Author’s response to reviews

Title: Exploring mechanisms of excess mortality with early fluid resuscitation: insights from the FEAST trial

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Major changes to the manuscript

1. Inclusion of a box – explaining the Presenting Syndromes (PS) and Terminal Clinical Events (TCE)

2. Redrawn Figure 1 to exclude FEAST B

3. Retained Figures 2a and 2b within main manuscript (see comment to reviewer 2)
4. Figures 3a-d have been retained as the contain important data (especially for important signs such as presence of crackles in the chest; evidence of hepatomegaly; stiff neck etc—all which previous commentaries had indicated were unethical to include in trial)

5. Figure 3e has been moved to the Extra Supplementary Material

6. Figure 4 remains Modes of Death (TCE)

7. Table 5a andb have been moved to ESM

Changes in the manuscript body

1. Removed Landmark analysis from the statistical methods

2. Within the discussion – addressing points raised by Reviewers two and three—indicating the level of evidence for the ACCM guidelines and that bundle based care was not the primary question – instead fluid resuscitation to inform WHO guidelines.

3. To indicate that these may be not relevant to other populations and that more research is required to understand the mechanisms for harm including some suggestions of why we think this may result in excess cardiovascular events.

(Other points raised by reviewers two and three – which don't comment on the data and require clarification - are covered in the response to reviewers).

4. Rewriting of the section in the discussion concentrating on mechanism of death (to address all 3 reviewers questions)- and downgrading or deleting sections on electrolyte and/or acid/base changes.

I have uploaded clean/net versions of the the revised manuscript. If you would like to have the original with tracked changes - I would be very happy to also supply this.