BAC DOOR: A Clinician Ranking Exercise for More Informative *Staphylococcus aureus* Bloodstream Infection Trial Design

Sarah B. Doernberg, MD, MAS1; Natalia A. Gouskova, PhD2; Scott R. Evans, PhD, MS3; Helen W. Boucher, MD4; G. Ralph Carey, MD4; Sara E. Cosgrove, MD5; Henry F. Chambers, MD1; Vance G. Fowler Jr, MD1; Thomas L. Holland, MD4

1 University of California San Francisco, California; 2 Harvard University, Boston, MA; 3 Tufts Medical Center, Boston, MA; 4 Duke University, Durham, NC; 5 Johns Hopkins University, Baltimore, MD

**Background**

- New therapies are needed for *S. aureus* bloodstream infection (SA-BSI).
- However, when comparing new antibiotic regimens, the standard noninferiority design fails to address the fundamental question of which treatment is better for patients.
- Desirability of Outcome Ranking (DOOR) and partial credit are novel methods for analysis of clinical trials. Patients are categorized according to overall outcomes, taking into account both benefits and harms.
- We conducted a study to develop a novel overall outcome to utilize DOOR or partial credit in future SA-BSI treatment trials.

**Methods**

- Twenty SA-BSI patient profiles were constructed to represent the range of experiences and outcomes observed in prior trials (Figure 1).
- Profiles described the efficacy, adverse events (AEs), symptomatic, and treatment adjustments of each patient during a trial for investigational comparing two treatments.
- Profiles were sent via a computerized survey to 43 ID clinicians working in the USA (28% pediatric). Respondents were asked to rank the 20 profiles from best to worst on the basis of desirability of overall outcome; profiles were presented in random order.
- We measured the consensus between respondent ranks. An overall outcome strategy based on the respondent consensus was developed using classification and regression tree (CART) analyses and team input.
- Consensus between ranks was measured with Spearman correlation and 95% confidence intervals

**Sample Patient Profiles**

1. 50 y/o M with diabetes and admitted with fever and left knee swelling. Initial blood cultures grow *MRSA* in 2/2 bottles, and he is taken to the OR the next day for ID. He is started on IV anti-staphylococcal antibiotic. She needs criteria for complicated SA-BSI and on day 14, she is randomized to oral therapy with drug A to complete 4 more weeks of therapy. There are no complications and on day 14, she is randomized to oral therapy with drug A to complete 4 more weeks of therapy. At test of cure visit he has no signs of infection.

2. 58 y/o M with diabetes and admitted with fever and left knee swelling. Initial blood cultures grow *MRSA* in 2/2 bottles, and he is taken to the OR the next day for ID. He is started on IV anti-staphylococcal antibiotic. She needs criteria for complicated SA-BSI and on day 14, he is randomized to oral therapy with drug A. Three days later he complains of new back pain and an MRI of his spine demonstrates an L1-2 discitis/myeloradiculitis with paravertebral psoas. A PICC is placed and he is switched back to IV therapy. He is evaluated by Neurosurgery, and no operative management is planned. He is discharged on day 28 to complete 2 more weeks of oral therapy. At test of cure visit he is wheelchair bound because of recurrent infection, although this has improved since discharge and has no signs of recurrent infection.

3. 24 y/o F with history of HIV/AIDS presents with fever and right thigh swelling at prior injection site. Blood cultures grow *MRSA*, so she is started on an IV anti-staphylococcal IV antibiotic. Imaging of the leg demonstrates a pseudoaneurysm, and she is taken to the OR for repair and grafting. Her post-op TEE does not show vegetations. She refuses TEE. She clears her blood cultures on day 4 and has a PICC placed for ongoing antibiotic therapy. She meets criteria for complicated SA-BSI. She is randomized on day 14 to oral drug A and discharged that day with a plan to complete 6 weeks of therapy. She returns to the emergency department on day 20 with severe nausea and vomiting, which resolves with anti-emetics. She meets criteria for complicated SA-BSI. She is randomized on day 14 to oral drug A and discharged that day with a plan to complete 6 weeks of therapy. She returns to the emergency department on day 20 with severe nausea and vomiting, which resolves with anti-emetics. She meets criteria for complicated SA-BSI.

**Conclusions**

- We created an ordinal outcome strategy incorporating benefits and harms as part of a global patient outcome in SA-BSI.
- When comparing SA-BSI outcomes, clinicians place value not only on cure, but also on AEs, infectious complications, and symptom resolution.
- This ordinal outcome can be used for future trials comparing treatment strategies for SA-BSI, with the goal of improved differentiation between management approaches.
- This exercise demonstrates the process for translating benefits and risks into a syndrome-specific DOOR algorithm; this process can be repeated for other clinical syndromes
- Validation studies are being planned, incorporating patient preferences, analyzing data from recently completed trials, and upcoming SA-BSI treatment trials.

**References**


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**Contact**

Thomas L. Holland, MD
Duke University Medical Center
Box 120359
Durham, NC 27710
thomas.holland@duke.edu

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Figure 1. Sample Patient Profiles

Figure 2. Distribution of Surveyed Respondent Rankings with Patient Profile Summaries

Figure 3. DOOR Algorithm Based on Clinician Rankings.