Figure 3. Preferred route of antimicrobial therapy in relation to pathogen

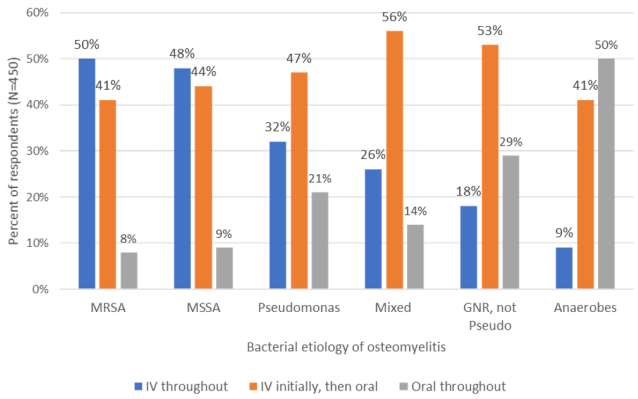

Chart shows percent of respondents who favor the indicated route of antimicrobial therapy (Y-axis) for various pathogens (X-axis), including methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA), *Pseudomonas,* mixed, Gram-negative bacilli (GNR), and anaerobes. Routes are shown as intravenous (IV) throughout (blue bars); IV initially, then oral (orange bars); and oral throughout (grey bars). There was no significant difference between route of therapy for MRSA and MSSA (P = 0.68). There was a significantly higher use of IV therapy throughout for *Staphylococcus aureus* (MRSA and MSSA) when compared to all other pathogens (P < 0.001), and a significantly higher use of oral therapy throughout for anaerobes when compared to all other pathogens (P < 0.001)

Figure 4: Duration of antimicrobial therapy in relation to extent of debridement

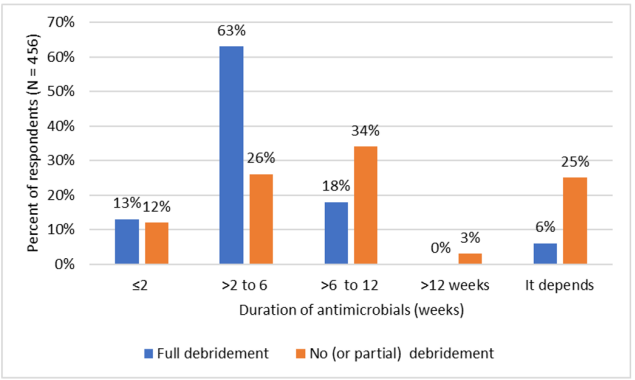

Chart shows percent of respondents (Y-axis) who favor the indicated duration of antimicrobial therapy, presuming full debridement (blue bars) or no (or partial) debridement (orange bars).

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1430. The Hidden Costs of Vancomycin Use During the Treatment of *Staphylococcus aureus* Bacteremia Concurrent with Acute Hematogenous Osteomyelitis

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Background. Current guidelines recommend the use of parenteral vancomycin for children with acute hematogenous osteomyelitis and concurrent *Staphylococcus aureus* bacteremia (SAB) due to Methicillin-Resistant *Staphylococcus aureus* (MRSA), despite vancomycin's slow bactericidal activity. This study explores the hidden costs of this approach.

Methods. Children with AHO and concurrent SAB, treated from 2009 to 2018, who had received vancomycin at some point during their treatment course were studied. Data collected included antibiotic susceptibilities; duration of bacteremia, blood culture results, duration of vancomycin; number of dose/interval changes; vancomycin trough and creatinine levels; rate of achieving target trough; use of other nephrotoxic agents; occurrence of acute kidney injury (AKI); and length of stay.

Results. 130 children diagnosed with AHO and concurrent SAB received vancomycin. Isolates were CR MSSA (3 or 2.3%), CR MRSA (5 or 3.8%), CS MSSA (35 or 26.9%), and CS MRSA (87 or 66.9%). Mean LOS was 14.6 days. 1,312 blood cultures were obtained (503 positive cultures and 809 negative cultures). Bacteremia persisted an average of 3.6 days. Target trough level (15–20 µg/mL) was achieved in 65 children (50%) within an average of 3.4 days of initial dosing. Attempts to reach therapeutic levels were abandoned in 32 children (24.6%) as MSSA was isolated before the trough. There were 319 vancomycin dose and/or interval changes, 1,192 serum creatinine levels, and 689 vancomycin trough levels obtained. Fourteen children (10.8%) experienced AKI. Additional nephrotoxicity exposure included: NSAIDs (127), IV contrast (100), loop diuretics (37), and aminoglycosides (11).

Conclusion. This study exposes and quantifies a substantial amount of resources devoted to dosing adjustments and serum level monitoring for vancomycin use in children with AHO and concurrent SAB. The cost differential in comparison to that of newer antibiotic alternatives is undermined by the effort to attain therapeutic target levels, resolve bacteremia, and address episodic AKI. If vancomycin is utilized, a deliberate approach should be taken to minimize risk of toxicity, including AUC/MIC ratio calculation, as opposed to therapeutic level monitoring, and avoid the concurrent use of other nephrotoxic agents.

Table 1. Parameters Associated with Vancomycin Treatment of 130 Children with AHO Concurrent with SAB

	n	Mean	Median	St. Dev	Min	Max
Length of Hospitalization (days)	130	14.6	11.5	10.7	3.9	63.1
Days in Intensive Care Unit	48	7.7	5.0	6.6	1	24
Duration of Bacteremia (days)	130	3.6	3	2.8	1	16
Number of Different Antibiotics Used†	130	3.2	3	1.3	2	9
Vancomycin Loading dose (mg/kg)	130	16.9	15.2	4.8	9	33
Vancomycin Dose/Interval Adjustments	77	3	2	2.5	1	11
Days Until Target Trough Reached	65	3.4	2.9	2.9	0.2	17.3
Serum Creatinine Levels	128	9.2	4	11.2	1	62
Serum Vancomycin Trough Levels	112	5.3	3	7.0	1	45
Highest Vancomycin Trough Level	112	21.6	17.1	16.6	1.3	85.3
Total Duration of IV Antibiotics (days)	130	17.0	10.9	17.0	1.2	82.4

†Including vancomycin

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1431. Comparison of Treatment Outcomes with Definitive Antibiotic Therapy and Empiric Antibiotic Therapy in Osteomyelitis

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Background. Definitive therapy for osteomyelitis (OM) is thought to be superior to empiric antimicrobial therapy; however, identifying causative pathogens is difficult.

Methods. This retrospective cohort study included patients treated with either definitive or empiric antimicrobial therapy for OM at VA St. Louis HCS between 1 January 2010 and 1 January 2018. Definitive antibiotic therapy was defined as a regimen tailored to susceptibilities of an organism(s) cultured from bone or deep tissue. The primary outcome was treatment failure, defined as a need for unplanned surgical intervention or re-initiation of antibiotic therapy for OM of the same anatomical site within 6-months after initial therapy was discontinued. Secondary outcomes included the incidence of acute kidney injury (AKI), *Clostridium difficile-associated* diarrhea (CDAD), and thrombocytopenia. Surgical intervention as part of initial therapy, presence of peripheral vascular disease (PVD), creatinine clearance < 50 mL/minute at initiation of therapy, receiving antibiotics at an extended care facility, age > 60 years, and receiving definitive antibiotics were included in a univariate analysis with variables with a $P < 0.2$ included in a multivariate logistic regression.

Results. There were 301 patients included; 179 in the definitive therapy group and 122 in the empiric therapy group. Baseline characteristics were similar among groups; however, more patients receiving definitive therapy had a bone biopsy compared with those treated with empiric therapy (58.1% (104/179) vs. 36.8% (45/122); $P < 0.05$). 33 percent (60/179) of patient treated with definitive therapy failed compared with 45% (55/122) treated with empiric therapy ($P = 0.109$). No significant differences were observed in secondary outcomes; however non-CDAD diarrhea occurred more in the empiric therapy group than definitive therapy group (3.9% (7/179) vs. 8.2% (10/122); $P > 0.05$). Receiving definitive therapy (OR 1.43, CI 0.89–2.313; $P = 0.138$) and presence of PVD (OR 1.34; CI 0.823–2.197; $P = 0.238$) were included in the multivariate logistic regression, but neither were independently associated with failure.

Conclusion. Definitive antibiotic therapy was not associated with a significant decrease in treatment failure.

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1432. Estimating the Incubation Period of *Salmonella* Urinary Tract Infection (UTI) Using Foodborne Outbreak Data

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Background. Urinary tract infections (UTI) are common bacterial infections that may occur as a part of foodborne outbreaks. Salmonella, a less common cause of UTI, has been identified during foodborne outbreaks, but the epidemiology and pathogenesis are poorly understood.

Methods. PulseNet, the United States national molecular subtyping network for foodborne disease surveillance, was used to identify Salmonella isolates associated with outbreaks from 2004 to 2013 containing at least one urine and one stool isolate in which the duration was ≤1 year and a food vehicle was suspected or confirmed. We standardized isolation dates across outbreaks by calculating the mean date for stool isolation within an outbreak and subtracting this from the date of each stool/urine

isolate in that outbreak. A linear-mixed model with random effect for stool/urine was used to estimate the difference in incubation periods between stool/urine isolates. We also surveyed patients from a 2012 Salmonella Cubana outbreak with many urinary isolates and associated with sprouts, to ask about diarrhea, UTI symptoms, diagnosis, and treatment. Descriptive statistics were calculated.

Results. Urine isolates had later isolation dates than stool isolates for 102 of the 110 outbreaks identified. The average difference between stool and urine isolates was 10.6 days (95% CI: 6.0, 15.2). Seven women from the Salmonella Cubana outbreak were reached. All women were diagnosed with either a UTI (6/7 = 86%) and/or kidney infection (2/7 = 29%) and were treated with antibiotics (7/7 = 100%). All six women completing the survey reported multiple signs and/or symptoms including frequency, urgency, dysuria, and hematuria with only two women reporting diarrhea prior to UTI.

Conclusion. Salmonella UTI seen during foodborne outbreaks are symptomatic foodborne infections not associated with diarrhea and appear to have a longer incubation period than Salmonella gastrointestinal (GI) illness. A 13- to 16-day incubation period for Salmonella UTI may be more appropriate, calculated by adding a 3- to 4-day GI illness incubation period plus delay in obtaining a stool isolate. Foodborne UTI investigation may need to change as the current method of obtaining a food history for the 6–72 hours prior to illness does not accurately reflect the incubation period for Salmonella UTI.

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1433. Predictive Models for Antibiotic Coverage of Gram-Negative Urinary Tract Infections

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Background. Providers use institutional recommendations, national guidelines, and antibiograms to decide on empiric antibiotics. As local antibiograms are most effective after organisms are known, we sought to use local microbiology and clinical data to develop predictive models for antibiotic coverage prior to identifying the organism. We focused on Gram-negative organisms as they are common urinary pathogens and are often the cause of sepsis originating in the urinary tract. As such, they are important to cover in hospitalized patients with urinary tract infections (UTI).

Methods. Hospitalized patients, with a diagnosis of UTI and a positive urine culture in the first 48 hours were included. Gram-positive organisms, yeast, and cultures without susceptibilities were excluded. Unknown susceptibilities were filled in using expert-derived rules. Clinical information from electronic health record (EHR) data were extracted on each patient. Penalized logistic regression with 10-fold cross validation was used to develop final models for coverage for five antibiotics (cefazolin, ceftriaxone, ciprofloxacin, cefepime, piperacillin–tazobactam). Final models were chosen based on their discrimination, calibration, and number of predictors, and then tested on a held-out validation dataset.

Results. Included were 5,096 patients (80% training; 20% validation). Coverage ranged from 65% for cefazolin to 90% for cefepime. Positive blood cultures were present in 544 (11%) with 388 (71%), including a urinary pathogen. In the first 24 hours, 2329 (46%) were hypotensive, 2179 (43%) had a respiratory rate > 22, 2049 (40%) had a WBC > 12, 1079 (21%) were febrile, and 584 (11%) required ICU care. Final model covariates included demographics, antibiotic exposure, prior resistant pathogens, and antibiotic allergies. The five predictive models had a point-estimate for the area under the ROC on the validation set that ranged from 0.70 for ciprofloxacin to 0.73 for ceftriaxone.

Conclusion. In this cohort of moderate to high acuity hospitalized patients with Gram-negative urinary pathogens, we used EHR data to develop 5 models that predict antibiotic coverage which could be used to support empiric prescribing. These models performed well in a held-out validation set.

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

1434. Risk Factors for Community-Acquired Urinary Tract Infections Caused by Extended-Spectrum β-Lactamase (ESBL) Producing *Escherichia coli* in Children: A Case–Control Study

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Background. In recent years, there has been an increasing incidence of community-acquired urinary tract infections (UTI) caused by extended-spectrum β-lactamase (ESBL) producing *Escherichia coli*. However, the risk factors of ESBL-producing bacteria in community-acquired (CA)-UTI in children in the USA remain unclear.

Methods. A retrospective case–control study of UTI due to CA-ESBL-producing *E. coli* during a 5-year period (2011–2016) was performed. Control cases of non-ESBL-producing *E. coli* UTI were matched by age, gender, and year of infection. Medical records were manually reviewed to collect data for potential risk factors for ESBL-positive infection.

Results. A total of 111 patients with ESBL-producing *E coli* UTI and 103 control patients were included. The proportion of ESBL-producing *E coli* UTI ranged from 7% to 15% per year. The median age was 4 years with female predominance (84%). The ESBL group was predominantly African American (32%) followed by patients of Middle Eastern (ME) ethnic background (31%). Risk factors by univariate analysis were vesicoureteral reflux (VUR): (20.9 ESBL group vs. 6% controls; $P = 0.002$), prior antibiotic usage in the previous 3 months (including β-lactams), prior UTI (last 3 months), recent hospitalization (last 3 months) and ME ethnic background. However, multivariate analysis showed that only prior antibiotic usage ($P = 0.001$) and ME ethnic background ($P < 0.001$) remained statistically significant. 18% (11/60) of patients exposed to prior antibiotic use in the ESBL group were on long-term antibiotic prophylaxis for VUR.

Conclusion. Risk factors for CA-ESBL-producing *E coli* UTI in children were: (1) antibiotic usage within the previous 3 months and (2) ME background. Prior antibiotic usage as a risk factor reinforces the need for judicious use of antibiotics. The high percentage of patients in this group (18%) receiving long-term antibiotic prophylaxis for VUR warrants further study as this practice may increase the prevalence of ESBL-producing infections in a population at high risk for UTI. The increased risk among children of ME ethnic background warrants further study to evaluate possible additional associated risk factors such as recent international travel or contact with international travelers.

Table 1: Demographic Information and Laboratory Values of Children with ESBL-Producing *E. coli* UTI compared to Controls

	ESBL-producing *E. coli* (n=109)	Non ESBL-producing *E. coli* (n=103)	*p-value*
Demographics[1]			
Median Age in years (range)	4 (1 mo-18 yrs, n=109)	4 (1 mo-18 yrs, n=103)	
Female Gender	84% (n=92)	88% (n=91)	
Ethnic Background			
Caucasian	17% (n=19)	17% (n=18)	
African American	32% (n=35)	49% (n=50)	
Hispanic	16% (n=17)	22% (n=23)	
Middle Eastern	31% (n=34)	10% (n=10)	
Other	4% (n=4)	2% (n=2)	
Laboratory Value (mean)			
WBC (10^3/mm^3)	14.5 (n=88)	14.3 (n=58)	0.340
Hemoglobin (g/dL)	11.9 (n=88)	11.4 (n=58)	0.340
Hematocrit (%)	34.9 (n=88)	33.7 (n=58)	0.212
Platelets (10^3/ml)	318.5 (n=88)	318.2 (n=58)	0.775
BUN (mg/dL)	13.4 (n=63)	11.6 (n=46)	0.437
Creatinine (mg/dL)	0.5 (n=62)	1.6 (n=46)	0.028
CRP (mg/dL)	81.5 (n=23)	60.8 (n=20)	0.661

ESBL: Extended spectrum β-lactamase; CRP: C-reactive protein
Denominators for percentages noted in header row of table
[1]All patients were case-controlled by age, sex, and year of UTI.

Table 2: Antimicrobial Resistance of ESBL-Producing *E. coli* compared to Non ESBL-Producing *E. coli*

Resistance to Antimicrobial Agents	ESBL-producing *E. coli*	Non ESBL-producing *E. coli*
Amikacin	0%	0%
Ampicillin/Sulbactam	92%	22%
Ampicillin	100%	63%
Aztreonam	81%	0%
Cefazolin	100%	0%
Cefepime	88%	0%
Cefoxitin	86%	0%
Ceftriaxone	100%	0%
Ciprofloxacin	73%	5%
Ertapenem	2%	0%
Gentamicin	36%	5%
Imipenem	0%	0%
Meropenem	0%	0%
Nitrofurantoin	1%	0%
Piperacillin/Tazobactam	75%	17%
Tobramycin	39%	2%
Trimethoprim/Sulfamethoxazole	72%	25%

Table 3: Univariate Analysis of Risk Factors for ESBL-Producing *E. coli* UTI compared to Controls

Risk Factors	ESBL-producing *E. coli*	Non ESBL-producing *E. coli*	*p-value*
VUR	20.9% (n=23)	5.9% (n=6)	0.002
Prior Antibiotic use (last 3 months)	54.5% (n=60)	14.6% (n=15)	<0.001
Prior β-lactam use (last 3 months)	30.9% (n=34)	8.8% (n=9)	<0.001
Prior UTI (last 3 months)	23.6% (n=26)	5.9% (n=6)	<0.001
Prior Hospitalization (last 3 months)	24.5% (n=27)	10.1% (n=10)	0.007
Prior Surgery (last 3 months)	7.3% (n=8)	3.9% (n=4)	0.378
Intraurinary tract intervention	4.6% (n=5)	3.9% (n=4)	1.000
Middle Eastern ethnic background	30.6% (n=34)	9.8% (n=10)	<0.001
GU Abnormalities[1]	22.2% (n=26)	30.8% (n=26)	0.182
Intraurinary tract device[2]	11.8% (n=13)	6.9% (n=7)	0.247
Functional abnormalities			
Neurogenic Bladder	7.9% (n=7)	1.4% (n=1)	0.077
Voiding Dysfunction	3.5% (n=3)	5.4% (n=4)	0.706
Neurogenic Bladder and voiding dysfunction	9.9% (n=9)	12.5% (n=15)	0.632
Constipation	10.9% (n=10)	19.5% (n=17)	0.143
Immunosuppression	8.2% (n=9)	4.9% (n=5)	0.412

[1]GU abnormalities included hydronephrosis, ureteropelvic junction obstruction, duplex collection system, duplex kidney, other renal/genitourinary tract abnormalities
[2]Intraurinary tract device included use of clean intermittent catherization and presence of any intraurinary tract stents