Setting the Stage: Inpatient Perspective

Notable Publications in Antimicrobial Stewardship

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Inpatient Antimicrobial Use:
Scope of the Problem

Original Investigation

Prevalence of Antimicrobial Use in US Acute Care Hospitals, May-September 2011

Shelley S. Magill, MD, PhD; Jonathan R. Edwards, MStat; Zintars G. Beldavs, MS; Ghinwa Dumyati, MD; Sarah J. Janelle, MPH; Marion A. Kainer, MBBS, MPH; Ruth Lynfield, MD; Joelle Nadle, MPH; Melinda M. Neuhauser, PharmD, MPH; Susan M. Ray, MD; Katherine Richards, MPH; Richard Rodriguez, MPH; Deborah L. Thompson, MD, MSPH; Scott K. Fridkin, MD; for the Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team

Magill S et al. JAMA 2014

ABX Use in U.S. Acute Care Hospitals, 2011

- One day point prevalence survey, 10 states, May-September 2011

- 11,282 patients in 183 hospitals; 49.9% got at least one antimicrobial drug
  - 77.5% of antimicrobial used to treat infections
  - 12.2% for surgical prophylaxis, 5.9% medical prophylaxis
  - Vancomycin (14.4%), piperacillin-tazobactam (10.3%), levofloxacin (9.1%)
  - 69% given for community onset infection, 81.6% outside of ICU

- Use of broad spectrum agents common including for treatment of community-onset infections and patients outside of ICU setting

Magill SS, et al JAMA 2014

Table 2. Infection Sites for Which Patients Received Antimicrobial Treatment

Infection Site[a]	No. of Drugs, (%) [95% CI] (n = 7641)	No. of Patients, (%) [95% CI] (n = 4278)
Lower respiratory tract	2607 (34.1) [33.1-35.2]	1480 (34.6) [33.2-36.0]
Urinary tract	1302 (17.0) [16.2-17.9]	955 (22.3) [21.1-23.6]
Skin and soft tissue	1177 (15.4) [14.6-16.2]	688 (16.1) [15.0-17.2]
Gastrointestinal tract	829 (10.8) [10.2-11.6]	537 (12.6) [11.6-13.6]
Undetermined/empirical	661 (8.7) [8.0-9.3]	364 (8.5) [7.7-9.4]
Bloodstream	639 (8.4) [7.8-9.0]	401 (9.4) [8.5-10.3]
Intra-abdominal	317 (4.1) [3.7-4.6]	178 (4.2) [3.6-4.8]
Bone and joint	291 (3.8) [3.4-4.3]	185 (4.3) [3.7-5.0]
Ear, nose, and throat	237 (3.1) [2.7-3.5]	183 (4.3) [3.7-4.9]
Hepatobiliary system	183 (2.4) [2.1-2.8]	109 (2.5) [2.1-3.1]
Central nervous system	137 (1.8) [1.5-2.1]	76 (1.8) [1.4-2.2]
Cardiovascular system	82 (1.1) [0.9-1.3]	50 (1.2) [0.9-1.5]
Reproductive tract	80 (1.0) [0.8-1.3]	46 (1.1) [0.8-1.4]
Disseminated	47 (0.6) [0.5-0.8]	38 (0.9) [0.6-1.2]
Unknown	34 (0.4) [0.3-0.6]	27 (0.6) [0.4-0.9]
Other	5 (0.07) [0.02-0.15]	3 (0.07) [0.02-0.19]

Magill S et al. JAMA 2014

Table 1. Antimicrobial Use Prevalence in Different Hospital Locations[a]

Location[b]	No. of Patients Receiving Antimicrobial Drugs	Total No. of Patients	Prevalence % (95% CI)
Surgical critical care unit	68	88	77.3 (67.7-85.1)
Medical-surgical pediatric critical care unit	47	66	71.2 (59.5-81.2)
Cardiothoracic critical care unit	51	75	68.0 (56.8-77.8)
Medical-surgical critical care unit	426	639	66.7 (62.9-70.2)
Medical critical care unit	156	243	64.2 (58.0-70.0)
Orthopedic ward	287	480	59.8 (55.4 -64.1)
Medical ward	918	1618	56.7 (54.3-59.1)
Medical-surgical ward	1475	2612	56.5 (54.6-58.4)
Cardiac critical care unit	28	50	56.0 (42.1-69.2)
Mixed acuity adult unit	59	106	55.7 (46.1-64.9)
Hematology-oncology pediatric specialty care area	29	54	53.7 (40.4-66.6)
Surgical ward	487	919	53.0 (49.8-56.2)
Hematology-oncology specialty care area	165	314	52.6 (47.0-58.0)
Stepdown unit	231	445	51.9 (47.3-56.5)
Medical-surgical pediatric ward	124	241	51.5 (45.1-57.7)
Medical pediatric ward	55	108	50.9 (41.5-60.3)

Magill S et al. JAMA 2014

Table 3. Five Most Common Antimicrobial Drugs Given to Treat Community-Onset Infections and Health Care Facility–Onset Infections[a]

Rank	No. of Drugs, (%) [95% CI]	
	Community-Onset Infections[b] (n = 5274)	Health Care Facility–Onset Infections[c] (n = 2220)
1	Vancomycin: 723 (13.7) [12.8-14.7][d]	Vancomycin: 354 (15.9) [14.5-17.5][d]
2	Ceftriaxone: 671 (12.7) [11.8-13.6]	Piperacillin-tazobactam: 259 (11.7) [10.4-13.1]
3	Levofloxacin: 518 (9.8) [9.0-10.7]	Levofloxacin: 170 (7.7) [6.6-8.8]
4	Piperacillin-tazobactam: 516 (9.8) [9.0-10.6]	Ceftriaxone: 147 (6.6) [5.6-7.7]
5	Azithromycin: 342 (6.5) [5.8-7.2]	Metronidazole: 101 (4.5) [3.7-5.5][d]

[a] Table does not include 147 antimicrobial drugs reported to have been given for infections with different onset locations (eg, for community- and health care facility–onset infections) or for infections with unknown onset location.

[b] Antimicrobial drugs are included if they were identified as being given for treatment of community-onset infections. Community-onset infections were defined as infections for which signs or symptoms began in community settings (eg, private residences, assisted living facilities, correctional facilities, homeless shelters, halfway houses, substance abuse rehabilitation facilities, etc).

[c] Antimicrobial drugs are included if they were identified as being given for treatment of health care facility–onset infections. Health care facility–onset infections were defined as infections for which signs or symptoms began in the survey hospital or in another health care facility (eg, another acute care hospital, long-term care facility, outpatient dialysis center, or infusion center, etc) prior to transfer to the survey hospital.

[d] Parenteral formulation of the drug.

Magill S et al. JAMA 2014

JAMA Internal Medicine | Original Investigation

Estimating National Trends in Inpatient Antibiotic Use Among US Hospitals From 2006 to 2012

James Baggs, PhD; Scott K. Fridkin, MD, MPH; Lori A. Pollack, MD, MPH; Arjun Srinivasan, MD, MPH;
John A. Jernigan, MD, MS

Baggs J et al. JAMA Int Med 2016

Inpatient ABX Use in U.S. Hospitals, 2006-12

- Retrospective, inpatient antibiotic use, Truven Health MarketScan
- 2006-2012, 300-383 hospitals per year
- Across all years, 55.1% of patients go at least one dose of ABX
- Overall national, 755 DOT/1000 patient-days
- Antibiotic use did not change over time
- Increases in broad spectrum agents
- Increases recorded for $3^{rd}/4^{th}$ generation cephalosporins, macrolides, glycopeptides, β-lactam/β-lactamase inhibitor combinations, carbapenems, and tetracyclines

Baggs J et al. JAMA Int Med 2016

Table 3. Extrapolated Estimates of Antibiotic Usage in the Truven MarketScan Hospital Drug Database by Year and Various Characteristics, 2006-2012 (continued)

Characteristic	DOT/1000 PDs							
	2006	2007	2008	2009	2010	2011	2012	All Years
Proportion of discharges by antibiotic class, %								
All	53.8	54.0	54.9	55.7	55.7	56.0	55.3	55.6
Aminoglycosides	5.7	5.6	5.3	4.6	4.3	4.0	3.9	4.8
First- and second-generation cephalosporins	20.4	20.3	20.1	20.2	20.1	19.5	18.9	20.0
Third- and fourth-generation cephalosporins	10.9	10.9	11.1	11.6	12.1	13.3	13.4	11.9
Lincosamide	3.4	3.4	3.5	3.5	3.5	3.5	3.5	3.5
Fluoroquinolones	16.8	16.7	16.9	16.4	15.8	15.7	15.0	16.2
Macrolides	4.9	4.9	5.3	5.7	5.5	6.1	6.0	5.5
Glycopeptide	8.2	8.9	9.9	10.7	11.3	12.3	12.9	10.6
Sulfa	1.8	1.9	2.0	2.0	1.9	1.8	1.8	1.9
β-Lactam/β-lactamase inhibitor combinations	7.5	8.0	8.6	9.1	9.5	10.2	10.4	9.0
Carbapenems	1.7	2.0	2.3	2.6	2.7	2.9	3.0	2.4
Penicillins	6.0	5.7	5.5	5.1	4.9	4.6	4.6	5.2
Tetracyclines	0.9	1.1	1.3	1.6	1.5	1.5	1.5	1.4
Metronidazole	5.1	5.2	5.1	5.1	5.2	5.3	5.3	5.2
Other	2.9	3.1	3.2	3.4	3.5	3.6	3.6	3.3

Abbreviations: DOT, days of therapy; PDs, patient-days.

Baggs J et al. JAMA Int Med 2016

Antimicrobial Stewardship: Current Status and Unanswered Questions

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

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Barlam TF et al. Clin Infect Dis 2016

Antibiotic Stewardship Programs in U.S. Acute Care Hospitals: Findings From the 2014 National Healthcare Safety Network Annual Hospital Survey

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Pollack LA, et al Clin Infect Dis 2016

Stewardship in U.S. Acute Care Hospitals

- 2014 NHSN Survey to describe ASP in acute care hospitals
- 4184 US hospitals, 39% had ASPs that met all 7 core components
- ASP implementation varies…(size, geographic region)
  - Hospitals greater than 200 beds, 59%
  - Hospitals less than 50 beds, 25%
  - Portion of hospitals in individual states varied (range 7% to 58%)

Pollack LA, et al Clin Infect Dis 2016

Table 1. Number and Percentage of US Acute Care Hospitals Reporting Implementation of Core Elements of Hospital Antibiotic Stewardship Programs, National Healthcare Safety Network, 2014

Core Element	NHSN ASP Question[a]	N	%
Infrastructure for antibiotic stewardship		**2298**	**54.9**
1. Hospital leadership commitment: Dedicate human, financial, and IT resources		2508	59.9
23	Written statement of support	2199	52.6
26	Salary support	1326	31.7
23, 26	Both	926	22.1
2. Program leadership (Accountability): Person responsible for outcomes		3016	72.1
24	Pharmacist	1540	36.8
24	Physician	1258	30.1
24	Other	218	5.2
3. Drug expertise: At least 1 pharmacist responsible for improving antibiotic use		3648	87.2
Implementation		**2112**	**50.5**
4. Act: Performance of at least one prescribing improvement action		3926	93.8
28	Facility-specific treatment recommendations	3232	77.3
31	Audit with feedback	3100	74.1
30	Prior-approval	2652	63.4
27	Requirement to document antibiotic indication	1105	26.4
29	Antibiotic time out	979	23.4
5. Track: Monitor prescribing and antibiotic resistance patterns.		3318	79.3
32	Monitor antibiotic use (consumption)	2881	68.9
28[b]	Facility-specific treatment recommendations and monitor adherence to facility-specific treatment recommendations	2203	52.7
27[b]	Requirement to document antibiotic indication and monitor adherence to indication documentation policy	736	17.6
6. Report: Regularly report to staff prescribing and resistance patterns		2822	67.5
33	Feedback to providers on how they can improve prescribing	2478	59.2
32[b]	Reports on antibiotic use shared with prescribers	1861	44.5
7. Educate about antibiotic resistance and improving prescribing practices		2589	61.9
34	Education provided to clinicians and other relevant staff		
Hospitals reporting all 7 core elements of hospital antibiotic stewardship programs		**1642**	**39.2**

Measuring Appropriate Antimicrobial Use: Attempts at Opening the Black Box

Emily S. Spivak,[1] Sara E. Cosgrove,[2] and Arjun Srinivasan[3]

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Indiscriminate antimicrobial use has plagued medicine since antibiotics were first introduced into clinical practice >70 years ago. Infectious diseases physicians and public health officials have advocated for preservation of these life-saving drugs for many years. With rising burden of antimicrobial-resistant organisms and *Clostridium difficile* infections, halting unnecessary antimicrobial use has become one of the largest public health concerns of our time. Inappropriate antimicrobial use has been quantified in various settings using numerous definitions; however, no established reference standard exists. With mounting national efforts to improve antimicrobial use, a consensus definition and standard method of measuring appropriate antimicrobial use is imperative. We review existing literature on systematic approaches to define and measure appropriate antimicrobial use, and describe a collaborative effort at developing standardized audit tools for assessing the quality of antimicrobial prescribing.

Keywords. antibiotic; quality; antimicrobial stewardship; drug resistance; utilization.

Spivak ES, Cosgrove SE, Srinivasan A. Clin Infect Dis 2016

Original Investigation

National Variability and Appropriateness of Surgical Antibiotic Prophylaxis in US Children's Hospitals

Thomas J. Sandora, MD, MPH; Monica Fung, MD; Patrice Melvin, MPH;
Dionne A. Graham, PhD; Shawn J. Rangel, MD, MSCE

Sandora TJ. JAMA Pediatr 2016

Surgical Prophylaxis in US Children's Hospitals

- Appropriate use of antibiotic prophylaxis reduces SSI rates
- Inappropriate has many negative consequences

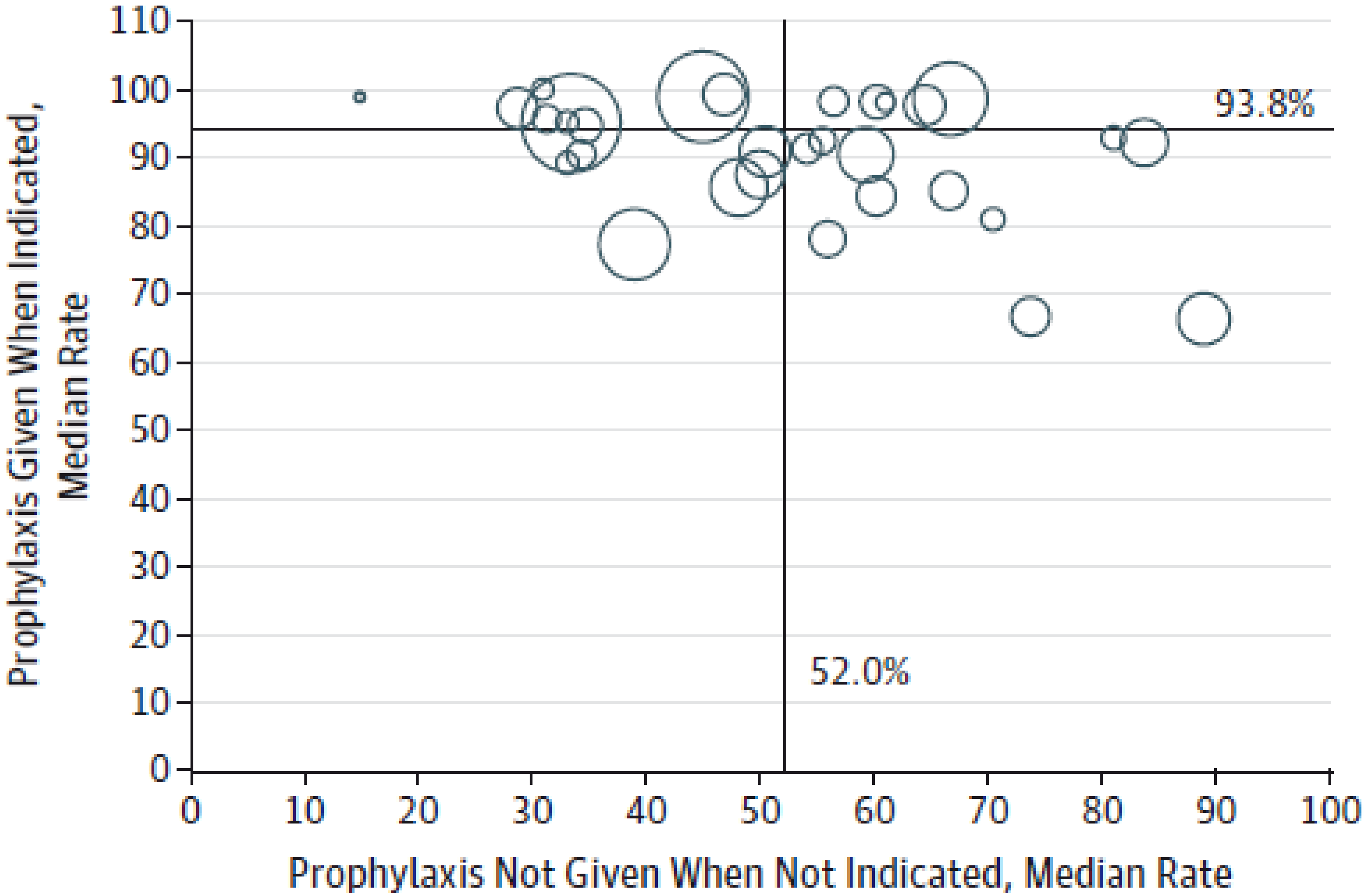
- Retrospective cohort study, 31 free-standing children's hospitals
- Rates of use, appropriateness, adverse events

- Appropriate Use (range 47.3% - 84.4%), variability by procedure
  - Prophylaxis indicated (median rate 93.8%)
  - Prophylaxis NOT indicated (median rate 52.0%)

- Odds of *C. difficile* (OR 3.3), epinephrine administration (OR 1.97)
- Higher among children who got antibiotic prophylaxis

Sandora TJ et al. JAMA Pediatr 2016

Figure 4. Interhospital Relationship Between Giving Prophylaxis When Indicated and Not Giving Prophylaxis When Not Indicated



Sandora TJ et al. JAMA Pediatr 2016

Original Investigation | LESS IS MORE

Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter–Associated Asymptomatic Bacteriuria

Barbara W. Trautner, MD, PhD; Larissa Grigoryan, MD, PhD; Nancy J. Petersen, PhD; Sylvia Hysong, PhD;
Jose Cadena, MD; Jan E. Patterson, MD, MS; Aanand D. Naik, MD

Trautner BW et al. JAMA Int Med 2016

Stewardship to Reduce CAUTI Overtreatment

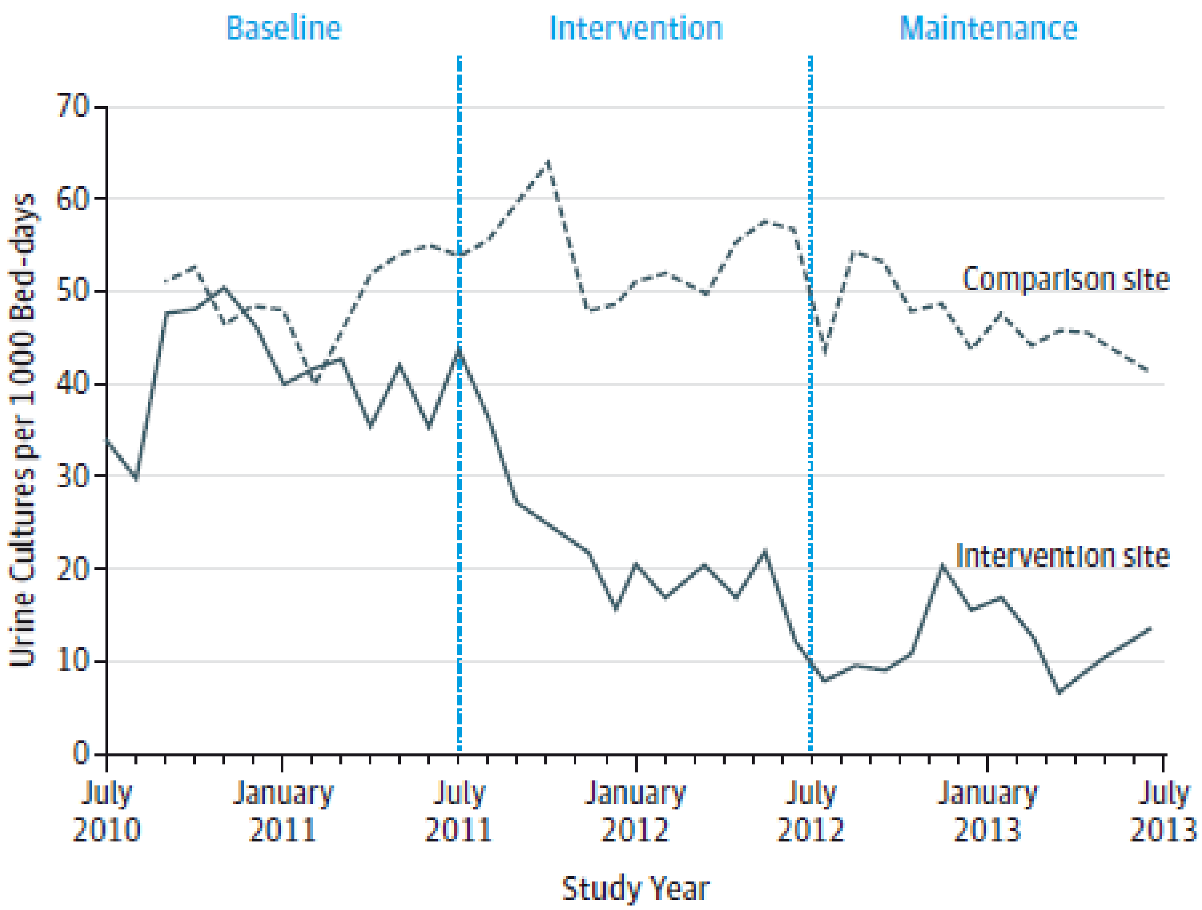
- “Kicking CAUTI”—intervention to reduce urine culture ordering and antimicrobial prescribing for catheter associated asymptomatic bacteriuria (multifaceted intervention that included “audit and feedback”)

- Overall rate of urine culture ordered decreased (41.2 to 23.3 per 1000 bed-days). Further decrease to 12.0 per 1000 bed days during maintenance period.

- Comparison site: no different in number of urine cultures ordered

Trautner BW, et al. JAMA Intern Med 2015

Figure. Monthly Rates of Urine Culture Orders per 1000 Bed-days



Shown are the intervention vs comparison sites across the 3 study periods ($P < .001$).

Trautner BW, et al. JAMA Intern Med 2015

Antibiotic Prescribing at the Transition from Hospitalization to Discharge: A Target for Antibiotic Stewardship

Norihiro Yogo, MD;[1,2] Michelle K. Haas, MD;[1,2,4,5] Bryan C. Knepper, MPH, MSc;[3,5] William J. Burman, MD;[1,2,4,5] Philip S. Mehler, MD;[1,2,5] Timothy C. Jenkins, MD[1,2,5]

Yogo N, et al. Infect Control Hosp Epidemiol 2015

Hospital Discharge: A Target for Stewardship

- Retrospective, single center study
- 300 patients prescribed oral antibiotics at the time of hospital discharge
- UTI, community acquired pneumonia, skin infections accounted for 181 (60%) treatment indications
- Half of prescriptions were antibiotics with broad Gram negative activity
- Discharge prescriptions were inappropriate in 79/150 cases reviewed (53%)

Yogo N, et al. Infect Control Hosp Epidemiol 2015

Original Investigation

Comparative Effectiveness of Intravenous vs Oral Antibiotics for Postdischarge Treatment of Acute Osteomyelitis in Children

Ron Keren, MD, MPH; Samir S. Shah, MD, MSCE; Rajendu Srivastava, MD, FRCPC, MPH; Shawn Rangel, MD; Michael Bendel-Stenzel, MD; Nada Harik, MD; John Hartley, DO; Michelle Lopez, MD; Luis Seguias, MD; Joel Tieder, MD; Matthew Bryan, PhD; Wu Gong, MS; Matt Hall, PhD; Russell Localio, PhD; Xianqun Luan, MS; Rachel deBerardinis, BA; Allison Parker, MS; for the Pediatric Research in Inpatient Settings Network

Keren R et al. JAMA Pediatr 2015

IV vs Oral ABX for Osteomyelitis in Children

- Post-discharge treatment of acute osteomyelitis in children requires extended therapy. Many downsides of PICCs
- Retrospective cohort study, PCORI ("comparative effectiveness")
- 2060 children: 1005 orals, 1055 therapy via PICC
- Propensity score-based matching to limit confounding
- Bottom-line
  - Children treated with orals did not have more treatment failures
  - Children with PICCs, 15% developed a PICC-related complication requiring ED visit and/or re-hospitalization
- Raises broader question of trying to use orals instead of IV for other conditions, populations (also duration of IV therapy)

Keren R et al. JAMA Pediatr 2015

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Receipt of Antibiotics in Hospitalized Patients and Risk for *Clostridium difficile* Infection in Subsequent Patients Who Occupy the Same Bed

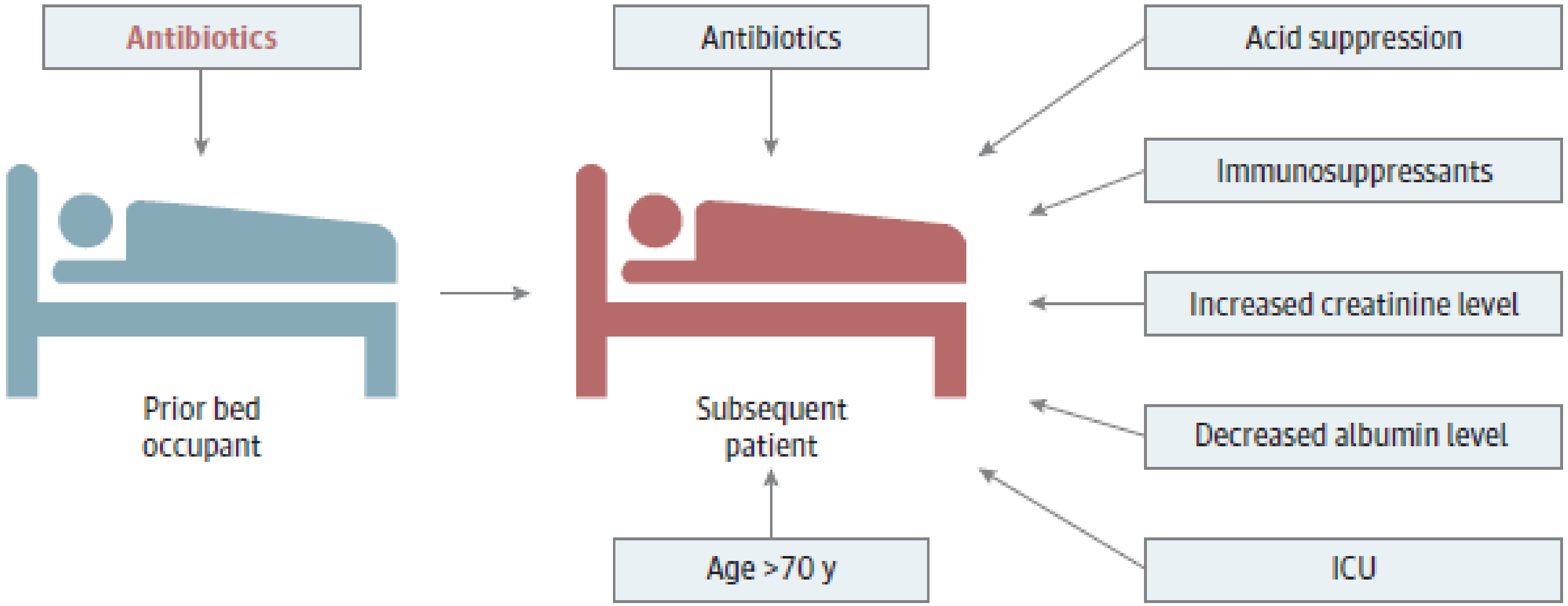
Daniel E. Freedberg, MD, MS; Hojjat Salmasian, MD, PhD; Bevin Cohen, MPH; Julian A. Abrams, MD, MS; Elaine L. Larson, RN, PhD

Freedberg DE et al. JAMA Intern Med 2016

- Retrospective cohort, adults hospitalized from 2010-2015
- 100,615 pairs of patients; 576 (0.57%) “subsequent” pts developed CDI; adjusted HR 1.22 95% CI 1.02-1.45
- Receipt of antibiotics by prior bed occupants associated with increased risk of CDI in subsequent patients
- WHY?
  - Patients colonized by *C. difficile* (spores shed into local environment)
  - Antibiotics affect microbiome more globally—decrease in bacterial species that protect again *C. difficile*

Freedberg DE, et al. JAMA Intern Med 2016

Figure 2. Schematic Depicting Risk Factors Significantly Associated With Increased Risk for *Clostridium difficile* Infection (CDI)



Multiple risk factors were identified related to the subsequent patient but, of all the potential risk factors examined that were related to the prior bed occupant, only antibiotics were associated with increased risk for CDI in subsequent patients. ICU indicates intensive care unit.

Freedberg DE et al. JAMA Intern Med 2016

Summary

- Inpatient setting still the primary location for ASP efforts
- Implementation studies (not just descriptive work) will be most influential in coming years
- Keep in mind resource limitations in non-tertiary care settings (important for generalizability)
- “In between” locations worth a closer look (transitions of care, surgical centers, LTACHs)
- Look for opportunities for “Out of the Box” studies