Results. The mean age of subjects was 63 years old and 85% had no history of prior *C. difficile* infection. The most common intervention was de-escalation of antibiotics (46%). The post-implementation SIR was 0.55 and hospital-onset *C. difficile* rate was 13, both of which were significantly lower than predicted.

Conclusion. Targeting patients who have a history of or are newly diagnosed with *C. difficile* infection may decrease hospital-onset *C. difficile* rates.

Disclosures. **All Authors**: No reported disclosures

55. Impact of Testing Methodology and Reporting on Time to Preferred Antibiotic Therapy in Extended Spectrum Beta-Lactamase producing Enterobacteriaceae (ESBL-E) Bloodstream Infections

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Session: P-04. Antimicrobial Stewardship: Outcomes Assessment (clinical and economic)

Background. Harborview Medical Center (HMC) identifies organisms and an ESBL genotype (CTX-M) via Verigene® Gram-Negative Blood Culture Nucleic Acid Test (BC-GN). University of Washington-Montlake (UWML) uses matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) for organism identification directly from positive blood cultures and ceftriaxone results by Kirby Bauer disk diffusion (KB) are reported 18 hours later. No ESBL comment is reported at UWML. We aimed to determine whether the methodology in identification and reporting of ESBL-E from blood cultures between two hospitals has an impact on time to preferred therapy with a carbapenem antibiotic.

Methods. Retrospective observational study conducted at UWML and HMC in Seattle, WA between 1/10/2015 and 9/15/2020. Adult patients were eligible if they had ≥1 positive blood culture with an Enterobacteriaceae isolate resistant to ceftriaxone and were on antibiotic treatment. The primary outcome was the difference in time to preferred definitive therapy with a carbapenem antibiotic in patients an ESBL-E bloodstream infection (BSI) identified by Verigene® vs. MALDI-TOF MS/KB.

Results. A total of 199 patients were screened; 67 were included for UWML and 68 at HMC. The average time to initiation of a carbapenem antibiotic was 42 ±26.5 hours at UWML and 28 ±19.7 hours at HMC. A t-test detected a difference in time to preferred therapy between a Verigene® vs. MALDI-TOF MS/KB tested ESBL-E BSI [95% confidence interval (CI), 5.3-22.9]. The hazard ratio to carbapenem initiation for HMC is 1.73643 [95% CI, 1.1405-2.644].

Conclusion. A statistically significant difference in time to preferred definitive therapy among patients with an ESBL-E BSI processed by Verigene® was found compared to MALDI-TOF MS. The results suggest standardization in protocols between the UWML and HMC hospitals is warranted.

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56. High Frequencies of Adverse Drug Events with Intravenous vs Oral High-Dose Trimethoprim-Sulfamethoxazole: An Opportunity for Antibiotic Stewardship

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Trimethoprim-sulfamethoxazole: intravenous versus oral therapy

Session: P-04. Antimicrobial Stewardship: Outcomes Assessment (clinical and economic)

Background. Trimethoprim-sulfamethoxazole (TMP-SMX) is a high-bioavailability antibiotic associated with potentially serious adverse drug events (ADE). The objective of this study was to evaluate the safety of intravenous (IV) and oral (PO) high-dose TMP-SMX.

Methods. IRB-approved retrospective cohort of hospitalized patients from January 2016 to November 2020. Inclusion: ≥ 18 years old and > 72 hours of renally adjusted high-dose TMP-SMX defined as ≥ 5 mg/kg/day of TMP. Exclusion: prophylaxis. Endpoints during treatment: hyponatremia with sodium < 135 mmol/L, hyperkalemia with potassium > 5 mmol/L, serum creatinine increase of ≥ 0.3 mg/dL or 1.5-1.9 times from baseline, and fluid overload on physical exam. Descriptive and bivariate statistics were performed.

Results. Each group included 50 patients (Table 1). Intensive care unit patients comprised 82% IV TMP-SMX compared to 32% PO. Most common infection: respiratory tract 86% IV and 68.1% PO. Most common organisms were *Stenotrophomonas maltophilia* (52% IV and 18% PO) and *Pneumocystis jiroveci* (16.3% IV and 62% PO). Median (IQR) days of inpatient therapy: 6 (5-7.5) PO vs. 7.5 (6-11.3) IV. Median (IQR) days of total duration: 9 (6-21.5) PO vs. 12 (7.8-14) IV (p=0.93). IV group: 88% of patients received >1 liter of D5W daily. Median (IQR) liters of D5W daily was 1 (1-1.5). 56% had a diuretic added, and 38% had a diuretic dose increase. Majority of patients (78%) on IV were taking other oral medications. 100% patients experienced any adverse event with IV vs. 70% with PO (unAdjOR 2.43; 95% CI 1.89-3.13). Most common ADE in both groups: hyponatremia, hyperkalemia, and elevated creatinine. Hyponatremia: 92% with IV and 32% with PO (unAdjOR 24.44; 95% CI 7.50-79.68). Edema on physical exam, an ADE specific to IV TMP-SMX, was the third most common side effect in the IV group. Relative changes from baseline in sodium, potassium, and creatinine from those who experienced hyponatremia, hyperkalemia and elevated creatinine were listed in Table 2.

Table 1. Baseline and Clinical Characteristics

Characteristics	Oral, n = 50	Intravenous, n = 50	p-value
Age, years- median (IQR)	62 (45-71)	60.0 (48-69.5)	0.63
Male sex- n (%)	31 (62)	29 (58)	0.68
Length of stay, days- median (IQR)	11 (8.5-20.5)	29.5 (15.5-44)	<0.05
Past Medical History, n (%)			
Congestive Heart Failure	5 (10)	8 (16)	0.37
End Stage Renal Disease	3 (6)	8 (16)	0.2
Acute Kidney Injury on Admission	13 (26)	18 (36)	0.28
Diabetes Mellitus, type 1 or 2	17 (34)	16 (32)	0.83
Active Oncologic Disorder	10 (20)	6 (12)	0.28
Immunocompromised	31 (62)	9 (18)	<0.05
Concomitant Medications Known to Increase Potassium- n (%)	19 (38)	4 (8)	<0.05
Type of Therapy at TMP-SMX Initiation- n (%)			
Empiric	23 (46)	16 (32)	-
Definitive	27 (54)	34 (68)	-

Table 2. Adverse Effects

Adverse Drug Event	Oral, n = 50	Intravenous, n = 50	p-value
Any- n (%)	35 (70%)	50 (100%)	<0.05
Hyponatremia- n (%)	16 (32%)	46 (92%)	<0.05
Observed Sodium Decrease, mmol/L- median (IQR)	*8.5 (3.0-14)*	*5.0 (4.0-7.8)*	-
Hyperkalemia- n (%)	25 (50%)	19 (38%)	0.23
Observed Potassium Increase, mmol/L, median (IQR)	*1.2 (0.7-1.7)*	*1.7 (1.3-2.2)*	-
Elevated Creatinine- n (%)	21 (42%)	23 (46%)	0.69
Observed Creatinine Increase, mmol/L, median (IQR)	*0.8 (0.5-1.2)*	*1.0 (0.4-1.6)*	-
Neutropenia- n (%)	1 (2%)	4 (8%)	0.36
Thrombocytopenia- n (%)	3 (6%)	7 (14%)	0.32
Hypoglycemia- n (%)	10 (20%)	6 (12%)	0.28
Documented Skin Reaction- n (%)	0	3 (6%)	0.24
Edema on Physical Exam- n (%)	0	29 (58%)	<0.05
Pulmonary Edema on Imaging- n (%)	0	15 (30%)	<0.05

Conclusion. Patients on IV TMP-SMX therapy were more likely to experience an ADE compared to PO, likely driven by the high volume of free water. Most patients on IV TMP-SMX were on other PO medications, suggesting a missed stewardship opportunity for IV to PO conversion to reduce patient harm.

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57. Financial Impact of a Regional Antimicrobial Stewardship Cost Saving Initiative in a Large Integrated Healthcare System

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Session: P-04. Antimicrobial Stewardship: Outcomes Assessment (clinical and economic)

Background. A regional antibiotic stewardship program (ASP) within a large integrated healthcare system covering two, non-academic, tertiary care medical centers and an additional six community hospitals implemented multiple interventions to optimize antimicrobial therapy and reduce unnecessary hospital costs, such as transition to extended-infusion (EI) piperacillin/tazobactam (TZP), formulary restriction of antimicrobials, and antimicrobial stewardship clinical review. The purpose of this study was to evaluate the cost savings associated with these regional ASP initiatives.

Methods. This was a multicenter, retrospective, observational review of regional stewardship interventions across eight inpatient medical centers in Oregon. Data was collected from January 2019 to December of 2020. Cost savings associated with reduced TZP administrations was based on the duration of therapy for each encounter in adults who received TZP for >24 hours in 2020. The regional antimicrobial restriction policy was implemented in February 2020. Cost savings attributed to antimicrobial formulary restrictions and reduction in overall days of therapy/1000 patient days (DOT) were based on EPIC costs.

Results. The reduction in number of administrations with implementation of EI TZP resulted in $226,420 saved in 2020. $182,837 was saved due to decreased usage of restricted antimicrobial agents. An additional $433,341 was saved for overall antimicrobial costs due to 19,775 days reduction in overall DOT/1000 patient days.

Conclusion. A community-based regional ASP has resulted in substantial financial impact and identified areas for future cost savings within the region.

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58. Impact of Order-set Modifications and Provider Education on Broad-Spectrum Antibiotic Use in Patients Admitted with Community Acquired Pneumonia

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