

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Intrapartum interventions and outcomes for women and children following induction of labour at term in uncomplicated pregnancies: A 16 year population based linked-data study
<b>AUTHORS</b>	Dahlen, Hannah; Thornton, Charlene; Downe, Soo; de Jonge, Ank; Seijmonsbergen-Schermer, Anna; Tracy, Sally; Tracy, Mark; Bisits, Andrew; Peters, Lilian

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Felice Petraglia University of Florence
<b>REVIEW RETURNED</b>	24-Jan-2021

<b>GENERAL COMMENTS</b>	<p>This original paper adds important informations in the scenario of IOL.</p> <p>I think the major strength is in the interpretation of the results considering parity (especially) and gestational age.</p> <p>As regard the neonatal outcomes I suggest to enclose the data about the arterial pH from umbilical cord at birth (main indicator of hypoxia) and to consider an APGAR score &lt;7 and not &lt;4.</p> <p>Despite the indisputable strengths of the study, I would like to have clarifications on some points that could reduce the power of the study:</p> <ul style="list-style-type: none"> <li>-have you comparison data on different methods of IOL?</li> <li>-how do you justify the bias due to the differences in population characteristics between the group of IOL vs the group of no-IOL?</li> <li>-are you sure that all the patients included in the group of IOL did not have any indication for induction?</li> </ul> <p>The data on instrumental birth is not clear. In the results you write that they were 23.9% in IOL and 28% in spontaneous birth, in the discussion you write that IOL is a risk factor for instrumental birth.</p>
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<b>REVIEWER</b>	Citra Mattar Natl Univ Singapore, Obstetrics & Gynaecology, Yong Loo Lin School of Medicine
<b>REVIEW RETURNED</b>	10-Feb-2021

<b>GENERAL COMMENTS</b>	<p>This large retrospective observational study of low-risk pregnancies undergoing labour induction and associated short and long-term outcomes is an important work that allows appreciation of certain outcomes such as successful vaginal deliveries, operative deliveries and major perinatal complications.</p> <p>Outcomes that are "worse" following IOL such as SVD rate and caesarean section rate may reflect more stringent medical labour management, and may not reflect the recent trend towards a more</p>
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	<p>physiological understanding and management of labour, especially in primigravidas.</p> <p>Significant limitations are related to the retrospective observational nature of the study and inability to examine cause and effect, inherent biases in the study population, and the understanding that the results may not truly reflect clinical outcomes because of the study design, which are adequately discussed.</p> <p>The paper reiterates the need for correct and appropriate utilization of IOL for sound clinical indications to avoid the described complications.</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

This original paper adds important informations in the scenario of IOL.  
I think the major strength is in the interpretation of the results considering parity (especially) and gestational age.

Thank you for your kind comments

As regard the neonatal outcomes I suggest to enclose the data about the arterial pH from umbilical cord at birth (main indicator of hypoxia) and to consider an APGAR score <7 and not <4.

Thank you for your comments. We don't have arterial pH in the linked data set. We would have loved to add this, but it is not available and not routinely done in Australia. We have used Apgar less than 4 as it is more associated with neonatal mortality and cerebral palsy than Apgar score less than 7. ACOG is warning that Apgar is not predictive of individual neurological outcome.  
<https://pediatrics.aappublications.org/content/pediatrics/early/2015/09/22/peds.2015-2651.full.pdf>  
We feel Apgar below 7 is not discriminating enough. In several large studies like this Apgar below 4 is being used.

We have added the following sentence to the limitations

"We did not have access to neonatal umbilical pH or Lactate in the population data set we analysed and this is not done routinely at every birth in Australia."

Despite the indisputable strengths of the study, I would like to have clarifications on some points that could reduce the power of the study:

-have you comparison data on different methods of IOL?

Thank you for this suggestion we have added the prevalences (n,%) of the different methods used for IOL in the results section of the manuscript:

"In the IOL group, 45 370 (65.4%) women were induced with a combination of two methods i.e. artificial rupture of membranes and oxytocin/prostaglandin. The other women in the IOL group were induced with one method, i.e. oxytocin/prostaglandin (n=16 974, 24.5%) or artificial rupture of membranes (n=6572, 9.5%) or other method such as foley catheter (n=481, 0.6%)."

-how do you justify the bias due to the differences in population characteristics between the group of IOL vs the group of no-IOL?

We have attempted to minimise the bias in the following way: In the total population, associations between IOL and short term maternal and children's outcomes were adjusted for maternal characteristics (i.e. maternal age, country of birth, socio economic position, gestational age, and parity). Next, associations were calculated separately for at term primiparous births (first birth) and at term multiparous births (subsequent births). All associations were adjusted for maternal age, country of birth, socio economic position, and gestational age. Afterwards, associations were calculated individually for each completed gestational week and adjustments were made for maternal age, country of birth, socio economic position and parity. This is all detailed in the paper

-are you sure that all the patients included in the group of IOL did not have any indication for induction?

As indicated in the limitations section we cannot guarantee that some of the inductions did not have some rare indication but on the whole we know there are many inductions done in Australia, especially in the private sector without medical indication and this is the closest we can get to non medically indicated inductions. To try and also increase the accuracy of this we have only included a very low risk population with no medical or pregnancy complications.

The data on instrumental birth is not clear. In the results you write that they were 23.9% in IOL and 28% in spontaneous birth, in the discussion you write that IOL is a risk factor for instrumental birth.

Thanks for picking this error up. We had this the wrong way around. It is 28.0% instrumental birth with IOL and 23.9% without IOL for primiparous women. We have now changed this.

Reviewer: 2

This large retrospective observational study of low-risk pregnancies undergoing labour induction and associated short and long-term outcomes is an important work that allows appreciation of certain outcomes such as successful vaginal deliveries, operative deliveries and major perinatal complications.

Outcomes that are "worse" following IOL such as SVD rate and caesarean section rate may reflect more stringent medical labour management, and may not reflect the recent trend towards a more physiological understanding and management of labour, especially in primigravida's.

In Australia the trend is away from physiological management and currently 45% of selected first time mothers (aged between 20 and 34 years, whose baby's gestational age at birth was between 37 and 41 completed weeks, with a singleton baby in the vertex presentation) were induced (34% overall, 25% in 2008). We have added this to the background.

"In Australia 45% of selected primiparous women (aged between 20 and 34 years, gestational age between 37 and 41 completed weeks, singleton baby in the vertex presentation) were induced 4. Overall the induction rate in the total Australian birthing population was 34% in 2018, almost a third increase in the last decade 4. Despite this there has been no change in the numbers of stillbirths or neonatal deaths in the last decade 4"

Significant limitations are related to the retrospective observational nature of the study and inability to examine cause and effect, inherent biases in the study population, and the understanding that the results may not truly reflect clinical outcomes because of the study design, which are adequately discussed.

Thanks, we agree these are limitations and have tried to be very transparent. We have added again to the limitations in the front of the paper too.

The paper reiterates the need for correct and appropriate utilization of IOL for sound clinical indications to avoid the described complications.

Thank you we agree.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Felice Petraglia University of Florence
<b>REVIEW RETURNED</b>	06-May-2021
<b>GENERAL COMMENTS</b>	The reviewer completed the checklist but made no further comments.