



The State of Stewardship Research – Success and Remaining Gaps

ACUTE INPATIENT

SHEA ASRW – November 15, 2017

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System Antimicrobial Stewardship Pharmacist Manager

Recent research successes in the acute inpatient setting

Two new systematic reviews, then select studies published in the last year



2017 COCHRANE REVIEW

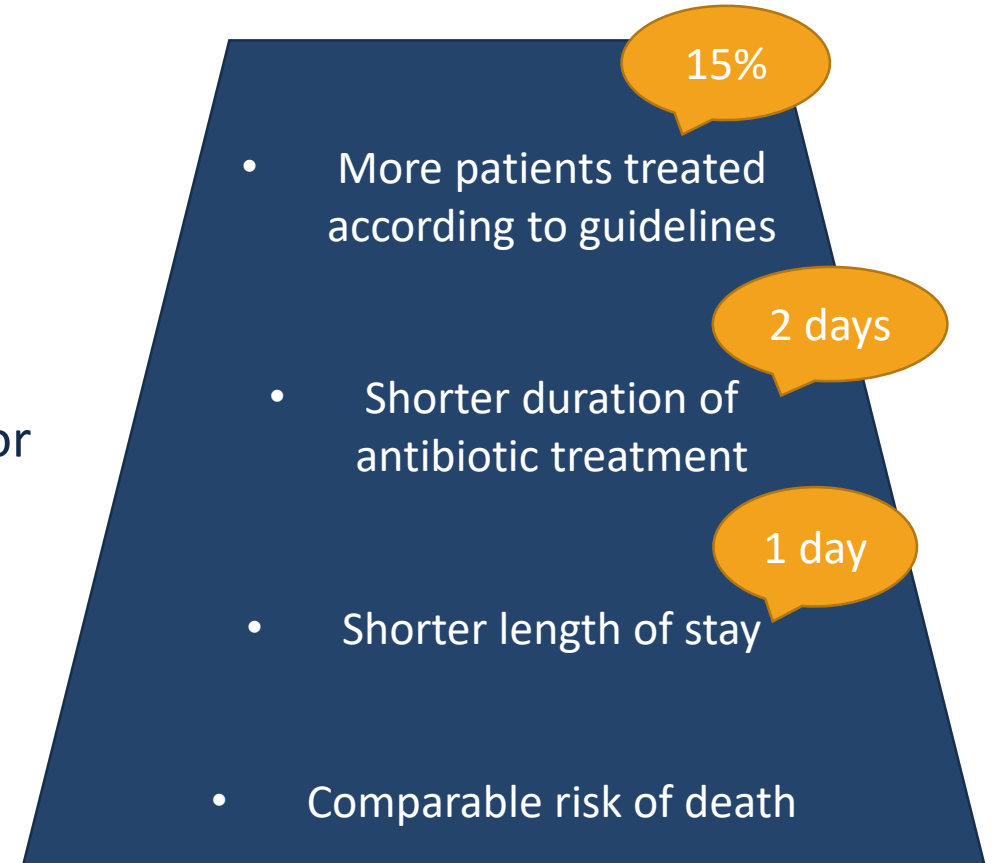
Previous version:

Restrictive intervention had greater immediate effect on prescribing than those that used education or persuasion

This update focused on “enabling”: increasing means or reducing barriers to increase capability or opportunity

Publications through January 2015:

- 221 studies (58 RCTs and 163 non-randomized)
- Most studies North America (96) or Europe (87)



RCT: Randomized Controlled Trial

Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4.

COCHRANE REVIEW

“The quality of reporting of interventions was poor, which makes it difficult for professionals and clinical teams to reliably implement interventions that have been shown to be useful and for other researchers to replicate or build on research findings.”

Hoffman TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687. DOI: 10.1136/bmj.g1687.

Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4.

COCHRANE REVIEW

LESS

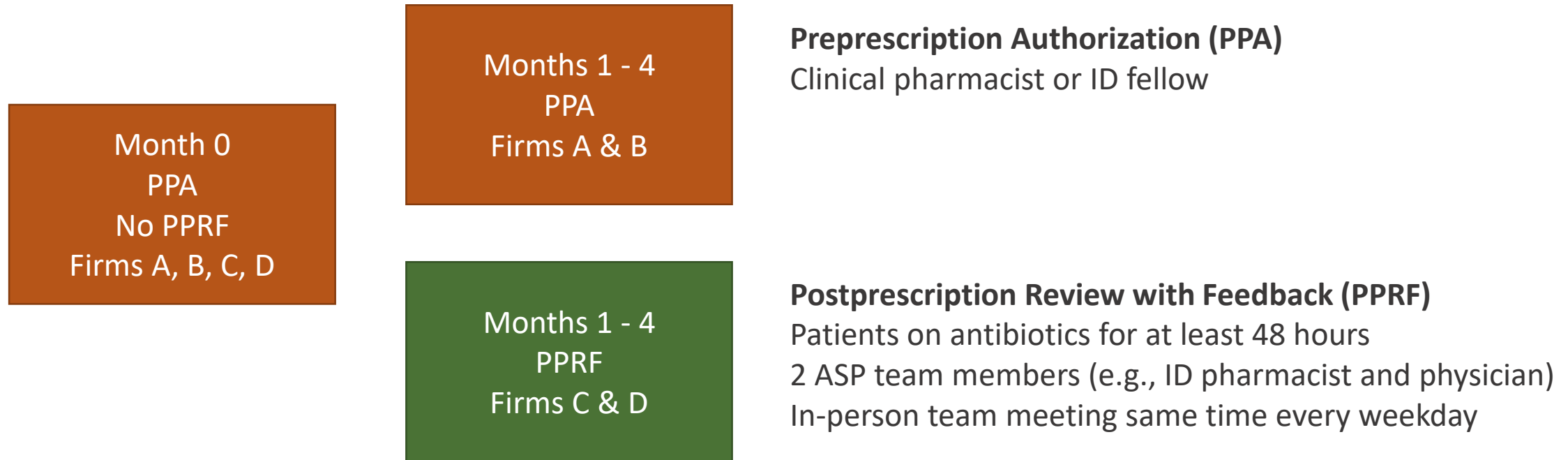
- Solely focusing on unnecessary treatment
- Comparing antibiotic stewardship to no intervention
 - Controlled before-after studies
 - Non-randomized trials

MORE

- Effective treatment of sepsis without also causing excessive antibiotic use
 - Comparing different interventions
 - Patient safety outcome measures
 - Microbial outcome measures
- Action planning, goal setting, feedback, self-reflection
 - Greater use of qualitative methods
 - Coordinated, multihospital RCTs

Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4.

PRE-AUTHORIZATION vs POST-PRESCRIPTION REVIEW



Tamma PD, Avdic E, Keenan JF, et al. What is the more effective antibiotic stewardship intervention: preprescription authorization or postprescription review with feedback? *Clinical Infectious Diseases* 2017;64(5):537-43.

PRE-AUTHORIZATION vs POST-PRESCRIPTION REVIEW



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PRE-AUTHORIZATION vs POST-PRESCRIPTION REVIEW

Primary outcome: patient DOT, including outpatient, per 1,000 patient-days

- PPA: 8 DOT per 1,000 patient-days; PPRF: 6 DOT per 1,000 patient-days ($p = 0.03$)

Length of therapy (LOT)

- PPA: 7 DOT per 1,000 patient-days; PPRF: 5 DOT per 1,000 patient-days ($p < 0.01$)

Antibiotic regimen inappropriate on Day 1

- Appropriate antibiotic regimen: PPA: 516 (66.3%); PPRF: 430 (58.9%)

No difference in *C. difficile*, length of stay, or in-hospital mortality

Tamma PD, Avdic E, Keenan JF, et al. What is the more effective antibiotic stewardship intervention: preprescription authorization or postprescription review with feedback? *Clin Infect Dis* 2017;64(5):537-43.

ADDITIONAL INTERVENTION AT HOSPITAL DISCHARGE

Quasi-experimental, retrospective cohort study

Syndrome-specific interventions for CAP and skin infections already implemented

DURATION for ALL
Laminated pocket-sized cards
Intranet resource
Smartphone app
Presentations to physicians
Staff pharmacist training to review & notify ID pharmacist

40% had PharmD review

Oral antibiotics filled at pharmacy within 48 hours of discharge

Pre-intervention Cohort
Random 50 of 300

Intervention Cohort
Random 50 of 200

3 blinded reviewers

Yogo N, Shihadeh K, Young H, et al. Intervention to reduce broad-spectrum antibiotics and treatment durations prescribed at the time of hospital discharge: a novel stewardship approach. *Infect Control Hosp Epidemiol* 2017;38(5):534-41.

ADDITIONAL INTERVENTION AT HOSPITAL DISCHARGE

	Broad	Total Duration	CAP Duration	Skin Duration	UTI Duration	Appropriate
Pre-intervention Cohort Random 50 of 300	51%	10 (7-13)	8 (6-9)	12 (8-15)	10 (8-13)	52%
	0.02		0.003	0.02		
Intervention Cohort Random 50 of 200	40%	9 (6-13)	6 (5-7)	9 (7-12)	9 (7-12)	66%

No difference in treatment failure, readmission, *C. difficile* or adverse events

Yogo N, Shihadeh K, Young H, et al. Intervention to reduce broad-spectrum antibiotics and treatment durations prescribed at the time of hospital discharge: a novel stewardship approach. *Infect Control Hosp Epidemiol* 2017;38(5):534-41.

PATIENT SAFETY OUTCOMES

Scotland – NHS Tayside Orthopaedic Antibiotic Prophylaxis Policy

Pre-October 2008
Cefuroxime

Oct 2008 to May 2012
Gentamicin 4 mg/kg x1
Flucloxacillin 1g x4

June 2012 to Dec 2013
Co-amoxclav 1.2 g x3

EXCEPT: neck of femur repair
operations – co-amoxclav

KDIGO criteria: SCr within year prior
to surgery compared to highest
within 7 days after surgery

Interrupted time series segmented
regression, multiple linear regression

KDIGO: Kidney Disease:
Improving Global Outcomes

Walker H, Patton A, Bayne G, et al. Reduction in post-operative acute kidney injury following a change in antibiotic prophylaxis policy for orthopaedic surgery: an observational study. *J Antimicrob Chemother* 2016;71:2598-605.

PATIENT SAFETY OUTCOMES

AKI Stage	Operations other than NOF repair, n (%)		NOF repair operations, n (%)	
	Before 2012 policy	After 2012 policy	Before 2012 policy	After 2012 policy
1	618 (9.86)	239 (8.03)	153 (12.24)	67 (13.09)
2	95 (1.52)	22 (0.74)	16 (1.28)	4 (0.78)
3	45 (0.72)	12 (0.4)	2 (0.16)	1 (0.2)
None	5509 (87.9)	2702 (90.8)	1079 (86.32)	440 (85.94)

ITS: 63% (-77 to -49) relative reduction in AKI at 18 months (control 10% (-35 to 15))

Higher 1-year mortality and length of stay in AKI group

Similar *C. difficile* and SSI (not consistently audited) pre/post policy change

Walker H, Patton A, Bayne G, et al. Reduction in post-operative acute kidney injury following a change in antibiotic prophylaxis policy for orthopaedic surgery: an observational study. *J Antimicrob Chemother* 2016;71:2598-605.

REVIEW OF PEDIATRIC LITERATURE

Found 17 original studies

- 9 studies described formal ASPs (originating from 4 centers)
- 8 studies evaluating specific intervention strategies
 - Guidelines (4), restriction/cycling (2), order form (1), clinical decision support (1)

“Prescribing errors” included as an antimicrobial stewardship metric

Gaps noted in this review:

- No formal economic studies
- No analysis of impact on *Clostridium difficile* rates
- Only 1 study compared results to other hospitals (days and length of therapy)
- Limited studies evaluating antibiotic appropriateness and intervention effectiveness

Smith MJ, Gerber JS, Hersh AL. Inpatient Antimicrobial Stewardship in Pediatrics: A Systematic Review. *J Pediatric Infect Dis Soc.* 2015 Dec;4(4):e127-35. doi: 10.1093/jpids/piu141. Epub 2015 Jan 23. PMID: 26582880

SHARPS



<http://www.sharpsgroup.org/>

ASP Strategies and Appropriate Antibiotic Use

Brian R. Lee, MPH, PhD; Alison Tribble, MD; Lori Handy, MD; Jeffrey Gerber, MD, PhD, MSCE; Adam Hersh, MD, PhD; Matthew Kronman, MD, MSCE; Cindy Terrill, BS; Jason Newland, MD, MEd; on behalf of the SHARPS Collaborative

Children's Mercy Kansas City, Kansas City, Mo.; C.S. Mott Children's Hospital, Ann Arbor, MI; The Children's Hospital of Philadelphia, Philadelphia, PA; Primary Children's Hospital, Salt Lake City, UT; Seattle Children's, Seattle, WA; Washington University School of Medicine, St. Louis, MO



<http://www.sharpsgroup.org/>

Background

- Antimicrobial stewardship programs decrease inappropriate antibiotic use among hospitalized children
- Data are limited on *which* ASP strategies have the greatest impact on inappropriate antibiotic use

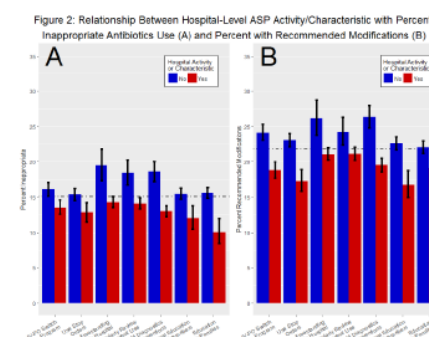
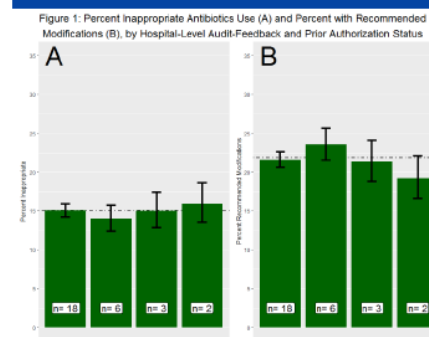
Methods

- In 2016, online survey data was collected from 30 hospitals:
 - Regularly review antimicrobial use
 - Use of audit-with-feedback
 - Use of restricted formularies or prior authorizations
 - Use rapid diagnostics results for ASP interventions
 - Dedicated ASP effort (FTE)
- In 2016, 3 quarterly one day point prevalence surveys (PPS) were conducted among all admitted patients <18 years who were receiving antibiotics. Data included:
 - Antibiotic type, dose, duration, & route
 - Indication for treatment
 - Appropriateness of antibiotic
 - Antimicrobial stewardship recommendation
- We report the unadjusted relationship between ASP-related strategy and hospital-level inappropriate antibiotic use and antibiotic modification recommendations from the PPS

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Results

- 6,921 patients were receiving at least one antibiotic
- 10,170 active antibiotic orders
 - Fifteen percent of antibiotics were categorized as inappropriate; inter-hospital range: 5.0% to 25.3%
 - Twenty-two percent of antibiotics required ASP modifications (e.g., change drug, change dose, etc.); inter-hospital range: 5.0% to 40.2%
- Total ASP FTE was not correlated with hospital-level inappropriate use ($Rho = -.091$; $p = .673$) or antibiotics modification recommendations ($Rho = -.052$; $p = .786$)
- Inappropriate antibiotic use and recommended modifications were significantly lower for hospitals that:
 - Have IV-PO conversion programs
 - Use automatic stop orders
 - Regularly review antimicrobial use
 - Use rapid diagnostic results for ASP interventions
- Audit-with-feedback and prior authorizations were not associated with inappropriate use or modification recommendations



Conclusions

- This is the most comprehensive survey of pediatric inpatient inappropriate antibiotic use to date
- Antibiotic use monitoring, integration of rapid diagnostics, and stop orders were associated with lower inappropriate use
- Audit-with-feedback and prior authorizations were not associated with less inappropriate prescribing

Newland JG, Gerber JS, Kronman MP, et al. Sharing Antimicrobial Reports for Pediatric Stewardship (SHARPS): a quality improvement collaborative. *J Pediatr Infect Dis Soc* 201 [Epub ahead of print] PMID: 28379408

Identify main areas where
research is acutely needed

to address unanswered stewardship
questions



OVERVIEW of FRAMEWORK FOR STEWARDSHIP GAPS

Population

- Multicenter, randomized trials

Intervention

- Standardized interventions for easier multicenter implementation

Comparison

- Comparing one intervention to another

Outcome

- Standardized outcomes
- Outcomes beyond antimicrobial use

POPULATION

Pediatric

Hurst AL, Child J, Pearce K, et al. Handshake stewardship: a highly effective rounding-based antimicrobial optimization service. *Pediatr Infect Dis J* 2016;35(10):1104-10. PMID: 27254036

Sepsis

Burston J, Adhikari S, Hayen A, et al. A role for antimicrobial stewardship in clinical sepsis pathways: a prospective interventional study. *Infect Control Hosp Epi* 2017;38(9):1032-8. PMID: 28693625

Immunocompromised

Webb BJ, Healy R, Majers J, et al. Prediction of Bloodstream Infection Due to Vancomycin-Resistant Enterococcus in Patients Undergoing Leukemia Induction or Hematopoietic Stem-Cell Transplantation. *Clin Infect Dis*. 2017 Jun 15;64(12):1753-1759. PMID: 28369204

INTERVENTION

WHO SHOULD PERFORM INTERVENTIONS?

Generalists

Carreno JJ, Kenney RM, Bloome M, et al. Evaluation of pharmacy generalists performing antimicrobial stewardship services. *Am J Health-Syst Pharm* 2015;72(15):1298-303. PMID: 26195656

Bessesen MT, Ma A, Clegg D, et al. Antimicrobial stewardship programs: comparison of a program with infectious diseases pharmacist support to a program with a geographic pharmacist staffing model. *Hosp Pharm* 2015;50(6):477-83.

Vaughn VN, Flanders SA. Annals for hospitalists inpatient notes – mindfulness and antibiotic appropriateness – how point-of-care stewardship begins with hospitalists. *Ann Intern Med* 2016;165(10):HO2-3. PMID: 27842418

Nurses

Monsees E, Goldman J, Popejoy L. Staff nurses as antimicrobial stewards: an integrative literature review. *Am J Infect Control* 2017;45(8):917-22. PMID: 28768593

Collaboratives

IDWeek 2017 platform on Colorado state based collaborative – Heidi Wald #1824

INTERVENTION

WHAT TYPES OF INTERVENTIONS ARE MOST EFFECTIVE?

Financial Incentives

Gong S, Qiu X, Song Y, et al. Effect of financially punished audit and feedback in a pediatric setting in China, within an antimicrobial stewardship program, and as part of an international accreditation process. *Front Public Health* 2016;4:99. PMID: 27242991

Patient Education

Heid C, Knobloch MJ, Schulz LT, Safdar N. Use of the health belief model to study patient perceptions of antimicrobial stewardship in the acute care setting. *Infect Control Hosp Epidemiol* 2016;37(5):576-82. PMID: 26809477

Micallef C, Kildonaviciute K, Castro-Sanchez E, et al. Patient and public understanding and knowledge of antimicrobial resistance and stewardship in a UK hospital: should public campaigns change focus? *J Antimicrob Chemother* 2017;72(1):311-4. PMID: 27655854

Diagnostic Interventions

Filice GA, Drekonja DM, Thurn JR, et al. Diagnostic errors that lead to inappropriate antimicrobial use. *Infect Contr Hosp Epidemiol* 2015;36(8):949-56. PMID: 25998898

Ng TM, Phang VY, Young B, et al. Clinical impact of non-antibiotic recommendations by a multi-disciplinary antimicrobial stewardship team. *Int J Antimicrob Agents* 2017;50:166-70. PMID: 28625717

INTERVENTION

WHERE CAN WE EXPAND OUR REACH?

Telemedicine

Siddiqui J, Herchline T, Kahlon S, et al. Infectious Diseases Society of America position statement on telehealth and telemedicine as applied to the practice of infectious diseases. *Clin Infect Dis* 2017;64(3):237-42. PMID: 28096274

Stenehjem E, Hyun DY, Septimus E, et al. Antibiotic stewardship in small hospitals: barriers and potential solutions. *Clin Infect Dis* 2017;65(4):691-6.

Additional Countries

Brink AJ, Messina Ap, Feldman C, et al. Antimicrobial stewardship across 47 South African hospitals: an implementation study. *Lancet Infect Dis* 2016;16:1017-25.

WHERE SHOULD WE DOCUMENT OUR INTERVENTIONS?

INTERVENTION

WHEN IS THE MOST VALUABLE TIME TO INTERVENE?

At 24, 48, 72 hours?

ATO platform at IDWeek 2017 – Kerri Thom #1747

Best CDSS Triggers

Huber SR, Fullas F, Nelson KR, et al. Retrospective evaluation of pharmacist interventions on use of antimicrobials using a clinical surveillance software in a small community hospital. *Pharmacy (Basel)* 2016;4(4). PMID: 28970405

Chow AL, Ang A, Chow CZ, et al. Implementation hurdles of an interactive, integrated, point-of-care computerized decision support system for hospital antibiotic prescription. *Int J Antimicrob Agents* 2016;47:132-9. PMID: 26774157

Upon Discharge

Jones JM, Leedahl ND, Losing A, et al. A pilot study for antimicrobial stewardship post-discharge. *J Pharm Pract* 2017. [Epub ahead of print] PMID: 28343444

Hersh AL, Olson J, Stockmann C, et al. Impact of antimicrobial stewardship for pediatric outpatient parenteral antibiotic therapy. *J Pediatr Infect Dis Soc* 2017; [Epub ahead of print] PMID: 28549165

COMPARISON

WHICH INTERVENTION FIRST?

WHICH INTERVENTION TYPES HAVE HIGHEST YIELD?

- New program
- Established program

WHICH IMPLEMENTATION STRATEGY?

- Implementation science

OUTCOME

Several recent reviews proposing antibiotic stewardship metrics

Akpan MR, Ahmad R, Shebl NA, Ashiru-Oredope D. A review of quality measures for assessing the impact of antimicrobial stewardship programs in hospitals. *Antibiotics (Basel)* 2016;5:5.

Kallen MC, Prins JM. A systematic review of quality indicators for appropriate antibiotic use in hospitalized adult patients. *Infect Dis Report* 2017;9:6821.

Moehring RW, Anderson DJ, Cochran RL, et al. Expert consensus on metrics to assess the impact of patient-level antimicrobial stewardship interventions in acute-care settings. *Clin Infect Dis* 2017;64:377-83.

Pollack LA, Plachouras D, Sinkowitz-Cochran R, et al. A concise set of structure and process indicators to assess and compare antimicrobial stewardship programs among EU and US hospitals: results from a multinational expert panel. *Infect Control Hosp Epidemiol* 2016;37(10):1201-11.

However, all of these antibiotic stewardship metrics need to be validated

OUTCOME (cont.)

Patient safety outcomes

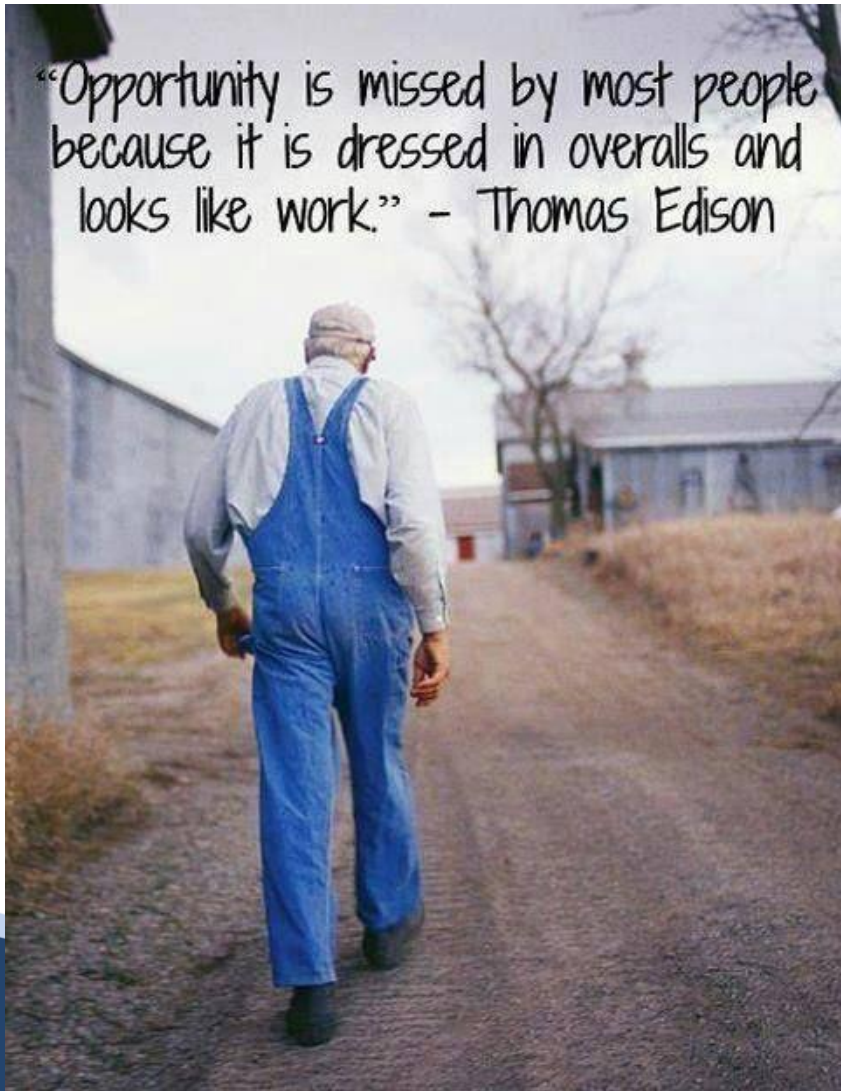
Significant variability in process and outcome measures methods

Limited studies evaluate robust outcome measures

- Patient outcomes: balancing measure vs targets

Baur D, Gladstone BP, Burkert F, et al. Effect of antibiotic stewardship on the incidence of infection and colonization with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:990-1001.

CONCLUSION



<https://quotlr.com/image/4954>



<https://twitter.com/ShawnFrankson/status/834090407331926017>

Let's get started!





The State of Stewardship Research – Success and Remaining Gaps

ACUTE INPATIENT

*Whitney R. Buckel, PharmD, BCPS-AQ ID
System Antimicrobial Stewardship Pharmacist Manager*

Select Studies after January 2015

Additional studies

Dalton BR, Sabuda DM, Bresee LC, Conly JM. Use of an electronic medication administration record (eMAR) for surveillance of medication omissions: results of a one year study of antimicrobials in the inpatient setting. *PLoS One* 2015;10(4):e0122422. PMID: 25856373

Graber CJ, Jones MM, Chou AF, et al. Association of inpatient antimicrobial utilization measures with antimicrobial stewardship activities and facility characteristics of Veterans Affairs medical centers. *J Hosp Med* 2017;12(5):301-9. PMID: 28459897

Boyles TH, Naicker V, Rawoot N, et al. Sustained reduction in antibiotic consumption in a South African public sector hospital; Four year outcomes from the Groote Schuur Hospital antibiotic stewardship program. *S Afr Med J* 2017;107(2):115-8. PMID: 28220735

Li DX, Ferrada MA, Avdic E, et al. Sustained impact of an antibiotic stewardship intervention for community-acquired pneumonia. *Infect Control Hosp Epidemiol.* 2016;37(10):1243-6. PMID: 27498601

Levy Hara G, Kanj SS, Pagani L, et al. Ten key points for the appropriate use of antibiotics in hospitalised patients: a consensus from the Antimicrobial Stewardship and Resistance Working Groups of the International Society of Chemotherapy. *Int J Antimicrob Agents.* 2016 Sep;48(3):239-46. PMID: 27502752

Tamma PD, Avdic E, Li DX, et al. Association of Adverse Events With Antibiotic Use in Hospitalized Patients. *JAMA Intern Med.* 2017 Sep 1;177(9):1308-1315. PMID: 28604925

Stenehjem E, Hersh A, Buckel WR, et al. The SCORE Study – IDWeek 2016 platform presentation

DOING THE LOW HANGING FRUIT WELL

<https://www.ncbi.nlm.nih.gov/pubmed/26198369> IV to PO criteria

<https://www.ncbi.nlm.nih.gov/pubmed/27811579> Pneumonia

<https://www.ncbi.nlm.nih.gov/pubmed/28336761> Timely antibiotic starts

<https://www.ncbi.nlm.nih.gov/pubmed/28483315> PCN allergies

<https://www.ncbi.nlm.nih.gov/pubmed/28254470> PCN allergies

<https://www.ncbi.nlm.nih.gov/pubmed/28531289> ASB

<https://www.ncbi.nlm.nih.gov/pubmed/28431847> SAB

<https://www.ncbi.nlm.nih.gov/pubmed/28961942> rapid diagnostics