Perinatal and maternal health inequalities:

effects of places of residence and delivery

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Perinatal and Maternal Health Inequalities:
effects of places of residence and delivery

Perinatale en Maternale Gezondheidsverschillen:
effecten van de woonplaats en plaats van bevalling

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Oh Lord,
grant me the serenity to accept the things I can not change,
the courage to change the things I can,
and the wisdom to know the differences.

Voor: mijn moeder, Anneke Kuijer †,
mijn zusje Petra en mijn vrienden,
die ik tijdens het promotietraject,
te weinig aandacht heb gegeven.

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Part I

General introduction

1.1 Aims of thesis

In the Netherlands, perinatal mortality has declined substantially since 1920, although the rate of decline seemed to have leveled off from 1978 onwards [1-7]. Last decades the decline was as not as steep as in other European countries [2-7]. As a consequence the Netherlands dropped from a number two position in 1960 to one at the bottom in 2004 in the ranking of the European countries according to perinatal mortality rate [2-7]. The same stagnating trend is observed for maternal mortality [8-12].

We may expect that in the Netherlands, an egalitarian prosperous society with universal access to education and (perinatal) health care, health inequalities by area of residence will be limited. But geographical health differences in the Netherlands are persistent, and extend to perinatal health [1,13,14].

Hence in the Netherlands, both the general level of perinatal mortality and its geographical distribution deserve attention. New evidence has emerged on (a) factors that may be responsible, among which factors related to obstetric care provision, and on (b) the interrelationships between these individual, geographic, and care-related, factors [15-21].

This thesis aims to capture the origin of, in particular, the inequalities in perinatal- and maternal outcomes in the Netherlands in relation to socio-economic and ethnic factors, to the area of residence, and to care-related factors in terms of setting and organization.

The studies, reported in this thesis, address the following questions:

1. To what extent do ethnic, socio-economic and geographic related differences exist in adverse perinatal and maternal outcomes in the Netherlands? How are ethnic and socio-economic effects, if existent, related?
2. Do perinatal adverse outcomes in the Netherlands differ according to time of birth (day, evening, night), and hospital-organisational aspects such as the annual number of deliveries (volume) and staffing during and outside office hours?
3. Is intrapartum and early neonatal death different between planned home and planned hospital births in the Netherlands, for assumed low risk women starting delivery under supervision of a community midwife?
4. Can a scavenging system for nitrous oxide-sedation during labour be safe used in a midwifery-led birth centre?

1.1.2 Outline of thesis

Part 1 provides an annotated history of the discussions on the key features of the unique Dutch obstetric care system (**Chapter 1.2**); next it presents new insights on - in particular non-medical - determinants explaining inequalities in perinatal and maternal health (**Chapter 1.3**).

Part 2 addresses the role of ethnic background and area of residence with perinatal and maternal health. In **Chapter 2.1** it examines whether living in deprived urban districts and a non-Western background are associated with higher risks of perinatal mortality and morbidity. Regional Dutch differences in maternal mortality and morbidity are presented in **Chapters 2.2 and 2.3**, with specific attention to the ethnic, socio-economic and geographic factors.

Part 3 presents studies on the potential role of care-related factors on perinatal outcome. **Chapter 3.1** addresses associations of time of delivery (day, evening and night), various staffing-models and volume of deliveries with perinatal outcomes. **Chapter 3.2** examines whether place of birth (planned home births and planned hospital births) is related with perinatal outcome in case of low-risk pregnancies starting their delivery under community midwife supervision. In **Chapter 3.3** the safety of occupational use of nitrous oxide during labour is examined in an innovative birth centre for low risk women. **Part 4** contains the general discussion and **Part 5** summarises the thesis. This chapter also includes a summary in Dutch.

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Chapter 1.2

Short history of Dutch obstetric care and birth centres in particular

Hanneke de Graaf
Hans Merkus
Anita Ravelli
Gouke Bonsel
Eric Steegers

1.2 Obstetric care in the Netherlands in a historical perspective.

1.2.1. Introduction.

Despite the fact that the Netherlands is among the 20 most prosperous countries in the world [1], the studies in this thesis show that levels of adverse outcomes of pregnancy appear to be unexpectedly high in some geographical areas in this country. The maternal place of residence – deprived neighbourhood, urban or rural setting -, socio-economic status, ethnical background as well as the organisation of obstetric care, all play an important role in this respect. The two latter factors are also important in a geographical sense.

To develop strategies to improve obstetric outcomes in the Netherlands, and in particular to reduce differences in outcomes, acknowledging the past history of societal and professional debates on the Dutch system and its (assumed) impact on fetal and maternal outcome is of great importance.

Section 1.2.2 of this chapter describes four different perinatal developments in their historical contexts: the emergence of preventive maternal services (consultatiebureaus), the transformation of multidisciplinary collaboration, the antenatal risk estimation as principle of task division between obstetrician (and neonatologist) and midwife and GP, and the persistence of the home setting as the location for the delivery. These are the pillars of the Dutch system.

In 1.2.3 we describe the development of hospital-like settings (in early days “kraaminstellingen” and since 2000 Midwife lead Birth Centres. In 1.2.4 we describe the development of profession-based registries in perinatal care since 1980, when three professional disciplines each started their own account of mother, fetus, child and the care delivered. Financing of the obstetric care system is next described in 1.2.5, perinatal mortality and its geographical differences in 1.2.6, and maternal mortality and its differences in 1.2.7. The chapter concludes in 1.2.8 with a description of the recent developments in Dutch obstetric care and a summary in 1.2.9.

1.2.2 A closer look at the debates around collaboration in obstetrics in the Netherlands.

In the early 20th century the medical professions in various countries introduced systematic prenatal care as a strategy to increase the likelihood of healthy survival of pregnancy and delivery for mother and child [2,3]. This development cannot be seen in isolation from the robust development of the public health sector and its associated services under the responsibility of national or local authorities. These strongly focus on the care for infants and young children. In the Netherlands Treub and later De Snoo were the ones to introduce these new insights around prenatal care [4].
The Netherlands, in contrast to other Western countries, opted to consider pregnancy as a physiological event based on trust in nature and the adequacy of its mechanisms. Increasingly 'physiological' was also explained in terms of low risk, and the trustworthiness of low-technological diagnostics and treatment approaches [5].
This view until today has given cause for occasionally very heated discussions, especially around the question whether there might be a link between the Dutch system and its less successful obstetric outcomes when compared to other Western countries [6]. For that matter, it must be pointed out that the foundations for the Dutch obstetric care organisation always have been and still are in accordance with the organisational basis of the Dutch healthcare system, i.e. obstetric care is provided as primary healthcare, unless secondary or tertiary healthcare assistance is needed.

1.2.2.1 <u>The special centre for perinatal care (consultatiebureau voor prenatale zorg)</u>
In 1928 Wijsenbeek was the first in the Netherlands to call for adjustments in the Dutch obstetric care system. He argued that there was a need to set up special centres for prenatal care (consultatiebureaus voor prenatale zorg (CBvPZ)), in analogy with the successful centres for the prevention of tuberculosis and lues [4,7]. In 1934 it was Salomonson who repeated the wish to have special CBvPZ, notably in rural areas, where mortality was high [8]. The authorities supported this initiative with radio broadcasts telling about the importance of prenatal care and by facilitating the planning of more CBvPZs. Due to the economic crisis and the Second World War quite a few CBvPZs opened their doors no sooner than 1951, financially supported by the government [9,10]. As the rule the CBvPZ was headed by an obstetrician, and its service was free of charge. The expectant mother usually visited the CBvPZ once or twice. Apart from a detailed history an obstetric physical examination was performed (including the pelvis, blood pressure and urine, among other things). Special attention was paid to blood group determination, lues- and Rhesus reaction and haemoglobin level. Also diet, and especially its composition, became a focus of attention, for which reason many CBvPZs appointed a dietician [9].
The foundation of the CBvPZs led to heated discussions between obstetricians and general practioners [11]. The GPs were of the opinion that the proposed socio-medical approach of prenatal care belonged to their sphere of work as family physicians. They rather considered the rationale for this approach as a strong argumentation against the interference of medical specialists. Kloosterman described the discussion as follows:

> *The aim of the Congress on Prenatal Care in Utrecht in 1947 (De Snoo's Congress), to draw more attention to this important element of preventive medicine, seems to have been reached to the extent that in the past years more than ever than before prenatal care became subject of discussions, letters to the editor, motions, etcetera.*

> *Regrettably these sometimes rather emotional effusions seldomly concern prenatal care itself, but more often its organisation. Rarely the question is posed what should be done to provide the best possible pregnancy monitoring; usually there is some quarrelling about the question who should do it. It does not seem likely that this would advance the matter at hand, namely to achieve the best possible Maternity care (Moederschapszorg) in our country [12].*

While according to Kloosterman the obstetricians expected that visits to the CBvPZ had no added value, they did not favour abolition [13].Kloosterman did not speak on behalf of all obstetricians, however, for in 1953 the Westland district of the Royal Dutch Medical Association (KNMG) adopted a resolution stating that the CBvPZs were superfluous; moreover, other districts were invited to support this resolution [14].

At the same time the Amsterdam district decided to have this problem studied by a committee composed of GPs, specialists and government-employed physicians [14].The purpose of this investigation was to answer the question whether this type of preventive care in itself could be considered satisfactory, or whether the activities of the CBvPZs were essential for it to succeed [14].

In spite of the perceived lacunas in prenatal care the committee concluded that this type of preventive medicine can be well practised by midwives and GPs since they receive adequate training. Special CBvPZs are not needed, therefore, the more so because they, too, must request specific aids such as lab tests and X-rays from third parties [14]. The committee provided two critical comments, however, i.e. on the medical-administrative and statistical registration procedures, and on the midwife’s remuneration for preventive care [14].

Elsewhere, too, it was doubted whether the CBvPZs would be able to help reduce perinatal mortality. In spite of the widely diverging opinions, various regions in our country actually welcomed the institution of the CBvPZs, which also appeared to be functioning well [15].

From the annual reports [15] it can be deduced that as from 1951 apart from the four largest cities 42 CBvPZs were instituted in eight provinces.

Table 1 Number of special centres for perinatal care per province in the period 1951 – 1966

Province	No. of CBvPZs	No. of sessions
Groningen	6	299
Friesland	1	48
Drenthe	4	185
Overijssel	9	197
Gelderland	4	182
Zuid-Holland	15	371
Zeeland	2	96
Noord-Brabant	1	24

The CBvPZs have been functioning for 15 years, as Van Luyn and his committee in 1966 advised the government to discontinue them [15]. After all, this committee held the view that this type of prenatal care fully belongs to the tasks of the one who will be in charge of the delivery, because:

> *The healthcare provision in our country is of such a nature that this is also feasible. Every physician and midwife is able to perform or have performed the examinations that currently are part of prenatal care.*

The committee furthermore stated that reduction of perinatal mortality could also be achieved also without the activities of CBvPZs; moreover the perinatal mortality rate was already low in comparison with international figures (see table 2).

> *The improvement should chiefly be obtained by stimulating and perfecting regular pregnancy monitoring by the "own midwife", in addition to measures aimed at reducing harm to the child during birth. In case of an uncomplicated pregnancy every midwife will be able to provide total prenatal care, notably when GP and midwife cooperate well. According to the committee, sympathetic cooperation between physicians and midwives will as well guarantee appropriate prenatal care in case of complications during pregnancy.*
>
> *Good mutual understanding then, in the committee's view, will not only benefit prenatal care but also ensure that supervision of the delivery is in good hands when taken care of by midwives and GPs. After all, the GP can always transfer care to the specialist- obstetrician is always open in case of complications; while midwives will take this route as a rule via the GP.*
>
> *The committee, in search for an explanation for the decrease in perinatal mortality over the past ten years, believed they might assume that this was mainly owing to the fact that the midwives had become aware of the great importance of good prenatal care (hypertension, imminent eclampsia, contracted pelvis, rhesus factor, lues reactions), in part by way of the reports on this issue published at the time and the ensuing discussions.*

Summarizing, the committee concluded that:

> *CBvPZs should not be considered the solution of the problem to further improve obstetric results. The committee recommends installing regional boards, formed from and by the KNMG and Midwife-union. On the one hand these boards are to accomplish optimal collaboration between GP and midwife and furthermore to achieve a reduction in perinatal mortality (autopsy of stillborn children, analysis of the placenta); on the other hand they will be responsible for having the necessary registration tasks performed. Voluntary participation of a large number of physicians could still help improve the obstetric outcomes – so the committee expects.*

Table 2 Perinatal mortality trend in the Netherlands (NL) versus those of other European countries (EU).

	Perinatal mortality (…/1,000 births)[a]		Ranking lowest perinatal mortality in EU	
Year	NL (‰)	Lowest perinatal mortality in Europe (‰)	Ranking NL	Country, lowest perinatal mortality
1920[16]	44.6	Not Available (NA)	Na	Na
1930[16]	41.4	Na	Na	Na
1940[16]	40.7	Na	Na	Na
1945[16]	35.0	Na	Na	Na
1950[16]	32.7	30	Na	Norway
1960[16]	25.3	25.0	2	Sweden
1970[17]	17.6	15.1	5	Finland
1980[17]	11.1	8.7	6	Sweden
1995[18]	10.7	6.9	11	Finland
1999[18]	10.9	5.6	15	Finland
2004[6]	10.0	4.8	15	Luxemburg

a) The perinatal mortality rate is defined as the number of stillbirths and deaths in the first week of life per 1,000 total births.

1.2.2.2 <u>The discussion around the organisation of obstetric care.</u>

In 1955 the first report from the Dutch Society for Obstetrics and Gynaecology (NVOG) was published: 'Report on the Form of Organisation of Prenatal Care' [20]. It proposed two points of departure for a novel approach to the prenatal care system. First, not social medicine physicians, but rather midwives, GPs and obstetricians are the primarily responsible professionals for the medical care of mother and child during pregnancy, delivery and postnatal period. Second, for all pregnant women home deliveries, under supervision of the midwife and GP, are preferred over giving birth in a hospital. The report emphasized that the results of perinatal care in other European countries were no reason to follow their examples. Moreover, there were still many options left to improve care without having to change the system, although it was known that in other countries a far greater proportion of pregnant women (80%) received regular prenatal care. This discrepancy was ascribed to organisational differences in obstetrical care. Prenatal care abroad was mostly organized by the authorities and was concentrated in hospitals; where most of the physicians and obstetricians were employed and where eventually also the delivery took place [21].

In 1962 a study on perinatal mortality in our country, initiated 10 years previously, yielded remarkable results [16]. It appeared that in many cases pregnancy-related conditions and impairments had not been identified. Referral to a physician consultation or hospital admission was often delayed. Common laboratory tests (blood group, rhesus (D) factor, lues and haemoglobin) had not been performed in almost half of the women. Circa 40% of the perinatal deaths occurred before birth of the child. One third of perinatal deaths were caused by complications during delivery. Economic factors appeared to be an important barrier for timely referral of the pregnant woman by the midwife to a specialist. Health insurers reimbursed referral and hospitalization only in case of severe maternal pathology [16]. This dissertation was one of the reasons for an increasing number of obstetricians to question the Dutch obstetric care model, certainly seen in the light of the recommendation made in 1972 by the Council for Healthcare (Centrale Raad voor de Volksgezondheid (CRV)) to maintain the current obstetrical care organisation [22]. The CRV justified its view by the good results obtained in the home deliveries. The NVOG early 1972 decided to appoint a committee itself entrusted with the task of providing a contemporary reflection and approach of obstetric and perinatal organisation [23]. This recommendation was presented to obstetricians, paediatricians, midwives and many other invitees during a seminar organized by the NVOG on 14 April 1973. The general consensus was that close collaboration between midwife, GP and obstetrician was indispensable for adequate obstetric care. The NVOG intended to reflect on an advice on the future structure of obstetric care after having consulted its members.

> *It is recommended that organisations of family physicians and midwives be heard. Perhaps it would be possible to come to a shared view. This would stimulate the much desired cooperation for the good of mother and child [24].*

According to obstetrician De Bruin, a number of midwives even intended to seek employment in a hospital. He said that:

> *Also midwives began to realise that they could not continue to work as self-employed persons. They wished to further develop their activities in the hospitals, based on a well-considered division of tasks. Notably younger midwives would prefer a clinical delivery in a dedicated maternity ward in the hospital. From experience they knew that instituting a Birth Centre detached from a hospital will only shift the limitations of the home delivery. Many hospitals appointed midwives [23].*

De Bruin's interpretation of the midwives' wishes was confirmed in 1975 in a letter to the editor of Medisch Contact by the general secretary of the Midwives Union (KNOV). She wrote that:

> W*ithin the context of obstetric care, cooperation with experts is to the good of the patient: an obstetric team consisting of a midwife, GP, obstetrician as well as maternity care [25].*

A recommendation from the CRV in 1972 also included a stand that provided for the formation of a cooperative of hospitals, obstetricians, GPs, midwives and maternity centres, to be achieved by means of subsidising Obstetrician led Birth Centre [22].

> *The experimental Obstetrician led Birth Centre Wormerveer served as a model for such a cooperative. The deliveries in this centre were supervised either by the women's own GP or midwife or by the obstetrician. Apart from the standard examination preceding the birth by GP or midwife, the pregnant woman was examined by an obstetrician as well. This procedure was aimed at achieving the best possible selection of women for whom for certain a hospital delivery would be necessary. In this novel organizational set-up, women who were expected to have an uncomplicated delivery would be able to opt for a home delivery or a delivery in the centre. The term used for the latter was "transferred home delivery". The experiment also opened the way to what was called "short-stay hospital delivery". This implied that delivery and maternity care in the first few days thereafter were provided in the obstetricians led Birth Centre, while further maternity care was continued at home. The Wormerveer experiment was also of interest because it enabled to compare outcomes and cost-effectiveness between home delivery, short-stay delivery and medical delivery [26].*

The concept of the obstetricians led Birth Centre was probably first used in the report entitled “Obstetric Care", prepared in 1968 by a working group of the Netherlands Health Care Inspectorate (IGZ) [27]. Van Geldrop et al. in their article described the Wormerveer Birth Centre as follows:

> *Daily management of '”the Wormerveer Birth Centre” is in the hands of a manageress assisted by a (part-time) medical superintendent. Both fulfil their tasks in conformity with the “Standards and conditions admission Maternity Centre”. The midwives employed by the Wormerveer Birth Centre have been given a broader medical function. For the sake of their clients they are entitled to directly contact GPs, self-employed midwives, hospitals, social workers, mother’s helpers, infant welfare centres, birth-control centres, as well as municipal authorities. Such a centre would well fit into a hospital organization, rather than functioning as a stand-alone maternity centre. A centre in the town of Enschede experimented with this working method, however, they did not include from the very start the mandatory prenatal examination by an obstetrician and did not have team meetings with the participating midwives and GPs.*
>
> *Several positions within the Wormerveer Birth Centre are subsidized in part; among others the directress-supervisor-instructor, the medical superintendent, the scientific traineeship of the gynaecological resident involving registration and evaluation of the centre’s activities. Experience in the Wormerveer Birth Centre learned that an annual number of 600 to 700 deliveries per year would be required to provide an acceptable economic basis. In order to reach this number a centre’s referral area needed to include about 1000 pregnant women willing to deliver their babies in the centre [27].*

In an article in the Dutch Journal of Medicine (Nederlands Tijdschrift voor Geneeskunde (NTVG)) published in 1978 Van Alten reported in detail the obstetric outcomes of the different types of obstetric care during delivery in the Wormerveer Birth Centre [28]. A comparable birth centre had been instituted in 1969, subsidized by the government, in a number of blocks of flats adjacent to the newly built hospital at Delfzijl. For various reasons, including discontinuation of the subsidy but also the low attendance at evaluation meetings, this centre was closed in 1973 [29].

In 1977 the CRV issued new recommendations on the Provision of Obstetric Care (Verstrekking van Verloskundige Hulp) [30]. One of the recommendations implied a preference for regional structuring of cooperatives between midwife, GP and specialist. Apart from the Wormerveer Birth Centre, the regional obstetric cooperatives of Hardenberg, Deventer and Alkmaar served as examples. Both the NVOG and the Dutch Society for Paediatrics (NVK) were reluctant to fully support the recommendations [31]. Both societies decided to install two committees that were to put to paper ideas on the organisation of obstetric care, curative neonatology and perinatal care. Both committees together published their interim reports, particularly emphasizing the need of scientific underpinning of the recommendations [32,33]. This scientific approach was discussed in a joint meeting of both associations in Utrecht on 26 March 1977 [31]. The new system proposed by the joint commissions of obstetricians and paediatricians entailed a fundamental change in the present system.

> *It aims to achieve a regulated yet voluntarily accepted team cooperation between GP, midwife, obstetrician and paediatrician, with a final accountability of the obstetrician for the functioning of the team and with early*

selection by means of prenatal examination. In addition a hospital policy change in relation to the increasing hospitalization of deliveries and concentration of intensive care facilities for mother and child.

The joint plan proposed concentration of intensive care facilities for mother and child in 10 to 15 central hospitals. Each region was to have one top hospital (around 2000 deliveries), 5 medium-sized hospitals (around 1500 deliveries) and 10 smaller hospitals (minimally 500 deliveries) [34]. The minimum number of births was based on evidence from other countries to the effect that both the perinatal and neonatal mortality of low birthweight children is considerably higher in hospitals with a low annual number of deliveries (< 500) than in hospital with a large number of deliveries [35].

Both committees are aware that great patience and much good will from all parties involved are required to realize this development within one generation, but trust it is not impossible. The Dutch system has been said to be unique in the world. "We are now given the opportunity to build a new system that is better equipped to meet the present-day demands. We cannot afford to miss this opportunity. [31]

Responding to the description by Van Alten (honorary secretary to this NVOG Committee) of the above-mentioned plans in 1978 the editors of the journal of the KNMG (Medisch Contact) wrote:

The hospitals with fewer than 300 births per year - the majority - had better clear out, read: reorganize regionally [36].

There upon various committees and steering groups at various moments called for collaboration between the professional disciplines involved in obstetrics, such as the Workinggroup Obstetric Care of the Council of Health insurances (Werkgroep Verloskunde van Ziekenfondsraad) in 1989, the steering group Modernisation Obstetric care (Stuurgroep "Modernisering Verloskunde") in 2000, and the steering group "Pregnancy and Birth" ("Zwangerschap en Geboorte") in 2009 [37,38].

As mentioned earlier in this chapter, discussions within the NVOG focussed on the question "who to give responsibility for the indication of medical supervision of the pregnancy and the delivery". Two points of view emerged that seemed to clash [16,31,39]. On the one side, that of a large group of obstetricians who took the stand that selection of pregnant women – i.e., distinguishing between increased risk and no increased risk – was feasible only if done by the most experienced person in the midwife-GP-obstetrician trio [16]. This was the approach applied from the 1950s both in the UK and the Scandinavian countries to the satisfaction of all professional disciplines. According to De Haas-Postuma supervision like this and the lack of competition will benefit the cooperation between midwife and obstetrician [16]. On the other side, that of the group of obstetricians, who just like the GPs maintained that with the use of appropriate lists of indications it would be possible to make the right choice for a low- or high-risk pregnancy and/or birth; and that only in the latter case a specialist would have to be consulted [31,39].

This type of needs assessment has a long history, as it was professor De Snoo who as early as 1930 recommended a first selection 'on the grounds of toxicosis during the pregnancy and for a complicated delivery on the grounds of malposition and/or contracted pelvis'. Furthermore, in 1958 the Council of Health Insurances (the precursor of the present CVZ) had endorsed the first Obstetric Indication List (Verloskundige Indicatielijst (VIL)) prepared by a medical advisor of a public health insurance company and the Amsterdam-based professor of obstetrics Kloosterman [40]. In 1966 professor Kloosterman published a new “VIL” in the NTVG [41].

The wide regional distribution of the number of medical indications (ranging from 40% to 80%) in the mid-1970s suggested that a medical indication for a hospital birth was in some cases made for spurious reasons. This is why the so-called Sikkel-report, the report of the Workinggroup Obstetric Organisation, installed by the Minister of Health, called for separate lists of medical indications for deliveries and maternity care [42]. This report also included recommendations for obstetric cooperation and at the time was adopted unanimously by all professional disciplines involved in obstetric care in the Netherlands.

Next, the CVZ in January 1982 proposed the professional disciplines involved, a number of independent experts as well as the medical advisor to the CVZ should consult with each other on preparing lists of medical indications for deliveries and maternity care; it was thought that these lists could serve to combat the improper use of medical indications [43]. Consultations went ahead right away and in first instance resulted in the Clinical Indication List Maternity Care (Indicatielijst Klinisch Kraambed) [43].

In 1987 the Workgroup Revision of the VIL (Werkgroep Bijstelling Kloostermanlijst (WBK)) of the CVZ presented the revised list of indications to the professional associations of obstetricians. Preparing this list had taken five years [44,45]. It was rejected by the NVOG, in part for the reason that the NVOG’s previous objections had been disregarded [44].

> *In this way the expectant mother can give birth at home (or as an outpatient under the supervision of her own midwife), unless prevented by a medical contra-indication. The indications listed in the VIL represent the “unlesses”. Decisions can be made at different moments: to avoid worse trouble, to timely recognize problems, and to provide an adequate intervention. The VIL by definition has important social implications: first of all for the woman involved, but also for the care providers. Remuneration of the latter is partly dependent on the list; for in principle the specialist is not entitled to receive a remuneration without indication. In this respect the VIL differs from other algorithms, for example for the treatment of specific tumors or for decision-making in blood transfusions. Such models are not primarily aimed at the question ‘who should do what’, but rather at what should be done. Yet the latter is also the starting point for the VIL, from which subsequently social consequences are drawn. On a number of indications opinions will differ only slightly, for example: providing care after recurrent miscarriage. However, some increased risks cannot be prevented, but can be recognized by primary caregivers, after which referral to secondary care is indicated. A grey area exists in which GP or midwife need to consult with a specialist, after which the former may decide on the who and where. Now that’s where the shoe pinches. After all, the NVOG would not do well to approve the proposed procedure. [44].*

The CVZ in 1988 decided to request the advice from professors Casparie and de Vries Robbé. The verdict of both professors supported the view of the NVOG-board that the scientific underpinning was wanting and that the procedure followed was not the correct one [40].

In 1990 the Amsterdam public healthcare insurance company (Ziekenfonds van Amsterdam) investigated the causes for the high percentage of medical indications for a hospital birth in Amsterdam compared to the rest of the Netherlands [46]. The percentage of primary medical indications for the public health insured in Amsterdam amounted to 40%. Nationwide this percentage was 22% [47] while in Haarlem and the obstetric outpatient department of the Slotervaart Hospital, which used the VIL, these percentages were 8.4% and 8.0%, respectively [48]. The study was performed among 30 midwifery-practices in Amsterdam by the head of the medical advisory office of Public Health Insurance Company of Amsterdam (AZA) and two midwives [46]. The question was whether the high percentage of referrals during pregnancy or delivery was a result of the:

> *Urban problems, such as a relatively high number of very young and old pregnant women, immigrants and marginally living women, or perhaps of other underlying causes in addition, such as "too" rapidly establishing a primary medical indication* and/or the refusal of obstetricians in Amsterdam to comply with the renewed VIL of 1987. The AZA suspected that a considerable proportion of the high number of medically indicated hospital births could be explained on the grounds of the latter factors. It was concluded that the needs assessment for a hospital birth in Amsterdam frequently was made on an unstable foundation and on other grounds than those provided in the VIL. For example, reported indications included infections of the female genitalia and infertility treatment. How to rectify this situation? The AZA rejected a police officer role but insisted the obstetricians were (medical) duty bound to thoroughly reflect on their contribution to the medicalization of birth. This reflection should result in adopting the VIL, acknowledging the midwife as a full-fledged expert in the field of physiological pregnancy and the birth process and her expertise in the field of selection to referral to secondary healthcare. Acting as a manager, AZA will together with all parties involved strive to design an action plan that could put an end to the perceived undesirable situation. Furthermore, the authorities and the umbrella organisations of health insurers should be made aware that the present midwifery remuneration policy has a demotivating effect on the midwives and individuals pursuing a midwife career. In any case financial stimuli should be provided to promote home birth and hospital birth under supervision of midwives, also for the public healthcare insured [46].*

Moreover, a questionnaire survey in 1990 by Netherlands Institute for Health Services Research (NIVEL) among the professional disciplines showed that the majority of obstetricians (82%) hardly ever made use of the new VIL [68]. The questionnaire was administered within the framework of the EVI study (Evaluatie Verloskundige Indicatielijst) [47].

To find a way out of this deadlock both the NVOG in 1991 and the KNOV in 1992 sought help from the CVZ [40]. The council suggested an informal dialogue between the two associations on the one side and the head of the medical advisory board of the CVZ on the other, which later was joined by the National Association of General Practitioners (Landelijke Huisartsen Vereniging (LHV)) [40]. Eventually it was agreed to "initiate obstetric working meetings dedicated not only to actualise the VIL but also to address other aspects of obstetric care, such as harmonization and collaboration" [40].

The working meetings went ahead in 1994. Participants were representatives of KNOV, LHV and NVOG. The IGZ and CVZ are represented as advisory members [40]. The paediatricians were not involved in these developments [40].

Regarding the indications list, it was agreed that ‘this should be the resultant of an agreement between the professional disciplines involved reached on the basis of professional grounds’ [50].

Eventually in 2003 the boards of the three professional associations (KNOV, NVOG and LHV) adopted the current Obstetric Practice Vademecum (Verloskundig Vademecum) as a successor to the VIL [50]. The members are requested to use this Vademecum as a consequential recommendation in individual obstetric care and in the collaborations with the other care providers involved in obstetrics [50]. In addition the CVZ proclaimed that health insurance companies would take the Vademecum point of departure in making agreements with the local/regional parties. Lastly, the IGZ listed the Vademecum among the general professional standards, which implies that it will serve as the standard for the inspection of quality of obstetric care [50].

1.2.2.3 <u>The debate on the home birth</u>

Simultaneously with the discussion on the above-mentioned proposed collaborations, in the 1970s the debate on the safety of the home birth and the 'alienating' character of the hospital birth flared up again in the the Netherlands. This debate overshadowed the above-mentioned proposals for structural changes in the obstetric care system. Even in spite of the fact that the proposed Equal Obstetric Partnership (Gelijkwaardige Verloskundige Samenwerkingsverband) was still regularly addressed, among others by the gynaecologist Meuwissen in the journal of the KNMG (Medisch Contact) [51].

From an analysis of the various standpoints in the debate on home births in 1970s it appears, according to Meuwissen, that 'safety' is not an unequivocal concept, but is defined differently in the various articles [51]:

> *According to authors such as Eskes and Hoogendoorn safety is on the one hand an epidemiological measure, to be calculated from registered deaths. On the other hand they relate safety to constant monitoring and accuracy, guaranteed by the application of medical technology during the delivery. The group of Kloosterman relates safety of the delivery to adequate risk selection. In contrast, the midwives relate safety to corporality, experience and social relations. This is why consensus on what does and what does not constitute a safe delivery is problematic and at most of a temporary nature [51,52].*

As from the 1970s obstetric care in the Netherlands finds itself on a fork in the road, namely having to choose from two mutually exclusive options: maintaining the risk-selected choice of location of the delivery or conforming to the international trend to have all expectant mothers to give birth in hospital. The French, for example, have considered delivery as 'high risk' since the 1970s, and 99.5% take place in the hospital, for the additional reason that in this way it can be monitored with the use of a cardiotocogram (CTG) [53].

On the basis of the same figures the above-mentioned two groups reached different conclusions. Kloosterman’s group concluded that home birth was a justified option, whereas the group headed by Eskes concluded that it was no longer justified [54,55]. The discrepancy was caused by having reached diverging conclusions from the different presuppositions, which did nothing but confirm these presuppositions.

There seems to be some reason to suppose that a further increase in hospitalization of women in labour will be associated with a further decline of perinatal mortality, notably in those provinces where the proportions of women giving birth in a hospital are relatively low [55].

The fact that hospital perinatal mortality is 6 times higher than that for home births (in 1974: 25.3‰ and 4.2‰, respectively) clearly shows that careful selection during pregnancy, based on frequent and painstakingly performed clinical examinations rather than on "sophisticated technology" will enable to adequately determine who can safely await birth at home [54].

According to Eskes et al. the much better results of hospital birth can be ascribed directly to accurate CTG monitoring of the fetal condition and the measuring of blood gas values in the fetus [56]. Eskes and colleagues at that time found an important ally: technology. Lievaart and De Jong drew the same conclusions as Eskes et al [57]. They report:

The better outcome of the infants born in the hospital under the care of an obstetrician is most probably (also) due to the tools of surveillance used in the supervision of the deliveries, i.e., electronic fetal monitoring and determination of fetal scalp blood pH and the capability to perform a caesarean section [57].

Lievaart and the Jong emphasize that the possibility of intervention provides for better perinatal outcomes. Medical technology and its application in childbirth constitute from this moment an important issue in the discussion on the delivery. A safe delivery is according to the group of Eskes only guaranteed under continuous fetal monitoring:

The fetale cardiotocogram (CTG) can be performed both during pregnancy with external (indirect) methods and during delivery with internal (direct) methods. The CTG allows, irrespective of the presence or absence of contractions, [...] collecting accurate data [...].CTG recording implies that at all times objective documentation of the fetal neural and circulatory condition is available, both for research and possible retrospective evaluation [56]

However, the group of Kloosterman posed that in case of proper risk selection, giving birth at home was safer than in het hospital:

"Any superfluous intervention (anaesthesia, episiotomy, assisted delivery) is bound to increase the risk for mother and child" [58].

In a society in which the woman is able to withdraw from a [...] rigid hospital regimen by staying at home [...] the consumer's wishes and desires will always be taken into account [...]. In short: a perfectly spontaneous delivery without any outside intervention, as manifestation of the fact that also in humans the process of birth is one of the normal life activities such as breathing, thinking, loving. A delivery like this must be strived for [58].

Furthermore, Stolte et al. [59] in 1979 made a plea in in this discussion about optimal obstetric care, i.e. to restrict the evaluation of the outcomes not only to perinatal mortality.

Low perinatal mortality is an indication only if perinatal morbidity is low as well. Since today we are able to assess perinatal morbidity reasonably well, this should be going to be considered as a standard for obstetric care. According to Stolte and colleagues this measure can also be related to the different factors that may be decisive for the choice of birth location [59].

In articles on safety aspects of the delivery the obstetricians made use of a vocabulary that rested on technical, statistical and medical terms [52]. Midwives had a different notion of safety than had obstetricians. Safety in their articles was given shape on an individual "emotional" level, of the woman in labour and her partner. They considered an epidemiological measure such as perinatal mortality as "one of the indicators of the quality of the obstetric care" [60].
Assessment and estimation of statistical risks in a specific context were to them more important than meaningless figures:

As a matter of course these risk estimations must be made on scientific grounds. More important, however, is the question whether the risks involved can be adequately dealt with or not by the primary care midwives [61].

Besides, midwives defended the safety of the home birth on quite different grounds than did the obstetricians [52]. In their studies they did not make use of blood gas values and laboratory results, but administered questionnaires to women and midwives informing after their opinions, feelings, needs and experiences regarding their delivery [50]. The material was evaluated by NIVEL. In the introduction to the NIVEL research report this choice was motivated as follows:

The midwives dissociated themselves from the virtual absence of the most concerned person, the (expectant) mother, except in statistics. The use of questionnaires instead of epidemiological mortality figures or blood gas values reflects that the woman and her child are seen as an entity and as individuals are central in the delivery. If the mother or child fares well (rather than the pH value) the delivery will be safe and can therefore also take place at home [62].

According to the NIVEL research report, midwives emphasized that in hospitals the expectant mothers were identified as patients:

It was feared that the Netherlands would conform to the international trend by which every pregnant woman is seen as a patient and is consequently forced with moral, financial and social measures to give birth in the hospital [62].

According to the midwives, the hospital, as an institution for the treatment of pathology, clashed with the concept of the delivery as a natural, normal and non-pathological process [52]. Under the key words medicalization and hospitalization midwives summarize the negative consequences of a hospital delivery [52]. Like the way in which the obstetricians unproblematically linked monitoring and registration with a better outcome of delivery, in the eyes of midwives considering medicalization, hospitalization and technology as a matter of course represented a hazard for the low risk deliveries [52].

Strukamp et al. [52] concluded from their review on of the articles and reports concerning the debate about home births that the midwives and obstetrician reasoned and formulated in different manners:

> *Both parties employ their own logic and own axiomas that not required further explanation. Because they do not speak the same language, they also do not address each other's arguments in this discussion on the optimal location of delivery [52].*

The Dutch Organisation of Midwives (currently KNOV) didn't publish opinionated articles in journals such as Medisch Contact or NTVG in which they could participate in this discussion, but directly addressed the authorities, like in 1979 when they requested to make all Dutch hospitals accessible for so-called outpatient deliveries under the supervision of the 'own' midwife [51].

Since the late 1980s the Dutch authorities and the public health insurers protect and support home delivery, on the advice of a research board specially set up to this aim [63]. Until now, however, researchers from various Western countries, including the Netherlands have continued to contribute to the debate on safety aspects of the home delivery on the basis of statistical analyses [64-69].

1.2.3 The history of birth centres

Deliveries in a maternity clinic, where women far from home and family give birth? The Rotterdam town council in 1868 shuddered at the very thought. How deeply the woman might have fallen, she needed not to stoop to the hospital. This was 'contrary to our national character' [70].

As from 1900 for various reasons maternity clinics were instituted in the Netherlands independent from the general hospitals. Thus, the Midwife school in Amsterdam from as early as 1883 disposed of its own model-delivery room for training purposes in which annually more than 100 deliveries took place; after having moved in 1900 the school had more of such rooms available [71]. Also the other Midwife schools in the Netherlands in this period organised their own clinics. In the school at Heerlen the emphasis was on the guidance of the unmarried pregnant woman and mother [72]. The number of deliveries in the Heerlen Clinic of Midwife school increased from 234 in the year 1925 to 737 in the year 1935 [72]. In contrast to other maternity clinics in the southern Netherlands specially intended for the single mother, the director of the Heerlen's Midwife school held the view that mother and kind after the delivery were not to be separated [73]. After 1900 especially the southern Netherlands saw the institution of a large number of maternity clinics for the unmarried mother. One of these, the "Moederheil" home, under the supervision of the "Kleine Zusters van the Heilige Jozef", was opened in Breda in 1924 [74]. This home was instituted and managed by the 'Magdalenastichting, Vereeniging ter bescherming van meisjes'. In 1948 Moederheil was the largest shelter-home in the Netherlands for single, pregnant women. In that very year alone the nuns took care of 101 single mothers and 897 babies were delivered in their maternity clinic [74].

Instigated by the housing shortage and bad housing situation, a large number of stand-alone maternity clinics were instituted before or immediately following the Second World War by various organisations and hospitals to cater for the transferred home birth. To name a few, in 1939, the Foundation General Protestant Gynaecological and Obstetric Clinics opened the maternity clinic "De Oranje Kliniek" in The Hague [75], and the public health insurance company "Azivo" opened a maternity clinic at Scheveningen in 1947 [76], another stand-alone maternity clinic in The Hague was run on anthroposophical grounds.

In Amsterdam two maternity clinics were instituted as annexes of the Academical Hospital from the University of Amsterdam (Wilhelmina Gasthuis) in 1949, the temporary maternity clinic "Zeeburgerdijk" and a luxury maternity clinic 'Minerva paviljoen' headed by Dr. Meurer [77]. In Haarlem the maternity clinic of the Mariastichting hospital was housed from 1958 to 1973 in the former homestead Uittenbosch [78]. The stand-alone maternity clinics were also instituted outside/independent of the hospitals in the various provinces, like in Franeker, although most of these already closed their doors before 1959 [79].

In the course of the 1970s and 1980s the majority of the above-mentioned maternity clinics were forced to close their doors. Their beds were the first to be sacrificed in the wake of the first so-called hospital bed reduction surge. A second reason was the availability and introduction of a financial remuneration of outpatient delivery in the hospital supervised by the midwives, on account of which the running costs could no longer be covered [80]. A number of maternity clinics were incorporated in hospitals, such as those of the Midwifery schools of Rotterdam and Amsterdam. However, the public health insurance company of The Hague (AZIVO) was granted approval in 1979 from the Parliamentary State Secretary of Health, Veder-Smit, to relocate the maternity clinic “Volharding” to the site of the Leyenburg hospital [81]. This new maternity clinic was linked to the hospital through a connecting corridor. A press release issued by AZIVO said:

> *This provides the opportunity to offer the pregnant woman a facility in conformity with the AZIVO view that the hospital is not a place for healthy expectantly mothers, while at the same time the whole range of modern hospital services is available should complications occur [81].*

Simultaneously, with the aid of a national experimental subsidy, a number of by obstetrician supervised birth centres arose, including Wormerveer, Delftzijl and Enschede, which enabled the midwives and GPs to perform deliveries in a medically safe manner in low-risk pregnant women [27], conform the report entitled “Obstetric Care” [82]. In the Birth Centre of Wormerveer the midwives were formally employed by the centre and gradually their activities developed towards a combination of prenatal- and delivery supervision. In this way they fulfilled a socio-medical function for their clients both during the pregnancy and the postnatal period. In addition they supervised the maternity care provided by the maternity assistants (kraamverzorgsters) [27]. Furthermore, consulting midwives or GPs were allowed to supervise their clients during delivery in this centre. The centre provided instruction to student maternity assistants, residents and student midwives, and registered and coded the social and medical data on prenatal care, deliveries and maternity care [27]. The Birth Centre of Wormerveer had to close its doors in 1984.

As far as is known, only the Maternity Clinic “de Meiboom” (a merger of the shelterhome for unmarried pregnant women and mothers called “Huize in the Bocht” and the maternity clinic called “Huize Moedervreugd” located at the same site) has continued to function from 1945 to the present day. At the end of 2005 the maternity clinic de Meiboom was relocated next to the hospital called “Tweestedenziekenhuis” in Tilburg and renamed Thebe “Kliniek” [83]. Around the turn of the century a new search was initiated for alternatives to the special hospital for women who, on account of their living situation, could not or did not want to give birth at home. For this reason the first by Midwives lead Birth Centres came into being, also in Dutch called “kraamhotels or geboortehotels”, like the one in Rotterdam Noord since 1997. Yet the advent of birth centres actually did not start until after the turn of the century, when a great shortage of obstetric care providers had occurred, especially in primary care but also in the delivery-room-complex of the hospitals [84,85]. Due to high workload midwives in several regions could no longer supervise home births and also could not without good reason take their clients to the hospital. An interim arrangement was provided in the shape of a birth centre, where the midwife could supervise multiple deliveries simultaneously without having to call on the hospital. In this way birth centres were established close to or sometimes even within the walls of a hospital, such as at the University Medical Centre Utrecht and the Martini Hospital in Groningen, or detached from a hospital such as the Geboortehoes in Enschede, as an emergency solution seeing that having waitlists for deliveries is no option. As the shortages were remedied a number of these birth centres were shut down.

Yet, meanwhile the views on obstetric care were changing indeed. Notably the hospitals, but also primary care midwives took an interest in the new alternative: a birth centre adjacent to or within the walls of a hospital or close to the hospital site, which would allow for closer contact between primary and secondary care, facilitate transfer and at the same time release the pressure on the hospital's delivery rooms, as fewer outpatient deliveries would be needed [84].

This (thought) development had already begun when the Netherlands was alarmed by the publications of EURO-PERISTAT [86] in which a picture emerged of high perinatal mortality in comparison with other European countries. The results of these studies were almost directly linked to the obstetric care system in the Netherlands, which was so different from that in the other countries after all. Consequently the focus of the debate on birth centres shifted from an alternative birth location to an alternative working method: the possibility to obtain further integration between primary and secondary care and to remove the clear dividing line between both echelons, in other words: 'decompartmentalisation'. Meanwhile around thirty birth centres are functioning, each with its own origin and organisation, and without the existence of an all-encompassing policy view on the position of birth centres in the obstetric care system and without insight on how they contribute to the quality of obstetric care. As mentioned earlier, these birth centres differ widely, from centres not adjacent to a hospital (e.g. Birth Centre Amsterdam) to centres fully integrated in a hospital, also called "kraamsuites". These centres also differ in the way they are managed. A large number was established by primary care midwives whether or not in collaboration with the "Foundation Homebirth the Netherlands" (STBN) or maternity care organisations or hospitals. Only few birth centres originate from collaboration between primary and secondary care (hospital) [84].

In the mid-1960s the public health insurance companies decided to only limitedly reimburse care provision in a maternity clinic without medical indication (the so-called legally required own contribution for delivery and postpartum care), except in case of a social indication and admission to a maternity clinic or a Midwifery school. Following on this decision the Committee "Social Obstetric Care [87] requested the "public health insurance companies to draw up a generally accepted agreement about medical and social criteria for treatment in a hospital/ maternity clinic during pregnancy and delivery; this request was disregarded. Subsequently in 1977 also the CVZ advised the Ministry of Health that, should a woman opt for giving birth in a hospital, without medical reason, she should not be penalized financially [88]. The recently founded Steeringgroup "Pregnancy and Delivery repeated this recommendation in 2009 [38]. Regrettably, so far the authorities have turned a deaf ear to these demands [89,90].

1.2.4 The history of obstetric registration and statistics.

In the early 20th century a number of organisations in the Netherlands became convinced that by publishing data on unacceptable differences in infant mortality the healthcare providers and policy makers could be persuaded to diminish these differences. As early as 1909 – 1928 first the national bureau of statistics (Statistics Netherlands (CBS)) and later the “Dutch Union for protecting Newborns” (Nederlandsche Bond tot Bescherming van Zuigelingen) founded in 1908, had published cartograms reporting infant mortality figures for individual municipalities [91].

> *These cards were, according to the Union, an excellent means to draw attention to the ‘disgrace of high infant mortality in places where thus far there was too little interest in this problem [91].*

In 1951 Rottinghuis made a plea in the NTvG to introduce a uniform statistical system for obstetric material in the Netherlands with the aim to draw solid and well-founded conclusions in the course of time [92]. Amsterdam based researchers investigating the added value of the CBvPZs made a similar plea [93].

Also a committee headed by Van Luyn concluded in 1966 that appropriate obstetric statistics were lacking in the Netherlands [15]. This conclusion was based on CBS data;

> *In 60% of cases of perinatal mortality the cause of death was reported as “e causa ignota". The committee held the opinion that anyone accurately reporting his data will personally gain a better insight into the causes of the perinatal mortality – which consequently by removing and combatting the identified causes may reduce mortality. Scientifically oriented coordination and registration obtained through the work of hundreds of physicians and midwives throughout the country cannot do without uniformity, which does not necessarily imply centralisation. For that matter, good registration is not only required from a scientific point of view, it is also of value for those who are monitoring the pregnancy and provide obstetric care. Van Luyn and his committee recommended the institution of regional boards, composed from and by the KNMG and KNOV [15].*

In the 1980s it was reported that the registration of perinatal mortality in the Enschede region was wanting [94]. Following this observation, the correct registration of perinatal mortality was evaluated in Amsterdam in the years 1981/'82 [95].

> *The perinatal mortality recorded in the registration books of deliveries (partusboeken) and the patient files of all the 13 hospitals were compared with civil registration data and CBS data using the mother’s name and the child’s birth date. Of the 343 perinatal mortality cases in the hospitals the data of 49 deceased children (14.3%) could not be traced in the CBS registry. The statistical analysis of the CBS proved highly accurate; the registration errors were owing to non-reporting of deaths. Reporting was relatively often omitted for live-born neonates with birth weight < 1000 g and a gestational age < 28 weeks and for children of Turkish and Moroccan parents. Still half (n = 25) of the non-reported children had a birth weight of over 1000 g and/or a gestational age of over 28 weeks [95].*

According to Treffers [95] the observation by Hoogendoorn “that in the seventies and eighties perinatal mortality in the Netherlands decreased less strongly than in the other European countries” could be explained by the fact that in those years in the Netherlands we had started to record more cases of perinatal mortality, which previously were overlooked. While the other European countries already for a long time had registries in place in which information on pregnancy, birth and status of the newborn was recorded, such nationwide registration was very limited in the Netherlands until the 1980s, consisting only of the CBS data [96].

To date the CBS registry only includes data on children of Dutch citizens born at a gestational age of 24 weeks or more even as they are not born in the Netherlands. Separately the municipal offices submit data on stillbirths to CBS. Stillbirth must be reported to the civil registration office if the child’s gestational age is at least 24 weeks. Live-born children are recorded in the Municipal Personal Records (gemeentelijke basisadministratie persoonsgegevens (GBA)) if the father or mother at the moment of birth have been registered in a municipality in the Netherlands. Gestational age is not recorded, however. On the basis of the available data the following perinatal mortality parameters are published: a) perinatal mortality of liveborns plus stilbirth after a pregnancy of at least 24 weeks; and b) perinatal mortality of liveborns plus stillbirth after a pregnancy of at least 28 weeks. These statistics include liveborn children at a gestational age of less than 24 and 28 weeks, respectively, who died within the first week of life, because the CBS-statistics on liveborn children do not include information about gestational age. In spite of these limitations the CBS-registry until today forms the basis for the comparisons of perinatal mortality between the European countries, such as Peristat.

Instigated by the registration systems abroad, eleven hospitals under the directorship of Oscar van Hemel decided in 1971 to set up the so-called “Shared Obstetrics Registration” (Gemeenschappelijke Verloskunde Registratie (GVR)) [97]. In 1983 this system was replaced with the so-called “National Perinatal Database by obstetricians” (Landelijke Verloskunde Registratie (LVR 2)), followed by the midwives in 1985 (LVR1).The neonatologists/paediatricians followed in their footsteps in 1992 with the “National Neonatal Database by neonatologists” (Landelijke Neonatologie Registratie (LNR)). With various initiatives the GPs complemented the registration process in the perinatal care chain [96]. In 1991, 74% of all Dutch births were recorded in the LVR. Registration rates varied per region and per professional discipline from 60% to 100%. The data were collected, stored and managed by the Dutch Medical Database Institution (Stichting Informatiecentrum voor de Gezondheidszorg (SIG, currently Prismant)) in Utrecht [96]. To stimulate scientific research using LVR-data in 1989 a partnership agreement was signed between the SIG and the foundation Perinatal Epidemiology The Netherlands (PEN), housed in the Netherlands Institute of Preventive Healthcare ((NIPG-TNO) at Leiden [96]

In 2001 the then Minister of Health, Welfare and Sports (hereafter: Minister of Health) provided funding for the improvement of the quality and the interrelation between the separate registrations (LVR1, LVR2, and LNR). This resulted in the establishment of a joint venture: the Foundation Dutch Perinatal Registry (Stichting Perinatale Registratie Nederland (PRN)) [98].

In spite of the introduction of the LVR it appeared that also in the 1990s not all cases of perinatal mortality were registered with the municipality and/or in the LVR in compliance with the then current regulations for registration of perinatal mortality. This appeared from, among other things, a comparison by Elferink and colleagues of the CBS data and the LVR 2 data [99].

According to CBS [18] the exact level of perinatal mortality is strongly dependent on the definition used, as well as on policy and practice differences. This is why according to Richardus et al.[100] the under registration of perinatal mortality up to and including the 1990s reached 20 percent and the perinatal mortality rate varied by up to 50 percent on the basis of the definition used.

To prevent under registration, the PRN data are linked with the GBA data and the CBS stillborn registry since 2004 [101, 102]. The CBS dataset covers the integral registration of all born children aged 24 weeks and more. The PRN data coverage is circa 94 percent, as a number of primary care practices (midwives and GPs) do not participate in the PRN registration [102]. Not all children included in the GBA registry and the stillborn registry could be matched with the PRN data. For this reason weighting factors have been calculated, so as to be able to present background characteristics for the total population [102]. The numbers of deceased children from the GBA and stillborn registries were used for the marginals. The weighting factors account for maternal age, country of origin, province, child's sex, month of birth, multiple pregnancy and the ratio of primary care and secondary care deliveries. It is assumed that the outcomes (mortality by birth weight and gestational age) in primary care by GPs and by midwives who not participate in the PRN registry are similar to those in primary care by midwives who do participate in the PRN registry and these small numbers have hardly any influence on the total [102].

Outcomes are not published until completeness, plausibility and consistency of the matched dataset has been checked using three methods: time series verification (consistency over time), parameter analysis (relations between variables) and confrontation with outcomes from other sources [102]. From this dataset we can retrieve gestational age of all live born and stillborn children born at gestational age 22 weeks or more or with a birthweight 500 gram or more in case of uncertain gestational age, which enables internal comparison of perinatal mortality rates [101].

1.2.5 Financing of obstetric care

When the national public health insurance system was introduced in 1941, pregnancy and delivery were ranked equally with disease, so that the insured were entitled to receive prenatal care from GP or midwife from early pregnancy onwards [16]. However, in the 1940s and 1950s criteria for hospital admission on medical grounds were quite strict due to the financial consequences. It was not until the end of 1956 that these criteria were slightly adjusted towards the fetus and child, for example in case of imminent preterm birth or rhesus antagonism [16]. In 1958 primiparity above the age of 40 years was added as an indication for hospital birth [4]. Nevertheless, in the 1950s most public health insured expectant mothers were admitted to hospital almosty exclusively for the sake of the mother, rarely for the sake of the child [4,16]. As from 1959 a list of medical indications for “hospital” obstetric care served as a guideline for the public health insurance package [42]. The Indication list of maternity care was added to this list in 1982 [43] and in 1987 the CVZ (Health Insurance Council) issued a revised list of indications [44].The most recent VIL was published in 2003 and has been endorsed by all parties [50]. It serves as the legal frame of reference for midwife, physician and (public) health insurer alike, which implies that medically non-indicated care from an obstetrician is not reimbursed [50].

At its introduction in 1941, the public health insurance system acknowledged the primacy of the midwife in common obstetric care:

> W*hose contribution to practical obstetrics showed a declining trend; this contribution was largely based on obstetric care practice among the poor [103].*

Public health insured persons since then were no longer entitled to obstetric care from the GP to be paid by the sick fund if a midwife was available. GPs received reimbursement of obstetric care only for privately insured patients. This arrangement was to put an end due to the fierce competition between GPs and midwives. In 2001 Minister of Health (Borst) deleted the midwives’ primacy from the Health Insurance Act [104]. Until 1956 midwives were not paid if they transferred the care for the pregnant woman to the GP antepartum [4]. As from 1956 they were entitled to receive one third of the fee for the total prenatal care excluding delivery [4].
Since 1980 the Health Insurance Funds Council provided for reimbursement of midwives supervising low-risk deliveries in hospital or maternity clinic, although the pregnant women in these cases were obliged to pay an own contribution in conformity with the “Regulations of own contribution for maternity care” (Regeling eigen bijdrage voor de kraamzorg) [105]. In 1984 the public health insurance company of Twente (RZT) discontinued reimbursement of outpatient deliveries, which implied that deliveries without foreseen complications were to take place at home. RZT argued that the shortage of midwives at the time had been the reason to introduce reimbursement of outpatient deliveries [106].

> *Now the shortage of midwives has been resolved, according to RZT, it seems justified to restrict reimbursement to home deliveries only. RZT in this way annually saved 600,000 Dutch guilders. The CVZ had no difficulty in supporting this measure: “We applaud the very fact that deliveries that need not necessarily take place in hospital can take place at home ". The CVZ in addition pointed to the increasing number of pleas from society*

> *members favouring home deliveries. Moreover, the shift from outpatient to home delivery was a good economy measure, "provided the conditions are present that guarantee safety of delivery at home"* [106].

Late December 1989 a large majority in the House of Representatives was in favour of scrapping reimbursement of outpatient delivery from the public health insurance package, so as to stimulate home birth [107]. This majority thus acted in line with a recommendation from the CVZ. Only the Christian Democrats group (CDA group) held a different opinion, they preferred the expectant mother to decide where to give birth. This diverging opinion was based on a verdict from the Workgroup Obstetric Care (Adviescommissie Verloskunde) to the effect that the expectant mother should be allowed giving birth where she felt safest. The State Secretary of Health thereupon attempted to bridge the gap between these two opinions by proposing that apart from medical indications also social and cultural considerations could be accepted as grounds for reimbursement of outpatient delivery [107]. Eventually the House of Representatives decided to retain outpatient delivery in the public health insurance package [63].

In 1966 the government introduced a system of legally required own contributions for maternity care, including postnatal care at home, in a maternity hospital, and in a general hospital, in the absence of a medical indication [108]. In 1979, however, the State Secretary of Health corrected the disparity in having to pay an own contribution for maternity care without medical indication versus not having to pay in case of a medical indication. The legally required own contribution for maternity care in a general hospital also was applicable in the case of a medical indication [109].

> *In the future one's own financial contribution for the provision of maternity care in hospital will be similar to that which at present is required for clinical delivery without medical indication, except in case of a medically indicated maternity care [109].*

In a court procedure started in 1991 at the Central Appeals Court (Centrale Raad van Beroep) an appeal was upheld that this policy was in defiance of the regulations in the treaties of the International Labour Organisation. The Dutch government acquiesced in his decision and withdrew the challenged Article 3a of the Decision of hospital maternity care public health insurance (Besluit hospital kraamverpleging ziekenfondsverzekering) as from 1 January 1996. The preamble to the document of withdrawal merely made mention of the international obligation to act in this way [110].

1.2.6 Regional differences

Until far into the 19th century we find a distinct regional bisection in infant mortality in the Netherlands [111]. The Historical Sample of the Dutch population (Historische Steekproef Nederlandse bevolking (HSN)) mapped the relative infant mortality rate per municipality for the period 1841-1860 on the basis of the birth records from 1812-1922. While a high infant mortality rate (25%) was found in the western coastal regions and the areas alongside the main rivers, the mortality rate in the higher regions in the north, east and south of the country was relatively low (10%) [112]. Van Poppel et al. ascribed the higher mortality in the western regions largely to ecological conditions, notably salinisation and pollution of surface water and subsoil water [111]. Many people therefore had no access to good quality drinking water. Moreover, malaria was endemic as a result of poor drainage [112].

The final decade of the 19th century saw a sharp shift in region-bound infant mortality; as from 1878 the areas with the lowest infant mortality were found in the western Netherlands [112]. This phenomenon was ascribed to the likely fact that knowledge about the desirability and the significance of all kinds of hygienic measures could be picked up earlier here [112]. Another contributing factor was the economic revival, which enabled improvement of nutritional status and further development of facilities such as water mains and drainage. In contrast, agricultural yields in the east and the south had declined [112]. Furthermore, female labour in the south was on the rise, which led to fewer mothers breastfeeding, fewer investments in child care, and a lagging behind of medicalisation [112].

In 1956 De Haas-Posthuma was the first to describe regional differences in perinatal mortality [113]. In her article she argues:

> *Now infant mortality is going to be a secondary problem in social pediatrics, it would seem to be increasingly necessary to promote not only child health but also newborn health, and to strive to obtain the best possible development of the newborn.*
>
> *Perinatal mortality in the Netherlands varied per province; it is lowest in Zeeland and South Holland; and highest in North Brabant and Limburg. Even larger differences are seen among the big cities [113].*

In 1962 De Haas-Posthuma reported in her doctoral dissertation also the regional differences in perinatal mortality in the Netherlands over 1950-1957 (see Table 3) [16].

Table 3 Trend of perinatal mortality[1] in the Netherlands, regional comparison

	1950-53[16]	1954-57[16]	1961-65[114]	1966-70[114]	1971-74[114]	2000-6[115,116]
Groningen	30.8	29.1	25.3	22.4	17.0	11.1
Friesland	31.3	28.5	23.6	21.8	18.7	11.3
Drenthe	33.3	30.5	26.8	23.6	19.5	9.5
Overijssel	34.5	30.7	26.1	21.9	17.5	9.8
Gelderland	34.1	31.0	24.2	20.5	16.8	9.9
Utrecht (pr)	29.6	27.3	23.6	20.3	16.1	10.2
Flevoland						10.4
Noord-Holland	29.3	25.7	22.4	18.8	16.0	9.6
Zuid-Holland	28.4	23.4	21.6	19.3	15.4	10.1
Zeeland	30.9	27.7	23.4	20.2	17.0	10.6
Noord-Brabant	34.4	31.0	25.1	20.7	16.5	9.2
Limburg	33.4	30.2	23.7	21.5	17.0	9.2
Amsterdam			23.9	19.6	16.5	10.1
Rotterdam	30.0		22.3	21.7	15.2	11.4
Den Haag			21.7	20.8	18.5	11.8
Utrecht (city)			23.6	19.3	13.8	11.6
Municipality < 20.000	31.9*	28.1**				
Municipality 20.000-100.000	29.9*	25.3**				
Municipality ≥ 100.000	28.8*	25.4**				
Deprived Neighbourhoods						13.6
The Netherlands	31.3	28.3	23.6	20.4	16.5	9.9

*1951-1955, **1956-1960

According to De Haas-Posthuma the differences in perinatale mortality between rural and urban areas will have been the result, in part, of the high number of stillbirths among children born out of wedlock in urban areas. After all, in 1951/1952 in this group the perinatal mortality rate in primiparity was 25% and in the other parities 50 to 100% higher than in the group of legitimate births of similar parity. In view of the relatively high number of children born out of wedlock in urban areas as compared with rural areas, the author expected a higher perinatal mortality rate in the cities. Nevertheless, it was quite the reverse. The author supposed this was due to more favourable medical-hygienic conditions and lower maternal age in the cities compared to the country. The perinatal mortality rates in the 1950s and 1960s were highest in Drenthe, Overijssel, Gelderland, Noord Brabant and Limburg provinces. The author could not provide an explanation for this finding other than religious conceptions [16].

In the 1970s and 1980s various publications attempted to link the differences in regional perinatal mortality rates to aspects of perinatal care such as the percentage of home births, the percentage of deliveries supervised by an obstetrician, and the presence of a 'level 2'- or 'level 3'-hospital [17,43,114,117,118]

> *Treffers et al. [114] concluded that there was no clear association between the hospitalization rate and the perinatal mortality rate. On the other hand, Hoogendoorn in 1978 proposed that there was some ground for the assumption that a further increase in hospitalization would be followed by a further decrease in perinatal mortality [17,119].*

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[1] Perinatal mortality is defined as the number of stillbirths and deaths in the first week of life per 1,000 total births.

Subsequently Mackenbach et al., taking into account the limitedly available data over the years 1980-1984, investigated through a more refined regional analysis the association between the percentage of home births (as well as some others aspects of perinatal care) and perinatal mortality rate [120].

> *The percentage of home births was clearly positively associated only with the stillborn rate. The percentage of deliveries supervised by an obstetrician was positively associated only with the first-week mortality as a result of a group of other causes [120].*

Next, the same research group investigated possible reasons for any regional differences in perinatal mortality in the period 1984-1994 [121].

> *They found striking differences in perinatal mortality in the twelve Dutch provinces, with the steepest decline in the period 1984-1994 in Flevoland, Noord-Brabant and Limburg provinces. These were the very provinces where perinatal mortality used to be highest. The differences could not be explained, however, by differences in the number of hospital births versus home births, supervision of the delivery (GP or midwife), complications during pregnancy or labour, maternal age and parity, socio-economic status, or the percentage of immigrants among the population.*
>
> *The only consistent association between a socio-demographic factor and mortality was found for the percentage of Roman-Catholics in 1985. This variable appeared to be associated with an initial high mortality in 1984-1986 and a subsequent rapidly decreasing mortality trend. Historically, a high perinatal mortality risk among Roman-Catholics can be explained by the high rate of births among this group, which persisted until long after the Second World War. In the 1960s, however, the birth rate among Roman-Catholics declined rapidly and after 1980 it was even below average. Thus, after 1984 the difference in perinatal mortality between the two provinces with the highest percentages of Roman-Catholics (mean 80%) and the other provinces (mean 20%) had largely disappeared [121].*

In 2009, Tromp et al [122] explained the regional differences in perinatal mortality in the years 2000-2004 as follows:

> *The elevated risk in the northern region could not be explained by regional variation in demographic risk factors like maternal age, parity and ethnicity. Socio-economic status and urbanisation grade only explained a small part of the excess risk. Analyses focussed on clinical relevant subgroups showed regional differences were most prominent among births from 32+0 weeks gestation onwards and especially among term births from women transferred from low to high risk during delivery [122].*

1.2.7 Maternal mortality throughout the years

In 1849 maternal mortality in the maternity clinic at Leiden was as high as 25%, and was mainly caused by the dreaded puerperal fever. Professor Lehmann in Amsterdam, however, attached no value to Semmelweiss's observation of a spectacular drop in mortality in his clinic in 1847 after the introduction of simple hygienic measures such as 'washing hands'. It was not until 1880 when Lehman's successor (Van der Mey) implemented these measures also in Amsterdam, upon which the maternal mortality declined to a mean of 16 promille [123].

In the UK from the mid-nineteenth century to the 1930s maternal mortality in contrast to other causes of death was often higher in the middle and upper classes than in the working class [124]. In 1898 Cullingworth [125] discovered that in London the districts with the highest maternal death rates were the middle class ones while those with the lowest were working; and in 1924 Dudfield stumbled on the same finding [126].

> *This reversed social class relationship was also shown by the national statistics, especially for deaths from puerperal sepsis. Researchers in those days reached the conclusion that because working class women give birth at home supervised by a well-trained midwife, these women in contrast to women from the higher classes, who gave birth in hospital, escaped exposure to the unhygienic intervention by the physicians. These, after all, acted on the assumption that they should not cause suffering and should accellerate the delivery (by means of an intervention) using a forceps [124].*

In the 1930s the risk of maternal mortality in the Netherlands was hovering around 300 per 100,000 live births, and then sharply decreased like in other Western countries (see Table 4).

Table 4 Comparison trend of maternal mortality in the Netherlands (NL) with that in other European countries (EU)

Year Country (region)	1927[127]	1937[127]	1947[127]	1941-1949[128]	1950[127]	1990[129]	2008[129]
USA	650	570	230		120	11.5	16.6
Australia	590	570	250		120	6.3	5.1
England & Wales	480	340	120		90	8.4	8.2
Sweden	320	320	100		70	6.3	4.6
The Netherlands	300	280	150	128	110	9.2*	7.6*

* The data of the Dutch Nationwide Confidential Enquiry into the Causes of Maternal Deaths during the period 1993-2005 showed a significant increase in the maternal mortality rate compared to the period 1983-1992: 12.1 per 100,000 live births versus 9.7 [130,131].

Loudon attempted to find an answer to the question why the maternal mortality started to drop as late as 1935, in spite of the introduction of anaesthetics (1847), antisepsis (1880s), and caesarean section for obstructed labour (1890-1900) [124].

> *The dramatic fall in maternal mortality from the late 1930s to the end of the twentieth century seems to have been initiated by the introduction of the sulphonamides and sustained by blood transfusion, penicillin, and a rising standard of obstetric education and obstetric care [124].*

In the Netherlands, Rottinghuis in 1949 introduced administration of prophylactic anticoagulants to prevent maternal death as a result of an embolism if three predisposing factors for thrombosis were present. In addition he proposed three guidelines to prevent maternal death from bleeding: a) manual removal of the placenta at an earlier stage; b) earlier administration of packed cells; and c) more frequent use of ermetrine [128].

In 2004 the Netherlands occupied the 18th position among the 25 neighbouring countries with regard to direct maternal mortality [132]. This was mainly due to the fact that eclampsia is relatively more frequent in the Netherlands [133,134]. This difference between the Netherlands and the neighbouring countries may be caused by epidemiological factors, classification issues or by differences in the care of high-risk pregnancies. Analysis of substandard care factors in the Netherlands in the period 1983–1992 demonstrated substandard care in 93% of women with hypertensive diseases in the period 1983–1992, a percentage that did not decline in the period 1993–2002 (90%) [130,134].

1.2.8 Recent developments in Dutch obstetric care.

In the past 5 years the quality and safety of obstetric care is frequently in the centre point of the audio-visual and written media.

The article “Beter Baren” of Prof. Visser and Prof. Steegers published in Medisch Contact in 2008 is one of the articles, which launched this interest of the media [135]. This article called for revision of the Dutch obstetric system, in response to the recent ranking of the Netherlands in the European Perinatal Health Report. Furthermore they reported hospital day and night differences in perinatal mortality. Where the reactions in the press were rather non-refined (" during the night more babies die“), those of politics and the Minister were nuanced and led to intensive constructive discussions.

In the same year, the former Minister of Health installed the Steering committee “Pregnancy and Birth” [38]. This committee was commissioned to develop proposals to optimize obstetric care and, where possible, to advise how to reduce perinatal mortality and morbidity. The Erasmus MC published a report (on request of the Netherlands Organisation for Health Research and Development (ZonMw)) on prioritizing research in midwifery and obstetrics. This report, for the first time, noticed suboptimal risk selection in the chain of care, as one of the contributing factors to perinatal mortality and morbidity [136].

In early 2010, this committee published their advice, named “A good start” [38]. In summary: act proactively and work together (midwives and obstetricians) in combination with more attention to women in disadvantaged situations. This also means: multidisciplinary care directives and standards: the current permissiveness within the various professional groups involved must end.

Again, the cooperation between the various separated obstetric professional groups is seen as one of the means to reduce perinatal mortality and morbidity. In contrast with the past, this pursuit is now supported by the government with research funds and enforced by the Health Care Inspectorate (IGZ) and restructuring of the financing structure.

Therefore ZonMw by order of the government has developed a research-program entitled “Pregnancy and Birth”. In this context end 2012 ZonMW launched the program “obstetric regional consortia”. This program aims those caregivers in the obstetric field to work together in care and research in the region, culminating in a joint knowledge infrastructure.

Cooperation between community health, professionals (GPs and midwives) and second and third caregivers (hospitals and perinatal centres) should contribute to reducing perinatal mortality and morbidity in the Netherlands.

Another part of this research program is the evaluation of birth centre care, in particular the effects of birth centres on quality of care, experiences of clients and caregivers, economic outcomes and implications for further implementation of birth centre care.

In the context of enforcement, the IGZ monitors the establishment of partnerships between the community midwives and the obstetricians since 2012.

In the context of this cooperation, but also to eliminate the various perverse incentives, the NZA advises the Dutch government to implement an integrated financing system of obstetric care in 2016 [137-139].

Finally to gain further insights in how perinatal mortality can be reduced, the NVOG has long endeavored for a national audit on this. Through a budget for the period 2008 to 2012, the Minister of Health created the possibility for this by installation of the Perinatal Audit of the Netherlands (PAN) [140].

1.2.9 Summary

This chapter illustrates through the description of a number of debates, among other things, the complex situation around the implementation of changes in the Dutch obstetric care system. Implementation was additionally complicated by the structuring of healthcare financing (see chapter 1.2.7), also due to the compartmentalisation in the chain of obstetric care (primary care by the GP and midwife and secondary care by the obstetrician). After all, primary care in the Netherlands is not only seen as gatekeeper to secondary care, but also as body preventing healthcare from becoming too expensive. From the above chapters it may be concluded that regarding costs, the Ministry of Health and the health insurers until 2003 considered primary care, and notably the primary care midwives as their ally [46].

Not only the financing system raised a wall between primary and secondary care, but also the manner of argumentation and the “public discussion medium” substantially differ between both professional disciplines. The midwives and obstetricians each make use of different types of arguments and channels. The obstetricians and health insurers make use of statistical data for their discussions and opinions and journals such as Medisch Contact and the NTVG, whereas the midwives make use of questionnaire data on experiences of pregnant women, their own professional journal and their contacts in politics and the health insurers.

Moreover, the implementation of changes especially in the 1970s and 1980s was also complicated by differing opinions of obstetricians on their role in determining in early pregnancy whether the pregnant woman is at low or high risk for unfavourable pregnancy outcomes.

Summarizing the whole obstetric history until 2000 has strongly been influenced by the Dutch philosophy: Pregnancy is not a disease and childbirth should therefore not take place in a hospital. This had and still has consequences for: a) the co-operation between the obstetric care providers, b) place of birth and the caregiver responsible, c) financial reimbursement and d) pregnancy outcome, in particular perinatal- and maternal mortality.

However, in 2010 both obstetric care providers, the government and health insurers came to the conclusion that decompartmentalisation of the chain of care represents one of the most important challenges to improve pregnancy outcome in the Netherlands.

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Chapter 1.3

Inequalities in perinatal and maternal health

Hanneke de Graaf
Eric Steegers
Gouke Bonsel

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Abstract

Purpose of review: To describe inequalities in perinatal and maternal mortality, and morbidity from an international high-income country perspective. Measures of inequalities are socio-economic status, ethnic background, and living area.

Recent findings: Despite decreasing overall perinatal and maternal mortality in high- income countries, perinatal and maternal health inequalities persist. Inequalities in fetal, neonatal, and maternal adverse outcome relate to specific groups of risk factors. They commonly have a background in socalled structural risk factors, that is low level of education and income, being a migrant and living in disadvantaged areas. Structural risk factors therefore drive inequalities, and simultaneously represent the common perspective to judge perinatal and maternal health gaps. The effect of risk factors is further magnified in urban areas through risk accumulation.

As mother and child share their background, neonatal, and maternal adverse health outcome patterns coincide, resulting in similar inequalities and similar epidemiological trends. The structural background explains the difficulty of improving this.

Summary: Inequalities in perinatal and maternal outcome persist in women from lower socio-economic groups, from specific ethnic groups, and from those living in deprived areas. In view of the lifelong consequences, these marked social disparities pose an important challenge for the political decision makers and the health care system.

Introduction

Worldwide health inequalities increase both in low and high-income countries despite a global increase of average health [1,2]. Following the World Health Organization (WHO) we define health inequalities as differences in health between defined groups that are avoidable and unjust [3]. The most important sources and measures of health inequalities are socio-economic status (SES), ethnic background, sex, and place of living [4] (Figure 1). Their separate causal attributions are not always clear because of mutual interactions. Inequalities in perinatal health are a special case [4]. Impaired health, and as we believe health inequality, starts at the very day of conception or arguably even some time before [3]. It becomes manifest in different forms of perinatal morbidity, which all show inequalities [5,6]. It also plays an overriding role in adult health (e.g. through the relation between fetal growth restriction, metabolic syndrome, and other diseases as adult) [7]. Health inequalities at birth thus represent a magnifying glass of pre-existent disadvantages and a forecast for adult inequalities. Increasingly, caregivers and public health authorities recognize this double relevance of perinatal inequalities [8]. Consequently, governments and caregivers from high-resource countries implement programs to decrease perinatal disparities [9-11].

This study provides a review of the current knowledge on inequality of perinatal health outcomes, and of its determinants. Focus is on evidence in high-income countries. A systematic comparison is made with maternal health inequalities, as similar patterns may be expected to the extent that determinants are the same. Reviews and studies were identified via keyword searching on PubMed, the Cochrane library, the WHO Regional Databases; additional studies were retrieved from reference lists. We selected the most pertinent reviews, preferably studies from United States and the United Kingdom given their longstanding tradition on health inequalities gradation, and from other European countries in particular the Netherlands with a focus on urban conditions [12].

First we describe inequalities in perinatal health and its associations with lifestyle, working conditions, SES and ethnic background, and area of living. Thereafter, we discuss maternal health inequalities in a similar way. For space reasons this review does not contain a review of interventions specifically developed to reduce perinatal or maternal inequalities.

Table 1 Definitions of the key terms

Perinatal health	Perinatal health refers to the state of health of the baby during pregnancy, birth and the early postpartum period. Conventional indicators of perinatal health (more precisely ill-health) are fetal and neonatal mortality and indicators of morbidity [13].
Neonatal and perinatal morbidity	Neonatal and perinatal morbidity is commonly indicated by the following outcomes measured as birth prevalence: congenital anomalies, fetal growth restriction (small-for-gestational age, SGA), preterm birth (PTB) and a low Apgar score [13].
Neonatal mortality rate	The neonatal mortality rate is defined as the number of deaths during the neonatal period (up to 28 completed days after birth) at or after 22 completed weeks of gestation in a given year, expressed per 1 000 live births in the same year [13].
Fetal growth restriction	Fetal growth restriction should be reported according to the third or tenth percentile of birth weight at each gestational age (small-for-gestational age, SGA) [13]. More recently, fetal size indicators can be derived from intra-uterine ultrasound measurement, applying so called customized reference curves [14].
Preterm birth	Preterm birth is defined as the number of live births and fetal deaths at each completed week of gestation (starting from 22 weeks) [13]. Preterm can be subdivided into 22-27 weeks (extremely (preterm), 28-31 weeks (very preterm), and 32 up to and including 36 weeks (moderately preterm) [13].
Obesity	Obesity is defined as a body mass index (BMI) exceeding 30 kg/m2 [15]
Maternal death	The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes [16].
Maternal mortality ratio	Number of maternal deaths during a given time period per 100 000 live births during the same time-period [16].
Maternal mortality rate	Number of maternal deaths in a given period per 100 000 women of reproductive age during the same time-period [16].
Severe acute maternal morbidity (SAMM)	WHO defined three categories to classify patients as being SAMM; (a) disease-specific (specified criteria for common conditions, e.g. pre-eclampsia, haemorrhage), (b) management-specific (specified criteria related to response to disease, e.g. admission to ICU) and (c) organ-system dysfunction/failure based (specified criteria for dysfunction or failure related to each organ system e.g. acute renal dysfunction, pulmonary oedema) [17].

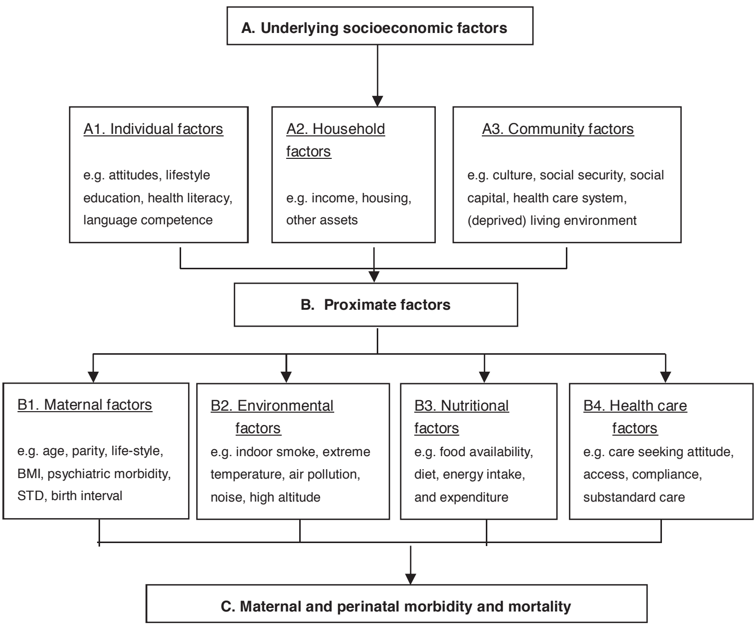
2 Perinatal health

Overall neonatal mortality rates (for definitions, see Table 1) in high-income countries have declined slowly over the last decades because of increased welfare, improved living conditions, and improved perinatal health care in particular in the domain of obstetric and neonatal treatment of premature birth [13,18].

Perinatal morbidity (for definitions, see Table 1) has, however, increased over the last decades, mainly as a consequence of the higher survival rate of previously untreatable premature birth and severe birth defects [13], while preterm birth prevalence increased [19]. Four key conditions of perinatal morbidity (see table 1) appeared to be responsible for 85% of perinatal mortality in the Dutch population; prematurity, fetal growth restriction, congenital abnormalities, low Apgar score at birth [20]. Prematurity was responsible for two-thirds of neonatal deaths in England and Wales [21].

The last two decades provided new evidence on what factors count, the interrelationship between individual, care-related, and environmental factors, the long- term effects of perinatal adverse outcome, and the reinforcement of risk factors being unequally distributed (for a scheme of perinatal risk factors, distinguishing between distal background and proximate factors, see Figure 1). In developed countries, geographical inequalities at the neighborhood level can be largely explained by risk accumulation in deprived areas [22,23]. Below we discuss five groups of risk factors associated with inequalities in perinatal outcome.

Figure 1 Factors influencing the health of mothers and their offspring (previously published by WHO [4])



Individual lifestyle inequalities

Any smoking, alcohol consumption, or drug use bears risks to the fetus. Unbalanced nutrition (vitamins, free fatty acids, dietary pattern in general) also appears to be a risk factor, yet the experimental confirming evidence from dietary intervention studies is still inconclusive, apart from the folic acid supplementation [24-28]. Working conditions are now accepted as key determinant acting through different pathways [29,30].

Maternal smoking

Maternal smoking during pregnancy increases the prevalence of several adverse perinatal outcomes, such as preterm birth, fetal growth restriction as well as fetal and neonatal death [31]. Despite it being the most important single risk factor for adverse perinatal outcome, women throughout the world continue to smoke during pregnancy [31]. In most developed countries maternal smoking during pregnancy decreases the last decade [31-33]. The downward trend in the Netherlands was most prominent in the highest-educated group [34].

Maternal smoking rates differ by socio-demographic characteristics, such as age, ethnicity and SES. In the United States Hispanic and Asian mothers are less likely to smoke than White and Black mothers [33], but in the Netherlands Turkish women smoke more (unhealthy adaptation) [35,36].

Alcohol consumption

Antenatal alcohol consumption during pregnancy even in so-called social quantities represents fetal risks. Excessive maternal alcohol consumption is associated with pregnancy complications, such as multiple birth defects, fetal alcohol syndrome and an increased risk of SGA [37,38]. Studies focusing on the effects of light-to-moderate alcohol consumption showed inconsistent results [39-41]. One retrospective study observed that any alcohol consumption in the first trimester increase the risk of spontaneous abortion by as much as four-fold [42].

Taking into account that self-report underestimates the degree of alcohol use [43], alcohol consumption during pregnancy is disturbingly common. Women's alcohol consumption during pregnancy increases with the rise of income, education, social class, and age; ethnic patterns exist [44-46].

Illicit drugs

Drugs abuse (e.g. marijuana, cocaine, heroin, methamphetamine, hallucinogens) during pregnancy is associated with birth defects, preterm birth, SGA, fetal distress, fetal death, and neurobehavioral abnormalities [47,48]. Substance drugs-abusing women often also have other characteristics that result in fetal harm, including high stress, lack of prenatal care, poor nutrition, sexually transmitted infections, and high-risk behaviors that expose them to violence [47,48]. Little is known on the extent to which reported adverse effects relate directly to drug-exposition or to these coinciding risks.

Nutrition in general

Although many associations exist between reproductive outcomes and maternal nutritional intake, as measured by self-report (dietary pattern, food groups, nutrients, and caloric content), and maternal nutrient deficiencies, as measured in blood. The interpretation in terms of attributable risk is difficult, as is their contribution to perinatal health inequality [24-26,49].

In non-experimental cohort studies, malnutrition and various nutrient deficiencies appears detrimental to birth outcomes, particularly malnutrition is associated with increased risk of SGA and stillbirths [24,25] iron deficiency is associated with increased risk of SGA, but excess iron supplement too is associated with SGA and preterm delivery [24,50,51], omega-3 fatty acids deficiency are associated with preterm birth [24,51]. In particular a low glycemic, Mediterranean-type diet is associated with less preterm birth and SGA [52,53]. Confirmatory evidence from nutrition intervention studies (beyond folic acid supplement, see section 2.1.6) is awaiting regarding vitamin D supplementation [54,55], balanced energy and protein supplementation [25,56], and magnesium supplementation [51,57].

Multiple nutrient deficiencies exist more often in low-SES populations as a result of poor diets (low amount of fruits, vegetables, fibre, fish, high amounts of sugar, fat, and salt); the expense of high-quality food may play a role [24,49,58].

Folic acid

Pregnant women with a folate deficiency are at an increased risk for congenital anomalies (in particular, neural tube defects), miscarriages, SGA and preterm birth [26,59,60].

Folic acid supplementation (starting prior to conception) either by individual intake or food fortification has repeatedly shown to be beneficial, primarily in terms of preventing neural tube defects [26-28]. Food fortification almost halves neural tube defects [61,62].

A sufficient folic acid status in many non-pregnant women of childbearing age relies on taking supplements, while a shorter interpregnancy interval represents additional risk [63]. The uptake of individual supplementation by women of reproductive age- is, however, incomplete (in the United States only 24%) [64-66].

Inadequate folic acid supplement use is associated with low SES, being immigrant, adverse dietary habits and smoking [62-64]. In urban populations indigenous population used recommended doses of periconceptional folic acid two to 10 times more than the immigrant population [66,67].

Obesity

Maternal obesity (for definition, see Table 1) represents an on-going reproductive risk from preconception period up to the puerperal period. Maternal obesity increases the risks of congenital fetal anomalies, preterm delivery, gestational diabetes, and fetal macrosomia with the associated risk of shoulder dystocia and other birth complications [68,69].

In the United Kingdom, 24% of women of reproductive age are now obese with an increasing trend in prevalence, which seems to occur worldwide [15,69].

Low SES, measured by level of education and health-related knowledge, is underlying different pathways to obesity. It may be a threshold to obtain the more expensive and less energy-dense foods (e.g. fruits, vegetables, and whole-grain cereals); and it is associated with fewer opportunities for recreational exercise [15].

Maternal age and parity

Generally, maternal age at the extremes (<20 year, >40 year), and high parity (>3) represent higher perinatal risk through different mechanisms [13,70]. Low socio-economic status and ethnic background are related to teenage pregnancies [71]. In some ethnic groups, high parity is more prevalent.

Working conditions

Although women in paid employment have better pregnancy outcomes than those without paid jobs, work-related factors such as exposure to chemicals, physically demanding work and psychological job strain adversely affect pregnancy outcomes [72-74].

Exposures to occupational chemicals periconceptionally and during pregnancy are associated with increased risk of spontaneous abortion, major malformations and SGA in the offspring [73,75,76].

Both physical work-related conditions, such as heavy lifting, prolonged standing or sitting, work with heavy machinery, and climbing stairs) as well as work processes related risks, such as hours worked, working shifts, job strain, machine-paced work, and speed of work are acknowledged to be related to adverse birth outcomes [30,72,74].

Two urban birth cohort studies [72,77] showed an independent association between high job strain and a long workweek during the first trimester with an average birth weight reduction of 150 g and 100% increased risk of SGA. The review of Bonzini et al [74] showed extensive evidence for a 40% increased risk of preterm birth of (a) shift work, (b) standing work, and (c) work for at least 40 per week.

The relation low SES and ethnic background with poor working conditions is accepted [78,79]. Ethnic differences in associations of job-related stress with adverse pregnancy outcomes were noted in several investigations [77]. African-American women consistently reported higher rates of job strain and were at greater risk for adverse pregnancy outcomes if compared with white or Hispanic women [78].

Socio-economic and ethnic determinants

SES is a construct conventionally defined by income, occupation, and educational attainment, where in the context of reproductive health educational attainment and wealth are the most important [3]. Through different pathways SES is a major source of health inequalities but it paradoxically also is the most commonly accepted normative yardstick to judge the absence of health inequalities [79,80].

Ethnic background can be defined in different ways, along citizenship (nationality), socio-cultural background (including language), or biological/racial ('black' referring to ancestry from former slavery countries in Africa) [78]. Minority groups represent a reproductive high- risk group, although exceptions exist, as illustrated through the Hispanic paradox in the

United States [82,83]. Ethnic reproductive inequalities are usually to the disadvantage of the immigrant group [78,80]. In most countries, perinatal health of defined indigenous minority groups is also at risk [1]. Possible pathways of SES and ethnicity towards reproductive disadvantages are explained below.

Socio-economic pathways

Most adverse birth outcomes are strongly associated with low SES, most importantly with through lower education and low income/wealth (through multiple pathways), and through occupational risk [84]. The reverse is also true. The highest education level is associated with better health through a healthier life style [2]. Preventive uptake and successful use of preventive and curative care also depend on educational level, as does coping with stress [84-86]. All these pathways apply in perinatal care. For instance, the date of the first prenatal visit strongly depends on SES, that is educational level and language competence [87,88]. Delayed first visit relates to increased perinatal mortality and preterm birth [87,88]. Decreased wealth and adverse social and material living conditions increase physiological and psychological stress [88]. Low income and material deprivation in general is associated with poor housing, nutrition, and health care access. It also negatively affects general health status and psychological health [1,3]. Finally, SES influences maternal age and parity. An in-depth study on SES mechanisms confirmed most of the above pathways [6].

Ethnic pathways

The pathways by which ethnicity affects perinatal health are of a different kind; besides lifestyle and socio-economic pathways (see above), ethnic groups have specific socio-cultural and biological pathways [90,91]. Across generations these pathways may alter [92,93]. Fetal growth restriction in some racial groups is partly explained by biological (genetic) differences, for example due to chronic and pregnancy-induced hypertension of women of African origin [91,94]. Recent immigrants may also be protected against risks for example when they retain the more favorable nutritional and behavioral (e.g. non-smoking) characteristics of the country they immigrated from [95].

Inequalities through the combined effects of socio-economic status and ethnicity

SES is differently distributed according to ethnicity, and their mutual contribution is not uniform. The combination of two deprived categories (low SES and black) yielded enhanced risks for adverse birth outcome [82,83]. In a Dutch national study however, low SES indigenous women represented the highest combined risk category, at least in generally deprived areas [70]. Perhaps this is due to selection bias, the white low SES group in deprived areas may represent (more than migrant groups) the very low end of the scale of being deprived from personal and social resources, unable to move to better areas and lacking any social cohesion.

Geographic disparities in perinatal health

Perinatal health differs widely both between countries. Within countries these differences are mainly related to urban versus rural differences and deprived-versus non-deprived neighborhoods differences [22,23].

Sources for area-differences are: social (e.g. quality living environment, education, access to community networks, and social welfare), economic (e.g. levels of employment, Gross Domestic Product per capita, working and environmental conditions), individual (e.g. lifestyle, nutrition), and access to health care [1,2]. Living in an urban neighborhood has important perinatal health-related effects, both favorable and unfavorable.

Neighborhood effects are no longer explained as single result of accumulation of risk factors related to individual SES and ethnicity, but as an interaction between the structural and contextual factors of the neighborhood and the life style and behaviors of their residents [96,97].

Living in a deprived neighborhood implies being exposed to urban environmental stressors and risk factors (e.g. crime, noise, physical insecurity, unemployment, lack of social support, and pollution) [22,23]. The pathways by which deprived neighborhood affects perinatal health are: promoting smoking, drugs and alcohol use and physical inactivity, inducing psychosocial stress (altered blood-pressure response and immune system comprise) and eliciting unhealthy food patterns [23,98]. Several studies showed that after controlling for individual socio-economic factors and ethnicity, living in deprived neighborhoods remained significantly associated with an increased risk of adverse birth outcomes, including preterm birth [99,100], SGA [101,102], and perinatal mortality [103,104]. In some Dutch-deprived neighborhoods perinatal mortality appears to be as high as 34‰ [104].

Inequalities in Maternal health

In 2008, the Maternal Mortality rate (MMR) in developing regions ranged from 640 maternal deaths per 100,000 live births in sub-Saharan Africa to an MMR of 41 in Eastern Asia. In developed countries rates are reported such as 24 in the United States and three in Ireland, accepting some heterogeneity in record completion [16]. The total MMR between 1990 and 2008 declined 34% in developing regions, versus 13% in the developed regions [16]. However, in several developed countries the MMR seems to have increased the last decade [16,105,106]. In part, this may be due to the fact that modern medicine successfully treats medical conditions that previously would have precluded pregnancy [107,108]. Additional to mortality, severe acute maternal morbidity (SAMM) has been used as maternal health indicator [110-111]. However, the definition of SAMM is still disputed and thus varies across studies [17,109]. The WHO defined three categories to classify patients as being SAMM (see table 1) [17]. In Western-Europe SAMM ranged from 6 to 14.7‰ [109,110]. As an additional indicator for severe maternal health states, we suggest psychiatric pathology, in particular depression and puerperal psychosis [105].

Below we discuss risk factors in the context of inequalities in maternal mortality, SAMM and post-partum health. Beyond the role of the factors discussed above as perinatal inequality factors, we add psychiatric conditions as being in particular relevant for maternal health inequalities (for a scheme of maternal risk factors, distinguishing between distal background and proximate factors, see Figure 1).

Lifestyle

Several studies have observed that SAMM and maternal mortality are associated with lifestyle in particular, heavy smoking, and obesity [112,113].

Smoking is responsible for a higher probability of IUGR and premature birth, which in turn induces more interventions and delivery complications. Although smoking generally decreases the risk of pre-eclampsia, on balance its effects on mother and child are detrimental [13,31].

Obesity represents also a risk to the pregnant woman and is associated with pre-eclampsia and gestational diabetes [112-114], delivery complications such as failure to progress in labor, increased requirement for induction of labor and increased frequency of caesarean delivery [112,115], and post-partum haemorrhage [112,115].

Pre-eclampsia rises with maternal weight from 2.8% in lean women to 10.2% in obese women [112]. A rule of the thumb suggests doubling of pre-eclampsia prevalence with each 5–7 kg/m^2 increase in pre-pregnancy BMI [115]. Extreme obesity during pregnancy is associated with a three- to four-fold increased risk of hypertensive complications [114,116]. The risk of gestational diabetes increases with rising maternal BMI; overweight and obese women having relative risks of 1.7 and 3.6, respectively [117]. Obese women with a family history of type 2 diabetes may be particularly at risk [113].

Age and parity

Teenagers and women aged 45+ are respectively three to 10 times at higher risk for maternal mortality [108]. Older women are more likely to be obese, have hypertension, or to develop gestational diabetes, pre-eclampsia or thrombo embolism [108,111]. Through this the risk of instrumental deliveries is enhanced. Age and parity also add to the risk of post-partum haemorrhage [118,119].

Work

One study reported unemployment during pregnancy to be associated with a twofold increased risk of dying from SAMM [111]. Bonzini et al. [74] found no unequivocal evidence for the association of occupational activities with gestational hypertension or pre-eclampsia. Two other recent studies support Bonzoni's conclusions [120,121].

Psychiatric and psychosocial background

Recent studies observed that maternal psychiatric illness is one of the leading causes of maternal death [105,122,123] and women with depressive illness were over-represented by five-fold amongst the women who died from severe obstetric morbidity [111]. In more than 50% of cases of maternal suicide an underlying psychiatric disorder could be identified, primarily a mood disorder [123,124]. Around 50% of these women with a known psychiatric disorder, had been in contact with mental health services [123,124]. Although post partum suicide is an unexpected and extreme high impact condition, from an epidemiological point of view we must add that the prevalence of non-pregnant women committing suicide in the same age group is considerably higher [105,123,124]. This ‘protective’ effect of pregnancy in terms of lower suicide rates is stronger during pregnancy compared with the postpartum period [104,123,124].

Socio-economic status and ethnicity

In low SES women maternal mortality as well as morbidity is increased [105]. Lack of education, resources (material, social, and family) and access to prenatal care, and living in a deprived area are hold responsible [105].

The racial disparity in maternal mortality and SAMM is only partially understood, key biological pathways are chronic-induced and pregnancy-induced hypertension and diabetes [125]. In the context of socio-cultural pathways mediating ethnic maternal disparities, substandard care may be involved [105,126]. Health illiteracy, which often coincides with greater need for care, results in suboptimal care due to delayed visits, underreporting of symptoms, and poor treatment compliance [125,126].

Geographic disparities in maternal mortality and severe acute maternal morbidity

Five recent regional studies [127-131] found substantially increased risks of MMR for their largest cities as compared with the rest of the countries. For example, the MMR in London compared with the rest of the United Kingdom was 19.3 versus 8.6 [127,128].

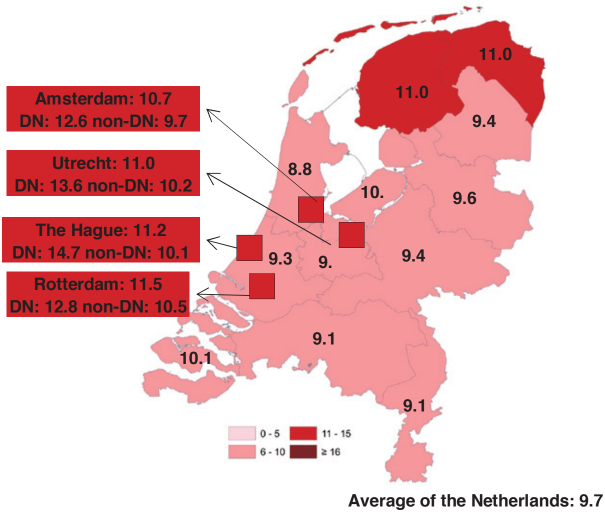
Perinatal- and maternal health inequalities compared

Generally the inequality patterns in perinatal health also apply to maternal health. Socio-economic, ethnic, and geographical gaps are here present too. In the figures 2a and 2b we show the corresponding perinatal and maternal mortality rates in the Netherlands.

Common pathways are related to low maternal education, low socio economic status, smoking, other unhealthy lifestyles and maternal age and parity. Maternal health inequality is additionally strongly influenced by the prevalence of medical and psychiatric conditions.

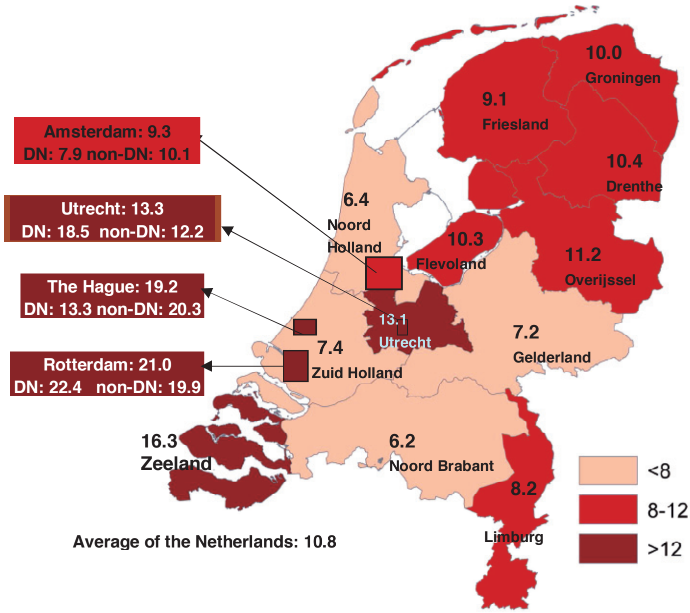
Despite lacking evidence, we expect that differential access to medical care inequalities plays a much stronger role in maternal morbidity and mortality as compared to fetal and neonatal outcome inequalities. Maternal conditions - if recognized - are to a larger extent preventable or even treatable according to current care standards.

Figure 2a Perinatal mortality (per 1 000 births) in the Netherlands by provinces and the 4 largest cities, 2000-2007 (Netherlands Perinatal Registration). (Previously published by Bonsel et al. [132])



***DN:** Deprived Neighborhood*

Figure 2b Maternal mortality (per 100.000 live births) in the Netherlands by provinces and the 4 largest cities, 1993-2008. (Previously published by de Graaf et al. [130])



DN: Deprived Neighborhood

Conclusion

Despite the reduction of the level of perinatal - and maternal mortality in most high-income countries during the last decades, perinatal and maternal health inequalities persist. This is particular true for women with lower SES in particular low education, for black women, and for women in regions characterized by social and physical deprivation. Emerging evidence suggests a strong biological mechanism behind the persistence of health inequalities. Perinatal disparities pose an important challenge for political decision makers and the health care and welfare systems of all countries.

Key points

- Adverse perinatal and maternal outcomes are subject to a common set of factors which underlie health inequalities. Consequently, the observed patterns of inequality in perinatal health, also apply to maternal health.
- An adverse perinatal event also is a determinant for adult health, and a major source of persistent adult health inequalities. The persistence of adult health inequalities may in part rest on this mechanism.

- The last two decades cohort studies have casted light on what perinatal and maternal factors count, the interrelationship between individual, care-related, and environmental factors, the long-term effects of perinatal adverse outcome, and the reinforcement or accumulation of risk factors being unequally distributed.
- Adverse perinatal outcome is strongly associated with low individual socio-economic background, most importantly with lower education and low income/wealth (through multiple pathways), and occupational risk. It seems less uniformly associated with ethnic background. Living in deprived neighborhoods appears to be an independent contributing factor.
- Maternal health inequality is additionally strongly influenced by age and parity at both extremes and by complex medical and psychiatric conditions.

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Part II

Place of residence and pregnancy outcome

Chapter 2.1

Living in deprived urban districts increases perinatal health inequalities

Hanneke de Graaf
Anita Ravelli
Marij de Haan
Eric Steegers
Gouke Bonsel

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Abstract

Objective: Analyses of the effects of place of residence, socioeconomic status and ethnicity on perinatal mortality and morbidity in the Netherlands.

Methods: Epidemiological analysis of all singleton deliveries > 22 gestational weeks (871,889 live born and 5927 stillborn) from the Dutch National Perinatal Registry 2002–2006. Multiple logistic regression analysis was used to determine whether place of residence (deprived neighborhood, or not) contributed to the adverse perinatal outcome (defined as perinatal mortality, preterm birth, small for gestational age, congenital abnormalities or Apgar score <7, 5 min after birth), additional to individual pregnancy characteristics, demographic characteristics, ethnic background and socioeconomic class.

Results: Incidence of adverse perinatal outcome was 16.7%. After adjustment the excess risk for perinatal mortality in deprived districts was 21%, for preterm birth 16%, for small for gestational age 11%, and for Apgar score <7 after 5 min 11%.

Conclusions: Perinatal inequalities appear impressive in both urban and nonurban areas, with a significant additive risk of living in a deprived neighborhood. Excess risk for perinatal mortality generally outranges that for morbidity, suggesting both an etiological and prognostic pathway for neighborhood effects.
A distinct pattern exists for congenital anomalies, for which first trimester adverse selection effects may be responsible.

Introduction

The increase of health inequalities is worldwide a recognized issue [1]. Health inequality refers to a difference in some defined health outcome among groups, where such a difference is regarded as unfair and undesirable, assuming unavoidable biological factors are not at stake. In this context ethnic background, socioeconomic status, gender and place of living are the most important sources of health inequalities, acknowledging part of their effect is unavoidable [2,3]. Health inequalities are not restricted to comparisons among countries; they also exist within countries, even if countries are highly developed [4].

The key indicator of perinatal health is perinatal mortality, and this indicator is well accepted to judge performance of care [5]. Other such indicators include preterm birth, fetal growth restriction, congenital malformations and/or the presence of perinatal asphyxia. Apart from mortality, most studies select low birth weight and/or preterm births as outcomes to establish perinatal health inequalities, although a plea for the other two can be made on similar grounds [6–10]. The presence of perinatal health inequalities has been established for ethnicity, socioeconomic class and, to a lesser extent, for the residential environment [3,8,9,11,12].

Perinatal health inequalities are particularly important in view of the future health of a newborn as it is difficult to redress disadvantages of an unhealthy start at birth, and detrimental effects range into adulthood and beyond [13].

Apart from the detrimental effects on the short term these adverse outcomes (at least small for gestational age and prematurity) are associated with impaired psychomotor functioning, learning and behavioral disabilities, and increased prevalence of diabetes and cardio-vascular disease later in life [13–16].

The Dutch government has adopted new strategies to reduce social and general health inequalities at adult age, with a focus on decreasing the impact of living in deprived neighborhoods or districts [17]. A deprived district is defined by the criteria: (un)employment, average income, the violent-crime rate as experienced by inhabitants and educational level, each criterion having its predefined threshold [18]. Forty districts have been formally defined as critical at the national level, most of them located in the four largest cities. Consequently 83% of women living in critically deprived neighborhoods, is a resident of one of the four largest cities. Contrarily to information on adult health inequalities, little is known of the presence and size of perinatal health inequalities.

The objective of this study is to establish the presence of perinatal health inequalities according to the place of living – in particular living in critically deprived neighborhoods – while accounting for ethnicity, and individual socioeconomic status. A previous paper on this study published in Dutch described some crude prevalence rates, not taking into account the differences in maternal background characteristics [19].

Materials and methods

Study population

Patient data were obtained from the Dutch Perinatal Registry (PRN), a linked professional database of all pregnancies, births and admissions after birth in the Netherlands, collected from midwives, obstetricians and paediatricians [20,21]. The registry information consists of detailed information of maternal demographic factors, pregnancy and delivery characteristics and neonatal outcomes on a personal level. Patient data in the PRN is anonymous. The national coverage is 96% near to complete as registration is compulsory (professional requirement to receive health insurance fees). The use of these patient data was with the explicit permission of the holder of the PRN. For this study all singleton deliveries from 22.0 weeks of gestation onwards during a five year period (1 January 2002 until 31 December 2006) were enrolled. We excluded the deliveries with missing gestational age or a birth weight less than 500 gram WHO [5]. Therefore, 877,816 (871,889 live born and 5,927 still born) singleton births remained for further analysis.

Outcome indicators

Adverse perinatal outcome was defined as the presence of any of the following outcomes: fetal mortality, early neonatal mortality (mortality within 7 days after live birth), perinatal mortality (fetal mortality and early neonatal mortality), preterm birth (birth before 37 completed weeks of gestation), small-for-gestational age (SGA) 10th percentile, based on the “Kloosterman” Dutch reference curves for birth weights [22], congenital anomalies (based on the caregivers diagnosis at birth or in the neonatal period, using a predefined checklist) and Apgar score after 5 min below 7 of the live born.

Population characteristics

The demographic characteristics studied were place of residence, ethnicity and socioeconomic status. Availability of postal code allowed for geographical assignment of living in the four largest cities (Amsterdam, Rotterdam, The Hague and Utrecht) and in the remainder of the Netherlands. The 40 most deprived neighborhoods (DN) have been determined by the Dutch government in 2007 [23]. The indicator used rests on rates of unemployment, of notified crime, insecurity and poor housing [24]. Previous research has used postal codes to characterize neighborhood effects [25,26] and has confirmed their utility in birth outcomes research [27]. Ethnicity of the women is reported by the woman’s care provider. For this study, we aggregated ethnic descent into Western (native Dutch and other European) and non-Western (including different ethnic groups like African/Surinamese Creole, Surinamese Hindustani, Moroccan and Turkish and other non-Western women).

Data on socioeconomic status were obtained from The Netherlands Institute for Social Research (SCP) on four-digit postal code level [28]. Using the woman’s postal code (4 digits) these data could be linked to the perinatal registry file. The socioeconomic status score of a postal code area is based on mean income level, the percentage of households with a low income, the percentage of inhabitants without a paid job and the percentage of households with on average a low education. The continuous socioeconomic status score was for our purpose categorized into a low, middle and high group based on percentile ranges (<20th percentile (low socioeconomic status) and >20th percentile (middle and high socio-economic status). The data on socioeconomic status were available for the year 2002. The categorized score was applied to the total population for the period 2002–2006 as large changes in socioeconomic status score for a postal code area within four years are unlikely. This could be confirmed for the city of Rotterdam, which made available annual sets of micro data underlying the geographical socioeconomic indicators like the local deprivation indicator (data not shown). Recent studies demonstrated the validity of this individual measure of socioeconomic status based on such small postal code areas [29]. The PRN-registry provides obstetrical data on determinants of perinatal outcomes: maternal age, parity, medical- and gynecological co morbidity, pregnancy complications, artificial reproductive treatment (ART) and calendar year. Maternal age is categorized into <20, 20–24, 25–34, 35–39 and ≥40 years. Parity is categorized into 0 (first birth), 1 (second birth) and 2+ (third and higher birth). Case mix is defined as: maternal age, parity, medical- and gynecological comorbidity, pregnancy complications and ART. Medical comorbidity includes the diseases; chronic hypertension, diabetes mellitus, neurological disorders, previous operations, abnormalities of the digestive, urological, and respiratory tract, thromboembolic, endocrine, cardiac, and psychiatric diseases and malignancies. Gynecological comorbidity includes the presence of congenital uterine anomalies, uterine fibroids, cervical amputation, prolapse surgery and diethylstilbestrol exposure. Furthermore this registry holds information on current pregnancy complications such as gestational hypertension, gestational diabetes, vaginal blood loss, Rhesus antagonism, cervical cerclage, placenta previae, solution placenta and includes the following risk factors: smoking, using drugs and sexually transmitted diseases. Whether pregnancy is achieved by artificial reproductive treatment is also coded.

Statistical analysis

Effect of all variables were interpreted as individual effects including the effect of living in deprived neighborhood, assuming that such an effect primarily covers an unmeasured individual characteristic.

First the incidence of each perinatal adverse outcome was analyzed by city of residence and by living in a deprived neighborhood (DN) or not. Second, we calculated the relative risk (RR) of the adverse perinatal outcome of a Western versus a non-Western woman living in the DN of the relevant city. As the reference we used the same risk outside the DN in the relevant city or in the rest of the Netherlands, whatever was appropriate A previous paper published in Dutch, using the same dataset, described some crude prevalence rates, not taking into account the differences in maternal background characteristics [19].

Complementary to this straightforward stratified analysis, we applied multivariable logistic regression analysis to explore whether any of the adverse perinatal outcomes related to living in a critically DN, after adjustment of all the other covariates. Adjustment followed a predefined sequential strategy. First we adjusted for case mix; maternal age, parity, medical and gynecological comorbidity, pregnancy complications, ART, and for calendar year to cover any unspecified annual trend. This set of adjustment variables was then treated as

forced case-mix control, to which other variables were added sequentially: ethnicity (Dutch, other European or non-Western), socioeconomic status, living in one of the four largest cities (with an indicator variable for each of these), and finally living in a critically deprived neighborhood. The stratified approach described above provides the maximum estimate of DN effects, including difficult to assign individual background effects (with the risk of over- estimation of the DN effect). Also interaction effects across strata, if present, become visible. The logistic stepwise procedure however, provides the most conservative estimate of the DN as the non DN factor included last, that is, the DN effect (if existent), as some of the adjustment factors (e.g. gynecological morbidity, diabetes) could be regarded at least partially as intermediate factor. Odds ratios, with 95% confidence intervals, were calculated
for each risk factor. Data was presented as frequencies and proportions (%) unless specified otherwise. The statistical software package SAS version 9.1 (SAS Institute Inc, Cary NC) was used for data analysis.

Results

About 15% of all deliveries took place in the 4 largest cities (C4 cities). These deliveries in C4 cities account for 41% of all births from non-Western women and for 82% of all births from women living in a deprived neighborhood (DN) (see Table 1).

Table 1. General characteristics of women and births 2002–2006

		Four largest cities (C4)												C4 total			Rest of the Netherlands			Netherlands Total
		Amsterdam			Rotterdam			The Hague			Utrecht									
Research Population (PRN)	Births (total)	49 651 (6% of births NL total)			35 237 (4% of births NL total)			30 214 (3% of births NL total)			20 890 (2% of births NL total)			135 992 (15% of NL Total)			741 824 (85% of NL total)			877 816 (100%)
	Births of non Western (NW) women	23 088 (47% of births Amsterdam total)			16 812 (48% of births Rotterdam total)			12 586 (42% of births The Hague total)			5 732 (27% of births Utrecht total)			58 218 (41% of nW births NL total)			83 427 (59% of nW births NL total)			141 645 (16% of births NL total)
	Birth in Deprived Neighborhood (DN)	19 372 (39% of births Amsterdam total)			15 843 (45% of births Rotterdam total)			4 792 (16% of births The Hague total)			3 829 (18% of births Utrecht total)			43 836 (82% of DN births NL total)			9 369 (18% of DN births NL total)			53 205 (6.1% of births NL total)
	Birth of non-Western women in DN	13 780 (28% of births Amsterdam total)			10 126 (29% of births Rotterdam total)			3 801 (13% of births The Hague total)			2 328 (11% of births Utrecht total)			30 045 (88% of nW/ DN births NL total)			3 394 (12% of nW /DN births NL total)			33 979 (3,9% of births NL total)
		DN yes	DN no	total	DN yes	DN no	Total	DN yes	DN no	total	DN yes	DN no	total	DN yes	DN no	Total	DN yes	DN no	total	total
Perinatal Outcomes	Perinatal mortality	258 13,0‰	245 8,1‰	503 10,1‰	194 12,2‰	208 10,7‰	402 11,4‰	84 17,5‰	272 10,7‰	356 11,8‰	55 14,4‰	187 11,0‰	242 11,6‰	591 13,5‰	912 9,9‰	1 503 11,1‰	128 13,7‰	6 760 9,2‰	6 888 9,3‰	8 391 (9,6‰)
	Fetal mortality (22.0 weeks - 0 day)	202 10,4‰	171 5,6‰	373 7,5‰	140 8,8‰	144 7,4‰	284 8,1‰	62 12,9‰	199 7,8‰	261 8,6‰	37 9,7‰	121 7,1‰	158 7,6‰	441 10,1‰	635 6,9‰	1 076 7,9‰	90 9,6‰	4 761 6,5‰	4 851 6,5‰	5 927 (6,8‰)
	Early neonatal mortality (< 7 days)	56 2,9‰	74 2,5‰	130 2,6‰	54 3,4‰	64 3,3‰	118 3,4‰	22 4,7‰	73 2,9‰	95 3,2‰	18 4,7‰	66 3,9‰	84 4,1‰	150 3,4‰	277 3,0‰	427 3,1‰	38 4,1‰	1 999 2,7‰	2 037 2,8‰	2 464 (2,8‰)
	Congenital abnormalities	420 21,7‰	584 19,3‰	1 004 20,2‰	387 24,4‰	476 24,5‰	863 24,5‰	130 27,1‰	572 22,5‰	702 23,2‰	78 20,4‰	338 19,8‰	416 19,9‰	1 015 23,2‰	1970 21,4‰	2 985 21,9‰	284 30,3‰	18 188 24,8‰	18 472 24,9‰	21 457 (24,4‰)
	Preterm birth (<37.0 weeks)	1 388 71,6‰	1 697 56,0‰	3 085 62,1‰	1 133 71,5‰	1 279 65,9‰	2 412 68,5‰	371 77,4‰	1 588 62,5‰	1 959 64,8‰	248 64,8‰	893 52,3‰	1 141 54,6‰	3 140 71,6‰	5457 59,2‰	8 597 63,2‰	677 72,3‰	43 539 59,4‰	44 216 59,6‰	52 813 (60,2‰)
	Small for gestational age (< P_{10})	1 708 88,2‰	1 788 59,1‰	3 496 70,4‰	1 439 90,8‰	1 438 74,1‰	2 877 81,6‰	473 98,7‰	1 915 75,3‰	2 388 79,0‰	278 72,6‰	889 52,1‰	1 167 55,9‰	3 898 88,9‰	6030 65,4‰	9 928 73,0‰	830 88,6‰	42 867 58,5‰	43 697 58,9‰	53 625 (61,1‰)
	Apgar score < 7 after 5 minutes	334 17,4‰	413 13,9‰	747 15,0‰	283 18,0‰	259 13,5‰	542 15,4‰	63 13,3‰	346 13,7‰	409 13,5‰	47 12,4‰	190 11,2‰	237 11,3‰	727 16,6‰	1208 13,1‰	1 935 14,3‰	150 16,2‰	8 204 11,3‰	8 354 11,3‰	10 289 (11,8‰)

DN=deprived Neighborhood
NW = Non Western
NA = not applicable

The population of the C4 cities showed a higher percentage of adverse outcomes (18.4 vs 16.4% of the remainder of the Netherlands). Perinatal mortality in the C4 cities was 11.1‰, versus 9.3‰ in the remainder of the Netherlands ($p < 0.001$), whereas the difference was larger for foetal mortality (7.9 vs 6.5‰; $p < 0.001$) compared to early neonatal mortality (3.1 vs 2.8‰; $p < 0.03$). Congenital anomalies were lower in the C4 cities (21.9 vs 24.9‰), while preterm birth (6.3% vs 6.0%), SGA (7.3 vs 5.9%), and low Apgar (14.3 vs 11.3‰) clearly showed differences to the disadvantage of the C4 cities.

While all C4 cities show higher mortality levels, Amsterdam (10.1‰) performed in between the other three cities (all exceeding 11‰) and the remainder of the Netherlands (9.3‰). Detailing the data to living in DN, showed large contrasts (both in the C4 cities, and the remainder of the Netherlands) which generally exceeded the contrasts between the C4 cities mutually, and between the C4 cities and the remainder of the Netherlands. For example fetal mortality in Amsterdam DN is 10.4 versus 5.6‰ outside DN, in Rotterdam DN 8.8 versus 7.4‰ outside DN, The Hague DN 12.9 versus 7.8‰ outside DN, Utrecht DN 9.7 versus 7.1‰ outside DN, in the remainder of the Netherlands DN 9.6 versus 6.5‰ outside DN. SGA showed similar large contrasts for example in Amsterdam: DN 88.2 versus 59.1‰ outside DN. Apgar scores generally showed similar contrasts. However, congenital anomalies did not show differences according to living in DN.

For C4 cities and the remainder of the Netherlands we repeated these analyses for ethnic groups separately showing perinatal outcomes universally worse in women from non-Western background, with moderate level differences in the C4 cities (detailed data supplement 1).

Table 2 shows the relative risks of living in a DN in all C4 cities, for ethnic groups separately. For Western women the great majority of indicators in all cities show significant risk associated with living in a DN; for non-Western this is true for only part of the indicators. Apart from neonatal mortality, all perinatal indicators in the C4 showed larger contrast between DN and non DN in Western women, compared to ethnic groups. Outside the C4 this differential effect of Western women living in DN was limited to SGA. In the adjusted logistic regression analysis the effect of living in the deprived neighborhoods appeared significant for all adverse perinatal outcomes. The excess risks for perinatal mortality, preterm birth, congenital abnormalities, SGA and low Apgar score were 21, 16, 8, 11, and 11% respectively (Tables 3 and 4). Non-Western ethnicity reflected a significantly higher risk for of all adverse perinatal outcomes. Low socioeconomic status was associated with a significant higher risk of the adverse perinatal outcomes, independent from living in a deprived neighborhood, except for congenital abnormalities.

Table2. Relative risk of the adverse perinatal outcome of (non)-Western pregnant women in the deprived neighborhood (DN)

Adverse perinatal outcome	deprived neighborhood in Amsterdam				deprived neighborhood in Rotterdam				deprived neighborhood in The Hague				deprived neighborhood in Utrecht				deprived neighborhood in the rest of the Netherlands			
	Western		non-Western		Western		non-Western		Western		non-Western		Western		non-Western		Western		non-Western	
	RR (95% -CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)		RR (95%-CI)	
Perinatal mortality (22.0 weeks - 7 days pp)	1,52	(1,12-2,05)*	1,36	(1,07-1,73)*	1,40	(1,05-1,87)*	0,88	(0,67-1,15)	1,96	(1,21-3,18)*	1,29	(0,96-1,74)	1,59	(1,04-2,42)*	1,00	(0,63-1,58)	1,34	(1,05-1,71)*	1,29	(1,00-1,65)
Fetal mortality (22.0 weeks - 0 days)	1,88	(1,34-2,63)*	1,45	(1,09-1,91)*	1,69	(1,21-2,36)*	0,81	(0,59-1,12)	2,23	(1,31-3,80)*	1,26	(0,89-1,80)	1,99	(1,25-3,18)*	0,94	(0,50-1,75)	1,31	(0,97-1,76)	1,29	(0,96-1,74)
Early neonatal mortality (< 7 days)	0,74	(0,36-1,50)	1,14	(0,71-1,82)	0,80	(0,44-1,47)	1,05	(0,64-1,73)	1,24	(0,38-3,99)	1,38	(0,78-2,42)	0,78	(0,28-2,16)	1,08	(0,54-2,14)	1,40	(0,90-2,18)	1,28	(0,80-2,07)
Congenital abnormalities	1,30	(1,07-1,58)*	0,96	(0,81-1,15)	0,99	(0,81-1,21)	1,00	(0,82-1,21)	1,47	(1,01-2,13)*	0,97	(0,77-1,22)	0,69	(0,44-1,08)	1,16	(0,83-1,63)	1,18	(1,01-1,37)*	1,18	(0,99-1,41)
Preterm birth (<37.0 weeks)	1,24	(1,11-1,39)*	1,26	(1,13-1,39)*	1,24	(1,11-1,38)*	0,97	(0,86-1,08)	1,76	(1,45-2,13)*	1,03	(0,90-1,19)	1,38	(1,14-1,67)*	1,30	(1,04-1,63)*	1,25	(1,14-1,37)*	1,15	(1,02-1,29)*
Small for gestational age (< P_{10})	1,49	(1,33-1,66)*	1,23	(1,12-1,34)*	1,46	(1,31-1,62)*	0,94	(0,85-1,03)	1,85	(1,55-2,22)*	0,95	(0,84-1,07)	1,78	(1,48-2,13)*	0,94	(0,77-1,15)	1,64	(1,51-1,79)*	1,07	(0,96-1,18)
Apgar score < 7 after 5 minutes	1,03	(0,80-1,33)	1,21	(0,99-1,48)	1,27	(0,98-1,65)	1,22	(0,96-1,54)	1,13	(0,67-1,90)	0,90	(0,65-1,27)	0,88	(0,51-1,53)	1,07	(0,69-1,67)	1,34	(1,08-1,67)*	1,29	(1,02-1,64)*
Total	1,34	(1,25-1,44)*	1,21	(1,14-1,28)*	1,24	(1,16-1,33)*	0,98	(0,92-1,05)	1,65	(1,46-1,87)*	1,00	(0,92-1,08)	1,43	(1,27-1,62)*	1,07	(0,93-1,22)	1,37	(1,29-1,44)*	1,11	(1,04-1,19)*

The risk outside a neighborhood as taken as reference either in the large city of interest or the remainder of the Netherlands.
RR. relative risk.
* = P<0,05

Table 3. Odds ratio (CI 95%) of perinatal mortality >22weeks and 7days post partum: prevalently, crude and the results of the separated four steps of the regression analysis.

Perinatal death >22weeks and 7days post partum		Prevalently ‰	Crude	Step 1 Casemix	Step 2 Casemix & ethnicity & SES	Step 3 Casemix & ethnicity & SES & C4	Step 4 Casemix & ethnicity & SES & C4 & Deprived neighbouhood
Deprived neighbourhood	Yes	13,5	1.46 (1.35-1.58)*				1.21 (1.09-1.34)*
	No	9,3	1				1
C4	Amsterdam	10,1	1.09 (1.00-1.20)			0.88 (0.80-0.97)*	0.83 (0.75-0.92)*
	Rotterdam	11,4	1.23 (1.11-1.36)*			0.97 (0.88-1.08)	0.91 (0.81-1.02)
	The Hague	11,8	1.27 (1.14-1.42)*			1.05 (0.94-1.17)	1.03 (0.92-1.15)
	Utrecht	11,6	1.25 (1.10-1.42)*			1.10 (0.96-1.25)	1.07 (0.94-1.22)
	rest NL - C4	9,3	1			1	1
Ethnicity	Dutch	8,9	1		1	1	1
	Other European	8,6	0.97 (0.84-1.12)		0.93 (0.80-1.07)	0.93 (0.81-1.08)	0.93 (0.81-1.08)
	Non western	12,9	1.46 (1.38-1.54)*		1.34 (1.26-1.42)*	1.35 (1.27-1.43)*	1.33 (1.25-1.41)*
SES	< p20 (low SES)	11,5	1.28 (1.22-1.34)*		1.12 (1.06-1.18)*	1.13 (1.07-1.20)*	1.09 (1.03-1.16)*
	> p20 (mid high SES)	9,1	1		1	1	1
Age	<20	15,0	1.75 (1.53-2.00)*	1.64 (1.43 - 1.88)*	1.46 (1.27-1.67)*	1.46 (1.27-1.67)*	1.45 (1.27-1.67)*
	20-24	11,5	1.34 (1.25-1.43)*	1.30 (1.21 - 1.39)*	1.19 (1.11-1.27)*	1.19 (1.11-1.27)*	1.18 (1.10-1.27)*
	25-34	8,7	1	1	1	1	1
	35-39	10,5	1.22 (1.15-1.29)*	1.21 (1.14 - 1.28)*	1.23 (1.16-1.30)*	1.23 (1.16-1.31)*	1.24 (1.17-1.31)*
	40+	15,3	1.78 (1.59-1.99)*	1.70 (1.52 - 1.90)*	1.68 (1.51-1.88)*	1.69 (1.51-1.89)*	1.70 (1.51-1.90)*
Parity	Nulliparae	10,5	1.38 (1.31-1.45)*	1.35 (1.28 - 1.42)*	1.36 (1.29-1.43)*	1.36 (1.29-1.43)*	1.36 (1.30-1.44)*
	par 1	7,6	1	1	1	1	1
	par 2+	11,0	1.45 (1.36-1.54)*	1.39 (1.31 - 1.48)*	1.32 (1.24-1.41)*	1.32 (1.24-1.41)*	1.32 (1.24-1.41)*
Medical comorbidity	No	9,4	1	1	1	1	1
	Yes	16,9	1.81 (1.63-2.02)*	1.76 (1.58 - 1.96)*	1.74 (1.56-1.94)*	1.73 (1.55-1.93)*	1.72 (1.55-1.92)*
Gynecological comorbidity and pregnancy complication	No	9,5	1	1	1	1	1
	Yes	16,5	1.74 (1.31-2.31)*	1.50 (1.12 – 2.00)*	1.45 (1.09-1.93)*	1.45 (1.08-1.93)*	1.45 (1.08-1.93)*
Assisted Reproductive Therapy (ART)	No	9,5	1	1	1	1	1
	Yes	18,7	1.99 (1.56-2.54)*	1.72 (1.34 - 2.20)*	1.71 (1.34-2.19)*	1.71 (1.33-2.18)*	1.70 (1.33-2.18)*

***= P<0,05**

Table 4. Odds ratio (CI 95%) of preterm birth, congenital abnormities, Small for Gestational Age and low Apgar score < 7 after 5 minutes before and after the regression analyses.

		Preterm birth			Congenital abnormalities			Small for Gestational Age (< P_{10})			Apgar score < 7 after 5 minutes		
		Preva-lenty %	crude	Step 4	Preva-lenty %	Crude	Step 4	Preva-lenty %	Crude	Step 4	Preva-lenty %	crude	Step 4
Deprived neigh-borhood	Yes	7,17	1.22 (1.18-1.27)*	1.16 (1.11-1.21)*	2,44	1.00 (0.94-1.06)	1.08 (1.00-1.16)	8,89	1.55 (1.50-1.60)*	1.11 (1.07-1.16)*	1,66	1.46 (1.36-1.56)*	1.11 (1.02-1.22)*
	No	5,94	1	1	2,44	1	1	5,93	1	1	1,15	1	1
C4	Amsterdam	6,21	1.05 (1.01-1.09)*	0.89 (0.86-0.93)*	2,02	0.81 (0.76-0.86)*	0.73 (0.68-0.78)*	7,04	1.21 (1.17-1.25)*	0.90 (0.86-0.94)*	1,52	1.34 (1.25-1.45)*	1.04 (0.96-1.14)
	Rotterdam	6,85	1.16 (1.11-1.21)*	0.98 (0.94-1.03)	2,45	0.98 (0.92-1.05)	0.89 (0.82-0.96)*	8,16	1.42 (1.37-1.48)*	1.03 (1.00-1.08)	1,55	1.37 (1.26-1.50)*	1.07 (0.97-1.18)
	The Hague	6,48	1.09 (1.04-1.15)*	0.98 (0.94-1.03)	2,32	0.93 (0.86-1.01)	0.86 (0.80-0.93)*	7,90	1.37 (1.31-1.43)*	1.09 (1.04-1.14)*	1,39	1.21 (1.09-1.33)*	1.00 (0.90-1.11)
	Utrecht	5,46	0.91 (0.86-0.97)*	0.81 (0.77-0.87)*	1,99	0.80 (0.72-0.88)*	0.74 (0.67-0.82)*	5,59	0.95 (0.89-1.00)	0.81 (0.76-0.86)*	1,14	1.01 (0.89-1.15)	0.86 (0.76-0.99)*
	rest NL- C4	5,96	1	1	2,49	1	1	5,89	1	1	1,13	1	1
Ethnicity	Dutch	5,98	1	1	2,42	1	1	5,68	1	1	1,11	1	1
	other European	5,31	0.88 (0.83-0.94)*	0.85 (0.80-0.90)*	2,31	0.95 (0.87-1.04)	0.97 (0.89-1.06)	6,04	1.07 (1.01-1.13)*	1.01 (0.95-1.07)	1,15	1.03 (0.91-1.17)	0.98 (0.86-1.11)
	Non-Western	6,32	1.06 (1.04-1.09)*	1.03 (1.01-1.06)*	2,59	1.07 (1.04-1.11)*	1.12 (1.08-1.17)*	8,29	1.50 (1.47-1.53)*	1.33 (1.29-1.36)*	1,53	1.38 (1.31-1.45)*	1.31 (1.24-1.38)*
SES	<p20 (low SES)	6,75	1.17 (1.14-1.19)*	1.11 (1.09-1.14)*	2,46	1.01 (0.97-1.04)	1.01 (0.97-1.06)	8,02	1.46 (1.43-1.49)*	1.28 (1.25-1.31)*	1,46	1.32 (1.26-1.38)*	1.15 (1.09-1.21)*
	>p20 (mid high SES)	5,84	1	1	2,44	1	1	5,63	1	1	1,11	1	1
Age	<20	8,88	1.56 (1.47-1.65)*	1.20 (1.13-1.27)*	2,67	1.14 (1.03-1.26)*	1.05 (0.95-1.16)	8,74	1.59 (1.50-1.68)*	1.31 (1.24-1.39)*	1,60	1.45 (1.27-1.66)*	1.05 (0.92-1.20)
	20-24	6,86	1.18 (1.15-1.21)*	1.01 (0.98-1.03)	2,57	1.10 (1.05-1.15)*	1.04 (1.00-1.09)	7,76	1.40 (1.36-1.43)*	1.21 (1.18-1.24)*	1,42	1.29 (1.21-1.37)*	1.04 (0.98-1.11)
	25-34	5,88	1	1	2,35	1	1	5,68	1	1	1,11	1	1
	35-39	5,63	0.96 (0.93-0.98)*	1.07 (1.04-1.10)*	2,58	1.10 (1.06-1.14)*	1.14 (1.10-1.18)*	6,27	1.11 (1.09-1.14)*	1.16 (1.13-1.18)*	1,20	1.08 (1.03-1.14)*	1.21 (1.14-1.27)*
	40+	6,91	1.19 (1.13-1.25)*	1.32 (1.25-1.39)*	3,30	1.42 (1.32-1.53)*	1.46 (1.35-1.57)*	7,88	1.42 (1.35-1.49)*	1.43 (1.36-1.51)*	1,67	1.51 (1.36-1.68)*	1.64 (1.47-1.82)*
Parity	Nulliparae	7,77	1.84 (1.81-1.88)*	1.84 (1.80-1.88)*	2,62	1.18 (1.14-1.21)*	1.19 (1.16-1.23)*	6,40	1.09 (1.07-1.11)*	1.07 (1.05-1.09)*	1,48	1.64 (1.57-1.72)*	1.66 (1.58-1.73)*
	par 1	4,37	1	1	2,23	1	1	5,90	1	1	0,90	1	1
	par 2+	4,86	1.12 (1.09-1.15)*	1.08 (1.05-1.11)*	2,43	1.09 (1.05-1.13)*	1.04 (1.00-1.08)	5,79	0.98 (0.96-1.01)	1.07 (1.05-1.09)*	0,98	1.08 (1.02-1.15)*	0.98 (0.92-1.05)
Medical co-mor bidity	No	5,91	1	1	2,40	1	1	6,06	1	1	1,16	1	1
	Yes	10,58	1.89 (1.80-1.97)*	1.84 (1.76-1.93)*	4,19	1.78 (1.66-1.91)*	1.76 (1.64-1.88)*	8,15	1.38 (1.31-1.45)*	1.34 (1.28-1.42)*	2,03	1.77 (1.60-1.95)*	1.71 (1.55-1.89)*
Gynecological comorbidity and pregnancy comp li-cation	No	6,00	1	1	2,44	1	1	6,10	1	1	1,18	1	1
	Yes	10,80	1.90 (1.69-2.13)*	1.64 (1.46-1.86)*	3,74	1.55 (1.28-1.88)*	1.39 (1.15-1.69)*	7,30	1.21 (1.05-1.39)*	1.09 (0.95-1.26)	1,91	1.63 (1.25-2.13)*	1.34 (1.02-1.75)*
ART	No	6,00	1	1	2,44	1	1	6,10	1	1	1,18	1	1
	Yes	9,90	1.72 (1.54-1.92)*	1.34 (1.20-1.50)*	3,49	1.45 (1.21-1.73)*	1.23 (1.03-1.48)*	7,88	1.32 (1.17-1.49)*	1.23 (1.09-1.39)*	1,90	1.63 (1.27-2.08)*	1.29 (1.01-1.66)*

*** = P<0,05**

Discussion

Despite the fact that the Netherlands belong to the twenty most prosperous countries in the world with a recognized egalitarian financial and medical system, this study demonstrates unexpected large perinatal health inequalities according to place of living – in particular deprived neighborhoods – as well as ethnicity and socioeconomic class [30–32]. We are not aware of similar studies which report both the full scale of perinatal outcomes, while separating the role of ethnicity, socioeconomic class, and living environment.

These inequalities add up to an already high national level of adverse perinatal outcomes, in particular perinatal mortality [19]. The observed levels of perinatal outcomes for some subpopulations come close to outcomes reported for countries regarded as poor and underdeveloped [33].

The excess risk for perinatal mortality in a deprived neighborhood is 21%, mainly through foetal mortality. The excess risk for other adverse perinatal outcomes like preterm birth and foetal growth restriction is about 10%. Non-Western-ethnicity and socioeconomic disadvantage mainly act through SGA and low Apgar (order of magnitude 30% excess risk), less through preterm birth and congenital abnormalities.

The analysis consistently showed independent effects of three major social determinants ethnicity, socioeconomic status and DN. The role of ethnicity on perinatal mortality, SGA, and preterm births has been reported before [11,12,34], as has been the role of socioeconomic background [7,8]. Limited number of studies, however, adjusted simultaneously for ethnicity and socioeconomic background; partial adjustment exaggerates the effect of other, related, variables [35,36]. We believe our strategy to adjust for all measured social variables, rather than a subset, explains that the odds ratio's for the separate social variables in this paper appear smaller than those reported before. Little evidence exists on the epidemiology of the Apgar score. In our data, a low Apgar coincided with one or more of the other adverse outcomes in about 65% of cases; these cases accounted for 95% of perinatal mortality in case of a low Apgar. Inequalities here too are substantial.

Our findings confirm observations among adults on strong social and geographical gradients for a wide range of health outcomes including mortality and morbidity [4,37]. That the mortality excess doubles the morbidity excess may be explained by two pathways. Patient risk factors underlying morbidity additionally affect prognosis, and also the prevalence of adverse care factors (primarily influencing mortality) may parallel the prevalence of adverse patient factors. Further analysis of what is behind 'deprived neighborhood' or 'large city' is required to enable improvement. At least three, nonmutually exclusive pathways, exist. First the accumulation of risks at the individual level [38,39]. Second, the provision of suboptimal care either through decreased access or lower performance, which may easily result from the high demands. Third, an aggregate stressor effect of living in a deprived area, as earlier shown in explaining small area variations in acute psychiatric disease [40]. The latter pathway consists of a negative effect of physical and social conditions, and lack of access to neighborhood resources [41,42]. Living in a DN implies being exposed to urban environmental stressors and risk factors (e.g. crime, noise, physical insecurity, unemployment, pollution [43,44]), which in turn can lead to psychosocial stress – including increased cortisol, altered blood-pressure response and immune system compromise – which finally may increase the risk of premature birth and foetal growth impairment, and subsequent perinatal mortality [45].

This paper suggests that perinatal inequalities primarily are associated with living in a particular neighborhood, rather than living in a city or region [46]. While we adjusted to the extent the registry data permitted including individual ethnicity and zip area socioeconomic class it is still possible that unmeasured individual life style, education and income differences exist, which explain part of the DN effect.

The differential effect of deprived neighborhoods on Western versus non-Western women is remarkable. Potential explanations are a protective effect of segregated neighborhoods, provided are belongs to the dominant ethnic group in that area; another explanation could be selection: only those native Dutch women stay in DN, who are unable to migrate upwards, where non-Western women move away when their socioeconomic status improve.

In large cities the incidence of congenital malformations is surprisingly low. This effect might be explained by 'healthy foetal survivor' effect. The great majority of foetal loss due to congenital anomalies occurs before the 22nd week, the lower gestational age range of foetal mortality according to WHO/FIGO definitions. The increased prevalence of risk factors in the greater cities and in particular in DN will also be true for a foetus with a congenital anomaly.

The extra burden of risk factors may accelerate early mortality in case of congenital anomalies which are severe yet not universally lethal. By such hypothetical mechanism the population miscarriage rate may increase, but the prevalence of congenital anomalies among those surviving 22 weeks will be lower.

Limitations and strengths

Although the national perinatal database consists of detailed information on perinatal care and outcome, the coverage of data on behavioral risks is limited. Smoking and alcohol abuse are, for example, insufficiently covered and the preconception use of folic acid is not recorded. However we assume that in the context of our study the individual refined background variables (ethnicity, socioeconomic status, age, parity) and the observed medical- and gynecological comorbidity, pregnancy complications and ART largely cover the lifestyle determinants. Separate indicators of individual educational level and family income of the pregnant women would be preferable to the current combined SES indicator, in particular as a tool to focus improvement in this domain. The place of residence was recorded at the time of delivery; in case women moved during pregnancy misclassification of neighborhood deprivation may have occurred. From detailed analysis of address changes during the perinatal period we know that the great majority of moving women stays within the same deprivation class of living area [47].

As it is difficult to separate the influence of genetic factors from lifestyle factors, and physical from psychosocial environmental factors, we cannot at this stage suggest interventions at the area level. Only detailed cohort studies [48–

50] are able to reveal the dominant pathway through which the deprived neighborhood effect acts on the perinatal outcome.

Conclusions

This is the first national study on the contribution of living in a critically deprived neighborhood to perinatal mortality and morbidity, apart from known effects of ethnicity, socioeconomic class, and standard factors like age and parity. Perinatal inequalities appear impressive in both urban and nonurban areas in the Netherlands, with a significant additive risk of living in a deprived neighborhood. Excess risk for perinatal mortality generally outranges that for morbidity, suggesting both an etiological and prognostic pathway for neighborhood effects. A distinct pattern exists for congenital anomalies, for which early adverse selection effects may be responsible.

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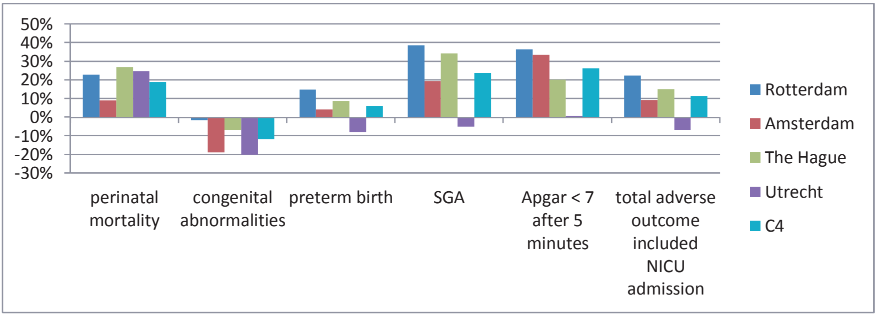
Supplements

Supplement 1. Perinatal outcome per 1000 births, to C4 and ethnic origin (Western (W) en non-Western (NW)).

	Amsterdam			Rotterdam			The Hague			Utrecht			C4 total			Rest of the Netherlands			The Netherlands total		
Adverse perinatal outcome	W	NW	Total	W	NW	Total	W	NW	total	W	NW	total	W	NW	total	W	NW	total	W	NW	total
	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰	‰
Perinatal death	7,7	12,9	10,1	10,4	12,5	11,4	9,8	14,6	11,8	11,1	12,9	11,6	9,5	13,2	11,1	8,8	12,8	9,3	8,9	12,9	9,6
Foetal death (22.0 weeks – 0 day)	5,6	9,7	7,5	7,5	8,6	8,1	7,3	10,6	8,6	7,7	7,2	7,6	6,9	9,3	7,9	6,2	9,2	6,5	6,3	9,2	6,8
Early neonatal death (< 7 days)	2,1	3,3	2,6	2,9	3,9	3,4	2,5	4,1	3,1	3,4	5,8	4,0	2,6	3,9	3,1	2,6	3,6	2,7	2,6	3,7	2,8
Congenital abnormalities	19,4	21,2	20,2	24,5	24,5	24,5	20,5	27,1	23,2	18,8	22,9	19,9	20,7	23,6	21,9	24,6	27,5	24,9	24,2	25,9	24,4
Preterm birth (<37.0 weeks)	58,0	66,9	62,1	68,8	68,0	68,5	62,1	68,6	64,8	56,2	50,4	54,6	61,2	66,0	63,2	59,4	61,2	59,6	59,6	63,2	60,2
Small for Gestational Age (< P_{10})	57,0	85,8	70,4	70,8	93,6	81,6	65,6	97,8	79,0	51,7	66,8	55,9	61,2	88,8	73,0	56,4	78,7	58,9	56,9	82,9	61,1
Apgar score < 7 after 5 minutes	12,8	17,8	15,1	13,1	18,0	15,4	13,6	13,5	13,5	10,5	13,6	11,4	12,6	16,5	14,3	10,9	14,2	11,3	11,1	15,3	11,8

Supplement 2. Adverse perinatal outcomes C4 compared with the rest of the Netherlands, average per year.



Relative differences in adverse perinatal outcomes in pregnant women in the four largest Dutch cities, compared to the rest of the Netherlands. The differences are expressed as a percentage of the national average per outcome (excluded the 4 largest cities).

Chapter 2.2

Regional differences in Dutch maternal mortality

Hanneke de Graaf
Joke Schutte
Jashvant Poeran
Jos van Roosmalen
Gouke Bonsel
Eric Steegers

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Abstract

Objective To study regional differences in maternal mortality in the Netherlands.

Design Confidential inquiry into the causes of maternal mortality.

Setting Nationwide.

Population A total of 3 108 235 live births and 337 maternal deaths.

Methods Data analysis of all maternal deaths in the period 1993–2008.

Main outcome measure Maternal mortality.

Results The overall national maternal mortality ratio was 10.8 per 100 000 live births. In the 12 provinces of the Netherlands, the maternal mortality ratio ranged from 6.2 in Noord Brabant to 16.3 per 100 000 live births in Zeeland. In the four largest cities, maternal mortality varied from 9.3 in Amsterdam to 21.0 in Rotterdam. At a national level, the most frequent direct cause was pre-eclampsia. Increased risks for maternal mortality were found for women living in deprived neighbourhoods (RR 1.41), women from non-Western origin (RR 1.59), and women who were 35 years or older (RR 1.61).

Conclusion There are significant variations in maternal mortality ratios in the Netherlands between cities, provinces, and neighbourhoods. In addition, higher maternal mortality was observed in women of non-Western origin and in women who were 35 years of age or older.

Introduction

Maternal mortality is a principal indicator of maternal health, and a sensitive indicator for both social disparities and substandard care [1]. Among human development indicators, maternal mortality shows the most pertinent inequalities between resource-rich and resource-poor countries, but also between the rich and the poor within countries. The maternal mortality ratio (MMR) is commonly defined as the number of maternal deaths during a given period of time per 100 000 live births in the same period of time [2]. According to recent reports, the mean MMR is 6.3 in Europe, [3] 11.0 in the USA, [4,5] and 498.0 in Africa [2].

Maternal health is influenced by many factors, including age, education, cultural norms, gender issues, obstetric care, and protective regulations from governments and employers [6–8].

Recent studies showed poor outcomes in deprived neighbourhoods for perinatal health and mortality [9–13]. It has been suggested that this may also be the case for maternal morbidity [12,13]. Consequently, we investigated the influence of the place of residence on maternal mortality in the Netherlands during the period 1993–2008.

Methods

Maternal mortality

This study investigates cases of maternal deaths as registered in the database of the Dutch Maternal Mortality Committee (MMC) in the period 1993–2008. The cases are reported by obstetricians, midwives, and general practitioners, using standard forms.

The level of adherence to and compliance with this reporting system is high. In order to avoid any missing cases, the database is cross-checked and complemented with data from Statistics Netherlands.

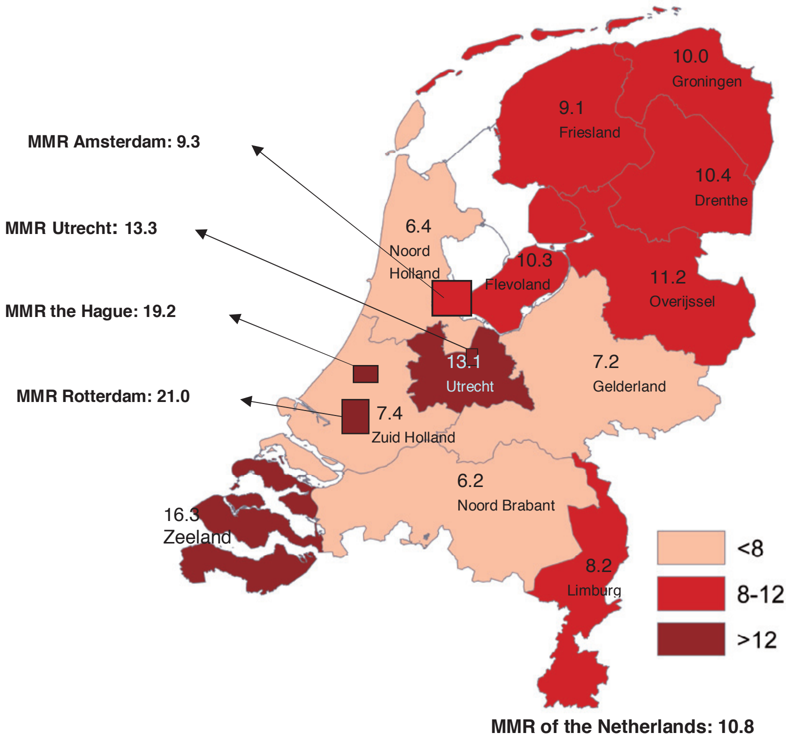
The MMC consists of eight obstetricians and one internist working in the field of maternal medicine. The Dutch Society of Obstetrics and Gynaecology is responsible for the appointment and supervision of the MMC [6].

Maternal death is defined and classified according to the World Health Organization's International Classification of Diseases [14], 10th revision (ICD-10). The MMR is defined as the number of direct and indirect maternal deaths per 100 000 live births up to 42 days after the termination of pregnancy [6]. Direct maternal death is the result of a complication of the pregnancy or delivery, or management thereof. Indirect maternal death is caused by pre-existing disease or morbidity that developed or deteriorated during pregnancy [15]. Late maternal death is defined as the sum of direct and indirect mortality, occurring between 42 and 365 days after pregnancy. Regions, cities, and deprived neighbourhoods in the Netherlands.

The Netherlands comprises 12 provinces (Figure 1) that represent legal administrative units sitting between municipalities and the national government. Regional differences in MMR were analysed according to province, the four largest cities

(C4), and deprived neighbourhoods (DNs). Previous studies have used postal codes and have confirmed their utility in birth outcome research [16–19]. Likewise, our study was also based on postal-code areas.

Figure 1. Maternal mortality ratio (MMR) in the provinces and four largest cities of the Netherlands.



In 2007, the Dutch government designated 40 neighbourhoods as DNs: 20 of these were in the four largest cities of the Netherlands and the remainder were scattered over 14 smaller cities across the country [20]. These neighbourhoods were characterised by high rates of unemployment, crime, insecurity, and poor housing. Designation as a DN was based on the number of these determinants associated with the geographical area [21].

Maternal characteristics

Maternal characteristics were categorised by age (<35 or ≥35 years), parity (0 and ≥1), and ethnicity. Ethnicity was defined by the care provider. In this study, we differentiated between Western (native Dutch and other Westerners) and non-Western (including different ethnic groups) women.

Statistical analysis

The frequency and relative risk (RR) of MMR were analysed according to region, cause of death, ethnicity, age, and parity. A chi-squared test was used for statistical analysis.

Results

In the study period of 1993–2008, a total of 3 108 235 live births and 337 maternal deaths were registered (MMR 10.8). Twenty percent of these cases occurred in the four largest cities (C4), whereas they account for 14% of births. When excluding the C4, the remaining MMR was 8.4. The difference between the MMR of the C4 (15.2) and the rest of the country is statistically significant ($P < 0.02$) (Table 1). No other significant differences in the MMR in Table 1 were observed.

Table 1 Characteristics of the 4 largest cities (C4) compared with the rest of The Netherlands (NL) 1993-2008.

Characteristics	NL total	C4		Rest of NL (= excl. C4)		Postal code unknown	
	N	N	% of NL total	N	% of NL total	N	% of NL total
Live Births total[1]	3,108,235	434,870	14%	2,673,359	86%	NA	NA
MMR	**10.8**	**15.2**		**8.4**		**NA**	
Pre-eclampsia/ Hypertension	92	18	20%	62	67%	12	13%
Thrombo-embolism	56	9	16%	39	70%	8	14%
Other Direct	79	15	19%	55	70%	9	11%
Indirect	110	24	22%	68	62%	18	16%
MM non-Western	87	40	46%	36	41%	11	13%
MM DN	29	26	90%	3	10%	NA	NA
MM age ≥ 35 year	99	22	22%	62	63%	15	15%

NA, not applicable.

[1]Source: Statistics Netherlands (CBS), available online at: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37259ned&D1=1,27&D2=0&D3=0-16&D4=20,33-48&HDR=T&STB=G2,G1,G3 &VW=T.

Table 2 Comparison of the causes of maternal mortality and MMRs in the four largest cities in the Netherlands

Characteristics	Amsterdam		Rotterdam		The Hague		Utrecht	
	N	% of C4	N	% of C4	N	% of C4	N	% of C4
Live Births total*	162,245	37%	118,845	27%	93,821	22%	59,959	14%
MM total	15	23%	25	38%	18	27%	8	12%
MMR	**9.3**		**21.0**		**19.2**		**13.3**	
Pre-eclampsia/ Hypertension	2	11%	9	50%	6	33%	1	6%
Thrombo-embolism	1	11%	3	33%	3	33%	2	22%
Other Direct	4	27%	4	27%	4	27%	3	20%
Indirect	8	33%	9	38%	5	21%	2	8%
MM non-Western	8	20%	16	40%	13	33%	3	8%
MM DN	5	19%	12	46%	7	27%	2	8%
MM ≥35 year	7	32%	7	32%	6	27%	2	9%

C4, the four largest Dutch cities (Amsterdam, Rotterdam, The Hague, Utrecht); MM, maternal mortality; DN, Deprived Neighbourhood

*Source: Statistics Netherlands (CBS), available online at: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37259ned&D1=1,27&D2=0&D3=0-16&D4=20,33-48&HDR=T&STB=G2,G1,G3&VW=T.

The highest MMR was seen in Rotterdam (21.0) and The Hague (19.2) (Table 2). The MMRs in these two cities were significantly higher compared with the MMR in the Netherlands once the C4 are excluded, as shown in Table 1 ($P < 0.001$). No other significant differences in relation to the MMRs listed in Table 2 were found.

Figure 1 presents the MMRs for the 12 provinces. Notably, the highest MMR occurred in the province of Zeeland (16.3). Compared with the national MMR excluding the C4, the high MMR in Zeeland was significant ($P < 0.05$). The MMR for the remaining provinces varied from 6.2 to 13.1. None of these ratios differed significantly from the national MMR.

Pre-eclampsia/hypertension is the most frequent direct cause of death (Table 1). Its related MMR of 3.0 is higher compared with other European countries (Table 3). Pre-eclampsia/hypertension-related maternal mortality appeared to be higher in women living in deprived neighbourhoods and in non-Western women, compared with women living in non-deprived neighbourhoods and Western women, respectively (Table 4).

Table 3 A comparison of direct, indirect and total MMR between the Netherlands and a selection of European countries

Causes of death	The Netherlands 1993-2008			United Kingdom 1994-2008 [42]	Denmark 2002-2006 [43]	Bavaria, Germany 1995- 2000 [44]	France 2001-2006 [45]
	non-DN	DN	total	total	total	total	total
All maternal deaths	**10.5**	**15.6**	**10.8**	**12.4**	**11.0**	**9.9**	**9.6**
Direct deaths	**7.1**	**10.7**	**7.3**	**5.5**	**5.4**	**4.0**	**6.9**
Pre-eclampsia/ Hypertension	2.6	8.6	3.0	0.8	0.5	1.2	1.0
Thrombo-embolism	1.9	0.5	1.8	1.6	2.6	1.2	1.0
Other Direct	2.6	1.6	2.5	NA	2.3	1.5	5.0
Indirect deaths	**3.5**	**4.8**	**3.5**	**6.9**	**5.6**	**5.9**	**2.7**
Cardiovascular	1.8	2.7	1.9	2.0	2.1	2.2	0.6
Neurological	0.8	2.1	0.8	1.8	0.5	0.9	1.0
Psychiatric	0.3	0	0.3	0.7	0.6	0.9	NA
Infectious	0.2	0	0.2	NA	0.4	NA	NA
Endocrine, metabolic and immune	0.1	0	0.1	NA	NA	NA	0.2
Malignant	0.1	0	0.1	0.3	0.4	0.6	0.2
Other indirect	0.2	0	0.2	2.1	1.6	1.2	0.7

DN, Deprived Neighbourhood, NA, not applicable

Table 4 Relative risk of maternal mortality by age, nulliparity, deprived neighbourhood (DN) and non-Western ethnicity

	Age ≥35 (vs <35)				Nulliparity (vs multiparity)				Deprived Neighbourhood (vs non-DN)				non-Western (vs Western)			
	N	RR	(95% CI)	p-value	N	RR	(95% CI)	p-value	N	RR	(95% CI)	p-value	N	RR	(95% CI)	p-value
Total deaths	**99**	**1.61**	**1.28-2.01**	**< 0.001**	**172**	**0.97**	**0.80-1.16**	**NS**	**29**	**1.41**	**0.97-2.06**	**NS**	**87**	**1.59**	**1.26-2.02**	**< 0.001**
Pre-eclampsia/ hypertension	23	1.37	0.87-2.16	NS	52	1.07	0.76-1.50	NS	16	2.85	1.68-4.85	< 0.001	31	2.08	1.38-3.12	< 0.001
Thrombo-embolism	18	1.76	1.03-2.99	< 0.01	25	0.84	0.53-1.35	NS	1	0.29	0.04-2.11	NS	11	1.21	0.64-2.31	NS
Other Direct	22	1.52	0.95-2.44	NS	39	0.93	0.64-1.37	NS	3	0.62	0.20-1.97	NS	23	1.80	1.13-2.86	< 0.01
Indirect	36	1.79	1.23-2.61	< 0.001	56	0.96	0.70-1.33	NS	9	1.34	0.68-2.65	NS	22	1.23	0.78-1.95	NS

NS, not significant, P is calculated using the chi-squared test.

Table 5. Relative Risk of maternal mortality in the 4 largest cities compared to the rest of The Netherlands

	Amsterdam				Rotterdam				The Hague				Utrecht			
	N	RR	(95% CI)	p-value	N	RR	(95% CI)	p-value	N	RR	(95% CI)	p-value	N	RR	(95% CI)	p-value
Total deaths	**15**	**1.10**	**0.65-1.86**	**NS**	**25**	**2.51**	**1.66-3.80**	< 0.001	**18**	**2.29**	**1.42-3.70**	< 0.001	**8**	**1.59**	**0.79-3.22**	**NS**
Pre-eclampsia/ Hypertension	2	0.53	0.13-2.17	NS	9	3.27	1.62-6.57	< 0.001	6	2.76	1.19-6.37	< 0.01	1	0.72	0.10-5.19	NS

NS, not significant. P is calculated using the chi-squared test.

Twenty-nine of the deceased women lived in deprived neighbourhoods. Twenty-six (90%) of them resided in the C4 (Table 1). Table 2 shows their distribution in the C4: almost half of them (46%) lived in the city of Rotterdam. The MMR for the DN group was 15.6 compared with 10.5 in the non-DN group (Table 3). The mean of the MMRs in the DN groups were 18.2 in the C4 and 6.8 in the rest of the Netherlands, respectively. Eighty-seven (26%) of the women who died were of non-Western origin (Table 1). The total maternal mortality was significantly higher in non-Western women compared with Western women (Table 4). Ninety-nine (29%) deceased women were 35 years or older (Table 1). The total maternal mortality in those women was higher compared with younger women (Table 4). Indirect causes of maternal death were also more frequent amongst the older women. Table 5 shows that total maternal mortality as well as maternal mortality caused by pre-eclampsia/hypertension was significantly increased in Rotterdam and the Hague, when compared with the rest of the Netherlands, excluding the C4.

Discussion

Despite the fact that the Netherlands is one of the 20 most prosperous countries in the world [22], with a free and universally accessible prenatal care system, the maternal mortality ratio has increased in the last two decades [6]. In this study, we analysed regional differences in maternal mortality in the C4, the 12 provinces, and in 40 DNs. Our study showed large regional differences. The C4 show a higher MMR compared with the rest of the Netherlands. For Rotterdam and the Hague, the differences were highly significant. This could be because urbanisation is associated with an increase in environmental health risks, risk behaviour, stress, and low socio-economic status [12,23–25].

Of the 12 provinces, Zeeland showed the highest MMR, which is significantly different from the rest of the Netherlands. Possible reasons for this poor outcome can be derived from Statistics Netherlands [26]: the frequency of hypertension in Zeeland is the highest in the country; there are fewer hospitals for the area and the travel times are long, which have been shown to be important risk factors [6,19]; and socio-economic status and lifestyle in the region are below the average standards. In addition, self-score questionnaires demonstrate that the inhabitants of Zeeland rate their health condition as the lowest in the country.

The high MMRs in DNs could be explained by an accumulation of heterogeneous risk factors present within these neighbourhoods [9,19,20], for example a lack of health insurance, low income, poor education, irregular consultation, and stress [27–30].

The MMR of non-Western women is also high, and this excess risk has been reported in several European studies [31–33]. The common denominator is low socio-economic status. However, in the Netherlands 75% of non-Western pregnant women do not live in deprived neighbourhoods [34]. A lack of proficiency in Dutch and therefore an inability to access adequate antenatal care is a more plausible explanation. This can result in late antenatal care [35], insufficient understanding of warning symptoms [6,36], inadequate diagnosis, and poor compliance with the advice of the midwife or doctor [36–38].

In this study, women aged 35 years or older were also at increased risk of maternal mortality, probably because of a deterioration of pre-existing disease. A growing number of women aged ≥35 years embark on a pregnancy, despite pre-existing medical problems.

The maternal mortality ratio (MMR) related to pre-eclampsia/hypertension in the Netherlands is higher than in other European countries (Table 3). Substandard care, both in community and hospital care, has previously been shown to be involved [36].

In 2005, the Dutch Society of Obstetrics and Gynaecology (DSOG) implemented the revised Guideline Hypertensive Disease in Pregnancy [39,40]. Since 2005, a total of eight regional audits were organised to evaluate adherence to these guidelines and compliance with its protocols. It appeared that common practice was inadequate. Consequently, the DSOG strongly advised an improvement and adherence to the guidelines in general and hospital practices. In addition, adequate prophylaxis of eclamptic seizures should be enhanced [41]. In general, well-organised programmes for education and information should be initiated, particularly for women with a low socio-economic status and of non-Western origin.

In conclusion, marked differences in maternal mortality are observed between cities, provinces and neighbourhoods in The Netherlands. Furthermore, higher maternal mortality was observed in women of non-Western origin and for women aged ≥35 years. This should be taken into account in current discussions on the quality of obstetric care.

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Chapter 2.3

Substantial regional differences in Dutch severe maternal morbidity

Hanneke de Graaf
Joost Zwart
Jos van Roosmalen
Gouke Bonsel
Eric Steegers

Submitted for publication

Abstract

Objective: To examine regional variation in Severe Acute Maternal Morbidity (SAMM) and case fatality in the Netherlands.

Design: Prospective population-based cohort study.

Setting: Nationwide.

Population: 346,469 live births and 2,545 SAMM cases.

Methods: Data analysis of all SAMM cases in the period 2004 - 2006.

Main outcome measure: SAMM (uterine rupture, eclampsia, major obstetric haemorrhage, miscellaneous cases and cases necessitating ICU admission) and case fatality rate.

Results: The overall national SAMM incidence was 7.4 per 1 000 live births. At the level of the 12 provinces, SAMM incidence ranged from 2.9 in Drenthe to 11.1 in Flevoland. In the four large cities (C4), SAMM incidence varied from 7.2 in Utrecht to 11.8 in The Hague.
Compared with the Netherlands excluding the four large cities (NL excluding C4), significantly increased risks for SAMM were found for the provinces of Flevoland (RR: 1.58 (1.30-1.92)), Zeeland (RR: 1.53 (1.20-1.94)), Noord Holland (RR: 1.23 (1.09-1.38)), Zuid Holland (RR: 1.20 (1.08-1.33)) and the C4 (RR: 1.29 (1.17-1.42)). Increased risks for SAMM were found for women from non-Western origin in NL excluding C4 (RR: 1.52 (1.35-1.71), as compared to Western women in NL excluding C4). Neither in the C4 nor in the remainder of the Netherlands significant differences were found between deprived neighbourhoods (DN) and non DN (table 2). The overall case fatality rate was 1.9%, ranging from 0 in Groningen and Limburg to 7.1% in Drenthe.

Conclusions: In the Netherlands, there are significant variations in SAMM rates between cities, provinces and ethnicity.

Introduction

Maternal mortality for long has been used as an indicator of quality of obstetric care and as yardstick for women's health after delivery. In high resource countries, two disadvantages are associated with this indicator. First, the prevalence of maternal mortality is very low [1], limiting its utility as monitor. Second, maternal mortality can be decomposed into morbidity prevalence and case fatality rate (CFR) from that morbidity, each with its own set of determinants.

Recent study showed considerable geographical variation in maternal mortality [2]. This was partially explained by patient-related determinants of morbidity (like age, parity, and pre-existing unhealthy lifestyle and disease). Variation was further explained by care-related factors (like difference in hospital density and effective management of (pre-)eclampsia). These factors which are primarily associated with CFR once morbidity is present. Such variations suggest important opportunities to reduce maternal mortality, which not only benefit outcome on short term but also prevents long-term sequelae [3].

In the present study we investigate regional variations in severe acute maternal morbidity (SAMM) [4] from CFR. In particular we focus on the potential role of living in a deprived area, as living here may represent both a higher risk exposure to morbidity and reduced access to health care facilities.

Methods

<u>Maternal morbidity</u>

All cases of SAMM in the Netherlands in the period 1 August 2004 to 1 august 2006 were prospectively collected in a large nationwide cohort study, the LEMMoN study [5]. The LEMMoN study was centrally approved by the medical ethics committee of Leiden University Medical Centre. All cases were centrally reported by local coordinators, using a standardised web-based form. Detailed methods of data collection were described previously [5].

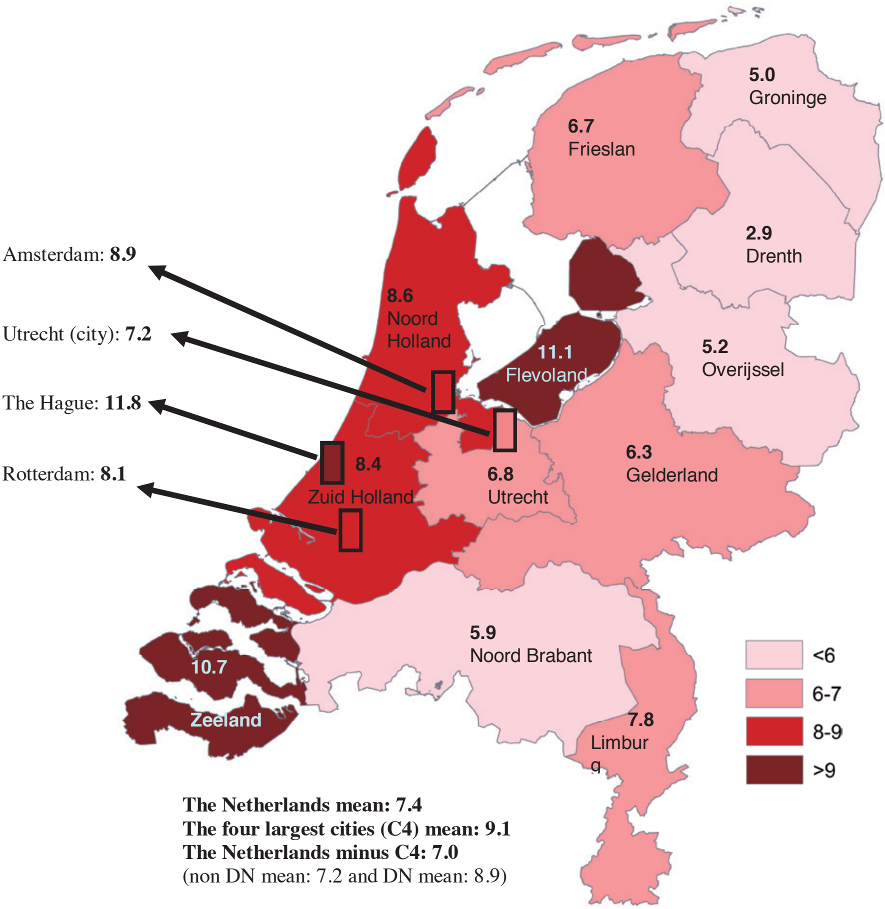
The subdivision of cases qualifying for SAMM were 1) uterine rupture, 2) eclampsia, 3) Major Obstetric Haemorrhage (MOH), with transfusion need of 4 or more units of packed cells or embolisation or hysterectomy for MOH, 4) miscellaneous (e.g. acute fatty liver of pregnancy, pulmonary embolism) as well as severe manifestations of generally less severe conditions (e.g. severe early pre-eclampsia) including all cases necessitating ICU admission.

Case fatality rate of SAMM (or any of its contributing conditions) was conventionally defined as the number of SAMM (or condition-specific) deaths divided by the total number of SAMM (or condition-specific) cases.

Regions, cities and deprived neighbourhoods in the Netherlands

The Netherlands consist of 12 provinces (Figure 1), which represent legal administrative units in-between municipalities and the national government. Regional differences in SAMM were analysed according to province, the four large cities (C4), and deprived neighbourhoods (DN).

Figure 1. SAMM Ratio by provinces and the 4 largest cities of the Netherlands (2004-2006), expressed in number of SAMM per 1 000 births.



In 2007, the Dutch government designated 40 neighbourhoods as “deprived neighbourhoods” of national importance; 20 of these where in the four large cities of the Netherlands and the remainder were scattered over

14 smaller cities in the country [6]. Neighbourhoods are the smallest administrative units in Dutch cities comprising of ≤ 5 postal code areas. The deprived neighbourhoods are characterised by high rates of unemployment, crime, insecurity and poor housing. DN-assignment was by the department of Internal Affairs, and based on the weighted quantification of these determinants; DN-assignment was unrelated to population health considerations [7]. Postal codes were used to determine place of residence and DN-assignment. These codes were retrieved from those hospital registries where the women were admitted for the first time. Four percent of the postal codes were missing. Previous studies have used postal codes and confirmed their utility in birth outcome research [2,8-12].

Maternal characteristics

Maternal characteristics were categorised by age, parity and ethnicity. Age: <20, 20-34, and ≥35 years. Parity: 0, 1- 4 and ≥4. Ethnicity was defined by the care provider based on geographical ethnic origin of the woman and her parents. In this study, we differentiated between Western (native Dutch and other Western) and non-Western (including different ethnic groups) women.

Other data sources

Denominator data regarding the number of live births of the non-Western women, the provinces, cities and deprived neighbourhoods, during the study period were obtained from the Netherlands Perinatal Registry, a linked professional database of all 20-weeks and above pregnancies in the Netherlands, collected from (referring) midwives, obstetricians and paediatricians [13,14]. All these registries are legally enforced and have close to 100% coverage.

The choice for using delivery data from the Netherlands Perinatal Registry rather than birth certificate data from CBS [5] to estimate the province denominators was by intent. In some outer regions part of the Dutch pregnant women give birth in the adjacent country (Germany at the East-border and Flanders-Belgium at the South-West border). Using civil administration data would overestimate the denominator. Asylum seekers and women which have no legal status are geographically concentrated and are unknown to the civil administration. Here, using civil data would underestimate the denominator. As data from the Netherlands Perinatal Registry and severe morbidity data both were collected through the same obstetrical caregiver, risk for a biased ratio is minimized.

Statistical analysis

Primary analysis addresses geographically defined risks. The prevalence of SAMM is expressed as the number of cases per thousand live births. Relative risks (RR) with 95% CI of SAMM in the provinces or in the four large cities (C4) were calculated taking the SAMM prevalence of the Netherlands excluding the C4 as reference. RRs of (1) being from Non-Western descent, and (2) of living in a deprived neighbourhood (DN) were calculated taking being from Western descent or living in a non-DN in the C4 or NL excluding the C4, as reference.

Results

In the study period 1 August 2004 to 1 August 2006, a total of 346,469 live births and 2552 SAMM cases were recorded in the database [5]. Seven cases were excluded, because these women had been living outside the Netherlands during their pregnancy.

Residing in Flevoland and Zeeland is associated with a significantly increased risk of SAMM as compared with the Netherlands excluding the four large cities (NL excluding C4) (respectively RR: 1.58 (1.30-1.92) and RR 1.53 (1.20-1.94)) (fig. 1 and table 1). These two provinces showed a significantly increased underlying risk for MOH (respectively RR: 1.56 (1.22-2.01) and RR: 1.53 (1.13-2.08)) table 1).

Prevalence of SAMM in the four largest cities (C4) was 9.1 per 1 000 live births, in the remainder of the Netherlands 7.0 per 1 000 live births, resulting in a national average of 7.4 per 1 000 live births.

Thirty-three percent of all women with SAMM had been admitted to the ICU. Women with SAMM living in the provinces of Drenthe and Gelderland showed a significant higher incidence of ICU admission.

Forty-eight maternal deaths were reported to the Audit Committee of Maternal Death of the Netherlands Society of Obstetrics & Gynaecology during the study period, giving an overall case fatality rate of 1:53 (1.9%). Living in the provinces of Drenthe and Utrecht was associated with increased case fatality rates.

The SAMM prevalence for the DN varied from 8.1 to 9.1 and the non-DN from 7.0 to 9.0. Neither in the C4 nor in the remainder of the Netherlands significant differences were found between DN and non DN (table 2).

Table 1 Prevalence & Relative Risk (RR) of severe maternal morbidity (SAMM) and the case fatality by province/ 4 large cities in the Netherlands, (RR by comparison the SAMM or case fatality of the region to the Netherlands minus the four large cities (NL- C4).

	Groningen	Friesland	Drenthe	Overijssel	Flevoland	Gelderland	Utrecht-C4	Noord Holland-C4	Zuid Holland-C4	Zeeland	Noord Brabant	Limburg	NL - C4	C4	NL Total
Total live births *n*	10699	12231	9520	26005	9464	42413	20620	37884	48705	6331	49190	18889	291951	54518	346469
Overall SAMM															
Total SAMM* *n*	53	82	28	134	105	266	141	327	409	68	290	148	2051	494	2545
Prevalence SAMM	5.0 ‰	6.7 ‰	2.9 ‰	5.2 ‰	11.1 ‰	6.3 ‰	6.8 ‰	8.6 ‰	8.4 ‰	10.7 ‰	5.9 ‰	7.8 ‰	7.0 ‰	9.1 ‰	7.4 ‰
RR SAMM	0.71 (0.54-0.93)	0.95 (0.77-1.19)	0.42 (0.29-0.61)	0.73 (0.62-0.73)	1.58 (1.30-1.92)	0.89 (0.79-1.01)	0.97 (0.82-1.15)	1.23 (1.09-1.38)	1.20 (1.08-1.33)	1.53 (1.20-1.94)	0.84 (0.74-0.95)	1.12 (0.95-1.32)	ref	1.29 (1.17-1.42)	-
Separate SAMM conditions															
prevalence MOH**	35 (3.3‰)	34 (2.8‰)	16 (1.7‰)	84 (3.2‰)	64 (6.8‰)	184 (4.3‰)	92 (4.5‰)	199 (5.3‰)	250 (5.1‰)	42 (6.6‰)	170 (3.5‰)	92 (4.9‰)	1262 (4.3‰)	338 (6.2‰)	1600 (4.6‰)
RR MOH***	0.76 (0.54-1.06)	0.64 (0.46-0.90)	0.39 (0.24-0.64)	0.75 (0.60-0.93)	1.56 (1.22-2.01)	1.00 (0.86-1.17)	1.03 (0.83-1.27)	1.22 (1.05-1.41)	1.19 (1.04-1.36)	1.53 (1.13-2.08)	0.80 (0.68-0.94)	1.13 (0.91-1.39)	ref	1.43 (1.27-1.63)	-
Prevalence Eclampsia	8 (0.8‰)	11 (0,9‰)	2 (0,2‰)	22 (0,9‰)	10 (1,1‰)	26 (0,6‰)	9 (0,4‰)	23 (0,6‰)	41 (0,8‰)	8 (0,8‰)	38 (0,6‰)	18 (1,0‰)	205 (0,7‰)	35(0,6‰)	240 (0,7‰)
RR Eclampsia***	1.06 (0.53-2.16)	1.28 (0.70-2.35)	0.30 (0.07-1.20)	1.20 (0.78-1.87)	1.50 (0.80-2.84)	0.87 (0.58-1.31)	0.62 (0.32-1.21)	0.87 (0.56-1.33)	1.20 (0.86-1.68)	1.12 (0.46-2.73)	0.87 (0.59-1.27)	1.36 (0.84-2.20)	ref	0.91 (0.64-1.31)	-
Prevalence Uterine rupture	1 (0.1‰)	9 (0.7‰)	3 (0.3‰)	13 (0.5‰)	7 (0.7‰)	21 (0.5‰)	15 (0.7‰)	26 (0.7‰)	31 (0.6‰)	8 (1.3‰)	38 (0.8‰)	18 (1.0‰)	190 (0.7‰)	27 (0.5‰)	217 (0.6‰)
RR Uterine rupture***	0.14 (0.02-1.02)	1.13 (0.58-2.21)	0.48 (0.16-1.51)	0.77 (0.44-1.35)	1.14 (0.54-2.42)	0.76 (0.49-1.19)	1.12 (0.66-1.89)	1.05 (0.70-1.59)	0.98 (0.67-1.43)	1.94 (0.96-3.94)	1.19 (0.84-1.68)	1.46 (0.90-2.37)	ref	0.76 (0.51-1.14)	
Prevalence Miscellaneous	11 (1.0‰)	30 (2.5‰)	8 (0.8‰)	24 (0.9‰)	27 (2.9‰)	44 (1.0‰)	29 (1.4‰)	86 (2.3‰)	97 (2.0‰)	17 (2.7‰)	60 (1.2‰)	24 (1.3‰)	457 (1.6‰)	104 (1.9‰)	561 (1.6‰)
IC admission															
Total IC admission/SAMM	14 (26.4%)	35 (42.7%)	15 (53.6%)	46 (34.3%)	27 (25.7%)	112 (42.1%)	50 (35.5%)	117 (35.8%)	118 (28.9%)	26 (38.2%)	96 (33.1%)	38 (25.7%)	694 (33.8%)	146 (29.6%)	840 (33%)
RR IC admission/SAMM***	0.78 0.50-1.23	1.26 0.98-1.63	1.58 1.12-2.25	1.01 0.80-1.29	0.76 0.55-1.06	1.24 1.07-1.45	1.05 0.83-1.32	1.06 0.90-1.24	0.85 0.72-1.00	1.13 0.83-1.54	0.98 0.82-1.16	0.76 0.57-1.00	ref	0.87 0.75-1.01	
Case fatality															
Maternal mortality *n*	0	2	2	4	2	4	6	7	8	1	5	0	41	7	48
Case fatality rate	0.0%	2.4%	7.1%	3.0%	1.9%	1.5%	4.3%	2.1%	2.0%	1.5%	1.7%	0.0%	2.0%	1.4%	1.9%
RR Case fatality***	0	1.22 (0.30-4.96)	3.57 (0.91-14.1)	1.49 (0.54-4.11)	0.95 (0.23-3.89)	0.75 (0.27-2.08)	2.13 (0.92-4.93)	1.07 (0.49-2.37)	0.98 (0.46-2.07)	0.74 (0.10-5.27)	0.86 (0.34-2.16)	0	ref	0.71 (0.32-1.57)	-

* numbers do not add to total as some women had more than one condition, ** MOH = Major Obstetric Haemorrhage, *** $p < 0.05$

Table 2 Prevalence of severe maternal morbidity (SAM 423 M), ICU admission and the case fatality per (non-)deprived neighbourhood (DN) and (non)Western ethnic background in the 4 large cities (C4) and the rest of the Netherlands (NL)

	Total live births	Prevalence SAMM	RR (95% CI) of SAMM	Prevalence Maternal Mortality	ICU admission / total SAMM
C4 non-DN	37184	336 (9.0‰)	ref	3 (0.9%)	28.0%
C4 DN	17334	158 (9.1‰)	1.01 (0.84-1.22)	4 (2.5%)	32.9%
NL-C4 non-DN	287977	2019 (7.0‰)	ref	40 (2.0%)	33.7%
NL-C4 DN	3974	32 (8.1‰)	1.15 (0.81-1.63)	1 (3.1%)	43.8%
C4 Western	31033	263 (8.5‰)	ref	4 (4.9%)	30.8%
C4 non-Western	23485	231 (9.8‰)	1.16 (0.97-1.38)	3 (4.6%)	28.1%
NL-C4 Western	259836	1727 (6.7‰)	ref	36 (6.3%)	32.8%
NL-C4 non-Western	32115	324 (10.1‰)	1.52 (1.35-1.71)	5 (3.9%)	39.2%

Non-Western women living outside the C4 showed a significantly increased risk for SAMM.

Figure 2 shows minimal variation in the mean age of overall group with SAMM, namely from 30.5 to 32.1 year. The average age of the group SAMM caused by MOH is comparable to that of the total group SAMM. However, in the group of SAMM caused by eclampsia, the mean age varies from 26.8 year in Zeeland to 35 year in Drenthe.

Figure 2 Mean age of women with SAMM (total) and SAMM caused by Eclampsia per region

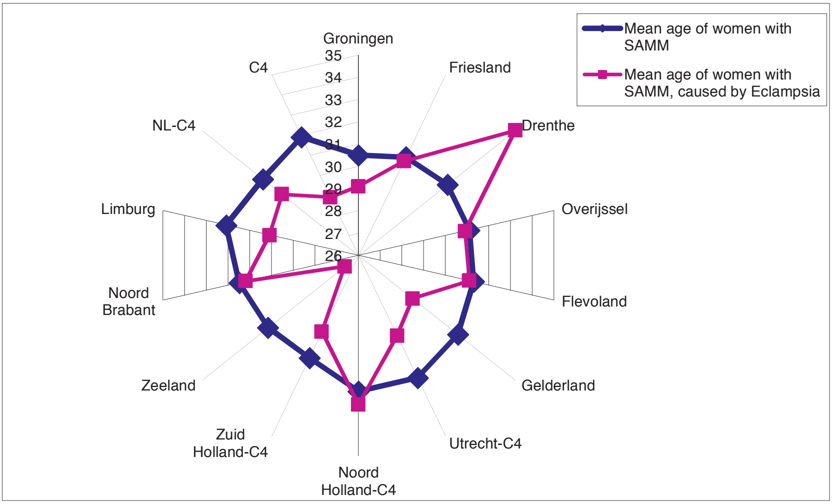
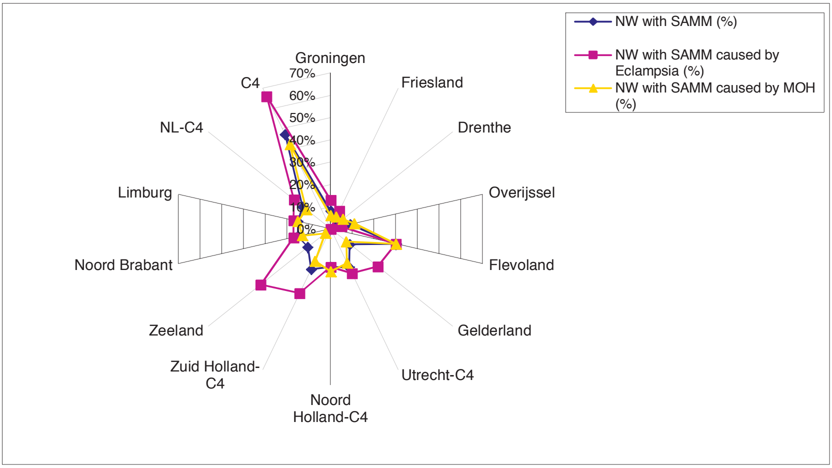


Figure 3 presents the differences in the prevalence per province of the total group of non-Western women with SAMM and the non-Western group with SAMM caused by MOH or eclampsia. The non-Western group of SAMM caused by eclampsia shows the largest variation. The prevalence of other risk factors for the total group of SAMM and the separate groups of SAMM caused by eclampsia or MOH like age and parity also differed per region (data not shown), e.g. in Zeeland more women had parity 4 or higher.

Figure 3 Rate of non-Western (NW) women in the different regions for SAMM (total) and for SAMM caused by Eclampsia or MOH



Discussion

This study demonstrates large differences in SAMM and case fatality rate among the 12 provinces, the four large cities (C4) and the 40 Deprived Neighbourhoods (DN). SAMM differences were most obvious in the group of MOH. Outside the 4 large cities, non-Western women showed considerably increased SAMM levels.

The overall national SAMM prevalence was 7.4 per 1000 live births which is comparable with other European countries, while the maternal mortality ratio in the Netherlands compared to other European countries is high [3]. An earlier European study on SAMM reported a range from 9.5 to 16 cases per 1 000 live births throughout Europe [15]. Others suggested a range from 1.0 to 10.1 per 1000 live births, differences being caused by heterogeneity of inclusion criteria [5,16,17].

Of the 12 provinces, Flevoland and Zeeland showed the highest SAMM prevalences. Patient-related factors are a likely cause [18]. Socio-economic status, education level and starting late with perinatal care, at 18 weeks of gestation [19] in Zeeland and Flevoland are below the Dutch average standards and in Flevoland the number and size of various risk groups (like unemployed, uninsured, crime, homelessness, psychiatric disease) is growing fast [20] as well as the non-Western population [19]. In addition, in both provinces the hospital density is low and travel time to the hospital has increased [11,21].

In our study regional variation in SAMM was dominated by differences in MOH incidence, which indeed was high in Zeeland and Flevoland (more than 50 percent excess risk). Zeeland contains the highest percentage of high parity (>4) women and is known for limited access to facilities, a factor which may also underlie the high prevalence of non-obstetric miscellaneous conditions. The 50 percent extra risk for eclampsia in Flevoland may be caused by overrepresentation of deprived women and in particular teenage pregnancies [22], since teenagers show an increased risk for pregnancy induced hypertension [23-25].

The four large cities (C4) show a significantly higher SAMM prevalence (9.1 per 1000 live births) compared to the remainder of the Netherlands (7 per 1000 live births). The high SAMM prevalence in the C4 may be explained by an accumulation of heterogeneous risk factors [12] present within these large cities including risk lifestyle and nutrition behaviours, sexually transmitted diseases, lack of health insurance, poor income, low education, environment, urban stress factors and irregular antenatal consultation [26-30]. In particular MOH prevalence is increased which may well be explained by patient factors overrepresented in these city areas: teenage pregnancies, elderly women, grande multiparae, non-Western women and women living in DN [22,31-33]. The increased SAMM prevalence among non-indigenous women may well be related to insufficient proficiency of the Dutch language and to unfamiliarity with the Dutch health care system [21,32-36].

Morbidity related to older age has public health implications, because there is a trend toward delayed childbearing in better-educated women [34,37,38].

The national ICU admission rates are difficult to judge as few comparable specific international data are available. The significant higher ICU admission rate in the two provinces may be caused by three mechanisms. First, through a limited anticipatory capacity as the non-tertiary hospitals of those provinces generally have low number of deliveries per year, no 24/7 hour presence of senior gynaecologists, and an extended travelling distance to the most nearby tertiary care. Second, these provinces do not have high care obstetrical units (without assisted ventilation facilities). Third, differences in IC admission between regions may also be caused by different admission criteria of intensive care units in practice [16,39-42].

Case-fatality in general did not parallel SAMM prevalence, pointing to a different background. Small numbers limit the strength of associations. The suggested highest case fatality in the province Drenthe could be related to decreased access to the hospital care [43]. In Drenthe hospital density is low and time of travel to obtain tertiary care is longer. In the larger cities, the case fatality rate is low compared with the remainder of the Netherlands. This may be caused by the presence of perinatal centres and a high hospital density in these cities.

Conclusions

The regional differences in maternal mortality in the Netherlands rest on substantial differences in both SAMM and case fatality from SAMM-conditions. The predominant role of MOH and eclampsia differences suggest that increased professional efforts may be instrumental, through improved adherence to guidelines, through local audits of SAMM, through implementation of multidisciplinary Managing Obstetric Emergencies & Trauma courses, and in particular through increased focus on pregnant women with a general high risk profile.

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Part III

Organisation of obstetric care, painrelief and pregnancy outcome

Chapter 3.1

Increased adverse perinatal outcome of hospital delivery at night

Hanneke de Graaf
Anita Ravelli
Gerard Visser
Chantal Hukkelhoven
Wing Tong
Gouke Bonsel
Eric Steegers

BJOG 2010; 117:1098-11

Abstract

Objective To determine whether delivery in the evening or at night and some organisational features of maternity units are related to perinatal adverse outcome.

Design A 7-year national registry-based cohort study.

Setting All 99 Dutch hospitals.

Population From nontertiary hospitals (*n* = 88), 655 961 singleton deliveries from 32 gestational weeks onwards, and, from tertiary centres (*n* = 10), 108 445 singleton deliveries from 22 gestational weeks onwards.

Methods Multiple logistic regression analysis of national perinatal registration data over the period 2000–2006. In addition, multilevel analysis was applied to investigate whether the effects of time of delivery and other variables systematically vary across different hospitals.

Main outcome measures Delivery-related perinatal mortality (intrapartum or early neonatal mortality) and combined delivery-related perinatal adverse outcome (any of the following: intrapartum or early neonatal mortality, 5-minute Apgar score below 7, or admission to neonatal intensive care).

Results After case mix adjustment, relative to daytime, increased perinatal mortality was found in nontertiary hospitals during the evening (OR, 1.32; 95% CI, 1.15–1.52) and at night (OR, 1.47; 95% CI, 1.28–1.69) and, in tertiary centres, at night only (OR, 1.20; 95% CI, 1.06–1.37). Similar significant effects were observed using the combined perinatal adverse outcome measure. Multilevel analysis was unsuccessful; extending the initial analysis with nominal hospital effects and hospital–delivery time interaction effects confirmed the significant effect of night in nontertiary hospitals, whereas other organisational effects (nontertiary, tertiary) were taken up by the hospital terms.

Conclusion Hospital deliveries at night are associated with increased perinatal mortality and adverse perinatal outcome. The time of delivery and other organisational features representing experience (seniority of staff, volume) explain hospital-to-hospital variation.

Introduction

Over 70% of Dutch women deliver at hospital [1]. At the time of delivery, care is focussed on risk surveillance and intervention, if indicated, including assisted delivery and neonatal intensive care. This requires the ready availability of experienced professionals and supportive facilities. High-care facilities and multiple expert competences cannot be represented at all hospitals on a 24-hour/7-day basis, however, because of issues of cost-effectiveness. In the Netherlands, 9% of deliveries are scheduled, but the majority of nonscheduled deliveries occur around the clock, with a biphasic pattern, including a peak – under natural conditions – in the early morning [2].

Heterogeneity with respect to facility and personnel coverage around the clock is the rule rather than the exception for most clinical care, even in surgery and intensive care. Studies have shown moderate to strong associations between patient outcomes and organisational features, both with regard to the volume of care and care that is daytime dependent, such as physician staffing and the immediate availability of anaesthesiological services [3-7].

In maternal and perinatal care, this evidence is not unequivocal. Different studies have demonstrated that high-risk newborns have better outcomes in high-volume hospitals [8-11], whereas controversy exists in the case of low- and moderate-risk newborns [12-18].

Little is known about the interaction between fixed and time-dependent organisational characteristics. The time of delivery may be regarded as an indirect expression of organisational vulnerability, as conditions may be more suboptimal during the evening and night. Indeed, recent studies have suggested that perinatal outcomes are compromised during the weekend and at night [17-24], and a recent analysis in the Netherlands – without elaborating on the specific organisational features – has suggested a similar relation for off-hour deliveries with regard to intrapartum and neonatal mortality [25-28].

The objective of this study was to evaluate the role of some organisational features (time of birth, volume of the maternity unit and physician staffing) in the performance of clinical maternity units of nontertiary hospitals and tertiary centres in the Netherlands, whilst adjusting for clinical risks. The organisational features of community midwifery care fall outside the aim of this study, as the organisation of more than 400 independent midwifery practices differs completely from that in hospitals, and possible differences in perinatal outcome in relation to the time of delivery may depend on other mechanisms. The scope of our evaluation was expanded from delivery-related perinatal mortality (about 2% in this population) to delivery-related perinatal adverse outcome, including intrapartum death, early neonatal death, a low Apgar score 5 minutes after birth and admission to a neonatal intensive care unit (altogether about 13% in this population), to enhance the sensitivity of the analysis.

Materials and methods

Study population

Patient data were obtained from the Netherlands Perinatal Registry, a linked professional database of all pregnancies, of 20 weeks and above, in the Netherlands, collected from (referring) midwives, obstetricians and paediatricians [27]. The registry information consists of maternal demographic factors, pregnancy and labour characteristics, and neonatal outcomes. The study was executed with the explicit permission of the holder of the patient registration data (Netherlands Perinatal Registry), which consists of representatives of all professional caregivers involved in the registry. The statistical analysis presented here was part of the required data application. The permission was subject to the strict requirement of nondisclosure of the identity of any individual hospital, directly or indirectly. Patient data in the Netherlands Perinatal Registry are anonymised.

From 1 January 2000 to 31 December 2006, all deliveries of each delivery hospital and home births in the Netherlands were enrolled. The national coverage is near to complete as registration is compulsory (professional requirement to receive health insurance fees).

Multiple deliveries of two or more were excluded (3.9%, 50 577 of 1 297 017). Home and transferred home deliveries in a hospital under the responsibility of community midwives (35.9%, 447 408 of 1 246 440) were also excluded from the analysis. In the case of the fusion of two hospitals during the study period, the records of both hospitals were combined. Deliveries at hospitals which had not participated in the registry for 2 years or more were also excluded (0.8%, 6078 of 799 032). The final database contained 792 954 births in 99 hospitals.

For the purpose of this study, the homogeneity of setting required the separation of the 10 tertiary perinatal centres (109 858 births, 13.9%). From the nontertiary hospitals, fetal deaths during gestation (n = 2585, 0.4%), children with congenital malformations (n = 17 516, 2.6%) and deliveries with a gestational age before 32.0 weeks or unknown gestational age (n = 7034, 1.0%) were excluded from the analysis. Outside tertiary centres, these deliveries are unexpected and unintended as to their location. Therefore, 655 961 singleton births of nontertiary hospitals remained for further analysis. From the tertiary centres, fetal deaths during gestation and deliveries with a gestational age before 22.0 weeks or unknown gestational age (n = 1413, 1.3%) were excluded from the analysis. From the tertiary centres, 108 445 singleton births were used for further analysis.

The sizes of the nontertiary hospitals were stratified into six categories based on the yearly number of deliveries, yielding about equal-sized groups. Although this number occasionally showed some fluctuation, the categorisation was primarily based on the category that was most prevalent.

Maternity units

All 99 participating maternity units were evaluated by a standard questionnaire to collect information on organisational factors. The information collected referred to teaching hospital (yes or no), and the number of obstetricians, clinical midwives, residents in training and residents not in training. In the Netherlands, after completing medical school and becoming a registered doctor, an individual attempts to obtain a formal training post to become a GP or in one of the specialities, such as obstetrics and gynaecology. Once accepted, the entire scheme of training (for 5 or 6 years) in peripheral and tertiary university hospitals is scheduled up to the moment of registration as a gynaecologist (or other speciality). Not all doctors manage to obtain such training posts immediately. Those doctors take jobs as Obstetrics and Gynaecology Residents (or other specialities), who are not formally in training, in order to obtain clinical experience.

The survey was executed prior to any data analysis. At the time of the study, no information was available on any of the primary study relations, at either the aggregate or individual hospital level. The information providers usually had an administrative background.

Definitions

Evening-time deliveries were defined as those taking place between 18.00 and 23.59 hours, and night-time deliveries as those taking place between 00.00 and 07.59 hours.

Based on the outcomes of the maternity unit enquiry, a senior index variable for non- tertiary hospitals was constructed [(number of obstetricians + residents in training) divided by the total staff of a hospital (obstetricians + residents in training + residents not in training + clinical midwives)]. A higher score implies a better qualified staff. Several weights for the numerator were tried, but the outcomes of these analyses were similar. The primary outcome parameter was perinatal mortality, defined as intrapartum or early neonatal death (number of deaths within 7 days after live birth); perinatal adverse outcome was defined as the presence of any of the following outcomes: intrapartum or early neonatal death (number of deaths within 7 days after live birth), 5-minute Apgar score below 7, or transfer of the newborn to a neonatal intensive care unit after birth.

Statistical analysis

The statistical software package SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) was used for data analysis. A multiple logistic regression analysis was used to determine whether the organisational factors, additional to pregnancy characteristics such as parity and gestational age, contributed independently to the outcome rates. For this purpose, we first estimated an optimal model including these pregnancy-related variables alone, and calendar year, as perinatal adverse outcomes show an annual trend. The resulting variable set was then treated as a forced case mix control to which organisational variables were added in two steps: first, time at delivery (daytime, evening, night and weekend or public holiday); second, organisational characteristics. To check for the general effect of the hospital on the predictors, we applied a multilevel analysis using the NLMIXED procedure of SAS. The first level was the hospital, which was reflected by a dummy. The second level was the remaining organisational and case mix variables listed previously. The a priori estimates of these variables, as required for the analysis, were drawn from the previous logistic regression analysis. When the model did not converge, we simplified the explanatory structure, re-estimated the basic logistic regression to obtain the priors, ran the analysis and increased the number of iterations. Special hardware was available to accommodate the memory requirements. If the analysis failed, we considered the introduction of a nominal hospital effect in the first analysis, together with an interaction term of hospital with time (evening, night; daytime was reference).

Odds ratios, with 95% confidence intervals, were calculated for each risk factor. A two-sided *P* value of <0.05 was considered to be statistically significant. Data were presented as frequencies and proportions (%), unless specified otherwise. The influence of maternity unit size (annual number of deliveries) and staff seniority was only analysed for the nontertiary hospitals, because there was little variety in the organisational features of the tertiary perinatal centres.

Results

A total of 655 961 deliveries in nontertiary hospitals was analysed, including 11 118 adverse outcomes (1.7%) [1206 (0.19%) with perinatal mortality]; 108 445 deliveries were analysed in tertiary centres, including 12 705 adverse outcomes (11.7%) [1915 cases (1.8%) of perinatal mortality].

The characteristics of the included births are shown in Table 1. Fifty-three per cent of the total population were nulliparous, 20% were above 35 years and 17% were non-Western. The time at delivery and hospital characteristics are depicted in Table 2. About one-half of the deliveries occurred during the evening or night-time. More than 75% of women were delivered in nontertiary hospitals with a volume of more than 1000 births per year. Tables 3 and 4 show, after adjustment for case mix, the associations of time of delivery and organisational characteristics with perinatal outcome in nontertiary and tertiary centres, respectively.In nontertiary hospitals, relative to daytime, increased perinatal mortality was found during the evenings (18.00–23.59 hours: OR, 1.32; 95% CI, 1.15–1.52) and nights (00.00–07.59 hours: OR,1.47; 95% CI, 1.28–1.69). In tertiary centres, increased perinatal mortality was found during the night only (OR,1.20; 95% CI, 1.06–1.37). Relative to weekdays, perinatal mortality was increased on Saturdays in nontertiary hospitals (OR, 1.28; 95% CI, 1.03–1.59). In both nontertiary hospitals and tertiary centres, perinatal adverse outcome was more frequent during the evenings (OR, 1.30; 95% CI, 1.24–1.36 and OR, 1.21; 95% CI, 1.13–1.30, respectively) and nights (OR, 1.28; 95% CI, 1.22–1.34 and OR, 1.25; 95% CI, 1.17–1.34, respectively). Perinatal adverse outcome in tertiary centres was higher on Saturdays (OR, 1.16; 95% CI, 1.05–1.30).In nontertiary hospitals, the seniority of staff was inversely associated with both perinatal mortality and perinatal adverse outcome (OR, 0.61; 95% CI, 0.32–1.15 and OR, 0.49; 95% CI, 0.39–0.61, respectively). Moderately small maternity units of nontertiary hospitals with between 750 and 999 deliveries showed an increased risk of perinatal adverse outcome (OR, 1.16; 95%, CI, 1.07–1.26).When multilevel analysis was applied, none of the four models converged satisfactorily. Partial results showed essentially the same coefficients (with larger confidence intervals; still significant in the case of time categories), but not all the case mix variables (e.g. the 22.0–27.6-week variable) could be estimated (too many so-called 'empty cells' in this hospital-specific estimation procedure). The addition of a nominal factor for each hospital and interaction terms for all hospital–time categories to the initial standard regression analysis revealed a significant effect of delivery at night-time in nontertiary hospitals (mortality, all adverse outcome); in tertiary hospitals, these interaction factors decreased the organisational effects to a nonsignificant level.

Table 1. Study population characteristics

	Non-tertiary hospitals n=655.961		Tertiary perinatal centres n=108.445	
	Frequency	Proportion (%)	Frequency	Proportion (%)
Maternal parity and age group				
- nulliparous and < 25 year	62.058	9.5	9484	8.8
- nulliparous and 25 - 29 year	124.567	19.0	17030	15.7
- nulliparous and 30 - 34 year	121.888	18.6	19424	17.9
- nulliparous and ≥ 35 year	41.600	6.3	8707	8.0
- multiparous and < 25 year	17.023	2.6	3195	3.0
- multiparous and 25 - 29 year	66.525	10.1	10685	9.9
- multiparous and 30 - 34 year	135.135	20.6	22039	20.3
- multiparous and 35 - 39 year	74.570	11.4	14825	13.7
- multiparous and ≥ 40 year	12.595	1.9	3056	2.8
Ethnicity				
- Non-Western	104.111	15.9	21.593	19.9
- Western	551.850	84.1	86.852	80.1
Gestational age at birth				
- 22 -27.6 weeks	0	0	2.260	2.1
- 28 –31.6 week	0	0	5.078	4.7
- 32 week	2.167	0.33	1.000	0.9
- 33 week	4.088	0.62	983	0.9
- 34 week	6.967	1.1	1.401	1.3
- 35 week	11.674	1.8	1.992	1.8
- 36 week	21.679	3.3	3.677	3.4
- 37 week	40.863	6.2	7.008	6.5
- 38 week	102.138	15.6	15.706	14.5
- 39 week	138.476	21.1	21.076	19.4
- 40 week	159.198	24.3	23.583	21.8
- 41 week	116.347	17.7	16.846	15.5
- ≥ 42.0 weeks	52.364	8.0	7.462	6.9
- Unknown	0.	0	373	0.3
Mode of delivery				
- spontaneous	403.019	61.4	66.726	61.5
- instrumental vaginal delivery	112.665	17.2	16.084	14.8
- elective cesarean section	60.609	9.2	13.497	12.5
- emergency cesarean section	79.668	12.2	12.138	11.2
Congenital anomalies	n.a.	n.a.	5.701	5.3
Outcome				
- intrapartum mortality	603	0.09	531	0.49
- neonatal mortality < 24 hours	300	0.05	944	0.87
- early neonatal mortality (1 – 7 days)	303	0.05	440	0.41
- Apgar after 5 minutes < 7	7.300	1.11	4.533	4.18
- admission to NICU	2.612	0.39	10.077	9.29
- total adverse outcome	11.118	1.69	12.705	11.7
- no adverse outcome	644.843	98.3	95.740	88.3

n.a. = not applicable, NICU, neonatal intensive care unit.

Table 2. Time at delivery and organisational characteristics

	Non-tertiary hospitals n=655.961		Tertiary perinatal centres n=108.445	
	Frequency	Proportion (%)	Frequency	Proportion (%)
Time at delivery				
- 0 – 8 am	151.002	23.0	28.752	26.5
- 8 am – 6 pm	355.922	54.3	54.021	49.8
- 6 pm – 12 pm	149.037	22.7	25.672	23.7
Day of the week				
- Saturday	79.101	12.1	13.086	12.1
- Sunday and public holiday	77.263	11.8	12.965	12.0
- Monday	97.617	14.8	15.691	14.5
- Tuesday	103.092	15.7	17.227	15.9
- Wednesday	103.487	15.8	16.918	15.6
- Thursday	102.336	15.6	16.556	15.3
- Friday	98.642	15.0	16.002	14.8
Maternity unit's characteristics				
Total number of staff (sum of gynaecologists, residents both in training and not and clinical midwives)				
- 0 - 9	214.681	32.7 (20 units)	0	0
- 10 – 19	250.372	38.2 (48 units)	0	0
- 20 – 29	190.908	29.1 (21 units)	30.883	28.5
- 30 – 60	0	0	77.562	71.5
Teaching hospital				
-Yes	338.519	51.6 (42 units)	108.445	100
-No	317.442	48.4 (57 units)	0	0
Annual number of deliveries				
- < 750 deliveries	54.316	8.3 (15 units)	0	0
- 750 - 999 deliveries	98.914	15.1 (19 units)	0	0
- 1000 - 1249 deliveries	141.869	21.6 (21 units)	16.300	15.0 (2 units)
- 1250 - 1499 deliveries	113.956	17.4 (13 units)	49.090	45.3 (5 units)
- 1500 - 1749 deliveries	110.807	16.9 (11 units)	0	0
- ≥ 1750 deliveries	136.099	20.7 (10 units)	43.055	39.7 (3 units)

Table 3 Organisation characteristics of non-tertiary hospitals. Perinatal mortality and perinatal adverse outcome adjusted for case mix (gestational age, maternal age, parity, mode of delivery ethnicity and calendar year trend). Odds ratios with 95% CI.

	Perinatal mortality (N=1.206)	**Perinatal adverse outcome** (N=11.118)
Time of delivery		
0 am - 8 am	1.47 (1.28-1.69)	1.28 (1.22-1.34)
8 am - 6 pm	1 [Ref]	1 [Ref]
6 pm - 12 pm	1.32 (1.15-1.52)	1.30 (1.24-1.36)
Day of delivery		
Saturday	1.28 (1.03-1.59)	1.01 (0.93-1.08)
Sunday	1.13 (0.91-1.41)	1.03 (0.95-1.11)
Monday	1.03 (0.84-1.28)	1.00 (0.93-1.08)
Tuesday	1 [Ref]	1 [Ref]
Wednesday	0.99 (0.80-1.22)	1.08 (1.01-1.15)
Thursday	1.16 (0.95-1.43)	1.04 (0.97-1.11)
Friday	1.07 (0.87-1.32)	1.06 (0.99-1.14)
Annual numbers of deliveries		
< 750	1.08 (0.83-1.40)	1.09 (0.99-1.19)
750- 999	0.89 (0.70-1.14)	1.16 (1.07-1.26)
1000- 1249	0.99 (0.81-1.20)	1.05 (0.98-1.12)
1250- 1499	1.01 (0.83-1.23)	1.00 (0.93-1.06)
1500 - 1749	0.97 (0.81-1.18)	1.06 (1.00-1.13)
≥1750	1 [Ref]	1 [Ref]
Seniority index		
continue	0.61 (0.32-1.15)	0.49 (0.39-0.61)
Teaching hospital		
Yes	1 [Ref]	1 [Ref]
No	0.91 (0.77-1.07)	1.28 (1.21-1.36)
Pregnancy characteristics (casemix adjustment)		
Gestational weeks		
32.0 - 32.6 week	11.5 (7.9-16.7)	20.5 (18.3-23.0)
33.0 - 33.6 week	9.50 (6.94-13.0)	12.6 (11.4-14.0)
34.0 - 34.6 week	4.76 (3.40-6.66)	7.30 (6.62-8.05)
35.0 - 35.6 week	4.72 (3.58-6.23)	4.42 (4.02-4.86)
36.0 - 36.6 week	2.58 (1.96-3.39)	2.21 (2.01-2.44)
37.0 - 37.6 week	1.99 (1.57-2.52)	1.55 (1.42-1.68)
38.0 - 38.6 week	1.11 (0.89-1.38)	0.96 (0.89-1.03)
39.0 - 39.6 week	1.11 (0.91-1.35)	0.93 (0.87-0.99)
40.0 - 40.6 week	1 [Ref]	1 [Ref]
41.0 - 41.6 week	1.42 (1.17-1.72)	1.21 (1.13-1.29)
≥ 42 weeks	1.08 (0.83-1.41)	1.19 (1.10-1.29)
Maternal parity and age group		
nulliparous and <25 year	1.27 (1.00-1.60)	1.14 (1.06-1.23)
nulliparous and 25 - 29 year	1 [Ref]	1 [Ref]
nulliparous and 30 - 34 year	1.25 (1.03-1.52)	1.03 (0.97-1.09)
nulliparous and ≥ 35 year	1.26 (0.97-1.64)	1.12 (1.03-1.21)
multiparous and <25 year	1.52 (1.05-2.20)	1.01 (0.88-1.15)
multiparous and 25 - 29 year	1.56 (1.24-1.96)	1.04 (0.96-1.13)
multiparous and 30 - 34 year	1.60 (1.32-1.94)	1.04 (0.98-1.11)
multiparous and 35 - 39 year	1.55 (1.24-1.94)	1.05 (0.97-1.13)
multiparous and ≥ 40 year	1.46 (0.96-2.22)	1.24 (1.08-1.42)
Mode of delivery		
spontaneous	1 [ref]	1 [Ref]
instrumental vaginal delivery	1.48 (1.25-1.77)	2.18 (2.07-2.30)
elective caesarean section	1.69 (1.39-2.05)	1.87 (1.75-1.99)
emergency caesarean section	3.04 (2.64-3.51)	2.97 (2.83-3.13)

Ethnicity		
Non-Western	1.43 (1.24-1.66)	1.28 (1.21-1.34)
Western	1 [Ref]	1[Ref]
Year of registration	0.99 (0.96-1.01)	1.00 (0.99-1.00)

Table 4 Organisation characteristics of tertiary hospitals. Perinatal mortality and perinatal adverse outcome adjusted for case mix (gestational age, maternal age, parity, mode of delivery ethnicity and calendar year trend). Odds ratios with 95% CI.

	Perinatal mortality (N=1.915)	Perinatal adverse outcome (N=12.705)
Time of delivery		
0 am - 8 am	1.20 (1.06-1.37)	1.25 (1.17-1.34)
8 am - 6 pm	1 [Ref]	1 [Ref]
6 pm - 12 pm	1.08 (0.95-1.24)	1.21 (1.13-1.30)
Day of delivery		
Saturday	0.86 (0.70-1.06)	1.16 (1.05-1.30)
Sunday	0.84 (0.69-1.04)	1.02 (0.91-1.13)
Monday	0.89 (0.73-1.08)	1.06 (0.96-1.17)
Tuesday	1 [Ref]	1 [Ref]
Wednesday	0.99 (0.81-1.198)	1.07 (0.97-1.18)
Thursday	0.94 (0.78-1.14)	1.16 (1.05-1.28)
Friday	1.03 (0.85-1.24)	1.08 (0.98-1.20)
Pregnancy characteristics		
Gestational weeks		
22.0 – 27.6 week	186 (148 - 232)	≈ (861 - ≈)
28.0 – 31.6 week	13.8 (10.8-17.6)	250 (221 - 284)
32.0 - 36.6 week	5.6 (4.40-7.10)	7.63 (6.97-8.35)
37.0 - 38.6 week	1.57 (1.22-2.03)	1.12 (1.01-1.23)
39.0 - 39.6 week	0.73 (0.53-1.01)	0.80 (0.72-0.89)
40.0 - 40.6 week+unknown	1[Ref]	1[Ref]
≥ 41 weeks	0.86 (0.64-1.16)	0.92 (0.83-1.02)
Maternal parity and age group		
nulliparous and <25 year	1.22 (1.00-1.51)	1.14 (1.02-1.28)
nulliparous and 25 - 29 year	1[Ref]	1[Ref]
nulliparous and 30 - 34 year	1.11 (0.91-1.34)	0.92 (0.83-1.01)
nulliparous and ≥ 35 year	1.09 (0.85-1.40)	0.86 (0.76-0.97)
multiparous and <25 year	1.15 (0.83-1.60)	1.07 (0.90-1.28)
multiparous and 25 - 29 year	1.47 (1.18-1.82)	1.01 (0.90-1.13)
multiparous and 30 - 34 year	1.45 (1.20-1.75)	0.99 (0.90-1.09)
multiparous and 35 - 39 year	1.60 (1.31-1.96)	0.97 (0.88-1.08)
multiparous and ≥ 40 year	1.28 (0.90-1.83)	0.98 (0.82-1.17)
Mode of delivery		
spontaneous	1[Ref]	1[Ref]
instrumental vaginal delivery	0.95 (0.77-1.17)	1.51 (1.38-1.65)
elective caesarean section	0.43 (0.37-0.51)	2.80 (2.60-3.01)
emergency caesarean section	0.47 (0.38-0.59)	2.87 (2.65-3.10)
Ethnicity		
Non-Western	0.97 (0.85-1.11)	1.07 (1.00-1.15)
Western	1[Ref]	1[Ref]
Congenital anomalies		
No	1[Ref]	1[Ref]
Yes	12.2 (10.8-13.8)	11.6 (10.8-12.5)
Year of registration	1.00 (0.98-1.03)	1.09 (1.07-1.10)

*Perinatal adverse outcome rate is 100%.

Discussion

To our knowledge, this is the first Dutch population-based report to demonstrate a strong association between time of delivery and hospital experience, and adverse obstetric outcomes, with care having been taken to correct for case mix. Delivery at night in all analyses was associated with an increased risk of perinatal mortality and adverse outcome in nontertiary hospitals. Smaller size and a lower seniority index of nontertiary hospitals emerged as two experience-related factors, which are additive if present together. Multilevel analysis to correct for the potential statistical effect of the hospital as a grouping unit of the data generally failed for this purpose, because of the unfavourable characteristics of the data: despite its size, the dataset contained too many ‘empty cells’ for rare outcomes, i.e. cases of mortality or adverse outcome, as specified by the variables, which did not exist in one or more hospitals. The alternative approach of adding nominal effects for each hospital and interaction terms for all hospitals with the time of delivery categories showed delivery at night to be significant in nontertiary hospitals for both outcomes. This analysis, however, yielded a severe loss of power (in nontertiary hospitals almost 300 coefficients were introduced), with the result that experience variables (volume, seniority) were obscured by the nominal hospital categories.

Our study suggests that this association may be related to the lower availability of experienced caregivers. In almost all nontertiary Dutch hospitals, the senior, experienced obstetrician and neonatologist are not present during the evenings, nights and weekends, but on call from home. Therefore, they are less likely to be involved in the judgement of (pre)critical conditions and the initial management of high-risk situations. Studies from intensive care units support such an interpretation. Increased mortality during off-hours in the case of non-24-hour availability of intensivists has been reported [28], and the introduction of 24-hour availability of senior intensivists was associated with decreased intensive care unit complication rates, hospital length of stay [29,30] and no differences in mortality between day, evening or night-time [31,32]. The same results were found in paediatric intensive care units [33] and maternity units [34]. Joyce *et al.*[35] observed a reverse correlation between stillbirth rate and consultant obstetric staffing levels. We assume that issues of 24-hour availability extend to the ready availability of anaesthesiologists and neonatologists as well.

Fatigue of the attending clinical midwife or resident may also be involved [36,37]. Changes in work schedules from days to nights may be too rapid to allow the circadian system to adapt to the scheduled wakefulness at night, placing many providers in a permanent state of ‘jet lag’ as they attempt to remain awake and work, and subsequently sleep, at the incorrect internal circadian phase [38,39]. Such circadian misalignment is responsible for the higher rates of accidents by night-shift industrial workers [40]. Independent of the circadian system, acute continuous sleep deprivation has a profound impact on fatigue. After about 16–18 hours of wakefulness, alertness and performance decline rapidly [41]. During the night, it is allowed for residents and midwives to take a nap. Furthermore, it has been shown that naps during the night induce post-nap impairment, where alertness and performance are particularly decreased during the 15–30 minutes after waking [35,42]. A Dutch law on labour conditions in 2007 issued limitations on resident work hours in an attempt to reduce fatigue-related medical errors. This law was not in force during the study period, when the practice of working for 24 hours was quite normal.

Volume–outcome relationships have been studied frequently in surgery and surgery-related specialities, and show that high surgeon volume and specialisation are associated with improved patient outcome, but high hospital volume is of limited benefit [4,6,7].

In our study, the moderately small maternity units with between 750 and 999 deliveries showed a higher risk of perinatal adverse outcome (15%) than the smallest units (7%). Further research may reveal whether this phenomenon reflects chance, selection uncovered by our case mix (e.g. referral to a tertiary perinatal centre at an earlier stage) or true performance.

One limitation of this observational study was our statistical approach of case mix adjustment. We deliberately included intervention during delivery as an adjustment factor. We were aware that, to some extent, this variable is not a true independent predictor of adverse outcome as it partially coincides with outcome. Nevertheless, it represents a useful and pragmatic coverage of risks at onset of delivery, yielding conservative estimates of the remaining factors. Using this procedure, we accepted a degree of overadjustment to arrive at nonexaggerated estimates of the organisational effects. Another limitation was the lack of information on actual staffing levels just before and during each delivery individually. Maternity ward staffing is typically a healthcare organisation issue that, despite its potential importance in clinical and economic outcomes, is not often studied [34]. Our seniority index essentially reflects availability, rather than actual use, of senior competence, although the former will always be a precondition for the latter. A third limitation was the use of the hour of birth as a proxy for the time of delivery effect, which implicitly defines this phase to be the time window of highest vulnerability for organisational effects. One may argue that such a critical phase starts, for example, 1 hour before delivery. When we tested the effect of such a change in the time definition (all time period definitions minus 1 hour), the results were unaffected. A fourth limitation was the inability to subject the dataset to a formal multilevel analysis without removing the standard case mix variables. The dataset was less suitable for this approach. Possibly, nonlinear algorithms will enable such an approach in the future. The application of a second best approach to test a hospital effect maintained a significant role for the time of delivery, where this can be interpreted as a conservative estimate in view of the large number of additional parameters introduced by this second approach. A fifth limitation, by intent, was the scope of our study. We did not address specific aspects of transfer, nor the roles of referring community midwives, and the availability and specific roles of anaesthesiologists and neonatologists. Finally, insufficient data were available to allow for an informed estimate of the economic and professional consequences of a change towards institutional concentration and full on-call coverage of off-hours. We could not therefore derive a crude estimate of the costs of constant staffing levels around the clock, allowing for a crude cost-effectiveness analysis if it is assumed that outcome levels in that case would return to those observed in the daytime.

Conclusion

Hospital deliveries at night are associated with increased perinatal mortality and adverse perinatal outcome. The time of delivery and other organisational features representing experience (seniority of staff, volume) can explain the hospital-to-hospital variation.

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Chapter 3.2

Planned home compared with planned hospital births in the Netherlands: intrapartum and early neonatal death in low-risk pregnancies

Jacoba van der Kooy
Jashvant Poeran
Hanneke de Graaf,
Erwin Birnie
Semiha Denktas
Eric Steegers
Gouke Bonsel

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Abstract

Objective: The purpose of our study was to compare the intrapartum and early neonatal mortality rate of planned home birth with planned hospital birth in community midwife-led deliveries after case mix adjustment.

Methods: The perinatal outcome of 679,952 low-risk women was obtained from the Netherlands Perinatal Registry (2000-2007). This group represents all women who had a choice between home and hospital birth. Two different analyses were performed: natural prospective approach (intention-to-treat-like analysis) and perfect guideline approach (per-protocol-like analysis). Unadjusted and adjusted odds ratios (ORs) were calculated. Case mix was based on the presence of at least one of the following: congenital abnormalities, small for gestational age, preterm birth, or low Apgar score. We also investigated the potential risk role of intended place of birth. Multivariate stepwise logistic regression was used to investigate the potential risk role of intended place of birth.

Results: Intrapartum and neonatal death at 0-7 days was observed in 0.15% of planned home compared with 0.18% in planned hospital births (crude relative risk 0.80, 95% confidence interval [CI] 0.71-0.91). After case mix adjustment, the relation is reversed, showing nonsignificant increased mortality risk of home birth (OR 1.05, 95% CI 0.91-1.21). In certain subgroups, additional mortality may arise at home if risk conditions emerge at birth (up to 20% increase).

Conclusion: Home birth, under routine conditions, is generally not associated with increased intrapartum and early neonatal death, yet in subgroups, additional risk cannot be excluded.

Introduction

The debate on the safety of home births continues in the literature as recently addressed in the Lancet [1]. In The Netherlands, approximately 50% of women give birth under the supervision of a community midwife. The community midwives are independent health care professionals in The Netherlands operating either solely or in group practices.

The proportion of home birth deliveries in The Netherlands has steadily decreased over the last decade but is currently stable at 25% of all births. Several Anglo-Saxon countries are considering the reintroduction of home births based on recent claims of sufficient safety [2]. The reverse trend is observed in The Netherlands, where the debate has intensified since the national perinatal mortality rate showed it to be one of the highest in Europe [3].

In the Dutch system, independently operating community midwives provide care for low- and medium-risk pregnant women (primary health care). High-risk pregnant women are referred to the gynecologist for remaining ante- and intrapartum care. If no or only a few risk factors are present, women can stay with the midwife and decide where the delivery will take place: at home or in the hospital, both supervised by the community midwife. For pregnant women with so-called medium risk, delivery in the hospital is obligatory but still can be under the supervision of the community midwife. A strict definition of medium risk, created and agreed on by midwives and gynecologists together, is defined in the Dutch guidelines [4]. The claimed benefits of planned home births include the reduction of maternal-fetal morbidity, a lower risk for unjustified medical interventions, and psychosocial advantages for the mother. These benefits may be counterbalanced by the disadvantages associated with a high intrapartum referral rate and an increased perinatal mortality, morbidity, and long-term negative effects [5-11].

This article readdresses the Dutch evidence focusing on two critical features of previous analyses. First, previous studies compared outcomes after exclusion of pregnant women who in view of the delivery guidelines should have been referred to a gynecologist. Second, previous studies did not apply case mix analysis, assuming risk equivalence of home and hospital groups [5,9,12–18]. Case mix may, however, differ across planned place of delivery as a result of self-selection or as a result of the midwife's proposal with the healthiest and most affluent women receiving home birth (confounding the comparison by indication bias) [5–7,11,19–21].

The purpose of our study was to compare the intrapartum and early neonatal mortality rate of planned home birth compared with planned hospital birth in community midwife-led deliveries after case mix adjustment. We compared a natural prospective approach without ex post exclusion of unsuitable midwife cases (intention-to-treat–like) with the conventional approach based on a theoretical midwife population under perfect guideline adherence (per-protocol–like). We hypothesized that although in general no difference may exist between home and hospital outcomes, for specific risk groups, the hospital setting is protective because obstetric and neonatal expertise and clinical facilities are directly available (so-called setting safety).

Materials and Methods

The Netherlands Perinatal Registry contains population-based information of 96% of all pregnancies in The Netherlands. Source data are collected by 95% of midwives, 99% of gynecologists, and 68% of pediatricians (including 100% of neonatal intensive care unit pediatricians) [3,22] (See web site for detailed description: www.perinatreg.nl.). Permission was obtained to use the anonymous registry data for this study from the board of The Netherlands Perinatal Registry. We selected the records of all singleton pregnant women between 2000 and 2007 who were under the supervision of a community midwife at the onset of labor (693,592 women).

The onset of labor was defined as spontaneous contractions or the spontaneous rupture of membranes by The Netherlands Perinatal Registry. Two subsets of pregnant women were further excluded from the original set of 693,592 women. First excluded were 13,384 women with so-called medium risk, for example, women with a history of postpartum hemorrhage or obesity (body mass index [calculated as weight (kg)/[height (m)]2] more than 30). Dutch guidelines prescribe a hospital delivery for these women that may be supervised by the community midwife. Secondly, we excluded records in which the data were incomplete (n=256).

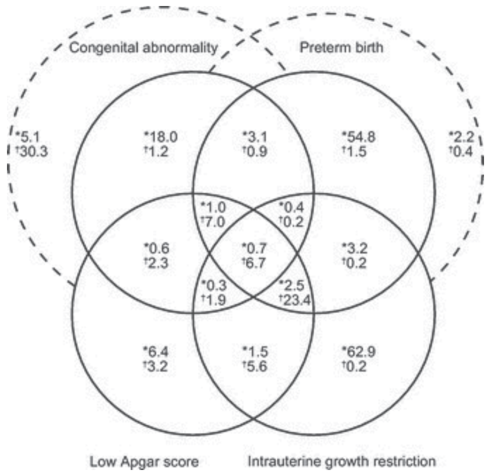
The remaining women (n=679,952) were categorized according to intended place of birth, which usually is concordant with the observed place of birth, either home or the hospital. For some women, the place was not decided until the onset of labor. This could be the result of indifference on the part of the woman or delayed antepartum care. The intended place then was coded “unknown.” This yielded three intention groups: home, hospital, and unknown.

Outcome was defined as intrapartum and early neonatal mortality, ie, 1) intrapartum death, 2) neonatal death up to 24 hours, and 3) neonatal death from 1 day to 7 days postpartum. In our low-risk group under midwife supervision, mortality beyond 8 days is rare and regarded to be unrelated to place of delivery. The Netherlands Perinatal Registry does not include long-term child outcomes, including psychomotor development and behavioral function.

Maternal risk factors were parity (nulliparous compared with multiparous), age, ethnicity (Western or non-Western based on a more refined classification in the registry), and living in a deprived neighborhood (yes or no based on four-digit zip codes and a public list of deprived, zip code-based, neighborhoods issued by the Dutch government).

Detailed risk information is unavailable in national registries. The case mix of any defined group of women was primarily represented by the prevalence (single or combined) of “Big 4” conditions (see below). From detailed analysis of the complete perinatal data set of the same Netherlands Perinatal Registry, years 2000–2007 (1.25 million records) [23], it appeared that the presence of any of four conditions preceded perinatal mortality in 85% of cases. These conditions were defined as congenital abnormalities (list defined), intrauterine growth restriction (small for gestational age, birth weight below the tenth percentile for gestational age, gender, and parity-specific), preterm birth (less than 37 weeks of gestation), or low Apgar score (less than 7 measured 5 minutes after birth). We will continue to refer to these four conditions as the Big 4. The main results of this detailed analysis are found in Figure 1.

Fig. 1. Perinatogram illustrating in a Venn diagram the relationship between (combinations of) Big 4 morbidities and perinatal mortality [1]

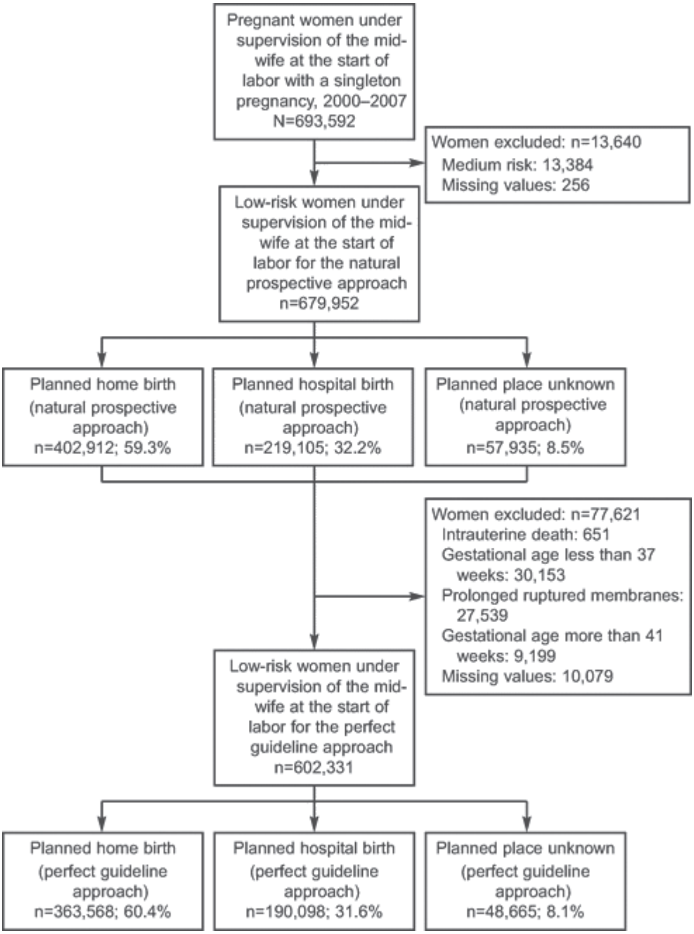


*[1] Big 4 morbidities and perinatal mortality defined as death from 22 weeks of gestational age until 7 days postpartum. In 85% of all cases of perinatal mortality, one or more Big 4 morbidities are present; for instance, a low Apgar score combined with preterm birth occurs in 30.3% of all cases of perinatal mortality. *Prevalence per 1,000 births of separate and combined Big 4 morbidities and their contribution to all cases of perinatal mortality (†percentage); this adds up to 85% of all cases of perinatal mortality. The dashed circles connect low Apgar score with preterm birth and congenital abnormality with intrauterine growth restriction.*

In our current analysis, these so-called Big 4 represent an objective estimate of the risk challenge at birth. The preventability of their occurrence, either antenatally or during delivery, is not at issue. We intentionally use it as a risk indicator, an explanatory factor at onset. By doing so, we ignore differential management effects of setting on the emergence of these Big 4, in particular low Apgar, should they exist.

As primary analysis, we present the results of the natural prospective approach resembling an intention-to-treat analysis (Fig. 2). For comparison, we added a perfect guideline approach resembling a per-protocol analysis. The natural prospective approach establishes, within observational constraints, the intrapartum and early neonatal death of planned home compared with planned hospital births. It stems from the viewpoint of a pregnant woman starting birth under supervision of a midwife (the denominator is n=679,952). The natural approach thus includes spontaneous preterm labor because to some extent this group was not referred to the gynecologist during labor or was referred late during (home) delivery. Therefore, a direct setting effect (admission to hospital at the onset of labor) may be visible to the advantage of the hospital. Furthermore, indirect setting effects may be present, for example, the timing of referral.

Fig. 2 Flow of women through the study



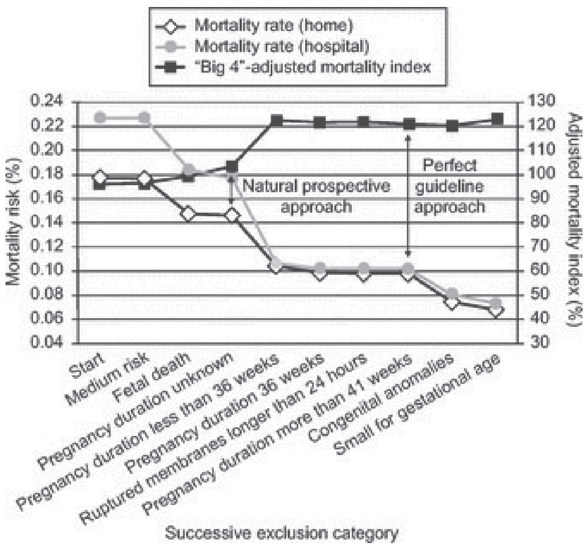
The perfect guideline approach includes the subset of women within the natural prospective approach population who in retrospect were compliant with the guidelines, which define low risk at the onset of labor and therefore are allowed to choose between a home or hospital birth under supervision of a midwife.

Noncompliance exists if a high-risk condition was already detectable at the onset of labor. These conditions applied to women with a gestational age less than 37 or more than 41 weeks, prolonged rupture of membranes (more than 24 hours), and intrauterine death with unclear timing relative to onset of labor (Fig. 2). The perfect guideline approach (n=602,331) still included undetected small for gestational age and congenital malformations that emerge at birth, because detection failure cannot be regarded as noncompliance from the viewpoint of current guidelines.

First we compared characteristics of the natural prospective approach and perfect guideline approach populations by intended place of birth (t tests for comparisons). Then we investigated the potential risk role of intended place of birth by a set of predefined nested multivariable logistic regression models (stepwise analysis, inclusion P<.05, exclusion P>.10) in which we added maternal and neonatal (case mix) explanatory variables. For these variables, hospital birth was set as the reference. All stepwise analyses were repeated with a forward and backward approach and finally forced inclusion of predictive variables (P<.05). Risk factor coefficients were only shown in case of significance of P<.05. Results across the three approaches were similar unless stated otherwise.

We graphically described the crude mortality of the planned home and planned hospital population for the series of populations that result from successive exclusion of women meeting a criterion for noncompliance (Fig. 3, dotted lines). This successive exclusion through noncompliance criteria gradually transforms the natural prospective approach population into the perfect guideline approach population. If the mortality rate of a noncompliance group is average, home and hospital mortality rates do not change on its exclusion. If the rates decrease at a different gradient (eg, hospital steeper than home, such as after exclusion of pregnancy duration less than 36 weeks), this may point to either differential prevalence of the noncompliance factor (such as here) or to differential case fatality by setting in which the largest mortality decrease is observed in the setting with the highest case fatality (interpretable as lowest setting safety).

Fig. 3 Big 4-adjusted mortality index of home birth (hospital-based birth under midwife supervision=100%).



To support this interpretation, we first divided the crude mortality of the home and hospital group by the respective prevalence of Big 4 conditions to obtain case mix adjustment. This assumes Big 4 prevalence to be a suitable risk indicator at the group level. Subsequent division of the resulting home and Big 4 mortality ratio by the hospital and Big4 mortality yields an index (Big 4-adjusted home birth mortality index; Fig. 3, black line). If this index is 100%, then relative mortality in home births and hospital births is equal. If the index is, for example, 120%, then home births have 20% excess mortality taking our case mix differences into account. Combining crude mortality changes with index changes allows for tentative interpretation of setting effects.

Results

Table 1 describes the baseline characteristics of both the natural prospective approach and perfect guideline approach populations (n=679,952 compared with 602,331). In both the natural prospective approach and perfect guideline approach populations, approximately 60% of women planned a home delivery and approximately 32% planned a hospital delivery. Compared with women who planned birth in the hospital or with an unknown location, the women with a planned home birth were more likely to be multiparous, 25 years of age or older, of Dutch origin, and to live in a privileged neighborhood (all of which are favorable conditions). In home birth women, neonatal case mix compared also favorably. Premature delivery was less common as was the prevalence of a Big 4 condition (natural prospective approach home birth 8.7% compared with hospital 10.8% compared with unknown 10.5%; perfect guideline approach home birth 6.5% compared with hospital 8.2% compared with unknown 7.5%, $P<.001$ in both cases).

Table 1. Characteristics and Outcomes of Women in Primary Care at the Onset of Labor (Natural Prospective Approach and Perfect Guideline Approach) *

	Planned Home Birth		**Planned Hospital Birth**		**Planned Place Unknown**		**Intrapartum and Early Neonatal Death**	
Variable	**NPA**	**PGA**	**NPA**	**PGA**	**NPA**	**PGA**	**NPA**	**PGA**
Parity †	402,912 (59.3)	363,568 (60.4)	219,105 (32.2)	190,098 (31.6)	57,935 (8.5)	48,665 (8.1)	679,952	602,331
Primiparous	171,986 (42.69)	148,082 (40.73)	104,249 (47.58)	88,110 (46.35)	26,254 (45.32)	21,047 (43.25)	614 (0.20)	283 (0.11)
Multiparous	230,926 (57.31)	215,486 (59.27)	114,856 (52.42)	101,988 (53.65)	31,681 (54.68)	27,618 (56.75)	485 (0.13)	268 (0.08)
Maternal age (y)†								
Younger than 19	4,036 (1.00)	3,502 (0.96)	6,713 (3.06)	5,770 (3.04)	1,190 (2.05)	910 (1.87)	42 (0.35)	13 (0.13)
20–25	34,661 (8.60)	30,787 (8.47)	32,617 (14.89)	28,669 (15.08)	6,823 (11.78)	5,611 (11.53)	133 (0.18)	65 (0.10)
25–34	296,128 (73.50)	267,408 (73.55)	142,597 (65.08)	124,071 (65.27)	39,526 (68.22)	33,583 (69.01)	693 (0.14)	348 (0.08)
Older than 35	68,087 (16.90)	61,871 (17.02)	37,178 (16.97)	31,588 (16.62)	10,396 (17.94)	8,559 (17.59)	231 (0.20)	125 (0.12)
Ethnic background†								
Western	364,796 (90.54)	329,677 (90.68)	143,677 (65.57)	124,144 (65.31)	45,205 (78.03)	38,508 (68.80)	880 (0.16)	452 (0.09)
Non-Western	38,116 (9.46)	33,891 (9.32)	75,428 (34.43)	65,954 (34.69)	12,730 (21.97)	17,461 (31.20)	219 (0.17)	99 (0.08)
Neighborhood†								
Privileged neighborhood	388,089 (96.32)	350,346 (96.36)	196,659 (89.76)	170,366 (89.62)	53,823 (92.90)	45,425 (93.34)	1,031 (0.16)	518 (0.09)
Underprivileged neighborhood	14,823 (3.68)	13,222 (3.64)	22,446 (10.24)	19,732 (10.38)	4,112 (7.10)	3,240 (6.66)	68 (0.16)	33 (0.09)
Gestational age (wk)†								
Less than 34	2,409 (0.60)		1,702 (0.78)		583 (1.01)		370 (7.88)	
35–36	6,510 (1.62)		4,064 (1.85)		1,206 (2.08)		65 (0.55)	
37	15,203 (3.77)	13,622 (3.75)	9,603 (4.38)	8,468 (4.45)	2,497 (4.31)	2,187 (4.49)	56 (0.21)	51 (0.21)
38–41	368,926 (91.56)	349,946 (96.25)	193,816 (88.46)	181,630 (95.55)	49,585 (85.59)	46,478 (95.51)	548 (0.09)	500 (0.09)
More than 41	9,864 (2.45)		9,920 (4.53)		4,064 (7.01)		60 (0.25)	
Big 4†								
Small for gestational age	18,786 (4.66)	17,089 (4.70)	13,114 (5.99)	11,604 (6.10)	3,081 (5.32)	2,665 (5.48)	71 (0.20)	59 (0.19)
Premature	8,090 (2.01)		5,117 (2.34)		1,547 (2.67)		92 (0.62)	0.00
Low Apgar score	1,692 (0.42)	1,483 (0.41)	1,180 (0.54)	959 (0.50)	289 (0.50)	228 (0.47)	97 (3.07)	86 (3.22)
Congenital Abnormality	4,874 (1.21)	4,366 (1.20)	2,941 (1.34)	2,531 (1.33)	778 (1.34)	655 (1.35)	74 (0.86)	60 (0.79)
Combination Big 4	1,648 (0.41)	693 (0.19)	1,279 (0.58)	453 (0.24)	391 (0.67)	92 (0.19)	458 (13.80)	85 (6.87)
Total Big 4	35,090 (8.71)	23,631 (6.50)	23,631 (10.79)	15,547 (8.18)	6,086 (10.50)	3,640 (7.48)	792 (1.22)	290 (0.68)

NPA, natural prospective approach; PGA, perfect guideline approach. Data are n (%).* Totals may not add up to 100 because of rounding error. † P.001.

Intrapartum and early neonatal mortality was 1,099 of 679,952 (1.62%) in the natural prospective approach women and 551 of 602,331 (0.91%) in perfect guideline approach women. Mortality was lower in women who were multiparous, between 24 and 34 years of age, of Dutch origin, or living in a privileged neighborhood (both natural prospective approach and perfect guideline approach; Table 1). Within the group with intrapartum and early neonatal mortality, Big 4 conditions were found in 792 of the 1,099 deaths (72.1%) in the natural prospective approach women compared with 290 of 551 deaths (52.6%) in the perfect guideline approach group.

In the natural prospective approach population, crude mortality risk was significantly lower for women who planned to give birth at home (relative risk 0.80, 95% confidence interval (CI) 0.71–0.91) and for women with unknown intention (relative risk 0.96, 95% CI 0.77–1.19) compared with those who intended to give birth in hospital (P<.05) (Table 2). All maternal and neonatal risk factors, except living in a deprived neighborhood, showed significant effect sizes in agreement with the expected direction. Mortality was significantly increased in neonates with a Big 4 outcome, especially in those with multiple Big 4 conditions (relative risk 276.6, 95% CI 240.3–318.3).

Table 2. Intrapartum and Neonatal Death 0–7 Days in Women Who Are in Primary Care at the Onset of Labor (Natural Prospective Approach)

				Model 1			Model 2			Model 3		
	Total	Mortality	P	Crude RR	95% CI	P	Adjusted OR	95% CI	P	Adjusted OR	95% CI	P
Intended place of birth			< .05			< .05			< .05			< .05
Home	402,912	594 (0.15)		0.80	0.71–0.91		nie			1.05	0.91–1.21	
Hospital (reference)	219,105	403 (0.18)		1						1		
Unknown	57,935	102 (0.18)		0.96	0.77–1.19		nie			0.77	0.61–0.97	
Parity			< .001			< .001			< .001			
Primiparous	302,489	614 (0.20)		1.58	1.40–1.78		1.67	1.47–1.89		nie		
Multiparous(reference)	377,463	485 (0.13)		1			1					
Maternal age (y)			< .001			< .001			< .001			< .001
Younger than 19	11,939	42 (0.35)		2.43	1.78–3.31		1.80	1.31–2.48		1.67	1.17–2.38	
20–25	74,101	133 (0.18)		1.24	1.03–1.49		1.03	0.85–1.24		0.92	0.75–1.13	
25–34 (reference)	478,017	693 (0.14)		1			1			1		
Older than 35	115,661	231 (0.20)		1.38	1.19–1.60		1.56	1.34–1.81		1.44	1.23–1.68	
Ethnic background			< .001			< .001			< .05			< .05
Western (reference)	571,185	880 (0.15)		1			1			1		
Non-Western	108,767	219 (0.20)		1.31	1.13–1.52		1.32	1.14–1.54		1.21	1.02–1.45	
Neighborhood						< .05						
Privileged neighborhood (reference)	638,571	1,031(0.16)		1								
Underprivileged Neighborhood	41,381	68 (0.16)		1.02	0.80–1.30		nie			nie		
Gestational age (wk)			< .001			< .001						< .001
Less than 34	4,694	370 (7.88)		88.08	77.44–100.18					15.74	12.56–19.72	
35–36	11,780	65 (0.55)		6.17	4.77–7.97					2.11	1.56–2.86	
37	27,303	56 (0.21)		2.29	1.74–3.02					2.26	1.71–2.99	
38–41 (reference)	612,327	548 (0.09)		1						1		
More than 41	23,848	60 (0.25)		2.81	2.15–3.67					2.10	1.60–2.77	
Big 4			< .001			< .001						< .001
Small for gestational age	34,910	71 (0.20)		1.27	1.00–1.62					3.64	2.82–4.69	
Prematurity	14,754	92 (0.62)		12.49	9.90–15.76							
Low Apgar score	3,161	97 (3.07)		21.35	17.28–26.38					53.41	42.55–67.04	
Congenital abnormality	8,593	74 (0.86)		5.68	4.48–7.20					14.53	11.30–18.67	
Combination Big 4	3,318	458 (13.80)		168.85	148.94–191.41					68.17	55.27–84.08	
No Big 4	615,145	307 (0.05)		1								

RR, relative risk; CI, confidence interval; OR, odds ratio; nie, not in equation, Data are n or n (%) unless otherwise specified. Model 1: crude RR. Model 2: adjusted for maternal factors including intended place of birth, parity, age, ethnic background, and neighborhood. Model 3: adjusted for maternal factors and child factors; model 2+ gestational age and presence of Big 4.

The nested multivariable logistic regression analysis showed that in the presence of adjusting maternal factors only (model 2), the intended place of birth had no significant effect on outcome. The maternal factors showed risks similar to the univariable (crude) analysis. The addition of Big 4 case mix adjustment (model 3) showed the intended place of birth to be a significant covariable, yet the contrast of planned home birth (odds ratio 1.05, 95% CI 0.91–1.21) compared with a hospital birth (reference=1) turned out to be nonsignificant. The effect of maternal risk factors was affected to a limited degree by the introduction of the Big 4 case mix.

We repeated the analysis for the perfect guideline approach population (Table 3). The results of the crude analysis were close to the natural prospective approach analysis. However, the effect of ethnic background was considerably stronger in the perfect guideline approach population. In all analyses, the intended place of birth showed a consistent, significant effect on intrapartum and early neonatal mortality, yet the contrast between home and hospital births never reached statistical difference. After Big 4 case mix adjustment, home birth showed a nonsignificant increased risk (odds ratio 1.11, 95% CI 0.93–1.34).

Table 3 Intrapartum and Neonatal Death 0–7 Days in Women Who Are in Primary Care at the Onset of Labor (Perfect Guideline Approach)

			Model 1			**Model 2**			**Model 3**		
	Total	Mortality	Crude RR	95% CI	P	Adjusted OR	95% CI	P	Adjusted OR	95% CI	P
Intended place of birth					< .05			< .05			< .05
Home	363,568	344 (0.09)	0.99	0.83–1.18		1.02	0.85–1.23		1.11	0.93–1.34	
Hospital (reference)	190,098	182 (0.10)	1			1			1		
Unknown	48,665	25 (0.05)	0.54	0.35–0.81		0.54	0.36–0.83		0.57	0.37–0.86	
Parity					< .001			< .001			
Primiparous	257,239	283 (0.11)	1.42	1.20–1.67		1.52	1.28–1.82		nie		
Multiparous (reference)	345,092	268 (0.08)	1			1					
Maternal age (y)					< .001			< .001			< .05
Younger than 19	10,182	13 (0.13)	1.56	0.90–2.71		1.31	0.75–2.30		1.29	0.73–2.26	
20–25	65,067	65 (0.10)	1.22	0.94–1.59		1.11	0.84–1.45		1.08	0.83–1.41	
25–34 (reference)	424,915	348 (0.08)	1			1			1		
Older than 35	102,018	125 (0.12)	1.50	1.22–1.84		1.66	1.34–2.04		1.50	1.22–1.85	
Ethnic background											
Western (reference)	507,063	452 (0.09)	1								
Non-Western	94,717	99 (0.10)	1.17	0.94–1.46		nie			nie		
Neighborhood											
Privileged neighborhood (reference)	566,137	518 (0.09)	1								
Underprivileged Neighborhood	36,194	33 (0.09)	1.00	0.70–1.42		nie			nie		
Gestational age (wk)					< .001						< .001
37	24,277	51 (0.21)	2.43	1.82–3.24					2.51	1.87–3.37	
38–41 (reference)	578,054	500 (0.09)	1						1		
Big 3					< .001						< .001
Small for gestational age	31,358	59 (0.19)	4.03	3.04–5.35					4.28	3.22–5.68	
Low Apgar score	2,670	86 (3.22)	69.05	54.28–87.84					71.52	55.87–91.56	
Congenital abnormality	7,552	60 (0.79)	17.03	12.88–22.53					16.76	12.64–22.23	
--Combination Big 3	1,238	85 (6.87)	147.19	115.97–186.80					159.49	123.86–205.38	
No Big 3	559,513	261 (0.05)	1						1		

RR, relative risk; CI, confidence interval; OR, odds ratio; nie, not in equation. Model 1: crude RR. Model 2: adjusted for maternal factors including intended place of birth, parity, age, ethnic background, and neighborhood. Model 3: adjusted for maternal factors and child factors; model 2+ gestational age and presence of Big 4.

Figure 3 describes the crude mortality risk (left Y-axis) and the Big 4-adjusted home birth mortality index (right Y-axis), in which each dot represents the mortality risk results after the group listed on the X-axis has been excluded from the population.The crude mortality (round and diamond shaped line) initially shows a difference in favor of home delivery (home: 0.18% compared with hospital: 0.22%), which converges toward a much lower average level if premature births are excluded. Further exclusions lower the crude mortality rate, leaving the small difference almost unaffected. The mortality index (squared shaped line) shows a distinct change from an initial level of approximately 100% toward approximately 120% after exclusion of the pregnancy duration less than 36 weeks. Combined with the similar crude mortality rates of home and hospital delivery from then onward, this suggests setting safety for the risk groups still included, ie, all groups to the right of the exclusion label “pregnancy duration less than 36 weeks.” For example, after exclusion of pregnancy duration more than 41 weeks (perfect guideline approach group), the adjusted mortality index is 120%, which is slightly larger than the nonsignificant regression result of 111% (Table 3).

Discussion

Planned home birth within the Dutch maternity care system has a lower crude mortality rate compared with a community midwife-led planned hospital birth. However, after case mix adjustment, the relation is reversed, showing a nonsignificant increased perinatal mortality rate of home birth. Excess setting-dependent mortality may arise at home if risk conditions are present or emerge at birth, yet remnant confounding by an indication effect (Big 4 conditions are more prevalent in the hospital) and low mortality prevalence limit statistical proof. Authors favoring a comparison of settings among “suitable” home births only (perfect guideline approach) usually exclude risk conditions with a potential setting effect. This mechanism may explain the apparently contradictory results from previous studies [1,5,7,10–15,17,18].

A strength of this study was the size of the study population, which reflects the complete Dutch experience from 2000 to 2007. The amount of missing explanatory data is negligible; mortality data have been shown to be complete. No annual trends are observed in the relations shown, except for a minimal gradual decrease in total perinatal mortality [3].

Our case mix adjustment proved to be essential. The assumption of comparability across home compared with hospital populations appeared not to be justifiable judging from the unequal prevalence of Big 4 conditions. These primarily have their origin in early negative fetal conditions and the disadvantaged genetic background of the parents. Only in the case of a low Apgar score, one may argue that the midwifery management during labor might influence its occurrence, whereas a management role in small for gestational age, spontaneous prematurity, and congenital anomalies at that stage is unlikely. We decided to include low Apgar cases assuming the role of management to be small compared with the disadvantage of the home setting once a child with a persistent low Apgar score is born. Thus, our point of departure starts from the risk challenge represented by Big 4 at the onset of labor and investigates whether setting matters in terms of prognosis. The mechanisms underlying the apparent favorable selection for home birth are still to be elucidated. Self-selection by pregnant women can coincide with implicit or explicit selection by the midwife who may tend to refer to the hospital if she feels uncomfortable with the risk level at home. The difference in the ratio home:hospital community midwifery-led deliveries among the four largest Dutch cities suggests the presence of substantial professional and setting effects. In Amsterdam and Utrecht, the ratio is 2:1, and in Rotterdam and the Hague, it is 1:2.

Several study limitations merit discussion. Although an improvement compared with previous studies, our case mix control is still incomplete because Big 4 is unrelated to 15% of deaths. In the perfect guideline approach population, this proportion is even 48%. Thus, we cannot rule out remnant confounding by indication because little is known of the factors underlying choice of setting.

Randomized controlled trials would be the superior design to address our research question. However, when home birth was part of a trial, participation was hampered [24] and selective participation was introduced, which limited generalizability. Moreover, if following one's choice affects outcome, estimates of setting effects are also biased [24–26]. Despite their shortcomings, in particular when considering the difficulty in overcoming the confounding by indication phenomenon, observational studies such as ours are therefore invaluable. A comparison with a 100% gynecologist hospital-based system is not included. The data from an otherwise very similar country such as Flanders [27] suggest that more favorable results may be expected in low-risk women in general from a hospital-based system. In Flanders, perinatal mortality is approximately 33% less than in The Netherlands, whereas the cesarean delivery rates show little difference.

This study primarily focuses on the disadvantages and neglects the claimed benefits when comparing planned home compared with planned hospital births. However, studies accessing a mother's opinion show that preventing these disadvantages easily outweighs the claimed benefits [28].

Our results appear compatible with most other reports, although previous studies show conflicting results. Planned home births attended by registered professional attendants are not associated with an increased risk of adverse perinatal outcomes in cohort studies in North America [7,12], the United Kingdom [14], Europe [5,11,15,17], Australia [29], and New Zealand [30]. In contrast, other cohort studies have shown a higher risk of perinatal mortality in planned home births compared with planned hospital births [10,13,16,18,30]. All studies are limited by voluntary submission of data [7,8,11–14,17,31,32], nonrepresentative sampling [5,13], lack of appropriate comparison groups [7,12,15,29], or insufficient statistical power [5,17,29,32]. A critical factor, as our study shows, is the in retrospect exclusion of unplanned and unsuitable home births from analysis [18].

Our results partly agree with those of Kennare et al [30] who found higher standardized perinatal mortality ratios among planned home deliveries after limited adjustment (birth weight, gestational age). Our results also partly agree with the meta-analysis by Wax et al [9]: differences in the prevalence of small for gestational age, premature births, and congenital anomalies seem equally present in planned home compared with hospital births. They reported a twofold higher neonatal mortality rate but no increase in perinatal mortality. These results are in agreement with Figure 3 in which the fetal death subgroup does not benefit from setting safety. It should be noted that the study of Wax et al received methodological criticisms [33–36] most notably the inclusion of the study of Pang and the exclusion of the study of De Jonge et al. Our conclusions apparently contradict those of De Jonge et al who concluded equal intrapartum and early neonatal outcome

of planned home birth compared with hospital birth in apparently the same population [15]. However, the point of departure is not the same. Of our two comparisons of home delivery compared with hospital delivery, one parallels the approach of De Jonge et al. Our principal approach (natural prospective approach) compares neonatal mortality in the actual populations delivering at home compared with the hospital, whereas the approach of De Jonge et al compares neonatal mortality in a hypothetical group resembling our perfect guideline approach population. Our adjustment procedure, however, goes further than the maternal factor adjustment of De Jonge et al.

From our study, we conclude that planned home birth, under routine conditions, is not associated with a higher intrapartum and early neonatal mortality rate. However, in subgroups, additional risk cannot be excluded.

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Chapter 3.3

A newly developed scavenging system for administration of nitrous oxide during labour: safe occupational use

Jacoba van der Kooy
Hanneke de Graaf
Zita Kolder
Karel Witters
Elaine Fitzpatrick
Hans Duvekot
Ilse Dons-Sinke
Eric Steegers
Gouke Bonsel

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Abstract

Objective Nitrous oxide (N2O) is routinely used as an analgesic in obstetrics during labour. Epidemiological studies have linked chronic occupational exposure to N2O to specific health problems, including reproductive risks. Occupational exposure limits (OELs) allow the use of N2O once appropriate preventive and safety measures have been taken. We assessed the effectiveness of a scavenger system (Anevac P-system®, Medicvent Heinen & Löwestein Benelux, Barneveld, the Netherlands) applied in N2O administration during labour in a midwifery-led birthing centre in the Netherlands.

Methods After informed consent, non-pregnant midwives were trained to administer N2O. N2O was delivered as a 50 : 50 mixture with oxygen and was self administered by the patient. The scavenging device, containing a double mask and a chin mask, was connected to the local evacuation system vented outside the building. Data on the 8-h time-weighted average (8-h TWA) as well as the 15-min TWA (15-min TWA) were obtained.

Results Thirteen patients were included. Six patients were included in the first study period. In this period the 8-h TWA was not exceeded, however, in all patients, the 15-min TWA occasionally exceeded the OELs. After four additional measures, seven patients were included. After implementation of these measures, the 8-h TWA and 15-min TWA never exceeded the OELs. System leakage was not observed during both study periods.

Conclusion The Anevac P-scavenging system during N2O analgesia in labour prevents exceeding OELs in professional workers. The scavenging system appeared acceptable and effective, and can be considered in hospital settings that use N2O as analgesic during labour.

Introduction

Nitrous oxide (N_2O) as analgesic is routinely used in dentistry, in the emergency room and during labour. It combines several advantages compared with intravenous alternatives like propofol or, in obstetrics, epidural analgesia, which makes it a preferred option in specific contexts [1,2]. Internationally, a wide variety in N_2O application as well as a wide variety in imposed safety regulations is observed. This may reflect uncertainty about how to apply N_2O in a truly safe manner.

Epidemiological studies have linked long-term occupational exposure to N_2O with reproductive risks such as spontaneous abortion, congenital anomalies and reduced rates of fertility [3-12]. Also, adverse effects on the haematological and nervous system have been described [4,13-16].

The recognition of the potential hazard to professional workers who are routinely exposed to N_2O elicited the introduction of occupational exposure limits (OELs) in different countries [17]. Governmental legislation enforces adherence to these OELs.

An OEL is expressed as a health-based OEL, an 8-h time-weighted average (8-h TWA). In some countries, a short-term exposure limit, 15-min TWA (15-min TWA), has been adopted. In the Netherlands, the 8-h TWA for N_2O is set on 152 mg/m^3, whereas the 15-min TWA is set on 304 mg/m^3. Studies have already shown that midwives are regularly exposed to higher levels of N_2O than permitted [18-20]. Furthermore, studies showed that the need for anaesthetic waste gas scavenging is of great importance in order not to exceed the OELs [20-23]. Strict University Hospital regulations in the Netherlands demand exposure levels to medical professionals that are less than or equal to only 25% of the recommended OELs (38 mg/m^3 respectively 76 mg/m^3). The use of N_2O has declined within obstetric care in the Netherlands because no scavenger system is available in standard settings.

In this study, we assessed the practical appliance, patient convenience and effectiveness of a scavenger system (Anevac P-system®, Medicvent Heinen & Löwestein Benelux, Barneveld, the Netherlands) given to women who received N_2O during labour in a midwifery-led birth centre in the Netherlands. This study was undertaken to apply for approval of the Dutch National Institute for Occupational Safety and Health.

Methods

The study protocol was approved by Medical Ethics Committee. This prospective observational intervention study was conducted during October 2009 and February 2010.

All midwives ($n = 15$) working in a midwifery-led birth centre were invited to participate and were asked to provide their written consent, unless they were pregnant or possibly pregnant or suffering from a known vitamin B deficiency. After informed consent was given, they were trained in the administration of N_2O and the use of the new scavenger system.

During the study period, patients were informed about the option for N_2O analgesic during labour and were asked to provide verbal consent. They were not permitted to use N_2O when acquaintances attending the birth were pregnant or possibly pregnant. In that case, they were offered another form of analgesia and were referred to the gynaecologist. If anyone attending the delivery was suffering from a vitamin B12 deficiency, they were excluded from the study because of possible adverse effects on the haematological system.

N_2O analgesic was administrated as a 50:50 mixture with oxygen, known as Relivopan® (Linde Gas, Benelux, Schiedam, the Netherlands). It was delivered from a portable N_2O gas cylinder using a pin index system (Linde Gas Benelux, Schiedam, the Netherlands). N_2O was self administered by the patient through a double mask containing a Carnét Demand valve (Medicvent Heinen & Löwenstein, Groningen, the Netherlands).

The scavenging device contained a double mask and a chin mask (Anevac P-system®); it was connected to the local evacuation system vented outside the building. The evacuation rate of the scavenging device was tested with an in-line flowmeter and was found to produce 34 m^3/h (17 m^3/h through the double mask, 17 m^3/h through the chin mask). (Fig. 1)

Figure 1. Scavenging device (photo with written permission of the patient).

(1) demand valve, (2) double mask and (3) chin mask

Room air-exchange rates were 6 air changes per hour for each individual delivery room. The patient was instructed to use the double mask and chin mask during the first stage of labour. Entering the second stage of labour, both the double mask and chin mask were removed after discontinuation of N_2O administration. During the first stage of labour, the use of the scavenging system was thoroughly observed to identify risk factors for possible leakage. Apart from the initial instruction, little correction during administration was given to obtain results close to practice.

Data on the 8-h TWA as well as information on 15-min TWA were obtained from the start of N_2O administration in the first stage till the third stage of labour. This was done to investigate N_2O levels while administrating and after discontinuation of administration. For the 8-h TWA exposure, a N_2O diffusion sampler was clipped to the midwives' lapel to keep it as close to the breathing area as possible. Diffusion samplers are generally designed to sample over a period of time for the determination of average concentrations. In contrast to active sampling, the transport of the contaminant molecules is achieved by diffusion processes, and not by using a pump. Contaminants from ambient air are adsorbed by the sorption agent (http://www.draeger.com). After sampling, the tubes were analysed with gas chromatography analysis and mass-spectrometry detection. They were asked to record the length of the shift and how long they spent on the labour suite. The measurement of the 15-min TWA was obtained by the 1312 Photoacoustic Multi-gas Monitor [(LumaSense Technologies Inc, Santa Clara, California, USA) detection limit for N_2O is 0.06 mg/m^3] which absorbs an air sample once every 60 s and directly analyses the concentration of N_2O. This sensitive technique allows for direct measurement of high-risk acts and system leakage. This technique was in permanent use during all observations. (for a more detailed description, see: http://www.lumasenseinc.com/EN/products/gas-monitoring-instruments/gas-monitoring/technical-information-of-gas/photoacoustic-detection-pas.html)

Patients as well as health-care workers/professionals were asked to fill out a questionnaire about the practical appliance and convenience of the administration of the scavenger system.

Interpretation of the exposure assessment was based upon 25% of the set OELs. Subsequently, we used the cut-off value of 38 mg/m^3 (20 ppm) resp. 76 mg/m^3 (39 ppm).

Having analysed the results of the first five patients, additional improvements to ensure maximum system effectiveness were performed in the second study period in February 2010. These included: (1) discontinuation of N_2O if the patient continued to be restless after 15 min, (2) permanent adequate position of chin mask during first and for at least 20 min in the second stage of labour, (3) extra 100% oxygen for 5 min, administered after discontinuation of N_2O administration when entering the second stage of labour and (4) increased evacuation rate (34 l/min) of the chin mask throughout second stage.

Results

In October 2009, six patients were included. One patient was excluded because N_2O was only given for 15 min. About 23 patient hours were continuously and intensely monitored; in 19 of 23 h, N_2O was actually administered. Analyses are shown in Table 1. In this study period, the 8-h TWA was not exceeded, however, in all patients, short-term peaks were observed. The 15-min TWA was exceeded when the chin mask was either not accurately positioned or was removed by the restless patient. Exceeding of the 15-min TWA was also noted during second stage after the discontinuation of N_2O when the chin mask was removed in agreement with protocol in the first study period, because the protocol prescribed the use of the scavenging system only while administrating N_2O.

Table 1. Results of the first study period in October 2009

Patient	Total time N2O administration (min)	Average occupational exposure (mg/m3) measured over total time	8-h TWA (mg/m^3)[a]	15-min TWA (mg/m3) only given when exceeding the OELs	Comments
1	180	35.0	13	170 231 --	Chin mask was not accepted. Referred to gynaecologist for other analgesia.
2	275	20.2	12	115 90 161	Chin mask removed when entering second stage of labour.
3	250	13.5	7	170 -- --	Chin mask removed when entering second stage of labour.
4	195	38.2	16	214 -- --	Patient restless, extremely vocal. Referred to gynaecologist for other analgesia.
5	207	31.5	14	101 -- --	Chin mask removed when entering second stage of labour.

[a] [Average occupational exposure (mg/m^3) measured over total time]/{(8*60)/[Total time N2O administration (min)]}. N2O, nitrous oxide; TWA, time-weighted average; OELs, occupational exposure limits.

After introducing the earlier-described improvements, seven more patients were included in February 2010. Two of these were excluded from the analysis because they remained restless after 15 min of N_2O administration. In this period, a total of 21 h (over five patients) was continuously observed. Within these 21 h, N_2O was given for 16 h. In the second study period, the 8-h TWA as well as the 15-min TWA were not exceeded. In this period, one control patient was included, in whom no scavenging was used. In this patient, both the 8-h TWA and the 15-min TWA substantially exceeded the OELs. Analyses are shown in Table 2.

Table 2. Results of the second study period in February 2010

Patient	Total time N2O administration (min)	Average occupational exposure (mg/m3) measured over total time	8-h TWA (mg/m^3)[a]	15-min TWA (mg/m3) only given when exceeding the OELs	Comments
7	186	12.0	5	No peaks observed	Oxygen for 5 min and chin mask continually worn.
8	250	26.9	14	No peaks observed	Oxygen for 5 min and chin mask continually worn.
9	195	23.8	10	No peaks observed	Oxygen for 5 min and chin mask continually worn.
10	135	21.7	6	No peaks observed	Oxygen for 5 min and chin mask continually worn. Referred to gynaecologist due to failure to progress.
11	188	15.9	6	No peaks observed	Oxygen for 5 min and chin mask continually worn
12	203	1582	663	Concentrations exceeding 76 mg/m3 continually	Control patient, no scavenging usedNo system leakage was found during both study periods.

[a] [Average occupational exposure (mg/m3) measured over total time]/{(8*60)/[Total time N2O administration (min)]}. N2O, nitrous oxide; TWA, time-weighted average; OELs, occupational exposure limits.

Equipment was found to be user-friendly by both patients and caregivers. After instruction to the patient, the 'on demand' administration of N_2O was found to be convenient. Only one patient removed the chin mask. The remaining patients showed no discomfort while using the mask.

Discussion

This study stresses the importance of using a scavenging system containing a double mask and chin mask and applying it with the four additional improvements to improve system effectiveness. It shows that the 8-h TWA and the 15-min TWA are met by the use of the Anevac P-scavenging system while administrating N_2O during labour. In addition, the introduction of four additional improvements increased system effectiveness. Limitations of the study include that the Anevac P-scavenging system was tested in the continuous presence of a health, safety and environment specialist. This may lead to a higher compliance to the study protocol. Protocol compliance should therefore be watched closely during and after implementation. A possible second limitation is the relative small number of patients included. Despite this, observations were performed thoroughly, including a sensitive technique which allowed for direct measurement of high-risk acts for the spilling of N_2O. The results of our qualitative evaluation of the multigas monitor, as well as the systemic evaluation and documentation suggest that the administration of N_2O should be discontinued when the patient remains restless after 15min or when no adequate position of chin mask is reached. To realize the expected effect of N_2O, a small 'run-in' period of 15min is needed, due to the instruction to the patient and the correct procedure to administer N_2O. When this state is not reached within 15min, it is highly unlikely that it be will with a longer 'run-in' period and is therefore likely to exceed the OELs.

After entering second stage of labour, saturated oxygen (100%) should be inhaled for 5min, and the chin mask should be worn continuous, with an increased evacuation rate (34l/min). Post-operative oxygen is commonly given to prevent hypoxaemia in patients and to wash out anaesthetic gases [24]. Studies showed that the need for anaesthetic waste gas scavenging during labour is of great importance in order not to exceed OELs [20-23].

Heath et al. [20] found average concentrations of 52 mg/m^3 with the use of a scavenging system, compared with 297 mg/m^3 where none was used. Munley et al.[22] found the same results seeing to lower exposure levels when a scavenging system was used.

In our study, the 8-h TWA concentrations ranged between 12.0 mg/m^3 and 38.2 mg/m^3. This it relatively low compared with others. Westberg et al. [21] found concentrations ranging between 2.5 mg/m^3 and 260 mg/m^3. After comparing a simple face mask with a double mask, they considered that their results favour the use of the double mask. The same result was seen by Chessor et al [23].

Comparing the use of a simple face mask with double mask, the observed exposure levels varied between 40 mg/m^3 and 216 mg/m^3 (average 125 mg/m^3) and 10 mg/m^3 and 306 mg/m^3 (average 72 mg/m^3), respectively. In addition, they highlighted one of the main difficulties with scavenging systems when used in labour and delivery, being under patient control, the mask is most frequently held at a distance too far from the face to allow scavenging of exhaled breath. Both these results confirm our findings on the use of the double mask and the relevance of the use of the chin mask. Newton et al. [18] compared exposure levels in two buildings; an older building where levels varied between 32 mg/m^3 and 2071 mg/m^3 and in a more modern facility comparable with ours, where levels varied between 14 mg/m^3 and 172 mg/m^3. This study might underline the importance of a good ventilation system.

Despite the use of scavenging systems, OELs are still exceeded in these studies [20-23]. This stresses the importance of using a scavenging system containing a double mask and chin mask and applying it with the four additional improvements to improve system effectiveness. Midwives must be trained regarding these improvements, understanding the reasons for implementation. To ensure that the use of N_2O as an analgesic during labour is continued, scavenging equipment is required. This scavenging system turns out to be practical and effective and should therefore be considered in clinics that use N_2O during labour.

After presenting the data, approval was granted by the Dutch National Institute for Occupational Safety and Health.

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Part IV

General discussion

4.1 Preamble

The studies reported in this thesis consistently showed independent effects of three social determinants on perinatal and maternal outcome; i.e. ethnicity, socio-economic status (SES) and living in a deprived neighbourhood.
As women with non-indigenous background and with low socio-economic status are substantially overrepresented in deprived neighbourhoods, the crude geographical differences in perinatal mortality and - morbidity are sizable and thus easy to observe. These differences can be seen at two levels: comparing the four large cities with other urban and rural areas, and within the large cities comparing neighbourhoods.
While most studies - as ours - focus on mortality, we demonstrated similar trends for fetal growth restriction (born small for gestational age) and premature birth.

As the Netherlands is an egalitarian society with universal access to education and (perinatal) health care, such differences in perinatal and maternal adverse outcomes would not have been expected and may be judged as unfair. Still, our findings are in line with reported inequalities in adult health, in particular between persons living in the large cities and elsewhere in the Netherlands. They also confirm the results of international perinatal research. While the general level of perinatal health in some countries may be better (e.g. the UK), perinatal and maternal inequalities do persist.

Another factor acting at the non-individual level is the organization of obstetric care. We showed the relevance for perinatal outcome of two organisational features: 7/24h hospital organisation and size and, to a lesser extent, birthplace setting in community midwifery care (home-hospital) which is a typical feature of the Dutch system. Moderately small maternity units of non-tertiary hospitals with between 750 and 999 deliveries per year show an increased risk of perinatal adverse outcome. In non-tertiary hospitals, perinatal mortality during the evenings and nights was higher than in the daytime. In tertiary centres it was higher at night time only, and generally effects were less.
The study about planned home birth versus planned hospital birth, among women starting the delivery under midwife's supervision, suggests some non-significant increased perinatal mortality in case of home birth, can be attributed to infrequent risk conditions that are present or emerge at birth. Remnant confounding of indication effects (Big 4 conditions [1]) are more prevalent among the hospital births under supervision of the midwife) and low mortality prevalence limited statistical proof.

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[1] BIG 4 conditions are indicated by the following outcomes measured as birth prevalence: congenital anomalies, fetal growth restriction (small-for-gestational age, SGA), preterm birth (PTB) and a low Apgar score.

4.2 Strengths and limitations of the studies.

Strengths and limitations of the separate studies in this thesis have been described in the previous chapters. This section provides a more general discussion of the methodological considerations and the implications of our findings for the future organisation of perinatal care and research.

4.2.1 Strengths and limitations of the studies about geographical differences in perinatal and maternal adverse outcomes.

A major strength of our studies is the level of detail and the sample size, which allowed to investigate the interaction between ethnicity and socio-economic status and to investigate the presence of an additional neighbourhood-effect (part 2). The collected perinatal outcome data from the Netherlands Perinatal Registry are the primary key factor. This registry is an integrated database of almost all pregnancies of 20 weeks and above in the Netherlands, with a standard set of data collected by (referring) midwives, obstetricians and paediatricians [1]. This dataset is less informative on maternal health. In addition we made use of data on maternal deaths registered in the database of the Dutch Maternal Mortality Committee (MMC) in the period 1993–2008. These cases are reported by obstetricians, midwives, and general practitioners, using standard forms. Furthermore we used maternal morbidity data prospectively collected in a large nationwide cohort study, the LEMMoN study [2]. The completeness of these datasets and assumed high quality for our purposes represents an important strength of our studies.

A second strength is our attempt to separate the roles of ethnicity, socio-economic class, and geographical area, and the parallel investigations of perinatal and maternal outcomes. The striking similarity of epidemiological patterns may add credibility to findings (in particular in maternal mortality) which suffer from lack of power due to the low prevalence of maternal mortality in general.

Making use of the national perinatal database also implies an important limitation. The set of individual risks contained is limited. For example, tobacco and alcohol abuse as well as the preconception use of folic acid are not recorded. The same holds for individual SES indicators such as educational level and family income, for which we used a zip code based proxy.

Another limitation refers to the classification of ethnicity and the place of residence. Any classification of ethnicity bears pros and cons, and the most obvious weakness of the one underlying the PRN registry is the combined category for Moroccan and Turkish women. We usually simplified the classification to a dichotomous one. In case of issues related to specific migrant groups (e.g. hypertensive disease in pregnancy in Surinamese Creoles) this can be a disadvantage. Place of residence can be subject to misclassification, as can be proxy variables based on this variable. First of all place of residence (actually 4 digit zip code) is recorded at the time of delivery, through the address provided by the women. The address may however not be valid at the time of recording - as in our experience is frequently the case in deprived and migrant groups, and if used as antenatal exposure variable, it may not be valid if women have moved house during pregnancy.

Furthermore, we used one available cross-sectional dataset for the translation of zip codes into socio-economic status. The socio-economic level of an area, however, may change over time. Finally, the general limitation of an aggregated proxy applies here: within a 4 digit zip code area heterogeneity may exist, in particular in large cities. This is not a source of bias, rather it limits power.

4.2.2. Strengths and limitations of the studies about the relation between organisational features and perinatal adverse outcomes.

We surveyed all 99 maternity units by a standard questionnaire on organisational factors. This information, while valuable and - as it appears - predictive, is subject to two weaknesses.

Firstly, these exposure data were used to explain outcome in a fixed in time dataset, while organisational features may have changed. This may have decreased power. Also, these data are at the hospital level and do not reflect the detailed actual staffing levels just before and during each individual delivery.

Another limitation was the use of the hour of birth as a proxy for the time of delivery effect, which implicitly defines this phase to be the time window of highest vulnerability for organisational effects. One may argue that phase starts to be critical as early as 1 hour before delivery. When we tested the effect of a different time definition (all time period definitions minus 1 hour), the results were unaffected, but other choices for the exposure window may be defined.

4.2.3 Implications for clinical practice and further research.

Researchers and politicians alike tend to ascribe the perinatal outcomes inequalities between cities/deprived neighbourhoods and other geographical areas in the Netherlands to the overrepresentation of migrants in deprived neighbourhoods. Our studies, however, reveal that while the average migrant women is worse off compared to the native Dutch women, it is rather the native Dutch pregnant women living in the most deprived neighbourhoods who shows the highest risk of adverse perinatal outcome. This finding could be explained by selection: only those native Dutch women who are unable to migrate upwards will continue to live in a deprived neighbourhood, whereas non-Western women move away when their socio-economic status improves. If truely individual socio-economic and additional data would be available this explanation could be tested.

Maternal health inequality is additionally strongly influenced by the prevalence of medical and psychiatric conditions. This finding can be explained by differential access to medical care, which may play a stronger role in maternal morbidity and mortality inequalities as compared to obstetric and neonatal care differences for foetal and neonatal outcome. This is an opportunity lost: maternal conditions - if recognized - are to a larger extent preventable or even treatable according to current care standards.

The relatively high prevalence of adverse perinatal outcomes in the group of native Dutch women, living in a deprived neighbourhood calls for new approaches to obstetric care.

Specific professional education programs for this group are needed. Also professional education in general medicine for non-Western women should be advocated to prevent maternal mortality and morbidity.

On the other side, more information should be provided to migrant women and women of very low socio-economic class about the consequences of an adverse lifestyle and of known medical conditions during pregnancy. Methods should be employed to overcome the current barriers of language, culture and social environment.

It is at this stage difficult to define straightforward clinical implications to decrease the remaining area-based inequalities as their background is unknown.

1. Detailed risk assessment during pregnancy including non-medical factors should elucidate the presence of additional individual risk factors which may be overrepresented in deprived neighbourhoods. Genetic factors belong to this explanation.
2. Sofar care factors were studied rather from the provider's perspective than from the woman's perspective. In this context health care provision (access, quality) should be studied to reveal area based differences.
3. In depth research should be dedicated to two true non-individual area-based factors: social structure and the physical environment. Social structure refers to social networks, cohesion (vs. isolation), and experienced safety. Physical environment refers to noise, air pollution, and seasonal effects.

In absence of more data we cannot at this stage suggest interventions at the area level.

With regard to organisational factors some clinical implications seem valid. The higher prevalence of adverse perinatal outcomes in the hospitals during evenings and nights might be prevented by 24-hour in-house continuous availability of senior, experienced obstetricians, neonatologists and anaesthesiologists. The introduction of senior staff in (paediatric) IC units and maternity units has been shown to decrease complications [3-5]. Financial barriers, however, are present, as availability costs are excluded from the current hospital tariff system. The solution of centralisation might solve efficiency and staffing of emergency care problems, but on the other hand carries with it other disadvantages.

4.3 General reflection on recent discussions and developments in Dutch obstetric care.

Reduction of the identified inequalities in perinatal and maternal outcomes are included in the recommendations of the steering group “Pregnancy and Birth”, in letters of the Minister of Health, the health insurers, the national program “Healthy pregnancy of All” and the programs of the recent regional obstetric consortia [6-10]. The Signalementstudy Pregnancy and Birth 2010 [11] makes clear that under the current obstetric care system the four major causes of perinatal mortality often are not timely recognized. For example: in 40% of births of a growth-restricted child antenatal care was performed and delivery started under responsibility of community midwives. Other research demonstrated that perinatal mortality in a low-risk group may exceed that in a high-risk group [12]. This goes to show that Rottinghuis’s statement in 1951 is still relevant; delivery should not be considered normal until it has been completed [13].
In response of these signals the steering group Pregnancy and Birth advised shared responsibility for the pregnant women by community midwives and obstetricians, specific and intensive focus on disadvantaged women and 7/24 hours availability of the caregivers. This advice has caused large movements in the field. Mainly due to the formation of formal obstetric partnerships (Verloskundige Samenwerkings Verbanden, VSV's) and in some cases birth centres, the distance between the various obstetric health care providers is reduced. Also in the field of another form of risk selection some projects started, but it remains to be seen whether this selection through a care-pathway commitment is feasible.
The Dutch Healthcare Authority (Nederlandse Zorgautoriteit, NZa) and health insurers support this movement by their advice to the Minister of Health for introducing of integrated financing of obstetric care in 2016, replacing the current separate funding [14]. However, they will not reimburse 24-hour availability in hospitals. Caution is required to already conclude that the above described actions have led to improvements. The Minister of Health concluded in December 2012 – referring to the NZa market scan - that the quality of care associated with pregnancy and birth is greatly improved, because perinatal mortality had declined since 2004 [15]. However in 2010 the Perinale Audit Nederland (PAN) [16] found that obstetrical care should be regarded substandard in 37% of cases and that in 42% of cases the policy of ‘wait and see’ was inappropriate; (a) insufficient alertness upon abnormalities on the cardiotocogram, or (b) too little response on suspicion of intrauterine growth retardation and overdue pregnancy.

4.4 The recent Dutch perinatal mortality figures compared with those of other European countries

In the Netherlands, perinatal mortality from 22 weeks gestational age up to and including 1 week after birth has dropped by 23%, from 12.2‰ in 2001 to 9.4‰ in 2008, while perinatal mortality from 37 weeks onwards has dropped by 39% in this period, from 651 cases (3.8‰) to 367 (2.3‰) [16]. Now, is this reason enough to assume that we as a country have fallen into step with other European regions or countries such as Flanders, Sweden, Finland and Norway? The answer must be no; for according to PAN the Netherlands is still lagging behind the other European countries [16]. The drop in perinatal mortality does, however, compare well with that in Ireland [17], i.e. from 8.6‰ in 2001 to 6.8‰ in 2008 (21%) and that in the UK [18], i.e. from 8.3‰ in 2000 to 7.5‰ in 2008 (10%). From these comparative figures we may conclude that although there is a decline in Dutch perinatal mortality, and one may assume perinatal morbidity, all parties should remain their ambitions to improve Dutch midwifery and obstetrics.

4.5 Final conclusions

Both patient-bound characteristics as well as geographical and organisational features are causes of the large differences in perinatal and maternal outcomes in the Netherlands. Important effects are noticed of hospital organisational characteristics. One may assume perverse financial stimuli in the healthcare funding system to be involved as well, within the context of the historical compartmentalisation of primary and secondary/tertiary care due to the principle of early risk selection. Equal access to proper midwifery and obstetrical care in the Netherlands will only be achieved after these barriers for both the expectant mothers and the professional disciplines have been removed.

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Part V

Summery and samenvatting

Summary

The focus of this thesis is on the achievements of perinatal care in the Netherlands, in terms of the outcomes for mother and child. These outcomes are quite valuable for the monitoring of quality of care. Furthermore, analysing possible differences may indeed alert us, so it appears, to motivating factors for quality improvement in practice.

The objective of this PhD-study was to determine to what extent the expectant mother's place of residence, her ethnicity, the organisation of (clinical) care and the (planned) setting for the delivery under the supervision of the community midwife affect outcomes for mother and child. Outcomes studied included perinatal mortality, perinatal morbidity (assessed by premature birth (< 37 weeks), growth retardation (birth weight < P10), low Apgar score (< 7 at 5 min postpartum), birth defect), admission to the neonatal intensive care unit, maternal mortality and severe maternal morbidity (uterine rupture, eclampsia, maternal haemorrhage and maternal intensive care admission).

Although important, outcome measures like the risk of perinatal mortality or need of intensive care treatment for the baby as such do not fully reflect the quality of the care delivered. After all, biological, medical and operational variables are in constant interplay, and the magnitude of the perinatal mortality risk does not necessarily point at a potential improvement opportunity. Perinatal outcomes, for that matter, are determined by patient factors (age, ethnicity, parity, lifestyle, socio-demographic characteristics), obstetric history, non-obstetric comorbidity, organisational factors (type of practice or hospital, size of the organisation, staff composition, training courses, 24-hours staffing), degree of interaction between links in the care chain (referral), and provider factors (knowledge, experience, skill). Generally, drawing a justified conclusion on the contribution of a variable to quality of care is not possible before having corrected for non-care factors. This is also called case-mix correction; and its success depends on what has been measured and recorded as well as on achieving the right balance between over- and under correction. In this thesis we therefore applied case-mix correction using different data sources and performed different statistical (regression) methods.

The influence of (unhealthy) living conditions on pregnancy outcomes is a major theme in this thesis. Research has shown large adult health disparities, and raising the overall lower health status of the population in urban areas to the national average is standing policy. So far, however, perinatal health disparities have received little attention. This is unwanted because by now we know that a bad start of life may have considerable effects on health in later life. For example, premature and small for gestational age children more often show learning and behaviour disorders and are at higher risk of diabetes and cardiovascular disease at adult age.

In a historical perspective the awareness of the importance of living conditions is not new. The first part of this thesis describes the history of obstetric care in the Netherlands with special attention to birth centres. It appears that such centres for over a century have been providing care to pregnant women in difficult social and/or economic circumstances. The past history therefore lends perspective to the findings from this thesis.

The complexity of changes in the Dutch obstetric care system is illustrated through several debates. Changes are hindered by ideological factors on the one side (pregnancy is not a disease) and the financing structure on the other side (compartmentalisation). In both aspects the system in the Netherlands deviates from that in most of the developed countries. The current Dutch obstetric structure has thus both a substantive and a financial background. Apart from this historical perspective the first part of this thesis further examines the most important social determinants (life style, employment and socio-economic status) with their parallel consequences for mother and child.

Part 2 shows the results of studies into geographical differences in perinatal and maternal outcomes. In the Netherlands we find large differences in both perinatal and maternal health and consequently the risk of a suboptimal pregnancy outcome. The study in chapter 2.1 describes the differences in perinatal health between the four largest Dutch cities, deprived neighbourhoods and other areas in the Netherlands. We used singleton pregnancy data of the linked professional database from the Netherlands Perinatal Registry over the five-year period 2002 – 2006. In this period the perinatal mortality rate in the four largest cities (11.1 per 1000 births) was significantly higher than in the rest of the Netherlands (9.3‰).

Women living in these cities also appeared to have a strongly increased risk of perinatal disease. Living in a deprived neighbourhood even carries a higher risk, especially for Western pregnant women. While in the Netherlands overall 6% of children are born in deprived neighbourhoods, this proportion in the largest cities can be as high as 45% in Rotterdam. Even after controlling for determinants such as socio-economic status, age, parity, comorbidity and ethnicity, living in a deprived neighbourhood was still associated with an extra risk of perinatal mortality of 21%. Concerning perinatal disease we found an extra risk of preterm birth of 16%, of small for gestational age (SGA) of 11% and of a low Apgar score at birth of 11%. Currently we have no explanation for this 'deprived neighbourhood' effect; we will need to obtain additional information as unexplored environmental factors and factors relating to the pregnant woman herself may be responsible.

The study presented in chapter 2.2 describes geographical and ethnic differences in maternal mortality based on data from the Dutch Maternal Mortality Committee over the period 1993 through 2008. Mean maternal mortality over this period in the Netherlands overall was 10.8 per 100,000 live births, ranging from 6.2 in the Noord Brabant province to 16.3 in the Zeeland province. Women living in Rotterdam or Den Haag had a significant higher risk of maternal mortality (respectively 21.0 and 19.2) compared with the nationwide average of 10.8. This could largely be ascribed to pre-eclampsia.

The increased maternal mortality risk of women living in Rotterdam or Den Haag is in line with the known health disparity between the four largest cities and the rest of the Netherlands and is possibly related to an increased risk of stress, low socio-economic status and a less healthy lifestyle.

Non-Western women also have a 59% increased risk of maternal morbidity, significantly related to pre-eclampsia.

Ultimately this may be the result of low command of the Dutch language on account of which these women have little access to information on prenatal care. They will therefore receive care with delay, are unaware of warning signs and cannot benefit from advice from the midwife or GP.

Chapter 2.3 presents a study on geographical and ethnic differences in maternal morbidity. As incidences of maternal mortality in most high income countries have dropped, severe acute maternal morbidity (SAMM) was introduced as a new marker for maternal health in the 1990s. For this study we used data from the LEMMoN study (a large nationwide cohort study on ethnic determinants of maternal morbidity in the Netherlands). We found a significantly increased risk of SAMM for pregnant women living in Flevoland and Zeeland provinces as compared with the other provinces. This was largely due to severe maternal haemorrhage.
In addition the increased prevalence of maternal morbidity in urban areas as a result of severe maternal haemorrhage was explained by factors that are over represented in urban areas: teen pregnancies, older women, grande multiparae and non-Western women. Joint professional efforts in all geographical areas could perhaps eliminate the impact of severe maternal haemorrhage on maternal morbidity rates, for example by improved compliance with guidelines and implementation of the multidisciplinary Managing Obstetrician Emergency & Trauma course.

In chapter 3.1 we evaluated the role of a number of organisational characteristics such as type of hospital (for example, peripheral hospitals or tertiary perinatal centres), yearly number of deliveries in the hospital and staffing on perinatal outcomes (intrapartum/early neonatal mortality and -morbidity) in the daytime, evening, night and weekend, corrected for the clinical case-mix. For this study we used PRN data over a seven-year period (2000 – 2006) of single pregnancies of 32 weeks and above as well as survey data on organisational characteristics of all 99 hospitals providing obstetric care in the year 2006.
After case-mix correction of the mother and child factors there was a significantly increased risk of perinatal death of 32% in the evening hours and 47% during the night as compared with the daytime for the non-perinatal centres. In the perinatal centres there was only a significantly increased risk of perinatal death of 20% for the night. Comparable significant effects were also found for the composite adverse outcomes (mortality, low Apgar score and/or NICU admission). These outcomes strongly suggest that giving birth in obstetric wards in the Netherlands outside normal working hours is less safe. We related this to the low availability of experienced care providers outside “office hours”. It appeared that in almost all non-perinatal centres the senior experienced obstetrician and neonatologist were not regularly present outside the normal working days, and could only be reached at home by telephone. Consequently they were less often involved in the assessment of (pre) critical circumstances and in the initial treatment of high-risk situations. This explanation of time and day effects is supported by intensive care research. In various studies the complications rate

dropped after the introduction of 24-hours availability of a senior intensivist in the IC department. In this regard, the advice "A Good Start" (January 2010) of the Steering group "Pregnancy and Birth" recommended 24-hours availability of senior care providers and initiating necessary interventions within 15 minutes.

Chapter 3.2 reports a study comparing the intrapartum and the early neonatal mortality rate in planned home births with that of community midwife-led planned hospital birth. We used the PRN data of term single pregnancies over the period 2000-2007. We only included pregnant women screened by primary care midwives at start of delivery. We hypothesized that although in general no difference may exist between home and hospital outcomes, for specific risk groups, the hospital setting is protective because obstetric and neonatal expertise and clinical facilities are directly available (so-called setting safety). Data analysis revealed that the pregnant women who preferred a home birth had a lower risk profile (often multiparity, 25 years or older, of Dutch origin and living in a non-deprived neighbourhood) than those who had planned to give birth in hospital. Possibly the unequal distribution of the women over the two groups explains why after case-mix correction there was no significantly increased risk for home births.

Finally in chapter 3.3 a study is described on the application of nitrous oxide sedation during delivery in a birth centre adjacent to a university hospital. We wished to confirm that this type of sedation with the use of adequate suction and a controlled setting could be applied safely in the Netherlands – anticipating a possible reintroduction of this method. In other countries N_2O is often used for pain relief in the last phase of the dilatation but also for other applications such as in dentistry. It is said to be beneficial to the patients as it is fast-acting, does not interfere with the contractions, and has no other direct effects during the first and second stages of labour. In this study safety was understood to mean that the caregivers would not be exposed to excess N_2O-concentrations. Epidemiological studies have shown that long-term professional exposure to N_2O can carry reproductive risks such as spontaneous abortion, birth defects and reduced fertility. On the basis of 12 analysed observations we concluded that, provided all regulations and protocols on exhaust gas evacuation are complied with, the N_2O exposure was in line with the national legal safety provisions.

Part 4, the Discussion, first addresses the strengths and limitations of the above studies, followed by an interpretation of the recently initiated restructuring of obstetric care in the Netherlands. Currently there seems to be readiness to accept change, but judging from the historical perspective, we expect that change will come slowly.

Samenvatting

In dit proefschrift staat het resultaat van de perinatale zorg in Nederland centraal, in termen van de uitkomsten van moeder en kind. Het vaststellen van deze uitkomsten speelt een belangrijke rol bij de bewaking van de kwaliteit van de perinatale zorg. Onderzoek naar variaties in uitkomstmaten biedt, zo blijkt, daadwerkelijk aangrijpingspunten voor kwaliteitsverbetering in de praktijk.

Het doel van dit promotieonderzoek was om vast te stellen wat de bijdrage van het woongebied van de zwangere, haar etniciteit, de organisatie van (klinische) zorg en de (geplande) plaats van een eerstelijns bevalling, was op uitkomsten van moeder en kind. Verschillende uitkomsten zijn bestudeerd zoals perinatale sterfte en perinatale morbiditeit; vroeggeboorte (geboorte < 37 weken), groeiachterstand (geboortegewicht < P10), lage Apgarscore (< 7 op 5 min na de geboorte) en aangeboren afwijking. Verder ook: opname op de neonatologische intensive care, maternale sterfte en ernstige maternale morbiditeit (uterus ruptuur, eclampsie, fluxus en Intensive Care opname van de vrouw).

Uitkomstmaten, zoals de kans op perinatale sterfte, of kans op NICU-opname zijn op zich onvoldoende als maat alleen voor de kwaliteit van de geleverde zorg. Er is immers een samenspel van biologische, medische en operationele variabelen, en de hoogte van de perinatale sterftekans leidt niet zonder meer naar een aangrijpingspunt voor verbetering. Zo worden de perinatale uitkomsten bepaald door patiëntfactoren (zoals leeftijd, etniciteit, pariteit, levensstijl, socio-demografische kenmerken), obstetrische voorgeschiedenis, niet-obstetrische comorbiditeit, organisatorische factoren (type praktijk/ziekenhuis, grootte van de organisatie, samenstelling van de staf, opleidingen, 24uurs bezetting), het proces van interactie tussen zorgschakels (verwijzing), en behandelaar-factoren (kennis, ervaring, kundigheid). Als men op basis van een uitkomst, conclusies wil trekken met betrekking tot de rol van de kwaliteit van zorg, moet men in het algemeen voor niet-zorgfactoren corrigeren. Dit heet ook wel case-mix correctie. Het welslagen van case-mix correctie hangt af van de gemeten en vastgelegde gegevens en van een goede balans tussen over- en ondercorrectie. In dit proefschrift zijn verschillende databronnen gebruikt voor de case-mix correctie, en verschillende statistische (regressie) methoden.

In dit proefschrift speelt de bijdrage van (ongezonde) woonomgeving van de zwangere een grote rol. Er was reeds bekend dat grote ongelijkheden bestonden in volwassen gezondheid, en het terugdringen van de gezondheids-achterstand in de grote steden naar het landelijke gemiddelde is staand beleid. Echter in onderzoek en beleid bestond weinig aandacht voor de gezondheidsachterstand van de pasgeborenen. Dat is ongewenst omdat toenemend duidelijk is geworden dat een slechte start van een pasgeborene grote gezondheidseffecten heeft voor de rest van het leven. Zo krijgen te vroeg en te licht geboren kinderen vaker leer- en gedragsstoornissen en hebben een hogere kans op diabetes en hart- en vaatziekten op volwassen leeftijd.

Deze aandacht voor de woonomgeving is in historisch perspectief overigens niet uniek. Het eerste deel van dit proefschrift beschrijft de historie van de verloskundige zorg in Nederland met speciale aandacht voor geboorte-centra. De context is dat dergelijke centra reeds een eeuw lang ingezet zijn voor zwangeren in moeilijke sociale en/of economische omstandigheden. Deze geschiedenis geeft perspectief aan de bevindingen van het proefschrift.

Aan de hand van enkele debatten wordt de complexiteit van veranderingen in het Nederlandse verloskundige zorgsysteem beschreven. Veranderingen worden enerzijds door ideologische factoren (zwangerschap is geen ziekte), anderzijds door financieringsstructuur (schotten) belemmerd. In beide opzichten is Nederland afwijkend ten opzichte van de meeste ontwikkelde landen. De lijnen/schotten structuur heeft dus zowel een inhoudelijke als een financiële achtergrond.
Naast dit historisch perspectief gaat het eerste deel in op de belangrijkste sociale determinanten (leefstijl, werk en SES) met hun parallelle gevolgen voor moeder en kind.

Deel 2 toont de resultaten van studies naar de geografische verschillen in de perinatale en maternale uitkomsten. In Nederland bestaan grote verschillen in de perinatale en maternale gezondheid en daarmee op risico's op een suboptimale zwangerschapsuitkomst. De studie in hoofdstuk 2.1 beschrijft de verschillen in perinatale gezondheid tussen de grote steden, achterstandswijken en de rest van Nederland. Voor deze studie werd gebruik gemaakt van de data van eenling zwangeren uit de gekoppelde bestanden van de Perinatale Registratie Nederland (PRN) over een periode van vijf jaar (2002 – 2006). In deze periode is het perinatale sterftecijfer met 11,1 per 1000 geboorten in de 4 grootste steden significant hoger dan in de rest van Nederland (9,3‰).
Vrouwen in de 4 grootste steden blijken ook een sterk verhoogde kans te hebben op perinatale ziekte. Het wonen in een achterstandswijk vormt een nog groter risico, vooral voor westerse zwangere vrouwen. In Nederland vindt 6% van de geboorten plaats in achterstandswijken, terwijl dit in de grote steden oploopt tot 45%, zoals in een stad als Rotterdam. Ook als wordt gecorrigeerd voor determinanten als sociaal economische klasse, leeftijd, pariteit, comorbiditeit en etniciteit blijkt dat het wonen in een achterstandswijk nog steeds gepaard gaat met een extra risico op perinatale sterfte van 21%. Wat betreft perinatale ziekte is er een extra risico op vroeggeboorte van 16%, op foetale groeivertraging van 11% en op een lage Apgarscore bij de geboorte van 11%. Zonder aanvullende informatie is dit 'achterstandswijk' effect op dit moment nog niet goed te duiden: zowel ongemeten factoren van de omgeving als van de zwangere zelf kunnen verantwoordelijk zijn.

De studie gepresenteerd in hoofdstuk 2.2 beschrijft de geografische en etnische verschillen in de maternale sterfte. Voor deze studie is gebruik gemaakt van de in de periode 1993 tot en met 2008 door de Commissie Moedersterfte (CMS) geregistreerde moedersterfte. Over deze periode is in Nederland de gemiddelde maternale sterfte 10.8 per 100.000 levend geborenen. De MMR varieerde van 6.2 in Noord Brabant tot 16.3 in Zeeland. Vrouwen, wonende in Rotterdam,

Den Haag bleken een verhoogde kans te hebben op maternale sterfte (respectievelijk 21.0, 19.2) in vergelijking tot het landelijk gemiddelde van 10,8. Pre-eclampsie als oorzaak van de maternale sterfte speelde hier een significante rol.
De verhoogde kans op maternale sterfte voor vrouwen in Rotterdam en Den Haag is in overeenstemming met de bekende gezondheidsverschillen tussen de grote steden en de rest van Nederland en zijn mogelijk gerelateerd aan een verhoogd risico op stress, lage sociaal-economische status en een minder gezonde leefstijl.
Ook niet-westerse vrouwen hebben een verhoogde kans van 59% op maternale sterfte, waarbij deze sterfte significant gerelateerd is aan pre-eclampsie. Mogelijk ligt hier - uiteindelijk – ook een matige beheersing door de zwangere van de Nederlandse taal aan ten grondslag. Hierdoor kan de zwangere de informatie op het gebied van prenatale zorg onvoldoende tot zich nemen. Met als gevolg: dat ze te laat in zorg komt, niet weet op welke waarschuwingssignalen zij moet letten en welke adviezen van de verloskundige of arts zij moet opvolgen.

In hoofdstuk 2.3 wordt de studie naar de geografische en etnische verschillen in de maternale morbiditeit gepresenteerd. Gezien de lage incidentie van maternale sterfte in de hoge inkomens landen wordt sinds de jaren 90 ernstige maternale morbiditeit (SAMM) gezien als een nieuwe marker voor de maternale gezondheid. Voor deze studie zijn de data gebruikt van de LEMMoN studie (acroniem van Landelijke studie naar Etnische determinanten van Maternale Morbiditeit in Nederland).
In deze studie werd voor zwangeren wonende in Flevoland en Zeeland in vergelijking met de rest van Nederland een significant verhoogd risico op ernstige maternale morbiditeit gevonden. Ernstige fluxus speelt hierin een significante rol. Daarnaast werd de verhoogde prevalentie van maternale morbiditeit in de grote steden ten gevolge van een ernstige fluxus verklaard door de oververtegenwoordiging van factoren in de stedelijke gebieden: tienerzwangerschappen, oudere vrouwen, grande multiparae en niet-westerse vrouwen.
De rol die fluxus speelt bij de verschillen in maternale morbiditeit, kan mogelijk worden teruggedrongen door een overal vergelijkbare professionele inspanning (verbetering in de naleving van richtlijnen en implementatie van multidisciplinaire Managing Verloskundige Noodgevallen & Trauma cursus).

In hoofdstuk 3.1 wordt de evaluatie beschreven van de rol van een aantal organisatorische kenmerken op perinatale uitkomsten (intrapartum/vroeg neonatale sterfte en -morbiditeit) in de dag, avond, nacht en weekend, gecorrigeerd voor de klinische casemix; type ziekenhuis (bijvoorbeeld, perifere ziekenhuizen of derdelijns perinatale centra), jaarlijks aantal bevallingen van het ziekenhuis en stafbezetting. Voor deze studie is gebruik gemaakt van de data uit de gekoppelde bestanden van de PRN over een periode van zeven jaar (2000 – 2006) van eenlingzwangerschappen vanaf 32 weken en met behulp van een survey verkregen data op ziekenhuisniveau met betrekking tot de organisatiekenmerken van alle 99 in het jaar 2006 verloskunde houdende ziekenhuizen.
Na case-mix correctie van de moeder- en kindfactoren werd ten opzichte van de dag een significant verhoogd risico op perinatale sterfte van 32% tijdens de avond uren en 47% tijdens de nacht gevonden voor de niet perinatale centra. In de perinatale centra werd alleen voor de nacht een significant verhoogd risico op perinatale sterfte van 20% gevonden.

Vergelijkbare significante effecten werden ook waargenomen voor de samengestelde perinatale ziektemaat (mortaliteit, lage Apgar en/of opname op de NICU). Deze uitkomsten doen sterk vermoeden dat het buiten de reguliere kantooruren minder veilig is op een verloskunde afdeling in Nederland. In de studie werd deze associatie gerelateerd aan de lagere beschikbaarheid van ervaren zorgverleners buiten “kantooruren”. In deze studieperiode waren buiten de normale werkdagen in bijna alle niet-perinatale centra ziekenhuizen de senior ervaren obstetricus en neonatoloog niet regulier aanwezig, en alleen via de telefoon thuis bereikbaar. Derhalve werden zij minder betrokken bij de beoordeling van (pre) kritische omstandigheden en bij de initiële behandeling van risicovolle situaties. Deze verklaring van tijd- en dageffecten wordt ondersteund door studies over de intensive care. Zo nam in diverse studies, na de introductie van 24 uur beschikbaarheid van een senior intensivist op de IC, het aantal complicaties af. In het Stuurgroeprapport “Een goed begin” (januari 2010) werd 24-uurs beschikbaarheid van senior zorgverleners en het starten met noodzakelijke interventies binnen 15 minuten aanbevolen.

In hoofdstuk 3.2 wordt de studie beschreven die de intrapartum en de vroege neonatale sterftecijfers van de geplande thuisbevallingen vergeleek met de geplande ziekenhuisbevallingen onder leiding van de eerstelijns verloskundige. In deze studie werd gebruik gemaakt van de PRN data van aterme eenling zwangerschappen over de periode 2000-2007. In deze studie werden alleen zwangeren, die bij aanvang van de bevalling werden begeleid door de eerstelijns verloskundigen, geïncludeerd.
Onze hypothese was dat, hoewel in het algemeen geen verschil mag bestaan tussen de uitkomsten van aterme laag riscio thuis- of ziekenhuisbevallingen, voor specifieke risicogroepen, het ziekenhuis een beschermende factor is omdat daar obstetrische en neonatale expertise evenals klinische faciliteiten direct beschikbaar zijn (zogenaamde settings afhankelijke veiligheid). Na analyse van de data bleek dat de zwangeren die thuis wilden bevallen in vergelijking met de zwangeren, die hun bevalling in het ziekenhuis hadden gepland, een lager risico profiel hebben (vaker multiparae, 25 jaar of ouder, van Nederlandse afkomst en woonden in een niet achterstandswijk). Mogelijk is de ongelijke verdeling van de vrouwen over de twee groepen de verklaring waarom na correctie voor de case-mix geen significant verhoogd risico voor thuisbevallingen in deze studie werd gevonden.
In hoofdstuk 3.3 wordt tenslotte een studie beschreven naar de toepassing van lachgas-sedatie (N2O) tijdens de bevalling in een aan een academisch ziekenhuis aanpalend geboortecentrum). Nagegaan is of met behulp van adequate afzuiging en een gecontroleerde setting lachgas-sedatie (N2O) tijdens de bevalling veilig kon worden toegepast. Dit ter voorbereiding van eventuele herintroductie. In de ons omliggende landen wordt voor pijnbestrijding in de laatste fase van de ontsluiting maar ook voor andere toepassingen zoals in de tandheelkunde veelvuldig N2O gebruikt. Vanuit patiëntperspectief heeft N2O namelijk gunstige eigenschappen. N2O werkt snel, interfereert niet met de contracties, en heeft ook geen effect op het verloop van de baring. In deze studie wordt met veilig bedoeld, dat de zorgverleners tijdens de lachgas-sedatie niet worden blootgesteld aan een te hoge N2O-concentratie. Epidemiologische studies hadden aangetoond dat langdurige beroepsmatige blootstelling aan N2O gepaard kan gaan met reproductieve risico's zoals

spontane abortus, aangeboren afwijkingen en verminderde vruchtbaarheid. Op basis van 12 geanalyseerde waarnemingen kon geconcludeerd worden dat, mits voldaan wordt aan alle voorschriften qua juiste toepassing van de afzuiging en de bijbehorende protocollen worden gevolgd, de blootstelling aan N2O voldeed aan de landelijk geldende wettelijke veiligheidsrichtlijnen.

In deel 4, de discussie, worden eerst de sterke en beperkende aspecten van de bovenbeschreven studies beschouwd, vervolgens wordt ingegaan op de recent ingezette herstructurering van de verloskundige zorg in Nederland. De bereidheid tot veranderen lijkt momenteel aanwezig, maar in het licht van de geschiedenis kan worden verwacht dat veranderingen geleidelijk zullen zijn.

About the author

Hanneke de Graaf was born on April 13th 1958 in a freestanding birth centre in Haarlem, the Netherlands. She studied nursing at the VU University Medical Center in Amsterdam and subsequently Health Science at the University of Maastricht, the Netherlands, obtaining her Master of Science degree in March 1994.

From 1977 to 1985, she worked as a nurse at the VU University Medical Center, from 1985 to 1998 in various management positions at the Mariastichting/Spaarne Hospital (internal medicine and oncology ward, paediatric and neonatal ward and subsequently as manager of the whole nursing department).

From 1998 to 2012 she was appointed as manager at the Erasmus MC, University Medical Center Rotterdam (1998-2000 at the departments of oncology and haematology and from 2000-2012 at the departments of obstetrics & gynaecology and urology). From 2012 onwards she is appointed as business developer of care innovations combined with a project leadership of innovations in obstetric care at the same centre and directorship of the birth centre Sophia in Rotterdam. In 2006, she started combining these activities with a PhD fellowship at the division of Obstetrics and Prenatal Medicine of the Erasmus MC. Her research focussed on inequalities in perinatal and maternal health (Supervisors Prof. E.A.P. Steegers, Prof. G.J. Bonsel and Dr. A.C.J. Ravelli).

Erasmus MC
Universitair Medisch Centrum Rotterdam

PhD Portfolio

Summary of PhD training and teaching

Name PhD student: drs. J.P. de Graaf Erasmus MC Department: Department of Obstetrics and Gynaecology	PhD period: Jan 2006 – Aug 2012 Promotor(s): Prof. dr. E.A.P. Steegers / Prof. dr. G.J. Bonsel Copromotor: Dr. A.C.J. Ravelli (AMC) Supervisor: Prof. dr. E.A.P. Steegers

1. PhD training

	Year	Workload ECTS
General courses		
- Biomedical English Writing and Communication	2007	5 ECTS
Specific courses (e.g. Research school, Medical Training)		
Seminars and workshops		
-		
Presentations		
- Grootstedelijke verloskundige uitkomsten	2008	1 ECTS
- Hoe bevalt regio Eindhoven	2009	1 ECTS
- Vormgeving polikliniek in de nieuwbouw	2011	1 ECTS
- Opening symposium ter gelegenheid van het 2,5 jarig bestaan van het Geboortecentrum Sophia	2012	0,2 ECTS
- Voor de sectie "obstetrische anesthesie" Lachgassedatie in het Geboortecentrum Sophia, Proof-of-principle en proof-of-safety	2012	1 ECTS
- Voor diverse medewerkers van HAGA ziekenhuis Lachgassedatie in het Geboortecentrum Sophia, Proof-of-principle en proof-of-safety	2012	0,2 ECTS
(Inter)national conferences		
- Grootstedelijke verloskundige gezondheid	2009	4 ECTS
- Redevelopment project, Conference "International experiences on care-focused hospitals"	2011	3 ECTS
- Sophia's Choice, Eerste resultaten uit het Geboortecentrum Sophia	2011	1 ECTS
- 1 ½ lijns geboortezorg	2011	2 ECTS

2. Teaching

	Year	Workload ECTS
Lecturing		
- Minor "Circle of life"	2012	1 ECTS

Supervising practicals and excursions, Tutoring		
- wiskundebijlessen aan HBOV verpleegkundigen als voorbereiding op deficiëntietoets Wiskunde A voor diverse universitaire studies	2008-2010	3 ECTS
- Begeleider keuzeonderzoek VAR studenten: 'Informatiebehoefte zwangeren'	2010	2 ECTS
- Praktijkbegeleider studenten tijdens hun van mastertheses aan BMG of verpleegwetenschappen: 1) effecten "anders werken" ovariumcarcinoom, 2) Vruchtbare samenwerking in de verloskundige zorg, 3) effecten programma patiënt prominent op prostaatcarcinoom patiënten	1&2) 2007 3) 2010	2 ECTS 1 ECTS
4) begeleiding masterstudent BMG zorgmanagement in geboortecentrum Sophia	4) 2012	2 ECTS
- Begeleiding TOP class student	2011	2 ECTS
- Tutoraat Erasmus MC	2012	2 ECTS
Supervising Master's theses	-	-
Other		
- Medewerking verleend aan de 'Signalementstudie Zwangerschap en Geboorte'	2009	1 ECTS

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