Reviewer’s report

Title: International standardisation of reporting of perinatal mortality for births following assisted reproductive technology treatment

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Reviewer: Rebecca RC Painter

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This paper displays the perinatal mortality rate (PMR) in a large number of ART deliveries in Australia in New Zealand, and demonstrates the effect of using various cut-offs for the definition of fetal/neonatal/perinatal mortality has on the PMR. Also, the authors show a comparison of PMR after ART reported in various international publications, reporting on the same time slot (2004-2008).

The authors advocate ART outcomes being reported in terms of PMR, in order to allow for international benchmarking. The focus of benchmarking in this paper is perinatal outcomes after SET/DET and multiple gestation.

The data presented by the authors is of interest and represents an important move towards improved quality of care after ART. Hopefully papers like this one will contribute to reporting PMRs after ART becoming standard international practice. The paper is generally clearly written, although there are some limitations that I feel need to be extensively addressed.

Major compulsory revisions

1. The research question is not clearly defined. The ‘Background’ section ends with the research aim: ‘To provide evidence of the need for a uniformed approach for reporting perinatal mortality we sought to apply different international definitions for fetal, neonatal and perinatal death to the Australian and New Zealand ART registry data; and to compare the resulting PMR by plurality and number of embryos transferred.’ This sentence summarizes the discrepancy between the aims of the study and the data the authors have used to achieve their aims: the authors are limited in their major comparison to Australia and New Zealand. Various cut-off points have been applied to the dataset, but other major issues in international comparisons have not been addressed. For example, confounding (see below) has not been studied, linkage to national perinatal databases was not attempted or performed (or availability and reliability for linkage studied for various countries).

The discrepancy is illustrated by the title and the abstract: the title suggests a study on standardised international outcomes, but in the abstract it does not become apparent which international aspects are being studied. I would suggest adapting the title and the background and discussion section to suit the scope of the study: Perinatal mortality in births following assisted reproductive technology treatment in Australia and New Zealand (or something along those lines) The alternative- adapting the paper to the title- is an option, but would require a lot
more work.

Minor essential revisions

1. Has the quality of data collection of ANZARD been assessed (for example by cross linkage to perinatal registries or death registries)? If so please include reference.

2. The paper states that Sweden and Denmark have defined perinatal mortality as >= 28 weeks, however (ref 27 and 29). However, reference 27 reports on Finland (and not Sweden or Denmark). Reference 29 reports on a Swedish study that chose to use >28 weeks for the PMR definition using data from the Swedish Medical Birth Registry. Sweden (Swedish Medical Birth Registry) was able to deliver data using >22 weeks for the Peristat report (http://www.européristat.com), which provides a useful overview for fetal, early and late neonatal mortality definitions across Europe which may be helpful for Box 1 too. Could the authors correct the references, and use more caution in their statements about the availability of data in various countries?

3. Which methods were used to search for the publications reporting on perinatal mortality after ART in various countries? Could the authors describe in more detail whether this was a comprehensive systematic search (which databases were studied? How many studies were found, and excluded?), or whether they display a number of examples (in which case how were the examples chosen) for their comparison to Australian and New Zealand ART perinatal outcomes?

4. Were any data from the ANZARD database extracted (or available) on known confounders including maternal age, BMI, smoking? Were other ART-related possible determinants of perinatal outcome besides SET/DET, including blastocyst/d3 embryo, fresh/frozen, indication for ART (tubal, male infertility, unknown) available?

5. Table 2 displays a comparison of frozen embryo cycles? How were the data obtained for this comparison?

6. Is this discussion about which cut-off to use new? In international obstetric outcome studies, comparing quality of care across countries, the discussion on determination of cut-offs for inclusion has been published on extensively. Euro-Peristat (European comparative perinatal mortality rates) struggles with the varied data input every few years, and others have looked at countries outside Europe: see for example Mohangoo et al, International comparisons of fetal and neonatal mortality rates in high-income countries: should exclusion thresholds be based on birth weight or gestational age? Plos One 2013; Joseph KS et al, Influence of definition based versus pragmatic birth registration on international comparisons of perinatal and infant mortality: population based retrospective study. BMJ 2012, Lawn JE et al, Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data, BMC Pregnancy and Childhood 2010. The authors could draw from and discuss the experience on for example the effects of and the methods of tackling under reporting.

7. Bias in PMR estimate: PMR reflects a broad composite of factors involved in
perinatal care. Underlying international differences in perinatal mortality unrelated to ART, for example population characteristics (including ethnicity, socio-economic factors, age at delivery, maternal smoking, maternal obesity) and health care system characteristics (including quality of care/availability of neonatal services, legislation on termination of pregnancy and gestational age limits for termination of pregnancy, health care insurance, quality registration) may confound international comparisons. This could be tackled by somehow correcting for national general (non-ART specific) perinatal mortality rate or by correcting as many of the available confounders as possible, the authors must comment on confounding or make an attempt to account for bias in their own data.

8. ART determinants of PMR: SET/DET and twinning rates are known important determinants of perinatal mortality after ART. But the strength of standardized international reporting of PMR after ART may also be the ability to assess the contribution of other factors. For example, patient selection (age, BMI, parity, indication for ART), financial/insurance/billing strategies (number of cycles reimbursed, percentage reimbursed, age limit reimbursement, duration of infertility before reimbursement) and features of ART treatment (culture conditions, IVF/ICSI, stimulation regimens) may each effect the perinatal outcome. In order for us to find out more about these risk factors, international registration would need to aim at including many more characteristics than SET/DET. Could the authors discuss these issues in the discussion?

9. Comparison to non-ART pregnancies: Embedding a suggested ART perinatal database in national perinatal databases or providing linkage to national perinatal databases may have advantages, as comparisons to non-ART pregnancies become possible. For example: the highest PMR (50.5 per 1000 SET births, 95% CI 36.5-64.5) was for twins following SET births would have greater meaning if it were possible to compare the PMR to that of monozygous/monochorionic twins after natural conception. Although this is beyond the scope of this paper, the authors could include a little more in their discussion on this topic of linkage. The comment in the last paragraph of the discussion about the lack of linkage to national perinatal database in Australia lacks clarity, or assumes more knowledge of the local situation than most readers will have.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests