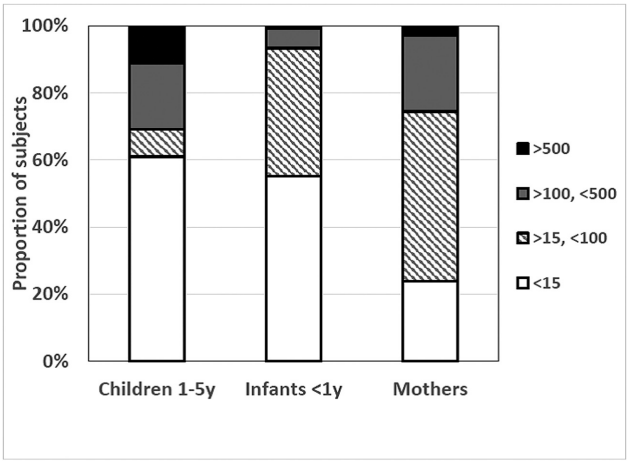

Figure 2. Proportion of subjects with detected ZIKV NAb by level and cohort at enrollment

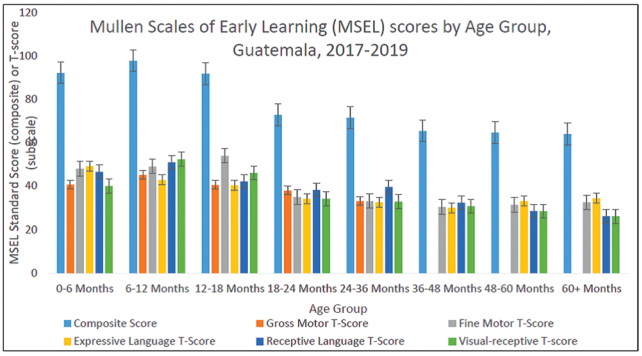

Figure 3. Mullen Scale of Early Learning (MSEL) composite (Standard score) and subdomain (T-score) results in infants and children by age.

Note: Composite score standard norm is 100, while subdomain standard norm is 50.

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847. The Effect of Antimicrobial Administration on Blood Culture Positivity in Patients with Severe Manifestations of Sepsis

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Background. Current guidelines recommend obtaining blood cultures prior to antimicrobial therapy in patients with sepsis. Administering antimicrobials immediately without waiting for blood cultures could potentially decrease time to treatment and improve outcomes, but it is unclear the degree to which this strategy impacts diagnostic yield.

Methods. We performed a patient-level, single-arm, diagnostic trial. Seven urban emergency departments affiliated with academic medical centers across Canada and the United States participated in the study. Adults ≥18 years of age presenting to the emergency department with evidence of severe manifestations of sepsis, including a systolic blood pressure <90 mmHg and/or a serum lactate ≥4 mmol/L were included. Study participants had 2 sets of blood cultures drawn prior to and immediately following antimicrobial administration. The primary outcome was the difference in blood culture pathogen recovery rates before and after administration of antimicrobial therapy.

Results. Of the 3,164 participants screened, 325 were included in the study (mean age, 65.6 years; 63.0% men) and had repeat blood cultures drawn after the initiation of antimicrobial therapy (median time of 70 minutes, IQR 50 to 110 minutes). Pre-antimicrobial blood cultures were positive for one or more microbial pathogens in 102/325 (31.4%) patients. Fifty-four participants (52.9%) had matching blood culture results after initiation of antimicrobial treatment. The absolute difference in pathogen recovery rates was 14.5% ([95% CI 8.0 to 21.0%]; $P < 0.0001$) between pre- and post-antimicrobial blood cultures. Results were consistent in an analysis of the per-protocol population (absolute difference, 13.3% [95% CI 6.1 to 20.4%]; $P < 0.0001$). Including the results of other microbiological cultures done as part of routine care, microbial pathogens were recovered in 69 of 102 (67.7%) participants (absolute difference, 10.2% [95% CI 3.4 to 16.8%]; $P < 0.0001$).

Conclusion. Among patients with severe manifestations of sepsis, the administration of empiric antimicrobial therapy significantly reduces the yield of pathogen recovery when blood cultures are drawn shortly after treatment initiation.

Figure 1 – Patient flow

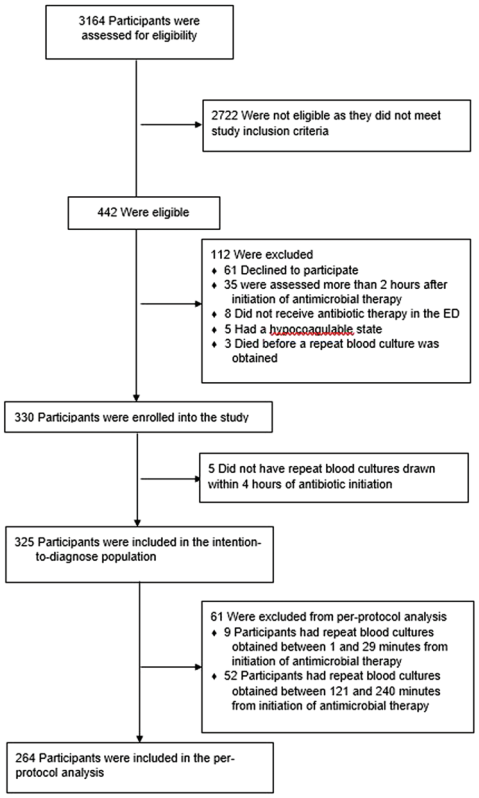

Figure 2– Difference in blood culture positivity rates between pre and post-antimicrobial blood cultures[1]

Time post-ABx administration	Total patients	Blood culture (+) pre-ABx	Blood culture (+) post-ABx	Absolute difference in positivity rates[2] [95% CI[3]]
30-60 minutes	124	45 (36.3%)	29 (23.4%)	12.9% [1.6-24.2]
61-120 minutes	140	35 (25.0%)	16 (11.4%)	13.6% [4.7-22.5]
121-240 minutes	52	21 (40.4%)	9 (17.3%)	23.1% [6.2-39.9]
Intention-to-diagnose population[4]	325	102 (31.4%)	54 (16.5%)	14.8% [8.3-21.2]
Per-protocol population[5]	264	80 (30.3%)	45 (17.0%)	13.3% [6.1-20.4]

[1]Compared to pathogens recovered in the pre-antimicrobial blood culture, excluding contaminants;
[2]Difference in blood culture positivity rates between pre and post-antimicrobial blood cultures;
[3]Exact binomial confidence intervals;
[4]Includes 9 patients who had their post-antimicrobial blood culture obtained within 30 minutes of initiation of antimicrobial therapy
[5]Defined as patients who had repeat blood cultures between 30 and 120 minutes from initiation of antimicrobial therapy

Table 1 – Patient characteristics

Characteristic	Blood Culture Negative[1] n= 223	Blood Culture Positive[1] n= 102	All n= 325
Mean age in years (SD)	65.4 (17.9)	66.1 (17.2)	65.6 (17.7)
Male sex, n (%)	141 (63.2)	63 (62.4)	204 (63.0)
Comorbidities, n (%)			
Hypertension	72 (32.3)	39 (38.2)	111 (34.3)
Diabetes Mellitus	57 (25.6)	31 (30.4)	88 (27.1)
Cancer	53 (23.8)	23 (22.6)	76 (23.4)
Chronic obstructive pulmonary disease	28 (12.6)	13 (12.8)	41 (12.6)
Atrial fibrillation	23 (10.3)	14 (13.7)	37 (11.4)
Congestive heart failure	21 (9.4)	16 (15.7)	37 (11.4)
Hepatitis C Virus	23 (10.3)	9 (8.8)	32 (9.8)
Intravenous drug use	19 (8.5)	8 (7.8)	27 (8.3)
Cerebral vascular disease	20 (9.0)	6 (5.9)	26 (8.0)
Coronary artery disease	14 (6.3)	12 (11.8)	26 (8.0)
Chronic kidney disease	15 (6.7)	10 (9.8)	25 (7.7)
Human Immunodeficiency Virus	13 (5.8)	3 (2.9)	16 (4.9)
Median Charlson Comorbidity score (IQR[2])	1 (1, 3)	1 (1, 3)	1 (1, 3)
Characteristics in the Emergency Department, n (%)			
Heart Rate > 90 beats per minute	185 (83.0)	82 (80.4)	267 (82.2)
Respiratory Rate > 20 per minute	135 (60.5)	61 (59.8)	196 (60.3)
Temperature >38°C or <36°C	106 (47.5)	61 (59.8)	167 (51.4)
White Blood Cell >12 or <4, x1,000/mL	177 (79.4)	78 (76.5)	255 (78.5)
Lactate ≥4.0 mmol/L	137 (61.4)	65 (63.7)	202 (62.2)
Systolic BP <90mmHg	127 (57.0)	57 (55.9)	184 (56.6)
Respiratory failure[3]	20 (8.9)	20 (19.6)	40 (12.3)
Ionotropic Support	33 (14.8)	18 (17.6)	51 (15.7)
Source of Infection, n (%)			
Respiratory	85 (38.1)	22 (21.6)	107 (32.9)
Genito-Urinary	31 (13.9)	27 (26.5)	58 (17.8)
Gastrointestinal	34 (15.2)	21 (20.6)	55 (16.9)
Skin and Soft Tissue	26 (11.7)	15 (14.7)	41 (12.6)
Other	6 (2.7)	9 (8.8)	15 (4.6)
Unknown	41 (18.4)	8 (7.8)	49 (15.1)
Initial Antimicrobial Regimen[4], n (%)[*,**]			
Piperacillin-tazobactam	74 (33.2)	36 (35.3)	110 (33.8)
Piperacillin-tazobactam + Vancomycin	27 (12.1)	19 (18.6)	46 (14.2)
Piperacillin-tazobactam + Other Antibiotic	29 (13.0)	12 (11.8)	41 (12.6)
3rd generation cephalosporin + azithromycin	34 (15.2)	5 (4.9)	39 (12.0)
3rd generation cephalosporin	24 (10.8)	13 (12.8)	37 (11.4)
Carbapenem ± Vancomycin	6 (2.7)	9 (8.8)	15 (4.6)
Fluoroquinolone ± Vancomycin	9 (4.0)	3 (3.0)	12 (3.7)
Other Regimen	20 (9.0)	5 (4.9)	25 (7.7)

[1]Blood culture obtained prior to administration of empiric antimicrobial therapy; specimens growing contaminant(s) only were treated as negative;
[2]Interquartile range;
[3]Respiratory failure was defined as requiring non-invasive ventilation (BiPAP) or invasive ventilation (endotracheal ventilation)
[4]See the Supplementary Appendix for a complete list of all antimicrobial regimens used
*p-value <0.05, **< 0.01, between groups; calculated by Fisher's Exact Test.

Table 2 – Relationship between timing of post-antimicrobial blood culture and pathogen recovery rates[1]

Time Between Antimicrobials and Repeat Blood Cultures	Positive Blood Culture Pre-Antimicrobials (n)	Positive Blood Culture Post-Antimicrobials (n)	Post-Antimicrobial Blood Culture Recovery Rate[2] (95% CI[3])	Initial Pathogen Recovered from Microbiological Cultures at Other Anatomic Sites[4] (n)	Overall Pathogen Recovery Rate Post Antimicrobials[5] (95% CI[3])
30 – 60 minutes	45	29	64.4% (48.8, 78.1)	6	77.8% (62.9, 88.8)
61 – 120 minutes	35	16	45.7% (28.8, 63.4)	4	57.1% (39.4, 73.7)
121 – 240 minutes	21	9	42.9% (21.8, 66.0)	5	66.7% (43.0, 85.4)
Intention-to-diagnose population[6]	102	54	52.9% (42.8, 62.9)	15	67.7% (57.7, 76.6)
Per-protocol population[7]	80	45	56.3% (44.7, 67.3)	10	68.8% (57.4, 78.7)

[1]Compared to pathogens recovered in the pre-antimicrobial blood culture, excluding contaminants
[2]Defined as the percentage of positive blood cultures after antimicrobial administration relative to the number of positive blood cultures prior to antimicrobial administration;
[3]Exact binomial confidence intervals;
[4]Pre-antimicrobial blood culture pathogen recovered from other microbiological cultures done as part of routine care, obtained either pre or post antimicrobial administration, including urine, sputum, and wound cultures;
[5]Defined as the percentage of pathogens recovered from positive blood cultures after antimicrobial administration as well as from other sources of microbiological data relative to the number of positive blood cultures prior to antimicrobial administration;
[6]Includes 9 patients who had their post-antimicrobial blood culture obtained within 30 minutes of initiation of antimicrobial therapy
[7]Defined as patients who had repeat blood cultures between 30 and 120 minutes from initiation of antimicrobial therapy

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

848. Low-Bioavailability vs. High-Bioavailability Oral Antibiotics for the Definitive Treatment of Enterobacteriaceae Bacteremia from Suspected Urine Source in Hospitalized Veterans

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Background. Limited and conflicting data exist evaluating low-bioavailability oral antibiotics (LOW) for definitive treatment of Enterobacteriaceae bacteremia (EB), and existing dogma limits their use. We compared outcomes for EB from a suspected urine source with LOW vs. high-bioavailability oral antibiotics (HIGH).

Methods. This was a retrospective cohort study across Veterans Affairs hospitals from 2006 to 2015. Inclusion criteria were monomicrobial EB and matching urine culture; receipt of active, empiric parenteral antibiotic(s); and conversion to a single oral LOW or HIGH between treatment day 2 and 6. Exclusion criteria were EB in the previous year, prior urologic abscess, or chronic prostatitis. HIGH included fluoroquinolones or trimethoprim-sulfamethoxazole. LOW included oral β-lactams. The primary outcome was all-cause 30-day mortality or recurrent EB. Patients were weighted using propensity-based overlap weights to make the groups more similar to each other at baseline. Log binomial regression models were used to estimate relative risks and risk differences.

Results. A total of 4,090 patients met inclusion criteria with 955 LOW and 3,135 HIGH. The median days of parenteral antibiotics before conversion to oral antibiotics were 4 (IQR 3, 5) in LOW and 4 (IQR 3, 4) in HIGH. The composite primary outcome occurred in 42 (4.4%) LOW and 94 (3.0%) HIGH. The adjusted relative risk (aRR) of the composite primary outcome with LOW was 1.28 (95% CI 0.86–1.89; risk difference [RD] 0.9%). Recurrent EB within 30-days occurred in 14 (1.5%) LOW and 12 (0.4%) HIGH (aRR 3.24, 95% CI, 0.46–22.8; RD 1.0%). Thirty-day mortality occurred in 29 (3.0%) LOW and 82 (2.6%) HIGH (aRR 1.0, 95% CI, 0.66–1.52; RD 0%). Similar outcomes were observed at 90 days.

Conclusion. There was no difference in the composite outcome of 30-day mortality and recurrent bacteremia comparing hospitalized patients who received LOW vs. HIGH for the definitive treatment of EB from a suspected urine source. While there was a nonsignificantly higher risk of 30-day recurrent EB with LOW, the absolute risk and risk difference were small, suggesting that definitive therapy with LOW may be considered. Future evaluation is needed to better understand risk factors for recurrent EB and which patients may fail LOW.

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

849. Reduced CIED Infections with an Antibacterial Envelope: Microbiologic Analysis of the WRAP-IT Study

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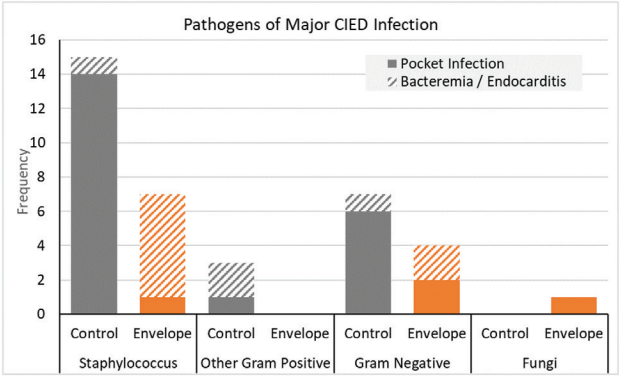
Background. Cardiovascular implantable electronic device (CIED) infections are associated with significant morbidity, mortality, and cost. There is limited evidence on antibiotic prophylactic strategies to prevent CIED infection. Recently, the TYRX Envelope, which elutes a combination of rifampin and minocycline for a minimum of 7 days, was shown to significantly reduce major CIED infections in the WRAP-IT trial. We sought to characterize the pathogens among patients who experienced an infection in the current era.

Methods. All patients undergoing CIED replacement, upgrade, revision, or *de novo* cardiac resynchronization therapy (CRT-D) received standard of care antibiotic prophylaxis and were randomized 1:1 to receive TYRX or not. The primary endpoint was major CIED infection within 12 months of the procedure. Major infection was defined as an infection resulting in (1) system extraction or revision, (2) long-term suppressive antibiotic therapy, or (3) death. Data were analyzed using the Cox proportional hazards regression model.

Results. A total of 6,983 patients were randomized worldwide with 3,495 randomized to receive an envelope and 3,488 randomized to the control. At 12 months, 25 major infections (0.7%) were observed in the envelope group and 42 major infections (1.2%) in the control group, resulting in a 40% reduction of major infections (HR: 0.60, 95% CI: 0.36–0.98, $P = 0.04$). Of 63 infections assayed, causative pathogens were identified in 36 infections whereas cultures were negative in 27 cases. Staphylococcus species ($n = 22$) were the predominate pathogens and a 53% reduction was observed with the use of TYRX (Figure 1). Moreover, there was only 1 CIED pocket infection with Staphylococcus species in the envelope group compared with 14 pocket infections in the control group. A comparison of timing of infection in the envelope group showed the presence of 11 endocarditis/bacteremia infections at 103 ± 84 days compared with 14 pocket infections presenting at 70 ± 78 days from the procedure.

Conclusion. In this large randomized trial, the use of the TYRX Envelope containing rifampin and minocycline resulted in a significant reduction of major CIED infections and was effective against staphylococcal species, which are the predominant cause of pocket infections.



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

850. Outcomes of Patients Discharged on Parenteral Ceftriaxone Compared with Oxacillin or Cefazolin in Methicillin-susceptible Staphylococcal aureus (MSSA) Bloodstream Infections

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