Figure. De-escalation, escalation, and unchanged outcomes among 39,226 antibiotic admissions.

N (%)		N Antibiotics		
		Lower	Same	Higher
Rank	Lower	10551 (27)	1269 (3)	146 (<1)
	Same	1218 (6)	19703 (50)	3048 (8)
	Higher	110 (<1)	732 (2)	1349 (3)

Note: De-escalation = green, Unchanged=yellow, Escalation=orange

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

961. The Role of Negative Methicillin-Resistant *Staphylococcus aureus* Nasal Surveillance Swabs in Predicting the Need for Empiric Vancomycin Therapy

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Session: 123. Stewardship Tools
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Background. The role of MRSA nasal surveillance swabs in guiding decisions about need for subsequent vancomycin therapy is unclear. Our objectives were to (1) determine the likelihood that patients with negative MRSA nasal swabs went on to develop MRSA infections during the same hospitalizations to assess if vancomycin therapy could be avoided once the nasal swab result returns negative, (2) assess days of vancomycin that potentially could be avoided, and (3) identify risk factors for having a negative MRSA nasal swab and developing an MRSA infection during the hospital stay.

Methods. This retrospective cohort study was conducted at six intensive care units (ICUs) at a tertiary care hospital in Baltimore from December 2013 to June 2015. MRSA nasal swabs are obtained at the time of admission and weekly thereafter for all ICU patients. The negative predictive value (NPV), defined as the ability of a negative MRSA nasal screening test to correctly predict no subsequent MRSA infection during the hospital stay, was calculated, accounting for the 3-day turnaround time of MRSA nasal surveillance swabs. Days of vancomycin therapy started or continued after 3 days from the first negative MRSA nasal swab were determined by chart review. A matched case–control study was performed to identify risk factors for patients with negative MRSA surveillance cultures who subsequently developed MRSA infections.

Results. Of 11,441 MRSA-nasal swab negative patients, the proportion of subsequent incident MRSA infections was 0.2%. Negative MRSA surveillance swabs had an NPV of 99.4% (95% CI 99.1–99.6%). Among 4,091 MRSA-negative patients receiving vancomycin, vancomycin was started or continued after 3 days since the first MRSA-negative nasal swab in 1,434 patients (35%), translating to 7,377 potentially avoidable vancomycin days. The matched case–control analysis did not identify risk factors associated with subsequent MRSA infection.

Conclusion. At our institution with robust infection control practices and low nosocomial MRSA transmission rates, patients with negative MRSA nasal swabs have a very low likelihood of subsequent MRSA infection during hospitalizations. MRSA nasal swabs can provide useful information when determining whether to initiate or stop empiric vancomycin.

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

983. Doing the Same with Less: A Randomized, Multinational, Open-Label, Adjudicator-Blinded Trial of an Algorithm vs. Standard of Care to Determine Treatment Duration for Staphylococcal Bacteremia

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Session: 132. Advances in Management of Bacteremia and Sepsis
Friday, October 6, 2017: 10:30 AM

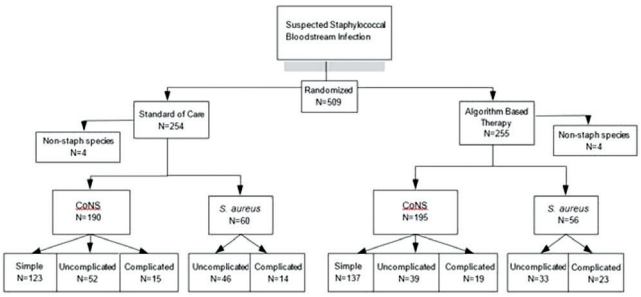
Background. The appropriate duration of antibiotics for staphylococcal bloodstream infection (BSI) is unknown. An algorithm to identify patients with staphylococcal BSI who can be safely treated with shorter courses of therapy would improve care and reduce total antibiotic use.

Methods. Adult patients with staphylococcal BSI were randomized to treatment based on algorithm-based therapy (ABT) or to standard of care (SOC). Co-primary outcomes were clinical success, as determined by a blinded Adjudication Committee, and serious adverse event (SAE) rates. The prespecified secondary outcome measure was antibiotic days by treatment group, among patients without complicated BSI. Prespecified durations of therapy in ABT were: *S. aureus* BSI (SAB): uncomplicated: 14 days; complicated: 4–6 weeks. Coagulase-negative staphylococci BSI (CoNSB): simple (1 positive blood culture) (0–3 days), uncomplicated (>1 positive blood culture) (5 days), complicated (7–28 days). Outcomes were compared using intention-to-treat principles. The target sample size was 500 patients, to ensure 90% power for establishing noninferiority within a margin of 15%.

Results. Between April 2011 and March 2017, 509 adults with suspected staphylococcal BSI at 16 sites in the US and Spain were randomized to ABT ($N = 255$) or SOC ($N = 254$). There were 116 patients with SAB (23%) and 385 (76%) with CoNSB (Figure 1). Overall success rate in the ABT group was 82.0% vs. 81.5% in the SOC group, difference 0.5%, 95% CI −5.2% to 6.1%. SAEs were reported in 32.9% of ABT vs. 28.3% of SOC patients (OR 1.2, 95% CI 0.9 to 1.8). Among evaluable patients without complicated BSI, mean duration of therapy was 4.4 days in the ABT group vs. 6.4 days in the SOC group (difference −2.0 days, 95% CI −3.3 to −-0.7, $P = 0.003$). Among patients with uncomplicated SAB, treatment durations were similar (15.3 days in ABT vs. 16.3 days in SOC, difference −1 day, 95% CI −3.89 to 1.91, $P = 0.497$), whereas for uncomplicated CoNSB, duration was shorter in the ABT group (5.3 days in ABT vs. 8.4 days in SOC, difference −3 days, 95% CI −4.87 to −1.34, $P < 0.001$).

Conclusion. The use of a treatment algorithm for staphylococcal BSI was associated with significant reductions in duration of antibiotic therapy in patients without complicated BSI, without significant differences in overall success or SAEs.

Figure 1. Schematic of Study Design



Disclosures. **V. Fowler Jr.**, NIH: Investigator, Contract HHSN272200900023C

984. Induced Hypothermia in Patients with Septic Shock and Ventilator-demanding Respiratory Failure

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Session: 132. Advances in Management of Bacteremia and Sepsis
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Background. Animal models of serious infection suggest that 24 hours of induced hypothermia improves circulatory and respiratory characteristics and enhances survival, but whether therapeutic mild hypothermia in such conditions is of clinical benefit remains unknown. We, therefore, tested whether reducing core temperature to 32–34°C in critically ill patients with septic shock and ventilator-demanding respiratory failure improves survival and reduces organ dysfunction.

Methods. In this multi-national trial, patients with septic shock were enrolled within 6 hours of onset of septic shock and ventilator-demanding respiratory failure and randomized 1:1, stratified by site (target sample = 560), to routine thermal management or 24 hours of induced hypothermia (target 32–34°C) followed by 48 hours of normothermia. Other aspects of care were per routine in each participating center. The primary endpoint was 30-day all-cause mortality.

Results. At the third ordinary interim analysis, after recruitment of 432 participants, the Data and Safety Monitoring Board recommended the trial be terminated for futility; the conditional power for rejection of the null hypothesis in favor of efficacy was null. In the induced hypothermia group, target temperature was reached within median 3.2 hours [IQR: 2.2, 4.8], and maintained for 24 hours [IQR: 24, 24] (Figure 1). There was no evidence for a difference in 30-day mortality risk in patients randomized to hypothermia (96/217) vs. routine thermal management (77/215): relative risk 1.24 [95% CI: 0.98, 1.56] (Figure 2). At the end of the temperature intervention (72 hours), more patients assigned to hypothermia were in continued shock (vasoactive medication 71% vs. 58%; P = 0.01), and fewer cooled patients had inflammatory control (32% vs. 47% had CRP decline of >30%, P = 0.005). More harm from cooling was seen in patients entering the trial with normal renal function and with normal platelet count (P for interaction < 0.05).

Conclusion. Among patients with septic shock and ventilator-demanding respiratory failure, induced hypothermia did not improve survival, but adversely affected the duration of shock, and inflammatory control. Induced hypothermia should not routinely be used in patients with septic shock.

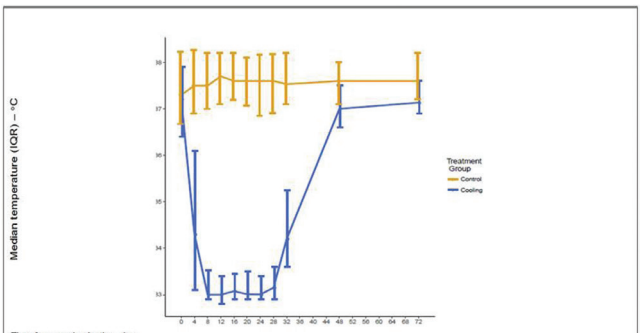

Figure 1. Median temperature the first 72 hours after randomization.

There was a significant difference in median temperature at all time points except baseline (Mann-Whitney U test, cooling vs. control).

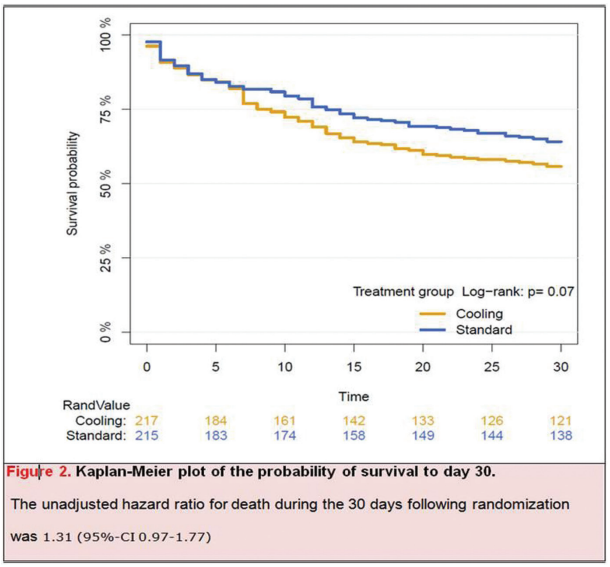

Figure 2. Kaplan-Meier plot of the probability of survival to day 30.

The unadjusted hazard ratio for death during the 30 days following randomization was 1.31 (95%-CI 0.97-1.77)

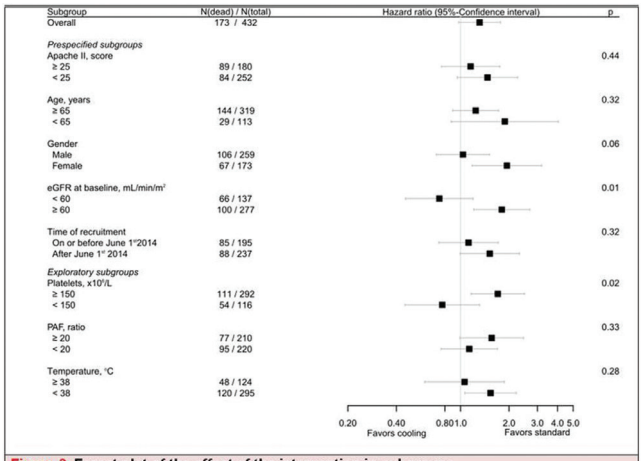

Figure 3. Forest plot of the effect of the intervention in subgroups

P values are interaction between treatment effect and subgroup. A test for interaction between site and intervention had a p value 0.41 (not shown).

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

985. The Emperor's New Clothes: Prospective Observational Evaluation of the Association between the Day 2 Vancomycin Exposure and Failure Rates among Adult Hospitalized Patients with MRSA Bloodstream Infections (PROVIDE)

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Session: 132. Advances in Management of Bacteremia and Sepsis
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Background. Current guidelines recommend vancomycin (VAN) dosing to achieve AUC/MIC ratio ≥400 for patients (pts) with serious MRSA bloodstream infections (BSI), but supporting data were largely derived in single center retrospective studies. A recent study using a Bayesian approach to estimate the VAN AUC found that patients with MRSA BSI who had an AUC_{DAY2}/MIC_{BMD} ≥ 650 or an AUC_{DAY2}/MIC_{ETEST} ≥ 320 had lower incidences of failure (*Clin Infect Dis* 59:666, 2014). This study prospectively evaluated if these VAN AUC_{DAY2}/MIC targets were associated with lower incidences of failure (PROVIDE, Award number UM1AI104681, Antibacterial Resistance Leadership Group).

Methods. Prospective, multi-center (n = 14), observational study (2014–2106) of hospitalized adults with confirmed MRSA BSI treated with VAN ≥ 72 h. Exclusion: (1) neutropenia; (2) cystic fibrosis; (3) renal replacement therapy; (4) APACHE-II score > 25; (5) previous MRSA BSI within 60 days. VAN exposures were estimated using maximum a posteriori probability procedure in ADAPT 5. MIC_{BMD} and MIC_{ETEST} were performed at a central laboratory. Outcomes: failure (30-day mortality or MRSA BSI ≥ 7 days); acute kidney injury (AKI), ≥1.5 × increase in serum creatinine (S_{cr}) among patients with a baseline S_{CR} < 2.0 mg/dl. The study was powered at 80% to detect a 17.5% difference in failure between AUC_{DAY2}/MIC groups.

Results. Among the 265 evaluable patients, mean (SD) age was 61 (17) and APACHE-II was 12 (6). Endocarditis was definite/possible in 29%. The $MIC_{50/90}$ by