

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Associations between maternal size and health outcomes for women undergoing caesarean section: a multicentre prospective observational study (The MUM SIZE Study)
AUTHORS	Dennis, Alicia; Lamb, Karen; Story, David; Tew, Michelle; Dalziel, Kim; Clarke, Philip; Lew, Jospeh; Parker, Anna; Hessian, Elizabeth; Teale, Gyln; Simmons, Scott; Casalaz, Dan

VERSION 1 - REVIEW

REVIEWER	Juan Jesús Fernández-Alba University Hospital of Puerto Real University of Cádiz Public health service of Andalusia SPAIN
REVIEW RETURNED	01-Feb-2017

GENERAL COMMENTS	<ul style="list-style-type: none">- The term "pregnancy specific BMI cut-off values" can be confusing. In all groups (underweight, overweight, obese and super-obese) gestational age at delivery is over 37 weeks. Therefore, it might be more correct to speak of "at term" or "3th trimester" specific BMI cut-off values. For example, it would not be correct to apply the proposed cut-offs in pregnant women between 12 and 32 weeks of gestation.- Please, check the reference at page 4, line 29.- In the study are included as potential confounders age, gestational age at delivery, multiple pregnancy, pre-eclampsia ... but does not include gestational diabetes. Consider including this variable if possible.- Infection of the surgical wound is one of the main complications in obese women undergoing cesarean section. It would be very interesting to include this variable to calculate the risk in each study group.
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REVIEWER	Jessica Pudwell Research Facilitator Queen's University, Department of Obstetrics and Gynaecology Kingston, Ontario, Canada
REVIEW RETURNED	28-Feb-2017

GENERAL COMMENTS	1) Anesthesia time has been defined as total theater time minus surgical time, with surgical time starting when abdominal prepping commenced. I wonder if a slightly different definition of anesthesia time would better describe difficulties in establishing appropriate anesthesia in the obese population?
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	<p>I would propose considering anesthesia time from the start time till the time of incision. In table 2, it can be seen that the current anesthesia times range from 0 to 113 minutes. The lower bound of 0 minutes is a little confusing, I assume it occurs because abdominal prepping and anesthesia may be done concurrently in an emergent or urgent situation. However, incision time may still be delayed for these patients if there is difficulty establishing appropriate anesthesia and the surgical team may have to wait between prepping and making the incision.</p> <p>If this information is available I would be interested to see if the outcomes change with this different definition. If this is not available, it may be worthwhile including a comment in the discussion section about why some anesthesia times were recorded as 0 minutes. Specifically stating that your definition of anesthesia time may not reflect total time to establish appropriate anesthesia based on your current definition.</p> <p>2) Please provide more information on your cost analysis in the methods section. Please specify that you are using AUD. You state that costs were estimated to 2020. How was this done? Did you use a specific inflation rate?</p>
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REVIEWER	Jenny Cresswell London School of Hygiene & Tropical Medicine, UK
REVIEW RETURNED	01-Mar-2017

GENERAL COMMENTS	<p>This paper is interesting and clearly-written, and represents a useful addition to the literature. However, I do have a few comments and clarifications, listed below, which should be addressed before the manuscript is ready for publication.</p> <p>Major comments:</p> <p>Introduction: The introduction currently ignores the substantial literature on gestational weight gain, instead giving the impression studies that usually only prefer to pre-pregnancy BMI. This is misleading since there has been a lot of debate over the relative contributions to increased risk that pre-pregnancy BMI vs excess gestational weight gain make that are directly relevant to this paper (delivery BMI is effectively a product of the two). Plenty of studies compare the joint and independent effects of the two measures. This literature should be summarised in the manuscript, and the contribution it makes positioned in this context.</p> <p>Page 7; lines 17-48: The authors should describe the regression diagnostics used for their linear regression models.</p> <p>Page 7; lines 17-47: Did the analysis take clustering (hospitals) into account? If so, this should be made clear in the methods section; if not, what was the reason?</p> <p>Discussion: The first major finding of the paper stated is that using pregnancy-specific cut offs for BMI of +5 kg/m² was successful. The authors should explain more clearly why they feel that this is the most important finding of their paper (it wasn't clear to me on what this was based, because the paper doesn't provide any diagnostic information, comparison of different cut-offs or model diagnostics).</p>
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	<p>Furthermore it would be useful if, in the discussion section, the authors clarified whether they believed delivery BMI to be a preferable measure to reporting pre-pregnancy BMI and gestational weight gain (linking to first comment above), and if so why.</p> <p>Minor/ optional comments that may improve the paper:</p> <p>Page 4; line 43: "there are fewer reports on obesity and caesarean" The authors might want to consider clarifying this sentence, since there is a large literature on obesity & caesarean including multiple systematic reviews. I presume they mean relating to something more specific relating to surgery?</p> <p>Page 6; line 9-10: A brief explanation of these categories should be given without the reader needing to refer to another citation (or could be done in relevant table/footnote).</p> <p>Page 8; line 17: Range gives a BMI of 16 kg/m² at the time of the delivery: is this figure correct in the text? It seems implausibly low.</p> <p>The manuscript doesn't currently mention the ethnic composition of the participants in either the methods or discussion sections. Different cut-offs are usually used for women of Asian ethnic backgrounds: to what extent was this an issue in this study?</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments: Dr Fernández-Alba

- The term "pregnancy specific BMI cut-off values" can be confusing. In all groups (underweight, overweight, obese and super-obese) gestational age at delivery is over 37 weeks. Therefore, it might be more correct to speak of "at term" or "3th trimester" specific BMI cut-off values. For example, it would not be correct to apply the proposed cut-offs in pregnant women between 12 and 32 weeks of gestation.

Thank you for your comment. Whilst the mean gestational age at delivery is 38 weeks, the range is from 25.0 – 42.0 weeks. This is shown in Table 1 and Table 2. The terms "at term" or "3rd trimester" therefore do not fit with what we are describing. We are describing pregnancy specific BMI cut-off values for women at delivery. I have added the term "for women at delivery" throughout the text to assist with clarification.

- Please, check the reference at page 4, line 29.

I have checked this reference. It is correct.

- In the study are included as potential confounders age, gestational age at delivery, multiple pregnancy, pre-eclampsia ... but does not include gestational diabetes. Consider including this variable if possible.

Thank you for your comment. We did not think that gestational diabetes would effect anaesthesia or surgical time so we did not include it as a confounding variable as it was no included in the case report form as a recordable variable. Cases of macrosomia (birth weight > 4000 g) and low birth weight (< 2500 g) were recorded and the association with birth weight and anaesthesia, surgical and total theatre time was poor.

- Infection of the surgical wound is one of the main complications in obese women undergoing cesarean section. It would be very interesting to include this variable to calculate the risk in each study group.

We have reviewed the case report form and data were collected on reasons for return to the operating theatre, one of which was infection. According to the data, only one of the nine women that returned to the operative room following caesarean section returned due to infection. This is too few for an analysis of this as an outcome.

Reviewer 2 comments: Dr Pudwell

- 1) Anesthesia time has been defined as total theater time minus surgical time, with surgical time starting when abdominal prepping commenced. I wonder if a slightly different definition of anesthesia time would better describe difficulties in establishing appropriate anesthesia in the obese population?

- I would propose considering anesthesia time from the start time till the time of incision. In table 2, it can be seen that the current anesthesia times range from 0 to 113 minutes. The lower bound of 0 minutes is a little confusing, I assume it occurs because abdominal prepping and anesthesia may be done concurrently in an emergent or urgent situation. However, incision time may still be delayed for these patients if there is difficulty establishing appropriate anesthesia and the surgical team may have to wait between prepping and making the incision.

- If this information is available I would be interested to see if the outcomes change with this different definition. If this is not available, it may be worthwhile including a comment in the discussion section about why some anesthesia times were recorded as 0 minutes. Specifically stating that your definition of anesthesia time may not reflect total time to establish appropriate anesthesia based on your current definition.

Thank you for your comments. We chose to record surgical time from when the abdomen is prepped to when the final dressing is applied, and then anaesthesia time being total theatre time – surgical time. The reason we chose these times were because hospital computer systems record these times routinely. We agree that for some patients the time between surgical prepping and surgical incision may be increased if there is difficulty establishing anaesthesia (in the case of difficult tracheal intubation for example). It is also true that the times when anaesthesia were recorded as zero minutes were when surgical prepping and anaesthesia commenced at the same time. As the incision time data is not available I have added a comment in the discussion section about why some anaesthesia times are recorded as zero minutes and specifically stated that according to our definition of anaesthesia time, in some cases this may not reflect the total time to establish anaesthesia if there is a delay between surgical prepping and incision time due to establishment of anaesthesia.

- 2) Please provide more information on your cost analysis in the methods section. Please specify that you are using AUD. You state that costs were estimated to 2020. How was this done? Did you use a specific inflation rate?

I have added additional information in the health economic data and cost analysis section of the manuscript, as well as two references, to answer these questions.

Reviewer 3 Dr Cresswell

- Introduction: The introduction currently ignores the substantial literature on gestational weight gain, instead giving the impression studies that usually only prefer to pre-pregnancy BMI. This is misleading since there has been a lot of debate over the relative contributions to increased risk that pre-

pregnancy BMI vs excess gestational weight gain make that are directly relevant to this paper (delivery BMI is effectively a product of the two). Plenty of studies compare the joint and independent effects of the two measures. This literature should be summarised in the manuscript, and the contribution it makes positioned in this context.

Thank you for your comments. Yes on re-reading this section the absence of a comment on gestational weight gain, and its importance in the pregnancy literature, is remiss of us. I have modified the second and third paragraphs of the introduction and included two references, and I now think it is much more balanced and logical.

- Page 7; lines 17-48: The authors should describe the regression diagnostics used for their linear regression models.

I have added a sentence in the statistical analysis section to describe this.

- Page 7; lines 17-47: Did the analysis take clustering (hospitals) into account? If so, this should be made clear in the methods section; if not, what was the reason?

All models included adjustment for hospital and this has been added to the statistical analysis section.

- Discussion: The first major finding of the paper stated is that using pregnancy-specific cut offs for BMI of +5 kg/m² was successful. The authors should explain more clearly why they feel that this is the most important finding of their paper (it wasn't clear to me on what this was based, because the paper doesn't provide any diagnostic information, comparison of different cut-offs or model diagnostics). Furthermore it would be useful if, in the discussion section, the authors clarified whether they believed delivery BMI to be a preferable measure to reporting pre-pregnancy BMI and gestational weight gain (linking to first comment above), and if so why.

Thank you for your comment. I have removed the somewhat confusing sentence at the beginning of the discussion about BMI increases and highlighted the major findings. I have added that recording of pre-pregnancy BMI and gestational weight gain are important and so too are height and weight measurements throughout pregnancy so that delivery BMI can be calculated enabling planning around the time of delivery.

- Page 4; line 43: "there are fewer reports on obesity and caesarean" The authors might want to consider clarifying this sentence, since there is a large literature on obesity & caesarean including multiple systematic reviews. I presume they mean relating to something more specific relating to surgery?

This has been clarified in the manuscript.

- Page 6; line 9-10: A brief explanation of these categories should be given without the reader needing to refer to another citation (or could be done in relevant table/footnote).

The categories have been added in a footnote.

- Page 8; line 17: Range gives a BMI of 16 kg/m² at the time of the delivery: is this figure correct in the text? It seems implausibly low.

Thank you for questioning this. We have rechecked the data and the calculation of BMI for these women used their pre-pregnancy weight therefore the BMI of 16 is incorrect. Using their delivery weight their BMIs are still low however not implausibly low (17.4 kg/m²). The next lowest was 18.94

kg/m².

- The manuscript doesn't currently mention the ethnic composition of the participants in either the methods or discussion sections. Different cut-offs are usually used for women of Asian ethnic backgrounds: to what extent was this an issue in this study?

We did not include ethnic composition. We do not think this is a significant issue in this study. Ethnicity is difficult to define and it is unclear how ethnicity by itself could contribute to the changes in this study related to time. In general, it is likely that socioeconomic status and educational status, independent of ethnicity, play a much larger role in observed differences in studies.

Thank you once again for reviewing our manuscript.

VERSION 2 – REVIEW

REVIEWER	Juan Jesús Fernández Alba Hospital Universitario de Puerto Real Servicio Andaluz de Salud Spain
REVIEW RETURNED	17-Apr-2017

GENERAL COMMENTS	<p>I think that the manuscript in its present form could be published.</p> <p>The comments for the authors are as follows:</p> <ul style="list-style-type: none">- The current manuscript clarifies that the BMI classification corresponds to the time of delivery.- The non-inclusion of diabetes as a potential confounder is a limitation of the present study. Consider including this comment as a limitation of the study.- In page 10 line 31 the words "can be" are repeated. <p>It is necessary to take into account that the results of the present study were published as a summary of a poster in the Obstetric Anaesthesia 2016 congress (MAY 19-20, 2016, MANCHESTER CENTRAL CONVENTION COMPLEX, UK). http://www.epostersonline.com/oa2016/node/46</p> <p>Thank you very much for giving me the opportunity to review this article.</p>
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REVIEWER	Jessica Pudwell Queen's University, Department of Obstetrics and Gynaecology Kingston, Ontario, Canada
REVIEW RETURNED	18-Apr-2017

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.
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REVIEWER	Jenny Cresswell London School of Hygiene & Tropical Medicine, UK
REVIEW RETURNED	10-Apr-2017

GENERAL COMMENTS	Thank you for addressing my comments on the previous version. This is an interesting paper.
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