Analysis of CAMERA S. aureus Bacteremia Trial Results Using the DOOR and Partial Credit Approaches

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Background

- Desirability of Outcome Ranking (DOOR)3 and partial credit analyses4 are novel approaches to measure benefits and risks in clinical trials.
- For a DOOR analysis, patients are categorized according to overall outcomes, using a composite endpoint that takes into account both benefits and harms.
- The partial credit approach then assigns a score, on a scale of 0 to 100, to each DOOR rank. Applying different partial credit weights allows nuanced differences between treatment strategies to be explored.
- CAMERA-1 was an RCT that evaluated the effect of combining flucloxacillin with vancomycin, compared to vancomycin monotherapy, for treatment of MRSA bloodstream infection2.
- CAMERA-1 found a trend to benefit for combination therapy in the endpoint of duration of bacteremia.
- We retrospectively applied a tailored version of a previously developed DOOR endpoint (Figure 1) to CAMERA-1.

Methods

- Using the DOOR endpoint that was developed for S. aureus bacteremia trials (Figure 1), the 60 CAMERA-1 participants were categorized into an overall ordinal outcome.
- This outcome incorporates mortality, treatment failure, infectious complications, and adverse events.
- The probability of a better DOOR rank with combination therapy was estimated. Various partial credit scores were applied to each observed DOOR category to reflect how different value judgments could influence the interpretation of the results.

Results

- The distribution of DOOR by treatment group is shown in Figure 2; rank 4 was not observed.
- The probability of a higher DOOR with combination therapy was 0.47 (95% CI 0.33-0.60). Thus, there was no evidence of a significant difference between treatment groups.
- Varying the partial credit scores suggested differences between treatment strategies (Figure 3).
- For example, Scenarios A represent a value judgement in which survival is the only thing that matters; death is assigned a score of 0 and all other ranks are given full credit. This would favor combination therapy, which had a lower proportion of deaths.
- Scenario C represents another extreme, in which any adverse outcome is seen as equivalent to death. This would favor standard therapy, which had more patients in the top rank.
- Scenarios B and D show the results of two other possible scoring systems.

Conclusions

- DOOR and partial credit analyses can be used to compare risks and benefits of different management strategies.
- Using the CAMERA-1 trial data, combination and standard therapy for MRSA BSI were associated with similar DOOR probabilities.
- These methodologies can inform and be adapted to other studies comparing treatment strategies, including the currently recruiting CAMERA-2 trial.
- This exercise demonstrates the process for evaluating benefits and risks using a syndrome-specific DOOR algorithm; this process can be repeated for other clinical syndromes.

References


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Figure 1. DOOR Endpoint

Figure 2. DOOR Component Summary

Figure 3. Contours of the Between-Treatment Difference for Range of Partial Credit Scores Combinations with Sample Scenarios