Effects of hospital delivery during off-hours on perinatal outcome in several subgroups: a retrospective cohort study

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Abstract

Background: Studies have demonstrated a higher risk of adverse outcomes among infants born or admitted during off-hours, as compared to office hours, leading to questions about quality of care provided during off-hours (weekend, evening or night). We aim to determine the relationship between off-hours delivery and adverse perinatal outcomes for subgroups of hospital births.

Methods: This retrospective cohort study was based on data from the Netherlands Perinatal Registry, a countrywide registry that covers 99% of all hospital births in the Netherlands. Data of 449,714 infants, born at 28 completed weeks or later, in the period 2003 through 2007 were used. Infants with a high a priori risk of morbidity or mortality were excluded. Outcome measures were intrapartum and early neonatal mortality, a low Apgar score (5 minute score of 0–6), and a composite adverse perinatal outcome measure (mortality, low Apgar score, severe birth trauma, admission to a neonatal intensive care unit).

Results: Evening and night-time deliveries that involved induction or augmentation of labour, or an emergency caesarean section, were associated with an increased risk of an adverse perinatal outcome when compared to similar daytime deliveries. Weekend deliveries were not associated with an increased risk when compared to weekday deliveries. It was estimated that each year, between 126 and 141 cases with an adverse perinatal outcomes could be attributed to this evening and night effect. Of these, 21 (15-16%) are intrapartum or early neonatal death. Among the 3100 infants in the study population who experience an adverse outcome each year, death accounted for only 5% (165) of these outcomes.

Conclusion: This study shows that for infants whose mothers require obstetric interventions during labour and delivery, birth in the evening or at night, are at an increased risk of an adverse perinatal outcomes.

Keywords: Time of birth, Night, Weekend, Delivery, Perinatal mortality, Perinatal morbidity, Hospital care, Quality of health care

Background

At present, a considerable amount of literature has been published about the relationship between hospital admissions that occur in the evening, at night, or during the weekend, and morbidity and mortality. In obstetrics and neonatal care, studies have focused on the time of birth, or admission to a neonatal intensive care unit (NICU) [1,2]. Studies have demonstrated a higher risk of adverse outcomes among infants born or admitted during off-hours (weekend, evening or night), as compared to office hours, leading to questions about the quality of care provided during off-hours. However, the findings of studies examining the effect of time of birth on perinatal mortality and morbidity have been inconsistent. Some studies reported increased risks for births during the weekend [3-9], during the evening or night [8-24], or during off-hours [8,25,26], while others did not find any effect [10,27-33]. In addition, many studies

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did not take into consideration that interventions like induction and augmentation of labour, administration of analgesics or anaesthetics, planned and emergency caesarean sections, or instrumental deliveries, are not randomly carried out throughout the day and week, and are directed to high-risk pregnancies.

In this paper, we aim to determine the relationship between off-hours delivery and adverse perinatal outcomes for subgroups of hospital births that require obstetric interventions. Focusing on subgroups may give important insight in specific processes of care. We also estimated the number of adverse outcomes attributable to the off-hours effect, among all births and within the subgroups. The expression of the risk as a number, instead of an odds ratio, may give a better indication of the impact of the off-hours effect on public health, and the potential gains of possible improvements in health care quality.

Methods
Data sources
For this retrospective cohort study we used data from the Netherlands Perinatal Registry (PRN). This countrywide registry covers 95% of the approximately 180,000 live-born infants and stillbirths per year in the Netherlands [34]. The PRN is based on a validated probabilistic linkage [35,36] of three voluntary independent registries owned by the professional organizations of midwives, obstetricians, and neonatologists/paediatricians. In 2007, the participation rates of midwife practices, obstetric departments, and paediatric departments were 94%, 99% and 68% respectively [34]. One hundred percent of the paediatric departments with a neonatal intensive care unit participated. Data on the mother, the pregnancy, childbirth, the child, and admission to a NICU on the same or the day after birth were available. Data on infants born to mothers who were transferred between hospitals (primary to secondary or tertiary care during labour or delivery ‘intrapartum transfer to the hospital’), from infants born to mothers who were already under hospital care before the onset of labour (‘antepartum transfer to the hospital’ or ‘referred before the onset of labour’). The latter group consists of both women who were under secondary care from the beginning of pregnancy, and women referred to secondary care during pregnancy before the onset of labour. The two groups, intrapartum and antepartum transfer to the hospital, may have different baseline risks and additional risks (as a consequence of a referral process under a certain level of urgency). We excluded birth records of women for whom it was unclear whether they were referred.

Outcome variables
We used three dichotomous outcome variables: (1) intrapartum and early neonatal mortality (death of the unborn child during labour or delivery, and death within 7 days after live birth, respectively), (2) a low Apgar score (5 minute score of 0–6), and (3) a composite measure. The composite measure combined intrapartum and early neonatal mortality, a low Apgar score, severe birth trauma (excluding cephalic haematoma, fracture of the clavicle, facial nerve injury and injury to the brachial plexus) [40], and admission to a NICU on the same or the day after birth.

Time of birth
Time of birth was examined using three different categorizations. The first was based on the day of the week and defined as weekday (Monday 8:00 am till Friday 10:59 pm) versus weekend (Friday 11:00 pm till Monday 7:59, and national holidays), the second was based on the time of the day and defined as day (from 8:00 am till 5:59 pm), evening (from 6:00 pm till 10:59 pm), and night (from 11:00 pm till 7:59 am). The third was based on an aggregation of the day of the week and time of the day into off-hours (evening, night, or the weekend) and office hours (daytime during weekdays).

Case-mix variables
We distinguished between two types of case-mix variables, namely (1) socio-biological factors and (2) characteristics of the delivery and obstetric interventions performed. Socio-biological factors included birth weight (in grams),
gestational age at delivery (28–36, 37–41, ≥42 completed weeks), congenital anomalies (infants with very severe anomalies were excluded; remaining anomalies were divided into mild and severe, based on perinatal mortality risks of congenital anomalies [41], fetal position (cephalic, breech, or transverse/other position), general medical or obstetric problems of the mother (as recorded by the midwife or gynaecologist), maternal age (<25, 25–34, ≥35 years), parity (0, 1, ≥2), single/multiple pregnancies, sex of the child, ethnicity of the mother (western, non-western countries), socioeconomic status (low, average, high), and the degree of urbanization of the maternal place of residence (5 classes). The characteristics of the delivery and obstetric interventions performed included induction and/or augmentation of labour (yes, no), administration of analgesics or anaesthetics (none/light analgesics, opiates, epidural...
anaesthesia in the first stage of labour, epidural/spinal an-
aesthesia during caesarean section, general anaesthesia),
mode of delivery (spontaneous delivery, instrumental vaginal
delivery - vacuum or forceps extraction -, emergency
caesarean section), hospital type (tertiary referral centre
with a NICU, teaching hospital without a NICU, general
hospital without a NICU), year of delivery, and the duration
of the second stage of labour (categorized as 0–29, 30–59,
60–119, ≥120 minutes). However, the start time of inter-
terventions is not registered in the PRN.

Statistical analyses
To analyse the outcome measures, we performed multi-
level logistic regression analyses controlling for case-mix
differences between infants born during the different time
periods used in the categorization of time of birth. Multi-
level models account for potential clustering of adverse
perinatal outcomes within hospitals. They also correct for
systematic differences between hospitals in the potential
association between time of birth and outcome.

All models included separate variables for time of the day
and day of the week. This enabled us to study the effect of
each factor separately by adjusting for the other one.

Based on the literature, we included case-mix variables
expected to influence perinatal outcome or the association
between time of birth and perinatal outcome in the ana-
lyses. Observations with missing values on any of these
variables were excluded from the data. For each subgroup,
our baseline model consisted of time of birth and socio-
biological factors. Subsequent models were extended by in-
cluding the characteristics of the delivery and the obstetric
interventions performed.

Observational studies are prone to ‘confounding by indi-
cation’. In this case, it refers to the situation in which a de-
terminant of adverse perinatal outcome is an indication for
stimulating delivery during a certain part of the day or
week. Induction or augmentation of labour and caesarean
section in particular, are means to influence the time of
birth of a high-risk pregnancy. To minimize this kind of
bias, we performed subgroup analyses, with subgroups
defined by induction and/or augmentation of labour, com-
bined with the mode of delivery (spontaneous delivery, in-
stumental delivery, emergency caesarean section). We
expected that the risk of adverse perinatal outcomes and
their distribution during the day and week would differ be-
tween these subgroups, and that within these subgroups
confounding by indication would be negligible. We com-
bined subgroups, in which the association between time of
birth and outcome did not differ (tested with interaction
terms of time of birth and mode of delivery).

The occurrence of the outcome intrapartum and early
neonatal mortality was rare. Therefore, only a limited
number of potential confounders could be included in the
models with mortality as outcome variable. We included
those variables that had a p-value <0.05 for testing the asso-
ciation in the corresponding models with the composite
measure. Additional, variables were removed through a
stepwise backward selection procedure, using restricted
likelihood ratio tests (critical p-value at 0.10).

The strength of the association between time of birth
and outcomes are expressed as odds ratios (OR) with
95% confidence intervals (CI). To adjust for multiple
comparisons, we used the adjustment method of Holm,
as explained by Aickin and Gensler [42]. The risk mod-
els were also used to calculate the number of cases with
an adverse perinatal outcome, attributable to the off-
hours effect [43]. Theoretically, this is the reduction in
adverse perinatal outcomes that would be observed if
the off-hours effect could be eliminated. In this scenario
infants born during off-hours have the same risk of an
adverse perinatal outcome as infants born during office
hours.

The statistical analyses were carried out using SAS ver-

cation 9.2 [44]. The multilevel logistic regression analysis was
done with the SAS procedure GLIMMIX.

Results
After applying our exclusion criteria (Figure 1), 449,714
infants were included in the study population. Most infants
were eliminated because they were born outside the
hospital. Of the study population, 310,776 (69%) were re-erred to a hospital before the onset of labour and 138,938
(31%) were referred during labour.

Table 1 shows the distribution of births by time of re-
ferral and time of birth, and the occurrence of the ad-
verse perinatal outcomes in each subgroup. Among
infants born to mothers referred to a hospital before the
onset of labour, differences were observed in the preva-
ience of all three adverse outcomes among all three time
categorizations (off-hours vs. office hours; day of the
week; time of the day). Among infants born to mothers
referred to a hospital during labour, differences were
observed in the prevalence of a low Apgar score, and the
composite measure within the time categorizations off-
hours vs. office hours, and time of the day, but not for
day of the week.

Tables 2 and 3 show the results of the analyses using the
multivariate models. Because the differences between the
results of the analyses using the baseline models and the
analyses using the extended models were small, we will
only describe the results of the extended models. An
increased risk of an adverse perinatal outcome was
observed among infants born during the evening or night
irrespective of whether the mother was under the care of a
hospital before the onset of labour or referred during
labour or delivery.
The risk of intrapartum or early neonatal death for infants born to mothers who were referred before the onset of labour is increased if labour was induced or augmented, and birth took place in the evening or at night. It was also increased if labour occurred naturally and delivery was performed by emergency caesarean section at night. Infants born in the evening or at night had an increased risk of a low Apgar score if their mothers were referred before the onset of labour, had labour induced or augmented, and achieved spontaneous or instrumental vaginal delivery. Irrespective of the mode of delivery, children of mothers referred during labour and in who labour was augmented were more likely to have a low Apgar score if the delivery occurred during the night. Increased risk of the composite outcome during evening or night birth was observed among subgroups similar to those at risk of a low Apgar score.

Among children born to mothers who were referred before the onset of labour, had no induction or augmentation of labour, and achieved spontaneous or instrumental delivery, we observed no increase in risk associated with birth during the evening, at night or during the weekend. Weekend birth was not associated with an increased risk in an adverse perinatal outcome for any subgroup when compared to weekday births.

After adjusting for multiple comparisons, using the Holm correction method, half of the findings remained significant at the 0.05 level (see Tables 2 and 3).

Table 4 shows the number of cases that can be attributed to the off-hours effect in the period 2003 through 2007, assuming that the effect measures as calculated and presented in Tables 2 and 3, are true. The predicted number of cases with an adverse perinatal outcome attributable to the off-hours effect is between 630 and 704, depending on the statistical model used. This represents 4% to 4.5% of all cases with adverse perinatal outcomes. The majority (64-67%) of these infants were born to mothers who were already under the care of the hospital before the onset of labour, whose labour was induced or augmented, and who achieved vaginal (spontaneous or instrumental) delivery. The number of cases of intrapartum and early neonatal death attributable to the off-hours effect is 103, in both models. Of these, 59 to 65% were under hospital care before the onset of labour and labour was induced or augmented. The population attributable risk (PAR) for this subgroup is over 20%. A substantial proportion (18-32%) of perinatal deaths among infants born to mothers who were neither induced nor augmented, and who eventually delivered by an emergency caesarean section is attributable to the of-hours effect, irrespective of referral before or during labour. For a low Apgar score and the composite outcome measure the picture is similar, although the PARs for a low Apgar score are somewhat higher.
Discussion

Results in perspective

Birth in the hospital in the evening or at night was associated with an increased risk of perinatal morbidity and/or mortality. These risks were concentrated in subgroups of deliveries that involved induction or augmentation of labour, or an emergency caesarean section. Infants born during off-hours to mothers referred before the onset of labour, whose labour was not induced and augmented, and who achieved vaginal delivery (spontaneous or instrumental) were not at increased risk of an adverse perinatal outcome. Birth during the weekend was not associated with an increased risk of adverse perinatal outcomes for any subgroup.

The PAR calculations demonstrated that about 4 to 4.5% of all cases with an adverse perinatal outcome, and 12.5% of all cases of intrapartum and early neonatal mortality, can be attributed to the evening and night effect. This theoretically established figure can be interpreted as the proportion of adverse outcomes that could be reduced by eliminating the off-hours effect, on the condition that unmeasured confounding does not bias the off-hours effects. Our PAR calculation of perinatal mortality is comparable with calculations from Sweden.
Health care quality improvement programs could target subgroups with both large absolute and relative numbers of cases that are attributable to the off-hours effect. In this case, it may be worthwhile to focus on deliveries among mothers referred before the onset of labour and whose labour is induced or augmented. Women under hospital care before the onset of labour, who are not induced or augmented, and who need an emergency caesarean section are the second largest contributor to the off-hours effect as it relates to intrapartum or early neonatal mortality.

The increased risks observed among infants born during the evening and night, confirm the results of those other studies accounting for the mode of delivery and/or several other risk factors [8,9,11-16,18-22,24].

### Table 3 Adjusted odds ratios (95% confidence intervals) for the effect of time of birth by referral status (intrapartum and antepartum) and outcome

| Subgroups                           | Odds ratio (95% CI) | Time of the day (reference group is day) | Part of the week (reference group is weekday) |
|-------------------------------------|---------------------|------------------------------------------|---------------------------------------------|
|                                     |                     | Evening (0.56-1.33)                      | Night (1.14-2.96)                           |
|                                     |                     | 0.99 (0.72-1.35)                         | 1.10 (0.81-1.49)                           |
|                                     |                     | 1.41 (0.92-2.17)                         |                                             |
|                                     |                     | 1.08 (0.82-1.41)                         |                                             |
|                                     |                     | 0.95 (0.63-1.42)                         |                                             |
|                                     |                     | 1.05 (0.58-1.89)                         |                                             |
|                                     |                     | 1.06 (0.67-1.67)                         |                                             |
|                                     |                     |                                          |                                             |
|                                     |                     | 1.00 (0.97-1.17)                         |                                             |
|                                     |                     | 1.02 (0.89-1.00)                         |                                             |
|                                     |                     | 1.03 (0.97-1.10)                         |                                             |
|                                     |                     | 0.92 (0.84-1.01)                         |                                             |
|                                     |                     | 1.00 (0.88-1.14)                         |                                             |
|                                     |                     | 0.93 (0.80-1.08)                         |                                             |
|                                     |                     | 1.06 (0.89-1.26)                         |                                             |
|                                     |                     | 0.93 (0.80-1.08)                         |                                             |
|                                     |                     | 0.93 (0.80-1.08)                         |                                             |
|                                     |                     | 0.90 (0.96-1.21)                         |                                             |
|                                     |                     | 1.05 (0.95-1.17)                         |                                             |
|                                     |                     | 0.93 (0.80-1.08)                         |                                             |
|                                     |                     | 1.06 (0.89-1.26)                         |                                             |
|                                     |                     | 1.00 (0.88-1.14)                         |                                             |
|                                     |                     | 0.97 (0.91-1.17)                         |                                             |
|                                     |                     | 0.92 (0.84-1.01)                         |                                             |
|                                     |                     | 1.07 (0.95-1.21)                         |                                             |
|                                     |                     | 0.98 (0.89-1.09)                         |                                             |
|                                     |                     | 1.04 (0.83-1.30)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 0.96 (0.70-1.30)                         |                                             |
|                                     |                     | 1.01 (0.95-1.05)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |
|                                     |                     | 1.00 (0.89-1.12)                         |                                             |

(12%) and Scotland (16.5%) [8,13]. Health care quality improvement programs could target subgroups with both large absolute and relative numbers of cases that are attributable to the off-hours effect. In this case, it may be worthwhile to focus on deliveries among mothers referred before the onset of labour and whose labour is induced or augmented. Women under hospital care before the onset of labour, who are not induced or augmented, and who need an emergency caesarean section are the second largest contributor to the off-hours effect as it relates to intrapartum or early neonatal mortality.

The increased risks observed among infants born during the evening and night, confirm the results of those other studies accounting for the mode of delivery and/or several other risk factors [8,9,11-16,18-22,24].
Table 4 Calculated number of cases attributable to the off-hours effect per subgroup and in total in the years 2003 through 2007

| Subgroups                        | Models with only social-biological factors | Models with social-biological factors, characteristics of the delivery and obstetric interventions performed |
|----------------------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------|
|                                  | Number of infants with adverse perinatal outcome | Number of infants with adverse perinatal outcome |
|                                  | Observed | Expected with elimination of off-hours effect | Attributable to off-hours effect | Observed | Expected with elimination of off-hours effect | Attributable to off-hours effect |
|                                  |          |                                      | PAR\(^a\) (in %)                  |          |                                      | PAR\(^a\) (in %)                  |
| **Intrapartum and early neonatal mortality** |                                      |                                      |                                      |          |                                      |                                      |
| Antepartum No                   | 187      | 188                                  | −1                                  | −0.4     | 187                                  | 186                                  | 1                                  | 0.3                           |
| Antepartum No                   | 88       | 60                                   | 28                                  | 32.2     | 88                                   | 60                                   | 28                                 | 32.3                          |
| Antepartum Yes                  | 298      | 237                                  | 61                                  | 20.5     | 297                                  | 230                                  | 67                                 | 22.5                          |
| Intrapartum No                  | 112      | 108                                  | 4                                   | 3.2      | 112                                  | 109                                  | 3                                  | 2.5                           |
| Intrapartum No                  | 53       | 40                                   | 13                                  | 25.1     | 53                                   | 43                                   | 10                                 | 18.2                          |
| Intrapartum Yes                 | 86       | 88                                   | −2                                  | −2.9     | 86                                   | 91                                   | −5                                 | −6.2                          |
| **Total**                       | 824      | 721                                  | 103                                 | 12.5     | 823                                  | 720                                  | 103                                | 12.5                          |
| **Apgar score 0-6**             |                                      |                                      |                                      |          |                                      |                                      |
| Antepartum No                   | 1525     | 1466                                 | 59                                  | 3.9      | 1520                                 | 1432                                 | 88                                 | 5.8                           |
| Antepartum Yes                  | 1030     | 844                                  | 186                                 | 18.0     | 1027                                 | 888                                  | 139                                | 13.5                          |
| Antepartum Yes                  | 698      | 569                                  | 129                                 | 18.5     | 697                                  | 573                                  | 124                                | 17.8                          |
| Antepartum Yes Instrumental     | 776      | 734                                  | 42                                  | 5.4      | 776                                  | 717                                  | 59                                 | 7.6                           |
| Intrapartum No                  | 688      | 689                                  | −1                                  | −0.1     | 688                                  | 684                                  | 4                                  | 0.5                           |
| Intrapartum No                  | 249      | 210                                  | 39                                  | 15.7     | 249                                  | 216                                  | 33                                 | 13.4                          |
| Intrapartum Yes                 | 791      | 698                                  | 93                                  | 11.8     | 790                                  | 721                                  | 69                                 | 8.8                           |
| **Total**                       | 5757     | 5209                                 | 548                                 | 9.5      | 5747                                 | 5230                                 | 517                                | 9.0                           |
| **Adverse perinatal outcome (composite measure)** |                                      |                                      |                                      |          |                                      |                                      |
| Antepartum No                   | 5919     | 5892                                 | 27                                  | 0.4      | 5903                                 | 5844                                 | 59                                 | 1.0                           |
| Antepartum Yes Instrumental     | 3078     | 2746                                 | 332                                 | 10.8     | 3065                                 | 2783                                 | 282                                | 9.2                           |
| Antepartum Yes Emergency CS     | 1394     | 1251                                 | 143                                 | 10.3     | 1387                                 | 1264                                 | 123                                | 8.9                           |
| Antepartum Yes Emergency CS     | 1553     | 1519                                 | 34                                  | 2.2      | 1553                                 | 1508                                 | 45                                 | 2.9                           |
| Intrapartum No                  | 1762     | 1733                                 | 29                                  | 1.7      | 1757                                 | 1712                                 | 45                                 | 2.6                           |
| Intrapartum No                  | 420      | 383                                  | 37                                  | 8.8      | 420                                  | 395                                  | 25                                 | 5.9                           |
| Intrapartum Yes                 | 1465     | 1362                                 | 103                                 | 7.0      | 1464                                 | 1414                                 | 50                                 | 3.4                           |
| **Total**                       | 15591    | 14887                                | 704                                 | 4.5      | 15549                                | 14919                                | 630                                | 4.0                           |

\(^a\) abbreviations: spont. = spontaneous, intr. = instrumental, CS = caesarean section, PAR = population attributable risk.
studies that adjust for several risk factors did not find an evening or night effect. However, all three studies were carried out in tertiary hospitals with round the clock in-house physicians [27,29,30].

In our study, the adjusted odds ratios for birth in the weekend did not differ from 1. This is comparable to the results of most other studies that took mode of delivery and/or other risk factors into account [13,14,21,24,28,29]. Three exceptions were a study among teenage mothers [3] and two studies in which the outcome measure was perinatal mortality due to asphyxia [7,8]. In one study an increased risk of perinatal mortality was demonstrated for infants born in nontertiary hospitals on Saturday. Also an increased risk of adverse perinatal outcome for infants born in tertiary hospitals on Saturday was found. Other combinations of type of hospital, day of the weekend, and outcome measure did not reach significance [9].

Methodological considerations
This observational study was carried out using a nationwide registry that included nearly all hospital births in the Netherlands. A limitation of observational studies is the sensitivity to ‘confounding by indication’. We minimized this effect by analysing subgroups of infants, defined on the basis of obstetric interventions. Moreover, we sought to compose a homogeneous group of cases, by excluding infants with a high a priori probability of an adverse perinatal outcome. This selection may limit the generalizability of the results, but prevents bias of strong confounding variables. Finally, in our analysis we included random effects for hospitals and adjusted for a large number of potentially confounding factors.

As with most observational studies there is the possibility of the presence of unmeasured confounding. One such factor may be the duration of the first stage of labour. Babies born during the evening or the night may have been exposed to a longer first stage of labour, and consequently have a higher risk of an adverse outcome. The duration of the first stage cannot be determined from the PRN, since the time of the onset of labour is not registered. In clinical practice this is also often omitted. Another potentially confounding factor among the subgroup of infants born to mothers who were referred before the onset of labour, may be the distinction between induction and augmentation. Induction of labour is often started for medical reasons, while augmentation is generally administered to mothers with a prolonged delivery after a spontaneous start. The perinatal risks can be different between these groups. In addition, in contrast to augmentation, induction is often planned, so the time of birth is more controlled. To obtain more insight into the off-hours effects within these subgroups, it may be interesting to differentiate between women who are induced and women who are augmented. However, the reliability of a distinction between the two obstetric interventions in a perinatal registry has to be ascertained.

We cannot rule out that some cases are misclassified, for example in the other caesarean section class (planned or emergency) or time of death class (antepartum death or intrapartum death). In a recent study, some of the cases initially classified as antepartum death, were reclassified as intrapartum deaths after review by a multidisciplinary team [45]. A mild underreporting of early neonatal mortality is expected, since one third of the paediatric departments in Dutch hospitals did not participate in the PRN at the time of our study. Furthermore, midwives, gynaecologists and paediatricians can make mistakes when entering the data. Some of these may remain undetected by the national registry office when checking the data. Finally, some cases had missing values on the examined variables, although, the number of cases with missing data was very limited (0.9% of the study population).

After adjustment for multiple comparisons, half of the associations remained significant. However, the discussion about the need to adjust for multiple comparisons is not yet settled [46]. Therefore, those associations that did not remain significant after adjustment for multiple comparisons may still represent a true relationship between the time of delivery and adverse outcomes.

Possible explanations of the associations
The off-hours effect convincingly demonstrated in our study may be caused by a delayed recognition of perinatal risks in the evening or at night, and an inappropriate response to hazardous situations. This may be the result of a multiple factors, like diminished numbers of and expertise of staff available, reduced access to diagnostic tests and procedures, a lower degree of supervision of residents, long-duration shifts and tiredness of personnel, no in-house obstetricians, anaesthesiologists and paediatricians, delays in availability of necessary personnel in case of emergency. In the Netherlands, the round-the-clock in-house presence of an obstetrician, anaesthesiologists, and the operating room team, is not warranted in the majority of the hospitals. Despite speculation about the impact of all these factors [47], they have not been extensively studied.

In our study, we did not demonstrate an increased risk of adverse perinatal outcomes among the subgroup of mothers who were referred before the onset of labour, whose labour was not induced or augmented, and who achieved vaginal delivery (spontaneously or instrumental). This suggests that for this subgroup differences in quality of obstetric care or other risk factors between birth during off-hours and daytime did not play an important role.

The absence of a weekend effect found in this study suggests that the quality of care during daytime, evening
and night during the weekend does not differ from corresponding parts of the day during weekdays. Despite the reduced staffing numbers in the weekend, during the daytime the available health personnel may be alert enough to prevent and reduce hazardous situations. Delays in availability of personnel, who are on duty during the weekend, may be comparable to those during corresponding parts of the day during weekdays.

Conclusion
Although confounding in our study cannot be entirely excluded, we recommend that the quality and organization of perinatal care should be optimized for the identified risk groups during the evening and the night, irrespective of how the causal pathway leads to adverse outcomes. This off-hours effect has also been demonstrated in other countries. Because we focused on hospital births, excluding home births which are rare in other countries, we think our results may be generalizable to other countries. A next step in research may be the identification of the factors that lead to the increased risks and an examination of the risks to infants not included in this study (like small for gestational age infants).

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
RG, CNWMH, CMAS, MBK, and GPW were primarily responsible for designing and drafts of the paper. This study was commissioned and funded by the Dutch Health Care Inspectorate. The Netherlands Perinatal Registry is thanked for their data and the authors thank Prof. Arie Franx for his valuable comments on the study. All authors participated in interpretation of the results. RG wrote the first draft of the paper and all authors contributed in the revision of the manuscript and approved the final version of the paper. All authors have critically read and approved the final manuscript.

Acknowledgements
The authors thank Prof. Arie Franx for his valuable comments on the study design and drafts of the paper. This study was commissioned and funded by the Dutch Health Care Inspectorate. The Netherlands Perinatal Registry is funded by the Dutch Ministry of Health, Welfare and Sport.

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Received: 10 December 2011 Accepted: 23 August 2012 Published: 8 September 2012

References
1. Abdel-Latif ME, Bakuj B, Oei J, Lui K: Mortality and morbidity among very premature infants admitted after hours in an Australian neonatal intensive care unit network. Pediatrics 2006, 117(5):1632–1639.
2. Lee SK, Lee DS, Andrews WL, Babaoal R, Pendray M, Stewart S: Higher mortality rates among inborn infants admitted to neonatal intensive care units at night. J Pediatr 2003, 143(5):592–597.
3. Hamilton P, Restrepo E: Weekend birth and higher neonatal mortality: a problem of patient acuity or quality of care? J Obstet Gynecol Neonatal Nurs 2003, 32(6):724–732.
4. Hamilton P, Restrepo E: Sociodemographic factors associated with weekend birth and increased risk of neonatal mortality. J Obstet Gynecol Neonatal Nurs 2006, 35(2):208–214.
5. Hake E, MacFarlane A: Daily and seasonal variation in live births, stillbirths and infant mortality in England and Wales, 1979–96. Health Stat Q 2001, (19 Spring):5–15.
6. Bendavid E, Kaganova Y, Needelman J, Gruenburg L, Weissman JS: Complication rates on weekends and weekdays in US hospitals. Am J Med 2007, 120(5):422–428.
7. Luo ZC, Liu S, Wilkins R, Kramer MS: Risks of stillbirth and early neonatal death by day of week. Cmaj 2004, 170(3):337–341.
8. Pasupathy D, Wood AM, Pell JP, Fleming M, Smith GC: Time of birth and risk of neonatal death at term: retrospective cohort study. BMJ 2010, 341:c3498.
9. De Graaf JF, Ravelli AC, Visser GH, Hukkelhoven C, Tong WH, Bonsel GJ, Steegers EA: Increased adverse perinatal outcome of hospital delivery at night. BJOG 2010, 117(9):1098–1107.
10. Chalmers JW, Shanks E, Paterson S, McNinneny K, Baird D, Penney G: Scottish data on intrapartum related deaths are in same direction as Welsh data. BMJ 1998, 317(7153):539–540.
11. Gould JB, Qin C, Chavez G: Time of birth and the risk of neonatal death. Obstet Gynecol 2005, 106(2):352–358.
12. Luo ZC, Karlberg J: Timing of birth and infant and early neonatal mortality in Sweden 1973–95: longitudinal birth register study. BMJ 2001, 323(7255):1327–1330.
13. Stephansson O, Dickman PW, Johansson AL, Kieler H, Nauctiong S: Time of birth and risk of intrapartum and early neonatal death. Epidemiology 2003, 14(2):218–222.
14. Stewart JH, Andrews J, Cartledge PH: Numbers of deaths related to intrapartum asphyxia and timing of birth in all Wales perinatal survey, 1993–5. BMJ 1998, 316(7132):657–660.
15. Thorgren-Jernel A, Herbst A Low 5-minute Apgar score: a population-based register study of 1 million term births. Obstet Gynecol 2001, 98(1):65–70.
16. Helfer G, Misselewitz B, Schmidt S: Early neonatal mortality, asphyxia related deaths, and timing of low birth risks in Hesse, Germany, 1990–8: observational study. BMJ 2000, 321(7256):274–275.
17. Ruffieux C, Marazzi A, Paccoud F: The circladian rhythm of the perinatal mortality rate in Switzerland. Am J Epidemiol 1992, 135(8):956–952.
18. Ustso AC, Craigo SD, Chelimow D, O’Brien WF: The association between time of birth and fetal injury resulting in death. Am J Obstet Gynecol 2006, 195(6):1521–1526.
19. Helfer G, Misselewitz B, Schmidt S: Diurnal mortality gradient in Hesse, Germany, an update including caesarean deliveries [Rapid response to: ZC Luo and J Karlberg, 2001]. BMJ 2001.
20. Helfer G, Schnell R, Misselewitz B, Schmidt S: Warum ist die Sterblichkeit von nachts geborenen Kindern erhöht? [Why are babies born at night at increased risk of early neonatal mortality?]. Z Geburtshilfe Neonatol 2003, 207(4):137–142.
21. Berglund S, Gruenwald C, Pettersson H, Nauctiong S: Risk factors for asphyxia associated with substandard care during labor. Acta Obstet Gynecol Scand 2010, 89(3):39–48.
22. Karlberg J: Diurnal mortality gradient for planned and not planned caesarean deliveries. [Rapid response to: ZC Luo and J Karlberg, 2001]. BMJ 2001.
23. Suzuki S, Nakai M, Hirazumi Y, Sato M: Time of delivery and perinatal outcome. J Nippon Med Sch 2010, 77(5):277–281.
24. Wu YW, Pham TN, Danieslian B, Towner D, Smith L, Johnston SC: Nighttime delivery and risk of neonatal encephalopathy. Am J Obstet Gynecol 2011, 204(1):e131–e36.
25. Rautava L, Lehtonen L, Pelto A, Konrennta M, Konrennta H, Linna M, Hallman M, Andersson S, Gillisler M, Leipaja J, et al: The effect of birth in secondary- or tertiary-level hospitals in Finland on mortality in very preterm infants: a birth-register study. Pediatrics 2007, 119(1): e257–e263.
26. O’Donoghue K, Sheridan CP, O’Sullivan K, Greene RA, Higgins JR: Timing of birth related to obstetric practice and neonatal outcome. J Med J 2008, 101(7):205–207.

27. Ballit JL, Landon MB, Thom E, Rouse DJ, Spong CY, Varner MW, Moawad AH, Caritis SN, Harper M, Wapner RJ, et al. The MFMU cesarean registry: impact of time of day on cesarean complications. Am J Obstet Gynecol 2006, 195(4):1132–1137.

28. Gould JB, Qin C, Marks AR, Chavez G: Neonatal mortality in weekend vs weekday births. JAMA 2003, 289(2):2958–2962.

29. Bell EF, Hansen NI, Morriss FH Jr, Stoll BJ, Ambalavanan N, Gould JB, Laptook AR, Walsh MC, Carlo WA, Shankaran S, et al. Impact of timing of birth and resident duty-hour restrictions on outcomes for small preterm infants. Pediatrics 2010, 126(2):e22–e31.

30. Caughey AB, Uroto AC, Lee KA, Thiet MP, Washington AE, Laros RK Jr: Time of delivery and neonatal morbidity and mortality. Am J Obstet Gynecol 2008, 199(5):496.e491-495.

31. Milot I, Laffont L, Thirion A, Niklasson A, Odeback A, Thornberg E: Influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population. Acta Obstet Gynecol Scand 2002, 81(10):909–917.

32. Kalogiannidis I, Margioula-Siarkou C, Petousis S, Goutzioulis M, Prapas N, Agorastos T: Infant births during the internal night were associated with increased risk for operative delivery and NICU admission. Arch Gynecol Obstet 2010, 284(1):65–71.

33. Routava L, Hakkinen LJ, Konovenranta E, Andersson S, Gissler M, Hallman M, Konovenranta H, Leipala J, Linna M, Peltola M, et al. Health-related quality of life in 5-year-old very low birth weight infants. J Pediatr 2009, 155(3):338–343. e331-333.

34. Stichting Perinatale Registratie Nederland [Netherlands Perinatal Registry Foundation]. Perinatal zorg in Nederland 2007 [Perinatal care in the Netherlands 2007]. Utrecht: Stichting Perinatale Registratie Nederland; 2009.

35. Meray N, Reitsma JB, Raveli 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(9):883–891.

36. Tromp M, Raveli AC, Meray N, Reitsma JB, Bonsel GJ: An efficient validation method of probabilistic record linkage including readmissions and twins. Methods Inf Med 2008, 47(4):356–363.

37. Claussnitzer V, Gensler L: Adjusting for multiple testing when reporting research results: the Bonferroni vs Holm methods. Am J Public Health 1996, 86(5):726–728.

38. Benichou J: A review of adjusted estimators of attributable risk. Stat Methods Med Res 2001, 10(3):195–216.

39. SAS Institute: SAS software. Version 9.2. Cary, NC: SAS Institute Inc; 2002–2008.

40. Evers AC, Brouwers HA, Hukkelhoven CW, Nikkels PG, Boon J, van Eegmond-Linden A, Hillegersberg J, Snuff YS, Stekken-Hoosima S, Bruijne HW, et al: Perinatal mortality and severe morbidity in low and high risk term pregnancies in the Netherlands: prospective cohort study. BMJ 2010, 341:c6539.

41. Perneger TV: What’s wrong with Bonferroni adjustments. BMJ 1998, 316(7139):1236–1238.

42. De Jonge A, Twisk J, Hutton E: Daytime births are associated with better perinatal outcomes in secondary and tertiary hospitals. Evid Based Med 2011, 16(2):59–60.

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