; Sally Gustafson, MS[2]; Rachel Stoecker, PharmD[1]; Brent Foster, PharmD, BCIDP[1]; Nicole Trower[1]; Laura Grangaard Johnson, MPH[2]; Elizabeth B. Hirsch, PharmD[3]; Stefan Colliau-Adler, MD, MPH[2]; Maxx Enzmann, PharmD, BCPS, BCIDP[4]; Ethan Ryberg, PharmD, BCPS[1]; Sarah Rebecca Peglow, MD[1]

[1]HealthPartners and Park Nicollet Health Services, Minneapolis, MN; [2]HealthPartners Research Institute, Minneapolis, MN; [3]University of North Carolina Health, Chapel Hill, NC; [4]University of Minnesota, College of Pharmacy, Minneapolis, MN

Study Design	8-hospital health system, pre-post quasi-experimental design 12 months pre-intervention (June 2022-May 2023) to 12 months post-intervention (July 2023-June 2024)
Population	Adult immunocompetent patients 4,774 patients (3,323 pre-/1,451 post-)
Intervention	Restricted remdesivir to adult patients meeting all: 1) symptomatic, 2) requiring supplemental oxygen and 3) immunocompromised OR ID consult

Christensen A, Nelson Z, Gustafson S, et al. Clinical Infectious Diseases 2025;ciaf217

Remdesivir Restriction Results

Pre-intervention	Post-intervention
37.7% patients received remdesivir	**4.1%** of patients received remdesivir

# of patients decreased by **33%**
$1.5 million in drug costs saved

Primary outcome	Adjusted outcomes using medium-risk covariate values: No difference in 14-day all-cause mortality (OR, 1.8; 95% CI 0.54 to 5.8, p=0.34)
Secondary outcomes	No difference in 28-day all-cause mortality, 30-day readmission, or length of stay between the two groups. For ICU admission and ventilator days, remdesivir was associated with lower risk in the pre-intervention group, and higher in the post-intervention group. Similar outcomes observed when high-risk covariates were modeled.
Limitations	Symptoms were not assessed and may have led to an imbalance between groups. Potentially underpowered to detect differences in mortality.

Christensen A, Nelson Z, Gustafson S, et al. Clinical Infectious Diseases 2025;ciaf217

Top 25 Drugs by Expenditures in Nonfederal Hospitals in 2024

Table 5. Top 25 Drugs by Expenditures in Nonfederal Hospitals in 2024

Drug*	2024 expenditures ($ thousands)	Percent change from 2023
Pembrolizumab	1,468,475	12.5
Immune globulin	1,040,191	6.4
Sugammadex	756,282	18.9
Daratumumab/hyaluronidase	707,513	23.9
Bictegravir/emtricitabine/tenofovir alafenamide	701,668	10.0
Remdesivir	642,653	–12.0
Nivolumab	555,420	3.3
Inactivated influenza virus vaccine	529,663	–4.5
Antithymocyte immunoglobulin	522,425	8.6
Pneumococcal conjugate vaccine	509,005	–14.3
Sodium intravenous solutions	507,739	6.6
Denosumab	455,068	8.3
Rituximab	452,083	–4.8
Alteplase	440,820	–7.2

#6??!!

Tichy EM, Rim MH, Cuellar S, et al. American Journal of Health-System Pharmacy, 2925;,zxaf092
The official Giphy page for the Office on Peacock. Retrieved from giphy.com/theoffice

Remdesivir Redo Takeaways

- Reasonable to re-evaluate criteria for use in modern era of widespread seropositivity
- May hesitate veering from guideline recommendations
- More studies needed – guidelines updated
- Fiscal stewardship is important to support other efforts
- Will likely see more institutions following suit

Overview – Hot Topics in Antimicrobial Stewardship

Precision Medicine	Inspire – ASP Pneumonia, UTI, IAI, and SSTI
Next-Level Stewardship	Opt-out electronic antimicrobial stewardship
Next-Level Beta-Lactam Allergy Management	PEN-FAST, CEPH-FAST, nurse documentation
Another Thing	Remdesivir recalibration

Thank you

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Asymptomatic Bacteriuria (ASB) Guideline Adherence

UTI Misdiagnosis Badness

- Antibiotics are not recommended in ASB (except pregnancy or urologic procedure)
- 1 in 3 patients with ASB are misdiagnosed with UTI
- 20% of hospitalized patients experience adverse events due to inappropriate treatment of ASB
- 1-3% of hospitalized patients developed *Clostridioides difficile* infection due to antibiotics

"Asymptomatic bacteriuria, the bane of my existence"

– every ASP pharmacist ever, probably

Michigan Hospital Safety Consortium (HMS) ASB Initiative

- National Quality Forum (NQF) endorsed metric “Inappropriate Diagnosis of UTI in Hospitalized Medical Patients”
- Percentage of hospitalized patients treated for UTI that don’t have a UTI (they have ASB)

Inappropriate Diagnosis of Urinary Tract infection (UTI) in Hospitalized Medical Patients

- National guidelines recommend against treating ASB in most hospitalized patients
- Up to 80% are treated with antibiotics

Study Design	3-year, prospective quality improvement study among 46 hospitals in the Michigan Hospital Medicine Safety Consortium
Population	• Hospitalized general care medicine patients with a positive urine culture (excluding *S. aureus* and *Candida* spp.) WITHOUT specific signs and symptoms of a UTI • Also excluded pregnancy, altered anatomy or urologic surgery (incl. stents, tubes) • Collected data to evaluate metric
Intervention	Triannual meetings and online toolkit, disseminated diagnostic and antibiotic stewardship strategies Data sharing, benchmarking, and pay-for-performance incentives through HMS

Vaughn VM, Gupta A, Petty LA, et al. JAMA Intern Med 2023;183(9):933-941

ASB Goal Metrics and Results

Diagnostic stewardship $\frac{\text{ASB all}}{\text{Positive urine cultures}}$	Decrease % of patients with positive culture who had ASB (Avoid cultures in asymptomatic patients) Declined from **34.1%** to **22.5%**
Antibiotic stewardship $\frac{\text{ASB treated}}{\text{ASB all}}$	Decrease % of patients treated for ASB Declined from **29.1%** to **17.1%**

Vaughn VM, Gupta A, Petty LA, et al. JAMA Intern Med 2023;183(9):933-941

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