Author's response to reviews

Title: Risk of surgical site infection and efficacy of antibiotic prophylaxis: A cohort study of appendectomy patients in Thailand.

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Author's response to reviews: see over
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Dear Editor,

Clariﬁcations to reviewers’ comments: manuscript 1873731254100613

Title: Risk of surgical site infection and efﬁcacy of antibiotic prophylaxis: A cohort study of appendectomy patients in Thailand.

Thank you very much for giving us the opportunity to revise and resubmit the above paper. We have gone carefully through the very constructive and pertinent comments from the reviewers and have revised the manuscript accordingly.

We hope that our revision of the paper will make it acceptable for publication, and we are of course willing to revise the paper further if necessary.

Yours sincerely,

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Below, please find our comments to the reviewers:

Reviewer # 1

1. From the paper there are no National guidelines, however, it should be stated if hospitals had their own internal prophylaxis guidelines.

Clarification 1: In order to address this important issue, we have inserted the following information on page 6, lines 11-12."
“some hospitals had their own internal antibiotic prophylaxis guidelines. However,”

2. On page 8 the use of antibiotic prophylaxis the authors write that 38.8% received a single dosing, 54.2% received dosing for 1 day and 38%. While I understand the numbers after looking in the table the wording sounds like single dose versus one day dosing versus > one day dosing and should be corrected.

Clarification 2: We confirm that the percentages in both text and Table 2 are correct. They may seem to be incorrect because the sample sizes of the antibiotic agent (1972) and the duration of antibiotic prophylaxis (2139) in Table 2 are different. The latter includes operations where no antibiotic prophylaxis was given. Please see page 10 lines 5-9, and page 23 Table 2.

3. I feel that the tables are too similar. For example duration of antibiotic prophylaxis is analyzed in all 3 tables, time of first antibiotic in Tables 2 and 3 and it is unclear why the risk factors included for statistical analysis for table 1 and 3 are different. It seems like most of the table data could be put in a single Table.

Clarification 3: The three tables are different. Actually, Table 1 presents a multivariable analysis of general risk factors for surgical site infection including antibiotic prophylaxis dichotomized as ≤1 day and >1 day. Table 2 presents characteristics of antibiotic prophylaxis together with observed rates of surgical site infection. Ultimately, Table 3 presents a multivariable analysis of risk associated with the various regimens used (the efficacy of antibiotic prophylaxis).

As pointed out by the reviewer, duration of antibiotic prophylaxis is included in all three tables, but this reflects the overall importance of this parameter. It must be noted that the actual incidence of infection is given in Table 2, and by comparing Tables 1 and 3 the reader has a possibility of checking that the reduced risk of infection associated with antibiotic prophylaxis is the choice of antibiotic regimen.

In addition, ‘length of preoperative stay’ and ‘type of operation’ are excluded from the model in Table 3, but included in Table 1. The reason is that these factors are risk factors for SSI, but they are not potential confounders for the efficacy of antibiotic prophylaxis. Please see pages 22-26.
4. On page 12 there is a discussion of the use of antibiotic prophylaxis. I do not believe that there is a consensus on appropriate length of prophylaxis for appendicitis (Mandell 2005). So what is the inappropriate length of prophylaxis definition used for this study?

Clarification 4: We agree and have deleted the word “Inappropriate” on page 13, line 4. (The definition of inappropriate length of prophylaxis was used to define ‘more than 1 day’.)

5. The tables in the text are with numbers while in the Tables they use roman numbers.

Clarification 5: We have changed the Table numbers from roman to times new roman, which is consistent with the text. Please see pages 22, 23, and 25.”

Reviewer # 2

1. What is missing is any evidence of technical factors (blood in wound, devitalized tissue, etc.)

Clarification 1: The reviewer has raised an important question. This study has a limitation in relation to the collection of technical evidence such as blood in wound, devitalized tissue, etc., because this is a big cohort study. We have, therefore, collected only the potential confounding factors. In addition, the technical factors for appendectomy are considered consistent in Thailand, which we have already stated on page 11, lines 12-15.

Reviewer # 3

1. Was informed consent obtained from the patients?

Clarification 1: No, informed consent was not obtained from the patients, because the patients in this study were anonymous and their identifications were removed from the records. We have, therefore, not provided this information in the text. However, this project was approved by the Ethical Review Committee for Research in Human Subjects, the Thai Ministry of Public Health, and the Ethical Committee and/or the directors of the participating hospitals. We have inserted the following information on page 7, lines 4-5: “, and the Ethical Committee and/or the directors of the participating hospitals.”
2. What were the hospitals?

**Clarification 2:** The participating hospitals were Chiangkham Hospital, Saraburi Hospital, Bhumibol Adulyadej Hospital, Vachira Phuket Hospital, Naradhiwas Rajanagarindra Hospital, Rayong Hospital, Chumphon Khet Udomsakdi Hospital, and Udonthani Hospital. We have added the names of the participating hospitals on page 6, line 24, and page 7, lines 1-2.

3. Were patients with or on antibiotic therapy excluded?

**Clarification 3:** Yes, the patients on antibiotic therapy were excluded from this study. We have inserted the following information on page 7, line 10: “and the patients who were on antibiotic therapy.”

4. What were the criteria for wound infections? Where there any degrees of wound severity. Any other parameters for infections? (I.e. fever, pus etc)

**Clarification 4:** We used the criteria of the US Centers for Disease Control and Prevention (CDC) NNIS System to diagnose SSI. Infections were classified as superficial incisional, deep incisional, or organ/space SSIs [20].” We have already provided this information on page 8, lines 2-4. We omitted the details in the manuscript because of the space limitation.

5. Any division between perforated and unperforated appendices?

**Clarification 5:** The perforated and non-perforated appendices are related to the degree of wound contamination. The non-perforated appendices were considered clean-contaminated wounds, whereas the perforated appendices were considered contaminated or dirty wounds depending on the degree of wound contamination. However, the latter was not included in this study. We have already defined uncomplicated appendicitis, which we studied on page 8, lines 10-12.

6. What was the dose of Metronidazole agent given?

**Clarification 6:** The dose of Metronidazole agent was 500 mg. We have not added this information, because we have chosen not to show the dose of any antibiotic prophylaxis. It should be consistent.

7. Any differences in results affected by age and other medical problems (i.e. chronic illness, HIV)

**Clarification 7:** After we adjusted for sex, age, length of preoperative stay, type of operation, ASA score, and duration of operation, the results did not show any substantial association between age and surgical site infection (SSI). Please see page 22, Table 1, and the discussion section page 12, lines 3-7.
Similar to age, other medical problems or underlying diseases that we presented as ASA score were not associated with SSI. This may be because most patients in this study had no severe underlying diseases. 1732 patients had ASA score equal to 1, and 402 patients had ASA score equal to 2. We, therefore, omitted these results from Table 1.

It should be noted that the ASA score was used to characterize the patients’ physical status as 1 (healthy), 2 (mild systemic disease), 3 (severe systemic disease), 4 (severe life-threatening systemic disease), or 5 (moribund).

We have added the following information on page 8, lines 5-6:
“1 (healthy), 2 (mild systemic disease), 3 (severe systemic disease), 4 (severe life-threatening systemic disease), or 5 (moribund)”