The State of Stewardship Research – Success and Remaining Gaps

ACUTE INPATIENT
SHEA ASRW – November 15, 2017

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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)

- More patients treated according to guidelines
- Shorter duration of antibiotic treatment
- Shorter length of stay
- Comparable risk of death

15%  
2 days  
1 day

RCT: Randomized Controlled Trial

“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.”


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

PRE-AUTHORIZATION vs POST-PRESCRIPTION REVIEW

**Preprescription Authorization (PPA)**
Clinical pharmacist or ID fellow

**Postprescription Review with Feedback (PPRF)**
Patients on antibiotics for at least 48 hours
2 ASP team members (e.g., ID pharmacist and physician)
In-person team meeting same time every weekday

Month 0
PPA
No PPRF
Firms A, B, C, D

Months 1 - 4
PPA
Firms A & B

Months 1 - 4
PPRF
Firms C & D

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

Month 0
PPA
No PPRF
Firms A, B, C, D

Months 1 - 4
PPA
Firms A & B

Month 5
Washout period

Months 6 - 9
PPRF
Firms A & B

Months 1 - 4
PPRF
Firms C & D

Months 6 - 9
PPA
Firms C & D

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.
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
- 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

### ADDITIONAL INTERVENTION AT HOSPITAL DISCHARGE

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention Cohort Random 50 of 300</th>
<th>Intervention Cohort Random 50 of 200</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Broad</strong></td>
<td>51%</td>
<td>40%</td>
</tr>
<tr>
<td><strong>Total Duration</strong></td>
<td>10 (7-13)</td>
<td>9 (6-13)</td>
</tr>
<tr>
<td><strong>CAP Duration</strong></td>
<td>8 (6-9)</td>
<td>6 (5-7)</td>
</tr>
<tr>
<td><strong>Skin Duration</strong></td>
<td>12 (8-15)</td>
<td>9 (7-12)</td>
</tr>
<tr>
<td><strong>UTI Duration</strong></td>
<td>10 (8-13)</td>
<td>9 (7-12)</td>
</tr>
<tr>
<td><strong>Appropriate</strong></td>
<td></td>
<td>52%</td>
</tr>
</tbody>
</table>

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

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

## PATIENT SAFETY OUTCOMES

<table>
<thead>
<tr>
<th>AKI Stage</th>
<th>Operations other than NOF repair, n (%)</th>
<th>NOF repair operations, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before 2012 policy</td>
<td>After 2012 policy</td>
</tr>
<tr>
<td>1</td>
<td>618 (9.86)</td>
<td>239 (8.03)</td>
</tr>
<tr>
<td>2</td>
<td>95 (1.52)</td>
<td>22 (0.74)</td>
</tr>
<tr>
<td>3</td>
<td>45 (0.72)</td>
<td>12 (0.4)</td>
</tr>
<tr>
<td>None</td>
<td>5509 (87.9)</td>
<td>2702 (90.8)</td>
</tr>
</tbody>
</table>

**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

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

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


INTERVENTION

WHO SHOULD PERFORM INTERVENTIONS?

**Generalists**


**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
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

Diagnostic Interventions


INTERVENTION

WHERE CAN WE EXPAND OUR REACH?

Telemedicine


Additional Countries

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


Upon Discharge


COMPARISON

WHICH INTERVENTION FIRST?

WHICH INTERVENTION TYPES HAVE HIGHEST YIELD?
- New program
- Established program

WHICH IMPLEMENTATION STRATEGY?
- Implementation science
Several recent reviews proposing antibiotic stewardship metrics


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

CONCLUSION

“Opportunity is missed by most people because it is dressed in overalls and looks like work.” - Thomas Edison

https://twitter.com/ShaunFrankson/status/834090407331926017

Alone we can do so little, together we can do so much

- Helen Keller

https://quotlr.com/image/4954

Let’s get started!
The State of Stewardship Research – Success and Remaining Gaps

ACUTE INPATIENT

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System Antimicrobial Stewardship Pharmacist Manager
Select Studies after January 2015

Additional studies


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/28336761  Timely antibiotic starts
https://www.ncbi.nlm.nih.gov/pubmed/28961942  rapid diagnostics