Author's response to reviews

Title: Standard abdominal wound edge protection with surgical dressings vs. coverage with a sterile circular polyethylene drape for prevention of surgical site infections. A patient and observer-blinded randomized controlled trial - BaFO

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Author's response to reviews: see over
Dear Madame/Sir,

Please find below a detailed list of changes made to the protocol to address all of the reviewer’s comments.

Sincerely,

Andre Mihaljevic

1. P(age) 2, p(aragraph) 4, l(ine) 1. Add the date of registration and the date the first patient was randomized if that has happened.  
   Answer: Dates were added

2. P 3, l 2. Replace [Rational] by [Rationale].  
   Answer: Done

3. P 3, p 1, l 3,5,6,10,11. Insert [,] rather than [.] to delimit each set of 3 digits.  
   Answer: Done

   Answer: Done

   Answer: Done

6. P 3, p 2, l 14 and 15. Are these rates in the correct order?  
   Answer: Done

7. P 3, p 2, l 19. Continue with the list and delete [etc.].  
   Answer: Done

8. P 3, p 3, l 2. Since [or] logically includes [and], delete [and/]. Also P 6, p 4, l 4. Also P 7, p 2, l 1. Also P 8, p 3, l 7 and 9. Also P 10, p 5, l 1. Also P 11, p 5, l 6 and 7. Also P 13, p 2, l 5.  
   Answer: Done

9. P 4, p 2, l 5. Did the study have a computed sample size justification and power analysis? Was this because of too little power?  
   Answer: The study had a computed sample size calculation only for the bundled interventions; one of which was the application of a wound edge protector. Power was set at 0.9

10. P 4, p 2, l 8. Replace [parameters] by [variables]. A parameter is a
characteristic of a distribution of a variable in a population and not the name for a variable in a sample.

Answer: Done

Answer: Done

12. P 4, p 3, l 3. Replace [Fig. 1] by [Figure 1] just as P 4, p 4, l 2 to be consistent.
Answer: Done

13. P 4, p 3, l 5. Insert a space to read [meta analysis].
Answer: Done

14. P 4, p 3, l 7. Should [folg] be [fold]? If so, on this and the previous line the relative risk should be stated and so should the comparison group. Fold is not a well defined term. The word increase is not needed, since values greater than 1 increase and those less than 1 decrease.
Answer: Relative risks were added

15. P 4, p 3, l 8. Suggest replacing [will] by [should]; presumably the results are not known!
Answer: Text changed as suggested

16. P 4, p 5, l 1 lists [14 sites] and P 6, p 4, l 1 lists [15 centres]; which is correct? Are they all listed on P 15?
Answer: 15 is the correct number

17. P 7, p 1, l 1 to 3. Are the envelopes individually numbered and will they be restricted to choosing one at a time?
Answer: Yes. The issue was clarified in the text.

18. P 7, p 3, l 2. Are the surgical dressings a standard list, if so which ones, and will they be recorded for each patient?
Answer: No. The exact number used will not be recorded for each patient.

Answer: CE was added to the list

20. P 8, p 1. Will these locations provide equivalent temperatures, and will they be measured with the same instrumentation? This should be recorded as it might be a source of variation that matters.
Answer: The text was clarified.

21. P 8, p 2, l 2. [CRF] is not in the list of short forms on P 16.
Answer: CRF was added to the list.
22. P 8, p 2, l 9. How is it sent? Electronically and secure? 
Answer: The issue was clarified in the text.

23. P 8, p 2, l 12. Insert a space to read [data management].
Answer: Done

24. P 8, p 2, l 13 to 16 should be described in more detail and the programs documented.
Answer: More details were added and the programs described. The BaFo data management plan (in German) was uploaded as appendix.

25. P 8, p 3, l 3 to 5. These should be documented.
Answer: Reference was added

26. P 9, p 1, l 1. Delete [her/his] and [his] to remain gender neutral.
Answer: Done

27. P 9, p 1, l 2. If copies of these are available they could be listed on the website as appendices.
Answer: The text was clarified for more detail.

28. P 9, p 3, l 4 and 5. Cite the R(eference) for these codes.
Answer: Done

29. P 9, 4, l 1 and 2. Here you use [subject] and [patient]; should this not be consistently used in the entire paper?
Answer: Done

30. P 9, p 4, l 3. Cite the website and the form; it could be included as an appendix to this paper.
Answer: The form was included as an appendix to the paper

31. P 9, p 4, l 6. Replace [significant] by [clinically important]. Who will make this determination? Are there any data on the reliability of this scoring?
Answer: The text was changed.

32. P 9, p 4, l 11. [SAE] is not defined in the list on P 16.
Answer: SAE is added to the list.

33. P 9, p 5, l 3. Replace [proportion] by [percentage].
Answer: Done

34. P 9, p 5, l 7. The Chi-Square does not seem to consider the stratification and blocking? Do you have software to do this? Cite the software.
Answer: Study site will be considered as the solely stratification variable. It
is assumed that if the sample size of each centre would be very large, there will be no difference in the effects between the centres (fixed effect model). Therefore analysis of the primary efficacy endpoint will be based on a Chi²-Test and not based on a random effects model which would assume different underlying effects within the centres. However, following the valuable suggestion of the reviewer, a generalized linear mixed effect model (logit link regression) will be fitted to the data in terms of a supportive sensitivity analysis which allows for assessment of the primary efficacy endpoint under consideration of random centre effects. This is also in line with the GCP-ICH E9 guideline (paragraph 5.7).

Blocking ensures balanced group sample sizes over the course of recruitment and has no impact on the statistical analysis. This issue is now clarified in the text.

35. P 10, p 1. Cite the method of the sample size calculation and the software used if relevant.
Answer: Sample size calculation was conducted by using nQuery Advisor® software version 7.0 which employs calculation formulas proposed by Fleiss et al. (1980) [Ref1]. The software is now mentioned in the text.

36. P 10, p 2. What will happen if fewer than 15 get recruited at any centre?
Answer: Centres with less than 15 patients will be excluded from the primary efficacy analysis. Therefore, recruitment will be continued until enough centres lead to the required total sample size by each enrolling a sufficient number of patients. This was clarified in the text.

37. P 10, p 2 ff into P 11. This whole analysis section is on need of Rs to justify the procedures listed. The principles used to justify the sub-groups analyses should be cited. The software planned to be used should be cited. Also on P 11, it does not appear that the stratification and blocking have been considered in the analyses.
Answer: In accordance with GCP-ICH E9 guideline, all intended subgroup analysis are pre-specified in the protocol. Adjustment for the stratification variable 'centre' will be conducted as supportive analysis but will not be considered in the primary efficacy analysis (this is now clearly stated in the text).

Procedures for the statistical analysis of the primary and secondary endpoints will be conducted in line with the GCP-ICH E9 guideline. For the statistical analysis, SAS® software version 9.2 or higher will be used.

38. P 10, dash 4, l 2. [NNIS] is not defined in the list on P 16.
Answer: NNIS was added to the list.
39. P 11, p 4, l 4. Until when?
   Answer: The text was clarified.

40. P 11, p 6, l 8. Suggest replacing [perceived] by [conceived].
   Answer: Done

41. P 12, p 4. Provide Rs to these guidelines.
   Answer: Done

42. P 13, p 1, l 3. Replace [last decades] with dates.
   Answer: Done

43. P 13, p 1, l 9 and 10. Delete [In order] and capitalize [To] as the words are redundant in English. Also P 14, p 2, l 5 and 11.
   Answer: Done

44. P 13, p 2, l 1 to 4. Does the R on l 4 give data on all of these?
   Answer: Yes.

45. P 13, p 2, l 7 to end. Is there a R to document these issues?
   Answer: No.

46. P 14, p 1, l 2. Replace [,] by [.] on both percentages.
   Answer: Done.

47. P 14, p 1. Is power an issue with any of these trials?
   Answer: Text was changed to clarify that power was indeed an issue in some of these trials.

48. P 14, p 2, l 1. Replace [is] by [are] since data is a plural word.
   Answer: Done.

49. P 14, p 2, l 2. How are they blinded to the patch?
   Answer: Text on page7 paragraph 1 was changed to clarify blinding.

50. P 15, p 2. Where is [CS] in this list?
   Answer: CS was added to the list.

51. P 16 does not contain all the items in the footnote to Table 2. This list should be checked to make sure it is complete.
   Answer: Items were added.

52. P 17. How big is the protector? Are there various sizes, and if so, how big are they. Will the size be recorded if they vary?
   Answer: Standard size (90cmx90cm) was added in the text.

53. P 19, criterion 10 does not seem to be referenced anywhere.
Answer: Reference was added.

54. P 20, footnote, l 4. Replace [optained] by [obtained].
   Answer: Done.

55. P 21, second level, l(tem) 3B, l 2. Insert a space as [> 38]
   Answer: Done.

56. P 21, last level, I 3A, l 1. The double dagger is not defined.
   Answer: Double dagger was defined.

57. P 23 ff. These Rs apart from R 29 do not need a citation date
   Answer: Citation dates were removed except for reference 29.

A random sample of 10 Rs was checked for citation accuracy.

58. P 24 ff. Rs 13, 19, 20, 24, 27, 39, 40 and 41 appear to be correct.
   Congratulations.
   Answer: Thank you.

59. P 24, R 21, l 3 should list [No 43] and provide the editors names.
   Which chapter is this?
   Answer: Missing information was added.

60. P 26, R 38, l 3. Delete the periods to read [J Int Med Res].
   Answer: Done.