Evaluating perinatal outcomes in different levels of care

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Intrapartum and neonatal mortality in primary midwife-led and secondary obstetrician-led care in the Amsterdam region of the Netherlands: a retrospective cohort study

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Abstract

Objective: To compare intrapartum- and neonatal mortality and intervention rates in term women starting labour in primary midwife-led versus secondary obstetrician-led care.
Design: Retrospective cohort study.
Setting: Amsterdam region of the Netherlands
Participants: Women with singleton pregnancies who gave birth beyond 37^{+0} weeks gestation in the years 2005 up to 2008 and lived in the catchment area of the neonatal intensive care units of both academic hospitals in Amsterdam. Women with a primary caesarean section or a pregnancy complicated by antepartum death or major congenital anomalies were excluded. For women in the midwife-led care group, a home or hospital birth could be planned.
Measurements: Analysis of linked data from the national perinatal register, and hospital- and midwifery record data. We assessed (unadjusted) relative risks with confidence intervals. Main outcome measures were incidences of intrapartum and neonatal (<28 days) mortality. Secondary outcomes included incidences of Caesarean section and vaginal instrumental delivery.
Findings: 53,123 women started labour in primary care and 30,166 women in secondary care. Intrapartum and neonatal mortality rates were 37/53,123 (0.70‰) in the primary care group and 24/30,166 (0.80‰) in the secondary care group (Relative Risk 0.88; 95% CI 0.52-1.46). Women in the primary care group were less likely to deliver by secondary caesarean section (5% versus 16%; RR 0.31; 95% CI 0.30- 0.32) or by instrumental delivery (10% versus 13%; RR 0.76; 95% CI 0.73-0.79).
Key conclusions: We found a low absolute risk of intrapartum and neonatal mortality, with a comparable risk for women who started labour in primary versus secondary care. The intervention rate was significantly lower in women who started labour in primary care.
Implications for practice: These findings suggest that it is possible to identify a group of women at low risk of complications that can start labour in primary care and have low rates of medical interventions while perinatal mortality is low.

Introduction

Safety of place of birth in term pregnancies has been subject of international debate. Dutch studies have found a comparable risk of perinatal mortality among low risk planned home versus planned hospital births.[1-3] Studies in Canada, North America and Britain showed similar results and moreover a lower intervention rate in the homebirth group.[4-6] However, these studies did not research whether women who start labour in primary care, regardless of their planned place of birth, have higher perinatal mortality risks than women who start labour in secondary care.

Obstetric care in the Netherlands is characterized by a formal distinction between primary care (led by midwives or general practitioners) and secondary care (led by obstetricians). Pregnant women who are considered low risk are usually looked after in primary care, although they can choose to be in secondary care. When complications or risk factors occur either during pregnancy or labour, women are referred to secondary care.

In 2010, a Dutch cohort study performed in the Utrecht region among women who gave birth after 37 weeks gestation to children without congenital abnormalities showed a significantly higher birth related perinatal mortality rate among women starting labour in primary midwife-led versus secondary obstetrician-led care (1.4‰ versus 0.60‰ respectively, (unadjusted) RR 2.3; 95% confidence interval (CI) 1.1 to 4.8).[7] It was unexpected that the population at highest risk (secondary care group) had a lower perinatal mortality rate in this cohort study[7] and additional research was recommended. To our knowledge, the study of Evers et al. was the first comparing pregnancy outcomes for women starting labour in primary versus secondary care in the Netherlands. However, concerns have been raised about its methodology.[8] First, the numerator and denominator were not taken from the same geographical region. Second, the study has not clearly distinguished ante- or intrapartum perinatal death, which is (sometimes) difficult but important when conducting a study on birth related perinatal mortality. Third, registration inaccuracies in the definition of 'level of care at the onset of labour' in the national database were not taken into account.

We aimed to conduct a study in a comparable Dutch region with a similar design, taking the points of criticism into account. The study was conducted in the Amsterdam region, where 19% of all women in the Netherlands give birth. Over a three-year period, we compared intrapartum and neonatal mortality and intervention rates among women who started labour in primary midwife-led versus secondary obstetrician-led care.

Methods

We performed a retrospective cohort study with use of linked data from the national perinatal register (PRN), together with additionally retrieved data from hospitals and midwife practices. The PRN database is a national database in which births of approximately 96% of primary care midwifery practices (national perinatal database-1 form) and of 99% secondary care units are registered (national perinatal database-2 form).[9] It contains population based information on all pregnancies, births from 22 weeks onwards and (re)admissions occurring until 28 days after delivery. This includes reason for referral to secondary care, medical indication, birth characteristics, complications, neonatal outcome and many other variables.

We studied women with singleton pregnancies who gave birth beyond 37^{+0} weeks gestation and excluded women with a pre-planned caesarean section and women with a pregnancy complicated by congenital anomalies or antepartum fetal death. Congenital anomalies were considered to be present if antenatal testing had demonstrated a significant chromosomal anomaly, if multiple anomalies were established at physical examination suggesting an underlying syndrome, or if an underlying syndrome was documented in the autopsy report. Level of care distinguished primary care (led by midwives or general practitioners) and secondary care (led by obstetricians). Women in tertiary care were included in the secondary care group. Groups were constituted by level of care at the onset of labour. Women who were transferred to secondary care during labour were analysed in the primary care group, thus mimicking an intention-to-treat approach. All women were included regardless of their risk profile. Antepartum death was defined as intrauterine death before the onset of labour. We defined start of labour as having uterine contractions every five minutes for at least one hour, or ruptured membranes, or dilatation of the cervix of 3 centimetres or more.

From the PRN database, we selected data from all women who gave birth at term between 2005 and 2008 in 'the perinatal region of Amsterdam' (women's zip code between 1000-2159, 8200 t/m 8245 and 8300-8324). This is one of the nine perinatal health care regions in the Netherlands that have neonatal intensive care (NICU) facilities. It consists of 18 hospitals with obstetric/paediatric care facilities, which form Perinatal Cooperation Groups (PCG's) with their surrounding community practices of independent midwives and general practitioners.[10] The study was limited to women with a home postal code within the perinatal health care region of Amsterdam regardless whether they gave birth within

the study region or in another postal code region. Women who lived outside the catchment area of Amsterdam, but who gave birth within this area (irrespective of the birth outcome), were not included in the study.

Identification of perinatal deaths

The selection of cases of perinatal mortality was limited to women who were registered in the cohort defined above. First, we selected all perinatal deaths that were registered in the PRN. In addition, all 18 hospitals (both obstetric and neonatal departments) in the region were requested to supply data about their perinatal deaths at term in the study period. The retrieved supplementary data were added to the cases identified in the PRN. Also, cases classified in the PRN as antenatal stillbirth, congenital anomalies or multiple pregnancy, although not subject of this study, were audited for eligibility to double-check the classification from the PRN and the annual reports. Patient records were retrieved from the hospitals and midwifery practices, and were examined by an expert panel for detailed classification.

A team consisting of a midwife in primary care, a midwife in secondary care, an obstetrician and a medical researcher classified all cases of perinatal death into the following categories: congenital anomaly versus no congenital anomaly, start of labour in midwife-led care or obstetrician-led care, and moment of death (antepartum, intrapartum, early neonatal <7 days, late neonatal >7 and <28 days). Perinatal deaths were included when classified as intrapartum or neonatal death up to 28 days of birth. In case of uncertainty or discrepant classification the case was again discussed in a larger group of professionals. If uncertainty remained, the case was labelled as such. Cases with antepartum mortality and with congenital anomalies were then excluded.

Secondary outcomes

Secondary outcomes included maternal intervention and morbidity rates including mode of delivery (spontaneous vaginal birth, instrumental birth, caesarean section), use of epidural, perineal trauma, post-partum haemorrhage and manual placental removal. Other neonatal outcomes included admission to a Neonatal Intensive Care Unit (NICU) of 24 hours or more and a five-minute Apgar score below 7.

Data analysis

Identification of intrapartum and neonatal deaths

First, we described the patient characteristics by level of care and intended place of birth. We compared women who started labour in secondary care with women who started labour in primary care. Secondly, we made an overview of all cases of intrapartum and neonatal mortality to gain more insight in all perinatal deaths. Thirdly, we described level of care at the onset of labour, type of foetal monitoring, obstetric interventions, risk factors (meconium stained liquor, augmentation of labour, etc.), whether there were previous consultations in secondary care, time of diagnosis of obstetric risk factor, time of transfer and time of start treatment, and mode of delivery.

We then calculated the incidence of intrapartum and neonatal mortality. The numerator was the number of deaths in each category, and the denominator the total number of women in each category. Calculations of Relative Risk (RR) rates (and 95% Confidence Intervals) were by start of labour in primary or secondary care. For discrete variables, we used $\chi 2$ tests to test the differences between the total primary versus secondary care groups. For continuous variables, we performed a Student's t-tests to compare the population averages and, depending on the variance (equal or unequal), used the matching pooled or Satterthwaite p-values to determine significance. We considered a two-sided p-value below 0.05 to be significant. Relative risks and confidence intervals were also calculated for our patient characteristics and secondary outcomes, as defined in the previous section.

Additional analyses

We planned two subgroup analyses. One by parity and one by intended place of birth (using hospital birth in secondary care as reference).

In addition, we planned three sensitivity analyses. One was based on a validity check for the denominator regarding level of care at the start of labour. We took a random sample of 100 women from our cohort and determined how often the information on level of care at the onset of labour was different from the information in the PRN database. In all samples, case notes were assessed by a primary care and secondary care professional from our research team. We then modified the denominator for the percentage of misclassifications and repeated our analyses for our primary outcome of intrapartum and neonatal mortality

within 28 days of birth in order to check the robustness of our findings. In a second sensitivity analysis, we excluded cases that were not registered in the PRN or cases that were only included in the PRN because the patient was referred to secondary care after the start of labour (but had no primary care data reported in the PRN). Rationale was to account for the fact that for every death that is not registered in the PRN, there will likely be an unknown number of uncomplicated births that are not registered and are therefore missing from the denominator. In a third sensitivity analyses we included all deaths in which we were unable to differentiate between antepartum and intrapartum death, in order to account for the unlikely possibility that all of these deaths were intrapartum and thus birth related.

In order to allow comparison of our findings to the Utrecht study, we planned an additional analysis in which we repeated our calculations after exclusion of cases of late neonatal mortality (day 7 to 28 of birth).

Findings

Denominator

Within our three-year time period, 83,909 women living in the Amsterdam perinatal health care region had a singleton pregnancy, with an intended vaginal birth of a child without congenital anomalies or antepartum fetal death and a term delivery. Of these, 53,123 (63.3%) started labour in primary care, 30,166 (36.0%) in secondary care and in 620 (0.7%) records the level of care at onset of delivery was not registered in the PRN database. According to the PRN database there were no perinatal deaths in this last group, and since it is a relatively small group, we excluded them from further analyses.

Baseline characteristics

Baseline characteristics of the 83,289 women are presented in Table 1. When compared to women who started labour in secondary care, women who started labour in primary care were younger (mean age 30.4 versus 31.4 years) and more often primiparous (48% versus 44%) and more often Western (76% versus 74%). Median gestational age at delivery was comparable between groups (40 (range 37-42) weeks). When subdividing gestational age per week the differences were statistically significant, as there was a higher rate of postdate (≥42 weeks) pregnancy in the secondary care group compared to the total primary care

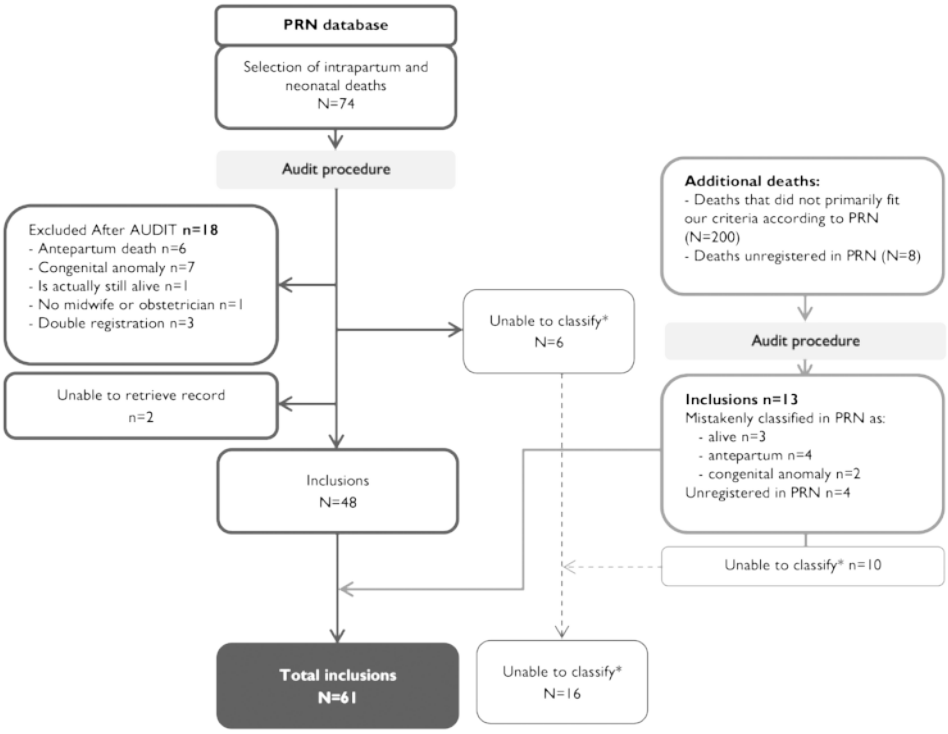
group (12% vs 2%), which was congruent with the fact that being post-term is an indication for referral to secondary care according to the 'Dutch obstetric indication list'.[11]

The medical indications for women starting labour in the secondary care group were diverse, including hypertension (17%), previous caesarean section (13%), postdate pregnancy (12%), prolonged rupture of membranes (7%), non-vertex position of the fetus (4%), and diabetes (2%) (Table S1).

Case selection

Within the PRN database of our study region a total of 74 intrapartum and neonatal deaths (up to 28 days postpartum) were identified that met our inclusion criteria based on PRN information (figure 1).

Figure 1. Flowchart showing the selection process of included cases of mortality



**unable to distinguish antepartum and intrapartum death*

Table 1. Patient characteristics by line of care and intended place of birth

		PRIMARY CARE								SECONDARY CARE		TOTAL	p-value primary total vs secondary care
		Start home		Start hospital		Unknown		Total		Start hospital			
	Births	26,128		21,362		5,633		53,123		30,166		83,289	
Characteristics													
Maternal age*		30.8	±4.7	30.0	±5.3	30.5	±5.1	30.4	±5.0	31.4	±5.2	30.8 ±5.1	<0.0001
Maternal age													
	< 25 years	2,568	10%	3,493	16%	779	14%	6,840	13%	3,161	10%	10,001	<0.0001
	25-29	7,449	29%	5,860	27%	1,496	27%	14,805	28%	7,163	24%	21,968	
	30-34	10,325	40%	7,530	35%	2,073	37%	19,928	38%	11,013	37%	30,941	
	>=35 years	5,786	22%	4,479	21%	1,285	23%	11,550	22%	8,829	29%	20,379	
Parity	Primiparous	11,214	43%	11,022	52%	3,365	60%	25,601	48%	13,131	44%	38,732	<0.0001
	Multiparous	14,914	57%	1,034	48%	2,268	40%	27,522	52%	17,035	56%	44,557	
Gestational age**		40	(37-42)	40	(37-42)	40	(37-42)	40	(37-42)	40	(37-42)	40 (37-42)	0.81
Mean gestational age													
	37	970	4%	898	4%	258	5%	2,126	4%	2,313	8%	4,439	<0.0001
	38	2,763	11%	2,543	12%	629	11%	5,935	11%	4,878	16%	10,813	
	39	6,669	26%	5,692	27%	1,403	25%	13,764	26%	6,524	22%	20,288	
	40	9,138	35%	7,419	35%	1,942	34%	18,499	35%	7,403	25%	25,902	
	41	6,178	24%	4,536	21%	1,287	23%	11,999	23%	5,401	18%	17,400	
	42	412	2%	274	1%	114	2%	800	2%	3,647	12%	4,447	
Birthweight*		3,579	±460	3,515	±460	3,543	±474	3549	±462	3509	±537.0	3535 ±491	<0.0001
Ethnicity													
	Non-Western	4,278	16%	7,282	34%	1,356	24%	12,916	24%	7,849	26%	20,765	<0.0001
	Western	21,850	84%	14,080	66%	4,277	76%	40,207	76%	22,317	74%	62,524	
SES	low	6,129	23%	6,128	29%	1,435	25%	13,692	26%	7,331	24%	21,023	<0.0001
	mid	13,494	52%	9,768	46%	2,763	49%	26,025	49%	14,641	49%	40,666	
	high	6,505	25%	5,466	26%	1,435	25%	13,406	25%	8,194	27%	2,1600	
Gender	Boy	13,307	51%	10,748	50%	2,933	52%	26,988	51%	15,377	51%	4,2365	0.63
	Girl	12,821	49%	10,614	50%	2,700	48%	26,135	49%	14,789	49%	4,0924	

** mean±SD* ***median (range)*

After the audit procedure by our multidisciplinary team of health care providers 18 deaths were excluded because of congenital anomaly (n=7), antenatal death (n=6), double registration in the PRN database (n=3), patient was still alive (n=1) or no midwife or obstetrician involved in patientcare (n=1). We were unable to retrieve data for 2 deaths. For another 6 deaths we were unable to distinguish antepartum and intrapartum. This left us with 48 inclusions. An additional audit was performed in order to identify deaths that were either misclassified or unreported in the PRN. We therefore audited 200 perinatal deaths that were classified in the PRN as antenatal stillbirth, congenital anomalies or multiple pregnancy and found 9 deaths that were actually eligible for inclusion. In 10 cases we were again unsure whether the timing of death was antepartum or intrapartum. Our effort to obtain mortality cases that were not registered in the PRN (by searching through annual reports an birth registries in the 18 hospitals of the region) resulted in the identification of another 8 mortality cases of which 4 met our inclusion criteria. This added up to a total of 61 inclusions. The 16 cases in which we were unable to distinguish antepartum and intrapartum death were added in a sensitivity analysis.

Neonatal outcomes

A total of 61 (0.68 ‰) cases of intrapartum and neonatal (<28 days of birth) mortality remained. Thirty-seven of these cases started labour in primary care (mortality rate 0.70‰), versus 24 in secondary care (mortality rate 0.80‰; Relative Risk of intrapartum and neonatal (<28days) mortality 0.88 (95% CI 0.52-1.46) (Table 2). Other neonatal outcomes, five minute Apgar score below 7 and NICU admission for at least 24 hours were less frequently observed in the primary midwife-led care group (Table 2).

Subgroup analyses

A further subdivision of intrapartum and neonatal mortality risk by parity, showed comparable risks for primiparous and multiparous women (Table S2). There were also no statistically significant differences between groups for the subgroup analysis by intended place of birth (intended midwife-led home versus obstetrician-led hospital birth; intended midwife-led hospital versus obstetrician-led hospital birth) (Table S3).

Table 2. Neonatal outcomes by line of care at onset of labour and by intended place of birth including relative risk of overall primary versus secondary care group

	PRIMARY CARE								SECONDARY CARE		Relative risk (95% CI)
	Start home		Start hospital		Unknown		Total				primary care total vs secondary care (reference)
Births	**26,128**	‰	**21,362**	‰	**5,633**	‰	**53,123**	‰	**30,166**	‰	
Intrapartum and neonatal mortality											
Yes	**23**	0.88‰	**12**	0.56‰	**2**	0.36‰	**37**	0.70‰	**24**	0.80‰	0.88 (0.52-1.46)
Intrapartum	**4**	0.15‰	**5**	0.23‰	**0**	0	**9**	0.17‰	**8**	0.27‰	0.64 (0.25-1.66)
Postpartum <28 days	**19**	0.73‰	**7**	0.33‰	**2**	0.36‰	**28**	0.53‰	**16**	0.53‰	0.99 (0.54-1.84)
- Day 0 to 6	**15**	0.57‰	**7**	0.33‰	**1**	0.18‰	**23**	0.43‰	**15**	0.50‰	0.87 (0.45-1.67)
- Day 7 to 27	**4**	0.15‰	**0**	0	**1**	0.18‰	**5**	0.09‰	**1**	0.03‰	
Five minute Apgar score											
< 7	**181**	6.93‰	**159**	7.44‰	**65**	11.53‰	**405**	7.62‰	**337**	11.17‰	**0.68 (0.59-0.79)**
NICU admittance > 24 hours	**43**	1.65‰	**55**	2.58‰	**24**	4.26‰	**122**	2.30‰	**135**	4.48‰	**0.51 (0.40-0.66)**

Sensitivity analyses

None of the sensitivity analyses that we planned significantly altered our findings regarding our primary outcome (Tables S4-S6). With our pre-planned validity check, we reviewed hospital charts of 100 random women in our cohort and determined whether we were able to reliably extract the level of care at the onset of birth from the PRN data. We found a nett misclassification rate of 1.8% (95% CI -0.5-5.1) for level of care at onset of birth. If we apply this to our data, the denominator in the primary care group decreases (N=51,506) and the denominator in the secondary care group increases (N=31,783). Modification of the denominator generated incidences of 0.72‰ in the primary care group and 0.76‰ in the secondary care group, with a comparable overall adjusted relative risk of intrapartum and neonatal (<28days) mortality of 0.95 (95% CI 0.57-1.59) (Table S4). The third sensitivity analysis including all 16 cases in which we were unable to differentiate between antepartum and intrapartum death, showed no difference in mortality between primary and secondary care (RR 0.99 (95% CI 0.62-1.58)) (Table S6).

The additional analysis excluding all cases of late neonatal death (7-28 days) resulted in a RR of 0.79 (95% CI 0.46-1.35) (Table S7).

Birth characteristics

Characteristics of all 83,289 births are presented in Table 3. Compared to women who started labour in secondary care, those who started in primary care were more likely to give birth spontaneously (86% vs 72%; RR 1.19 95%CI (1.18-1.20)). Correspondingly, there was a lower rate of secondary C-sections (5% vs 16%; RR 0.31; 95% CI 0.30- 0.32) and a lower rate of instrumental vaginal delivery (10 vs 13%; RR 0.76 (0.73-0.79)). For both groups failure to progress in labour was most frequently reported as the main indication for intervention. In the primary care group there was a lower rate of women receiving pain relief either by epidural (4% versus 11%, RR 0.38 (0.36-0.40)) or non-epidural analgesia (9% versus 21%, RR 0.45 (0.43-0.46)) and the risk of post-partum haemorrhage was lower (4% versus 7%, RR 0.68 (0.64-0.72). For women with a vaginal delivery, the risk of manual removal of placenta was also lower in the primary care group (2% versus 3%, RR 0.45 (0.40- 0.49)), as was the number of episiotomies among vaginal births (20% versus 29%, RR 0.68 (0.67-0.70)). Of the women who started labour in primary care, 39% were referred to secondary care during labour.

Clinical overview of perinatal deaths

An overview of the most relevant clinical diagnoses of the included mortality cases can be found in Tables 4a and 4b. For both groups (primary and secondary care) asphyxia without a further known or specified cause is the most common reported clinical condition followed by infection in the primary care group, and uterine rupture in the secondary care group. In the secondary care group, a previous Caesarean section was the medical indication most often reported and 4 out of these 10 cases were complicated by a uterine rupture. In the primary care group, there was also one case of uterine rupture in a woman without a previous C-section. In the secondary care group, poor fetal condition was diagnosed after spontaneous labour in 42% of the cases (10/24), while the majority (58%) had received prostaglandins or oxytocin prior to the diagnosis of poor fetal condition.

Table 3: Birth outcomes by line of care at onset of labour, and by intended place of birth

	PRIMARY CARE								SECONDARY CARE		Relative risk (95%CI)
	Start home		Start hospital		Unkown		Total				Primary care total vs secondary care (reference)
ALL BIRTHS	**26,128**		**21,362**		**5,633**		**53,123**		**30,166**		
Induction of labour											
yes	**127**	0%	**141**	1%	**25**	0%	**293**	1%	**10,679**	35%	Not applicable
no	**26,001**	100%	**21,221**	99%	**5,608**	100%	**52,830**	99%	**19,487**	65%	
Mode of delivery											
Spontaneous	**23,055**	88%	**18,166**	85%	**4,202**	75%	**45,423**	86%	**21,602**	72%	**1.19 (1.18-1.20)**
C-section											
Secondary:	**988**	4%	**1,131**	5%	**467**	8%	**2,586**	5%	**4,735**	16%	**0.31 (0.30-0.32)**
> suspected fetal distress	**172**	17%	**230**	20%	**82**	18%	**484**	1%	**1,215**	4%	**0.23 (0.20-0.25)**
> failure to progress	**614**	62%	**680**	60%	**293**	63%	**1,587**	3%	**2,329**	8%	**0.39 (0.36-0.41)**
> combined	**125**	13%	**142**	13%	**50**	11%	**317**	1%	**475**	2%	**0.38 (0.33-0.44)**
> other reason	**67**	7%	**75**	7%	**39**	8%	**181**	0%	**707**	2%	**-**
Instrumental vaginal delivery	**2,085**	8%	**2,065**	10%	**964**	17%	**5,114**	10%	**3,829**	13%	**0.76 (0.73-0.79)**
> suspected fetal distress	**517**	25%	**577**	28%	**247**	26%	**1,341**	3%	**1,442**	5%	**0.53 (0.49-0.57)**
> non-progression	**1,277**	61%	**1,205**	58%	**588**	61%	**3,070**	6%	**1,842**	6%	0.95 (0.89-1.00)
> combined	**278**	13%	**263**	13%	**122**	13%	**663**	1%	**495**	2%	**0.76 (0.68-0.85)**
> other reason	**11**	1%	**14**	1%	**5**	1%	**30**	0%	**46**	0%	**-**
Postpartum hemorrhage	**928**	4%	**1,096**	5%	**362**	6%	**2,386**	4%	**1,989**	7%	**0.68 (0.64-0.72)**
Manual placenta removal	**299**	1%	**343**	2%	**131**	2%	**773**	1%	**874**	3%	**0.50 (0.46-0.55)**
Pain relief											
Epidural	**702**	3%	**1,063**	5%	**398**	7%	**2,163**	4%	**3,229**	11%	**0.38 (0.36-0.40)**
Other	**1,700**	7%	**2,307**	11%	**882**	16%	**4,889**	9%	**6,212**	21%	**0.45 (0.43-0.46)**

	PRIMARY CARE								SECONDARY CARE		Relative risk (95%CI)
	Start home		Start hospital		Unkown		Total				Primary care total vs secondary care (reference)
ALL BIRTHS	**26,128**		**21,362**		**5,633**		**53,123**		**30,166**		
Line of care at birth											
Primary care	**18,297**	70%	**12,165**	57%	**1,872**	33%	**32,334**	61%	**10**	0%	Not applicable
Secondary care	**7,831**	30%	**9,197**	43%	**3,761**	67%	**20,789**	39%	**30,156**	100%	
	PRIMARY CARE								SECONDARY CARE		Relative risk (95%CI)
	Start home		Start hospital		Unkown		Total				Primary care total vs secondary care (reference)
VAGINAL DELIVERIES ONLY	**25,140**		**20,231**		**5,166**		**50,537**		**25,431**		
Manual placenta removal	**436**	2%	**343**	2%	**131**	3%	**773**	2%	**874**	3%	**0.45 (0.40- 0.49)**
Ruptures											
Perineum											
> intact	**12,949**	52%	**10,352**	51%	**3,314**	64%	**24,029**	48%	**14,852**	58%	**0.81 (0.80-0.83)**
> third degree tear	**407**	2%	**407**	2%	**106**	2%	**920**	2%	**433**	2%	1.07 (0.95-1.20)
> fourth degree tear	**236**	1%	**208**	1%	**76**	1%	**520**	1%	**264**	1%	0.99 (0.86-1.15)
Episiotomy overall	**4,400**	18%	**4,267**	21%	**1,507**	29%	**10,174**	20%	**7,490**	29%	**0.68 (0.67-0.70)**
> without instrumental delivery*	**2,767**	11%	**2,696**	13%	**767**	15%	**6,230**	12%	**4,661**	18%	**0.64 (0.61-0.66)**
> with instrumental delivery**	**1,622**	78%	**1,562**	76%	**738**	77%	**3,922**	77%	**2,812**	73%	1.04 (1.02-1.07)

** To calculate incidences and relative risks we used all spontaneous vaginal deliveries for the numerator*

*** To calculate incidences and relative risks we used all instrumental deliveries for the numerator*

Table 4a: Timing and most relevant clinical condition for all mortality cases starting labour in **primary care group**

Suspected cause of death	Planned home/ died at home	Planned hospital/ died at home	Planned home/ Poor perinatal condition on arrival in hospital	Planned hospital/ poor perinatal condition on arrival in hospital	Planned hospital with good perinatal condition on arrival in hospital but poor condition at time of referral	Good perinatal condition at time of referral	Mortality not directly related to birth	Total
Asphyxia, unknown origin	2		4[1]	4[1]	2	4		**16**
Meconium aspiration syndrome			1[2]					**1**
Asphyxia and nuchal cord		1						**1**
Perinatal infection			1			5	2	**8**
Cord prolapse			1	1	1			**3**
Placental abruption				1				**1**
Uterine rupture						1		**1**
Vasa praevia			1					**1**
Bleeding due to velamentous insertion of umbilical cord				1				**1**
Sinus transversus thrombosis							1	**1**
Postpartum death of unknown origign after initial good neonatal condition							1	**1**
Unsupervised homebirth	1		1[3]					**2**
Total	**3**	**1**	**9**	**7**	**3**	**10**	**4**	**37**

[1] Unexpected poor neonatal condition after home birth, neonate transferred by ambulance to hospital (2 cases)

[2] Nuchal cord and meconium aspiration leading to severe asphyxia, home birth, neonate transferred by ambulance to hospital

[3] unsupervised homebirth, midwife arrives 12 minutes later, no evident signs of neonatal distress, 4 hours later hypothermia and acute cardiac arrest, obduction: asphyxia, meconiumaspiration syndrome with persisting pulmonary hypertension.

Table 4b: Medical indication for secondary care and most relevant clinical condition for all mortality cases starting labour in **secondary care group**

	Indication for Obstetrician led-care before onset of labour						Total
	Previous C-section	Postdate pregnancy	Hypertensive disorder	Vaginal bleeding >20 weeks gestation	Diabetes	Other	
Asphyxia, unknown origin	3	4	1	1		2[3,4]	**11**
Asphyxia, either nuchal cord or true cord knot	1						**1**
Meconium aspiration		2			1		**3**
Shoulder dystocia					1		**1**
Perinatal infection	1		1			1[5]	**3**
Placental abruption	1						**1**
Uterine rupture	4[1,2]						**4**
Total	**10**	**6**	**2**	**1**	**2**	**3**	**24**

[1] one woman had a combined medical indication of previous C-section AND a hypertensive disorder
[2] one women underwent induction of labour because of previous uterine rupture and gestational age approaching 42 weeks
[3] Medical indication for secondary care was decreased fetal movements
[4] Medical indication for secondary care was request for pain medication (pethidine) before onset of active labour, spontaneous labour followed.
[5] Medical indication for secondary care was request for pain medication (pethidine) before onset of active labour. Suspected cause of death was a combination of asphyxia and group B streptococcal infection

Discussion

Main findings

In this study, we compared perinatal and maternal outcomes among women who started labour in primary versus secondary care in the Amsterdam perinatal health care region of the Netherlands, and found that women who started labour in primary care had a similar risk of intrapartum and neonatal mortality when compared to women who started labour in secondary care, with a lower risk of interventions during birth. Results were comparable for primi- and multiparous women.

Strengths and limitations.

A major strength of our study is the multidisciplinary approach with collaboration of midwives, obstetricians, a paediatrician and epidemiologists within our study group. By thoroughly searching through all annual reports we were able to retrieve additional cases of mortality that were unregistered in the PRN. We also performed an extensive validity check to make sure that classification of level of care at onset of labour was valid, in order to strengthen our findings.

Our study has some limitations. First, we did not do a multivariable regression analysis because of the small number of perinatal deaths and limitations of the use of national PRN data for the denominator combined with patient record data for the numerators which had some incomplete data.

Another limitation is that the groups are not restricted to low risk women. To compare these groups would be more appropriate for the study question but depends on a consistent registry of high risk factors in the PRN registry.

We limited our study to intrapartum and neonatal mortality because we focussed on mortality after the onset of labour. We are therefore unable to draw any conclusions regarding antepartum fetal death and total perinatal mortality. As antepartum death is the largest group it would be very interesting to review these cases in a separate study.

Our data referred to the period 2005 up to December 31, 2007. Data from 2008 and onwards were not yet available in the national database when we started the project. The study was

conducted from 2011 to 2015 without funding. Data collection for the main study and for the validation checks was cumbersome as almost 600 case notes had to be examined. There were some changes in obstetric care in the Netherlands over the last few years, including increasing initiatives for closer collaboration between primary and secondary care and the implementation of a systematic method of internal perinatal audit of mortality cases. Recent research has shown that term perinatal mortality rates have declined over the years 2010 to 2012.[10]

Our study has the power to exclude a difference in mortality of 0.7 per 1000 between groups, based on a non-inferiority design with an alpha of 5% and a mortality incidence of 0.8 per 1000. Although, smaller differences are also relevant, we can exclude the existence of a larger difference, as was previously suggested by Evers et al. Studies with stronger power require either larger sample sizes, or a meta-analysis of smaller studies.

Interpretation

This is the second study in the Netherlands comparing incidence rates of intrapartum and neonatal mortality between women starting labour in midwife led primary care and obstetrician led secondary care. Our study does not confirm the findings of the study of Evers et al. which showed a significantly higher incidence of birth related perinatal death among women who started labour in primary midwife-led care compared to those who started labour in secondary obstetrician-led care (relative risk 2.3, 95% CI 1.1 to 4.8) in the Utrecht region of the Netherlands (Evers et al., 2010). Furthermore, we found that the overall incidence rate of intrapartum and neonatal (<7days) mortality was lower than expected, with an incidence of 0.66 ‰ versus 1.01 ‰ in the Utrecht study. In the unlikely event that all cases in which the audit team was unable to classify death as antepartum or intrapartum were in fact intrapartum, our incidence rate of intrapartum and early (<7days) neonatal mortality would have been 0.85 ‰. These differences could be due to chance (large confidence interval), due to methodological differences between studies or actual differences between regions.

Differences in methodological approach include a different approach for defining the region for inclusion of the population. We restricted our inclusion to women with a postal code in the perinatal health care region of Amsterdam for the cases (numerator) as well as for the total number of births (denominator). The Utrecht group included intrapartum and neonatal deaths among women who delivered within their perinatal health care region of Utrecht re-

gardless of their own postal code, but for the denominator they only included women with a postal code in the Utrecht region (Evers et al., 2010). Hence, the numerator and denominator did not come from the same groups. Furthermore, onset of labour was not specified in the Utrecht study, so definitions might have been different between the groups, although it is unclear whether this had an influence on the results. A final hypothesis could be that the Utrecht and Amsterdam regions in fact have a different risk profile. Previous research has shown differences in perinatal mortality between regions in the Netherlands.[12-16]

Mortality is only the tip of the iceberg, and it would be interesting to know more about the incidences of perinatal morbidity. Our study showed lower incidences in NICU admission and five-minute Apgar score below 7 in the primary care group. Caution is needed with the interpretation of these findings because neonatal morbidity is a difficult outcome measure, and NICU admission is even considered an invalid outcome measure when comparing different lines of care.[17]

A recent Lancet series showed the need for a system-level shift in maternal and newborn care from identification and treatment of pathology for the minority to skilled care for all, in which midwifery plays a pivotal role.[18, 19] A Cochrane review including over 16,000 women showed that women who had received midwife-led continuity models of care were less likely to experience regional analgesia, episiotomy and instrumental birth, and were more likely to give spontaneous vaginal birth without a differences in caesarean births.[20] With respect to fetal and neonatal outcomes, women in the midwife-led continuity model group were less likely to experience preterm birth and fetal loss before 24 weeks' gestation, although there were no differences in fetal loss/neonatal death after 24 weeks or in overall fetal/neonatal death. These findings contributed to the current international discussion emphasizing the positive aspects of midwife-led continuity care models.[19, 21-23] However, there is still uncertainty regarding the optimal organization of these models and the application in existing obstetric care systems.[20, 22, 24, 25]

In this study, we compared intrapartum and neonatal mortality outcomes by intended place of birth, and found no differences in women with an intended home birth compared to women in secondary care, or in women with an intended hospital birth compared to women in secondary care. We did not compare outcomes within the primary care group (home versus hospital) as the aim of our study was to compare the primary to secondary care

group. Other national and international studies, however, showed no differences in perinatal mortality between women who started their labour in midwife-led care at home versus midwife-led care in hospital.[2-6] As for our low intervention rates in the primary care group, these findings are consistent with existing literature.[20]

Our study compares two groups selected before labour to have a different risk for adverse outcome of birth and each group received an estimated appropriate, though different, level of care. Women who started labour in primary care had a similar risk of intrapartum and neonatal mortality when compared to women who started labour in secondary care, with a lower intervention risk during labour. These findings suggest that it is possible to identify a group of women at low risk of complications that can start labour in primary care and have low rates of medical interventions while perinatal mortality is low.

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Supplement Information

Table S1: Risk factors by line of care at onset of labour and by intended place of birth

	PRIMARY CARE								SECONDARY CARE		**p-value** primary care total vs secondary care
	Start home		Start hospital		Unknown		Total				
Births	**26,128**		**21,362**		**5,633**		**53,123**		**30,166**		
Risk factors											
Non vertex position	**316**	1%	**329**	2%	**140**	2%	**785**	1%	**1,187**	4%	<0.0001
Postdate pregnancy (≥42 weeks)	**412**	2%	**274**	1%	**114**	2%	**800**	2%	**3,647**	12%	<0.0001
Previous Caesarean section	**444**	2%	**498**	2%	**60**	1%	**1,002**	2%	**3,909**	13%	<0.0001
Hypertension	**246**	1%	**251**	1%	**76**	1%	**573**	1%	**5,257**	17%	<0.0001
Diabetes	**1**	0%	**6**	0%	**1**	0%	**8**	0%	**557**	2%	<0.0001
Vaginal bleeding in second half of pregnancy	**9**	0%	**9**	0%	**4**	0%	**22**	0%	**96**	0%	<0.0001
Prolonged rupture of membranes	**1,616**	6%	**1,555**	7%	**545**	10%	**3,716**	7%	**2,527**	8%	<0.0001

Table S2: Relative risk of Intrapartum and postpartum (<28days) mortality for onset of labour in primary versus secondary care, by parity

Onset of labour, intended place of birth	mortality cases	Total number of births	Incidence ‰	RR	95% CI	
Overall population					**Low**	**High**
Primiparous						
> Primary care	27	25,601	1.05	**1.26**	**0.62**	**2.54**
> Secondary care	11	13,131	0.84	Reference		
Multiparous						
> Primary care	10	27,522	0.36	**0.48**	**0.21**	**1.09**
> Secondary care	13	17,035	0.76	Reference		

Table S3: Relative risk of Intrapartum and postpartum (<28days) mortality for onset of labur in primary versus secondary care, by intended place of birth

Onset of labour, intended place of birth	Cases of mortality	Total number of births	Incidence ‰	RR	95% CI	
Overall population*					**Low**	**High**
Primary care , Home	22	26,128	0.84	**1.06**	**0.59**	**1.89**
Secondary care, Hospital	24	30,166	0.80	Reference		
Primary care, Hospital	13	21,349	0.61	**0.77**	**0.39**	**1.50**
Secondary care , Hospital	24	30,166	0.80	Reference		

** Note: Unknown intended place of birth (2 cases of perinatal death) and intended place of birth in a birth centre (N=13, no cases of death) not reported in this analysis*

Table S4: Intrapartum and neonatal mortality (<28days) in women starting labour in primary versus secondary care: unmodified denominator and denominator modified for validity check regarding the variable "line of care at onset of labour"

	Unmodified denominator						Modified denominator					
Onset of labour, intended place of birth	**mortality cases=**	**N**	**Incidence ‰**	**RR**	**95% CI**		**mortality cases=**	**N**	**Incidence ‰**	**RR**	**95% CI**	
Overall population					**Low**	**High**					**Low**	**High**
Primary care	**37**	53,123	**0.70**	**0.88**	**0.52**	**1.46**	**37**	51,506	**0.72**	**0.95**	**0.57**	**1.59**
Secondary care	**24**	30,166	**0.80**	Reference			**24**	31,783	**0.76**	Reference		
Total	**61**	83,289	**0.73**				**61**	83,289	**0.73**			

Denominator was modified based on a validity check of 100 records. Relative risks based on the lower and upper limit of the 95% CI of the modified denominator did not lead to different conclusions (no statistical significant difference between groups).

Table S5: Sensitivity analysis: Excluding all cases that are unregistered in the PRN (n=4) or cases that were only included in the PRN because of referral to secondary care (but had no primary care data reported to the PRN, n=3).

	Cases of mortality	Total number of births	Incidence ‰	Relative Risk	95% CI	
Onset of labour					**low**	**high**
Primary care	30	53,123	0.80	0.71	0.42	1.21
Secondary care	24	30,166	0.57	Reference		
Total	54	83,289				

Table S6: Sensitivity analysis 3: including all cases in which we were unable to distinguish antepartum from intrapartum death

	Deaths (<28 days)	Number of births	Incidence ‰	RR	95% CI	
Onset of labour					**low**	**high**
Primary care	49	53123	0,92	0,99	0,62	1,58
Secondary care	28	30166	0,93	Reference		
Total	77	83289	0,92			

Table S7: Relative risk of Intrapartum and early postpartum (<7days) mortality for onset of labour in primary versus secondary care (all cases of late neonatal mortality excluded)

	Cases of mortality	Total number of births	Incidence ‰	Relative risk	95% CI	
Onset of labour					**low**	**high**
Primary care	32	53,123	0.60	**0.79**	**0.46**	**1.35**
Secondary care	23	30,166	0.76	Reference		
Total	55	83,289	0.66			