Reviewer’s report

Title: Wound Healing In Surgery for Trauma (WHIST): statistical analysis plan for a randomised controlled trial comparing standard wound management with negative pressure wound therapy

Version: 0 Date: 29 Nov 2018

Reviewer: W den Hollander

Reviewer’s report:

The current manuscript describes a proposed statistical analysis plan for assessing a reduction in the rate of deep surgical site infection post major trauma. This study is of high relevance to the field, which currently appears to lack studies which have been appropriately performed statistically. The manuscript is clearly written, but I suggest to incorporate the following points to further improve it:

1) Could the authors supply the actual power calculation they have performed to define their sample size to be 615 (or 770 when accounting for dropout) per arm. This would be appropriate given they will be using mixed-effect models, and do not appear to have ran simulation studies to determine the sample size.

2) The authors should elaborate on "major protocol deviations" (R143-146). They do give an example which seems clear to be deemed as such, but apart from that the extent of deviation seems arbitrarily defined and thus yields a somewhat vague exclusion criterium.

3) I would suggest to rewrite the phrase "a sufficient number of deaths" on R205-206, and perhaps even define a fraction of the sample size to be "sufficient".

4) For analysis of the secondary outcomes the authors describe they will be assessing the relevant variables for approximate normality (R218-219), and if absent will be transformed to achieve so (R230-232). However, given they will be fitting mixed models for these outcomes (R220-223), there is no need to have them be normally distributed. What is, however, explicitly necessary for these mixed models to make sense, is whether the resulting residuals are normally distributed. Mixed models assume the outcome to be normally distributed, conditional on the random effects. If the authors wish to deposit a statistically sound paper, they should address this issue.

5) The authors will include interaction effects between time and treatment in the secondary analyses (R225-226) if trends over time appear appropriate to do so. The authors should define appropriate here.

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