Author’s response to reviews

Title: VALUE OF PARENTAL CONCERN AND CLINICIAN’S GUT FEELING IN RECOGNITION OF SERIOUS BACTERIAL INFECTIONS: A PROSPECTIVE OBSERVATIONAL STUDY

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Dear Editors,

On behalf of the group of authors, I thank you for your consideration of our original research article entitled “Value of parental concern and clinician’s gut feeling in recognition of serious bacterial infections: a prospective observational study” by Urzula Nora Urbane, Dita Gaidule-Logina, Dace Gardovska, and Jana Pavare, for consideration for publication in BMC Pediatrics.

We have carefully read the comments and questions from the editor and the reviewers and are happy to provide the answers to their remarks in the following pages of this letter. We have tried our best to provide answers to all questions made by the reviewers.

Thank you again for your consideration!
Sincerely,

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Editor Comments (EC): I have a few questions which should be clarified. In particular, more information is required for your methods and results.

Comment No.1: Some more information about the study setting would be useful. What types of patients attend the ED? What is the admission rate?

Response to EC No.1:

Thank you for the suggestion.
The following information has been added to the manuscript at the end of the Background section (lines 105-115, page 5):

“Description of the clinical settings for the study.

This study was conducted at the emergency department (ED) of the Children’s Clinical University Hospital in Riga, Latvia. It is attended by patients aged 0 to 18 years, with problems ranging from trauma and surgical emergencies to various childhood illnesses. The annual attendance of the ED is around 65 thousand patients, among them around nine thousand febrile cases. Children with fever constitute for up to 22% of ED visits (excluding trauma patients). Around 70% of all febrile patients seen in the ED undergo clinical and laboratory investigations, and the admission rate of febrile children is up to 27%. Thirty per-cent of febrile patients are discharged from the emergency department without undergoing any investigations. Most of these patients have been evaluated as clinically stable and triaged into the lowest level of urgency, where they are seen by a direct-access paediatrician in a separate section of the ED.”

Comment No.2: In particular, how many children with fever were seen during the study period? How many days did recruitment occur for? How many eligible children were missed?

Response to EC No.2:

Thank you for your comment. No overall data collection of precise number of febrile cases within the study period was collected as a part of this study. The data on children with febrile episodes during 2017, including number of patients seen each month, admissions, prescriptions of antibiotics etc. was collected for another international study, unfortunately the data remain unpublished to this date and are therefore confidential.

The recruitment was done over 88 days. All patients with febrile illness were theoretically eligible for the study if there were no exclusion criteria. However, not all patients agreed to participate in the questionnaire during the acute illness of their child, and the specifics of methodology require that the doctor of each patient enrolled agreed and had managed to fill the questionnaire before familiarizing oneself with the investigation results. We approached all patients who were present at the emergency department during recruitment hours and met these conditions, except the patients seen by the direct-
access paediatrician, and only 162 patients were included in the final data analysis.

We have updated the manuscript by adding this information in more detail to the methods and results section:

“The recruitment occurred over 88 days during the study period. All patients who were eligible according to conditions described above were approached, and each day one to six patients were enrolled.

Overall, 266 patients were approached. Twenty-four patients were excluded as the clinicians did not manage to fill the clinician questionnaire before viewing the investigation results. Forty-six parents refused participation in the questionnaire, and 33 failed to submit the completed questionnaire within the specified time period. One patient was excluded as the evidence on the parental questionnaire suggested it was filled by the child and not the parent. In total, 162 patients were included in the study.” (Lines 179-187 on page 8).

Reviewer reports:

Fidelis Njokanma (Reviewer 1):

1. The "Abstract" is a bit too long - in all, much more than 300 words.

Response to F.N. 1:

Thank you for your assessment. The submission guidelines for BMC paediatrics state that the abstract should not exceed 350 words, which was the length of the original abstract. However, we have shortened it for the convenience to less than 300 words in the revised version.

2. The "Abstract" contains a statement to the effect that "gut feeling" is associated with "increased likelihood" of "developing" SBI. It might be better to state that "gut feeling" is associated with a "higher likelihood" of "having" SBI.

Response to F.N. No. 2:

Thank you for this commentary. Yes, we agree that your version is more accurate and have therefore corrected this statement in the abstract, results and conclusion sections:

“‘Gut feeling’ as stated by certified paediatricians was associated with higher likelihood of having SBI” (lines 46-47, pages 2-3).

3. It is preferable not to start sentences with Arabic numerals - see page 7, line 49.

Response to F.N. No. 3:

Thank you for the reminder. We have carefully re-read the whole manuscript and made our best attempts in correcting this wherever necessary, for example:

“Twenty-two patients were younger than one year, and 80 patients were 1 to 5 years old.” (lines 188-189 on page 9).
4. Table 2: Identifying "True Positives" etc raises some concern. According to the authors, "Sense of reassurance in case of absent SBI was considered as true positive". As long as this understanding is stated as a footnote to the table, there need not be any problems. However, in the opinion of the reviewer, it should be considered "True Negative" instead. And here is the logic:

When there is a sense of reassurance, the doctor is saying "I do not think there is SB!". If it turns out there is no SBI, then the "test" is truly negative. If on the other hand, it turns out there is really SBI, the doctor's sense of reassurance has been wrongly placed and the "test" is falsely negative.

Response to F.N. No.4:

Thank you for your reasoning. There seems to be a slight confusion in understanding what question is asked to the doctor when assessing sense of reassurance. “I do not think there is SBI” is a negative response to “gut feeling” rather than positive answer to “sense of reassurance”.

As explained in the methods section:

“The clinicians who first examined the patients were asked to fill a questionnaire reporting their clinical impression on the degree of severity of the child’s illness. The “Gut feeling”, defined as an intuitive feeling that the child may have a serious illness, as well as the “Sense of reassurance”, defined as an intuitive feeling that the child has a self-limiting illness, were noted as present, or unsure/absent.”

(Slines 135-139 on page No. 6).

Sense of reassurance is when we ask the doctor if he or she feels sure that there is a self-limiting illness (therefore no SBI), and this is not the same question as for gut feeling. The definitions used in this study were derived from other studies [1, 2]

We interpreted that a true positive is when a doctor says there is “No SBI” and there really IS “No SBI” (the expectation matches the result, so the test is positive). In other words, “No SBI” is negative for SBI but positive for what the doctor expected, which is the absence of SBI. Similarly, when a doctor did not have a sense of reassurance (or in other words, the doctor denies or doubts the absence of SBI) and there is no absence of SBI (SBI is present), this is true negative.

When the doctor has stated that there is no SBI, but there really is SBI, the test is falsely positive for the expectation (that there is No SBI). And when the doctor has no sense of reassurance (negative answer) but turns out there really is “No SBI” (positive result if absence of SBI is what you are looking for), the test is falsely negative.

Therefore, if it is acceptable and not too confusing for the readers, we would like to leave this as it was in the original manuscript. We realize though that coming from a country with double negatives used in the language slightly affects our judgement. But for as long as we have thought about the interpretation in this case, we always come to the same conclusion.

5. The use of the term "this study" can sometimes lead to confusion. For example, within the last three lines of page 12 and the first two lines of page 13, that expression was used twice in reference to two separate studies - a reference study and the study under review. It is probably better to find alternative terms altogether.

Response to F.N. No. 5:
Thank you for the correction, this has been revised and the corrections can be viewed in lines 282-291 (page 14):

“However, in our study there were significant differences in the diagnostic performance of “gut feeling” when expressed by senior and junior clinicians, in contrast to one observational study conducted in primary care settings in Belgium published in 2012, where it was equal. In the same Belgian study, another term, “clinical impression”, a subjective observation that the illness is serious based on objective information (history, observation, examination), was distinguished from the more intuitive “gut feeling”. The specificity of gut feeling was higher than clinical impression, suggesting that more holistic approach to evaluation of a patient’s leads to a better recognition of serious illness. The discrimination of the two terms was not applied to our research, as clinical impression was replaced with the presence or absence of “red flag” signs.”

6. Do the authors agree that "gut feeling" of respondent doctors was heavily driven by "red flag" signs? In other word, the study indirectly tested the usefulness of "red flag" signs in identifying SBI!

Response to F.N. No.6:

We did not statistically assess the predictive value of “red flag” signs as this was not the aim of the study, but we must agree that the presence of these clinical signs was indeed associated with triggering “gut feeling”, especially in cases where it successfully identified children who developed SBI. As we stated in discussion:

“It was evident that clinical presentation was suggestive of serious illness in great majority of cases when gut feeling correctly identified SBI, which together with the role of experience leads to a conclusion that “gut feeling”, although defined as an intuitive feeling, may be reliant on conscious evaluation rather than unconscious instincts.” (lines 291-295 on page 14).

Karen Dunn (Reviewer 2):

Diagnosing serious bacterial infection particularly in young children is a challenge. This paper aimed to determine the association between clinician gut feeling and parental concern and the presence of SBI. It is clearly written and is easy to read. However, I have questions about the methodology and the findings.

1. The study was conducted over 9 months and included the winter period. Inclusion were children 2mth -17yrs with a temperature of >38C, however it is not stated how or when the temperature was measured. Eg were children included only if an elevated temperature was recorded in the ED by reliable means or was a reported fever at home also included?

Response to K.D. No.1:

Thank you for your question. In the hospital, we use axillary alcohol thermometers to assess the temperature of the child. All patients enrolled in the study had axillary temperature higher than 38.0C, or history of it on the day of admission. As children were commonly given antipyretics at home, it was not obligatory for enrolment to have a documented temperature above 38.0C at the point of admission to the emergency department. Parent-reported temperature higher than this was considered as reliable if it had
been measured by axillary electronic or alcohol thermometer, in some cases mercury thermometers had also been used. We acquired this information upon enrolment of the patient, and the presence of fever had to be confirmed and documented later during their stay in the emergency department.

We have updated the methods section of our manuscript to clarify this information for the readers (lines 121-126 on page 6):

“Patients aged 0 to 18 years who presented to the ED with fever (body temperature above 38°C) or history of fever during the day of admission to the emergency department were considered eligible. Axillary alcohol thermometers were used to assess the body temperature of patients on admission to the emergency department and during their stay in the hospital.”

2. After the child was examined by the physician, the physician completed a questionnaire regarding their 'gut instinct' about the child having an SBI. However they were also asked about the presence of red flags at the same time which could bias their interpretation of their 'gut instinct' if they hadn't previously paid particular attention to these signs or symptoms.

Response to K.D. No.2:

Thank you for the remark. The goal of including these clinical signs in the clinician’s questionnaire was to assess the influence of the presence of these “red flag” signs on the judgement of the clinician, in order to see their importance in triggering “gut feeling”. We wanted to avoid having to rely on secondary data from the medical records of the patients, for example when they would be written retrospectively in case of intensive flow of patients. We agree that this could theoretically serve as a checklist and make the doctor re-evaluate the patient’s condition. In fact, we discussed this with local and foreign colleagues specializing in studies of “gut feeling”, and an agreement was made to place the question on clinical signs after the questions on “gut feeling”, on the other side of the sheet.

3. Parent responses were recorded within 48hr of admission and as most children were admitted and underwent investigation it would be difficult to isolate the parents from the knowledge of the results before they completed their survey.

Response to K.D. No.3

Thank you for this remark. To clarify on this, the goal of the parental questionnaire was not to see if parents could predict the outcome of the child’s illness by relying on their evaluation alone. Rather it was used to assess their feelings and observations during the episode, and to see if they felt this illness was different/more severe than other febrile illnesses the child had had during his or her life, according to the definition of “parental concern” derived from a previous study [3]. We agree that being consulted by a doctor could provide assurance or in some cases raise even more concern, but we did not consider it ethical to approach parents and ask them to participate in research before their child’s urgent medical needs were met first. After the child was in a stable condition, the parent could fully concentrate on filling the survey. In most cases it was filled within a few hours since admission to emergency department while waiting for test results, the 48-hour window was reserved for cases in which this was not possible, for example, when the child had to be held on arms, or the patient’s condition on admission was very severe. We believe that applying more strict conditions on filling the parental questionnaire would have significantly reduced the response rate.

4. There were only 162 children included in the study, it is not stated how many children presented to
the ED with a fever in the study period and were not included. Were these children a biased sample?

Response to K.D. No.4:

Thank you for your question. In Children’s Clinical University Hospital, each year roughly 9 thousand visits to ED are febrile children. No overall data collection of precise number of febrile cases within the study period was collected as a part if this study. The data on children with febrile episodes during 2017, including number of patients seen each month, admissions, prescriptions of antibiotics etc. was collected for another international study, unfortunately the data remain unpublished to this date and are therefore confidential.

We did not perform a consecutive enrollment of all febrile episodes. The recruitment was done over 88 days, which were evenly distributed within the study period. All patients with febrile illness were theoretically eligible for the study if there were no exclusion criteria. However, not all patients agreed to participate in the questionnaire during the acute illness of their child, and the specifics of methodology require that the doctor of each patient enrolled agreed and had managed to fill the questionnaire before familiarizing oneself with the investigation results. We approached all patients who were present at the emergency department during recruitment hours and met these conditions, except the patients triaged as non-urgent and referred to the direct-access paediatrician, and only 162 patients were included in the final data analysis.

We have updated the methods and results section of the manuscript with a detailed information on patient recruitment which we had previously omitted.

Results section: “The recruitment occurred over 88 days during the study period. All patients who were eligible according to conditions described above were approached, and each day one to six patients were enrolled.

Overall, 266 patients were approached. Twenty-four patients were excluded as the clinicians did not manage to fill the clinician questionnaire before viewing the investigation results. Forty-six parents refused participation in the questionnaire, and 33 failed to submit the completed questionnaire within the specified time period. One patient was excluded as the evidence on the parental questionnaire suggested it was filled by the child and not the parent. In total, 162 patients were included in the study.” (Lines 179-187 on page 8).

5. The incidence of SBI was 28% which is much higher than in other studies and it is not fully explained why the rate is so high. The incidence of pneumonia was 17.3%. Pneumonia was defined as consolidation on CXR, and I wondered if some of these children had viral LRTI or was the entire sample biased toward sicker children?

Response to K.D. No.5

Thank you for your question. We are aware that the incidence of the SBI in the study population does not reflect the overall prevalence of SBI seen at the ED in the hospital. We have explained this in the discussion section of the manuscript:

“The prevalence of serious bacterial infections in the study sample was nearly 30%, which does not represent the overall prevalence of SBI in the study site. However, as the patients were recruited prospectively, the final diagnosis at the time of recruitment was unknown. Patients receiving intravenous fluids and requested awaiting blood test results were more likely to stay longer at the
emergency department and thus their parents were more prone to voluntarily participate in the parental survey and complete it by the end of their stay. As a result, some parents failed to submit the survey and were therefore excluded, and the patients classified as lower risk and discharged after examination or rapid antigen testing were scarcely enrolled (the study population included four such patients).” (Lines 328-337, pages 15-16).

We also did not approach the non-urgent patients seen by direct access paediatrician due to limited amount of time reserved for each patient. As a result, the study sample was indeed unintentionally biased towards sicker children.

As for pneumonia, the causative agent was not always identified, and none of the patients included in the study had pneumonia with confirmed viral aetiology. These patients were classified as SBI according to definition described in Methods [4].

6. Most children underwent investigations and 60% were admitted to hospital. This is a very high rate of admission and I wonder why they were admitted, especially if the clinician thought there was a low chance of SBI.

Response to K.D. No.6:

Thank you for your question. As we stated previously, the study sample did include children who are clinically more ill than patients attending the ED on average, which may partially explain the high admission rates. Comparatively high admission rates have also been noted in other studies conducted in Children’s Clinical University Hospital, and three reasons have been proposed for this, which are: 1) this is the only tertiary children’s hospital in the country and receives seriously ill children from the whole country; 2) the health-care system has traditionally been more hospital-centred when it comes to paediatric care, even though attempts are being made to transition towards predominantly outpatient management of mild to moderate childhood illnesses; 3) the parents of patients are generally not very compliant with oral rehydration strategies.

We did not collect and analyse information on the specific reasons for hospitalization among these patients, however indications other than SBI are usually need for intravenous rehydration, severe diarrhoea and vomiting, inability to reduce fever effectively, wheezing and respiratory failure (which is often viral-induced), viral meningitis etc, which often have little to do with the presence or absence of SBI. As our patients included some of the conditions mentioned above, this could also explain the need for hospitalization in their case.

6. The results of gut feeling/parent concern and the sensitivity and specificity for SBI cannot be reliably interpreted without accounting for the potential for bias as written above. And if the results were valid they do not provide reassurance to the ED physician that an SBI could be reliably detected on gut instinct alone.

Response to K.D. No.6:

We are aware that the selection bias could affect the applicability of the results to population outside the research sample, and therefore future research is necessary. However, the association of “gut feeling” with higher likelihood of the patient having SBI does provide assurance that it is a useful tool when evaluating a child with fever presenting not only to primary care but also to emergency department. It was not our aim to create assurance that SBI can be diagnosed based on gut feeling of the clinician or parent alone, but that it is a useful additional sign that can be applied in identification of
higher risk patients, and it may indicate the need for further investigations and assessment.

References: