Reviewer’s report

Title: Distinct regional differences in perinatal mortality in the Netherlands

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Reviewer: Bengt Källén

Reviewer’s report:

This is a well written and interesting paper. The authors pose a clear question and use a national perinatal register as source of information.

Major compulsory revisions

1. Title of article. The title just tells that there are regional differences in perinatal mortality but the article also tries to explain these differences. ‘Should this not be apparent in the title?’


a) On p 5 it is said that the register used contains information on about 96% of all deliveries in the Netherlands. The drop-out rate is not large but may be skewed. At least in our country, we know that the cases missed in the central medical birth register are to some extent selected and with an excess of complicated deliveries, including infant deaths, multiple birth and severe congenital malformations. This may not be so in the Netherlands but I think this must be discussed. Furthermore, it is not clear if the drop out rate is the same in the different regions. As the authors know that there is about 4% missing, I suppose there is an administrative register which can be used for checking the completeness of the data in the various regions.

b) On p 5-6 it is said that the preterm birth and low birth weight were analyzed as mediating outcome measures. The authors have chosen <37 weeks, <2500g and low Apgar (<7 at 5 minutes). These are cut-off values which are often used in reproduction epidemiology but if one is interested in risk factors for perinatal death, I think one should choose lower limits, perhaps <32 week, <1500g weight (or even <1000g), and <4 Apgar score. Later on they distinguish between preterm and very preterm but this should be clarified already in the methodological description.

c) On p. 8 the authors describe the statistical analysis as logistic modeling, but no further details on the actual modeling is given. They have, for instance, used maternal age as one dependent variable. Was that a linear regression or did one take into consideration the U-formed association between maternal age and perinatal death risk (seen in Table 3). If you have a U-formed association and puts a straight line into the model, the association may seem non-existent. The same is true for parity and to this can be added that maternal age and parity interact: low maternal age and high parity and high maternal age and low parity
are high risk strata. It is not clear how these problems have been solved. By
giving each maternal age stratum a 0-1 variable etc.??

d) Also on p. 8 the categorization into severe congenital anomalies and without
such anomalies is described but no definition of what is meant with severe
congenital anomalies. There are many severe anomalies which are no death
risks (e.g., absent of a hand). I suppose what would have been more relevant
was the presence of a malformation which carries a marked death risk, e.g.,
diaphragmatic hernia and omphalocele but not gastroschisis. Anyway, the
authors must describe how they defined severe congenital anomalies and tell
how they were identified and give some ideas about prevalence at birth, total and
by region. – The authors do not mention the phenomenon on prenatal diagnosis
and selective abortion. Could regional differences in the extent and efficiency of
prenatal diagnosis (and perhaps acceptance of induced abortion when a severe
malformation is found) contribute to the variability in death rate (p. 13).

e) The authors miss important data on smoking and BMI on an individual level.
They do adjust for regional differences between these characteristics which I
suppose is as close they could come. I suppose these data refer to the smoking
rate in the population and not to smoking among pregnant women (which may
differ) and the same is probably true for BMI. The authors should specify what
type of data they have. They quote papers from other parts of the world where it
is made likely that socioeconomic and ethnic adjustments take care also of
smoking and BMI. If this is true in the Netherlands is just a guess, I suppose.
How do the authors define heavy smoking (Table 2)? The rates given in that
Table are very low which indicates that they have a rather high cut-off rate. Also
moderate maternal smoking is a risk factor for perinatal mortality ref. 23).

3. Data presentation.

a) Figure 1: I must confess that I do not understand this Figure. What do the
black circles mean? Obviously they should mark the province contribution to the
total birth rate. The proportions of births are given as percentages in Table 1 and
I think that is enough. Figure 1 could be kept in order to describe the geography if
that really is of importance for the reader but I think the black circles are only
confusing.

b) Figure 2. What does this Figure add? Rates of stillbirths per region and
province – but those numbers could equally well be given in a Table which could
contain the actual numbers (similar to Table 1). I would suggest that Table 1
contains data on total number of children, number of preterm birth (preferably for
<32 weeks), low birth weight (preferably for <1500 or <1000g) and low Apgar
score (preferably <4) and that all information on stillbirth, early neonatal death
and perinatal death is given in a separate table.

Minor revisions

The authors use weeks.days for gestational length which is confusing because it
looks like a decimal point. Usually one writes weeks+days, e.g., 20+0-25+6.
Level of interest: An article whose findings are important to those with closely related research interests

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.