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Pitfalls in the use of register-based data for comparing adverse maternal and perinatal outcomes in different birth settings

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Routinely collected registration data are an efficient source for conducting research. In particular, they are useful for studies with rare outcomes, as these require large sample sizes, which are difficult to obtain through targeted data collection. Registration data are often used to compare severe, adverse maternal and perinatal outcomes in different birth settings. However, registration data are primarily recorded for purposes other than research, such as supporting care processes. Subsequently, if these data are used for scientific studies, the analyses are, by definition, 'secondary' and therefore are likely to have more limitations compared with prospectively and purposely collected research data. We wanted to show how some of these limitations can lead to erroneous conclusions, using the Dutch perinatal register as an example. This may help researchers to avoid some of the pitfalls of using register-based data and help service users, professionals and policy makers to recognise these limitations when interpreting study findings.
We use the framework in Figure 1 to illustrate the following three categories of limitations when analysing register-based data for comparing maternal and perinatal outcomes in different birth settings[1]: (1) *the study numerator and denominator* represent different populations; (2) *choice of comparison groups* is not appropriate for the research question; (3) *limited representativeness and external validity*.

THE NETHERLANDS PERINATAL REGISTER (PERINED)

Data on perinatal care in the Netherlands are routinely collected in three databases by primary care midwives (perinatal database-1), obstetricians (perinatal database-2) and paediatricians (neonatal database). Via a validated linkage method, these data are combined into one perinatal database (Perined).[2] The variable 'start of labour in midwife-led or obstetrician-led care' has been created using information from other variables, such as referral from midwife-led to obstetrician-led care, timing of referral, and place of birth. Filling in some variables, such as place of birth, is compulsory and professionals are notified if they did not record any information or if the information is not consistent with other variables (for example, a woman cannot give birth at home if the obstetrician was responsible for her care at the time of birth). Other variables are not compulsory and are therefore not always recorded.

[FIGURE 1.]

When comparing rates of adverse outcomes for different birth settings it is important that cases in the *numerator and the denominator* come from the same study group. Problems with the selection of the numerator and denominator were present in an analysis conducted by Evers et al. in 2010.[3, 4] They compared rates of perinatal mortality and morbidity among 37 735 births that started in midwife-led versus obstetrician-led care (group a versus group b in Figure 1). The researchers collected maternity care records of all neonates who died during labour or in the first week of life and of their mothers from all primary midwifery care practices and hospitals located in the Utrecht Neonatal Intensive Care (NICU) region. For the denominator, information was used from Perined of women with a postal code of their home address in the Utrecht NICU region.

Births attended by professionals in primary care practices and hospitals in the Utrecht region were not included in the denominator if women lived in another region. However, an unknown number of neonates born to these women in other regions who died, were included in the numerator if their primary care practice or hospital was located in the Utrecht region. Therefore, births in groups a and b came from a different geographical area in the numerator and denominator; births outside the Utrecht NICU region that met the inclusion criteria were included in the numerator but not in the denominator. When the analysis was repeated in the Amsterdam area, this problem was addressed by selecting births in the numerator as well as the denominator from the Amsterdam NICU region.[5] In this analysis among 83 909 births, no significant difference in intrapartum and neonatal death rates was found among births that started in midwife-led versus obstetrician-led care.

The second limitation concerns the *choice of comparison groups*. In the Netherlands, most low-risk women receive midwife-led care.[6] If risk factors or complications arise, they are referred to obstetrician-led care. Indications for referral are listed in the so-called obstetric indication list.[7] Although a minority of low-risk women choose to have obstetrician-led care throughout their pregnancy, the majority of women have a medical indication for obstetrician-led care, such as hypertension or post-term pregnancy. When studying the association between type of care at the onset of labour and maternal and perinatal outcomes, controlled for other factors, one should preferably compare women with the *same low-risk profile* who start labour in midwife-led versus obstetrician-led care (group c versus e). This is what the research team of the Amsterdam study set out to do. Ideally, the obstetrician-led care

subgroup should only consist of women who would have had no indication for referral if they had been in midwife-led care.

However, not all indications for referral are registered in Perined. For example, in a study into severe acute maternal morbidity, 27% of women with a previous caesarean section had no record of this risk factor in Perined.[8] Again, this can lead to *problems in the definition of the numerator and denominator*. In the Amsterdam study, information on the cases of intrapartum and neonatal death was collected from maternity care records. If risk factors that would be indications for referral were present, these cases were removed from the numerator so that only low-risk women remained (group e). For the denominator, information was taken from Perined. If information on risk factors was missing, cases (from group f) would mistakenly not be removed from the denominator. The rate of intrapartum and neonatal death would then appear to be lower than it was in reality.

Therefore, the researchers of the Amsterdam study examined the magnitude of the problem of missing information on risk factors by comparing information in maternity care records with register data in Perined (article in preparation). Two samples of 100 records each were randomly selected among women in obstetrician-led care at the onset of labour. One sample was taken from women for whom no indication for referral according to the obstetric indication list was recorded in Perined. In 37% of these cases, at least one indication was mentioned in the maternity care records, which was not registered in Perined. For an additional 22% of cases, labour started in midwife-led care, whereas information in the register suggested that it started in obstetrician-led care. The second sample was taken from women who did not have one of eight risk factors, such as caesarean section. In 13% of these cases, information on one or more of these eight risk factors was recorded in the maternity care records but was missing in Perined, and an additional 12% of women started labour in midwife-led care, whereas starting labour in obstetrician-led care was recorded in Perined. These findings demonstrate a substantial rate of misclassification and illustrate that it is not possible to compare low-risk women who started labour in midwife-led versus obstetrician-led care (group c versus e) in the Netherlands reliably on the basis of Perined data.

If risk levels in study groups are not equal, a comparison of outcomes provides little information on a possible difference in quality of care if confounding cannot be adequately controlled for. For example, lower rates of severe acute maternal morbidity have been found among women who start labour in midwife-led versus in obstetrician-led care (group a versus b).[8] To a large extent, this is most probably attributable to the fact that women in midwife-led care have fewer obstetric risk factors, rather than due to the care women receive in either setting. The rate of adverse outcomes in midwife-led groups is expected to be equal to or lower than the rate in obstetrician-led groups.

On the other hand, some Dutch studies found higher rates of adverse perinatal outcomes among women who were referred during labour versus those who were in either midwife-led or obstetrician-led care throughout labour.[3, 9] The midwife-led care group only included women that were referred because of risk factors or complications, whereas women who were not referred, both in midwife-led and obstetrician-led care, included those with low-risk births (group k versus i, j, l and m). Hence, the groups of referred and non-referred women were not comparable. Therefore, these findings do not answer the question of whether women who develop

complications during labour have a higher chance of adverse outcomes if they started labour in midwife-led care compared to women with the same risk profile who started labour in obstetrician-led care (group k versus m).
Equally, studies comparing *actual* places of birth without taking the responsible caregiver into account (group i versus j and k), are not comparing like with like, because women with risk factors or complications are referred to obstetrician-led care and give birth in hospital.[10] To study the association between place of birth and adverse outcomes, different *planned* places of birth should be compared regardless of the *actual* place of birth (group g versus h), similar to intention-to-treat analyses in clinical trials.
Finally, findings from well-conducted studies based on registers may be informative for the setting in which they were conducted, but may *not be representative for other settings*, for example where characteristics of midwife-led care may be different (group a). Studies in the Netherlands did not show any increased rates of adverse outcomes among planned home versus planned hospital births (group g versus h).[6, 11] These studies have been conducted in a country with a good risk selection and emergency transportation system and well-trained, licensed midwives. The findings may therefore not apply to other maternity care settings. Indeed, a study in Oregon found a higher rate of perinatal mortality among planned out-of-hospital births compared with planned hospital births.[12] However, the out-of-hospital birth group included women with risk factors (group d) that would be indications for hospital birth in other settings and not all women were assisted by licensed midwives.
In short, large datasets of routinely collected data are the best available resources to compare rare, adverse maternal and perinatal outcomes in different birth settings. Because these data are primarily recorded for other reasons than to be used for research, they have several limitations. Considering the importance of registration data for studying rare outcomes, it is vital that the quality of these data is monitored and continuously improved. The limitations of these data should be kept in mind when designing secondary analyses using these data and interpreting their results. Failure to do so will lead to misinforming women, professionals and policy makers about the implications for clinical practice of studies comparing different birth settings.

DISCLOSURE OF INTEREST

None declared. Completed disclosure of interests form available to view online as supporting information

CONTRIBUTION TO AUTHORSHIP

AJ conceived the idea for the commentary and wrote the draft text. MW, JK, JB, JZ, JvD, HvdH and FS critically revised earlier drafts of the commentary for important intellectual content and gave final approval of the version to be published.

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REFERENCES

1 Van Walraven C, Austin P. Administrative database research has unique characteristics that can risk biased results. J Clin Epidemiol 2012;65:126–31.
2 Meray N, Reitsma JB, Ravelli AC, Bonsel GJ. Probabilistic record linkage is a valid and transparent tool to combine databases without a patient identification number. J Clin Epidemiol 2007;60:883–91.
3 Evers AC, Brouwers HA, Hukkelhoven CW, Nikkels PG, Boon J, van Egmond-Linden A, et al. Perinatal mortality and severe morbidity in low and high risk term pregnancies in the Netherlands: prospective cohort study. BMJ 2010;341:c5639.
4 De Jonge A, Mol BW, Van der Goes BY, Nijhuis JG, van der Post JA, Buitendijk SE. Dutch perinatal mortality. Too early to question effectiveness of Dutch system. BMJ 2010;341:c7020.
5 Wiegerinck MMJ, Van der Goes BY, Ravelli ACJ, van der Post JAM, Klinkert J, Brandenbarg J, et al. Intrapartum and neonatal mortality in primary midwife-led and secondary obstetrician-led care in the Amsterdam region of the Netherlands: A retrospective cohort study. Midwifery 2015;31:1168–76.
6 De Jonge A, Geerts CC, Van Der Goes BY, Mol BW, Buitendijk SE, Nijhuis JG. Perinatal mortality and morbidity up to 28 days after birth among 743 070 low-risk planned home and hospital births: A cohort study based on three merged national perinatal databases. BJOG 2015;122:720–8.
7 College voor Zorgverzekeringen. [Obstetric manual]. Diemen, 2003.
8 De Jonge A, Mesman JAJM, Manniën J, Zwart JJ, Buitendijk SE, van Roosmalen J, et al. Severe adverse maternal outcomes among women in midwife-led versus obstetrician-led care at the onset of labour in the Netherlands: a nationwide cohort study. PLoS ONE 2015;10:e0126266.
9 Ravelli ACJ, Jager KJ, De Groot MH, Erwich JJHM, Rijninks-van Driel GC, Tromp M, et al. Travel time from home to hospital and adverse perinatal outcomes in women at term in the Netherlands. BJOG 2011;118:457–65.
10 Daysal NM, Trandafir M, Van Ewijk R. Saving lives at birth: the impact of home births on infant outcomes. Am Econ J Appl Econ 2015;7:28–50.
11 De Jonge A, Mesman JA, Mannien J, Zwart JJ, Van Dillen J, Van Roosmalen J. Severe adverse maternal outcomes among low risk women with planned home versus hospital births in the Netherlands: nationwide cohort study. BMJ 2013;346:f3263.
12 Snowden JM, Tilden EL, Snyder J, Quigley B, Caughey AB, Cheng YW. Planned out-of-hospital birth and birth outcomes. N Engl J Med 2015;373:2642–53.