Author's response to reviews

Title: How many preterm births in England are due to excision of the cervical transformation zone? Nested case control study

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Author's response to reviews: see over
Dear Mr Jason Pepito,

Re: 4046138691595367 - How many preterm births in England are due to excision of the cervical transformation zone? Nested case control study
Rekha Wuntakal, Alejandra Castanon, Rebecca Landy and Peter D Sasieni

We would like to thank the reviewers for their general positive comments on our manuscript. Our responses to their comments are below. We have endeavoured to be as thorough as possible in our responses, both here and in the main manuscript.

Reviewer#1:
Thank you for asking me to review this paper, which I have read and enjoyed. The paper is devoted to a highly topical and important subject in clinical practice and is worthy of publication in the journal. I would recommend acceptance and have just one comment which relates to the terminology used. In the methods section (line 91) the authors describe three documented measurements which were entered into the study database

Pathology reports were entered into the study database by two trained individuals (AP and TP) to ensure measurements were entered in a standardised way, facilitating the identification of the length, width and depth of specimens.

We apologise for the confusion in the text. Study sites entered details of the specimen (i.e date, type of sample, clear margins) into the database and additionally submitted the anonymised pathology reports to Barts and the London where two individuals entered each measurement into another database. We have rephrased the paragraph to make it clearer that by having two people entering the measurements we tried to ensure the measurements were always entered in the same order.

We will additionally change the measurement terminology used in the paper to come in line with that used in the Borenstein et al colposcopy terminology document.

In line 113 of the manuscript the authors define the depth of excision???.?Depth of excision was defined as the distance from the distal or external margin to the proximal or internal margin of the excised specimen? In the plethora of papers relating excision dimensions to risk of preterm labour there is some confusion of nomenclature. Terms like height, depth and length are not clearly defined and mean different things in different publications. As a result of this the IFCPC included excised specimen dimensions in their updated nomenclature. The definition of depth in this study is actually length as defined in other papers, and most importantly in the IFCPC nomenclature of 2012.

In this excellent paper by Wuntakal and colleagues it would help readers understand the implications of excised specimen dimensions if these dimensions were clearly defined and consistent with the IFCPC nomenclature (Bornstein et al 2012). The authors should define both in the text and in an illustration precisely what is meant by depth, length and width and, ideally, should use terms consistent with the IFCPC nomenclature. Many of the individual measurements in the study database may not have used terms that are easily understood but as far as possible the terms length, thickness and circumference...
should be used as these are in the IFCPC nomenclature and are clearly understood. Three pictures may be helpful in clarifying what is meant. These are: [http://www.biomedcentral.com/manuscript/review/attachment/pdf/1456811178167159.pdf]

We defined depth to mean length as defined by Bornstein et al in their 2012 guidelines. We agree that this may cause confusion. We have changed the terminology and replaced any mention of depth with length. The other two measurements are referred to by Bornstein as thickness and circumference (we had previously called them width and length). We hope that the terminology in this paper is now in line with the guidelines.

We are happy to add a diagram to illustrate the terms. However it is unclear whether any of the diagrams suggested by the reviewer are protected by copyright. We could use the same one used by Bornstein et al, but we are unsure how to obtain permission from Obstetrics and gynaecology where the images were initially published. As a compromise we could provide an email link to the Bornstein publication which contains the images. We have added this link to the end of reference 13. If the editor so wishes we are happy to obtain copyright permission from the journal to replicate the original image illustrating depth, thickness and circumference.

Reviewer#2:
This is an extremely well constructed and presented paper by one of the leading UK cancer epidemiological units in the UK. There have been many individual studies and meta-analyses suggesting increased premature deliveries after excision treatment to the cervix. Many have been biased towards adverse events as they have included knife cone biopsies and deep excisions as a reflection of Scandinavian practice which is more radical than current UK practice. The authors present the outcomes derived from English colposcopy clinics which are quality assured and practice standard out-patient loop excisional treatment. The authors have presented the risk of preterm delivery after excisions treatment stratified by depth of treatment in previous publications. This is an important paper as it is the first paper to my knowledge that has attempted to quantify the total number of preterm deliveries (and extreme preterm deliveries) in England giving the total number and the rate. This gives the reader an estimate of the contribution of colposcopy treatment to preterm deliveries. This has not been done before and therefore is original and will be cited. This is robust data on how the management of cervical disease impacts on reproductive outcomes and can be utilised in health economic evaluations particularly on the impact of HPV vaccination etc.

We thank the reviewer for their comments and hope that other readers feel the same way.

We hope that you find our response satisfactory.

Kind regards,
Alejandra Castanon