

INSPIRE Abdominal Infection Trial

I**N**telligent S**t**ewardship P**r**ompts to I**m**prove R**e**al-time E**m**piric
A**n**tibiotic S**e**lection for P**a**tients

ID Week

October 18, 2024



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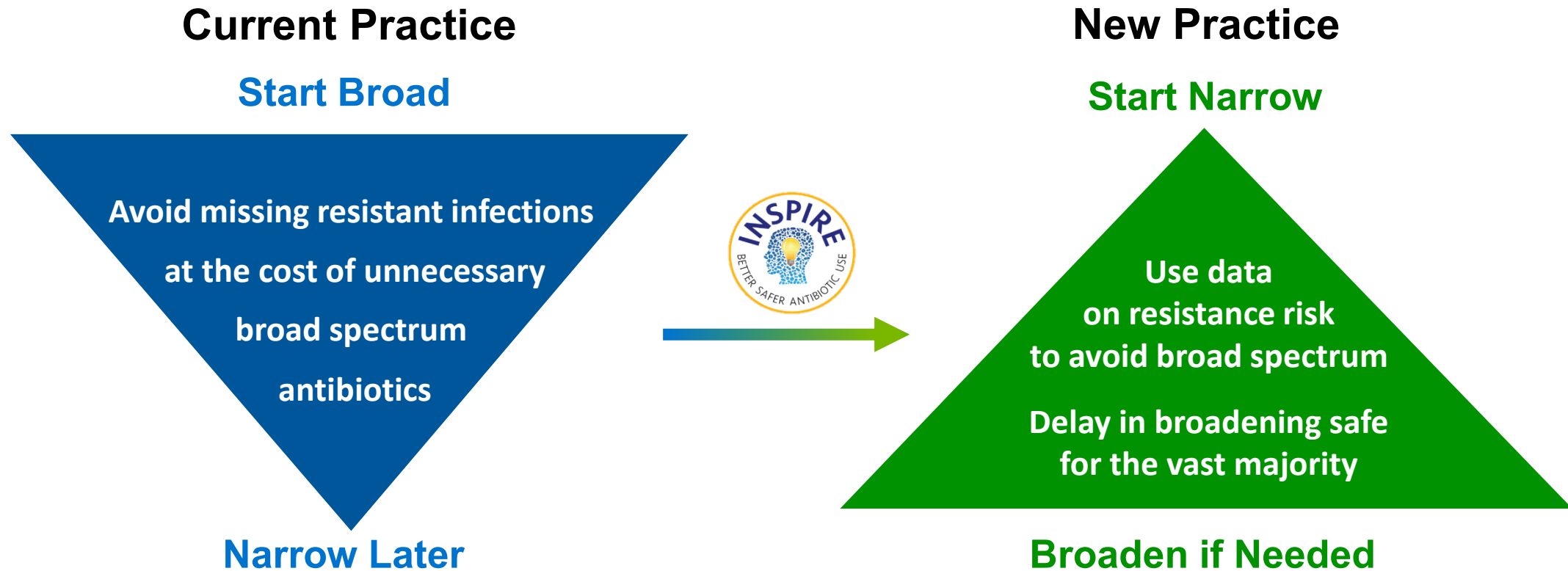
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Can We Change the Culture of Empiric Antibiotic Selection in Non-Critically Patients?

- More than 2.8 million antibiotic-resistant infections annually in US alone
- Overprescribing is a major contributor: 40% of inpatient antibiotics too broad



Infections & Bacteria That Account for Antibiotic Use

- **Most commonly treated infections in US hospitals**
 - Pneumonia¹
 - Urinary tract infection (UTI)²
 - **Abdominal infections**
 - Skin/soft tissue infections³
- **Multidrug-resistant organisms physicians worry most about**
 - Methicillin resistant *Staphylococcus aureus* (MRSA)
 - *Pseudomonas* species
 - Extended-Spectrum Beta-Lactamase producing *Enterobacterales* (ESBL)
 - Vancomycin Resistant *Enterococci* (VRE)
 - Carbapenem Resistant *Enterobacterales* (CRE)

¹Gohil SK, Stewardship Prompts to Improve Antibiotic Selection for Pneumonia: The INSPIRE Randomized Clinical Trial. JAMA. April 19, 2024. doi:10.1001/jama.2024.6248

²Gohil SK, Stewardship Prompts to Improve Antibiotic Selection for Urinary Tract Infection: The INSPIRE Randomized Clinical Trial. JAMA. April 19, 2024. doi:10.1001/jama.2024.6259

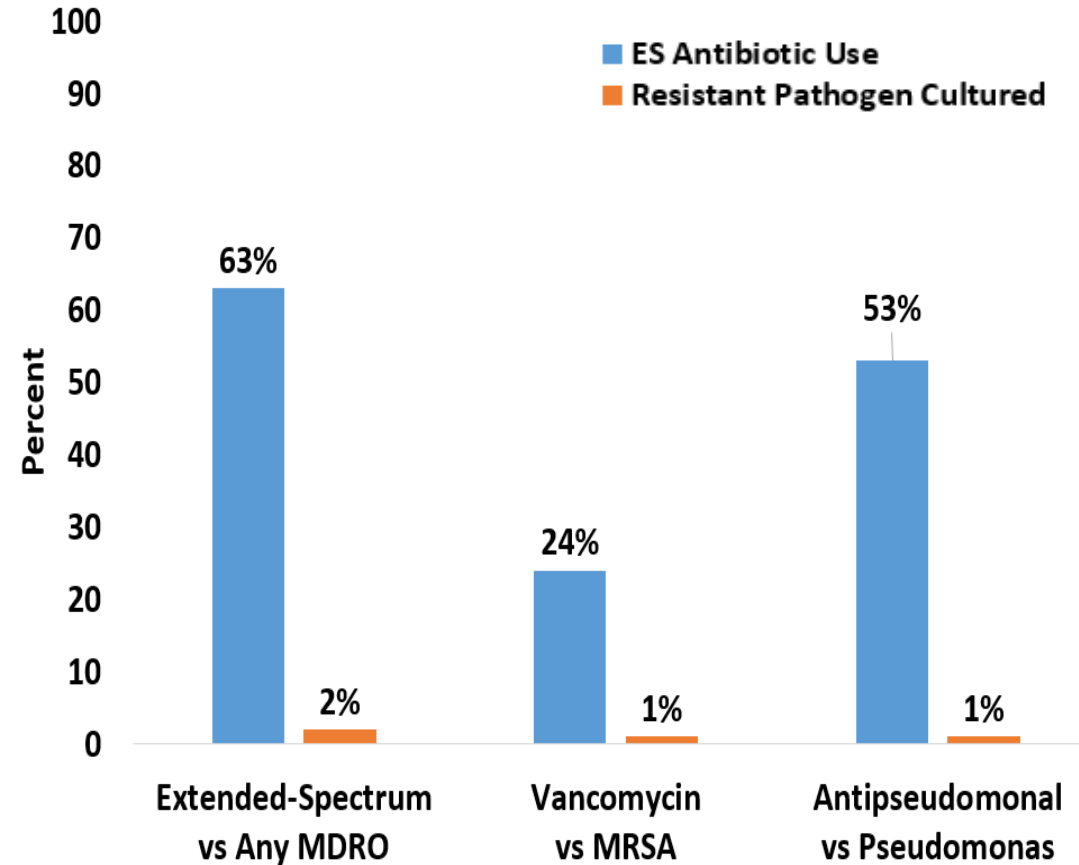
³Gohil SK, ID Week 2024 Oral Abstract #179



Empiric Antibiotic Selection in Abdominal Infections?

Extended-spectrum use far exceeds resistance

Abdominal Infections <2% with Resistant Bacteria



Among 200,000 HCA Healthcare patients admitted with abdominal infection, 2017-2019

*Abbreviations: MDRO=multidrug-resistant organism; MRSA=methicillin-resistant *Staphylococcus aureus*





INSPIRE Abdominal Infection Cluster Randomized Trial

INSPIRE Abdominal Trial – Design

92-hospital, cluster-randomized trial

Arm 1: Routine Care – 46 Hospitals

- Standard-of-care antibiotic stewardship

Arm 2: INSPIRE Computerized Physician Order Entry (CPOE) Bundle

Intervention – 46 Hospitals

- Physician “CPOE smart prompts” for patient-specific resistant organism risk
- Recommends appropriate antibiotic choice
- Provider encouragement and feedback reports (by local study champions)

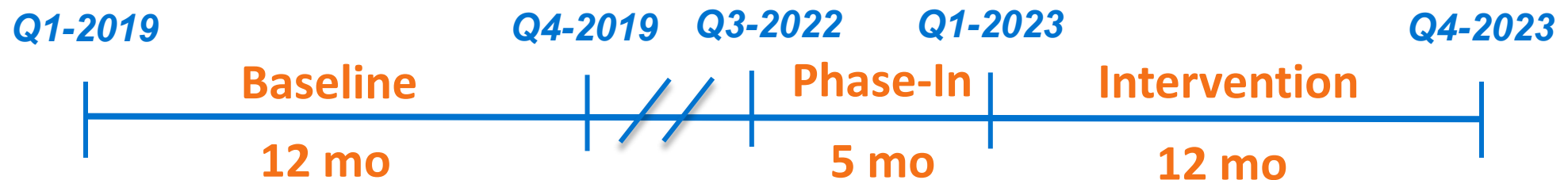


INSPIRE Study Population and Timeline

Setting

- HCA Healthcare (largest private hospital system in the nation) – 200+
- Pragmatic – community hospitals
- Adults admitted for **Abdominal Infections**
- Excludes patients admitted to ICUs
- Focuses on first 3 days of admission

Trial Timeline



CPOE Prompt Activated Via Indication Screens

- INSPIRE prompts activated when physicians select extended-spectrum antibiotics to treat abdominal infections
- Programmed to fire only in non-ICU locations
- Provides **absolute risk** of infection due to a multidrug-resistant organism:
 - ✓ Patient-specific
 - ✓ Infection syndrome-specific
 - ✓ Pathogen-specific
 - ✓ Hospital-specific



What Antibiotics Are Considered “Extended-Spectrum”?

Category	Extended–Spectrum Antibiotics Included in CPOE Alerts
Anti-MRSA	Ceftaroline, Daptomycin, Linezolid ¹ , Vancomycin ²
Anti-Vancomycin Resistant <i>Enterococcus</i>	Daptomycin, Linezolid ¹
Anti-<i>Pseudomonas</i>	Aztreonam, Cefepime, Ceftazidime, Piperacillin/Tazobactam
Anti-Extended Spectrum Beta Lactamase-producing <i>Enterobacterales</i>	Ertapenem, Imipenem, Meropenem, Ceftolozane/Tazobactam

¹Both oral and intravenous (IV) formulations; ²IV formulation only

Note: Fluoroquinolones not included as extended-spectrum.



INSPIRE Prompt Approach

- Risk estimate and guidance *tailored to drug and pathogen*.
 - If vancomycin ordered → returns MRSA risk and recommends alternative
 - If cefepime ordered → returns *Pseudomonas* risk
 - If meropenem ordered → returns ESBL or *Pseudomonas* risk
- Real-time, patient-specific.
 - MD orders cefepime for abdominal infection indication
 - Prompt pulls patient characteristics from EHR to generate risk estimate
 - Prompt recommends ceftriaxone if *Pseudomonas* abdominal infection **risk is < 10%**

INSPIRE Abdominal Infection **Absolute Risk Models**

- Based on 225,000 patients with abdominal infection (2017-2019)
- Used recursive partitioning to identify algorithm for MDRO infection
- Evaluated >60 variables: demographics, comorbidities, prior antibiotics, nursing home, hospitalization, admission labs, prior MDRO

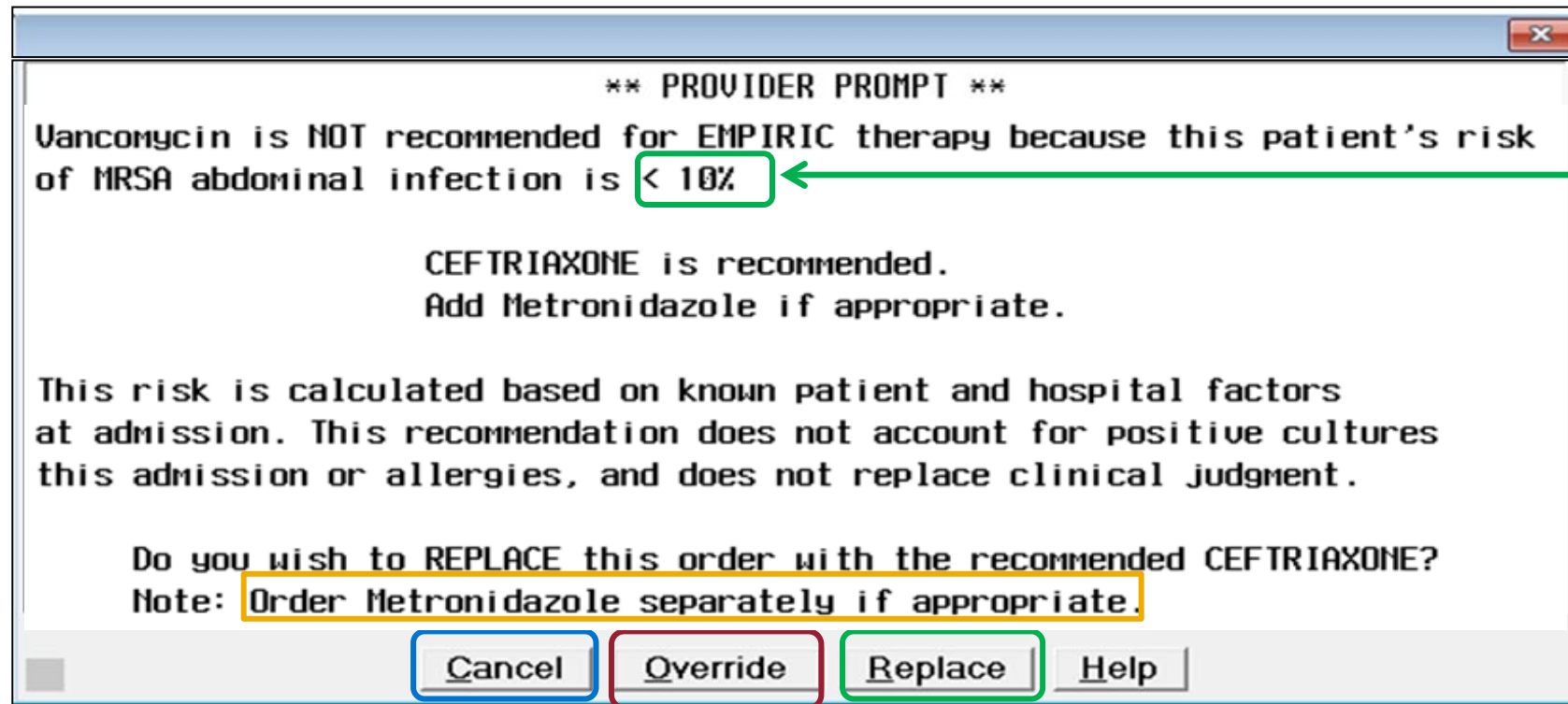
Target Pathogen	Elements Predictive of Absolute Risk $\geq 10\%$
MRSA	History of MRSA, history of abdominal surgery
<i>Pseudomonas</i>	History of <i>Pseudomonas</i> , history of abdominal surgery
ESBL	History of ESBL, Facility %ESBL among abdominal infection admissions
CRE	No risk factors predicted $\geq 10\%$ risk

MRSA - Methicillin Resistant *Staphylococcus aureus*; ESBL – Extended-Spectrum Beta-Lactamase producing *Enterobacterales*; CRE – Carbapenem Resistant *Enterobacterales*.



INSPIRE Prompt Provides Patient-Specific Risk Estimates

- Physician orders vancomycin for **abdominal infection** and risk of MRSA abdominal infection calculated to be low (<10%)



Patient & syndrome-specific risk estimate

Returns to order screen

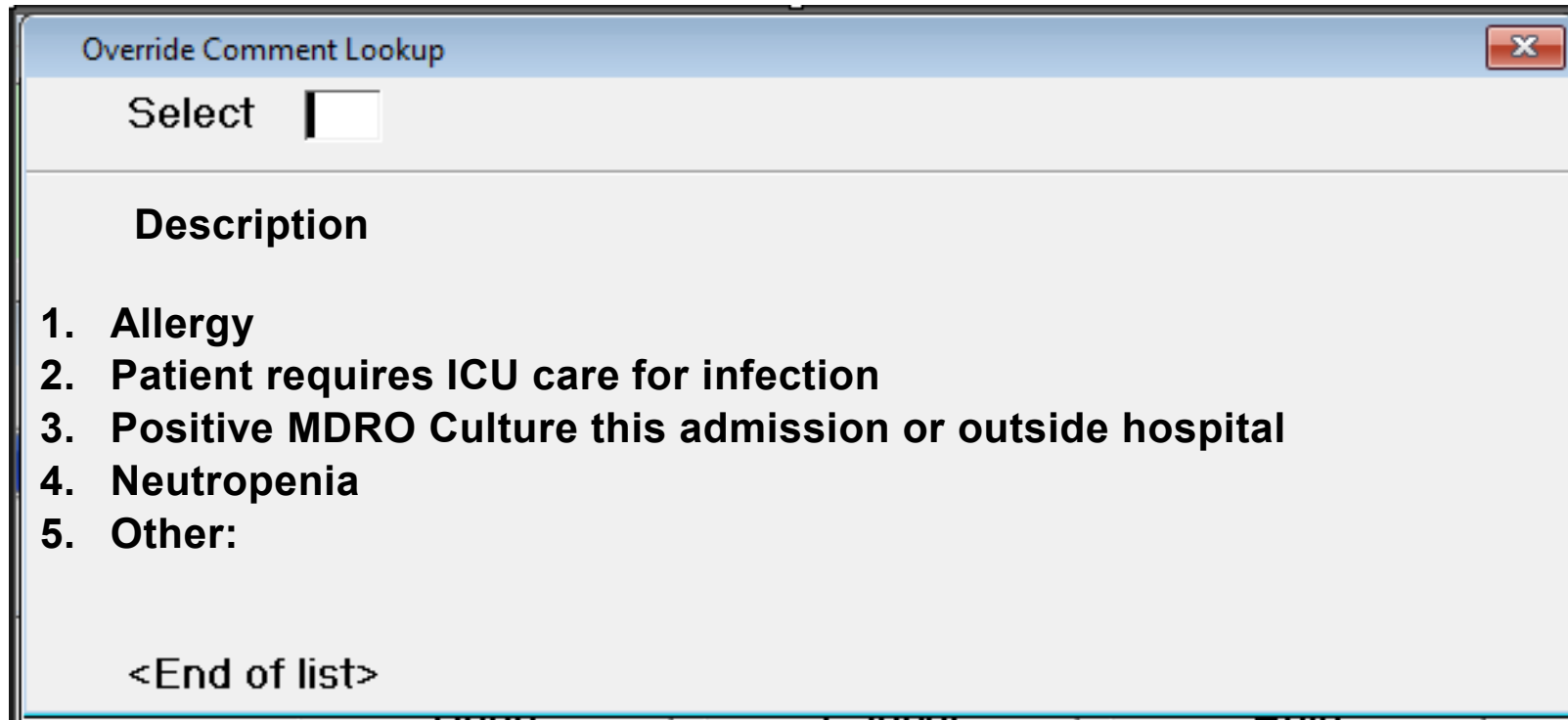
Next screen asks reason to keep vancomycin

Taken to ceftriaxone order screen



Override Screen and Options

- Alert supports, but does not replace clinical judgment
- Clinicians choosing to override must give a reason:



Override Comment Lookup

Select

Description

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

<End of list>

INSPIRE Abdominal Infection Trial Outcomes

Primary Outcome

- Extended-spectrum antibiotic days of therapy during first 3 days of admission

Secondary Outcomes

- Vancomycin days of therapy during first 3 days of admission
- Antipseudomonal days of therapy during first 3 days of admission

Safety Outcomes

- Days to ICU transfer
- Length-of-stay

Statistical Analysis

- Main results are as-randomized, unadjusted, admission level
- **Primary/secondary outcomes:** generalized linear mixed effects model (GLIMMIX)
 - Multivariable regression model
 - Compares intervention to baseline rates between arms, accounting for clustering within hospital and period
- **Safety Outcomes:** Proportional hazards models
 - With shared frailties to account for clustering within hospital and period (baseline vs intervention)
- Adjusted analyses



INSPIRE Abdominal Infection Trial

Results

INSPIRE Trial Participants

- 92 hospitals in 15 states
- Non-ICU intervention period patients admitted with **Abdominal Infection: 105,044**

Arm 1: Routine Care

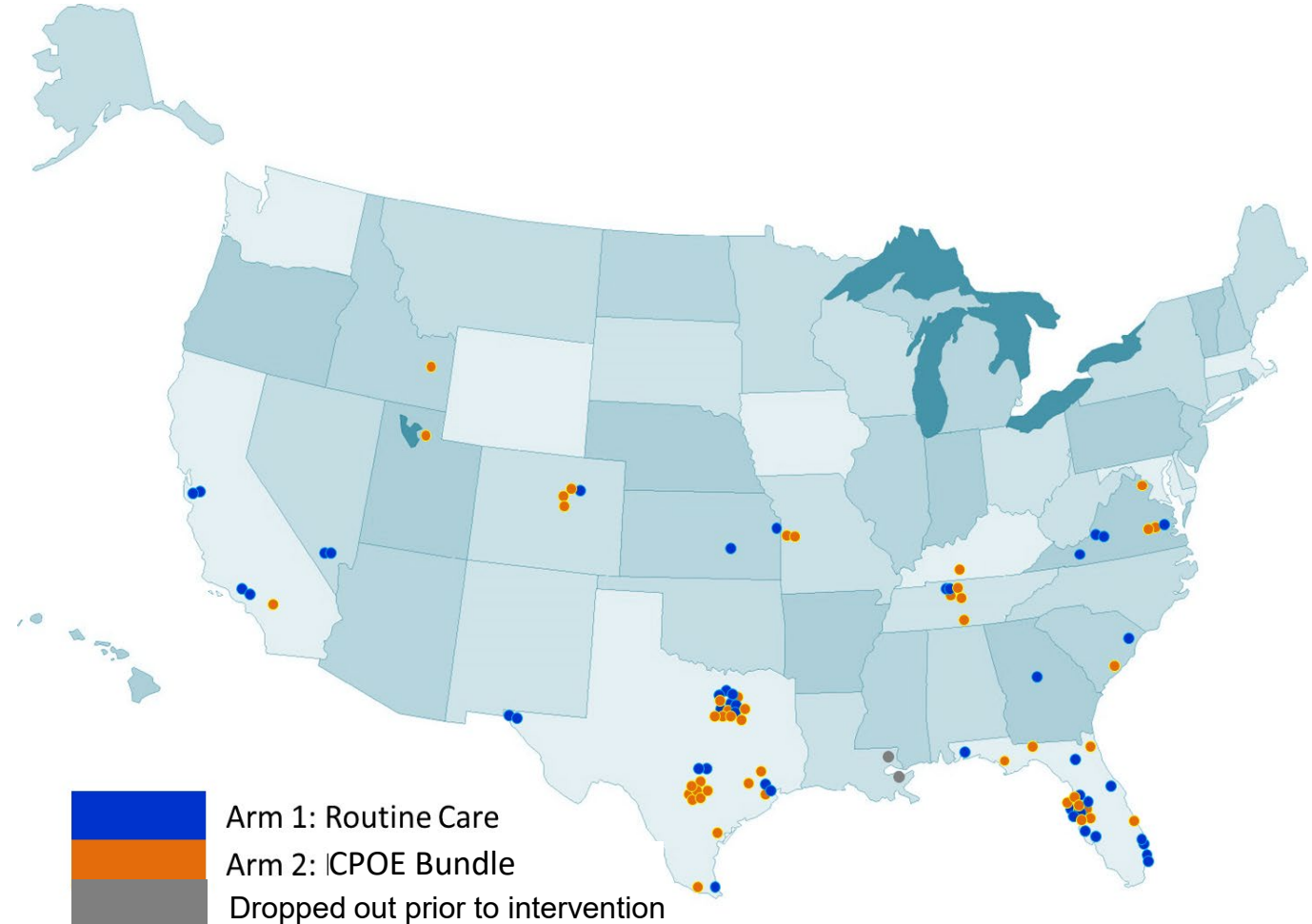
46 Hospitals

Abdominal Infection Trial: N = 54,384

Arm 2: CPOE Bundle

44 Hospitals

Abdominal Infection Trial: N = 50,620



Participant Characteristics (Intervention Period)

Characteristics	Abdominal Infection	
	Routine (N=54,136)	CPOE Bundle (N=50,701)
Mean Age	61	59
Female	59%	59%
Non-White	27%	30%
Hispanic	24%	25%
Medicaid Insured	24%	24%
Hospitalization - Past Year	30%	30%
Antibiotic use - Past Year	24%	24%
Nursing Home Visit - Past Year	7%	7%
Length of Stay (mean days)	6.2	6.1
Comorbidity Score ¹	3	3



INSPIRE Participants - MDRO History (Intervention Period)

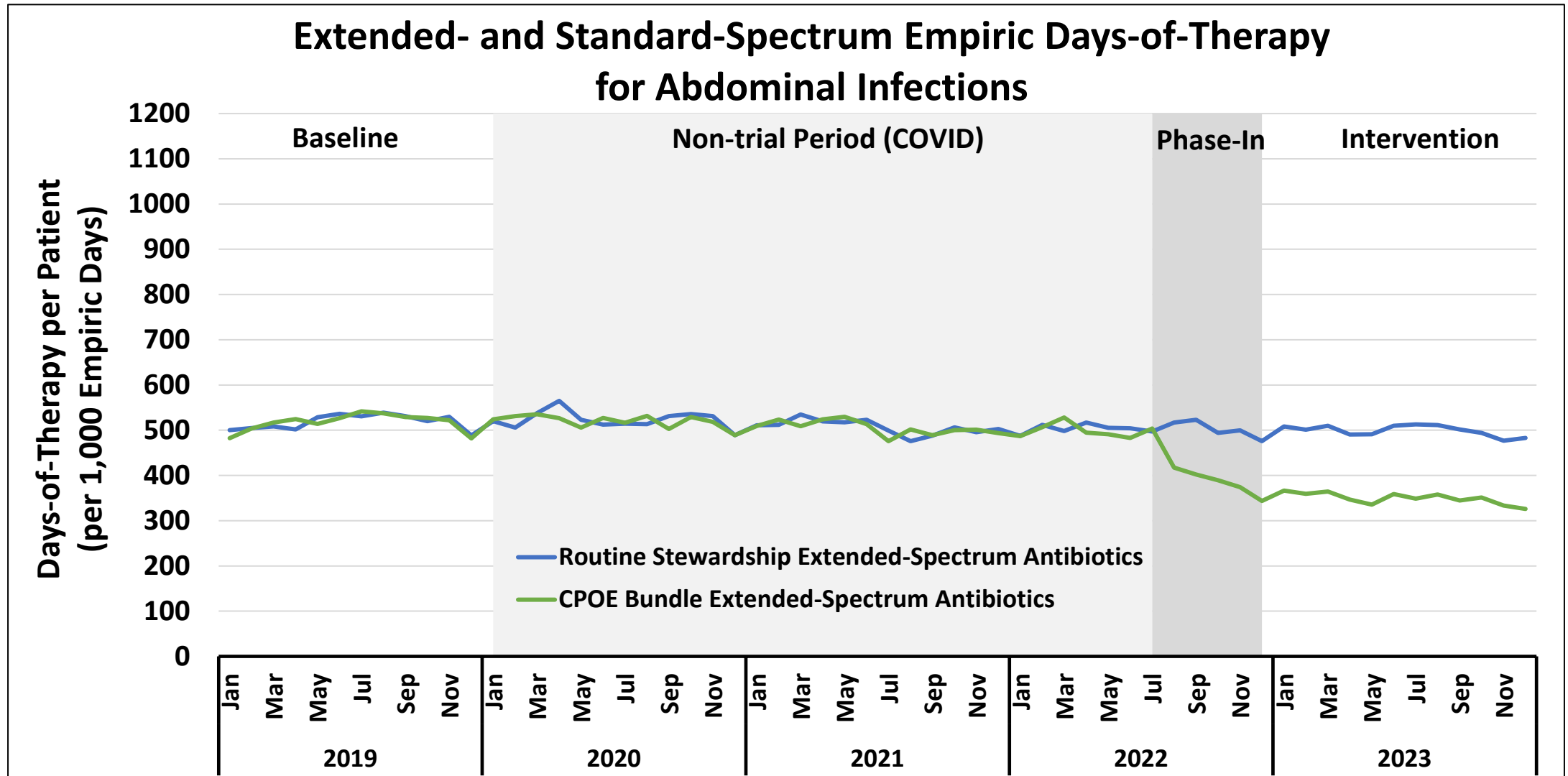
Patient Characteristic	Abdominal Infection	
	Routine (N=54,136)	CPOE Bundle (N=50,701)
History of Any MDRO	9.4%	9.8%
MRSA	4.8%	4.9%
VRE	0.7%	0.7%
<i>Pseudomonas</i>	2.5%	2.7%
ESBL	4.3%	4.6%
CRE	0.1%	0.3%
MDR Gram Negative Rods*	0.5%	0.6%

*MDR Gram Negative Rods – includes MDR *Enterobacteriaceae*, MDR/carbapenem resistant *Pseudomonas*, *Acinetobacter*. Abbreviations: MDRO – multidrug resistant organism; MRSA - Methicillin Resistant *Staphylococcus aureus*; ESBL – Extended Spectrum Beta Lactamase producer; VRE – Vancomycin Resistant *Enterococci*; CRE – Carbapenem Resistant *Enterobacteriaceae*; MDR- Multi-Drug Resistant



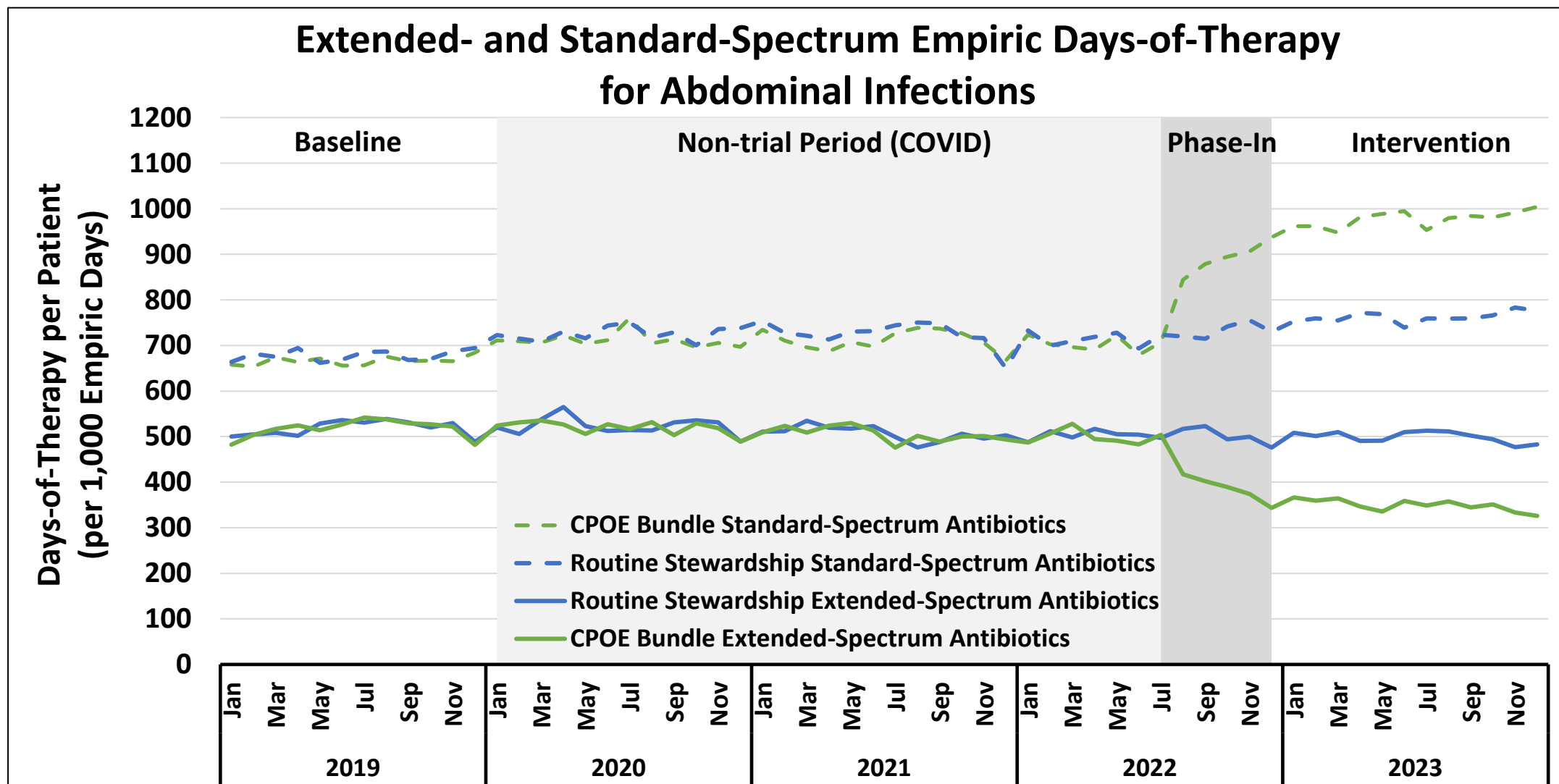
Empiric Extended-Spectrum Use Across Study Period - Abdominal Infection

- 30% crude absolute reduction with INSPIRE CPOE bundle

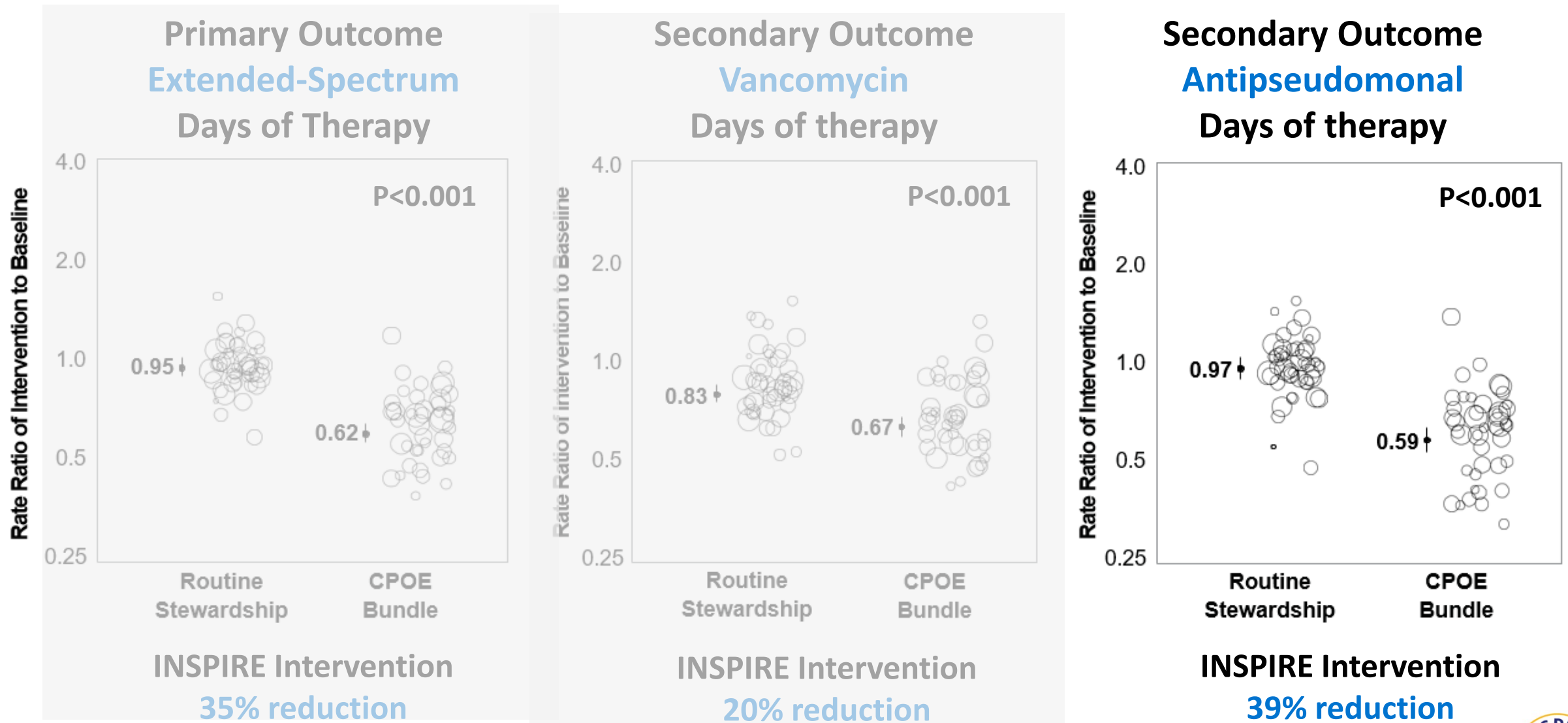


Empiric Extended-Spectrum Use Across Study Period - Abdominal Infection

- 30% crude absolute reduction with INSPIRE CPOE bundle



INSPIRE Abdominal Infection Trial Effectiveness Outcomes – As Randomized



INSPIRE Abdominal Infection Trial Safety Outcomes

- Days to ICU Transfer
 - No difference between groups
 - HR (CI) = 1.10 (0.96-1.26), p = 0.15
- Length of Stay
 - No difference between groups
 - HR (CI) = 1.02 (0.98-1.06), p = 0.27

Limitations

- Effect of individual components of bundle unknown
 - Need for education and feedback components by site-based pharmacist and physician champion is unknown
- Requires CPOE capability and live link to electronic health record
- Lower alert thresholds could have spared additional ES antibiotic use

Summary

- Real-time, personalized prompts can reduce empiric extended-spectrum use
- Benefits of automated approach:
 - Reduction despite disruptions in hospital operations (e.g., weather, COVID-19)
 - Active hospital-wide, nights/weekends
 - Risk documented in EHR may address clinician medical-legal concerns



INSPIRE Abdominal Infection Trial Hospital Participants

Arm 1 Facilities

CJW Medical Center – Chippenham, Johnston Willis Campuses	HCA Florida Northwest Hospital	LewisGale Medical Center	Southern Hills Hospital & Medical Center
Overland Park Regional Medical Center	HCA Florida Oak Hill Hospital	Good Samaritan Hospital	Regional Medical Center of San Jose
Grand Strand Medical Center	HCA Florida Pasadena Hospital	Medical City Alliance	St. David's North Austin Medical Center
HCA Florida Bayonet Point Hospital	HCA Florida Sarasota Doctors Hospital	Medical City Dallas	St. David's Round Rock Medical Center
HCA Florida Blake Hospital	HCA Florida South Tampa Hospital	Medical City Denton	Sunrise Hospital & Medical Center
HCA Florida Englewood Hospital	HCA Florida West Tampa Hospital	Medical City Frisco	The Medical Center of Aurora
HCA Florida Fort Walton-Destin Hospital	HCA Florida Trinity Hospital	Medical City Las Colinas	TriStar Centennial Medical Center
HCA Florida JFK North Hospital	HCA Houston Healthcare Kingwood	Medical City McKinney	TriStar Southern Hills Medical Center
HCA Florida Kendall Hospital	HCA Houston Healthcare Southeast	Medical City Plano	Valley Regional Medical Center
HCA Florida Lake City Hospital	Las Palmas Medical Center	Menorah Medical Center	Wesley Medical Center
HCA Florida Mercy Hospital	Lee's Summit Medical Center	Orange Park Medical Center	Wesley Woodlawn Hospital & ER
Los Robles Hospital & Medical Center	LewisGale Hospital Montgomery	Fairview Park Hospital	West Hills Hospital & Medical Center
Del Sol Medical Center	LewisGale Hospital Pulaski	Oviedo Medical Center	

Arm 2 Facilities

Corpus Christi Medical Center – Bay Area, Doctors, Heart Hospital	HCA Florida Brandon Hospital	Medical City North Hills	Eastern Idaho Regional Medical Center
Henrico Doctors' Hospital – Forest, Parham, Retreat Campuses	HCA Florida Capital Hospital	Medical City Weatherford	St. David's Medical Center
Rio Grande Regional Hospital Main Campus	HCA Florida Fawcett Hospital	Methodist Hospital Northeast	HCA Houston Healthcare Clear Lake
HCA Florida Gulf Coast Hospital	HCA Houston Healthcare Conroe	Centerpoint Medical Center	Swedish Medical Center
HCA Florida Largo Hospital	HCA Houston Healthcare Mainland	Methodist Hospital	Trident Medical Center
HCA Florida Lawnwood Hospital	HCA Houston Healthcare Pearland	Methodist Hospital Texsan	TriStar Greenview Regional Hospital
HCA Florida Memorial Hospital	HCA Houston Healthcare West	North Suburban Medical Center	TriStar Hendersonville Medical Center
HCA Florida Northside Hospital	Methodist Hospital Metropolitan	Ogden Regional Medical Center	TriStar Horizon Medical Center
HCA Florida South Shore Hospital	Medical City Arlington	Parkridge East Hospital	TriStar StoneCrest Medical Center
HCA Florida St. Lucie Hospital	Medical City Fort Worth	Parkridge Medical Center	HCA Florida St. Petersburg Hospital
Riverside Community Hospital	Medical City Lewisville	Research Medical Center	Tulane Medical Center
Methodist Hospital Specialty and Transplant	Sky Ridge Medical Center	Reston Hospital Center	Lakeview Regional Medical Center

INSPIRE Investigative Team



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