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 (AE), symptomatology, and treatment adjustments of each patient during a theoretical trial 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.

Based on the CART analyses, the team developed an overall outcome strategy (Figure 3), which correlated strongly with the surveyed respondent ranking: r=0.89, 95% CI (0.73, 0.95).

Results

Forty-two (97%) respondents completed the survey. The distribution of pairwise responses demonstrated moderately strong consensus (median correlation = 0.89, 95% CI [0.73, 0.95]).

Respondents tended to differentiate best and worst profiles. However, a larger spread in responses was apparent for profiles in the middle (Figure 2).

Features most discriminating rank were survival, severe AE, cure, infectious complications, and ongoing symptoms.

Based on the CART analyses, the team developed an overall outcome strategy (Figure 3), which correlated strongly with the surveyed respondent ranking: r=0.89, 95% CI (0.73, 0.95).

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 the new overall outcome in future SA-BSI trials.

Figure 1. Sample Patient Profiles

1. A 65 y old woman with complicated S. aureus bacteremia presents for treatment of a symptomatic right ankle abscess. She is initiated on IV anti-staphylococcal antibiotic. She meets criteria for complicated SA-BSI and on day 4, she is randomized to oral therapy with antibiotic A for 6 weeks. She is discharged from the hospital and returns to the emergency department on day 20 with severe nausea and vomiting, which is controlled by IV fluids and anti-emetics. She is restarted on antibiotics. The team developed an overall outcome strategy based on the respondent consensus was developed using classification and regression tree (CART) analyses and team input.

Based on the CART analyses, the team developed an overall outcome strategy (Figure 3), which correlated strongly with the surveyed respondent ranking: r=0.89, 95% CI (0.73, 0.95).

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

Figure 3. DOOR Algorithm Based on Clinician Rankings.

Tables

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<tr>
<th>Characteristic</th>
<th>CHF, Severe comorbidities, 60+</th>
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<td>Shock</td>
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References


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