Author’s response to reviews

Title: Optimising trial designs for identifying appropriate antibiotic treatment durations

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We thank the reviewer and editor for their helpful comments.

Point-by-point responses are provided below.

Editor:
1. Please remove the figures from the main manuscript, and upload them as separate files.
Response:
We have removed the figures from the main manuscript and uploaded them as separate files.

2. Please add an acknowledgments section
Response:
We have added an acknowledgements section

3. Please add headers to your abstract (Background, Main Body, Conclusions)
Response:
We have added the requested headers to our abstract.

Reviewer #1:
1. Line 132-137 - In the paragraph on DOOR/RADAR the authors conclude that "its ranking assumes that the shorter of two durations is beneficial" and "this unverified strong assumption could lead to
demonstration of non-inferiority using DOOR/RADAR when conventional trial designs may show that shorter durations are not non-inferior." - I believe this is incorrect since in the DOOR/RADAR approach first the clinical patient-relevant outcomes are compared. Only if no difference in these is detected, will the duration come into play with the shorter duration gaining. The condition for the latter is that there is no difference in clinical outcomes between the short and long treatment duration.

Response: To address this comment we changed this sentence now to:

‘However in its ranking this approach implicitly assumes that the shorter of two durations is beneficial when other patient/clinical outcomes are identical.’

The second point of this sentence – ‘this unverified strong assumption could lead to demonstration of non-inferiority using DOOR/RADAR when conventional trial designs may show that shorter durations are not non-inferior’ - is correct as the letter from Phillips et al. (ref 24) demonstrates. Of note, this has also recently been demonstrated by another study: https://www.ncbi.nlm.nih.gov/pubmed/28501668