

IMPACT OF REQUIRED DURATION
OF THERAPY ON ANTIBIOTIC
UTILIZATION FOR SEPSIS

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DISCLOSURE

- Elizabeth Sandmann
- Potential conflicts of interest: none
- Sponsorship: none
- Proprietary information or results of ongoing research may be subject to different interpretations
- Speaker's presentation is educational in nature and indicates agreement to abide by the non-commercialism guidelines provided.

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LEARNING OBJECTIVES

1. Apply the results of the study to the correct population
2. Interpret the impact of required duration of antibiotic therapy in the sepsis population

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BACKGROUND

- The Centers for Disease Control and Prevention (CDC)
 - Core Elements of Hospital Antibiotic Stewardship
 - Implementing policies that will support optimal antibiotic use
- The Infectious Diseases Society of America (IDSA)
 - Stewardship program guidelines
 - Strongly recommend utilizing strategies to optimize antibiotic therapy
 - An accepted strategy is to require a duration of therapy at time of order

DeLitt TH. *Clinical Infectious Diseases*. 2007;44(2):159-77. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. CDC; 2014.

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STUDY RATIONALE

- Duration of therapy requirement on all antibiotic orders
 - Began on February 15, 2017
 - Prescribers must indicate length of therapy at the time of order input
- Sepsis population
 - Known use of antibiotics in this population
 - Overuse of the term sepsis to describe acutely ill patients

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DEFINITIONS

- **Apache IV score**
 - Assesses acuity of illness in ICU patients
 - Predicts risk of death and length of ICU stay
- **Multi-drug resistant (MDR)**
 - Bacteria resistant to ≥ 3 antibiotics in different classes
- **De-escalation**
 - Change in antibiotic regimen after first culture result
- **Difficult to treat pathogens**
 - Pathogens that may require longer duration of therapy
 - *Acinetobacter sp.*, ESBL, MRSA, *Pseudomonas sp.*, *Stenotrophomonas maltophilia*

ESBL = Extended-spectrum beta-lactamases
MRSA = Methicillin resistant *Staphylococcus aureus*

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DURATION DEFINITIONS

Antibiotic	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Vancomycin	X	X				
Cefepime		X	X	X	X	X

- Length of Therapy (LOT)
 - Vancomycin LOT = 2 days
 - Cefepime LOT = 5 days
- Cumulative Duration (CD)
 - Vancomycin LOT + Cefepime LOT = 7 days
- Total Duration (TD)
 - Continuous antibiotic days = 6 days

STUDY DESIGN

- Purpose**
 - Determine the impact of required duration of therapy on antibiotic utilization in septic patients
- Methods**
 - Randomized, retrospective chart review
 - Included 200 patients
- Time-frame**
 - Before implementation: March – June 2016 (n=100)
 - After implementation: March – June 2017 (n=100)

OUTCOMES

- Primary
 - Total duration of therapy
 - Cumulative duration of therapy
- Secondary
 - New *Clostridium difficile* infection within 30 days of admission
 - 30-day all cause readmission rates
 - In hospital all-cause mortality
 - Length of hospital stay
 - Length of ICU stay
 - Sepsis order-set utilization
 - Institution-wide days of therapy per 1,000 patient days

INCLUSION AND EXCLUSION CRITERIA

- Inclusion Criteria
 - 18 years of age or older
 - Diagnosis of sepsis upon admission
 - Received antibiotics for 24 hours or longer
- Exclusion Criteria
 - Immunocompromised receiving prophylactic antibiotics
 - Received more than one dose of IV antibiotics prior to admission
 - Discharge diagnosis of: osteomyelitis, endocarditis, diabetic foot infection, or cystic fibrosis

STUDY RANDOMIZATION

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    graph TD
      A[Patients with sepsis diagnosis (n=790)] --> B[Randomly assessed for inclusion (n=225)]
      B --> C[Included in final analysis (N=200)]
      B --> D[Excluded (n=25)]
      D --- E["Osteomyelitis (n=7)  
Immunocompromised (n=6)  
More than 1 dose prior to transfer (n=5)  
Diabetic foot infection (n=4)  
Prophylactic antibiotics (n=3)"]
      C --> F[2016 (n=100)]
      C --> G[2017 (n=100)]
    
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BASELINE DEMOGRAPHICS

Characteristic	2016 n=100	2017 n=100
Age, years		
Average	59.9	61.6
Range	18-91	24-98
Male, %	46	51
Comorbidities, %		
Asthma	12	12
COPD	24	27
ESRD	7	5
DM	31	30
CHF	13	17
Tobacco use	12	19
Illicit drug use	4	4
Antibiotic allergy, %	33	37

BASELINE DEMOGRAPHICS, CONTINUED

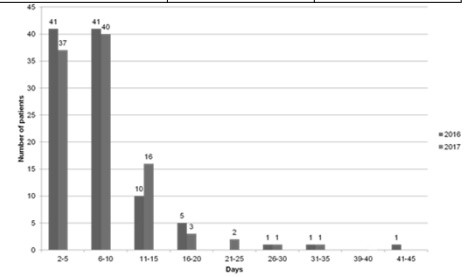
Characteristic	2016 n=100	2017 n=100
Apache IV Score, avg (range)	7.3 (1-35.9)	9.6 (0.8-39.3)
Apache IV Score, median (IQR)	4.6 (3.2-8.1)	6.3 (3.7-9.7)
Initial Lactic Acid Level, avg (range)	2.0 (0.5-7.4)	2.7 (0.6-11.6)
Initial Lactic Acid Level, median (IQR)	1.9 (1.3-2.5)	2.2 (1.3-3)
ID Physician Consult, %	5	17
ICU Patients, %	49	50
Mechanically Ventilated, %	13	18
Mechanical ventilation (MV) duration, days median IQR	2.3 1-7.3	5.3 2-7.5

IQR = Inner Quartile Range

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PRIMARY OUTCOME-TOTAL DURATION

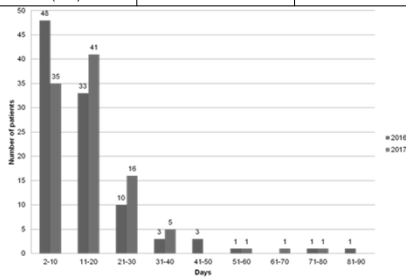
Outcome	2016 n=100	2017 n=100
Total Duration, days median (IQR)	6 (4-9)	7 (4-10)



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PRIMARY OUTCOME-CUMULATIVE DURATION

Outcome	2016 n=100	2017 n=100
Cumulative Duration, days median (IQR)	11 (7-17)	13 (8-20)



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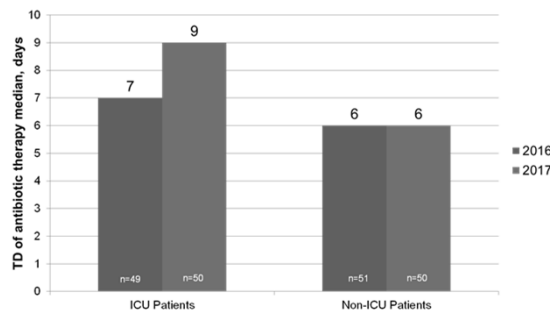
SECONDARY OUTCOMES

Measure	2016 n=100	2017 n=100
<i>Clostridium difficile</i> incidence	3%	1%
All-cause readmission within 30 days	13%	13%
Order set utilization	55%	58%
All-cause mortality	2%	8%
Inpatient LOS, days Median IQR	5.9 3.7-8.9	6.2 3.8-10.2
ICU LOS, days Median IQR	4.4 2.7-7.8	4.9 2.9-10.0

IQR = Inner Quartile Range
LOS = Length of Stay
ICU = Intensive Care Unit

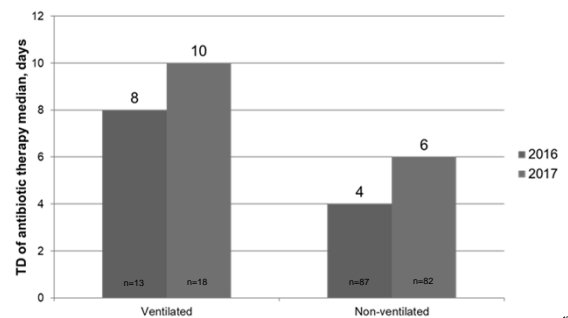
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PATIENT SETTING VS TOTAL DURATION

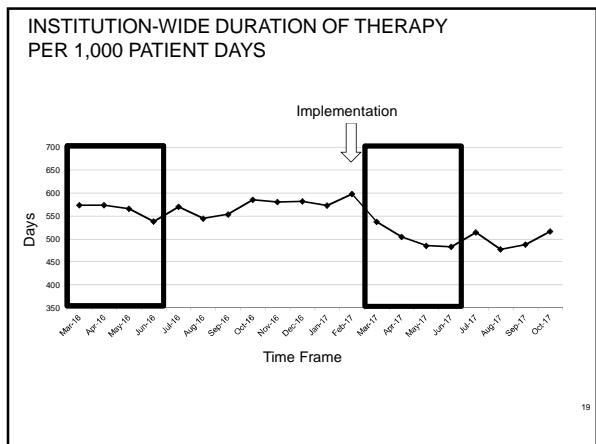


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VENTILATION STATUS VS TOTAL DURATION



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SUB-ANALYSIS

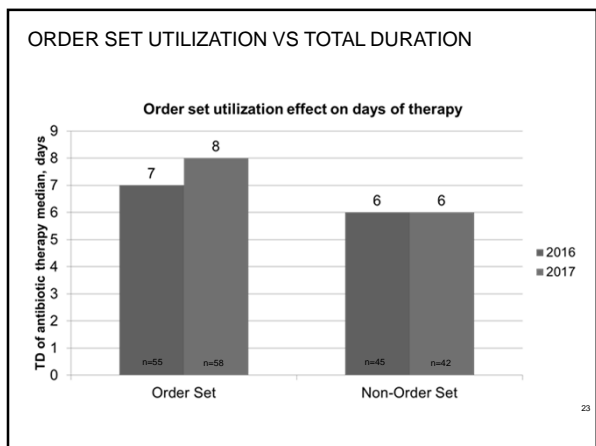
Microbiology Results

BACTERIAL GROWTH

Measure	2016 n=100	2017 n=100
Culture growth, n	41	39
Multi-drug resistant pathogens, n	12	10
De-escalation, n	35	27
Difficult to treat pathogens, n	9	10

SUB-ANALYSIS

Order Set Utilization



SUMMARY OF FINDINGS

Measure	Post-implementation
Total duration	=
Cumulative duration	=
Length of ICU stay	=
Length of stay	↑
Number of difficult to treat pathogens	↑
Number of cultures with growth	↓
Number of MDR's	↓

LIMITATIONS

- ID physician staffing changes- may have contributed to difference with ID consults
- Only sepsis order sets were counted for data collection
- Did not assess appropriateness of treatment
- Did not collect the prescriber's initial duration
- Did not obtain discharge infection diagnosis
- Did not differentiate truly septic patients

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FUTURE DIRECTIONS

- Impact of required duration of therapy in other populations including other infection types or order set utilization
- Duration of therapy for difficult to treat pathogens

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SUMMARY

- The strategy evaluated in this study is a guideline accepted implementation strategy to decrease the length of antibiotic therapy.
- Possible higher acuity in the post-implementation group
- Patients in 2016 had more positive cultures and MDR's
- The study found no differences in length of therapy after implementation of the duration of therapy requirement in the sepsis population.

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REFERENCES

1. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. *Clinical Infectious Diseases*. 2007;44(2):159-77.
2. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at: <http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>.

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ASSESSMENT QUESTION 1

1. The study discussed today applies to which of the following patients?
 - A. A 12-year-old female with septic shock secondary to pneumonia
 - B. A 25-year-old male with sepsis secondary to osteomyelitis
 - C. A 65-year-old female with pneumonia
 - D. A 55-year-old female with a history of hypertension and diabetes with a diagnosis of sepsis secondary to a urinary tract infection

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ASSESSMENT QUESTION 2

The study discussed today found which of the following:

- A. The duration of therapy was significantly **lower** after the implementation of the duration strategy
- B. The duration of therapy was significantly **higher** after the implementation of the duration strategy
- C. The duration of therapy was **unchanged** after the implementation of the duration strategy
- D. None of the above

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