Obstetric care in Norway - the role of institution availability and place of delivery for maternal and perinatal outcomes

Population-based retrospective cohort studies

Hilde Marie Engjom

Thesis for the Degree of Philosophiae Doctor (PhD)
University of Bergen, Norway
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Scientific environment

This PhD work has been conducted in a cross-disciplinary scientific environment.

During the first PhD phase, when my research focus was on global maternal health and service improvement in rural Ethiopia, Ole Frithjof Norheim was my main supervisor and Bernt Lindtjørn at the Centre of International Health provided valuable insights as a co-supervisor. When local political circumstances in Southern Ethiopia lead to challenges, we decided to change setting and perspectives to a Norwegian project. Kari Klungsøyr took over responsibility as main supervisor and project group member Nils-Halvdan Morken agreed to be co-supervisor along with Ole-Frithjof Norheim.

My Norwegian research project has been based at the research group for registry-based studies of familial risks, led by Rolv Skjærven. I have kept the association with the research group for Global Health Priorities, led by Ole Frithjof Norheim, and the studies have been linked to his project "Priority setting across clinical specialities", funded by the Western Regional Health Authority. Both groups are located at the Department of Global Public Health and Primary Care, Faculty of Medicine and Dentistry, University of Bergen.

I have been a member of the EPINOR program. This is the national research school for epidemiology, and I have participated in local and national activities related to the research school.

Some international networks have been valuable sources of insights and knowledge; The Nordic and international research networks for obstetric surveillance and research, NOSS and INOSS, the Norwegian Forum for Global Health Research and European Federation of Societies for research in Tropical Medicine and International Health, FESTMIH. From 2011 to 2016 I have also been member of the Health Systems Global-network with the main interests in research on and teaching about health systems.

Acknowledgements

I would like to thank Kari Klungsøyr, my main supervisor, for the dedication, encouragement, and persistent pursuit of excellence in academic work and in her approach to supervision. The cross-disciplinary supervisor team laid a strong foundation for the project. Nils-Halvdan Morken provided a pragmatic and firm emphasis on combining scientific quality with a clinical perspective and practical relevance. Ole Frithjof Norheim played the key role in initiating the project, and without his open mind and willingness to explore new perspectives this project would not have been possible. Bjørn Thorsdalen at Statistics Norway provided valuable insights in the initial planning of the project, and Even Høydahl deserves special thanks for the effort in planning and performing estimates on this scale.

I am very obliged to the members of the research groups in global health priorities and registry-based studies of familial risks for valuable feed-back and comments. I sincerely thank my colleagues at the Department of Global Public Health and Primary Care for their interest and active involvement in promoting a welcoming and scientifically excellent working environment.

Clinical work offers the opportunity for skills acquisition, expanded clinical knowledge as well as critical reflections concerning the factors that impact our work. I would like to thank all my present and former colleagues for the professional companionship and inspiring discussions. In particular, I would like to thank Susanne Albrechtsen for her patience and encouragement in the concluding phase of the project, and Kathrine Woie and Line Bjørge for allowing me time for academic work despite staff shortages and heavy workloads.

Family and friends have made invaluable contributions to recreation and practical help. Halvor and Ragnhild eagerly embarked on long and short journeys during the course of this research, and Trond kept it all together by combining love and a steady hand.

Abbreviations

BOC	Basic Obstetric Care
CI	Confidence Interval
EmONC	Emergency Obstetric and Newborn Care
HELLP	haemolysis, elevated liver enzymes and low platelets
ICC	intracluster correlation coefficient
MBRN	Medical Birth Registry of Norway
OR	odds ratio
RR	relative risk
UN	The United Nations
WHO	The World Health Organization

Abstract

Background: Obstetric care in midwife-led institutions may be more cost-effective and reduce the number of interventions during labour. On the other hand, large obstetric institutions may offer more technologically advanced and specialised care. Knowledge of how availability of and access to different types of obstetric institutions impact maternal and perinatal clinical outcomes in a high-income context is lacking.

Aims: The aim of this thesis was to assess availability of and access to obstetric institutions in Norway during recent decades and to assess perinatal and maternal clinical outcomes by travel time to institution and place of birth.

The first study assessed changes in travel time on a population level, the risk of unplanned birth outside institution over time, as well as the risk of maternal morbidity. The second study aimed to assess the association of mother's travel time to an obstetric institution and place of birth with peripartum perinatal mortality. The aim of the third study was to assess risk of eclampsia and HELLP syndrome by the mother's travel time to an obstetric institution and place of delivery.

Material and methods: The studies were conducted using population-based data from Norway. The primary data source was the Medical Birth Registry of Norway (MBRN), and we included births from 1979 to 2009. The mother's unique national identification number was used to link births in the MBRN to her registered address. Statistics Norway provided geographic coordinates linked to National Registry addresses for two ecological cross-sectional studies and two cohort analyses.

We also used the mother's unique identification number to link births to their mother in a sibling-structure to assess clinical outcomes in subsequent pregnancies.

Obstetric institutions were categorised by function and annual number of births. Availability of and access to obstetric institutions was based on the woman's travel time to the nearest obstetric institution. Travel time was estimated using geographic

information systems software combined with the Norwegian digital road database. Population proportions and risks were assessed using cross-tables. Logistic regression and generalized linear models were used to calculate odds ratios and relative risks with 95% confidence intervals and to adjust for confounders. Travel time ≤ 1 hour was used as reference for all travel time analyses. Multilevel regression models were used to account for clustering by several births to the same mother and by births in the same institution. Sibling structures with the mother as the observation unit were used to assess outcomes in successive pregnancies.

Results: In the first study, we found a 10% increase in the proportion of women of reproductive age living outside the 1-hour travel zone to all obstetric institutions and to Emergency Obstetric and Newborn Care (EmONC) institutions from 2000 to 2010. On a national level, the risk of unplanned birth outside institution doubled from 1979-83 to 2004-09 and the differences between counties increased. The risk of maternal morbidity increased by 40% from 2000 to 2009 on a national level, with increasing regional differences.

The second study showed that unplanned birth outside institution was associated with higher risk of peripartum perinatal death (death during delivery or within the first 24 hours). Women with travel time exceeding one hour to any obstetric institution had higher risk of unplanned birth outside institution compared to women with less than 1 hour travel time. On a population level, 2 % of peripartum perinatal deaths could be attributed to unplanned birth outside institution.

In the third study, we found that nulliparous women who had to travel more than one hour to any obstetric institutions had a 50 % higher risk of eclampsia or HELLP-syndrome. These complications occurred in all categories of obstetric institutions. Women with risk factors such as preeclampsia or previous preeclampsia delivered in the larger EmONC institutions. Deliveries prior to 35 gestational weeks were also referred to the largest EmONC institutions. Women with previous preeclampsia had a higher risk of recurrence, but the majority of parous women with eclampsia or HELLP did not have previous preeclampsia.

Conclusion: Access to obstetric institutions and skilled birth attendance play an important role to reduce the risk of adverse clinical maternal and fetal outcomes. In planning or evaluating changes in the obstetric healthcare structure, associated changes in the distribution of benefits and burdens should be considered. Further work must aim at assessing risk of a wider range of maternal complications as well as neonatal morbidity and mortality.

List of publications

Paper I
Engjom, Hilde Marie; Morken, Nils-Halvdan; Norheim, Ole Frithjof; Klungsøyr, Kari. Availability and access in modern obstetric care: a retrospective population-based study. BJOG: an International Journal of Obstetrics and Gynaecology 2014 ;Volume 121.(3) p.290-299

Paper II
Engjom, Hilde Marie; Morken, Nils-Halvdan; Høydahl, Even; Norheim, Ole Frithjof; Klungsøyr, Kari.
Increased risk of peripartum perinatal mortality in unplanned births outside institution: a retrospective population-based study. American Journal of Obstetrics and Gynecology, August 2017 DOI: http://dx.doi.org/10.1016/j.ajog.2017.03.033

Paper III
Engjom, Hilde Marie; Morken, Nils-Halvdan; Høydahl, Even; Norheim, Ole Frithjof; Klungsøyr, Kari.
Risk of eclampsia and HELLP by travel time to institution and institution category; a population-based cohort study (submitted)

The papers have been published as open access articles. No permissions were needed for reprints in the thesis.

1 Introduction

The aim of the present thesis was to examine health systems factors in obstetric care in relation to maternal and perinatal outcomes. We examined how availability of obstetric institutions, as well as institution type and volume, were associated with unplanned delivery outside institution, peripartum perinatal death and maternal complications due to pregnancy and childbirth.

The thesis comprises three papers. Paper I examined availability of institutions by estimating distribution of and changes in travel time to obstetric institutions on a population level for women of reproductive age in 2000 and 2010. The study further examined access to obstetric institutions from 1979 to 2009 by analysing the risk of unplanned delivery outside institution, and described the WHO Emergency Obstetric Care Indicators applied on Norwegian births in 2000 and 2009 using maternal morbidity as a main clinical maternal outcome.

Paper II examined the mothers travel time to institution using individual travel time data. We used travel time and place of birth as main exposures in the analyses of the risk of perinatal death during labour or within 24 hours.

Paper III examined the mother´s risk of severe hypertensive complications in pregnancy related to her travel time to an obstetric institution and also examined where mothers with severe hypertensive complications delivered taking into account whether she had known risk factors.

The research was based on national registry data of good quality, combined with new technological approaches and demographic tools. By applying an international maternal health approach we were also able to evaluate Norwegian obstetric care from a global perspective.

The registry linkages will be described in further detail in the thesis. The linkages provided a larger dataset than would have been achievable in a prospective study, but the linkage process as well as the travel zone estimations were complicated and time consuming. Hence, the data collection had to be limited to 2009 and the data set was not completed before 2015.

1.1 Background

1.1.1 Health systems and the right to health

Caught between high-technology services and the care for normal uncomplicated deliveries, obstetric care has been a core issue in the current health-system debate in several high-income countries.(1-10) The right to health was declared by the United Nations (UN) in 1948, and further elaborated in the International Covenant of Economic, Social and Cultural rights in 1966. The role of health systems in providing this right was emphasised in the World Health Report in 2000, and in a general comments issued by the UN Committee on Economic, Social and Cultural rights in 2000 and 2016.(11-13) Both the UN and the World Health Organization (WHO) list available and accessible institutions, as well as acceptable health services of sufficient medical and scientific quality, as core elements in providing the right to health.

1.1.2 Obstetric health services

Birth-related complications may arise quickly and threaten life and future health of both mother and child. Prevention of death and adverse outcomes requires urgent and skilled interventions and thus access to institution based care.(13-15) The WHO has addressed maternal and newborn care specifically, and developed tools for monitoring emergency obstetric care including geographic distribution of institutions, access, utilization and the type of services provided.(15, 16) These guidelines list eight indicators for Emergency Obstetric and Newborn Care (EmONC) and nine signal functions describing treatment that should be available. Registration of severe maternal morbidity adds information about the health service performance in all types of resource settings.(17, 18)

In studies of maternal mortality, the “Three Delays Model” has been used to conceptualize the process of seeking and receiving adequate treatment and how barriers can increase the risk of maternal death: first, the decision to seek medical care, second, the process of getting there, and third, the diagnostic and therapeutic care provided by health personnel.(19, 20) Practical implications of addressing the core elements in a health system have also been elaborated and conceptualised for maternal and newborn health; in the table below, the concept of quality evaluation using system, process and outcome factors has been combined with the core elements of the health system as outlined by the UN and WHO. (21)

Table 5
Typology of quality of health care.

Model	Quality of structure	Quality of process	Quality of outcome
Dimensions of health system e.g. Donabedian	• Policy • Resources • Organisation • Management system	• Service delivery	• Outputs • Health status
Characteristics of quality e.g. Maxwell	• Accessibility • Availability • Affordability • Relevance to need • Goodness of amenities • Equity • Sustainability	• Appropriateness • Acceptability • Technical competence • Safety • Goodness of interpersonal relationship	• Coverage • Effectiveness • Efficiency • Health impact • User satisfaction
Perspectives of quality e.g. Ovretveit	Client quality <-> Professional quality <-> Management quality		
Elements of quality e.g. Hulton et al.	• Human and physical resources • Referral system • Information system	• Use of appropriate technologies • Internationally recognised good practices • Management of emergencies	• Experience of care

Adapted from Health Care Quality Assurance Manual—LSTM (1995).

Raven et al, Midwifery, 2012, reproduced with permission

The focus of the national health policy in Norway has shifted from equality and geographic access in the 1970s to efficiency and patient empowerment in the 1990s and the first decade of the new millennium.(22) However, recent parliament decisions emphasized the need for decentralized care in order to provide safe services of high quality near a woman´s home.(23) Nevertheless, according to combined information from several public sources, the number of obstetric institutions in Norway declined from 95 to 51 between 1979 and 2009.(24) (http://statistikkbank.fhi.no/mfr/)

1.1.3 Institution volume and function

Within other fields in medicine, such as cancer treatment, surgery, and intervention cardiology, centralisation to larger units improve the patient outcome although the mechanisms are complex.(25-27) The need for sufficient skills and competence in technologically or scientifically demanding treatment has been emphasized. Volume measured as procedures or treatments per year was frequently used as a proxy measure for potential quality, but methodological concerns and concern for accessibility were raised.(25, 27-31) Studies by initiatives benefiting from centralisation, such as the Leapfrog-initiative in the US, did show stronger volume-outcome associations than studies in a different financing setting.(32, 33) Access and utilization of specialised procedures such as percutaneous coronary interventions have been shown to vary across countries and regions, (34, 35) and Norwegian studies have indicated similar regional underutilization.(36)

1.1.4 Obstetric volume and perinatal outcomes

In obstetrics, delivery in large institutions has been associated with an increased frequency of interventions for low-risk women and the benefit for neonatal outcome in low-risk infants remains unclear.(1, 9, 37, 38) Whether delivery care in smaller obstetric institutions and midwife-led institutions is safe and cost-effective compared to centralized care in larger obstetric institutions has been heavily debated.(1, 2, 9, 39-42) With the exception of access to neonatal intensive care units and neonatal outcome, the availability of and access to obstetric institutions has received little attention in high-income countries. (43, 44)

Typically, previous studies comparing planned place of delivery have excluded unplanned births outside institution.(39, 40, 45, 46) Additionally, key studies have included only neonatal deaths and thus failed to address how lack of adequate monitoring and interventions during labour may result in intrapartum death.(37, 40, 41, 43, 45, 47) Several authors have raised concerns about adverse consequences of reduced accessibility to obstetric and neonatal care, as well as risk of unnecessary interventions in the larger institutions.(1, 8, 9, 48-51) However, conclusive studies linking structural factors and perinatal mortality are lacking.

1.1.5 Obstetric volume and maternal outcomes

Contrary to publications concerning volume and outcomes in surgical procedures, few studies on institution volume and obstetric outcomes have been published. In the

United States, peripartum hysterectomy following caesarean sections in large institutions was associated with lower maternal mortality rates.(52) However, this study did not discriminate between planned and emergency hysterectomies. A Dutch study on severe maternal morbidity linked cases of severe morbidity to inadequacies in provided care and identified socio-demographic risk factors, but this study did not assess the place of birth as a risk factor.(5) A previous study in Norway, as part of a European collaboration to assess severe maternal morbidity, only collected data from one county and institutional differences could not be assessed.(53) A Scandinavian study on eclampsia identified cases of substandard care, but did not categorise the institutions.(54) Higher rates of severe maternal morbidity and lower rates of antihypertensive medication were reported for women with severe hypertension admitted to low-volume hospitals in California and Arizona.(55) In France, lack of an anaesthetist and volume < 500 births annually was associated with higher risk of substandard care for post-partum haemorrhage.(56)

1.1.6 Severe hypertensive complications in pregnancy

Globally, severe hypertensive complications in pregnancy remain one of the unsolved challenges in obstetric care.(57-59) Hypertensive complications have been the most common cause of direct maternal deaths in Norway since 1980, causing 14/47 deaths in 1980-2000 and 6/14 deaths in 2005-09.(60, 61)

Hypertensive complications in pregnancy include isolated hypertension, preeclampsia, eclampsia, and HELLP syndrome. Preeclampsia is usually defined as hypertension and proteinuria occurring after 20 gestational weeks.(62) Severe hypertensive complications have been defined either by preeclampsia and systolic blood pressure above 160 mmHg, by the occurrence of seizures (eclampsia) or by liver-, platelet- and coagulation disturbance in HELLP-syndrome. The term “imminent eclampsia” has been used to categorise symptoms associated with or prodromal to eclampsia; hyperreflexia in deep tendon reflexes, frontal headache, visual disturbance and epigastric pain. Eclampsia and HELLP syndrome are associated with increased risk of pregnancy-related death and morbidity in infant and mother, and also with long-term risk of maternal cardiovascular mortality and death in epidemiological studies and familial studies (63-70)

The aetiology and pathogenesis of preeclampsia is still not fully understood, but involve a complex interplay between genetic predisposition and protection,(71, 72) complex immunologic and vascular factors,(73) and socioeconomic and environmental risk factors.(59, 74) Proposed prevention strategies range from public health interventions to targeted individual interventions, for example pre-pregnancy counselling and reduction of cardiovascular and metabolic risk factors, prevention of teenage pregnancies, and approaches using information about individual or familial risk to guide targeted testing and examinations, medication, and dietary supplements.(59, 62, 74)

Delays in diagnosis and management in obstetric institutions have been highlighted as risk factors for eclampsia.(54, 75) Despite the well-established recognition of the importance of prompt diagnosis and adequate treatment, recently proposed quality indicators for intrapartum obstetric care in hospitals do not include severe hypertensive complications, except if the mother is admitted to an intensive care unit.(76, 77)

While preeclampsia can be identified at antenatal visits in primary care, some women experience a sudden and rapid progression of severe disease at the time of term delivery.(54, 73) In women with symptoms of imminent eclampsia or severe hypertension, magnesium sulphate reduces the risk of seizures and prevents recurrent seizures, and has reduced the incidence of eclampsia.(78-80) Definitive treatment is delivery when the woman has been stabilized, sometimes involving difficult considerations regarding maternal and fetal benefits and risks in preterm delivery. Previous research has aimed at identifying maternal characteristics that may be risk factors for progression of preeclampsia to more severe disease or death.(81) We lack knowledge about how health system factors are related to risk of severe hypertensive complications.

2 Hypothesis and aims

The main hypothesis of the studies comprised in this thesis was that centralisation of obstetric care increases the travel time to institution but improves the clinical outcomes for mother and child.

The overall aim was to assess the impact of institution availability, access and function on maternal and perinatal outcomes in Norway

Paper I had the following specific aims; to assess the travel time to the nearest obstetric institution for women of reproductive age, to assess the risk of unplanned birth outside institution nationally and by county, to assess maternal morbidity, and to assess the number and classification of obstetric institutions and the WHO EmONC indicators and change over time.

Paper II aimed to assess the risk of perinatal death during labour or within 24 hours by maternal travel time to the nearest obstetric institution and by place of birth for births from 1999 to 2009.

The aim of paper III was to assess the risk of eclampsia, HELLP-syndrome, and preterm delivery prior to 35 weeks in pregnancies with preeclampsia, by place of delivery and travel time to the nearest obstetric institution

3 Material and methods

3.1 Data sources

The thesis was based on population data from two main sources: the Medical Birth Registry of Norway (MBRN) and Statistics Norway. In addition we had data on maternal address from the National Registry at Skatteetaten (TaxNorway) and on level of education from the National Education Database. All citizens and non-citizen residents in Norway receive a unique national identification number. Foreigners who live in Norway less than 6 months are assigned a unique D-number.(82) We used these national identification numbers to link births in the MBRN to the address coordinates. D-numbers could not be used to link successive births to the mother.

The MBRN has received mandatory standardized notifications of all live births and stillbirths (from 16 weeks gestation) since 1967. The registry is routinely linked with the National Registry through the mother's national identification number, given to all individuals residing in the country. This linkage provides identification numbers to all live births, ensures complete notification to the MBRN and also provides data on all dates of death.

The notification includes information about demographic characteristics, maternal health before and during pregnancy, pregnancy complications, the delivery (including induction, complications and interventions), complications after delivery until discharge from the institution, and information about the infant (vital status, time of death, anthropometric measurements, Apgar scores and neonatal diagnoses including congenital malformations). Notifications are mandatory, but the mother can opt-out from registration of tobacco use/smoking. Gestational age was based on last menstrual period until 1998, and on ultrasound estimates thereafter. Ultrasound estimates are usually from a routine scan in the second trimester. If ultrasound is missing, gestational age is based on the last menstrual period.

The MBRN notification form was revised and extended in 1999 to include more detailed information about the mother, the neonate, and the place of birth. Before 1999, all outcomes were notified only as free text and coded at the MBRN using the International classifications of Diseases version 8 (ICD-8). From 1999, the form also included check boxes for the most common risk factors and clinical outcomes. Since 1999, additional free text has been coded at the MBRN using the ICD-10, and place of delivery has also been notified by check boxes on the notification form. Planned home birth is a separate category, as is unplanned birth at home, during transport or with unknown location.

The notification of stillbirths specifies time of death in relation to labour (antepartum, intrapartum or unknown) and to arrival at the institution (prior to arrival or after). Unexplained antepartum fetal death registration in the MBRN has been validated for the years 1985-2007 with acceptable results.(83) The MBRN receives the autopsy report or, if autopsy is not performed, a written conclusion on likely cause of death for all stillbirths from 22 weeks gestation. Neonatal deaths during the first 24 hours are identified by the date and hour of birth and the number of hours lived, as registered on the MBRN notification form.

The main direct maternal complications are notified by check boxes as well as options for free text on the notification form. The check boxes includes intensive care treatment and the following severe maternal complications: puerperal sepsis or sepsis during delivery, thromboembolic disease, eclampsia, and haemorrhage >1500 ml or blood transfusion.

Validation studies of preeclampsia registration in the MBRN have concluded that the information has acceptable accuracy.(84, 85) Mild preeclampsia at term has shown lower ascertainment than more severe preeclampsia with preterm delivery and intrauterine growth restriction.(85) A study on eclampsia in Scandinavia found over-reporting of eclampsia to the MBRN after the revised notification form was introduced in 1999,(54) and this was confirmed in a validation study at the

MBRN.(86) Based on these observations all notifications of eclampsia and HELLP from 1999 onwards are routinely verified through patient records.

The Central Bureau of Statistics was established in 1876. Presently known in English as Statistics Norway, this is the national statistical institute and the main producer of official statistics related to economy, population and society. Since 2000, Statistics Norway has assigned geographic coordinates to the National Registry addresses and updates addresses and coordinates on 1 January each year. The coverage of individual coordinates was 98% of all addresses in 2000, with a range between counties from 95.5 to 99%. In 2010 the coverage of individual coordinates was 99%, with a county range from 98.2 to 100%. In Paper I we used address coordinates for women of reproductive age, 15 to 49 years, in two ecological analyses on travel time to all obstetric institutions and to EmONC institutions on 1 January 2000 and 1 January 2010.

In paper II and paper III, linkage between the MBRN and the National Registry also provided data on each mother´s registered address, these addresses were then combined with address coordinates from Statistics Norway to estimate individual travel time to the nearest obstetric institution.

Statistics Norway was also the source of demographic data about the mother's country of birth for those born outside Norway, categorised by world region, and of data from the National education database on the mother's highest attained level of education.

3.2 Study populations

Due to delays in the registry-linkage process this PhD work has been conducted on two datasets from the same birth population with all deliveries in Norway from 22 weeks of gestation or with birth weight from 500g.

Paper I used MBRN data from the period of 1979 to 2009. All deliveries from 1979 to 2009 (n=1 807 714) were categorized according to place of delivery (definitions on page 23). All deliveries in the years 2000 (n= 58 632) and 2009 (n= 61 895) were used to analyse maternal morbidity and to perform the WHO EmONC indicator analysis. We also used population data from Statistics Norway for two ecological analyses, 1 January 2000 (n= 1 050 269) and 1 January 2010 (n=1 127 665), and estimated travel time to the nearest obstetric institution for women of reproductive age (15-45 years). At the county level, we compared the proportion of women living outside the 1-hour zone and the risk of unplanned birth outside institution.

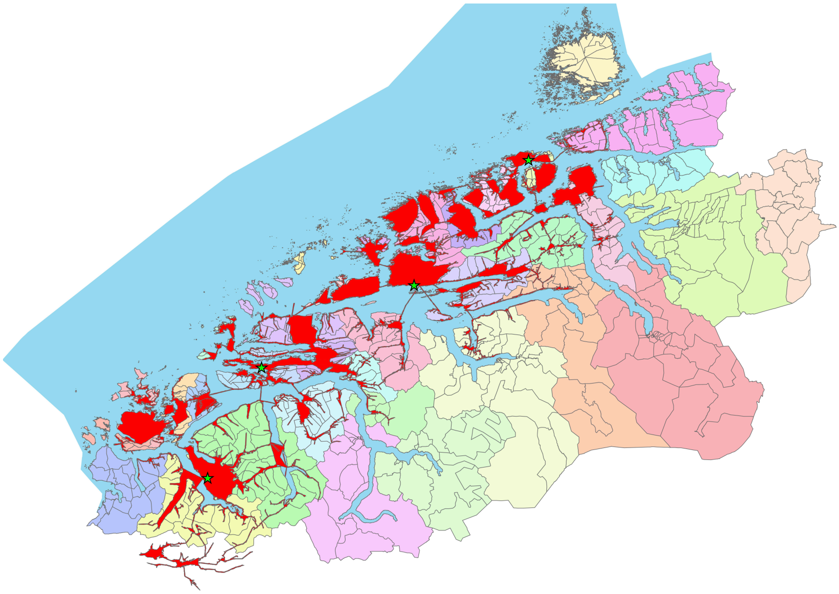
The source population for paper II was all infants born during the period from 1999 to 2009 (n= 648 555). We excluded 404 births (0.06%) due to lack of travel time estimates for the mother. Further, planned home births (n= 1 253, 0.2%) were described but excluded from the analyses. The final study population was 646 898 births.

In paper III, the source population was all women who delivered from 1999 to 2009 (n= 636 738). We excluded 398 (0.06%) women lacking travel time information. We described planned home deliveries (n= 1 252, 0.2%) and unplanned deliveries outside institution (n= 4 519, 0.7%), but they were excluded from the analyses. The final study population was 630 255 deliveries.

3.3 Exposures, covariates and outcomes

3.3.1 Main exposures

Travel time A travel zone was defined as the geographic area in which all women were estimated to reach the nearest obstetric institution within the given time. Institutions were registered by geographic coordinates and surrounding travel zones were calculated based on the Norwegian electronic road database.(87) Estimates were based on registered speed limits and standard duration of ferry/boat journeys and represented the minimum time for non-emergency transport. A merged area (polygon) was created for the travel zones (<1 hour, 1-2 hours and ≥2 hours).



Emergency obstetric institutions and travel time in Møre and Romsdal county. EmONC institutions are marked by asterisks. Estimated travel time < 1 hour in red, municipalities with varying colours.

Place of birth/delivery Place of birth was categorized as unplanned outside obstetric institution, in basic obstetric care institution (BOC), and in emergency obstetric and newborn care institution (EmONC). Unplanned birth outside institution was defined as birth at home, during transportation, or in a non-obstetric institution or unknown location (e.g. health centre) for a woman who planned an institutional birth. The WHO Handbook for Monitoring Emergency Obstetric and Newborn Care was used to categorize institutions by the available treatment options.(16) BOC institutions provided midwife-led care for normal deliveries, and intravenous administration of drugs and basic newborn resuscitation if needed before transfer. EmONC institutions provided intravenous administration of uterotonic drugs, antibiotics and magnesium sulphate, removal of placenta or retained products of conception, newborn resuscitation, assisted vaginal delivery, caesarean section, and blood transfusion. All EmONC institutions had a specialist in obstetrics and gynaecology on call. For papers II and III we further classified EmONC institutions according to annual number of births (<500, 500-1499 and ≥1500). Institution closure or change in level of care was corrected at the start of each calendar year. We included all institutions reporting ≥10 births annually.

3.3.2 Main outcomes

Paper I had three main outcomes; 1) number and proportion of women of reproductive age living in the different travel zones, 2) place of birth categorised as unplanned outside institution or in an obstetric institution, and 3) maternal morbidity. Planned home births arranged with an attending midwife were excluded. Maternal morbidity was defined as maternal intensive care, puerperal sepsis or sepsis during delivery, thromboembolic disease (with the exception of peripheral venous thrombophlebitis), eclampsia, and haemorrhage >1500 ml or blood transfusion.

In paper II the main clinical outcomes were unplanned birth outside institution and peripartum perinatal death. The definition of unplanned birth outside institution was similar to paper I. Peripartum perinatal death was defined as death during labour or within 24 hours after birth. Intrauterine fetal death prior to start of labour was described but excluded from main analyses.

In paper III the main clinical outcomes were eclampsia, HELLP syndrome, or preterm delivery in pregnancies with preeclampsia. Eclampsia was defined as seizures in a woman with preeclampsia/pregnancy hypertension after exclusion of other medical causes. HELLP was defined as intravascular haemolysis, elevated liver enzymes, and thrombocytopenia (<100 x10^9/L). Since delivery can prevent progression to eclampsia and HELLP syndrome, preterm delivery in pregnancies with preeclampsia was a third clinical outcome. Defined as delivery prior to 35 gestational weeks in pregnancies with preeclampsia and no eclampsia or HELLP, this outcome included all modes of labour start and route of delivery; induced and spontaneous deliveries, vaginal or by caesarean section.

3.3.3 Secondary outcomes

The WHO EmONC indicators were secondary outcomes in paper I. These eights indicators benchmark institution availability and access, caesarean section rate, direct obstetric case fatality rate, intrapartum and very early neonatal mortality (perinatal deaths during labour or within 24 hours), and maternal mortality from direct causes. Maternal mortality was low in Norway during this period and we chose to use maternal morbidity as a maternal clinical outcome. The number of maternal deaths was obtained from the on-going maternal death audit addressing this time period (Siri Vangen, personal communication).(60)

The WHO guideline advices three months data collection, we chose to use a full year for observation as some of the outcomes were rare and the data were readily available.

Births at term to healthy women with a singleton pregnancy, no major congenital malformations, cephalic presentation, and normal vaginal delivery, have been used to define a low-risk category in the literature.(1, 88, 89) We used these births as a secondary outcome in paper II to assess outcomes in low-risk births in the different EmONC institution categories.

3.3.4 Potential confounders

Paper I took into account a limited range of potential confounders; maternal age (>20, 20-24, 25-29 (reference), 30-34, 35+), parity (0, 1, 2+(reference)), education (<11, 11-14, 14+ years (reference)), and partner status (living with partner (reference), single). Maternal morbidity was also adjusted for tobacco use (daily smoking/occasional smoking, or non-smoking (reference)).

In paper II we examined a range of known risk factors for perinatal death, both by stratification and by adjustment in the full regression model. The following variables were assessed: gestational age (<37 weeks, ≥37 weeks (reference)), maternal age (<20, 20-35 (reference), >35), parity (0, 1+ (reference)), education (<11, ≥11 (reference)), partner status (partner (reference), single), ethnicity (Western (reference), Non-Western), chronic disease (asthma, thyroid disease, epilepsy, rheumatoid arthritis, diabetes prior to or in pregnancy, chronic hypertension, chronic renal disease, cardiac disease), plurality (singleton (reference) or multiple birth), major congenital malformation as defined by the EUROCAT collaboration (http://www.eurocat-network.eu/content/EUROCAT-Guide-1. 4-Section-3.3.pdf) (no severe malformation (reference), severe malformation), small for gestational age (<10th percentile, ≥10th percentile (reference)), severe maternal morbidity (haemorrhage <1,5 l or haemorrhage and blood transfusion, eclampsia, HELLP-syndrome, sepsis, pulmonary embolism, organ failure, placental abruption with disseminated coagulation, hysterectomy or uterine rupture), and previous stillbirth at gestation age ≥24 weeks. We stratified by smoking habits; non-smoker (reference), no information, smoker. We used sex-specific birth weight by gestational age z-scores to evaluate misclassification of gestational age, defined as z>4.(90) If gestational age was misclassified (n=330, 0,05%) or only birth weight was notified, births were categorised as prior to 37 weeks if birth weight was below 2 standard deviations from the national average at 37 weeks (2285 g for males and 2200 g for females, n=677, 0,1%).

In paper III we included covariates known to impact the maternal risk of severe hypertensive complications. Analyses were stratified on parity and preeclampsia, and adjusted for the following socio-demographic and maternal medical risk factors: maternal age (<20 years, 20-34 (reference), 35+), partner status (living with partner (reference), single), maternal education (11years or more (reference), <11 years), chronic hypertension (no (reference), yes), diabetes (no (reference), yes), smoking (no (reference), yes and no information), and time period (1999-2004 (reference), 2005-2009). When analysing overall risk of severe hypertensive complications, parity was also included in the model (0/1+). As in paper II, we used sex-specific birth weight by gestational age z-score (90) to identify misclassified gestational age as births with z>4. If gestational age was misclassified (n= 19, 0.1% of deliveries) or only birth weight was recorded, we categorized deliveries as occurring prior to week 35 if birth weight was 2 standard deviations below average weight at 35 weeks gestation (weight <2 020 g for males and < 1 950g for females, n= 203, 1.2 % of deliveries before 35 weeks).(90)

3.4 Analyses

3.4.1 Cross tables and regression

Cross tables were used to calculate proportions and risk, both overall and stratified by potential confounders. Odds ratios (OR) with 95 % confidence intervals (CI) were estimated using logistic regression, crude and adjusted for potential confounders. Relative risks (RR) were estimated using generalised linear models with log-binomial regression, crude and adjusted for potential confounders. Travel time ≤ 1 hour was used as reference in all travel time analyses. For the other main exposures and potential confounders, the category with the lowest risk was generally used as the reference group.

3.4.2 Attributable risk and population attributable risk

The attributable risk or fraction among the exposed quantifies the fraction of disease that can be ascribed to one or more exposures of interest. This fraction depends on the relative risk associated with the exposure. The population attributable risk or fraction describes how much of the outcome in a population that can be ascibed to the exposure of interest. The population attributable risk depends both on the relative risk associated with the exposure and the risk of being exposed in the population.(91, 92) The adjusted relative risk models were used to estimate attributable risk and population attributable risk for peripartum perinatal mortality in unplanned birth outside institution.

3.4.3 Multilevel analyses

Regular statistical methods assume that observations are independent, however, births to the same mother or in the same institution may be more similar than births to another mother or at another institution. In paper II we used multilevel generalized linear models to assess odds ratios and intraclass correlation coefficients (ICC) using the mother, the institution and both as clusters.

3.4.4 Sibling data

By means of the mothers' national identification numbers, deliveries in paper III were also organized in a sibling structure, linking each infant to its mother with the mother as the observation unit (n= 410 841). A total of 2 459 women (0.6%) lacked identification numbers and were not included. The sibling structure enabled analyses of how previous preeclampsia influenced the risk of eclampsia, HELLP-syndrome, and preterm delivery in preeclamptic pregnancies, in the subsequent pregnancies.

3.4.5 Unmeasured confounders

A confounder in an epidemiological study is a factor associated with the exposure and an independent risk factor for the outcome, that may fully or partly explain the observed association between the exposure and the outcome.(93) If information is available, such factors are taken into the analyses in the adjustment phase, either by stratification or by inclusion as covariates in a multivariable model.

In most observational studies, there will be lacking information for potential confounders, so called unmeasured confounding. Different sensitivity analyses can evaluate potential bias associated with unmeasured confounding, a recently proposed approach is to calculate the E-value.(94) The E-value describes the minimum strength of association that an unmeasured confounder would need to have with both the exposure and the outcome in order to explain away the observed exposure-outcome association, conditional on measured covariates.(94) The E-value for a RR estimate >1 is given by RR + sqrt(RR*(RR-1)). The lower (LL) and upper (UL) confidence interval values are given by the similar formula using LL or UL instead of RR if the lower confidence interval is above 1. We performed E-value calculations for the main clinical outcomes in paper III.

3.4.6 Geographic analyses

In paper I, travel time for women of reproductive age to the nearest institution was assessed by two ecological studies at the start and end of the decade. Address coordinates were placed in the different travel zones and the number of women living in each travel zone was counted.

In paper II and paper III all births from 1999 to 2009 were identified in the MBRN and the mothers' addresses were retrieved from the National Registry. Address coordinates at Statistics Norway were then used to assign each birth/delivery to the travel zone of the mother at the time of birth. The mother´s national identification number, or the D-number, was used to link births/deliveries in the MBRN to her registered address in the National Registry and then to the address coordinates (98.4%). For each birth/delivery the registered address was placed in a travel zone. Births to women lacking address coordinates (1.5%) were assigned to the travel zone of the majority of mothers in their municipality in the corresponding year. Few births lacked both address coordinates and municipality (0.06%), and these were excluded from the travel zone analyses.

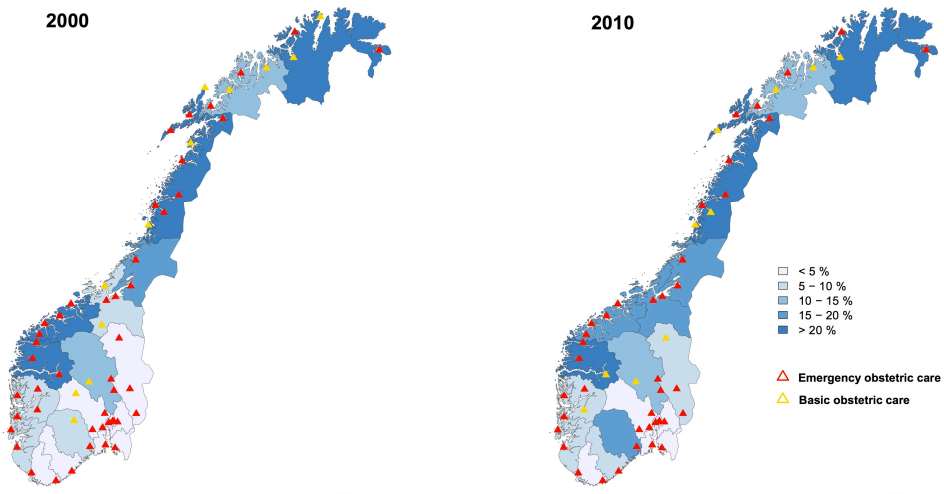
3.4.6 Ethical approval

The study was approved by the Regional Medical Ethical Committee for Western Norway (REK-VEST 2010/3243) and was exempted from the principle of individual consent.

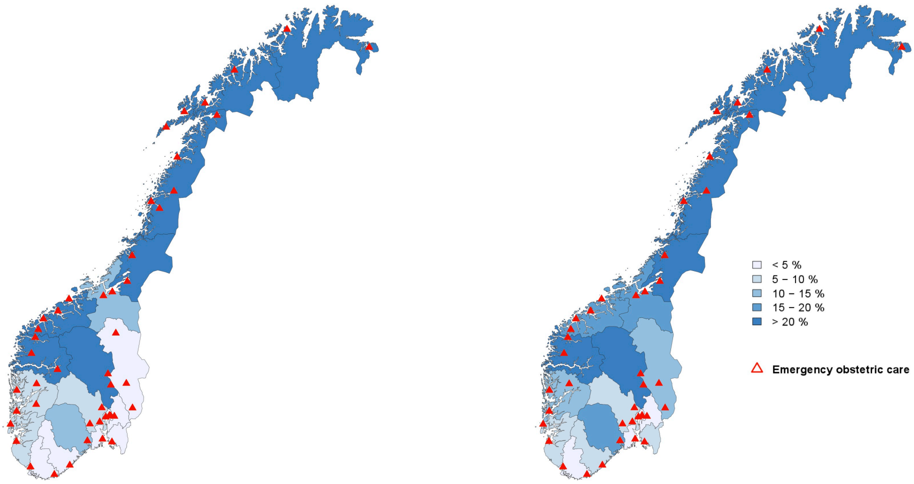
4 Results

4.1 Paper I

Travel time to an obstetric institution The proportion of women of reproductive age who lived outside the 1-hour travel zone to any obstetric increased from 7.9% to 8.8% from 2000 to 2010 (RR 1.11; 95% CI 1.10-1.12). The proportion of women living outside the 1-hour zone to EmONC institutions increased from 11.0% to 12.1% from 2000 to 2010 (RR 1.1; 1.09-1.11). Increases in proportions were observed in counties where obstetric institutions closed during this period, whereas decreases related to major infrastructure projects were observed in two counties. Although the numbers were low, the proportion of women living outside the 2-hour zone to EmONC institutions increased from 3.4 to 4.8% nationally (RR 1.4; 1.39-1.43) and also increased in three of the five health regions.



All obstetric institutions and the proportion of women in fertile age living outside the 1-hour travel zone by county. Norway 2000 and 2010.



EmONC institutions and the proportion of women living outside the 1-hour travel zone by county. Norway 2000 and 2010.

Unplanned delivery outside an obstetric institution During 1979 to 2009, a total of 11 537 deliveries outside an institution were registered among the 1 807 714 deliveries in this period. On a national level, the risk of unplanned delivery outside an institution almost doubled from 0.4% in 1979-83 to 0.7% in 2004-09.[1] The risk range among the counties increased from 0.1 to 0.7% in the first period to 0.3-1.8% in the last period, with the highest risks in counties where more women lived outside the 1-hour zone. However, even in urban counties where less than 1% of the women lived outside the 1-hour zone, the risk more than doubled.

Maternal morbidity Nationally, the maternal morbidity risk increased from 1.7% to 2.2% from 2000 to 2009 (adjusted OR, 1.4; 1.2-1.5), regional comparisons yielded similar risks in 2000 and increasing regional differences in 2009.

[1] In table 3 in the paper there is an error in number of deliveries for 2004-2009. These columns describe the number of deliveries from 2003 to 2009, both total and unplanned outside institution. The error in numbers had no consequences for the reported risks in the last time period. The odds ratios were calculated using the time period from 2004 to 2009 and are correct.

4.2 Paper II

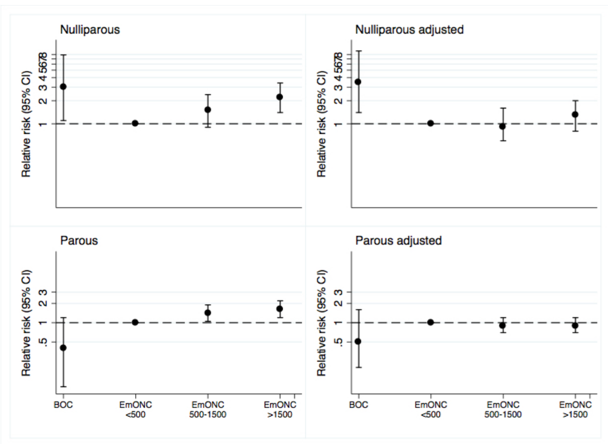
Travel zone and place of birth Travel zone information was available for 646 898 births (99.94%). Births were more likely to occur unplanned outside an obstetric institution, in BOC institutions or in the lowest volume EmONC institutions when mothers lived in rural areas with long travel time to institutions. A total of 9 490 births occurred in BOC institutions. Few nulliparous women delivered in BOC institutions (n=1 680, 18%), among these 87% would need to travel more than one hour to reach an EmONC institution.

4 538 infants with available travel zone information were born unplanned outside institution. Compared to births within the 1-hour zone, the risk of unplanned birth outside institution was five times higher in the 1-2 hour travel zone to all institutions (adjusted RR 5.3; 4.9-5.7) and seven times higher when travel time was two hours or more (adjusted RR 7.1; 6.3-8.1). The majority of unplanned births outside institutions occurred to low-risk women.

Peripartum mortality in unplanned birth outside institution Among 645 063 births we identified 1 586 peripartum perinatal deaths, of which 773 (48.7%) were stillborn. Unplanned birth outside institution was strongly associated with mortality risk (adjusted RR 3.9; 2.8-5.3). Although the absolute mortality risk was higher for preterm births than term births (25.4/1000 versus 0.7/1000), the relative mortality risk associated with unplanned birth outside institution was increased for both preterm and term births. The stratified analyses illustrated higher absolute mortality rates in high-risk groups, but similar RRs associated with unplanned birth outside institution except for single, young and nulliparous women. The relative mortality risk was particularly high for births to nulliparous women (adjusted RR 14.9; 8.8-25.1), but also births to parous women had a doubled risk of death if born unplanned outside institution (adjusted RR 2.2; 1.4-3.4). The risk of death ascribable to unplanned birth outside institutions was high with an attributable risk of 0.7 (95% CI; 0.6-0.8), and these births accounted for 2.1% (95% CI; 1.2-3.0%) of the peripartum mortality in the population.

Peripartum mortality in obstetric institutions Infants with severe congenital malformations were born in the larger EmONC institutions. When we excluded severe congenital malformations, the mortality rate in BOC institutions was lower for parous women (0.5/1000) than nulliparous women (3.6/1000). The peripartum mortality rate in EmONC institutions ranged from 1.3 % in the smallest institutions to 2.6 % in the largest. After adjustment for socio-demographic factors and maternal and fetal risk factors and using the smallest EmONC institutions as reference, we did not find evidence of different mortality by annual number of births in EmONC institutions. Restricting the analyses to healthy women with vaginal delivery at term of a singleton infant with cephalic presentation and no severe congenital malformation, the peripartum mortality ranged from 0.5/1000 to 0.6/1000 in the EmONC institutions, and we found no difference in mortality by volume category.

Regardless of place of birth and not restricted to unplanned birth outside institution, mortality increased during the winter season for births at term to parous women with travel time 2 hours or more to all institutions (2.5/1000) compared to births where the mother lived within the 1-hour zone (0.6/1000, RR 3.8; 1.4-10.5).



Risk of peripartum perinatal mortality in obstetric institutions, stratified by parity and using the smallest EmONC institutions with <500 births/year as reference. Births with no severe congenital malformations, adjusted for sociodemographic factors and maternal and fetal medical risk factors. Norway 1999-2009.

4.3 Paper III

Hypertensive complications Among 630 255 deliveries, we identified 1 387 (2.2/1000) women with eclampsia/HELLP and 3 004 (4.8/1000) deliveries prior to 35 weeks to women with preeclampsia and no eclampsia or HELLP. The risk of eclampsia/HELLP was higher among women with preeclampsia, but women without preeclampsia accounted for a major proportion of cases among parous (56%) and nulliparous (45%) women.

Travel time to any obstetric institution The overall risk of eclampsia/HELLP was 30% higher outside compared to inside the 1-hour zone (adjusted RR 1.3; 1.05-1.7). The risk increase was particularly high among nulliparous women without preeclampsia (0.26 vs 0.16%, adjusted RR 1.7; 1.2 to 2.6). Among nulliparous women, only one case occurred in a BOC institution, and the risk increase associated with long travel time was similar in the different EmONC volume categories. Among parous women, longer travel time was not associated with increased risk of eclampsia/HELLP.

Travel time to EmONC institutions As described for all obstetric institutions, the overall risk increased by 30% when the women had to travel 1 hour or more to an EmONC institution, and the risk increase was similar across the institution volume categories. In nulliparous women, travel time ≥1 hour was associated with a 40% increase in risk of eclampsia/HELLP, while there was no risk increase among parous women. However, for parous women with preeclampsia and delivery after 35 weeks, the risk of eclampsia/HELLP was almost doubled outside the 1-hour zone (1.8% versus 1.0%, adjusted RR 1.8; 1.0 to 3.1)

Delivery prior to 35 weeks in women with preeclampsia and no eclampsia/HELLP Delivery prior to 35 weeks in women with preeclampsia was highest among nulliparous women; 0.6% outside the 1-hour zone to any institution versus 0.7% within the 1-hour zone (adjusted RR 0.8; 0.6 to 1.1).

Hypertensive complications and place of delivery Women with preeclampsia who developed eclampsia/HELLP received care in EmONC institutions with >500 births annually. Women with preeclampsia and no eclampsia/HELLP who delivered before 35 weeks constituted nearly 20% of all deliveries before 35 weeks. These women delivered in EmONC institutions with more than 500 births annually.

All eclampsia/HELLP cases in BOC institutions occurred in women without preeclampsia. In EmONC institutions, 42 % of cases delivering after 35 weeks did not have a registered preeclampsia.

Hypertensive complications in successive pregnancies Among 260 388 women who delivered a first infant in the study period, 138 111 (53%) had a second and 27 714 (11%) a third delivery. We defined previous preeclampsia as preeclampsia, eclampsia or HELLP in a previous pregnancy. Among women with previous preeclampsia, 38 (0.5%) had eclampsia/HELLP in the second delivery. None of these women delivered in a BOC institution, and the majority delivered in the largest EmONC institutions. Two women with eclampsia/HELLP at the third delivery had previous preeclampsia, and they delivered in the largest EmONC institutions.

The risk of eclampsia/HELLP in the second and third delivery among women without previous preeclampsia was 0.1%. These 135 women accounted for all eclampsia/HELLP cases in BOC institutions, and 70% or more of the cases in EmONC institutions.

5 Discussion

5.1 Principal findings

Paper I

The risk of unplanned delivery outside an institution doubled in Norway over 30 years and maternal morbidity increased from 2000 to 2009. These changes coincided with an increasing proportion of women of reproductive age living farther away from obstetric institutions, and with a reduction in the number of emergency obstetric care institutions to a level below the estimated need according to WHO guidelines.

Paper II

Unplanned birth outside an institution was associated with the peripartum mortality risk both for births to women with risk factors and for births to women usually regarded as low-risk. Elimination of unplanned births outside institution was estimated to reduce the peripartum perinatal mortality in the population by 2.1%. The risk of unplanned birth outside institution was strongly associated with travel time to the nearest obstetric institution. Few high-risk births in the smallest institution categories and comparable mortality rates in EmONC institutions indicated well functioning routines for selective referral.

Paper III

Nulliparous women living outside the 1-hour travel zone to all obstetric institutions had a 50% increased risk of eclampsia/ HELLP. This risk was also increased in parous women with preeclampsia and delivery after 35 weeks if travel time was 1 hour or more to EmONC institutions.

All eclampsia/HELLP cases occurring in BOC institutions were in women without preeclampsia registered in the present pregnancy. Although previous preeclampsia was a major risk factor for eclampsia/HELLP in later pregnancies, the majority of eclampsia and HELLP cases occurred in women without previous preeclampsia. All women with previous preeclampsia delivered in EmONC institutions. Similarly, deliveries prior to 35 gestational weeks in women with preeclampsia received care in EmONC institutions, the majority in the largest volume categories.

5.2 Strengths

We used population-based registry and census data, and we combined various methods and data sources in order to provide a more comprehensive description of the health system during the study period. The registries are based on mandatory notification/registration and cover the entire country. The national identification numbers allowed linkage between registries, enabled individual travel time estimations and allowed linkage of all births to their mother in a sibling structure to analyse outcomes in successive pregnancies.

The MBRN database permitted a long observation period and the large samples necessary to study rare events. In papers II and III, the use of geographic technology combined with individual address coordinates allowed individual estimates of travel time.

We had data for a range of potential confounders and risk factors and were able to take into account clustering of births to the same mother and in the same institution. In contrast to other studies using hospital discharge data, we had verified information about eclampsia and HELLP,(95, 96) and the registration of preeclampsia has been validated. When analysing successive deliveries, the long observation time allowed sufficient observation time for new pregnancies to occur.

5.3 Methodological considerations and limitations

5.3.1 Design

With the register based retrospective cohort design, we could use data from registries covering the entire country over decades, and this approach allowed for a longer observation time than would have been feasible in a prospective study. The data consists of recorded information for predefined variables in the registry, and the variables were not primarily designed for health systems research purposes. The registry has more extensive data on factors known to be relevant for perinatal outcomes than data from hospital admissions or other sources of routine data.(97) Notification of all births also collects information from the women without complications. However, the information available for women experiencing the main study outcomes may be restricted compared to a prospective cohort study where more extensive information about exposures and factors believed to influence the outcome can be collected. In such studies there may be less information available for selected controls. Quality control was implemented by the MBRN to exclude false-positive outcomes. Routines to assess false-negative registrations were not implemented at the MBRN, so we do not know the proportion of women with complications that were not registered. Previous studies have shown underreporting of diagnoses and procedures such as uterine rupture and hysterectomy in the MBRN.(98-100)

5.3.2 Information bias

Misclassification of exposures

Very few women in our population lacked information about the main exposures (travel time and place of birth), and individual travel time data was available for the majority in papers II and III. The travel time estimates were based on standardized conditions and may underestimate actual travel time. The estimates did not take into account factors such as seasonal variations in driving conditions, but higher perinatal mortality during the winter season suggests potential consequences of reduced accessibility. The geographic travel zones were checked for topographic barriers such as rivers and islands. Women living on islands or more than 500 m from a road, might lack geographic coordinates. Assigning women who lacked geographic coordinates to the travel time of the majority of women in the municipality could lead to underreporting of women with long travel time. Consequently, such information bias could lead to underestimation of the risk ratio.

In paper I, travel time estimates were based on population data on women in reproductive age and not on individual estimates for the women giving birth.

Relocation and travel time estimates in paper II and III

The annual relocation rate was 14% in 2000, 8.6% relocated within the municipality, and 4.8% to another municipality. Relocation from a rural to an urban area during the year of birth could lead to the lower risk of urban residence being assigned to rural residence and thus an underestimation of the rural risk. Similarly, relocation from an urban to a rural residence during the year of birth would lead to an increased rural risk being registered as urban in the analyses. Thus, relocation bias could lead to overestimation of the urban risk (the reference group) and a lower relative risk associated with rural residence.

Classification of place of birth

Planned home deliveries were not registered separately in the MBRN before 1999. Consequently, the increase in risk of unplanned delivery outside institutions over time may be underestimated in paper I. However, planned home deliveries were rare in the reference period (1979-1983), in 1975-76 the prevalence was 0.037 % (20/54492).(101)

While working on with paper II, we identified that some births in former obstetric institutions were categorised by the MBRN as institutional births during the period from 1999 to 2009. The closed institution had lower volumes, and these errors could bias both the risk associated with unplanned birth outside institution and with births in the assigned birth volume category if not corrected. The increase in risk of unplanned birth outside institution over time may be underestimated in paper I as births in closed institutions would not be counted in the primary outcome during the last time period. However, the number was limited to 129 births from 1999 to 2009.

Misclassification of outcomes

In paper I, the definition of maternal morbidity included the main direct potentially life threatening complications.(17) The increase in maternal morbidity over time may have several explanations, and we could not discriminate improved diagnosis or improved reporting from other contributing factors. National guidelines for diagnosis, monitoring and treatment of maternal and fetal complications have been updated regularly since 1995, but lack of adherence has been reported.(54, 102-104)

Perinatal peripartum mortality (paper II) constitutes a hard endpoint insofar as mortality is a definitive state. The MBRN notification included time of death prior to, during or after delivery. Some stillbirths were classified as having unknown time of death, the proportion of unknown time of death was 0.07% of all institutional births and 0.35% of unplanned births outside institution. We used unplanned birth outside institution as a measure of inadequate access to obstetric institutions, and unknown time of death could be a consequence of lacking skilled attendance and monitoring at the start of labour. Thus, we included stillbirths with unknown time of death in our definition of peripartum perinatal mortality in paper II, while antepartum deaths were excluded.

In paper I, delivery related perinatal death (death during labour or within the first 24 hours) in institutional births was used to describe mortality in institutions, and here we excluded both antepartum stillbirths and stillbirth with unknown time of death.

Although all eclampsia and HELLP cases (paper III) notified to the MBRN were verified, we could not rule out false negative cases in. Previous studies from the MBRN have also shown that mild preeclampsia may be underreported. However, underreporting is not likely linked to women´s travel time and would thus represent a non-differential bias.

5.3.3 Potential confounders

Paper I

In the analyses we adjusted for a limited number of potential confounders; maternal age, parity, and partner status, and there was little difference between crude and adjusted odds ratios. Mode of delivery, such as caesarean section, also increases the risk of maternal complications both in the actual and subsequent pregnancies.(105, 106) Within-country variation of caesarean section rates may have an impact on maternal morbidity and these rates were reported at a regional level in the WHO indicator analysis. Women with long travel time may have increased risk of caesarean section if they arrive at the institution too late for other interventions or if they more frequently have a planned caesarean section, but in such cases the mode of delivery would be a mediator. Adjustment for maternal diabetes did not change the estimates and was not included in the final regression models. Adjustment for maternal smoking slightly increased the estimates, probably due to decreasing frequency of daily smoking over time. Daily smoking was reported by 24 % of the pregnant women in 2000, compared to 17 % in 2009 (the MBRN, http://mfr-nesstar.uib.no/mfr/). We could not adjust for maternal obesity, and we commented that women with a Non-Western county of birth may have higher risk of adverse pregnancy outcomes and that ethnicity must be included among the risk factors in future studies. (5, 105, 107, 108)

Paper II

In paper II, we both stratified analyses and adjusted for a range of potential risk factors for peripartum mortality that theoretically could be associated with travel time or place of birth. The adjustment slightly strengthened the overall relative risk estimate. The MBRN lacked information on some potential confounders that could be of importance, such as obesity. Although obesity is a significant risk factor for perinatal mortality, it is less likely to be strongly associated with travel time or place of birth, except with referral of women with very high BMI. Maternal obesity is also associated with education level and maternal chronic disease and these risk factors were included in the analyses. Similarly, higher alcohol consumption during pregnancy has been shown to be associated with smoking and older age, we adjusted for both smoking and maternal age, so residual confounding by alcohol consumption is not likely to explain the observed differences in peripartum mortality by place of birth and travel time.(109)

When defining severe congenital malformations, we applied published definitions from the European network of congenital anomaly registers, EUROCAT (http://www.eurocat-network.eu/content/EUROCAT-Definition-New-Subgroups-Feb-2007). Other risk factors for peripartum mortality, such as fetal sex or fetal presentation, are not associated with travel time and were therefore no confounders in our analyses. Differences in available intrapartum care probably explain most of the differences in mortality by place of birth and are a likely mediator in our data.

Some births in the MBRN had missing information on gestational age, or gestational age was misclassified and not in accordance with birth weight. In paper II and III, the majority of births with misclassified gestational age or only recorded birth weight, had birth weights indicating that they were born either at 37 weeks or later, or at 35 weeks or later. By reclassifying these births manually using birth weight by gestational age standards(90) we retained these births in the adjusted analyses.

Women can opt out from registration of smoking information. Because of this, the proportion of births/deliveries with missing information about smoking was quite high (17%). In paper I, we adjusted for two categories of tobacco use; smoking or non-smoking, and the women with missing information were excluded from the adjusted analyses. As smoking is related to risk of peripartum perinatal death and to risk of preeclampsia, we included women with missing smoking information as an additional category in paper II and III. If all women with missing information were non-smokers, the relative risk of peripartum mortality rate in unplanned births outside institution versus institution births would be 3.96; 2.9-5.5 after adjustment for smoking. If all the women with missing information were indeed smokers, the adjusted relative risk of peripartum perinatal mortality in unplanned birth outside institution would be 3.94; 2.8-5.5 after adjustment for smoking.

Paper III

The absolute risk of hypertensive complications varied with gestational age, parity and whether the mother had preeclampsia. Obesity increases the risk of preeclampsia and since we lacked data about maternal BMI we could not adjust for obesity. In the Norwegian Mother and Child cohort from 19998-2008, 10 % of women with a singleton pregnancy, no severe congenital malformations and no prepreganacy diabetes had a prepregnancy body mass index (BMI) of 30 or more (7% BMI 30-35, 2.6% BMI >35).(110) However, the cohort contains a selected group of women with a higher level of education, a lower proportion of daily smoking women, and fewer women with low socioeconomic status than the general population.

Obesity increases with parity and our results showed the highest risk of severe hypertensive complications related to travel time in nulliparous women. Findings from the UK suggest that obesity as a single risk factor play a modest role for adverse maternal and perinatal outcomes in parous women.(111) In a hospital case-control study in Norway, weight more than 70 kg was associated with increased risk of severe preeclampsia in parous women with a history of preeclampsia in previous pregnancy.(112) A recent study from the US did show increased risk of preeclampsia with severe features at or after 34 gestational weeks with increasing BMI.(113)

While we could not adjust for obesity as a separate risk factor, adjustment for risk factors related to obesity, such as diabetes, chronic hypertension, partner status, education and smoking, did not change the relative risk associated with longer travel time. Low availability of institutions may be associated with a rural lifestyle associated with higher *or* lower risk of obesity, we thus believe the potential association between travel time and obesity to be modest. Women with chronic renal disease and systemic lupus erytematosus have increased risk of preeclampsia.(114) Chronic renal disease was rare and adjustment did not change the risk estimates. Accordingly, we removed chronic renal disease from the model. No cases of eclampsia/HELLP were described among the 340 women with systemic lupus erytematosus. (115)

Sensitivity analyses

The potential consequences of unmeasured confounding need to be taken into account in observational studies. As mentioned earlier, the E-value measures the minimum strength of association that an unmeasured confounder must have with both the exposure and the outcome in order to explain away the exposure-outcome association.(94) In paper III, we performed sensitivity analyses and computed E-values for the main exposure-outcome associations. Unmeasured confounders can never be ruled out, but would have to be strongly associated with both travel time and hypertensive complications to explain the observed associations. In order to explain away the results in paper III, an unmeasured confounder needs be associated with both travel time and eclampsia/HELLP with a relative risk of 2 or more, which we judge to be unlikely.

5.3.4 Cluster analyses

Births within the same institution may share socio-demographic and health characteristics, will be treated in the same clinical setting, and may thus have more similar health outcomes compared to births in another institution. Births to the same mother will also have more similar outcomes than births to different women.(116-118) In studies on public health interventions in groups (clusters), the intraclass correlation coefficient (ICC) describes the degree to which individuals within a group share similarities; if it is close to 0 the individuals within a cluster are no more similar than individuals outside the cluster, if it is close to 1 the individuals in the cluster are similar.(119) If births within the same cluster are very similar (low within-cluster variation) this will artificially magnify differences in outcomes between clusters and reduce the power to detect true differences between exposure groups in observational studies.

We applied a multilevel statistical model to the analysis of peripartum perinatal mortality using the institutions as a cluster variable. The multilevel statistical models yielded similar odds ratios as the relative risk of large groups, as expected. In the comparison between births in BOC and EmONC institutions at term, ICC for institution was 0.012 (0.03 to 0.057). Among term EmONC births the ICC for institution was 0.011 (0.002 to 0.060). Adding the mother as a further cluster variable for term births, the ICC for the institution was 0.01 (0.003 to 0.029) and the ICC for mother was 0.31 (0.20 to 0.44). ICC for the mother in smaller, high-risk groups, such as preterm birth, was high.

Although we had a relatively similar number of clusters, the ICC for the institution clusters in our study was lower than in a US study comparing maternal and neonatal outcomes by institution practices for induction and caesarean section rate in low-risk women.(120) Our results were slightly higher than modelled estimates for perinatal outcomes in trials assessing community interventions in maternal and newborn health.(119) Both the number of births per cluster and a limited number of clusters may contribute to this and need to be considered because the power to detect a true difference may be reduced.

Multilevel analyses yielded comparative or slightly higher odds ratios to the relative risks, except for higher odds ratios than the relative risks in smaller, high-risk groups. Hence, we completed the analyses using the relative risk to aid comparison across strata and the communication of the findings.

5.4 Comparison with other studies

Paper I

Travel time When analysing availability of institutions, we considered hourly time categories to be a realistic approach to the Norwegian demography. The Netherlands has a higher proportion of planned home deliveries compared to Norway, there, estimated travel time exceeding 20 minutes was associated with increased risk of adverse neonatal outcome in home deliveries with subsequent hospital transfer.(51) Travel time exceeding 45 minutes was associated with higher risk of fetal mortality in France.(121) Few studies have assessed travel time to obstetric institutions with different levels of care. In the United States, the proportion of women who lived outside the one-hour travel zone was three times higher than in Norway when all obstetric institutions were included, and almost twice as high when including only emergency obstetric care institutions.(50)

Indigenous population It is worth noting that a higher proportion of Native American women (18.8%) lived outside the one-hour drive to the US equivalent of EmONC institutions.(50) Similarly, we found higher proportions of women (35 to 72%) who lived outside the 1-hour zone to EmONC institutions in the Northern region of Norway. This region covers the main Sami cultural and economic areas in Norway.(122) Neither Statistics Norway, nor the MBRN, register the indigenous identity of Sami women. Consequently, it was not possible to assess availability for this group in particular.

The risk of unplanned delivery outside institutions This risk increased in both urban and rural counties in our study. The risk in Norway during the period 2004-2009 was higher than the previously reported 0.1% of births in national data from Finland.(123) In our study, the risk was 0.3 to 0.5% in the three most urban counties, this was lower than the 0.6% reported from an urban area in Scotland and relatively similar to studies from France.(48, 124) In urban areas other factors than the time of the journey may also increase the difference between actual and estimated travel time,(125) and the institution workload or policies may impact admission.(126)

Maternal morbidity The 2.2 % risk of maternal morbidity in paper I was higher than previous reports from Norway and Europe, but differences in risk may partly be due to different definitions of maternal morbidity. The Mothers Mortality and severe Morbidity Survey B (MOMS-B) reported a Norwegian incidence rate 0.86/1000 deliveries based on data collected for 1 year in the capital county, Oslo, The study did not address differences between Norwegian hospitals and regions and did not include thromboembolism. European rates of maternal morbidity in the MOMS-B study ranged from 0.6 to 1.5 %.(53) The incidence of severe maternal morbidity was 0.71 % in a prospective Dutch study that applied a more strict definition of severe maternal morbidity.(5, 17) The fact that our inclusion criteria were wider was also reflected by a morbidity/mortality ratio of 266:1, compared to other studies reporting ratios of 118:1 and 49:1.(127, 128) While the wider definition influenced the reported risk, the definitions and the MBRN notification form were similar throughout the period, thus allowing for evaluation of change over time as well as regional differences. However, we could not exclude the possibility of changes in the reporting to the MBRN over time and potential influences of notification practices on the time trends in maternal morbidity.

Annual number of births in institutions We observed a reduction in the number of small institutions, and an increasing proportion of the deliveries took place in the largest institutions. In France, small institutions had higher frequency of inadequate/inappropriate management of severe post-partum haemorrhage.(56) A study from the United States reported increased risk of maternal complications in the institutions with the lowest volumes, which also included non-obstetric institutions.(129) Low volume of deliveries and rural location were also associated with increased risk of postpartum haemorrhage in a US study where maternal morbidity included severe perineal lacerations and wound infections, but excluded hypertensive complications and thromboembolism. Urban teaching hospitals also had higher morbidity risk among the high volume institutions.(130)

Paper II

Theoretically, reduced access to specialist health care could influence antepartum stillbirths due to factors such as lower detection of risk pregnancies and less monitoring to assist timely delivery.(131, 132) However, we found no difference in antepartum stillbirth rates in the different travel zones, and these births were referred to EmONC institutions.

Avoidance of institutions Lack of acceptability resulting in deliberate avoidance of institutions and planned home delivery with an unskilled attendant has been described in the US and Australia .(46, 133) Avoidance of institutions has not been a major risk factor for unplanned birth outside institution in Europe.(134, 135) In Canada, the Society for Obstetricians and Gynaecologists have stated that skilled birth attendance needs to be available in remote communities(136) Few women with risk factors gave birth in BOC institutions and in the lowest volume category of EmONC institutions in our study, indicating that the national guidelines for referral were well implemented. In accordance with recent publications, the peripartum mortality was higher in births to nulliparous than to parous women in BOC institutions.(45, 137) However, the mortality risk was lower than for unplanned birth outside institution for this group.

Previous studies have shown an association between reduced availability of institutions and higher neonatal morbidity, thus suggesting an increased risk of neonatal mortality.(123, 138) Potential increases in neonatal mortality have also been modelled (139) and reported as a co-finding.(45) We found a clear association between unplanned birth outside obstetric institution and peripartum mortality, and the increase in mortality was not confined to preterm birth or vulnerable groups, as shown in previous studies.(49, 51, 131)

Paper III

Prediction models Models using symptoms and laboratory findings may be helpful in identifying short-term risk of rapid progression to severe hypertensive complications in women with preeclampsia.(140) Previous hospital based studies from the US reported few women with diagnosed preeclampsia among eclampsia cases and identified delay in recognition of prodromal symptoms, care seeking, as well as diagnosis and treatment by the physician.(75, 141)

In our study, the proportion of women with eclampsia/HELLP and preeclampsia differed by gestational age, and more than 50% of cases occurring after 35 weeks did not have preeclampsia, although mild preeclampsia may be underreported.(85) Preeclampsia incidence in Norway has been comparable to other high-income settings,(142) and although there may be underreporting of mild preeclampsia at term, our results are comparable to previous European studies where 42% of the women had preeclampsia prior to eclampsia.(143)

It is also worth noting that a similar shift in the proportion of women with preeclampsia prior to eclampsia was observed in the UK following the introduction of magnesium-sulphate to treat and prevent seizures; improved management reduced the risk of eclampsia in women with preeclampsia, but not for women without established preeclampsia.(80) In Scandinavia, eclampsia in 1998-2000 was linked to suboptimal care and low use of magnesium-sulphate, and 84 % of the women had preeclampsia prior to seizures.(54) In our study, the proportion of eclampsia/HELLP cases with preeclampsia was almost 70 % in deliveries prior to 35 weeks and 42 % in deliveries at 35 weeks or later. Similarly, previous preeclampsia was a risk factor for eclampsia/HELLP in the present pregnancy, but in the sibling analyses, 78 % of parous women with eclampsia/HELLP in the second or third delivery did not have previous preeclampsia. The proportion of parous women with previous preeclampsia was 34% in the study from 1998-2000.(54) While prevention and treatment of eclampsia with magnesium-sulphate was not addressed in our study, the reduction in the risk of preeclampsia among women with preeclampsia may indicate a transition comparable to the reduction of eclampsia among women with preeclampsia in the UK.

Our findings illustrate potential shortcomings in the “linear” preeclampsia to eclampsia approach(141) and shows that it may not be possible to predict severe hypertensive complications based on preeclampsia alone.

5.4.2 Distribution of health and social determinants

National policy in Norway has emphasized the need for decentralized care in order to provide safe services of high quality near a woman´s home.(23) National policy also aims to reduce economic barriers to healthcare in pregnancy. Both primary and specialist healthcare related to pregnancy and childbirth is free for residents in Norway, and prenatal care is widely attended.(144)

Norwegian research, policy and plans regarding social, economic and cultural inequalities in health have focused on socioeconomic inequalities using income and education as determinants; the recent national knowledge summary did not address geographic inequalities but stated that there were small geographic differences in service utilization and outcomes for cancer and chronic disease.(145) Social inequality in fetal outcomes has been identified in most of the Nordic countries, where education level has been the most frequent measure of social status.(146) However, the above review article also concluded that studies using data from the 1980-ies were not conclusive with regard to social differences in perinatal mortality in the Nordic countries. Differences in risk of antenatal fetal death by low maternal education declined in Norway during the period from 1967 to 1998.(147) Geographic differences in health have been addressed in studies of cancer survival.(148)

The delivery rate before 35 weeks in women with preeclampsia was lower among nulliparous women who lived outside the 1-hour travel zone. While the difference was not statistically significant, the lower delivery rate and the higher risk of eclampsia/ HELLP may jointly indicate lower access to adequate and timely health services in rural areas.

Parous women with preeclampsia who delivered after 35 weeks had a low absolute risk of eclampsia/HELLP, but the risk was higher outside the 1-hour travel zone to EmONC institutions. When counselling these women, clinicians need to discuss potential benefits and disadvantages of planned early delivery or closer monitoring.(149) A previous study on Scottish women's preferences and considerations in choice of place of birth has shown how women take several factors into account.(134) The studies in this thesis were not designed to address the women's concerns and considerations.

A Dutch study on maternal mortality caused by hypertensive complications identified geographic as well as socioeconomic and ethnic disparities in mortality.(150) Increased risk of severe disease or death, and barriers to access care for immigrants have been documented in high-income countries (107, 108, 125, 151). In our study, women born in non-Western countries had a higher risk of unplanned birth outside institution and peripartum perinatal mortality. The risk of eclampsia/HELLP was similar in parous non-Western women (0.12 versus 0.13%) and nulliparous non-Western women (0.24 versus 0.36%) when compared to women born in Western countries. The approach to measurement of inequality also matters, in a US study on opportunities for improvement in care for women with severe maternal morbidity, social conditions and barriers to access care was labelled as a patient and not a system factor in a hospital-based study.(152)

Our studies illustrate how institution availability in itself can be a barrier to access care. Increased travel time was not linked to different outcomes in the high-risk groups for perinatal death and severe hypertensive complications, such as nulliparous women with pre-eclampsia. However, we found increase in risk related to travel time among women usually not regarded as high-risk; unplanned birth outside institution to parous women and births at term, nulliparous women without preeclampsia, and parous women with preeclampsia who delivered after 35 weeks. The decision-making process and potential delays among women and health personnel has not been studied for such intermediate/low-risk groups. We may speculate that the emergency transport for small groups of high-risk patients work well, although it may not always be available.(153)

5.4.3 Evaluating quality of care

Maternal clinical outcomes

Concluding on the findings in paper I, we would expect the risk of morbidity to be unchanged or reduced following the centralisation. The maternal mortality was low and indicate good quality of clinical care in the institutions. Still, we found an increase in the risk of maternal morbidity and increasing regional differences in such risk. We do not believe that our findings could be fully explained by differences in diagnoses, reporting practices or increases in risk factors where information was lacking, although these factors may play a role.

The definition of maternal morbidity in paper I comprised the main direct maternal morbidities as well as intensive care as a management indicator of severe disease, although thresholds for transfer to intensive care units may vary.(154)

An initial aim of the research in this thesis was to assess severe maternal morbidity using both notifications to the MBRN and the ICD-10 and procedure codes reported to the Norwegian Patient registry (NPR) for the last 2 study years. We aimed to apply variable definitions in line with recent emphasis on organ failure and procedures.(5, 17, 67, 155-157) Comparison of registrations in the MBRN and the NPR in 2008 and 2009 did show discrepancies in frequencies of severe maternal morbidity in accordance with previous research and preliminary analyses of on-going Nordic research collaborations.(98-100) Thus, for the present paper III we chose to use verified clinical outcomes. The findings concerning severe maternal morbidity have led to a project to compare and validate notification of severe maternal morbidity in the MBRN and the NPR. The findings from that project show under-reporting to the MBRN for a number of sever maternal complications, but over-reporting and false-positive registrations in the NPR. Our conclusion was that neither the MBRN nor the NPR have data on severe maternal morbidity that is of adequate quality to make a sound basis for comparing different institutions or regions. A routine linkage of the registries followed by prospective validation of a prioritized number of defined complications could be one way of improving the quality of these data.

Perinatal clinical outcomes

Improvement in monitoring and interventions during delivery has been proposed as an explanation for reduced intrapartum and 7-day neonatal mortality in term births during recent decades.(88) However, as much as 30 % of the deaths in low-risk births at term occurred intrapartum in Scotland.(88) Our findings added to the evidence that including only neonatal deaths would lead to an underestimation of delivery related mortality.

In the thesis, we assessed perinatal mortality during birth and within 24 hours. Infants surviving with severe morbidity or dying within 28 days would be expected to depend on availability of pediatric care or neonatal intensive care. Given the decentralised structure of obstetric and pediatric care in Norway, this should be addressed in a separate study.

Recent publications about risk factors for stillbirths in high-income countries have refrained from investigating health system factors, some have only targeted “modifiable maternal risk factors”,(158) other studies have also included indicators of socioeconomic and demographic factors.(132, 159-163) Lack of attention to modifiable health systems factors may lead to unidentified socio-demographic inequalities and lack of relevant information in the debate on existing and emerging inequities.

Process measures of quality

In the thesis we have used health system characteristics as exposures and clinical outcomes as main outcomes. We have not assessed the process of treatment provision, such as the proportion of women receiving care according to treatment guidelines. Such actions, often referred to as process indicators, may be more readily available for study than rare clinical outcomes. However, process indicators for best-practice have not been shown to be associated with improved clinical maternal and neonatal outcomes in low-risk births.(120)

5.5 Generalisability

While travel distances in Norway may be longer than in many high-income countries, we complied with international standard definitions and indicator frameworks to aid comparison over time and across settings.(16) By classifying the obstetric institutions according to both function and annual number of deliveries we were able to discriminate the emergency services provided and exclude non-obstetric institutions. Emergency obstetric care in Norway has a tiered organisation with increasing subspecialisation following increasing annual volume comparable to other high-income settings.(164, 165)

6 Conclusion and future research

The present thesis found support for the importance of available and accessible obstetric institutions also in a high-income setting. We show that the addition of geographic tools to traditional epidemiology can be useful for service evaluation as well as for planning. We found that structural factors such as travel time have important impact on maternal and perinatal health, also for low-risk births. The results show the importance of skilled birth attendance and warrant attention to negative consequences of reduced access to institutions.

The findings in paper I indicated reduced quality from the health system perspective, as demonstrated by a reduced availability of emergency obstetric care institutions to a level below the estimated need according to the WHO guidelines, and an increased risk of unplanned delivery outside institutions over time.

In paper II, unplanned birth outside institution was associated with an increased risk of peripartum mortality, and the risk of unplanned birth outside institutions increased with long travel time to an obstetric institution. Skilled birth attendants with access to medical and technical equipment plays a key role to maintain low peripartum mortality.

In paper III, we concluded that reduced availability of obstetric institutions was associated with higher risk of eclampsia/HELLP in nulliparous women. A large proportion of cases occurred in women without present or previous preeclampsia. Emphasis on antenatal identification of maternal risk factors in research and clinical guidelines may mask the importance of awareness among women and clinicians concerning early recognition of prodromal symptoms. All obstetric institutions need to be prepared to provide emergency stabilization and treatment.

Future perspectives

A more comprehensive evaluation of the health system structure should take severe maternal and neonatal morbidity into account.

Further research should aim to inform the debate concerning distribution of benefits and burden in the centralisation of obstetric care. The studies in this thesis point to emerging inequalities in availability of and access to obstetric care, and potential consequences of this inequality. Our studies were not designed to answer whether these differences were acceptable or unacceptable from an ethical perspective; if they were inequitable or not. However, the studies were able to describe emerging inequalities and inform the public and political debate about these issues.

7 References

1. Birthplace in England Collaborative G, Brocklehurst P, Hardy P, Hollowell J, Linsell L, Macfarlane A, et al. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. BMJ. 2011;343:d7400.
2. Schroeder E, Petrou S, Patel N, Hollowell J, Puddicombe D, Redshaw M, et al. Cost effectiveness of alternative planned places of birth in woman at low risk of complications: evidence from the Birthplace in England national prospective cohort study. BMJ. 2012;344:e2292.
3. Christiaens W, Bracke P. Place of birth and satisfaction with childbirth in Belgium and the Netherlands. Midwifery. 2009;25(2):e11-9.
4. Benoit C, Zadoroznyj M, Hallgrimsdottir H, Treloar A, Taylor K. Medical dominance and neoliberalisation in maternal care provision: the evidence from Canada and Australia. Soc Sci Med. 2010;71(3):475-81.
5. Zwart JJ, Richters JM, Ory F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies. BJOG. 2008;115(7):842-50.
6. Couchie C, Contributing A. A report on best practices for returning birth to rural and remote aboriginal communities. J Obstet Gynaecol Can. 2007;29(3):250-4.
7. Escuriet R, White J, Beeckman K, Frith L, Leon-Larios F, Loytved C, et al. Assessing the performance of maternity care in Europe: a critical exploration of tools and indicators. BMC Health Serv Res. 2015;15:491.
8. Hemminki E, Heino A, Gissler M. Should births be centralised in higher level hospitals? Experiences from regionalised health care in Finland. BJOG. 2011;118(10):1186-95.
9. Tracy SK, Sullivan E, Dahlen H, Black D, Wang YA, Tracy MB. Does size matter? A population-based study of birth in lower volume maternity hospitals for low risk women. BJOG. 2006;113(1):86-96.
10. Klein M, Johnston S, Christilaw J, Carty E. Mothers, babies, and communities. Centralizing maternity care exposes mothers and babies to complications and endangers community sustainability. Can Fam Physician. 2002;48:1177-9, 83-5.
11. Committee on Economic S, and Cultural Rights. General Comment No 14. United Nations, 2000.
12. WHO. Health systems: improving performance. Geneva: 2000 ISSN 1020-3311.
13. Committee on Economic S, and Cultural Rights. General comment no 22 on the right to sexual and reproductive health. United Nations, 2016.
14. Paxton A, Bailey P, Lobis S, Fry D. Global patterns in availability of emergency obstetric care. Int J Gynaecol Obstet. 2006;93(3):300-7.
15. WHO. Make every mother and child count. Geneva: 2005.
16. WHO, UNFPA, UNICEF, AMDD. Monitoring emergency obstetric care- a handbook. Geneva: 2009.
17. Say L, Souza JP, Pattinson RC. Maternal near miss--towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol. 2009;23(3):287-96.
18. van Roosmalen J, Zwart J. Severe acute maternal morbidity in high-income countries. Best Pract Res Clin Obstet Gynaecol. 2009;23(3):297-304.

19. Thaddeus S, Maine D. Too far to walk: maternal mortality in context. Soc Sci Med. 1994;38(8):1091-110.
20. Binder P, Johnsdotter S, Essen B. Conceptualising the prevention of adverse obstetric outcomes among immigrants using the 'three delays' framework in a high-income context. Soc Sci Med. 2012;75(11):2028-36.
21. Raven JH, Tolhurst RJ, Tang S, van den Broek N. What is quality in maternal and neonatal health care? Midwifery. 2012;28(5):e676-83.
22. Ringard ÅS, A. Saunes, I. S. Lindahl, A.K. Norway Health System Review. Copenhagen Norwegian Knowledge Centre for the Health Services, 2013 Contract No.: 8.
23. White paper nr 12. "En gledelig begivenhet". Oslo: Ministry of Health and Care Services; 2008.
24. Sykehusstruktur i endring. de lange linjer og utviklingen siste tiår. Trondheim: SINTEF Unimed NIS SAMDATA, 2001.
25. Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Ann Intern Med. 2002;137(6):511-20.
26. Urbach DR, Baxter NN. Does it matter what a hospital is "high volume" for? Specificity of hospital volume-outcome associations for surgical procedures: analysis of administrative data. BMJ. 2004;328(7442):737-40.
27. Billingsley KG, Morris AM, Dominitz JA, Matthews B, Dobie S, Barlow W, et al. Surgeon and hospital characteristics as predictors of major adverse outcomes following colon cancer surgery: understanding the volume-outcome relationship. Arch Surg. 2007;142(1):23-31; discussion 2.
28. Urbach DR, Austin PC. Conventional models overestimate the statistical significance of volume-outcome associations, compared with multilevel models. J Clin Epidemiol. 2005;58(4):391-400.
29. Epstein AJ, Gray BH, Schlesinger M. Racial and ethnic differences in the use of high-volume hospitals and surgeons. Arch Surg. 2010;145(2):179-86.
30. Liu JH, Zingmond DS, McGory ML, SooHoo NF, Ettner SL, Brook RH, et al. Disparities in the utilization of high-volume hospitals for complex surgery. JAMA. 2006;296(16):1973-80.
31. Archampong D, Borowski D, Wille-Jorgensen P, Iversen LH. Workload and surgeon's specialty for outcome after colorectal cancer surgery. Cochrane Database Syst Rev. 2012(3):CD005391.
32. Urbach DR, Croxford R, MacCallum NL, Stukel TA. How are volume-outcome associations related to models of health care funding and delivery? A comparison of the United States and Canada. World J Surg. 2005;29(10):1230-3.
33. Christian CK, Gustafson ML, Betensky RA, Daley J, Zinner MJ. The volume-outcome relationship: don't believe everything you see. World J Surg. 2005;29(10):1241-4.
34. Laut KG, Gale CP, Lash TL, Kristensen SD. Determinants and patterns of utilization of primary percutaneous coronary intervention across 12 European countries: 2003-2008. Int J Cardiol. 2013;168(3):2745-53.
35. Laut KG, Gale CP, Pedersen AB, Fox KA, Lash TL, Kristensen SD. Persistent geographical disparities in the use of primary percutaneous coronary intervention in 120 European regions: exploring the variation. EuroIntervention. 2013;9(4):469-76.
36. Jortveit J, Govatsmark RE, Digre TA, Risoe C, Hole T, Mannsverk J, et al. Myocardial infarction in Norway in 2013. Tidsskr Nor Laegeforen. 2014;134(19):1841-6.
37. Moster D, Lie RT, Markestad T. Neonatal mortality rates in communities with small maternity units compared with those having larger maternity units. BJOG. 2001;108(9):904-9.

38. Wildman K, Blondel B, Nijhuis J, Defoort P, Bakoula C. European indicators of health care during pregnancy, delivery and the postpartum period. Eur J Obstet Gynecol Reprod Biol. 2003;111 Suppl 1:S53-65.
39. Heller G, Richardson DK, Schnell R, Misselwitz B, Kunzel W, Schmidt S. Are we regionalized enough? Early-neonatal deaths in low-risk births by the size of delivery units in Hesse, Germany 1990-1999. Int J Epidemiol. 2002;31(5):1061-8.
40. Moster D, Lie RT, Markestad T. Relation between size of delivery unit and neonatal death in low risk deliveries: population based study. Arch Dis Child Fetal Neonatal Ed. 1999;80(3):F221-5.
41. Snowden JM, Cheng YW, Kontgis CP, Caughey AB. The association between hospital obstetric volume and perinatal outcomes in California. Am J Obstet Gynecol. 2012;207(6):478 e1-7.
42. Hendrix MJ, Evers SM, Basten MC, Nijhuis JG, Severens JL. Cost analysis of the Dutch obstetric system: low-risk nulliparous women preferring home or short-stay hospital birth--a prospective non-randomised controlled study. BMC Health Serv Res. 2009;9:211.
43. Merlo J, Gerdtham UG, Eckerlund I, Hakansson S, Otterblad-Olausson P, Pakkanen M, et al. Hospital level of care and neonatal mortality in low- and high-risk deliveries: reassessing the question in Sweden by multilevel analysis. Med Care. 2005;43(11):1092-100.
44. Chung JH, Phibbs CS, Boscardin WJ, Kominski GF, Ortega AN, Needleman J. The effect of neonatal intensive care level and hospital volume on mortality of very low birth weight infants. Med Care. 2010;48(7):635-44.
45. Grunebaum A, McCullough LB, Sapra KJ, Brent RL, Levene MI, Arabin B, et al. Early and total neonatal mortality in relation to birth setting in the United States, 2006-2009. Am J Obstet Gynecol. 2014;211(4):390 e1-7.
46. Snowden JM, Tilden EL, Snyder J, Quigley B, Caughey AB, Cheng YW. Planned Out-of-Hospital Birth and Birth Outcomes. N Engl J Med. 2015;373(27):2642-53.
47. Pyykonen A, Gissler M, Jakobsson M, Petaja J, Tapper AM. Determining obstetric patient safety indicators: the differences in neonatal outcome measures between different-sized delivery units. BJOG. 2014;121(4):430-7.
48. Blondel B, Drewniak N, Pilkington H, Zeitlin J. Out-of-hospital births and the supply of maternity units in France. Health Place. 2011;17(5):1170-3.
49. Pilkington H, Blondel B, Papiernik E, Cuttini M, Charreire H, Maier RF, et al. Distribution of maternity units and spatial access to specialised care for women delivering before 32 weeks of gestation in Europe. Health Place. 2010;16(3):531-8.
50. Rayburn WF, Richards ME, Elwell EC. Drive times to hospitals with perinatal care in the United States. Obstet Gynecol. 2012;119(3):611-6.
51. Ravelli AC, Jager KJ, de Groot MH, Erwich JJ, Rijninks-van Driel GC, Tromp M, et al. Travel time from home to hospital and adverse perinatal outcomes in women at term in the Netherlands. BJOG. 2011;118(4):457-65.
52. Wright JD, Herzog TJ, Shah M, Bonanno C, Lewin SN, Cleary K, et al. Regionalization of care for obstetric hemorrhage and its effect on maternal mortality. Obstet Gynecol. 2010;115(6):1194-200.
53. Zhang WH, Alexander S, Bouvier-Colle MH, Macfarlane A. Incidence of severe pre-eclampsia, postpartum haemorrhage and sepsis as a surrogate marker for severe maternal morbidity in a European population-based study: the MOMS-B survey. BJOG. 2005;112(1):89-96.
54. Andersgaard AB, Herbst A, Johansen M, Ivarsson A, Ingemarsson I, Langhoff-Roos J, et al. Eclampsia in Scandinavia: incidence, substandard care, and potentially preventable cases. Acta Obstet Gynecol Scand. 2006;85(8):929-36.

55. Kilpatrick SJ, Abreo A, Greene N, Melsop K, Peterson N, Shields LE, et al. Severe maternal morbidity in a large cohort of women with acute severe intrapartum hypertension. Am J Obstet Gynecol. 2016;215(1):91 e1-7.
56. Bouvier-Colle MH, Ould El Joud D, Varnoux N, Goffinet F, Alexander S, Bayoumeu F, et al. Evaluation of the quality of care for severe obstetrical haemorrhage in three French regions. BJOG. 2001;108(9):898-903.
57. Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987-2004. Am J Hypertens. 2008;21(5):521-6.
58. Klungsoyr K, Morken NH, Irgens L, Vollset SE, Skjaerven R. Secular trends in the epidemiology of pre-eclampsia throughout 40 years in Norway: prevalence, risk factors and perinatal survival. Paediatric and perinatal epidemiology. 2012;26(3):190-8.
59. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet. 2010;376(9741):631-44.
60. Vangen S, Ellingsen L, Andersgaard AB, Jacobsen AF, Lorentzen B, Nyflot LT, et al. Maternal deaths in Norway 2005-2009. Tidsskr Nor Laegeforen. 2014;134(8):836-9.
61. Vangen S, Bergsjo P. [Do women die from pregnancy these days?]. Tidsskr Nor Laegeforen. 2003;123(24):3544-5.
62. American College of O, Gynecologists, Task Force on Hypertension in P. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol. 2013;122(5):1122-31.
63. Skjaerven R, Wilcox AJ, Klungsoyr K, Irgens LM, Vikse BE, Vatten LJ, et al. Cardiovascular mortality after pre-eclampsia in one child mothers: prospective, population based cohort study. BMJ. 2012;345:e7677.
64. Andersgaard AB, Herbst A, Johansen M, Borgstrom A, Bille AG, Oian P. Follow-up interviews after eclampsia. Gynecol Obstet Invest. 2009;67(1):49-52.
65. Andersgaard AB, Acharya G, Mathiesen EB, Johnsen SH, Straume B, Oian P. Recurrence and long-term maternal health risks of hypertensive disorders of pregnancy: a population-based study. Am J Obstet Gynecol. 2012;206(2):143 e1-8.
66. Creanga AA, Berg CJ, Syverson C, Seed K, Bruce FC, Callaghan WM. Pregnancy-related mortality in the United States, 2006-2010. Obstet Gynecol. 2015;125(1):5-12.
67. Callaghan WM, Creanga AA, Kuklina EV. Severe maternal morbidity among delivery and postpartum hospitalizations in the United States. Obstet Gynecol. 2012;120(5):1029-36.
68. Kuklina EV, Ayala C, Callaghan WM. Hypertensive disorders and severe obstetric morbidity in the United States. Obstet Gynecol. 2009;113(6):1299-306.
69. Paauw ND, Luijken K, Franx A, Verhaar MC, Lely AT. Long-term renal and cardiovascular risk after preeclampsia: towards screening and prevention. Clin Sci (Lond). 2016;130(4):239-46.
70. Thomsen LC, Melton PE, Tollaksen K, Lyslo I, Roten LT, Odland ML, et al. Refined phenotyping identifies links between preeclampsia and related diseases in a Norwegian preeclampsia family cohort. J Hypertens. 2015;33(11):2294-302.
71. McGinnis R, Steinthorsdottir V, Williams NO, Thorleifsson G, Shooter S, Hjartardottir S, et al. Variants in the fetal genome near FLT1 are associated with risk of preeclampsia. Nat Genet. 2017;49(8):1255-60.
72. Thomsen LC, McCarthy NS, Melton PE, Cadby G, Austgulen R, Nygard OK, et al. The antihypertensive MTHFR gene polymorphism rs17367504-G is a possible novel protective locus for preeclampsia. J Hypertens. 2017;35(1):132-9.

73. Staff AC, Benton SJ, von Dadelszen P, Roberts JM, Taylor RN, Powers RW, et al. Redefining preeclampsia using placenta-derived biomarkers. Hypertension. 2013;61(5):932-42.
74. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. Lancet. 2016;387(10022):999-1011.
75. Chames MC, Livingston JC, Ivester TS, Barton JR, Sibai BM. Late postpartum eclampsia: a preventable disease? Am J Obstet Gynecol. 2002;186(6):1174-7.
76. Boulkedid R, Sibony O, Goffinet F, Fauconnier A, Branger B, Alberti C. Quality indicators for continuous monitoring to improve maternal and infant health in maternity departments: a modified Delphi survey of an international multidisciplinary panel. PLoS One. 2013;8(4):e60663.
77. Sibanda T, Fox R, Draycott TJ, Mahmood T, Richmond D, Simms RA. Intrapartum care quality indicators: a systematic approach for achieving consensus. Eur J Obstet Gynecol Reprod Biol. 2013;166(1):23-9.
78. Jaatinen N, Ekholm E. Eclampsia in Finland; 2006 to 2010. Acta Obstet Gynecol Scand. 2016;95(7):787-92.
79. Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet. 2002;359(9321):1877-90.
80. Knight M, Ukoss. Eclampsia in the United Kingdom 2005. BJOG. 2007;114(9):1072-8.
81. Kayem G, Kurinczuk J, Lewis G, Golightly S, Brocklehurst P, Knight M. Risk factors for progression from severe maternal morbidity to death: a national cohort study. PLoS One. 2011;6(12):e29077.
82. TaxNorway-Skatteetaten. Norwegian national ID numbers [Available from: http://www.skatteetaten.no/en/international-pages/felles-innhold-benyttes-i-flere-malgrupper/articles/norwegian-national-id-numbers/.
83. Rasmussen S, Albrechtsen S, Irgens LM, Dalaker K, Maartmann-Moe H, Vlatkovic L, et al. Unexplained antepartum fetal death in Norway, 1985-97: diagnostic validation and some epidemiologic aspects. Acta Obstet Gynecol Scand. 2003;82(2):109-15.
84. Thomsen LC, Klungsoyr K, Roten LT, Tappert C, Araya E, Baerheim G, et al. Validity of the diagnosis of pre-eclampsia in the Medical Birth Registry of Norway. Acta Obstet Gynecol Scand. 2013;92(8):943-50.
85. Klungsoyr K, Harmon QE, Skard LB, Simonsen I, Austvoll ET, Alsaker ER, et al. Validity of pre-eclampsia registration in the medical birth registry of norway for women participating in the norwegian mother and child cohort study, 1999-2010. Paediatric and perinatal epidemiology. 2014;28(5):362-71.
86. Klungsøyr K. Validation of eclampsia notifications to the Medical Birth Registry of Norway 2000-2006. The Norwegian Institute of Public Health, Norway TMBRo; 2009.
87. Elveg- the electronic road database: The Norwegian Mapping Authority; 2009 [Available from: http://www.statkart.no/nor/Land/Fagomrader/Vegdatasamarbeidet/Elektronisk_vegnett/.
88. Pasupathy D, Wood AM, Pell JP, Fleming M, Smith GC. Rates of and factors associated with delivery-related perinatal death among term infants in Scotland. JAMA. 2009;302(6):660-8.
89. de Jonge A, Geerts CC, van der Goes BY, Mol BW, Buitendijk SE, Nijhuis JG. Perinatal mortality and morbidity up to 28 days after birth among 743 070 low-risk planned home and hospital births: a cohort study based on three merged national perinatal databases. BJOG. 2015;122(5):720-8.

90. Skjaerven R, Gjessing HK, Bakketeig LS. Birthweight by gestational age in Norway. Acta Obstet Gynecol Scand. 2000;79(6):440-9.
91. Eide GE. Attributable fractions for partitioning risk and evaluating disease prevention: a practical guide. Clin Respir J. 2008;2 Suppl 1:92-103.
92. Eide GE, Heuch I. Average attributable fractions: a coherent theory for apportioning excess risk to individual risk factors and subpopulations. Biom J. 2006;48(5):820-37.
93. Rothman K; Greenland S; Lash T. Modern Epidemiology 3ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
94. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. Ann Intern Med. 2017;167(4):268-74.
95. Sigakis MJ, Leffert LR, Mirzakhani H, Sharawi N, Rajala B, Callaghan WM, et al. The Validity of Discharge Billing Codes Reflecting Severe Maternal Morbidity. Anesth Analg. 2016;123(3):731-8.
96. Geller SE, Ahmed S, Brown ML, Cox SM, Rosenberg D, Kilpatrick SJ. International Classification of Diseases-9th revision coding for preeclampsia: how accurate is it? Am J Obstet Gynecol. 2004;190(6):1629-33; discussion 33-4.
97. Knight M. Studies using routine data versus specific data collection: What can we learn about the epidemiology of eclampsia and the impact of changes in management of gestational hypertensive disorders? Pregnancy Hypertens. 2011;1(1):109-16.
98. Al-Zirqi I, Stray-Pedersen B, Forsen L, Kjersti Daltveit A, Vangen S. Validation study of uterine rupture registration in the Medical Birth Registry of Norway. Acta Obstet Gynecol Scand. 2013;92(9):1086-93.
99. Colmorn LB, Petersen KB, Jakobsson M, Lindqvist PG, Klungsoyr K, Kallen K, et al. The Nordic Obstetric Surveillance Study: a study of complete uterine rupture, abnormally invasive placenta, peripartum hysterectomy, and severe blood loss at delivery. Acta Obstet Gynecol Scand. 2015;94(7):734-44.
100. Jakobsson M, Tapper AM, Colmorn LB, Lindqvist PG, Klungsoyr K, Krebs L, et al. Emergency peripartum hysterectomy: results from the prospective Nordic Obstetric Surveillance Study (NOSS). Acta Obstet Gynecol Scand. 2015;94(7):745-54.
101. Bakketeig LS, Bergsjo P. [Birth during transportation in Norway. An analysis of births outside an instittion from 1 February 1975 to 31 January 1976]. Tidsskr Nor Laegeforen. 1977;97(17-18):923-70.
102. Guidelines for obstetrics: The Norwegian Society for Obstetrics and Gynecology, The Norwegian Medical Association; 2008. Available from: http://legeforeningen.no/Fagmed/Norsk-gynekologisk-forening/Veiledere/veileder-i-fodselshjelp-2008/.
103. Winter C, Macfarlane A, Deneux-Tharaux C, Zhang WH, Alexander S, Brocklehurst P, et al. Variations in policies for management of the third stage of labour and the immediate management of postpartum haemorrhage in Europe. BJOG. 2007;114(7):845-54.
104. Bjornerem A, Acharya G, Oian P, Maltau JM. [Postpartum hemorrhage--prophylaxis and treatment in Norway]. Tidsskr Nor Laegeforen. 2002;122(26):2536-7.
105. Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of severe obstetric haemorrhage. BJOG. 2008;115(10):1265-72.
106. Al-Zirqi I, Stray-Pedersen B, Forsen L, Vangen S. Uterine rupture after previous caesarean section. BJOG. 2010;117(7):809-20.
107. Philibert M, Deneux-Tharaux C, Bouvier-Colle MH. Can excess maternal mortality among women of foreign nationality be explained by suboptimal obstetric care? BJOG. 2008;115(11):1411-8.

108. Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities. BMJ. 2009;338:b542.
109. Alvik A, Heyerdahl S, Haldorsen T, Lindemann R. Alcohol use before and during pregnancy: a population-based study. Acta Obstet Gynecol Scand. 2006;85(11):1292-8.
110. Sorbye LM, Klungsoyr K, Samdal O, Owe KM, Morken NH. Pre-pregnant body mass index and recreational physical activity: effects on perinatal mortality in a prospective pregnancy cohort. BJOG. 2015;122(10):1322-30.
111. Hollowell J, Pillas D, Rowe R, Linsell L, Knight M, Brocklehurst P. The impact of maternal obesity on intrapartum outcomes in otherwise low risk women: secondary analysis of the Birthplace national prospective cohort study. BJOG. 2014;121(3):343-55.
112. Odegard RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgulen R. Risk factors and clinical manifestations of pre-eclampsia. BJOG. 2000;107(11):1410-6.
113. Durst JK, Tuuli MG, Stout MJ, Macones GA, Cahill AG. Degree of obesity at delivery and risk of preeclampsia with severe features. Am J Obstet Gynecol. 2016;214(5):651 e1-5.
114. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. BMJ. 2005;330(7491):565.
115. Wallenius M, Salvesen KA, Daltveit AK, Skomsvoll JF. Systemic lupus erythematosus and outcomes in first and subsequent births based on data from a national birth registry. Arthritis Care Res (Hoboken). 2014;66(11):1718-24.
116. Melve KK, Skjaerven R, Rasmussen S, Irgens LM. Recurrence of stillbirth in sibships: Population-based cohort study. American journal of epidemiology. 2010;172(10):1123-30.
117. Saemundsson Y, Svantesson H, Gudmundsson S. Abnormal uterine artery Doppler in pregnancies suspected of a SGA fetus is related to increased risk of recurrence during next pregnancy. Acta Obstet Gynecol Scand. 2009;88(7):814-7.
118. Skjaerven R, Gjessing HK, Bakketeig LS. New standards for birth weight by gestational age using family data. Am J Obstet Gynecol. 2000;183(3):689-96.
119. Pagel C, Prost A, Lewycka S, Das S, Colbourn T, Mahapatra R, et al. Intracluster correlation coefficients and coefficients of variation for perinatal outcomes from five cluster-randomised controlled trials in low and middle-income countries: results and methodological implications. Trials. 2011;12:151.
120. Howell EA, Zeitlin J, Hebert PL, Balbierz A, Egorova N. Association between hospital-level obstetric quality indicators and maternal and neonatal morbidity. JAMA. 2014;312(15):1531-41.
121. Pilkington H, Blondel B, Drewniak N, Zeitlin J. Where does distance matter? Distance to the closest maternity unit and risk of foetal and neonatal mortality in France. Eur J Public Health. 2014;24(6):905-10.
122. Sami statistics. Oslo/Kongsvinger: Statistics Norway, 2010 ISBN 978-82-537-7742-9 Elektronisk versjon.
123. Viisainen K, Gissler M, Hartikainen AL, Hemminki E. Accidental out-of-hospital births in Finland: incidence and geographical distribution 1963-1995. Acta Obstet Gynecol Scand. 1999;78(5):372-8.
124. Rodie VA, Thomson AJ, Norman JE. Accidental out-of-hospital deliveries: an obstetric and neonatal case control study. Acta Obstet Gynecol Scand. 2002;81(1):50-4.
125. Pilkington H, Prunet C, Blondel B, Charreire H, Combier E, Le Vaillant M, et al. Travel Time to Hospital for Childbirth: Comparing Calculated Versus Reported Travel Times in France. Matern Child Health J. 2017.

126. Vik ES, Haukeland GT, Dahl B. Women's experiences with giving birth before arrival. Midwifery. 2016;42:10-5.
127. Waterstone M, Bewley S, Wolfe C. Incidence and predictors of severe obstetric morbidity: case-control study. BMJ. 2001;322(7294):1089-93; discussion 93-4.
128. Brace V, Penney G, Hall M. Quantifying severe maternal morbidity: a Scottish population study. BJOG. 2004;111(5):481-4.
129. Kyser KL, Lu X, Santillan DA, Santillan MK, Hunter SK, Cahill AG, et al. The association between hospital obstetrical volume and maternal postpartum complications. Am J Obstet Gynecol. 2012;207(1):42 e1-17.
130. Kozhimannil KB, Thao V, Hung P, Tilden E, Caughey AB, Snowden JM. Association between Hospital Birth Volume and Maternal Morbidity among Low-Risk Pregnancies in Rural, Urban, and Teaching Hospitals in the United States. Am J Perinatol. 2016;33(6):590-9.
131. Luo ZC, Wilkins R. Degree of rural isolation and birth outcomes. Paediatric and perinatal epidemiology. 2008;22(4):341-9.
132. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for stillbirth: population based study. BMJ. 2013;346:f108.
133. Jackson M, Dahlen H, Schmied V. Birthing outside the system: perceptions of risk amongst Australian women who have freebirths and high risk homebirths. Midwifery. 2012;28(5):561-7.
134. Pitchforth E, Watson V, Tucker J, Ryan M, van Teijlingen E, Farmer J, et al. Models of intrapartum care and women's trade-offs in remote and rural Scotland: a mixed-methods study. BJOG. 2008;115(5):560-9.
135. Pilkington H, Blondel B, Drewniak N, Zeitlin J. Choice in maternity care: associations with unit supply, geographic accessibility and user characteristics. Int J Health Geogr. 2012;11:35.
136. Society of O, Gynaecologists of C. SOGC policy statement. No. 251, December 2010. Returning birth to aboriginal, rural, and remote communities. J Obstet Gynaecol Can. 2010;32(12):1186-8.
137. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. BMJ. 2011;343:d7400.
138. Combier E, Charreire H, Le Vaillant M, Michaut F, Ferdynus C, Amat-Roze JM, et al. Perinatal health inequalities and accessibility of maternity services in a rural French region: closing maternity units in Burgundy. Health Place. 2013;24:225-33.
139. Poeran J, Borsboom GJ, de Graaf JP, Birnie E, Steegers EA, Mackenbach JP, et al. Does centralisation of acute obstetric care reduce intrapartum and first-week mortality? An empirical study of over 1 million births in the Netherlands. Health Policy. 2014;117(1):28-38.
140. von Dadelszen P, Payne B, Li J, Ansermino JM, Broughton Pipkin F, Cote AM, et al. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. Lancet. 2011;377(9761):219-27.
141. Katz VL, Farmer R, Kuller JA. Preeclampsia into eclampsia: toward a new paradigm. Am J Obstet Gynecol. 2000;182(6):1389-96.
142. Thornton C, Dahlen H, Korda A, Hennessy A. The incidence of preeclampsia and eclampsia and associated maternal mortality in Australia from population-linked datasets: 2000-2008. Am J Obstet Gynecol. 2013;208(6):476 e1-5.
143. Schaap TP, Knight M, Zwart JJ, Kurinczuk JJ, Brocklehurst P, van Roosmalen J, et al. Eclampsia, a comparison within the International Network of Obstetric Survey Systems. BJOG. 2014;121(12):1521-8.

144. Delvaux T, Buekens P. Disparity in prenatal care in Europe. Study group on barriers and incentives to prenatal care in Europe. Eur J Obstet Gynecol Reprod Biol. 1999;83(2):185-90.
145. Dahl EB, H. van der Wel, K. eds. Social inequalities in health, a Norwegian knowledge base. . Oslo and Akershus University College of Applied Sciences, 2014.
146. Jorgensen T, Mortensen LH, Andersen AM. Social inequality in fetal and perinatal mortality in the Nordic countries. Scand J Public Health. 2008;36(6):635-49.
147. Rasmussen S, Albrechtsen S, Irgens LM, Dalaker K, Maartmann-Moe H, Vlatkovic L, et al. Risk factors for unexplained antepartum fetal death in Norway 1967-1998. Early Hum Dev. 2003;71(1):39-52.
148. Kravdal O. Does place matter for cancer survival in Norway? A multilevel analysis of the importance of hospital affiliation and municipality socio-economic resources. Health Place. 2006;12(4):527-37.
149. Cluver C, Novikova N, Koopmans CM, West HM. Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term. Cochrane Database Syst Rev. 2017;1:CD009273.
150. de Graaf JP, Schutte JM, Poeran JJ, van Roosmalen J, Bonsel GJ, Steegers EA. Regional differences in Dutch maternal mortality. BJOG. 2012;119(5):582-8.
151. Wahlberg A, Roost M, Haglund B, Hogberg U, Essen B. Increased risk of severe maternal morbidity (near-miss) among immigrant women in Sweden: a population register-based study. BJOG. 2013;120(13):1605-11; discussion 12.
152. Ozimek JA, Eddins RM, Greene N, Karagyozyan D, Pak S, Wong M, et al. Opportunities for improvement in care among women with severe maternal morbidity. Am J Obstet Gynecol. 2016;215(4):509 e1-6.
153. Haug B, Avall A, Monsen SA. [Reliability of air ambulances--a survey in three municipalities in Helgeland?]. Tidsskr Nor Laegeforen. 2009;129(11):1089-93.
154. Senanayake H, Dias T, Jayawardena A. Maternal mortality and morbidity: Epidemiology of intensive care admissions in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2013.
155. Wen SW, Huang L, Liston R, Heaman M, Baskett T, Rusen ID, et al. Severe maternal morbidity in Canada, 1991-2001. CMAJ. 2005;173(7):759-64.
156. Callaghan WM, Grobman WA, Kilpatrick SJ, Main EK, D'Alton M. Facility-based identification of women with severe maternal morbidity: it is time to start. Obstet Gynecol. 2014;123(5):978-81.
157. Schaap T, Bloemenkamp K, Deneux-Tharaux C, Knight M, Langhoff-Roos J, Sullivan E, et al. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG. 2017.
158. Flenady V, Koopmans L, Middleton P, Froen JF, Smith GC, Gibbons K, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. Lancet. 2011;377(9774):1331-40.
159. Stillbirth Collaborative Research Network Writing G. Association between stillbirth and risk factors known at pregnancy confirmation. JAMA. 2011;306(22):2469-79.
160. Stacey T, Thompson JM, Mitchell EA, Ekeroma AJ, Zuccollo JM, McCowan LM. The Auckland Stillbirth study, a case-control study exploring modifiable risk factors for third trimester stillbirth: methods and rationale. Aust N Z J Obstet Gynaecol. 2011;51(1):3-8.
161. Reddy UM, Laughon SK, Sun L, Troendle J, Willinger M, Zhang J. Prepregnancy risk factors for antepartum stillbirth in the United States. Obstet Gynecol. 2010;116(5):1119-26.

162. Hirst JE, Villar J, Victora CG, Papageorghiou AT, Finkton D, Barros FC, et al. The antepartum stillbirth syndrome: risk factors and pregnancy conditions identified from the INTERGROWTH-21st Project. BJOG. 2016.
163. Oster RT, Toth EL. A retrospective analysis of stillbirth epidemiology and risk factors among First Nations and non-First Nations pregnancies in Alberta from 2000 to 2009. J Obstet Gynaecol Can. 2015;37(2):117-21.
164. American College of O, Gynecologists, Society for Maternal-Fetal M, Menard MK, Kilpatrick S, Saade G, et al. Levels of maternal care. Am J Obstet Gynecol. 2015;212(3):259-71.
165. Janakiraman V, Lazar J, Joynt KE, Jha AK. Hospital volume, provider volume, and complications after childbirth in U.S. hospitals. Obstet Gynecol. 2011;118(3):521-7.

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Epidemiology

Availability and access in modern obstetric care: a retrospective population-based study

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Objective To assess the availability of obstetric institutions, the risk of unplanned delivery outside an institution and maternal morbidity in a national setting in which the number of institutions declined from 95 to 51 during 30 years.

Design Retrospective population-based, three cohorts and two cross-sectional analyses.

Setting Census data, Statistics Norway. The Medical Birth Registry of Norway from 1979 to 2009.

Population Women (15–49 years), 2000 (n = 1 050 269) and 2010 (n = 1 127 665). Women who delivered during the period 1979–2009 (n = 1 807 714).

Methods Geographic Information Systems software for travel zone calculations. Cross-table and multiple logistic regression analysis of change over time and regional differences. World Health Organization Emergency Obstetric and Newborn Care (EmOC) indicators.

Main outcome measures Proportion of women living outside the 1-hour travel zone to obstetric institutions. Risk of unplanned delivery outside obstetric institutions. Maternal morbidity.

Results The proportion of women living outside the 1-hour zone for all obstetric institutions increased from 7.9% to 8.8% from 2000 to 2010 (relative risk, 1.1; 95% confidence interval, 1.11–1.12), and for emergency obstetric care from 11.0% to 12.1% (relative risk, 1.1; 95% confidence interval, 1.09–1.11). The risk of unplanned delivery outside institutions increased from 0.4% in 1979–83 to 0.7% in 2004–09 (adjusted odds ratio, 2.0; 95% confidence interval, 1.9–2.2). Maternal morbidity increased from 1.7% in 2000 to 2.2% in 2009 (adjusted odds ratio, 1.4; 95% confidence interval, 1.2–1.5) and the regional differences increased.

Conclusions The availability of and access to obstetric institutions was reduced and we did not observe the expected decrease in maternal morbidity following the centralisation.

Keywords Access, availability, emergency obstetric care indicators, Geographic Information Systems, healthcare quality.

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Introduction

Caught between high-technology services and the care for normal uncomplicated deliveries, obstetric care has been a core issue in the current health system debate in several high-income countries.[1–5] Within other fields in medicine, such as cancer treatment, surgery and intervention cardiology, centralisation to larger units improves patient outcome, although the mechanisms are complex.[6–8] In obstetrics, however, delivery in large institutions has been associated with an increased frequency of interventions for low-risk women and the benefit for neonatal outcome in low-risk infants remains a matter of debate.[1,9,10] With the exception of access to neonatal intensive care units and neonatal outcome, the availability of and access to obstetric institutions has received little attention in high-income countries.[11,12] Treatment of obstetric complications requires skills and medical and technical resources, and thus access to institution-based care.[13] The World Health Organization (WHO) has developed tools to monitor emergency obstetric care, including the geographical distribution of institutions, access, utilisation and the type of services provided.[14] Registration of severe maternal morbidity adds information about the health service performance in all types of resource settings.[15] National policy in Norway has emphasised the need for decentralised care in order to provide safe services of high quality near a woman's home.[16] However, the number of obstetric institutions in Norway declined from 95 to 51 between 1979 and 2009.

Knowledge of how centralisation of obstetric services affects availability and access to obstetric institutions is lacking in high-income countries. In particular, the consequences are unclear for maternal outcomes. Our objective was to study the time trends and regional variations in travel distance to institutions, the risk of unplanned delivery outside institutions and maternal morbidity using nationwide population-based registries to design three cohort and two cross-sectional analyses. Our hypothesis was that the centralisation has led to reduced availability of and access to institutions, but a reduced risk of maternal morbidity.

Methods

Core definitions

Basic obstetric care was defined as care for a normal delivery and referral if complications occurred. Emergency obstetric care institutions provided all the nine signal functions outlined in Table 1. A travel zone was defined as the geographical area in which all women were estimated to reach the nearest institution within the given time limit. An unplanned delivery outside an institution was defined as delivery at home, during transportation or in a non-obstetric institution (e.g. health centre) for a woman who had planned an institutional delivery. Maternal morbidity from causes related to pregnancy and childbirth was assessed using the following diagnoses or treatment-based categories: maternal intensive care, puerperal sepsis and sepsis during delivery, thromboembolic disease with the exception of peripheral venous thrombophlebitis, eclampsia and haemorrhage >1500 ml or blood transfusion. We defined delivery-related perinatal mortality as intrapartum death or neonatal death within 24 hours at a gestational age of ≥22 weeks or birth weight of ≥500 g.

Table 1. World Health Organization (WHO) Emergency Obstetric Care (EmOC) indicators and signal functions

Indicators (8)
Institution availability and geographic distribution. Recommendation: 5 institutions per 500 000 inhabitants including one institution providing comprehensive emergency care
Proportion of all births in emergency obstetric care institutions. Recommendation: to be determined locally
Met need of emergency obstetric care. The proportion of women with major direct complications who are treated in EmOC facilities. Recommendation: 100%
Caesarean section rate as a proportion of all births. Recommendation: 5–15%
Direct obstetric case fatality rate. Recommendation: <1%
Intrapartum and very early neonatal mortality. Recommendation not given
Maternal mortality from indirect causes. Recommendation not given
Signal functions (9)
Basic emergency obstetric care
Perform parenteral administration of antibiotics (1), uterotonic drugs (2) and anticonvulsants (3)
Perform manual removal of placenta (4) and removal of retained products (5)
Perform assisted vaginal delivery (6)
Perform basic neonatal resuscitation (7)
Comprehensive emergency obstetric care include the above plus
Perform surgery, e.g. hysterectomy and caesarean section (8)
Perform blood transfusion (9)

WHO.[14]

Availability of institutions

Women of fertile age (15–49 years) who lived more than 1 or 2 hours away from the nearest obstetric institution were counted. Institutions were included if they were registered to provide obstetric care and reported more than 10 deliveries in 2000 or 2009. Cross-sectional assessments were performed for 1 January 2000 (n = 1 050 269 women, 59 institutions) and 1 January 2010 (n = 1 127 665 women, 51 institutions). Four basic obstetric care institutions in the Northern region had fewer than 10 deliveries in 2000 and were therefore excluded.

Since 2000, Statistics Norway has assigned geographical coordinates to individual addresses as part of the census update on 1 January each year. Individual coordinates had been assigned to 98% of the census addresses in 2000 (county range, 95.5–99%), whereas the coverage was 99% in 2010 (county range, 98.2–100%). We registered the institutions with geographical coordinates, and the surrounding travel zones were calculated based on the national road database for the corresponding year. A merged area (polygon) was created for the travel zones, and the number of women registered to live fully within the area was counted. The women were counted in the area of the nearest institution, irrespective of county and health region borders. Estimates were based on registered speed limits and standard duration of ferry/boat journeys, but did not take into account such factors as harbour waiting times, difficult driving conditions or temporary route changes. The estimates thus represented the minimum time for non-emergency transport.

Access to obstetric institutions at the time of delivery, the risk of unplanned delivery outside an institution

We performed a retrospective cohort analysis of unplanned deliveries outside institutions from 1979 to 2009 using data from the Medical Birth Registry of Norway (MBRN). The registry has received mandatory notifications of all births since 1967, both live births and stillbirths from 16 weeks of gestation (12 weeks since 2002). The notification form is standardised and was revised in 1999 to include more information about the mother, the neonate and the birthplace, including planned home deliveries. Notification is given as free text and, after 1999, also as check boxes/predefined variables. Free text is coded at the MBRN using the *International Classification of Diseases, 8th Revision* for births in 1967–1998 and *10th Revision* for births from 1999 onwards. Birth notifications are sent from the institutions to the MBRN at the time of discharge. Inclusion criteria were the known place of birth and either gestational age ≥22 completed weeks or birth weight ≥500 g (n = 1 807 714). Planned home deliveries from 1999 to 2009 were excluded (n = 1267); these constituted 0.2% of the study population during these years. The year of delivery was categorised in 5-year groups; the last group covered 6 years.

Maternal morbidity and emergency obstetric care indicators

Two national retrospective cohort analyses were performed using all deliveries from 1 January to 31 December 2000 (n = 58 632) and 2009 (n = 61 895). The inclusion criterion was gestational age ≥22 completed weeks or birth weight ≥500 g. Deliveries categorised as unknown birthplace (2000, n = 11; 2009, n = 22) or lacking registered maternal address (2000, n = 103; 2009, n = 33) were excluded from the regional analyses. Population data were obtained from Statistics Norway. We applied the WHO emergency obstetric care signal functions (Table 1) to classify institutions, and used the indicators to assess the geographical distribution of institutions, access, use and maternal and neonatal outcomes in 2000 and 2009. The WHO handbook was developed as a tool for low-income countries, but the indicators have also been used to evaluate services in high- and middle-income countries.[13] We used the 1-year cohorts rather than the proposed 3 months registration, as some indicators represent rare events. Caesarean section rates were assessed on a national and regional level. Data on maternal deaths were obtained from the Norwegian Cause of Death Registry and from a Norwegian maternal mortality audit study. The Norwegian Air Ambulance records for 2009 documented the number of urgent emergency transports as a result of suspected or diagnosed complications during pregnancy or after delivery. The records included information about indication and whether the transport was from the woman's home (primary) or was a transfer between institutions (secondary).

Direct maternal deaths were rare, and maternal deaths from indirect causes were not registered in Norway. We used maternal morbidity from causes related to pregnancy and childbirth (see Core definitions) as well as the delivery-related perinatal mortality to assess the quality of clinical care according to the WHO guidelines.

Analyses

The cross-sectional travel zone analyses were performed with the Geographic Information Systems (GIS) software Arc Info with Network Analyst (Environmental Systems Research Institute Inc. (Esri), Redlands, CA, USA). The GIS tool integrates hardware, software and data, and is used for the capture, analysis and display of geographically referenced information. Arc Info is the software currently used by Statistics Norway. Travel zones were estimated by combining the institution coordinates with the national road database.[17] The number of women living within or outside the zone was counted. The differences in the proportions of women who lived outside the 1-hour and 2-hour travel zones in 2000 and 2010 were calculated by cross tables providing relative risk (RR) with 95% confidence intervals (CIs), using 2000 as the reference year.

Cross tables were used to calculate the risk of unplanned delivery outside an institution in all 5-year groups from 1979–83 to 2004–09, and we evaluated time trends across these groups using logistic regression analyses. Cross tables were also used to calculate odds ratios (ORs) with 95% CIs for maternal morbidity in 2009 relative to 2000. Finally, we analysed regional differences in maternal morbidity and delivery-related perinatal mortality using the region with the lowest risk as reference. Logistic regression analyses were used to adjust for confounding by maternal age (<20, 20–24, 25–29, 30–34, 35 + years), parity (0, 1, 2+), education (<11, 11–14, 14 + years) and partner status (single or married/cohabiting). Maternal morbidity was also adjusted for tobacco use (daily smoking, occasional smoking, or non-smoking). All outcomes were rare and ORs were considered to be close approximations to RRs in these analyses. We used IBM SPSS Statistics version 19 (IBM SPSS Inc., Chicago, IL, USA) for all calculations.

Results

Availability

The proportion of women who lived outside the 1-hour zone of all institutions increased from 7.9% to 8.8% from 2000 to 2010 (RR, 1.11; 95% CI, 1.10–1.12; Table 2). The number of counties in which more than 10% of women lived outside the 1-hour zone increased from seven to nine from 2000 to 2010 (Figure 1, Appendix S1, see Supporting information). Increases in proportions were observed in counties in which obstetric care institutions closed during this period, whereas decreases related to major infrastructure projects were observed in two counties.

Table 2. National and regional numbers and proportions of women living outside the 1-hour zone of all institutions and emergency obstetric care institutions in 2000 and 2010. Based on institution data from the Medical Birth Registry of Norway, population data from Statistics Norway and the Norwegian road database

	Total population of women 15–49 years*		All institutions**			Emergency obstetric care institutions***		
	2000	2010	2000 Outside 1 hour (%)	2010 Outside 1 hour (%)	Relative risk (95% CI)	2000 Outside 1 hour (%)	2010 Outside 1 hour (%)	Relative risk (95% CI)
Norway	1 050 269	1 127 665	82 671 (7.9)	98 720 (8.8)	1.1 (1.10–1.12)	115 701 (11.0)	136 208 (12.1)	1.1 (1.09–1.11)
Eastern region	386 227	426 030	7682 (2.0)	11 001 (2.6)	1.3 (1.26–1.34)	11 341 (2.9)	18 419 (4.3)	1.5 (1.44–1.51)
Southern region	200 868	211 541	5029 (2.5)	11 985 (5.7)	2.3 (2.19–2.34)	11 438 (5.7)	14 849 (7.0)	1.2 (1.20–1.26)
Western region	214 827	236 258	21 640 (10.1)	25 374 (10.7)	1.07 (1.05–1.09)	21 640 (10.1)	30 749 (13.0)	1.3 (1.27–1.31)
Central region	142 830	150 868	23 161 (16.2)	24 983 (16.6)	1.02 (1.01–1.04)	29 208 (20.5)	26 035 (17.3)	0.8 (0.83–0.86)
Northern region	105 517	102 968	25 159 (23.8)	25 377 (24.7)	1.03 (1.02–1.05)	42 074 (39.9)	46 156 (44.8)	1.1 (1.11–1.14)

*Women 15–49 years with registered address on 1 January 2000 and 1 January 2010.
**Institutions provided only basic obstetric care or all nine emergency obstetric care signal functions; 59 institutions in 2000 and 51 institutions in 2009.
***Institutions provided all the nine signal functions; intravenous administration of drugs, removal of placenta/retained products, assisted vaginal delivery, basic neonatal resuscitation, surgery and blood transfusion; 47 institutions in 2000 and 41 institutions in 2009.

The availability of emergency obstetric care institutions was also reduced. The proportion of women living outside the 1-hour zone for emergency obstetric care institutions increased from 11.0% to 12.1% from 2000 to 2010 (RR, 1.1; 95% CI, 1.09–1.11; Table 2). The number of counties in which more than 10% of women lived outside the 1-hour zone increased from nine to 11 (Figure 1, Appendix S2, see Supporting information). Although the absolute numbers were low, the proportion of women living outside the 2-hour zone increased from 3.4% to 4.8% nationally (RR, 1.4; 95% CI, 1.39–1.43), from 0.29% to 1.6% in the Eastern region (RR, 5.6; 95% CI, 5.2–5.9), from 0.81% to 2.9% in the Southern region (RR, 3.6; 95% CI, 3.4–3.8) and from 21% to 28% in the Northern region (RR, 1.3; 95% CI, 1.28–1.32).

Risk of unplanned delivery outside an institution

During 1979–2009, the number of institutions declined from 95 to 51, and 11 537 deliveries outside an institution were registered among the included deliveries (n = 1 807 714). On a national level, the risk of unplanned delivery outside an institution was doubled in 2004–09 relative to 1979–83 (Table 3). The risk increased successively from 0.4% in 1979–83 to 0.8% in 1994–98 and to 0.7% in 1999–2003 and 2004–09 (test for trend [Wald]: $P < 0.001$). During 1979 to 1998, we were unable to exclude planned home deliveries from these figures (approximately 0.2% per 5-year period after 1999). The geographical variation increased, and the risk in different counties ranged from 0.1% to 0.7% in the first period and from 0.3% to 1.8% in the last period. Two counties experienced a fivefold increase in risk. We observed that the risk of unplanned delivery outside an institution was higher in counties with a decentralised population pattern (Figure 2). However, even in urban counties, where <1% of women lived outside the 1-hour zone, the risk more than doubled (counties 2, 3 and 7; Table 3, Appendix S1).

Emergency obstetric care indicators and maternal morbidity

From 2000 to 2009, the total population increased from 4 478 497 to 4 858 159, whereas the number of emergency obstetric care institutions decreased from 47 to 41 (Table 4). Thus, the national number of institutions was lower than the estimated need in 2009. At the regional level, the number of emergency obstetric care institutions was lower than the estimated need in the Southern and Eastern regions in 2000. The coverage in these regions declined further during the decade. The Western region also had fewer institutions than the estimated need in 2009. From 2000 to 2009, the proportion of deliveries in institutions with more than 3000 births per year increased from 34% in four institutions to 46% in five institutions. A total of 31 institutions with fewer than 500 births per year provided care for 10% of all deliveries in 2000, whereas the corresponding numbers were 21 institutions and 9.0% of all deliveries in 2009. The national average caesarean section rate was 14% in 2000 and 17% in 2009, with a regional range of 11–15% in the first period and 13–19% in the latter (Table 4). There were 12 institutions that provided only basic obstetric care in 2000 and 10 in 2009. The majority of basic obstetric care institutions were rural and

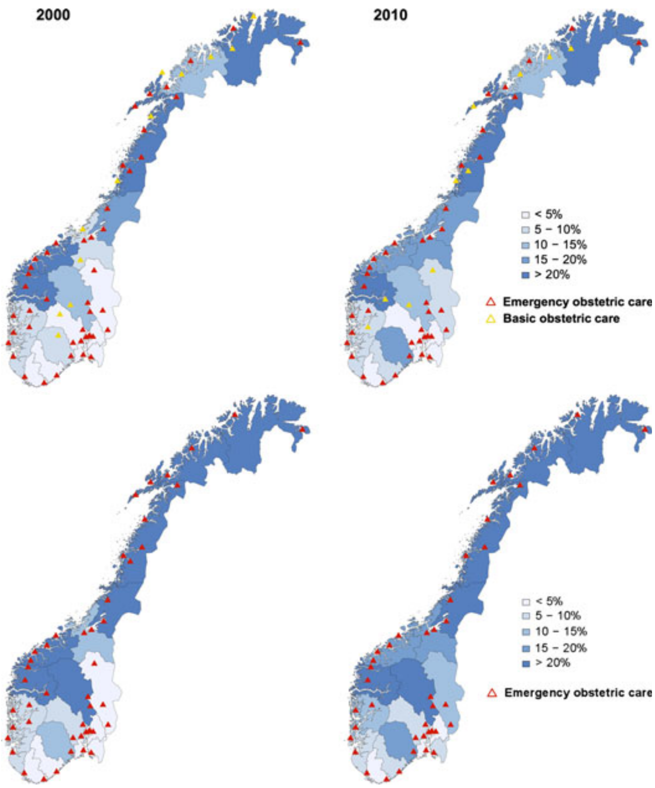

Figure 1. Travel time to all institutions and emergency obstetric care institutions. The proportion of women living outside the 1-hour zone in the 19 counties on 1 January 2000 and 2010 (%) is shown in the background colour scale for all institutions (top) and emergency obstetric care institutions (bottom). The institutions are marked according to the level of care. Based on census data from Statistics Norway and the Norwegian road database.

had a helicopter response time exceeding 20 minutes and a road ambulance transfer time of 1–3 hours to the nearest emergency institution. The Norwegian Air Ambulance recorded 444 transports related to pregnancy and childbirth in 2009: 257 primary transports from home to institution and 187 secondary transports between institutions (P. Madsen, the Norwegian Air Ambulance, personal communication, 2011). The maternal death audit identified five direct maternal deaths in 2009, and the direct maternal mortality rate was 8.1 per 100 000 live births (5/61 674). Transport delay was not a major factor in any of these deaths (S. Vangen, University of Oslo, personal communication, 2012). As shown in Table 4, the delivery-related perinatal death rate declined from 2.1 per 1000 in 2000 to 1.6 per 1000 in 2009 (adjusted OR, 0.6; 95% CI, 0.4–0.9). The regional differences in 2000 and 2009 were not statistically significant (2000, $P = 0.35$; 2009, $P = 0.16$; Wald test). Table 4 also shows the numbers and risk of maternal morbidity on national and regional levels. Nationally, the maternal morbidity risk increased from 1.7% to 2.2% from 2000 to 2009 (adjusted OR, 1.4; 95% CI, 1.2–1.5). The maternal morbidity risk also increased in three health regions: Northern region (adjusted OR, 1.5; 95% CI, 1.1–1.9), Southern region (adjusted OR, 1.5; 95% CI, 1.2–1.8) and Eastern region (adjusted OR, 1.3; 95% CI, 1.1–1.5). The Western region had the lowest risk of maternal morbidity in both 2000 and 2009, and was used as reference for regional comparisons. In 2000, there were no significant regional differences when adjusting for confounding variables ($P = 0.3$, Wald test), whereas, in 2009, the maternal morbidity risk was significantly higher than the reference in three regions: Northern region (adjusted OR, 1.8; 95% CI, 1.4–2.2), Southern region (adjusted OR, 1.8; 95% CI, 1.5–2.1) and Eastern region (adjusted OR, 1.3; 95% CI, 1.05–1.5).

Table 3. Risk of unplanned delivery outside an institution in 2004–09 versus 1979–83. Data from the Medical Birth Registry of Norway on deliveries at gestational age ≥22 weeks or birth weight ≥500 g

Region and country number		1979–83		2004–09		Odds ratio, crude	95% CI	Odds ratio, adjusted***	95% CI
		Total deliveries*	Outside institution** (%)	Total deliveries*	Outside institution** (%)				
Norway		252 621	984 (0.39)	409 432	2832 (0.69)	1.8	1.6–1.9	2.0	1.9–2.2
Eastern region	1	12 768	18 (0.14)	20 447	131 (0.64)	4.5	2.8–7.4	5.7	3.1–10
	2	21 629	51 (0.24)	42 682	232 (0.54)	2.3	1.6–3.1	2.3	1.7–3.2
	3	25 910	35 (0.13)	66 818	229 (0.34)	2.5	1.7–3.7	2.6	1.7–3.8
	4	9246	28 (0.30)	12 604	80 (0.63)	2.1	1.4–3.2	2.3	1.4–3.7
	5	9329	56 (0.60)	12 641	101 (0.79)	1.3	0.96–1.8	1.7	1.2–2.5
Southern region	6	11 901	40 (0.33)	19 709	107 (0.54)	1.6	1.1–2.3	1.9	1.3–2.9
	7	10 343	17 (0.16)	16 739	73 (0.43)	2.7	1.6–4.4	2.8	1.6–4.9
	8	9087	42 (0.46)	11 694	110 (0.93)	2.0	1.4–2.9	2.3	1.6–3.4
	9	5856	12 (0.20)	8462	45 (0.53)	2.6	1.4–4.9	2.8	1.4–5.4
	10	9685	39 (0.40)	14 812	99 (0.66)	1.7	1.1–2.4	2.0	1.3–3.0
Western region	11	23 663	101 (0.43)	40 629	235 (0.58)	1.4	1.1–1.7	1.6	1.2–2.0
	12	26 680	103 (0.38)	42 132	340 (0.80)	2.1	1.7–2.7	2.1	1.7–2.7
	14	6945	45 (0.64)	8476	113 (1.32)	2.1	1.5–2.9	2.1	1.4–3.1
Central region	15	15 622	99 (0.63)	19 425	190 (0.97)	1.5	1.2–1.9	2.0	1.5–2.6
	16	15 484	56 (0.36)	25 176	199 (0.78)	2.2	1.6–2.9	2.6	1.9–3.5
	17	7771	53 (0.68)	10 073	141 (1.38)	2.1	1.5–2.8	2.5	1.8–3.5
Northern region	18	15 472	99 (0.64)	17 498	180 (1.02)	1.6	1.3–2.1	2.0	1.5–2.6
	19	9873	68 (0.68)	13 125	118 (0.89)	1.3	0.97–1.8	1.4	1.0–1.9
	20	5303	21 (0.39)	5897	105 (1.75)	4.5	2.8–7.2	5.4	3.2–8.8

*Deliveries with known place of birth; planned home deliveries were excluded in 2004–09.
**Delivery at home, during transportation or in a non-obstetric institution.
***Adjusted for maternal age, parity, education level and partner status.

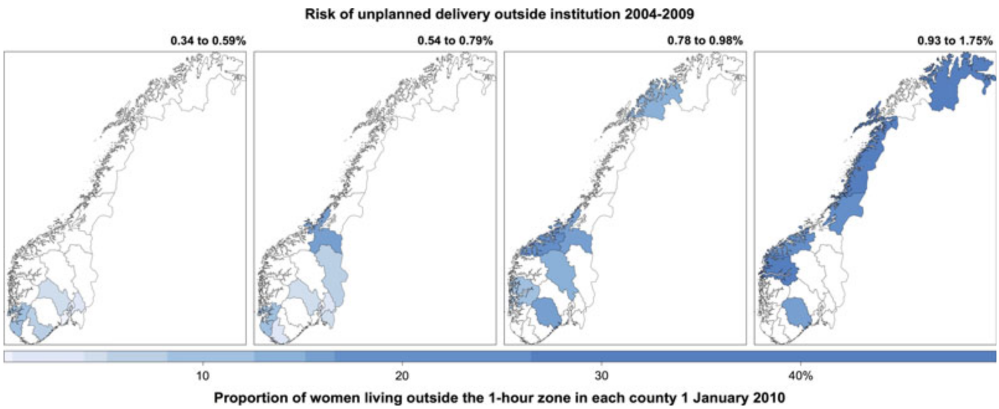

Figure 2. Risk of unplanned delivery outside institutions and travel time to institutions. The counties were sorted into four levels of risk based on the period 2004–09. The colour scale shows the proportion of women living outside the 1-hour zone in each county (%) on 1 January 2010. Based on data from the Medical Birth Registry of Norway, and on census data from Statistics Norway combined with the Norwegian road database.

Table 4. The World Health Organization (WHO) Emergency Obstetric Care (EmOC) indicators as applied to national and regional levels, Norway, 2000 and 2009. Data from the Medical Birth Registry of Norway on deliveries ≥22 weeks of gestation or birth weight ≥500 g. Population data from Statistics Norway

Regions	Population	EmOC* estimated need**	EmOC number (coverage) (%)	Basic OC***	Deliveries (*n*)	Outside EmOC**** *n* (%)	Caesarean sections *n* (%)	Maternal morbidity***** *n* (%)	Perinatal mortality****** *n* (%)
2000									
Norway	4 478 497	45	47 (100)	12	58 632	1068 (1.8)	7653 (13.1)	988 (1.7)	124 (2.1)
Eastern	1 592 540	16	11 (69)	1	20 786	229 (1.1)	3032 (14.6)	341 (1.6)	47 (2.2)
Southern	872 493	9	8 (89)	2	10 480	130 (1.2)	1354 (12.9)	189 (1.8)	22 (2.1)
Western	916 018	9	9 (100)	0	13 078	70 (0.5)	1381 (10.6)	194 (1.5)	29 (2.2)
Central	633 118	6	8 (100)	2	8172	144 (1.8)	1050 (12.8)	143 (1.8)	9 (1.1)
Northern	464 328	5	11 (100)	7	6013	495 (8.2)	825 (14.6)	119 (2.0)	16 (2.6)
2009									
Norway	4 852 197	49	41 (83)	10	61 895	1289 (2.1)	10 154 (16.4)	1331 (2.2)	99 (1.6)
Eastern	1 770 946	18	9 (50)	2	23 642	299 (1.3)	4286 (18.1)	507 (2.1)	37 (1.5)
Southern	936 066	10	8 (80)	0	10 682	84 (0.8)	1863 (17.4)	299 (2.8)	21 (1.9)
Western	1 006 202	10	7 (70)	2	13 822	254 (1.8)	1760 (12.7)	225 (1.6)	20 (1.4)
Central	673 364	7	8 (100)	0	8272	78 (0.9)	1376 (16.6)	152 (1.8)	11 (1.3)
Northern	465 619	5	9 (100)	6	5443	574 (10.6)	862 (15.8)	147 (2.7)	7 (1.3)

*Emergency obstetric care defined by the provision of all nine WHO signal functions.
**Five institutions per 500 000.
***Basic obstetric care defined as care for normal, uncomplicated deliveries.
****Deliveries at basic obstetric care institutions, unplanned deliveries outside institution and planned home deliveries.
*****Maternal morbidity included the following: maternal intensive care, eclampsia, puerperal sepsis and sepsis during delivery, thromboembolism and haemorrhage ≥1500 ml or blood transfusion.
******Intrapartum death and neonatal death before 24 hours per 1000 births (both live and stillborn).

Discussion

Main findings

The risk of unplanned delivery outside an institution has doubled in Norway over the last 30 years and the risk of maternal morbidity increased from 2000 to 2009. These changes coincided with an increasing proportion of women of fertile age living further away from obstetric institutions, and with a reduction in the number of emergency obstetric care institutions to a level below the estimated need.

Strengths and weaknesses

We used population-based registry and census data, and combined various methods and data sources in order to provide a more comprehensive description of the health system during the study period. The MBRN database permitted a long observation period and the large samples necessary to study rare events. We show that the addition of geographical tools to traditional epidemiology can be useful for service evaluation as well as planning.

However, our study had some limitations. Travel zone calculations were based on standardised conditions and may underestimate actual travel time. Further, planned home deliveries were not registered separately in the MBRN before 1999, and the risk increase for unplanned delivery outside institutions may be underestimated. Planned home deliveries were rare in the reference period (1979–83) and constituted 0.037% (20/54492) of the deliveries in 1975–6.[18] Finally, our definition of maternal morbidity included the main causes of potentially life-threatening complications.[15] The increase in maternal morbidity over time may have several explanations, and we could not separate improved diagnosis and reporting from other contributing factors. National guidelines for diagnosis, monitoring and treatment of maternal and fetal complications have been updated regularly since 1995, but lack of adherence has been reported.[19–22] Caesarean section also increases the risk of maternal complications both in the actual and subsequent pregnancies.[23,24] Within-country variation of caesarean section rates may have an impact on maternal morbidity. The increase in maternal morbidity may also be related to changes in maternal risk factors, rather than reduced timeliness and adequacy of the provided care. Adjustment for maternal diabetes did not change the estimates and was not included in the final regression models. Adjustment for maternal smoking increased the estimates slightly, probably as a result of decreasing frequency of daily smoking. Daily smoking was reported by 24% of pregnant women in 2000, compared with 17% in 2009 (MBRN, http://mfr-nesstar.uib.no/mfr/). We could not adjust for maternal obesity, and ethnicity must be included among the risk factors in future studies.[2,23,25,26]

Interpretation

Although travel distances in Norway may be longer than in many high-income countries, we complied with international standard definitions and indicator frameworks to aid comparison over time and across settings.[14] When analysing the availability of institutions, we considered hourly time categories to be a realistic approach to the Norwegian demographics. In the Netherlands, an estimated travel time exceeding 20 minutes was associated with increased risk of adverse neonatal outcome in home deliveries with subsequent hospital transfer.[11] Compared with a recent study from the USA, the proportion of women who lived outside the 1-hour travel zone was three times higher in Norway when including all obstetric institutions, and almost twice as high when including only emergency obstetric care institutions.[27] A higher proportion of Native American women (18.8%) lived outside the 1-hour drive to a perinatal centre.[27] Similarly, we found higher proportions of women (35–72%) who lived outside the 1-hour zone to emergency obstetric care institutions in the Northern region. This region covers the main Sami cultural and economic areas in Norway.[28] Neither Statistics Norway nor the MBRN register the indigenous identity of Sami women. Consequently, it was not possible to assess the availability for this group in particular.

The risk of unplanned delivery outside institutions increased in both urban and rural counties in our study. The risk in Norway during the period 2004–09 was higher than the previously reported 0.1% of births in national data from Finland.[29] In our study, the risk was 0.3–0.5% in the three most urban counties; this was lower than the 0.6% reported from an urban area in Scotland.[30] However, the risk more than doubled in all three counties from 1979–83 to 2004–09. Mechanisms may differ between locations and involve factors such as geographical distance and traffic constraints, as well as admission criteria in large, busy obstetric departments.

The 2.2% incidence of maternal morbidity in our study was higher than previous reports from Norway and Europe. The Mothers Mortality and Severe Morbidity Survey B (MOMS-B) reported a Norwegian incidence rate of 0.86% for severe maternal morbidity based on data collected from the capital county, Oslo, during 1995. European rates ranged from 0.6 to 1.5%, and the MOMS-B studies did not include thromboembolism.[31] The incidence of severe maternal morbidity was 0.71% in a prospective Dutch study which applied a stricter definition of severe maternal morbidity.[2,15] The wider case definition in our study was also reflected by a morbidity/mortality ratio of 266 : 1; other studies have reported ratios of 118 : 1 and 49 : 1.[32,33] Although the wider definition influenced the reported rates, the definitions and report form were similar throughout the period, thus allowing for the evaluation of change over time as well as regional differences.

Our study focused on institution numbers and not on institution size. However, we observed a reduction in the number of small institutions and an increasing proportion of the deliveries took place in the largest institutions. In France, small institutions had a higher frequency of inadequate/inappropriate management of severe post-partum haemorrhage.[34] A recent study from the USA reported increased risk of maternal complications in the institutions with the lowest volumes, which apparently also included non-obstetric institutions.[35]

Conclusions

The findings in the current study indicated reduced quality from the health system perspective, as demonstrated by a reduced availability of institutions and an increased risk of unplanned delivery outside institutions. The WHO indicators were secondary outcomes in our study. However, they were useful in the Norwegian high-income context and the indicator assessment pointed to the emerging inequalities described in the cross-sectional and cohort analyses. Availability and access must be considered to a larger extent in service planning and evaluation, and structural issues, such as the risk factors for unplanned delivery outside institutions in urban and rural areas, need to be addressed.

We would expect the risk of morbidity to be unchanged or reduced following centralisation. The maternal mortality and delivery-related perinatal mortality were low and indicated good quality of clinical care in the institutions. Nevertheless, we reported an increase in the risk of maternal morbidity and increasing regional differences in such risk. We do not believe that our findings can be fully explained by differences in diagnoses, reporting practices or increases in risk factors where information was lacking. More knowledge is needed to understand the interaction between structural factors and clinical outcomes. A comprehensive analysis of neonatal mortality and morbidity was beyond the scope of this study, but must be included when drawing the final conclusions on quality in obstetric care. Further research should aim to inform the debate concerning the distribution of benefits and burden in the centralisation of obstetric care. Whether mothers pay the price for efforts to improve neonatal outcome remains to be answered.

Disclosure of interests

None.

Contribution to authorship

HME and OFN outlined the initial idea. HME, N-HM, OFN and KK contributed to the definition of the research question and to the development of the final study design. HME and KK performed the statistical analyses. HME drafted the manuscript, tables and figures. HME, NHM, OFN and KK participated in the interpretation of the results, draft revision and approved the final version of the manuscript.

Details of ethics approval

The regional ethical council, REK-Vest, approved the study and granted exemption from the principle of individual consent (ID 2010/3243/R).

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Travel time to all obstetric institutions.

Appendix S2. Travel time to emergency obstetric care institutions. ■

References

1 BiEC Group. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. *BMJ* 2011;343:d7400.

2 Zwart JJ, Richters JM, Ory F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies. *BJOG* 2008;115:842–50.

3 Christiaens W, Bracke P. Place of birth and satisfaction with childbirth in Belgium and the Netherlands. *Midwifery* 2009;25:e11–9.

4 Schroeder E, Petrou S, Patel N, Hollowell J, Puddicombe D, Redshaw M, et al. Cost effectiveness of alternative planned places of birth in women at low risk of complications: evidence from the Birthplace in England national prospective cohort study. *BMJ* 2012;344:e2292.

5 Benoit C, Zadoroznyj M, Hallgrimsdottir H, Treloar A, Taylor K. Medical dominance and neoliberalisation in maternal care provision: the evidence from Canada and Australia. *Soc Sci Med* 2010;71:475–81.

6 Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. *Ann Intern Med* 2002;137:511–20.

7 Urbach DR, Baxter NN. Does it matter what a hospital is "high volume" for? Specificity of hospital volume–outcome associations for surgical procedures: analysis of administrative data. *BMJ* 2004;328:737–40.

8 Billingsley KG, Morris AM, Dominitz JA, Matthews B, Dobie S, Barlow W, et al. Surgeon and hospital characteristics as predictors of major adverse outcomes following colon cancer surgery: understanding the volume–outcome relationship. *Arch Surg* 2007;142:23–31. discussion 2.

9 Tracy SK, Sullivan E, Dahlen H, Black D, Wang YA, Tracy MB. Does size matter? A population-based study of birth in lower volume maternity hospitals for low risk women. *BJOG* 2006;113:86–96.

10 Moster D, Lie RT, Markestad T. Neonatal mortality rates in communities with small maternity units compared with those having larger maternity units. *BJOG* 2001;108:904–9.

11 Ravelli AC, Jager KJ, de Groot MH, Erwich JJ, Rijninks-van Driel GC, Tromp M, et al. Travel time from home to hospital and adverse perinatal outcomes in women at term in the Netherlands. *BJOG* 2011;118:457–65.

12 Dummer TJ, Parker L. Hospital accessibility and infant death risk. *Arch Dis Child* 2004;89:232–4.

13 Paxton A, Bailey P, Lobis S, Fry D. Global patterns in availability of emergency obstetric care. *Int J Gynaecol Obstet* 2006;93:300–7.

14 WHO, UNFPA, UNICEF, AMDD. *Monitoring Emergency Obstetric Care – A Handbook*. Geneva: WHO, 2009.

15 Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. *Best Pract Res Clin Obstet Gynaecol* 2009;23:287–96.

16 White paper nr 12. En gledelig begivenhet. Oslo: Ministry of Health and Care Services, 2008.

17 Elveg – the electronic road database. 2009 [www.statkart.no/nor/Land/Fagomrader/Vegdatasamarbeidet/Elektronisk_vegnett/]. Accessed 9 July 2012.

18 Bakketeig LS, Bergsjo P. Birth during transportation in Norway. An analysis of births outside an institution from 1 February 1975 to 31 January 1976. *Tidsskr Nor Laegeforen* 1977;97:923–70.

19 Bjørge L, Henriksen T, Øian P, Hordnes K, Sand S, editors. *Guidelines for obstetric care*. In Bjørge L, Henriksen T, Øian P, Hordnes K, Sand S, editors. *The Norwegian Society for Obstetrics and Gynecology*. Oslo: The Norwegian Medical Association, 2008.

20 Andersgaard AB, Herbst A, Johansen M, Ivarsson A, Ingemarsson I, Langhoff-Roos J, et al. Eclampsia in Scandinavia: incidence, substandard care, and potentially preventable cases. *Acta Obstet Gynecol Scand* 2006;85:929–36.

21 Winter C, Macfarlane A, Deneux-Tharaux C, Zhang WH, Alexander S, Brocklehurst P, et al. Variations in policies for management of the third stage of labour and the immediate management of postpartum haemorrhage in Europe. *BJOG* 2007;114:845–54.

22 Bjornerem A, Acharya G, Oian P, Maltau JM. Postpartum hemorrhage – prophylaxis and treatment in Norway. *Tidsskr Nor Laegeforen* 2002;122:2536–7.

23 Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of severe obstetric haemorrhage. *BJOG* 2008;115:1265–72.

24 Al-Zirqi I, Stray-Pedersen B, Forsen L, Vangen S. Uterine rupture after previous caesarean section. *BJOG* 2010;117:809–20.

25 Philibert M, Deneux-Tharaux C, Bouvier-Colle MH. Can excess maternal mortality among women of foreign nationality be explained by suboptimal obstetric care? *BJOG* 2008;115:1411–8.

26 Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities. *BMJ* 2009;338:b542.

27 Rayburn WF, Richards ME, Elwell EC. Drive times to hospitals with perinatal care in the United States. *Obstet Gynecol* 2012;119:611–6.

28 Sami statistics. Oslo, Kongsvinger: Statistics Norway, 2010. Report No.: ISBN 978-82-537-7742-9 Elektronisk versjon.

29 Viisainen K, Gissler M, Hartikainen AL, Hemminki E. Accidental out-of-hospital births in Finland: incidence and geographical distribution 1963–1995. *Acta Obstet Gynecol Scand* 1999;78:372–8.

30 Rodie VA, Thomson AJ, Norman JE. Accidental out-of-hospital deliveries: an obstetric and neonatal case control study. *Acta Obstet Gynecol Scand* 2002;81:50–4.

31 Zhang WH, Alexander S, Bouvier-Colle MH, Macfarlane A. Incidence of severe pre-eclampsia, postpartum haemorrhage and sepsis as a surrogate marker for severe maternal morbidity in a European population-based study: the MOMS-B survey. *BJOG* 2005;112: 89–96.

32 Waterstone M, Bewley S, Wolfe C. Incidence and predictors of severe obstetric morbidity: case–control study. *BMJ* 2001;322:1089–93. discussion 93–4.

33 Brace V, Penney G, Hall M. Quantifying severe maternal morbidity: a Scottish population study. *BJOG* 2004;111:481–4.

34 Bouvier-Colle MH, Ould El Joud D, Varnoux N, Goffinet F, Alexander S, Bayoumeu F, et al. Evaluation of the quality of care for severe obstetrical haemorrhage in three French regions. *BJOG* 2001;108:898–903.

35 Kyser KL, Lu X, Santillan DA, Santillan MK, Hunter SK, Cahill AG, et al. The association between hospital obstetrical volume and maternal postpartum complications. *Am J Obstet Gynecol* 2012;207:42e1–17.

Paper I. Erratum and supplementary online files.

In table 3 in the paper there is an error in number of deliveries for 2004-2009. These columns describe the number of deliveries from 2003 to 2009, both total and unplanned outside institution. The error in numbers had no consequences for the reported risks in the last time period. The odds ratios were calculated using the time period from 2004 to 2009 and are correct.

Appendix S1. Travel time to all obstetric institutions.
Numbers and proportions of women living outside the one-hour and two-hour travel zone in 2000 and 2010. Based on census data from Statistics Norway and the Norwegian road database

Region, county and county number		Women 15- 49 years[a]		Women living outside the 1 hour zone for any institution[b] Number (%)				Women living outside the 2 hour zone for any institution[b] Number (%)			
		2000	2010	2000		2010		2000		2010	
	Norway	1 050 269	1 127 665	82 671	(7.9)	102 895	(8.8)	23 581	(2.3)	27 571	(2.4)
Eastern Region	**1 Østfold**	57 260	60 489	829	(1.4)	2431	(4.0)	155	(0.3)	345	(0.6)
	2 Akershus	113 817	126 415	58	(0.1)	530	(0.4)	2			0
	3 Oslo	134 749	159 156		0	13	(0.01)		0		0
	4 Hedmark	40 321	40 350	1 305	(3.2)	2 088	(5.2)	35	(0.9)	30	(0.1)
	5 Oppland	40 080	39 620	5 490	(13.7)	5 939	(15.0)	344	(0.9)	453	(1.1)
Southern Region	**6 Buskerud**	54 518	58 497	647	(1.2)	2 757	(4.7)	28	(0.05)	29	(0.05)
	7 Vestfold	49 819	52 352	115	(0.2)	125	(0.2)	74	(0.2)	162	(0.3)
	8 Telemark	37 277	37 018	2 633	(7.1)	5 906	(15.0)	223	(0.6)	277	(0.8)
	9 Aust-Agder	23 387	24 193	1 138	(4.9)	1 947	(8.0)	239	(1.0)	422	(1.7)
	10 Vest-Agder	35 867	39 481	496	(1.4)	1 250	(3.2)	178	(0.5)	459	(1.2)
Western Region	**11 Rogaland**	90 446	102 028	5 905	(6.5)	8 710	(8.5)	896	(1.0)	1 271	(1.2)
	12 Hordaland	101 172	111 589	9 897	(9.8)	9 150	(8.2)	3 599	(3.6)	4 621	(4.1)
	14 Sogn og Fjordane	23 209	22 641	5 838	(25.2)	7 514	(33.2)	1 210	(5.2)	1 216	(5.4)
Central Region	**15 Møre og Romsdal**	53 795	53 948	14 047	(26.1)	8 956	(16.6)	1 486	(2.8)	1 558	(2.8)
	16 Sør-Trøndelag	61 495	68 640	4 201	(6.8)	10 376	(15.1)	1 125	(1.8)	1 940	(2.8)
	17 Nord-Trøndelag	27 540	28 280	4 913	(17.8)	5 651	(20.0)	1 759	(6.4)	1 796	(6.4)
Northern Region	**18 Nordland**	52 493	50 926	12 748	(24.3)	13 471	(26.4)	5 236	(10.0)	6120	(12.0)
	19 Troms	35 422	35 620	4 190	(11.8)	4 474	(12.6)	1 276	(3.6)	1 505	(4.2)
	20 Finnmark	17 602	16 422	8 221	(46.7)	7 432	(45.2)	5 716	(32.5)	5 405	(32.9)

[a] Data from Statistics Norway for all women in fertile age (15 -49 years) with registered address on 1 January 2000 and 1 January 2010. 59 institutions in 2000 and 51 institutions in 2010.

[b] Included institutions provided either basic obstetric care for normal deliveries or both basic obstetric care and emergency obstetric care.

Appendix S2. Travel time to emergency obstetric care institutions.

Numbers and proportions of women who lived outside the one-hour and two-hour travel zone to emergency obstetric care (EmOC) institutions in 2000 and 2010. Based on census data from Statistics Norway and the Norwegian road database.

		Women 15- 49 years[a]		Outside the 1 hour zone for EmOC[b] Number (%)				Outside the 2 hour zone for EmOC[b] Number (%)			
		2000	2010	2000		2010		2000		2010	
	Norway	1 050 269	1 127 665	115 701	(11.1)	136 208	(12.1)	36 074	(3.4)	54 567	(4.8)
Eastern Region	**1 Østfold**	57 260	60 489	829	(1.4)	3 157	(5.2)	155	(0.3)	85	(0.1)
	2 Akershus	113 817	126 415	58	(0.05)	559	(0.4)	2	(<0.01)	14	(0.01)
	3 Oslo	134 749	159 156	0		28	(0.01)	0		0	
	4 Hedmark	40 321	40 350	1 320	(3.3)	5 061	(12.5)	35	(0.1)	3 022	(7.5)
	5 Oppland	40 080	39 620	9 134	(22.8)	9 614	(24.3)	946	(2.4)	3 862	(9.8)
Southern Region	**6 Buskerud**	54 518	58 497	5 023	(9.2)	5 390	(9.2)	739	(1.4)	3489	(6.0)
	7 Vestfold	49 819	52 352	115	(0.2)	126	(0.2)	74	(0.1)	119	(0.2)
	8 Telemark	37 277	37 018	4 666	(12.5)	6 043	(16.3)	237	(0.6)	1636	(4.4)
	9 Aust-Agder	23 387	24 193	1 138	(4.9)	2 030	(8.4)	405	(1.7)	745	(3.1)
	10 Vest-Agder	35 867	39 481	496	(1.4)	1 260	(3.2)	178	(0.5)	212	(0.5)
Western Region	**11 Rogaland**	90 446	102 028	5 905	(6.5)	9 167	(9.0)	896	(1.0)	931	(0.9)
	12 Hordaland	101 172	111 589	9 897	(9.8)	11 653	(10.5)	3 599	(3.6)	1250	(1.1)
	14 Sogn og Fjordane	23 209	22 641	5 838	(25.2)	9 929	(43.9)	1 212	(5.2)	4618	(20.4)
Central Region	**15 Møre og Romsdal**	53 795	53 948	15 321	(28.5)	8 975	(16.6)	1 491	(2.7)	451	(0.8)
	16 Sør-Trøndelag	61 495	68 640	8 922	(14.5)	11 385	(16.6)	1 846	(3.0)	3096	(4.5)
	17 Nord-Trøndelag	27 540	28 280	4 965	(18.0)	5 675	(20.0)	1 759	(6.4)	2446	(8.7)
Northern Region	**18 Nordland**	52 493	50 926	16 424	(31.3)	21 933	(43.0)	8 130	(15.5)	10123	(19.9)
	19 Troms	35 422	35 620	12 591	(35.5)	12 389	(34.8)	6 633	(18.7)	7 106	(20.0)
	20 Finnmark	17 602	16 422	13 059	(74.2)	11 834	(72.1)	7 737	(44.0)	11 362	(69.2)

[a] Data from Statistics Norway for all women 15 -49 years who had a registered address on January 1 2000 and January 1 2010. 47 institutions in 2000 and 41 institutions in 2010.

[b] Emergency obstetric care included the following nine signal functions; intravenous administration of drugs, removal of retained placenta/products, assisted vaginal delivery, basic neonatal resuscitation, surgery, and blood transfusion.

OBSTETRICS

Increased risk of peripartum perinatal mortality in unplanned births outside an institution: a retrospective population-based study

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BACKGROUND: Births in midwife-led institutions may reduce the frequency of medical interventions and provide cost-effective care, while larger institutions offer medically and technically advanced obstetric care. Unplanned births outside an institution and intrapartum stillbirths have frequently been excluded in previous studies on adverse outcomes by place of birth.

OBJECTIVE: The objective of the study was to assess peripartum mortality by place of birth and travel time to obstetric institutions, with the hypothesis that centralization reduces institution availability but improves mortality.

STUDY DESIGN: This was a national population-based retrospective cohort study of all births in Norway from 1999 to 2009 (n = 648,555) using data from the Medical Birth Registry of Norway and Statistics Norway and including births from 22 gestational weeks or birthweight ≥500 g. Main exposures were travel time to the nearest obstetric institution and place of birth. The main clinical outcome was peripartum mortality, defined as death during birth or within 24 hours. Intrauterine fetal deaths prior to start of labor were excluded from the primary outcome.

RESULTS: A total of 1586 peripartum deaths were identified (2.5 per 1000 births). Unplanned birth outside an institution had a 3 times higher mortality (8.4 per 1000) than institutional births (2.4 per 1000), relative risk, 3.5 (95% confidence interval, 2.5–4.9) and contributed 2% (95% confidence interval, 1.2–3.0%) of the peripartum mortality at the population level. The risk of unplanned birth outside an institution increased from 0.5% to 3.3% and 4.5% with travel time <1 hour, 1–2 hours, and >2 hours, respectively. In obstetric institutions the mortality rate at term ranged from 0.7 per 1000 to 0.9 per 1000. Comparable mortality rates in different obstetric institutions indicated well-functioning routines for referral.

CONCLUSION: Unplanned birth outside an institution was associated with increased peripartum mortality and with long travel time to obstetric institutions. Structural determinants have an important impact on perinatal health in high-income countries and also for low-risk births. The results show the importance of skilled birth attendance and warrant attention from clinicians and policy makers to negative consequences of reduced access to institutions.

Key words: access, availability, emergency obstetric and newborn care, health systems, perinatal mortality

Birth-related complications may arise quickly and threaten the life and future health of both the mother and child. Prevention of death and adverse outcomes requires urgent, skilled interventions. Whether delivery care in smaller obstetric institutions and midwife-led institutions is safe and cost effective compared with centralized care in larger obstetric institutions has been heavily debated.[1-6] Typically, previous studies comparing the planned place of birth have excluded unplanned births outside an institution.[3,4,7,8] Additionally, key studies have included only neonatal deaths and thus failed to address how a lack of adequate monitoring and interventions during labor may result in intrapartum death.[4,6,7,9,10]

Several authors have raised concerns about adverse consequences of reduced accessibility to obstetric and neonatal care as well as a risk of unnecessary interventions in the larger institutions.[1,5,11-15] However, conclusive studies linking structural factors and perinatal mortality are lacking. In Norway, the number of obstetric institutions was reduced from 95 to 51 during 1979–2009. The rate of unplanned births outside an institution increased in both rural and urban areas during this period.[16]

The aim of the present study was to assess peripartum mortality associated with the place of birth and availability of obstetric institutions, with the hypothesis that centralization reduces institution availability but improves the peripartum mortality.

Material and Methods

Study design, setting, and data sources

We designed a retrospective population-based cohort study of all births in Norway from Jan. 1, 1999, to Dec. 31, 2009 (n = 648,555 births). Data sources were the Medical Birth Registry of Norway (MBRN) and Statistics Norway. Inclusion criteria were births with a gestational age ≥22 completed weeks or birthweight ≥500 g.

The MBRN has received mandatory standardized notifications of all live births and stillbirths (≥16 weeks' gestation) since 1967. The registry is routinely linked with the National Registry through the mother's national identification number, given to all individuals residing in the country. This linkage provides identification numbers to all live births, ensures complete notification

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to the MBRN, and provides data on all dates of death.

The MBRN notification form was extended in 1999 to include more information about the mother, the neonate, and the birthplace. The notification of stillbirths specifies time of death in relation to labor (antepartum, intrapartum, or unknown) and to arrival in the institution (prior to or after). Stillbirth registration in the MBRN has been validated,[17] and the MBRN receives the autopsy report or, if autopsy is not performed, a written conclusion on likely cause of death for all stillbirths from 22 weeks' gestation.

In the present study, linkage with the National Registry provided data on each mother's registered address. Since 2000, Statistics Norway has assigned geographic coordinates to the National Registry addresses and updated addresses and coordinates on Jan. 1 each year. Coverage of individual coordinates was 98% of all addresses in 2000 and 99% in 2010.

Primary perinatal outcome

Peripartum mortality was defined as intrapartum death or neonatal death within 24 hours and will in the following text be referred to as mortality. Fetal death prior to labor (antepartum stillbirths) were excluded from the primary perinatal outcome.

Place of birth

Place of birth was categorized as unplanned outside an obstetric institution, in basic obstetric care institution (BOC), and in emergency obstetric and newborn care institution (EmONC). Unplanned birth outside an institution was defined as a birth at home, during transportation, or in a nonobstetric institution (eg, health center) for a woman who planned an institutional birth.

The World Health Organization Handbook for Monitoring Emergency Obstetric and Newborn Care was used to categorize institutions by the available treatment options.[18] BOC institutions provided midwife-led care for normal deliveries and intravenous administration of drugs and basic newborn resuscitation if needed before transfer.

EmONC institutions provided intravenous administration of uterotonic drugs, antibiotics, and magnesium sulphate, removal of the placenta or retained products of conception, newborn resuscitation, assisted vaginal delivery, cesarean delivery, and blood transfusion. All EmONC institutions had a specialist in obstetrics and gynecology on call.

We further classified EmONC institutions according to the annual number of deliveries (<500, 500−1499, and >1500). Institution closure or change in the level of care was corrected at the start of each calendar year, included institutions reported ≥10 births annually. Planned home births were rare (1253, 0.2%); 96% of these mothers lived within the 1 hour travel zone to all obstetric institutions. There were no peripartum deaths. These births have been described previously[19] and were excluded (Figure 1).

Travel zone

A travel zone was defined as the geographic area in which all women were estimated to reach the nearest obstetric institution within the given time. Institutions were registered by geographic coordinates, and surrounding travel zones were calculated based on the Norwegian electronic road database.[20] Estimates were based on registered speed limits and the standard duration of ferry/boat journeys and represented the minimum time for nonemergency transport. A merged area (polygon) was created for the travel zones (<1 hour, 1−2 hours, and >2 hours).

The mother's national identification number, or a substitute identification number for resident noncitizens, was used to link births in the MBRN to her registered address in the National Registry and then to the address coordinates (n = 638,155 births, 98.4%). For each birth the registered address was placed in a travel zone. Births to women lacking address coordinates were assigned to the travel zone of the majority of mothers in their municipality in the corresponding year (n = 9996 births, 1.5%). Few births lacked both address coordinates and municipality (n = 404, 0.06%), and these were excluded from the travel zone analyses. The annual relocation rate was 14% in 2000, 8.6% within the municipality, and 4.8% to another municipality.

Analyses

The infant/birth was the observation unit in all analyses. Cross-tables and generalized linear models were used to compute rates and relative risks (RRs) with 95% confidence intervals (CIs), while taking into account clustering by births to the same mother or in the same institution.

Multilevel models were used to assess both cluster levels. Attributable risk was calculated from the adjusted relative risk model.[21,22] Analyses were stratified on socioeconomic risk factors and maternal and fetal medical risk factors for perinatal mortality.

We also stratified analyses by season (summer, April to September; and winter, October to March) and by 5 year period (1999−2004 and 2005−2009). We used standardized sex-specific birthweight by gestational age (z-scores) to identify misclassified gestational age (z-score above 4, n = 330 births, 0.05%).[23] If gestational age was misclassified or only birthweight was recorded (n = 4810, 0.7%), we categorized births as preterm if birthweight was more than 2 SD below the average weight at 37 weeks (<2285 g for males and <2200 g for females, n = 677, 0.1%).

Statistical analyses were performed with SPSS (IBM SPSS Statistics for Mac, version 23.0; IBM Corp, Armonk, NY) and STATA 14 IC (StataCorp LP, College Station, TX). Travel zone analyses were performed with the GIS software Arc Info with Network Analyst (Environmental Systems Research Institute Inc, Redlands, CA).

Ethical approval

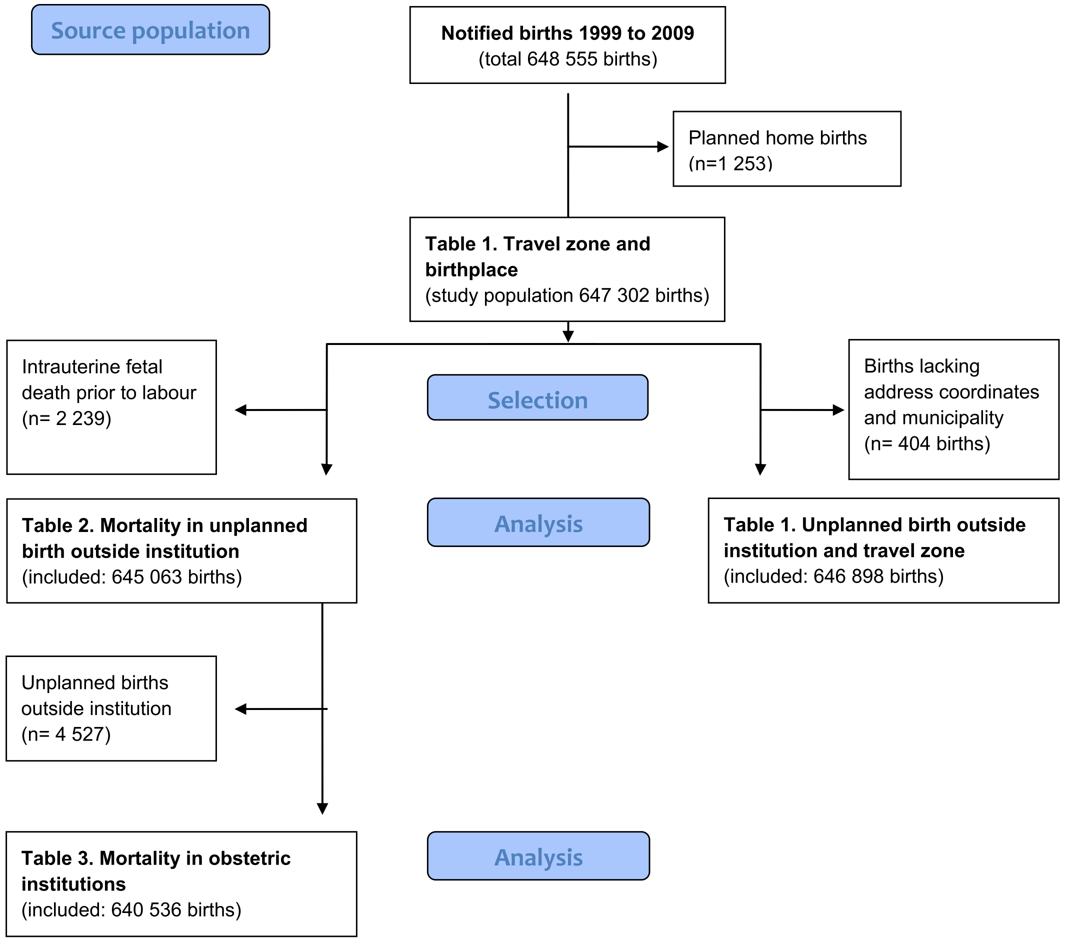
The Regional Medical Ethical Committee for Western Norway approved the study (REK-VEST 2010/3243).

Results

Travel zone and place of birth

Travel zone information was available for 646,898 births and the distribution

FIGURE 1
Study population flow diagram



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of travel zones and place of birth in the population is described in Table 1. Births were more likely to occur unplanned outside an institution, in BOC institutions, or in the lowest-volume EmONC institutions when mothers lived in rural areas with long travel time to institutions. A total of 9490 births occurred in BOC institutions. Few nulliparous women delivered in BOC institutions (n = 1680); among these, 87% would need to travel more than 1 hour to reach an EmONC institution.

A total of 4538 children with available travel zone information were born unplanned outside an institution: 1759 at home, 2148 during transport, 121 in former obstetric institutions, and 510 in other locations. Risk of unplanned birth outside an institution was 5 times higher in the 1–2 hour travel zone to all institutions compared with the <1 hour zone (adjusted RR, 5.3; 95% CI, 4.9–5.7) and 7 times higher when travel time exceeded 2 hours (adjusted RR, 7.1; I, 6.3–8.1).

The majority of unplanned births outside institutions occurred to low-risk women (online Appendix 1). There were no differences in frequency from the first to the last 5 year period (data not shown, $P = .48$). Stratified on the risk factors outlined in Table 2, analyses yielded similar relative risks as the crude relative risk, but women with medical risk

TABLE 1
Place of birth and the mother's travel zone to all obstetric institutions and to EmONC institutions

Institution	Travel zone	Total, n	Basic obstetric care, n	Emergency obstetric care <1500/y, n	Emergency obstetric care >1500/y, n	Unplanned birth outside institution n	Relative risk (95% CI)[a]	Adjusted relative risk[b]
	Total births[c]	647,302	9490 (1.5)	204,612 (31.6)	428,654 (66.2)	4546 (0.7)		
	Travel zone available, n, %	646,898	9487 (1.5)	204,508 (31.6)	428,365 (66.2)	4538 (0.7)		
All institutions	Travel zone 1 h, n, %	615,896	8638 (1.4)	182,202 (29.6)	421,608 (68.5)	3488 (0.6)	Reference	Reference
	Travel zone 1–2 h, n, %	25,494	787 (3.1)	17,600 (69.0)	6263 (24.6)	844 (3.3)	5.9 (5.5–6.4)	5.3 (5.0–5.8)
	Travel zone >2 h, n, %	5508	62 (1.2)	4706 (85.4)	494 (9.0)	246 (4.5)	8.0 (7.0–9.1)	7.2 (6.3–8.2)
EmONC institutions	Travel zone <1 h, n, %	591,836	1187 (0.2)	170,512 (28.8)	417,067 (70.5)	3070 (0.5)		
	Travel zone 1–2 h, n, %	40,189	5148 (12.8)	25,031 (62.3)	8947 (22.3)	1063 (2.7)		
	Travel zone >2 h, n, %	14,873	3152 (21.2)	8965 (60.3)	2351 (15.8)	405 (2.7)		

Data from Statistics Norway and the Medical Birth Registry of Norway, 1999–2009.

EmONC, Emergency Obstetric Care.

[a] Relative risks adjusted for births to the same mother; [b] Relative risk adjusted for all risk factors outlined in Table 2; [c] Births at gestational age ≥22 weeks or birthweight ≥500 g; planned home births were excluded.

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factors were less likely to deliver unplanned outside an institution (online Appendix 1). Most resident noncitizen women lived within the 1 hour travel zone (n = 2315, 94%). Their rate of unplanned births outside an institution was 1.2% (n = 30), with no deaths.

Peripartum mortality in unplanned birth outside an institution

Antepartum fetal deaths occurred at a similar rate in the travel zones (overall number, 2239, 3.4 per 1000). Nearly all were delivered in EmONC institutions (n = 2208), 19 were born unplanned outside an institution, and 12 in BOC institutions. These births were excluded from further analyses (Figure 1).

Among the remaining 645,063 births, we identified 1586 deaths (Table 2), of which 773 (48.7%) were stillborn. Unplanned birth outside an institution was strongly associated with mortality risk (crude RR, 3.5; 95% CI, 2.5–4.9). Although the absolute mortality rate was higher for preterm births than term births (25.4 per 1000 versus 0.7 per 1000), the relative mortality risk associated with unplanned birth outside an institution was increased for both preterm and term births. There was no difference between the first and last 5 year period (data not shown, $P = .3$).

The stratified analyses shown in Table 2 illustrate higher absolute mortality rates in high-risk groups but similar RRs associated with unplanned birth outside an institution except for single, young, and nulliparous women.

The relative mortality risk was particularly high for births to nulliparous women (RR, 14.9; 95% CI, 8.8–25.1), but also births to parous women had a doubled risk of death if born unplanned outside an institution (RR, 2.2; 95% CI, 1.4–3.4). Few births with severe congenital malformations took place unplanned outside an institution (n = 170, 0.5%), and there were no peripartum deaths. We therefore excluded severe congenital malformations before adjusting for all tabulated risk factors (Table 2). The adjusted relative risk for peripartum mortality in an unplanned birth outside an institution was then 3.9 (95% CI, 2.8–5.3).

Attributable risk

Peripartum deaths were rare and occurred most frequently in institutional preterm births. However, among unplanned births outside an institution, the risk of death attributable to this exposure was high (attributable fraction, 0.7; range, 0.6–0.8) and accounted for 2.1% (95% confidence interval, 1.2–3.0%) of the peripartum mortality in the population.

Mortality in obstetric institutions

Figure 2 shows the relative risk of peripartum death in the different institution categories stratified on parity. After adjustment for socioeconomic factors and maternal and fetal risk factors and using the smallest EmONC institutions as reference, we did not find evidence of different mortality by annual number of births in EmONC institutions (Table 3).

In births with no major congenital malformations, the mortality rate in BOC institutions was lower for parous women

TABLE 2
Peripartum mortality comparing unplanned births outside an institution and births in obstetric institutions, overall and stratified by maternal and fetal risk factors

Variables	Category	Number of births, n = 645,063[a]	Unplanned outside institution, n = 4527, deaths (per 1000)	In obstetric institutions, n = 640,536, deaths (per 1000)	Relative risk (95% CI)
Overall mortality, n (per 1000)[b]			38 (8.4)	1548 (2.4)	3.5 (2.5–4.9)[c]
					3.9 (2.7–5.6)[d]
Gestational age, wks	≥37	600,129	7 (1.7)	429 (0.7)	2.3 (1.1–4.9)
	<37	44,934	31 (100.3)	1119 (25.4)	3.9 (2.8–5.6)
Maternal age, y	<20	15,251	6 (96.8)	56 (3.7)	19.3 (8.6–43.6)
	20–35	520,589	28 (7.8)	1163 (2.2)	3.4 (2.3–4.9)
	>35	109,183	4 (4.7)	329 (3.0)	1.5 (0.6–4.1)
Parity	1 or more	378,687	20 (4.9)	855 (2.3)	2.2 (1.4–3.4)
	0	266,376	18 (39.5)	693 (2.6)	14.4 (9.0–23.2)
Education, y	≥11	497,697	24 (7.3)	1038 (2.1)	3.5 (2.3–5.2)
	<11	148,431	14 (11.2)	510 (3.5)	3.1 (1.8–5.3)
Partner status	Partner	592,153	27 (6.5)	1358 (2.3)	2.7 (1.9–4.0)
	Single	43,598	11 (32.1)	158 (3.6)	8.8 (4.8–16.1)
Ethnicity	Western	585,324	35 (8.6)	1136 (2.3)	3.6 (2.6–5.1)
	Non-Western	59,739	3 (6.8)	212 (3.6)	1.9 (0.6–6.0)
Smoking	Nonsmoker	435,910	15 (5.1)	944 (2.2)	2.4 (1.4–3.9)
	No information[e]	106,533	11 (15.6)	335 (3.2)	4.5 (2.4–8.5)
	Any smoking	102,620	12 (13.4)	269 (2.6)	5.1 (2.9–9.0)
Chronic disease	No	583,274	35 (8.4)	1390 (2.4)	3.4 (2.4–4.8)
	Yes[f]	61,789	3 (7.9)	158 (2.6)	3.1 (0.99–9.7)
Plural	Singleton	621,789	33 (7.4)	1256 (2.0)	3.5 (2.5–5.0)
	Multiple	23,274	5 (87.7)	292 (12.6)	7.1 (3.0–16.5)
Major malformation[g]	No	623,064	38 (8.6)	1313 (2.1)	4.0 (2.9–5.5)
	Yes	21,999	0	235 (10.7)	n.a.
SGA[h]	≥10th percentile	590,418	31 (7.5)	1157 (2.0)	3.8 (2.7–5.4)
	<10th percentile	55,898	7 (19.0)	391 (7.0)	2.3 (1.0–5.2)
Severe maternal morbidity	No	630,105	37 (8.2)	1443 (2.3)	3.5 (2.5–4.9)
	Yes[i]	14,958	1 (20.4)	105 (7.0)	3.0 (0.4–20.7)
Previous CD	No	589,679	37 (8.5)	1380 (2.4)	3.5 (2.5–4.9)
	Yes	55,384	1 (5.9)	168 (3.0)	1.9 (0.3–13.8)
Previous stillbirth[j]	No	552,968	28 (7.6)	1239 (2.3)	3.3 (2.2–4.8)
	Yes	5437	1 (34.5)	41 (7.6)	4.8 (0.7–33.6)

Data are from the Medical Birth Registry of Norway and Statistics Norway, 1999–2009.

CD, cesarean delivery; *CI*, confidence interval; *n.a.*, not applicable; *SGA*, small for gestational age.

[a] Births from 22 weeks' gestational age or birthweight above 500 g. Antepartum fetal deaths and planned home births were excluded; [b] Intrapartum stillbirth and neonatal death, 0–24 hours; [c] Relative risks using institutional births as reference. Estimates were adjusted for clustering by births to the same mother; [d] Adjusted for all the maternal and fetal risk factors listed in Table 2 for births with no major malformations; [e] Women can decline to register information about smoking, and these births were analyzed separately; [f] Asthma, thyroid disease, epilepsy, rheumatoid arthritis, diabetes prior to and in pregnancy, chronic hypertension, epilepsy, chronic renal disease, and cardiac disease; [g] Eurocat definitions of severe malformations (http://www.eurocat-network.eu/content/EUROCAT-Guide-1.4-Section-3.3.pdf); [h] Small for gestational age, birthweight by gestational age classified according to Norwegian standards[16]; [i] Severe maternal morbidity: hemorrhage, >1.5 l, or hemorrhage and blood transfusion, eclampsia, hemolysis, elevated liver enzymes, and low platelet count (HELLP), sepsis, pulmonary embolism, organ failure, placental abruption with disseminated coagulation disorder, hysterectomy, or uterine rupture; [j] Previous stillbirth at gestation age ≥24 weeks; 86,658 births with missing information on this variable were excluded from the stratified analysis.

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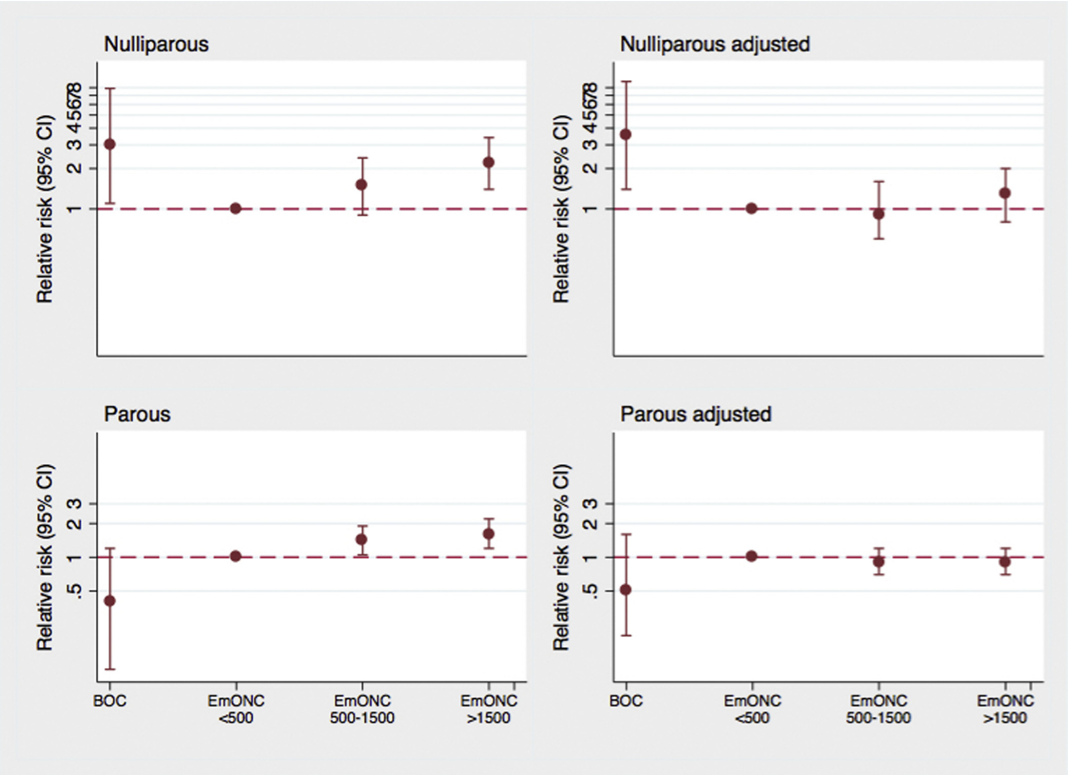
FIGURE 2
Relative risk of peripartum mortality by institution category, stratified on parity



Relative risks were calculated for births with no major malformations and adjusted for socioeconomic factors and medical maternal and fetal risk factors.
CI, confidence interval; *BOC*, basic obstetric care institution; *EmONC*, emergency obstetric and newborn care institution.
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(0.5 per 1000) than nulliparous women (3.6 per 1000), as shown in Figure 2 and Table 3. There was no difference between the first and last 5 year period in births with no major malformations (data not shown, $P > .6$ for nulliparous women and $P > .3$ for parous women).

In births with major malformations, the mortality was lower in the last 5 year period for both nulliparous and parous women (RR, 0.6; 95% CI, 0.5–0.8), these births took place in the EmONC institutions, and there were no difference between the different EmONC categories ($P > .4$). Results of stratified analyses are reported in online Appendix 2. Resident noncitizen women delivered in the largest EmONC institutions (n = 2021, 87%) with a mortality rate of 1.4% (n = 32).

Births at term to healthy women with a singleton pregnancy, no major congenital malformations, cephalic presentation, and normal vaginal delivery has been used to define a low-risk category in the literature.[1,24,25] In our study the mortality for this group ranged from 0.5 per 1000 to 0.6 per 1000 in the EmONC institutions ($P > .3$, data not shown).

Seasonal variations

During the winter season, from October to March, mortality was higher for births at term to parous women living outside the 2 hour zone to all institutions (2.5 per 1000) compared with births in which the mother lived within the 1 hour zone (0.6 per 1000, RR, 3.8; 95% CI, 1.4–10.5). For these births, residence outside the 2 hour travel zone to EmONC institutions was also associated with a seasonal increase in mortality risk (1.6 per 1000 vs 0.6 per 1000, RR, 2.5; 95% CI, 1.2–5.5).

Comment

Principal findings

Unplanned birth outside an institution was associated with the highest peripartum mortality rates both for births to women with risk factors and for births to women usually regarded as low risk.

TABLE 3
Peripartum mortality in obstetric institutions by institution function and volume category, total and stratified by parity

Category	n	Basic obstetric care, n (rate per 1000)	Emergency obstetric care, n (rate per 1000) <500	500–1499	>1500
Total births[a]	640,532	9478	55,161	148,812	427,081
Peripartum deaths, n (per 1000)	1548 (2.4)	10 (1.1)	79 (1.4)	301 (2.0)	1158 (2.6)
Nulliparous births[b]	256,228	1650	20,224	56,137	178,830
Deaths, n (per 1000)	609 (2.4)	6 (3.6)	27 (1.3)	117 (2.0)	543 (2.9)
Relative risk[c]		3.0 (1.1–7.9)	Reference	1.5 (0.9–2.3)	2.2 (1.4–3.4)
Relative risk adjusted[d]		3.5 (1.4–8.9)	Reference	0.9 (0.6–1.6)	1.3 (0.8–2.0)
Parous total births[b]	362,421	7662	33,998	87,917	232,844
Deaths, n (per 1000)	704 (1.9)	4 (0.5)	44 (1.3)	161 (1.8)	495 (2.1)
Relative risk[c]		0.4 (0.1–1.2)	Reference	1.4 (1.0–1.9)	1.6 (1.2 –2.2)
Relative risk adjusted[d]		0.5 (0.2–1.6)	Reference	0.9 (0.7–1.2)	0.9 (0.7–1.2)

Data are from the Medical Birth Registry of Norway and Statistics Norway.

EmONC, emergency obstetric and newborn care.

[a] Births from 22 weeks' gestational age or birthweight >500 g. Planned home births, unplanned birth outside aninstitution, and antepartum fetal deaths were excluded. Institutions were classified according to the provided care: basic obstetric care for normal deliveries or EmONC in which emergency interventions were available. Births in EmONC institutions with volume <500 births was used as reference. Complete stratified analyses are presented in online Supplemental Table 2; [b] Births with no major congenital malformations (Eurocat definitions of major congenital malformations, http://www.eurocat-network.eu/content/EUROCAT-Guide-1.4-Section-3.3.pdf); [c] Relative risks in births with no major malformations; [d] Births with no major congenital malformations, adjusted for all risk factors in Table 2 except previous stillbirth and previous caesarean delivery in births to nulliparous women. All models included clustering by births in the same institution.

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Elimination of unplanned births outside an institution was estimated to reduce the peripartum perinatal mortality in the population by 2.1%. The risk of unplanned birth outside an institution was strongly associated with travel time to the nearest obstetric institution. Few high-risk births in the smallest institution categories and comparable mortality rates in obstetric institutions indicated well-functioning routines for selective referral.

Comparison with other studies

Previous studies have shown an association between reduced availability of institutions and higher neonatal morbidity, thus suggesting an increased risk of neonatal mortality.[26,27] Potential increases in neonatal mortality have also been modeled[28] and reported as a cofinding.[7] By combining traditional epidemiology with new geographic technologies, we were able to use population-based databases over a decade and obtain individual information about travel time and clinical outcomes, thus linking structural determinants and perinatal mortality. We found a clear association between unplanned birth outside an institution and mortality, and the increase in mortality was not confined to preterm birth or vulnerable groups as shown in previous studies.[13,15,29]

Improvement in monitoring and interventions during delivery has been proposed as an explanation for reduced intrapartum and 7 day neonatal mortality in term births during recent decades.[24] However, as much as 30% of the deaths in low-risk births at term occurred intrapartum in Scotland.[24] Our findings add to the evidence that including only neonatal deaths would lead to an underestimation of mortality.

Strengths and limitations

The cohort in this study covered the entire population and was large enough to study a rare outcome in relation to individual travel time. We had data for a range of potential covariates and risk factors and were able to take into account clustering of births to the same mother and in the same institution. Multilevel analyses yielded comparative odds ratios to the relative risks, except for higher odds ratios than the relative risks in smaller, high-risk groups. We thus chose to complete the analyses using generalized linear models and report the relative risks.

The MBRN lacked information on some covariates/risk factors that could be of importance, such as obesity. Although obesity is a significant risk factor for perinatal mortality, it is less likely to be strongly associated with the exposures under study. Similarly, alcohol consumption during pregnancy has been shown to be associated with smoking and older age, not with education or income, and it is not likely to explain the observed differences.[30]

Norway has a clear policy aim to reduce economic barriers to health care in pregnancy. Both primary and specialist health care related to pregnancy and childbirth is free for residents in Norway, and prenatal care is widely attended.[31]

The annual relocation outside the municipality was approximately 5% but could lead to an underestimation of the relative risk. The travel time analyses did not take into account factors such as seasonal variations in driving conditions, but higher perinatal mortality during the winter season suggests potential consequences of reduced accessibility.

The registry linkages provide a larger data set than would have been achievable in a prospective study, but linkages had to be performed retrospectively, and the linkage process as well as the travel zone estimations were complicated and time consuming. Hence, the data collection had to be limited to births up to 2009, and the data set was completed by 2015. The individual travel zone calculations provided individual information using uniform methods. The institutional structure reported in this study is representative for the present annual statistics (http://statistikk.fhi.no/mfr/).

Theoretically, reduced access to specialist health care could influence antepartum stillbirths because of factors such as lower detection of risk pregnancies and less monitoring to assist timely delivery. However, we found no difference antepartum stillbirth rates in the different travel zones, and these births were referred to EmONC institutions. Other risk factors, such as fetal sex, are not associated with travel time and therefore no confounders in our analyses. Differences in available intrapartum care probably explain most of the differences in mortality by place of birth and are a likely mediator in our data.

Lack of acceptability resulting in deliberate avoidance of institutions has not been described as a major risk factor for unplanned birth outside an institution in Europe.[32,33] Few women with risk factors gave birth in BOC institutions and in the lowest volume category of EmONC institutions, indicating that the national guidelines for referral were well implemented. In accordance with recent publications, the mortality was higher in births to nulliparous than to parous women in BOC institutions.[1,7] However, the mortality rate was lower than for unplanned birth outside an institution for this group.

Some of the BOC institutions were based in rural hospitals. The lack of formalized obstetrician-led services disqualified them from classification as EmONC institutions. However, notifications included preterm births, instrumental vaginal births, breech births, and cesarean deliveries. These interventions highlight the importance of training, clinical guidelines, and preparedness to tackle emergency situations also in this setting.

Unanswered questions and future research

We identified and stratified on severe maternal morbidity that may increase the risk of fetal or neonatal death. A thorough assessment of maternal morbidity was beyond the scope of this study. A more comprehensive evaluation of the health system structure should take severe maternal and neonatal morbidity into account.[34] We found that structural determinants have an important impact on perinatal health in high-income countries and also for low-risk births. The results show the importance of skilled birth attendance and warrant attention to negative consequences of reduced access to institutions. ■

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References

1. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. BMJ 2011;343:d7400.

2. Schroeder E, Petrou S, Patel N, et al. Cost effectiveness of alternative planned places of birth in woman at low risk of complications: evidence from the Birthplace in England national prospective cohort study. BMJ 2012;344:e2292.

3. Heller G, Richardson DK, Schnell R, Misselwitz B, Kunzel W, Schmidt S. Are we regionalized enough? Early-neonatal deaths in low-risk births by the size of delivery units in Hesse, Germany 1990–1999. Int J Epidemiol 2002;31:1061-8.

4. Moster D, Lie RT, Markestad T. Relation between size of delivery unit and neonatal death in low risk deliveries: population based study. Arch Dis Child Fetal Neonatal Ed 1999;80:F221-5.

5. Tracy SK, Sullivan E, Dahlen H, Black D, Wang YA, Tracy MB. Does size matter? A population-based study of birth in lower volume maternity hospitals for low risk women. BJOG 2006;113:86-96.

6. Snowden JM, Cheng YW, Kontgis CP, Caughey AB. The association between hospital obstetric volume and perinatal outcomes in California. Am J Obstet Gynecol 2012;207:478.e1-7.

7. Grunebaum A, McCullough LB, Sapra KJ, et al. Early and total neonatal mortality in relation to birth setting in the United States, 2006–2009. Am J Obstet Gynecol 2014;211:390.e1-7.

8. Snowden JM, Tilden EL, Snyder J, Quigley B, Caughey AB, Cheng YW. Planned out-of-hospital birth and birth outcomes. N Engl J Med 2015;373:2642-53.

9. Merlo J, Gerdtham UG, Eckerlund I, et al. Hospital level of care and neonatal mortality in low- and high-risk deliveries: reassessing the question in Sweden by multilevel analysis. Med Care 2005;43:1092-100.

10. Moster D, Lie RT, Markestad T. Neonatal mortality rates in communities with small maternity units compared with those having larger maternity units. BJOG 2001;108:904-9.

11. Blondel B, Drewniak N, Pilkington H, Zeitlin J. Out-of-hospital births and the supply of maternity units in France. Health Place 2011;17:1170-3.

12. Hemminki E, Heino A, Gissler M. Should births be centralised in higher level hospitals? Experiences from regionalised health care in Finland. BJOG 2011;118:1186-95.

13. Pilkington H, Blondel B, Papiernik E, et al. Distribution of maternity units and spatial access to specialised care for women delivering before 32 weeks of gestation in Europe. Health Place 2010;16:531-8.

14. Rayburn WF, Richards ME, Elwell EC. Drive times to hospitals with perinatal care in the United States. Obstet Gynecol 2012;119:611-6.

15. Ravelli AC, Jager KJ, de Groot MH, et al. Travel time from home to hospital and adverse perinatal outcomes in women at term in the Netherlands. BJOG 2011;118:457-65.

16. Engjom H, Morken NH, Norheim O, Klungsoyr K. Availability and access in modern obstetric care: a retrospective population-based study. BJOG 2014;121:290-9.

17. Rasmussen S, Albrechtsen S, Irgens LM, et al. Unexplained antepartum fetal death in Norway, 1985–97: diagnostic validation and some epidemiologic aspects. Acta Obstet Gynecol Scand 2003;82:109-15.

18. World Health Organization, United Nations Population Fund, United Nations Children's Fund, Averting Maternal Death and Disability. Monitoring emergency obstetric care—a handbook. Geneva (Switzerland); 2009. ISBN: 978 92 4 154773 4.
19. Blix E, Huitfeldt AS, Oian P, Straume B, Kumle M. Outcomes of planned home births and planned hospital births in low-risk women in Norway between 1990 and 2007: a retrospective cohort study. Sex Reprod Healthc 2012;3:147-53.
20. Elveg- the electronic road database. 2009. Available at: http://www.kartverket.no/en/data/Open-and-Free-geospatial-data-from-Norway/. Accessed May 5, 2017.
21. Eide GE. Attributable fractions for partitioning risk and evaluating disease prevention: a practical guide. Clin Respir J 2008;2(Suppl 1):92-103.
22. Eide GE, Heuch I. Average attributable fractions: a coherent theory for apportioning excess risk to individual risk factors and subpopulations. Biomed J 2006;48:820-37.
23. Skjaerven R, Gjessing HK, Bakketeig LS. Birthweight by gestational age in Norway. Acta Obstet Gynecol Scand 2000;79:440-9.
24. Pasupathy D, Wood AM, Pell JP, Fleming M, Smith GC. Rates of and factors associated with delivery-related perinatal death among term infants in Scotland. JAMA 2009;302:660-8.
25. de Jonge A, Geerts CC, van der Goes BY, Mol BW, Buitendijk SE, Nijhuis JG. Perinatal mortality and morbidity up to 28 days after birth among 743,070 low-risk planned home and hospital births: a cohort study based on three merged national perinatal databases. BJOG 2015;122:720-8.
26. Combier E, Charreire H, Le Vaillant M, et al. Perinatal health inequalities and accessibility of maternity services in a rural French region: closing maternity units in Burgundy. Health Place 2013;24:225-33.
27. Viisainen K, Gissler M, Hartikainen AL, Hemminki E. Accidental out-of-hospital births in Finland: incidence and geographical distribution 1963—1995. Acta Obstet Gynecol Scand 1999;78:372-8.
28. Poeran J, Borsboom GJ, de Graaf JP, et al. Does centralisation of acute obstetric care reduce intrapartum and first-week mortality? An empirical study of over 1 million births in the Netherlands. Health Policy 2014;117:28-38.
29. Luo ZC, Wilkins R. Degree of rural isolation and birth outcomes. Paediatr Perinat Epidemiol 2008;22:341-9.
30. Alvik A, Heyerdahl S, Haldorsen T, Lindemann R. Alcohol use before and during pregnancy: a population-based study. Acta Obstet Gynecol Scand 2006;85:1292-8.
31. Delvaux T, Buekens P. Disparity in prenatal care in Europe. Study Group on Barriers and Incentives to Prenatal Care in Europe. Eur J Obstet Gynecol Reprod Biol 1999;83:185-90.
32. Pitchforth E, Watson V, Tucker J, et al. Models of intrapartum care and women's trade-offs in remote and rural Scotland: a mixed-methods study. BJOG 2008;115:560-9.
33. Pilkington H, Blondel B, Drewniak N, Zeitlin J. Choice in maternity care: associations with unit supply, geographic accessibility and user characteristics. Int J Health Geogr 2012;11:35.
34. Raven JH, Tolhurst RJ, Tang S, van den Broek N. What is quality in maternal and neonatal health care? Midwifery 2012;28:e676-83.

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APPENDIX 1

Risk of unplanned delivery outside an institution and travel time to the nearest institution

Variables	Category	Total births	Unplanned deliveries outside institution, n, %	Outside institution travel zone >1 h, n, %	Outside institution travel zone >2 h, n, %	Risk ratio (95% CI), 1–2 h vs <1 h	Risk ratio (95% CI), >2 h vs <1 h
Overall		646,898	4546 (0.7)	844/25,494 (3.3)	246/5508 (4.5)	5.9 (5.4–6.4)[a]	8.0 (7.0–9.1)[a]
Gestational age, wks	≥37	600,582	4218 (0.7)	805/23 820 (3.4)	229/5107 (4.5)	6.1 (5.6–6.6)	8.1 (7.1–9.3)
	<37	46,316	320 (0.7)	39/1717 (2.3)	17/407 (4.2)	3.8 (2.7–5.4)	7.0 (4.3–11.3)
Maternal age, y	<20	15,295	86 (0.6)	22/933 (2.4)	12/263 (4.6)	6.6 (4.0–10.9)	12.7 (6.9–23.7)
	20–35	521,941	3590 (0.7)	690/20,462 (3.4)	187/4318 (4.3)	6.2 (5.7–6.7)	8.0 (6.9–9.3)
	>35	109,625	861 (0.8)	132/4099 (3.2)	47/927 (5.1)	4.9 (4.1–6.0)	7.6 (5.7–10.2)
Parity	1 or more	379,749	4076 (1.1)	771/16,780 (4.6)	219/3576 (6.1)	5.4 (4.9–5.8)	7.1 (6.2–8.2)
	0	267,149	462 (0.2)	73/8714 (0.8)	27/1932 (1.4)	5.9 (4.6–7.6)	10.0 (6.8–14.8)
Education, y	≥11	498,143	3286 (0.7)	647/19,601 (3.3)	162/3875 (4.2)	6.3 (5.8–6.9)	8.0 (6.8–9.5)
	<11	148,755	1252 (0.8)	197/5893 (3.3)	84/1633 (5.1)	4.9 (4.1–5.7)	7.5 (6.0–9.4)
Partner status	Partner	593,783	4153 (0.7)	795/23,340 (3.4)	225/4941 (4.6)	6.2 (5.6–6.7)	9.0 (7.9–10.3)
	Single	43,762	344 (0.8)	41/1848 (2.2)	21/487 (4.3)	3.3 (2.3–4.6)	6.6 (4.3–10.3)
Ethnicity	Western	586,902	4099 (0.7)	801/24,372 (3.3)	223/5192 (4.3)	6.0 (5.5–6.5)	7.8 (6.8–9.0)
	Non-Western	59,996	439 (0.7)	43/1122 (3.8)	23/316 (7.3)	6.0 (4.3–8.3)	11.4 (7.5–17.4)
Smoking	Nonsmoker	436,983	2934 (0.7)	585/16,964 (3.5)	132/3246 (4.1)	6.5 (5.9–7.1)	7.6 (6.4–9.1)
	No information	106,928	707 (0.7)	92 (3.0)	40 (4.6)	5.3 (4.2–6.6)	8.2 (6.0–11.2)
	Any smoking	102,987	897 (0.9)	167/5411 (3.1)	74/1389 (5.3)	4.5 (3.8–5.4)	7.8 (6.2–9.9)
Chronic illness	No	584,909	4156 (0.7)	778/22,928 (3.4)	231/4963 (4.7)	6.0 (5.6–6.5)	8.3 (7.2–9.5)
	Yes[b]	61,987	382 (0.6)	66/2567 (2.6)	15/545 (2.8)	4.9 (3.8–6.5)	5.4 (3.1–9.3)
Plural	Singleton	623,408	4479 (0.7)	836/24,651 (3.4)	246/5323 (4.6)	5.9 (5.5–6.4)	8.1 (7.1–9.3)
	Multiple	23,490	59 (0.3)	8/843 (1.0)	0/185	4.2 (1.6–11.2)	NA
Major malformation	No	624,783	4421 (0.7)	822/24,611 (3.3)	243/5357 (4.9)	5.9 (5.5–6.4)	8.7 (7.7–9.9)
	Eurocat[c]	22,115	117 (0.5)	22/885 (2.5)	3/151 (2.7)	5.7 (3.6–9.0)	6.1 (2.3–16.3)
SGA	≥10th percentile	591,419	4162 (0.7)	797/23,573 (3.4)	222/5048 (4.4)	6.1 (5.6–6.6)	8.7 (7.6–9.9)
	<10th percentile	56,675	376 (0.7)	47/1961 (2.4)	24/465 (5.2)	4.1 (3.0–5.7)	9.2 (6.0–14.0)
Previous	No	592,524	4368 (0.7)	819/23,072 (3.6)	241/4962 (4.9)	6.1 (5.6–6.5)	8.3 (7.3–9.5)
CD	Yes	55,593	170 (0.3)	25/2422 (1.0)	5/546 (0.9)	3.9 (2.6–6.0)	3.4 (1.4–8.4)
Previous stillbirth	No	554,536	3687 (0.7)	670/20,860 (3.2)	178/4343 (4.1)	6.0 (5.5–6.5)	7.7 (6.6–8.9)
	Yes[d]	5488	29 (0.5)	5/241 (2.1)	2/21 (3.9)	4.9 (1.9–12.9)	9.2 (2.2–37.6)

Births were at gestational age ≥22 weeks or birthweight ≥500 g. Residence within the 1 hour travel zone to all institutions was used as reference. Data are from Statistics Norway and the Medical Birth Registry of Norway, 1999–2009.

CD, cesarean delivery; *CI*, confidence interval.

[a] Relative risks are adjusted for clustering in the mother; [b] Athma, thyroid disease, rheumatoid artritis, epilepsy, chronic hypertension, chronic cardiac or renal disease, diabetes before or in pregnancy; [c] Eurocat definitions of severe malformations (http://www.eurocat-network.eu/content/EUROCAT-Guide-1.4-Section-3.3.pdf); [d] Previous stillbirth at gestational age ≥24 weeks.

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Peripartum mortality in obstetric institutions, stratified on maternal and fetal risk factors

Variable		Total mortality[a]	Basic obstetric care		Emergency obstetric care, annual volume					
					<500[b]		500–1499		>1500	
Risk factor	Category	n (per 1000)	n (per 1000)	Relative risk (95% CI)	n (per 1000)	Reference	n (per 1000)	Relative risk (95%CI)	n (per 1000)	Relative risk (95% CI)
Gestational age, wks	≥37	429 (0,7)	8 (0.9)	1.2 (0.6–2.4)	38 (0.7)	1	104 (0.7)	1.1 (0.7–1.5)	279 (0.7)	1.0 (0.7–1.3)
	<37	1119 (25.1)	2 (11.2)	0.5 (0.2–1.5)	41 (21.5)	1	197 (19.8)	0.9 (0.7–0.3)	879 (27.0)	1.3 (0.9–1.7)
Maternal age, y	<20	56 (3.7)	1 (4.4)	1.6 (0.2–15.7)	6 (2.8)	1	19 (4.1)	1.5 (0.5–4.2)	30 (3.6)	1.3 (0.4–3.5)
	20–35	1163 (2.2)	9 (1.2)	0.9 (0.5–1.5)	61 (1.4)	1	227 (1.9)	1.4 (0.98–1.9)	866 (2.5)	1.9 (1.3–2.6)
	>35	329 (3.0)	0		12 (1.4)	1	55 (2.4)	1.7 (0.8–3.7)	262 (3.6)	2.5 (1.1–5.5)
Parity	≥1	855 (2.3)	4 (0.5)	0.3 (0.1–0.99)[c]	52 (1.5)	1	184 (2.0)	1.4 (1.04–1.8)	615 (2.5)	1.6 (0.97–2.8)
	0	693 (2.6)	6 (3.6)	2.7 (0.99–7.2)[c]	27 (1.3)	1	117 (2.0)	1.5 (0.9–2.5)	543 (2.9)	2.3 (1.2–4.2)
Education, y	≥11	1038 (2.1)	8 (1.1)	0.8 (0.5–1.6)	55 (1.3)	1	198 (1.7)	1.3 (0.98–1.8)	777 (2.4)	1.9 (1.1–3.2)
	<11	510 (3.5)	2 (0.9)	0.5 (0.06–3.8)	24 (1.9)	1	103 (3.1)	1.7 (1.01–2.8)	381 (3.7)	2.0 (1.06–3.6)
Partner status	Partner	1358 (2.3)	8 (0.9)	0.7 (0.3–1.4)	67 (1.3)	1	260 (1.9)	1.4 (1.04–1.9)	1 023 (2.7)	2.0 (1.2–3.2)
	Single	158 (3.7)	2 (3.9)	1.5 (0.4–5.5)	11 (2.6)	1	36 (3.7)	1.4 (0.7–2.8)	109 (3.1)	1.2 (0.5–2.7)
Western		1336 (2.3)	9 (1.0)	0.7 (0.4–1.3)	70 (1.3)	1	285 (2.0)	1.5 (1.1–2.0)	972 (2.6)	2.0 (1.2–3.2)
Non-Western		212 (3.6)	1 (2.7)	0.9 (0.1–7.4)	9 (3.1)	1	16 (2.1)	0.7 (0.3–1.7)	186 (3.8)	1.1 (0.5–2.7)
Smoking	No	959 (2.2)	3 (0.5)	0.4 (0.1–1.1)	44 (1.2)	1	198 (1.9)	1.6 (1.1–2.2)	699 (2.4)	2.0 (1.3–2.9)
	No information	335 (3.2)	3 (2.4)	1.1 (0.3–3.6)	19 (2.1)	1	29 (2.0)	0.9 (0.5–1.6)	284 (3.5)	1.6 (1.1–2.4)
	Yes	269 (2.6)	4 (2.2)	1.4 (0.6–3.8)	16 (1.5)	1	74 (2.3)	1.6 (0.9–2.7)	175 (3.1)	2.1 (1.2–3.4)
Chronic disease[d]	No	1390 (2.4)	10 (1.1)	0.8 (0.4–1.5)	71 (1.4)	1	272 (2.0)	1.4 (1.03–1.9)	1 047 (2.7)	1.9 (1.4–2.6)
	Yes	158 (2.6)	0		8 (1.5)	1	39 (2.5)	1.6 (0.8–3.3)	111 (2.5)	1.8 (0.9–3.5)
Plural	Singleton	1256 (2.0)	10 (1.1)	0.8 (0.2–1.5)	70 (1.3)	1	255 (1.8)	1.4 (1.08–1.8)	921 (2.2)	1.7 (1.1–2.6)
	Multiple	292 (12.6)	0		9 (10.3)	1	46 (9.0)	0.9 (0.4–2.1)	237 (14.0)	1.4 (0.5–3.5)
Major malformation[e]	No	1313 (2.1)	10 (1.1)	0.8 (0.5–1.5)	68 (1.3)	1	261 (1.8)	1.4 (1.1–1.9)	974 (2.4)	1.9 (1.4–2.4)
	Yes	235 (10.7)	0		11 (7.1)	1	40 (8.4)	1.2 (0.6–2.2)	184 (11.9)	1.7 (0.9–3.2)
SGA	≥10	1157 (2.0)	9 (1.0)	0.9 (0.4–1.6)	60 (1.2)	1	235 (1.7)	1.5 (1.1–1.9)	853 (2.2)	1.9 (1.1–3.1)
	<10	391 (7.0)	1 (2.1)	0.4 (0.08–2.3)	19 (5.0)	1	66 (5.6)	1.1 (0.7–1.9)	305 (8.2)	1.6 (0.95–2.8)
Maternal morbidity[f]	No	1443 (2.3)	10 (1.1)	0.8 (0.4–1.5)	72 (1.3)	1	277 (1.9)	1.4 (1.06–1.9)	1084 (2.6)	1.9 (1.2–3.2)
	Yes	105 (7.0)	0		7 (5.6)	1	24 (6.8)	1.2 (0.6–2.7)	74 (7.1)	1.3 (0.6–2.6)

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(continued)

APPENDIX 2

Peripartum mortality in obstetric institutions, stratified on maternal and fetal risk factors *(continued)*

Variable		Total mortality[a]	Basic obstetric care		Emergency obstetric care, annual volume					
					<500[b]		500–1499		>1500	
Risk factor	Category	n (per 1000)	n (per 1000)	Relative risk (95% CI)	n (per 1000)	Reference	n (per 1000)	Relative risk (95%CI)	n (per 1000)	Relative risk (95% CI)
Previous CD	No	1380 (2.4)	8 (0.9)	0.7 (0.3–1.4)	64 (1.3)	1	275 (2.0)	1.6 (1.1–2.2)	1033 (2.6)	2.0 (1.4–2.9)
	Yes	168 (3.0)	2 (7.0)	2.5 (.3–19.7)	15 (2.7)	1	26 (1.9)	0.7 (0.4–1.3)	125 (3.5)	1.3 (0.7–2.4)
Previous stillbirth[g]	No	1239 (2.3)	8 (1.1)	0.9 (0.5–1.8)	54 (1.2)	1	231 (1.9)	1.6 (1.1–2.3)	946 (2.4)	2.1 (1.4–3.0)
	Yes	41 (7.6)	0		2 (4.7)	1	12 (9.1)	2.0 (0.5–8.4)	27 (7.5)	1.6 (0.4–6.4)

CD, cesarean delivery; *CI*, confidence interval; *EmONC*, emergency obstetric and newborn care; *SGA*, small for gestational age.

[a] Intrapartum death and neonatal death 0–24 hours. Births from 22 weeks' gestation or birthweight >500 g. Planned home births, unplanned births outside an institution and intrauterine fetal death prior to the start of labor were excluded. Data are from the Medical Birth Registry of Norway and Statistics Norway; [b] Births in EmONC institutions annual volume <500 are used as reference; [c] $P = .05$; [d] Asthma, thyroid disease, epilepsy, rheumatoid arthritis, diabetes prior to and in pregnancy, chronic hypertension, epilepsy, chronic renal disease, and cardiac disease; [e] Eurocat definitions of major congenital malformations (http://www.eurocat-network.eu/content/EUROCAT-Guide-1.4-Section-3.3.pdf); [f] Severe maternal morbidity included the following: hemorrhage >1.5 l or hemorrhage and coagulation disorder, blood transfusion or manual removal of placenta, placental abruption with disseminated intravascular coagulation, eclampsia, hemolysis, elevated liver enzymes, and low platelet count (HELLP), pulmonary embolism, sepsis, organ failure, or complications to anesthesia; [g] Previous stillbirth at gestational age ≥24 weeks.

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Risk of eclampsia or HELLP-syndrome by institution availability and place of delivery - a population-based cohort study

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Abstract

Objective: To examine the association between availability of obstetric institutions and risk of eclampsia, HELLP-syndrome, or delivery before 35 gestational weeks in preeclamptic pregnancies

Study design: National population-based retrospective cohort study of deliveries in Norway, 1999-2009 (n= 636738) using data from The Medical Birth Registry of Norway and Statistics Norway. Main exposures were institution availability, measured by travel time to the nearest obstetric institution, and place of delivery.
We computed relative risks (RR) with 95 % confidence intervals (CI) using travel time ≤1 hour as reference. We stratified analyses by parity and preeclampsia, and adjusted for socio-demographic and medical risk factors. Successive deliveries were linked using the national identification number.

Results: We identified 1387 eclampsia/HELLP cases (0.2%) and 3004 (0.5%) deliveries before 35 weeks in preeclamptic pregnancies. Nulliparous women living >1 hour from any obstetric institution had 50% increased risk of eclampsia/HELLP (0.50 versus 0.35%, adjusted RR 1.5; 95 %CI 1.1-1.9). Parous women with preeclampsia and delivery after 35 gestational weeks living >1 hour from emergency institutions had a similar increased risk (1.8% versus 1.0%, adjusted RR 1.8; 1.0-3.1). Women without present/previous preeclampsia constituted all eclampsia/HELLP cases in midwife-led institutions, 39%-50% of cases in emergency institutions, and 78% of cases (135/173) in successive pregnancies. Women with risk factors delivered in the emergency institutions, indicating well-implemented selective referral.

Conclusion: the study shows the importance of available obstetric institutions. Policymakers and clinicians should consider the distribution of potential benefits and burdens when planning and evaluating the obstetric health service structure.

Key words: Eclampsia, emergency obstetric care, health systems, HELLP-syndrome, preterm delivery

Introduction

Severe hypertensive complications in pregnancy remain one of the unsolved challenges in obstetric care globally.(1-3) Known risk factors and causes of preeclampsia include genetic factors, immunologic processes, socio-economic and environmental factors. Prevention strategies range from reduction of obesity and teenage pregnancies to individual approaches with targeted testing, medication and dietary supplements.(3-5) Severity has usually been defined by either systolic blood pressure above 160 mmHg, occurrence of seizures (eclampsia) or by liver-, platelet- and coagulation disturbance in HELLP-syndrome. Eclampsia and HELLP are associated with increased risk of pregnancy-related death and morbidity in infants and mothers, and long-term risk of maternal cardiovascular morbidity and death.(6-12)

While preeclampsia can be identified at antenatal visits, some women experience a sudden and rapid progression of severe disease at delivery.(13) Late care seeking and delays in diagnosis and management in obstetric institutions have been highlighted as risk factors for increased morbidity and mortality among women with preeclampsia.(13, 14) Treatment with magnesium-sulphate reduces the risk of seizures, prevents recurrent seizures, and reduced the incidence of eclampsia.(15-17) Definitive treatment is delivery when the woman has been stabilized, sometimes involving difficult considerations regarding maternal and fetal benefits and risks associated with preterm delivery.

Previous research has aimed at identifying maternal factors predicting risk for progression of preeclampsia to severe morbidity or death.(18) Severe hypertensive complications were the major direct cause of maternal deaths in Norway with 6/14 fatalities in 2005 to 2009 (19). Although the relation between health system factors and progression to severe morbidity has been acknowledged, it has been less studied than health interventions among women at risk.(20) The aim of the present study was to assess the risk of eclampsia, HELLP and delivery before 35 weeks in preeclamptic pregnancies by travel time to obstetric institutions and place of delivery.

Material and methods

Study design, setting and data sources

We designed a retrospective population-based cohort study of all deliveries in Norway from 1999 to 2009 (n= 636 738). Data sources were the Medical Birth Registry of Norway (MBRN) and Statistics Norway (SN). Inclusion criteria were deliveries with gestational age ≥22 completed weeks or birth weight ≥500 grams.

The MBRN has received mandatory standardized notifications of all live births and stillbirths (>16 weeks gestation) since 1967. The registry is routinely linked with the National Registry through the mother's unique national identification number. This linkage provides identification numbers to all live births, ensures complete notification to the MBRN and provides data on all dates of death. Registration of preeclampsia in the MBRN has been validated.(21, 22) Mild preeclampsia at term had lower ascertainment than more severe preeclampsia with preterm delivery and intrauterine growth restriction.(22) Over-reporting of eclampsia to the MBRN was identified following the introduction of a revised notification form in 1999,(13) and confirmed by the MBRN.(23) Consequently, all notifications of eclampsia and HELLP from 1999 onwards were routinely verified through patient records.

In the present study, linkage with the National Registry also provided data on each mother´s registered address. Since 2000, SN has assigned geographic coordinates to addresses, and updates addresses and coordinates yearly. The coverage of individual coordinates was 98% of all addresses in 2000, and 99% in 2010.

Primary clinical outcomes

The primary clinical outcomes were eclampsia, HELLP-syndrome, or delivery before 35 gestational weeks in women with preeclampsia but no eclampsia or HELLP. Preeclampsia was defined as hypertension (≥140/90 mmHg) from 20 gestational weeks and either proteinuria ≥0.3 g/24 hours or urine dipstick protein ≥1+. Eclampsia was defined as generalized seizures in women with preeclampsia or pregnancy hypertension after exclusion of other causes of seizures. HELLP-syndrome was defined by intravascular hemolysis, elevated liver enzymes, and thrombocytopenia (<100 x10^9/L). National guidelines advises referral of deliveries prior to 35 gestational weeks to obstetric institutions with a paediatric ward.(24, 25) National clinical guidelines on management of hypertensive pregnancy complications was first published in 1995 and updated regularly.(26) In cases of severe early preeclampsia, preterm delivery may prevent clinical deterioration and development of eclampsia or

HELLP-syndrome. Accordingly, delivery before 35 weeks in preeclamptic women without eclampsia or HELLP was defined as a clinical outcome.

Place of delivery

Place of delivery was categorized according to institution function and volume. The WHO Handbook for Monitoring Emergency Obstetric and Newborn Care was used to categorize institutions by available treatment options.(27) Basic obstetric care (BOC) institutions provided midwife-led care for normal deliveries and intravenous administration of drugs and basic newborn resuscitation before transfer. Emergency obstetric and newborn care (EmONC) institutions provided intravenous administration of uterotonic drugs, antibiotics and magnesium sulphate, removal of placenta or retained products of conception, newborn resuscitation, assisted vaginal delivery, caesarean section, and blood transfusion. All EmONC institutions had an on-call obstetrician. EmONC institutions were further classified by annual volume of births (<500, 500-1499 and ≥1500). Institution closure or change in level of care was corrected at the start of each calendar year. Included institutions reported ≥10 births annually.

Planned home deliveries and deliveries outside obstetric institutions

Planned home deliveries (0.2%) and unplanned deliveries outside institution (0.7%) were rare, with no primary clinical outcomes, and all were excluded from further analyses (Figure 1).

Travel time

Estimated travel time to the nearest obstetric institution was used to describe institution availability. A travel zone was defined as the geographic area in which all women were estimated to reach the nearest obstetric institution within the given time. Institutions were registered by geographic coordinates, and surrounding travel zones were calculated based on the Norwegian electronic road database.(28) Estimates were based on registered speed limits and standard duration of ferry/boat journeys and represented the minimum time for non-emergency transport. A merged area (polygon) was created for the travel zones (≤1 hour, >1 hour).

The mother´s national identification number was used to link births in the MBRN to her registered address and coordinates (n= 617 654 births, 98.4%). For each delivery, the address was placed in a travel zone. Deliveries to women lacking coordinates were assigned to the travel zone of the majority of mothers in their municipality in the corresponding year (n= 9 601 deliveries, 1.5%). Few deliveries lacked both address coordinates and municipality (n= 389, 0.06%), and these were excluded (Figure 1).

Sibling data

By means of the national identification numbers, we also linked deliveries to the same mother (n= 410 841). 2 459 women (0.6%) lacked identification numbers and were not included. These analyses enabled assessment of how preeclampsia, eclampsia or HELLP in previous pregnancies influenced the primary outcome.

Analyses

The mother/delivery was the observation unit in all analyses. Cross-tables and generalized linear models were used to compute rates and relative risks (RR) with

95% confidence intervals (CI) using travel time ≤1 hour as reference. We stratified by parity and preeclampsia, and adjusted for the socio-demographic and maternal medical risk factors listed in footnotes to Tables 1 and 2 and described in supplementary table 1. When analysing overall risk of severe hypertensive complications, parity was included in the model (0/1+). We used sex-specific birth weight by gestational age z-scores (29) to identify misclassified gestational age (deliveries with z>4). If gestational age was misclassified (n= 19, 0.1%) or only birth weight was recorded, we categorized deliveries as occurring before 35 weeks if birth weight was two standard deviations or more below mean weight at 35 weeks (males <2 020g, females <1 950g, n= 203, 1.2% of deliveries before 35 weeks).(29) We did sensitivity analyses by computing E-values to assess the robustness of the associations to unmeasured or uncontrolled confounders.(30)

Travel zone analyses were performed with the GIS software Arc Info with Network Analyst (Environmental Systems Research Institute Inc. (Esri), California, USA). Statistical analyses were performed with SPSS (IBM SPSS Statistics for Mac, Version 22.0. IBM Corp., New York, USA) and STATA 14 IC (StataCorp LLC, Texas, USA.)

Results

Among 630 255 deliveries, we identified 1 387 (0.22%) women with eclampsia/HELLP and 3 004 (0.48%) deliveries before 35 weeks to women with preeclampsia and no eclampsia/ HELLP. The risk of preeclampsia was 5.6% among nulliparous women (n=14684) and 2.6% among parous women (n=9854). The risk of eclampsia/HELLP in nulliparous women was 0.35%, 0.17 % in women without preeclampsia and 3.5% in women with preeclampsia. In parous women the corresponding risks were lower, 0.13 %, 0.07% and 2.1%, respectively. However, women without preeclampsia accounted for a major proportion of cases among parous (56%) and nulliparous (45%) women.

Travel time to any obstetric institution

Table 1 shows risk of hypertensive complications by travel time to all institutions, overall and stratified by parity and preeclampsia. The risk of eclampsia/HELLP was 30% higher outside the 1-hour zone (adjusted RR 1.3; 1.05-1.7). Socio-demographic and medical risk factors had a similar distribution across travel zones (supplementary table 1). Women with longer travel time were more likely to deliver in the smallest institutions (supplementary table 2).

Among nulliparous women, the risk of eclampsia/HELLP was 0.35%, and travel time >1 hour was associated with a 50% increased risk (adjusted RR 1.5; 1.1-2.0). The risk increase was particularly high in women without preeclampsia (adjusted RR 1.7; 1.2-2.6). Only one case occurred in a BOC institution, and the risk increase associated with long travel time was similar across the different EmONC volume categories (supplementary table 3). Among parous women, travel time was not associated with increased risk of eclampsia/HELLP.

Travel time to EmONC institutions

Table 2 shows severe hypertensive complications by travel time to EmONC institutions. The overall risk increased by 30% outside the 1-hour zone, and the risk increase was similar across the institution volume categories (supplementary table 3). In nulliparous women, travel time >1 hour was associated with a 40% increase in risk of eclampsia/HELLP, while there was no risk increase among parous women.

However, for parous women with preeclampsia and delivery after 35 weeks, the risk of eclampsia/HELLP was almost doubled outside the 1-hour zone (1.8 versus 1.0%, adjusted RR 1.8; 1.01-3.1, data not tabulated).

Delivery prior to 35 weeks in women with preeclampsia and no eclampsia/HELLP

Delivery prior to 35 weeks in women with preeclampsia occurred in 0.6% of nulliparous women outside the 1-hour zone to any institution versus 0.7% within the 1-hour zone (adjusted RR 0.8; 0.6-1.1, Table 1). The corresponding risks in parous women were 0.32% versus 0.34% (adjusted RR 0.9; 0.7-1.2). Similar risks and RR estimates were found for EmONC institutions (Table 2).

Hypertensive complications and place of delivery

Women with preeclampsia who developed eclampsia/HELLP received care in EmONC institutions with >500 births annually (Table 3). All eclampsia/HELLP cases in BOC institutions occurred in women without preeclampsia. In EmONC institutions, 42% of cases delivering after 35 weeks did not have preeclampsia.

Women with preeclampsia who delivered before 35 weeks constituted nearly 20% of all deliveries before 35 weeks. These women delivered in EmONC institutions with more than 500 births annually.

Hypertensive complications in successive pregnancies

Among 260388 women who delivered a first infant in the study period, 138111 had a second and 27787 a third delivery (Figure 2). We defined previous preeclampsia as preeclampsia, eclampsia or HELLP in a previous pregnancy. Among women with previous preeclampsia, there were 38 eclampsia/HELLP cases; 36 (0.5%) at second and 2 (0.4%) at third delivery. 37 deliveries took place in the largest EmONC institution categories.

Among women without previous preeclampsia the risk of eclampsia/HELLP in the second or third pregnancy was 0.1%. These 135 women accounted for all eclampsia/HELLP cases in BOC institutions, 92% (11/12) of cases in EmONC institutions <500/year and a majority of cases in the remaining EmONC categories (89% (40/45) and 74% (83/112) respectively, not tabulated).

Discussion

Principal findings

Nulliparous women living outside the 1-hour travel zone to all obstetric institutions had a 50% increased risk of eclampsia/ HELLP. This risk was also increased in parous women with preeclampsia and travel time >1 hour to EmONC institutions, if delivery occurred after 35 weeks.

All eclampsia/HELLP cases occurring in BOC institutions were women without preeclampsia in the present or previous pregnancies. Although previous preeclampsia was a risk factor for eclampsia/HELLP in later pregnancies, the majority of cases occurred in women without previous preeclampsia.

Deliveries prior to 35 gestational weeks in women with preeclampsia, eclampsia or HELLP took place in EmONC institutions with paediatric services, and all women with previous preeclampsia delivered in EmONC institutions. This indicates adherence to national guidelines for referral.

A strength of this population-based cohort study was estimation of individual travel time to the nearest obstetric institution by using updated address coordinates. Because of the large study population we could study rare clinical outcomes, perform stratified analyses and adjust for a range of potential confounders. In contrast to other studies using hospital discharge data we had verified information about eclampsia and HELLP,(31, 32) and the registration of preeclampsia had been validated. The long observation time enabled analysis of outcomes in successive pregnancies for all women, and was not restricted to women with preeclampsia in the first pregnancy.

The possibility of registry linkage and unique individual travel distance data constituted the major scientific achievement of this study. These linkages and estimations required considerable time before the final dataset was available in 2015. The study was, however, based on extensive national population data and the complete birth population was described, thus avoiding the selection bias often found in previous hospital-based studies. Although 2009 was our most recent year of deliveries, the dataset is representative for the present institutional structure in Norway (http://statistikkbank.fhi.no/mfr/).

Limitations

The study lacked information about some risk factors, such as obesity. However, obesity increases with parity and our results showed the highest increase in risk of eclampsia/HELLP related to travel time in nulliparous women. The socio-demographic and medical risk factors were distributed similarly (supplementary table 1), and adjustment did not change the relative risk associated with longer travel time. Chronic renal disease was rare, did not change the estimates, and was removed from the model. No eclampsia/HELLP cases occurred in the 340 women with systemic lupus erytematosus.(33)

We used sensitivity analyses and calculated E-values to assess the robustness of the observed associations.(30) The E-value for eclampsia/HELLP in nulliparous women with travel time >1 hour was 2.4 (95%CI 1.3-3.4). Similarly the E-value for eclampsia/HELLP in parous women with preeclampsia and delivery after 35 weeks was 3.0 (95% CI 1.1-3.8). Thus, to explain the associations found in the present study, an unmeasured confounder would need to be associated with the both the exposure and the clinical outcome by a risk ratio of at least 2.4 and 3.

Although all eclampsia and HELLP cases notified to the MBRN were verified, we cannot rule out false negative cases. However, underreporting is not likely to be linked to women´s travel time. The model for travel time estimates did not take into account seasonal variations in driving conditions, temporary route changes or harbour waiting times and may have underestimated actual travel time. Travel time categories were used to describe availability of obstetric institutions and were adapted to the Norwegian setting where alternative obstetric institutions rarely would be available within the 1-hour travel zone.

The absolute risk of hypertensive complications varied with gestational age, parity and whether the mother had preeclampsia. Women with medical risk factors delivered in the larger EmONC institutions, and selective referral appeared to be well implemented. A previous US study has reported an association between low hospital obstetric volume and increased risk of postpartum complications, but included non-obstetric institutions and did not address hypertensive complications.(34) By classifying the obstetric institutions according to both function and volume, we were able to discriminate between the emergency services provided and exclude non-obstetric institutions. Emergency obstetric care in Norway has a tiered organisation with increasing subspecialisation following increasing annual volume comparable to other high-income settings.(35, 36) Prenatal care is provided in the community health services and is very well attended.(37) All health care during pregnancy is free of charge, including emergency transport with car- or air-ambulance.(38) Low differences in risk related to travel time among high-risk women may indicate that available and responsive emergency services mitigate differences in outcome for these women. Longer travel time was associated with increased risk in groups with low absolute risk. Our study cannot identify the causal chain of events in these deliveries. However, available obstetric institutions appear to play an important role to reduce the risk.

Prediction models using symptoms and laboratory findings may be helpful in identifying short-term risk of rapid progression to severe morbidity in women with preeclampsia.(39) However, our study calls for caution if prediction of risk is based on preeclampsia alone. Previous studies from the US reported few women with diagnosed preeclampsia among eclampsia cases, and identified delays in recognition of symptoms, care seeking, and diagnosis and treatment.(40, 41) In our study, the proportion of women with eclampsia/HELLP and preeclampsia differed by gestational age, and more than 50% of cases occurring after 35 weeks did not have preeclampsia. Preeclampsia incidence in Norway has been comparable to other high-income settings.(42) Despite potential underreporting of mild preeclampsia at term, our results are comparable to previous reports where 42% of the women had preeclampsia prior to eclampsia.(43) This illustrates potential shortcomings in the "linear" preeclampsia to eclampsia approach.(41)

Similarly, previous preeclampsia was a risk factor for eclampsia/HELLP in the present pregnancy, but the majority of parous women with eclampsia/HELLP did not have previous preeclampsia. Improved monitoring of women with preeclampsia and timely delivery may reduce the risk of complications in pregnancies with preeclampsia.(17) The delivery rate before 35 weeks in nulliparous women with preeclampsia was slightly lower outside the 1-hour travel zone, concomitant higher risk of eclampsia/ HELLP may indicate barriers to adequate and timely health services in rural areas. Similarly, parous women with preeclampsia who delivered after 35 weeks had a low absolute risk of eclampsia/HELLP, but the risk was higher outside the 1-hour travel zone to EmONC institutions. When counselling these women, clinicians need to discuss potential benefits and disadvantages of planned early delivery or closer monitoring.(44)

In conclusion, the study shows the importance of available obstetric institutions also in a high-income country. Policymakers need to consider the distribution of potential benefits and burdens when planning and evaluating the obstetric health service structure.

HME, KK, NHM, OFN and EH designed the study. EH had access to the SN address coordinates and performed the travel time analyses. HME and KK had full access to the final, linked dataset and performed the statistical analyses. All authors contributed to interpretation and communication of the results and approved the final manuscript. The authors thank Arild Osen at the MBRN for assistance with the registry linkages, Rolv Skjærven at the University of Bergen for his contribution to the sibling analyses, and Bjørn Thorsdalen at Statistics Norway/The Norwegian Institute of Public Health for his contribution to planning the travel time analyses.

Ethics approval

The study was approved by the Regional Medical Ethical Committee for Western Norway (REK-VEST 2010/3243) and was exempted from the principle of individual consent.

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All authors declare no conflict of interest.

No dataset available for sharing.

References

1. Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987-2004. Am J Hypertens. 2008;21(5):521-6. doi:10.1038/ajh.2008.20
2. Klungsoyr K, Morken NH, Irgens L, Vollset SE, Skjaerven R. Secular trends in the epidemiology of pre-eclampsia throughout 40 years in Norway: prevalence, risk factors and perinatal survival. Paediatr Perinat Epidemiol. 2012;26(3):190-8. doi:10.1111/j.1365-3016.2012.01260.x
3. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet. 2010;376(9741):631-44. doi:10.1016/S0140-6736(10)60279-6
4. American College of O, Gynecologists, Task Force on Hypertension in P. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol. 2013;122(5):1122-31. doi:10.1097/01.AOG.0000437382.03963.88
5. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. Lancet. 2016;387(10022):999-1011. doi:10.1016/S0140-6736(15)00070-7
6. Skjaerven R, Wilcox AJ, Klungsoyr K, et al. Cardiovascular mortality after pre-eclampsia in one child mothers: prospective, population based cohort study. BMJ. 2012;345:e7677. doi:10.1136/bmj.e7677
7. Andersgaard AB, Herbst A, Johansen M, Borgstrom A, Bille AG, Oian P. Follow-up interviews after eclampsia. Gynecol Obstet Invest. 2009;67(1):49-52. doi:000161569 [pii]
10.1159/000161569
8. Andersgaard AB, Acharya G, Mathiesen EB, Johnsen SH, Straume B, Oian P. Recurrence and long-term maternal health risks of hypertensive disorders of pregnancy: a population-based study. Am J Obstet Gynecol. 2012;206(2):143 e1-8. doi:10.1016/j.ajog.2011.09.032
9. Creanga AA, Berg CJ, Syverson C, Seed K, Bruce FC, Callaghan WM. Pregnancy-related mortality in the United States, 2006-2010. Obstet Gynecol. 2015;125(1):5-12. doi:10.1097/AOG.0000000000000564
10. Callaghan WM, Creanga AA, Kuklina EV. Severe Maternal Morbidity Among Delivery and Postpartum Hospitalizations in the United States. Obstet Gynecol. 2012. doi:10.1097/AOG.0b013e31826d60c5
11. Kuklina EV, Ayala C, Callaghan WM. Hypertensive disorders and severe obstetric morbidity in the United States. Obstet Gynecol. 2009;113(6):1299-306. doi:10.1097/AOG.0b013e3181a45b25
00006250-200906000-00016 [pii]
12. Paauw ND, Luijken K, Franx A, Verhaar MC, Lely AT. Long-term renal and cardiovascular risk after preeclampsia: towards screening and prevention. Clin Sci (Lond). 2016;130(4):239-46. doi:10.1042/CS20150567
13. Andersgaard AB, Herbst A, Johansen M, et al. Eclampsia in Scandinavia: incidence, substandard care, and potentially preventable cases. Acta Obstet Gynecol Scand. 2006;85(8):929-36. doi:748296053 [pii]
10.1080/00016340600607149
14. van Dillen J, Mesman JA, Zwart JJ, Bloemenkamp KW, van Roosmalen J. Introducing maternal morbidity audit in the Netherlands. BJOG : an international journal of obstetrics and gynaecology. 2010;117(4):416-21. doi:10.1111/j.1471-0528.2009.02480.x
15. Jaatinen N, Ekholm E. Eclampsia in Finland; 2006 to 2010. Acta Obstet Gynecol Scand. 2016;95(7):787-92. doi:10.1111/aogs.12882

16. Altman D, Carroli G, Duley L, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet. 2002;359(9321):1877-90.
17. Knight M, Ukoss. Eclampsia in the United Kingdom 2005. BJOG. 2007;114(9):1072-8. doi:10.1111/j.1471-0528.2007.01423.x
18. Kayem G, Kurinczuk J, Lewis G, Golightly S, Brocklehurst P, Knight M. Risk factors for progression from severe maternal morbidity to death: a national cohort study. PLoS One. 2011;6(12):e29077. doi:10.1371/journal.pone.0029077
19. Vangen S, Ellingsen L, Andersgaard AB, et al. Maternal deaths in Norway 2005-2009. Tidsskr Nor Laegeforen. 2014;134(8):836-9. doi:10.4045/tidsskr.13.0203
20. Geller SE, Rosenberg D, Cox SM, et al. The continuum of maternal morbidity and mortality: factors associated with severity. Am J Obstet Gynecol. 2004;191(3):939-44. doi:10.1016/j.ajog.2004.05.099
21. Thomsen LC, Klungsoyr K, Roten LT, et al. Validity of the diagnosis of pre-eclampsia in the Medical Birth Registry of Norway. Acta Obstet Gynecol Scand. 2013;92(8):943-50. doi:10.1111/aogs.12159
22. Klungsoyr K, Harmon QE, Skard LB, et al. Validity of pre-eclampsia registration in the medical birth registry of norway for women participating in the norwegian mother and child cohort study, 1999-2010. Paediatr Perinat Epidemiol. 2014;28(5):362-71. doi:10.1111/ppe.12138
23. Klungsøyr K. Validation of eclampsia notifications to the Medical Birth Registry of Norway 2000-2006: The Norwegian Institute of Public Health, Norway TMBRo;2009.
24. Helsetilsynet. Faglige krav til fødeinstitusjoner1997.
25. Helsedirektoratet. Kvalitetskrav for fødeinstitusjoner. Oslo: The Norwegian Directorate of Health2011.
26. Guidelines for obstetrics: The Norwegian Society for Obstetrics and Gynecology, The Norwegian Medical Association; 2008. Available from: http://legeforeningen.no/Fagmed/Norsk-gynekologisk-forening/Veiledere/veileder-i-fodselshjelp-2008/.
27. WHO, UNFPA, UNICEF, AMDD. Monitoring emergency obstetric care- a handbook. Geneva2009.
28. Elveg- the electronic road database. The Norwegian Mapping Authority. 2009. http://www.kartverket.no/en/data/Open-and-Free-geospatial-data-from-Norway/. June 2012 to February 2015.
29. Skjaerven R, Gjessing HK, Bakketeig LS. Birthweight by gestational age in Norway. Acta Obstet Gynecol Scand. 2000;79(6):440-9.
30. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. Ann Intern Med. 2017;167(4):268-74. doi:10.7326/M16-2607
31. Sigakis MJ, Leffert LR, Mirzakhani H, et al. The Validity of Discharge Billing Codes Reflecting Severe Maternal Morbidity. Anesth Analg. 2016;123(3):731-8. doi:10.1213/ANE.0000000000001436
32. Geller SE, Ahmed S, Brown ML, Cox SM, Rosenberg D, Kilpatrick SJ. International Classification of Diseases-9th revision coding for preeclampsia: how accurate is it? Am J Obstet Gynecol. 2004;190(6):1629-33; discussion 33-4. doi:10.1016/j.ajog.2004.03.061
33. Wallenius M, Salvesen KA, Daltveit AK, Skomsvoll JF. Systemic lupus erythematosus and outcomes in first and subsequent births based on data from a national birth registry. Arthritis Care Res (Hoboken). 2014;66(11):1718-24. doi:10.1002/acr.22373

34. Kyser KL, Lu X, Santillan DA, et al. The association between hospital obstetrical volume and maternal postpartum complications. Am J Obstet Gynecol. 2012;207(1):42 e1-17. doi:S0002-9378(12)00508-X [pii]
10.1016/j.ajog.2012.05.010
35. American College of O, Gynecologists, Society for Maternal-Fetal M, et al. Levels of maternal care. Am J Obstet Gynecol. 2015;212(3):259-71.
doi:10.1016/j.ajog.2014.12.030
36. Janakiraman V, Lazar J, Joynt KE, Jha AK. Hospital volume, provider volume, and complications after childbirth in U.S. hospitals. Obstet Gynecol. 2011;118(3):521-7.
doi:10.1097/AOG.0b013e31822a65e4
37. Delvaux T, Buekens P. Disparity in prenatal care in Europe. Study group on barriers and incentives to prenatal care in Europe. Eur J Obstet Gynecol Reprod Biol. 1999;83(2):185-90.
38. White paper on emergency response services outside hospitals "Først og fremst", (2015).
39. von Dadelszen P, Payne B, Li J, et al. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. Lancet. 2011;377(9761):219-27. doi:S0140-6736(10)61351-7 [pii]
10.1016/S0140-6736(10)61351-7
40. Chames MC, Livingston JC, Ivester TS, Barton JR, Sibai BM. Late postpartum eclampsia: a preventable disease? Am J Obstet Gynecol. 2002;186(6):1174-7.
41. Katz VL, Farmer R, Kuller JA. Preeclampsia into eclampsia: toward a new paradigm. Am J Obstet Gynecol. 2000;182(6):1389-96. doi:10.1067/mob.2000.106178
42. Thornton C, Dahlen H, Korda A, Hennessy A. The incidence of preeclampsia and eclampsia and associated maternal mortality in Australia from population-linked datasets: 2000-2008. Am J Obstet Gynecol. 2013;208(6):476 e1-5.
doi:10.1016/j.ajog.2013.02.042
43. Schaap TP, Knight M, Zwart JJ, et al. Eclampsia, a comparison within the International Network of Obstetric Survey Systems. BJOG. 2014;121(12):1521-8.
doi:10.1111/1471-0528.12712
44. Cluver C, Novikova N, Koopmans CM, West HM. Planned early delivery versus expectant management for hypertensive disorders from 34 weeks gestation to term. Cochrane Database Syst Rev. 2017;1:CD009273.
doi:10.1002/14651858.CD009273.pub2

Figure legends

Figure 1. Study population flow chart.

Figure 2. Successive deliveries for women who had a first delivery in the study period. Eclampsia or HELLP-syndrome, and delivery before 35 weeks in pregnancies with preeclampsia but no eclampsia or HELLP, by preeclampsia in first pregnancy or previous delivery with preeclampsia, eclampsia, or HELLP. Norway 1999-2009. Data from the Medical Birth Registry of Norway.

Table 1. Travel time to any obstetric institution and severe hypertensive complications, overall and stratified by parity and preeclampsia. Norway, 1999-2009.

	Total N (%)	<1 hour N (%)	≥ 1hour N (%)	RR ≥1 hour (95% CI)[a]	RR adjusted (95% CI)[b]
All deliveries	630 255	600 872	29 364		
Eclampsia/HELLP (E/H) total	1 387 (0.22)	1 309 (0.22)	78 (0.27)	1.2 (0.97-1.5)	1.3 (1.05-1.7)
Delivery <35 weeks and preeclampsia (PE)	3004 (0.48)	2 887 (0.48)	117 (0.40)	0.9 (0.7 -1.0)	0.9 (0.7 -1.05)
Nulliparous					
Deliveries	261 310	250 932	10 378		
Eclampsia/HELLP total	918 (0.35)	866 (0.35)	52 (0.50)	1.5 (1.1-1.9)	1.5 (1.1-2.0)
E/H and PE	510 (3.5)	484 (3.45)	26 (3.93)	1.1 (0.8-1.7)	1.2 (0.8-1.7)
E/H and no PE	408 (0.17)	382 (0.16)	26 (0.26)	1.7 (1.2-2.5)	1.7 (1.1-2.6)
Delivery <35 weeks and PE	1 763 (0.68)	1 706 (0.68)	57 (0.55)	0.8 (0.6-1.05)	0.8 (0.6-1.07)
Parous					
Deliveries	368 945	349 940	19 005		
Eclampsia/HELLP total	469 (0.13)	443 (0.13)	26 (0.14)	1.1 (0.7 -1.6)	1.1 (0.7 -1.6)
E/H and PE	207 (2.1)	191 (2.06)	16 (2.8)	1.4 (0.8-2.3)	1.4 (0.8-2.3)
E/H and no PE	262 (0.07)	252 (0.07)	10 (0.05)	0.7 (0.4-1.3)	0.7 (0.4-1.4)
Delivery <35 weeks and PE	1 241 (0.34)	1 181 (0.34)	60 (0.32)	0.9 (0.7 -1.2)	0.9 (0.7 -1.2)

[a] Relative risks using travel time <1 hour as reference.
[b] Relative risk adjusted for maternal age (<20 years, 20-34 (reference), 35+), partner status (living with partner/single), maternal education (<11 years/ 11years or more), chronic hypertension (yes/no), diabetes (yes/no), smoking (yes/no info/no), and time period (1999-2004/2005-2009).

Data from the Medical Birth Registry of Norway and Statistics Norway

Table 2. Travel time to the nearest EmONC institution and severe hypertensive complications, overall and stratified by parity and preeclampsia. Norway, 1999-2009.

	Total (%)	<1 hour N (%)	≥1hour N (%)	RR (95% CI) ≥1 hour crude[a]	RR (95% CI) ≥ 1 hour adjusted[b]
All deliveries	630 255	577 608	52 647		
Eclampsia/HELLP (E/H)	1 387 (0.22)	1 250 (0.22)	137 (0.26)	1.2 (1.01-1.4)	1.3 (1.1-1.6)
Delivery <35 weeks and preeclampsia (PE)	3 004 (17.8)	2 789 (0.48)	215 (0.41)	0.9 (0.8-1.0)	0.9 (0.8-1.0)
		Nulliparous			
Deliveries	261 310	242 515	18 795		
Eclampsia/HELLP	918 (0.35)	833 (0.35)	85 (0.45)	1.3 (1.05-1.6)	1.4 (1.1-1.7)
E/H and PE	510 (3.47)	467 (3.4)	43 (3.8)	1.1 (0.8-1.5)	1.1 (0.8-1.5)
E/H and no PE	408 (0.17)	366 (0.16)	42 (0.24)	1.5 (1.1-2.1)	1.6 (1.1-2.2)
Delivery <35 weeks and PE	1 763 (0.68)	1 656 (0.68)	107 (0.57)	0.8 (0.7-1.0)	0.85 (0.7-1.04)
		Parous			
Deliveries	368 945	335 093	33 852		
Eclampsia/HELLP	469 (0.13)	417 (0.12)	52 (0.15)	1.23 (0.9-1.6)	1.26 (0.9-1.7)
EH and PE	207 (2.1)	181 (2.03)	26 (2.7)	1.32 (0.9-2.0)	1.37 (0.9-2.1)
EH and no PE	262 (0.07)	236 (0.07)	26 (0.08)	1.06 (0.7-1.6)	1.1 (0.7-1.7)
Delivery < 35 weeks and PE	1 241 (0.3)	1 133 (0.34)	108 (0.32)	0.94 (0.8-1.1)	0.95 (0.8-1.2)

[a] Relative risks using travel time <1 hour as reference.

[b] Relative risk adjusted for maternal age (<20 years, 20-34 (reference), 35+), partner status (living with partner/single), maternal education (<11 years/ 11years or more), chronic hypertension (yes/no), diabetes (yes/no), smoking (yes/no info/no), and time period (1999-2004/2005-2009).

Data from the Medical Birth Registry of Norway and Statistics Norway

Table 3. Hypertensive complications by place of delivery and preeclampsia, total and stratified by 35 weeks gestational age. Norway, 1999-2009.

	Pre-eclampsia No/Yes	Total N (%)	BOC N (%)	EmONC <500 N (%)	EmONC 500-1499 N (%)	EmONC ≥ 1500 N (%)
Deliveries		630 255	9 474	54 844	146 528	419 409
Eclampsia /HELLP		1 387 (0.22)	7 (0.07)	68 (0.12)	381 (0.26)	931 (0.22)
Delivery <35 weeks and PE		3004 (0.48)	0	20 (0.04)	578 (0.39)	2 406 (0.6)
≥ 35 weeks		612 986	9 438	54 479	142 929	406 140
≥35 and PE		20 793 (3.4)	50 (0.5)	1 708 (3.1)	4 958 (3.5)	14 077 (3.5)
Eclampsia/ HELLP		886 (0.14)	7 (0.07)	67 (0.12)	252 (0.18)	560 (0.14)
	No (%)[a]	517 (58.4) [a]	7	26 (38.8) [a]	165 (65.5) [a]	319 (57.0) [a]
	Yes (%)[a]	369 (41.6) [a]	0	41 (61.2) [a]	87 (34.5) [a]	241 (43.0) [a]
<35 weeks		17 269	36	365	3 599	13 269
<35 weeks and PE		3 004 (17.6)	0	20 (5.5)	578 (16.4)	2 406 (18.5)
Eclampsia or HELLP		501 (2.9)	0	1 (0.3)	129 (3.6)	371 (2.8)
	No (%)[a]	153 (30.5) [a]	0	1 (0.3) [a]	50 (38.8) [a]	102 (27.5) [a]
	Yes (%)[a]	348 (69.4) [a]	0	0	79 (61.2) [a]	269 (72.5) [a]

[a] percentage of eclampsia and HELLP cases with or without preeclampsia

Data from the Medical Birth Registry of Norway

Online supplementary 1. Socio-demographic variables, maternal medical risk factors and travel time to the nearest obstetric institution.
Deliveries in obstetric institutions, Norway 1999 to 2009.

		All institutions		**EmONC institutions**	
Covariates	category	Travel time <1 hour n (%)	Travel time ≥1 hour n (%)	Travel time < 1 hour n (%)	Travel time ≥1 hour n (%)
Maternal age	mean +/- sd	29.5 +/-5.1	28.9 +/-5.4	29.5 +/-5.1	29.0 +/- 5.4
	<20	13 942 (2.3)	1 154 (3.9)	13 023 (2.3)	2 073 (3.9)
	20-34	485 692 (80.8)	23 492 (80.0)	467 224 (80.9)	41 960 (79.7)
	≥35	101 204 (16.8)	4 737 (16.1)	97 328 (16.9)	8 613 (16.4)
Education years	≥11	462 926 (77.0)	22 249 (75.7)	445 183 (77.1)	39 992 (76.0)
	<11	132 946 (23.0)	7 134 (24.3)	132 475 (22.9)	12 655 (24.0)
Smoking	no	406 602 (67.7)	19 128 (65.1)	391 244 (67.7)	34 486 (65.5)
	no info[a]	100 381 (16.7)	3 796 (12.9)	97 183 (16.8)	6 994 (13.3)
	yes	93 889 (15.6)	6 459 (22.0)	89 181 (15.4)	11 167 (21.2)
Partner status	partner	551 517 (93.1)	26 766 (92.3)	530 100 (93.2)	48 183 (92.6)
	single	40 594 (6.9)	2 246 (7.7)	39 009 (6.9)	3 831 (7.4)
Diabetes[b]	no	590 447 (98.3)	28 882 (98.3)	567 562 (98.3)	51 767 (98.3)
	yes	10 425 (1.7)	501 (1.7)	10 046 (1.7)	880 (1.7)
Chronic hypertension	no	597 582 (99.5)	29 152 (99.2)	574 491 (99.5)	52 243 (99.2)
	yes	3 290 (0.6)	231 (0.8)	3 117 (0.5)	404 (0.8)
Gestational age at delivery	≥35 weeks	584 366 (97.3)	28 620 (97.4)	561 714 (97.3)	51 272 (97.4)
	<35 weeks	16 506 (2.8)	763 (2.6)	15 894 (2.8)	1 375 (2.6)
Etnicity	Western	543 495 (90.5)	28 019 (95.4)	521 351 (90.3)	50 163 (95.3)
	Non-Western	57 377 (9.6)	1 364 (4.6)	56 257 (9.7)	2 484 (4.7)

[a] Women can opt-out from registration of information about smoking.
[b] Insulin dependent diabetes or non-insulin dependent diabetes prior to pregnancy, and gestational diabetes.

Data from the Medical Birth Registry of Norway and Statistics Norway.

Online supplementary 2. Travel time to all obstetric institutions and the nearest emergency obstetric and newborn care (EmONC) institution by place of delivery. Norway 1999-2009.

	Travel time (hour)	Total N (%)	BOC N (%)	EmONC <500 N (%)	EmONC 500-1499 N (%)	EmONC ≥ 1500 N (%)
Total Deliveries[a]		630 255	9474	54 884	146 528	419 409
All[b]	≤1	600 872(95.3)	8 627 (91.1)	45 834 (83.6)	130 546 (91.2)	412 865 (98.4)
institutions	1-2	24 217 (3.8)	785 (8.3)	6 185 (11.3)	11 169 (7.6)	6 078 (1.5)
	>2	5 166 (0.8)	62 (0.7)	2 825 (5.2)	1 813 (1.2)	466 (0.1)
EmONC[c]	≤1	577 608 (91.7)	1 184 (12.5)	42 973 (78.4)	124 982 (85.3)	408 469(97.4)
institutions	1-2	38 438 (6.1)	5 142 (54.3)	8 026 (14.6)	16600 (11.3)	8 670 (2.1)
	>2	14 209 (2.3)	3 148 (33.2)	3 845 (7.0)	4 946 (3.4)	2 270 (0.5)

[a]All deliveries at gestational week 22 to 45. Planned home deliveries, unplanned deliveries outside institution, and deliveries lacking travel zone information were excluded (n=6 160)

[b] Travel time to the nearest obstetric institution of any category

[c] Travel time to the nearest EmONC institution.

Data from the Medical Birth Registry of Norway and Statistics Norway

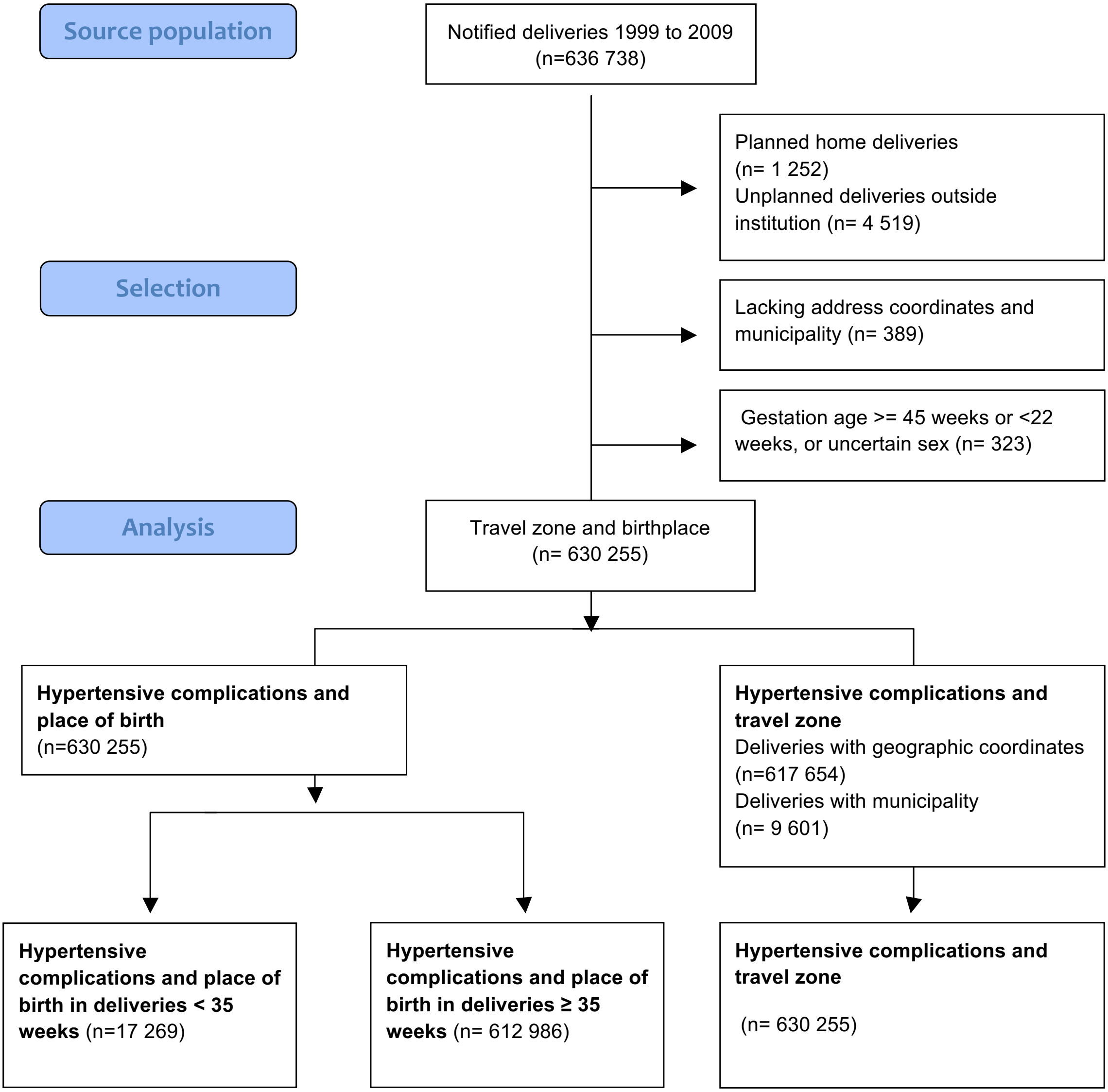
Online supplementary 3. Risk of eclampsia or HELLP by travel time to obstetric institutions, stratified by parity and EmONC volume category.
Norway 1999-2009

Institution Volume category	Deliveries	Eclampsia HELLP N total (risk %)	Eclampsia HELLP travel time ≥ 1 hour to all institutions N (risk %)	Relative risk crude	Relative risk adjusted[a]	Eclampsia HELLP travel time ≥1 hour to EmONC institutions N (risk %)	Relative risk crude	Relative risk adjusted[a]
Nulliparous								
EmONC <500	20 126	43 (0.21)	9 (0.29)	1.4 (0.7-3.0)	1.3 (0.6-2.8)	12 (0.27)	1.4 (0.7-3.0)	1.3 (0.4-2.5)
EmONC 500-1499	57 285	245 (0.43)	29 (0.63)	1. 5 (1.1-2.3)	1.6 (1.04-2.3)	50 (0.59)	1.5 (1.1-2.0)	1.5 (1.1-2.0)
EmONC ≥1500	182 217	629 (0.35)	14 (0.56)	1.6 (0.97-2.8)	1.7 (0.98-2.8)	22 (0.50)	1.5 (0.95-2.2)	1.5 (0.97-2.3)
Parous								
EmONC <500	34 718	25 (0.07)	7 (0.12)	1.9 (0.8-4.6)	1.6 (0.6-4.1)	9 (0.12)	2.1 (0.9-4.7)	1.8 (0.8-4.2)
EmONC 500-1499	89 243	136 (0.15)	10 (0.12)	0.8 (0.4-1.5)	0.8 (0.4-1.5)	24 (0.18)	1.2 (0.8-1.9)	1.2 (0.8-1.9)
EmONC ≥1500	237 192	302 (0.13)	9 (0.22)	1.8 (0.9-3.4)	1.6 (0.9-2.8)	13 (0.20)	1.6 (0.9-2.8)	1.6 (0.9-2.8)

[a] Relative risk adjusted for maternal age, eduation level, partner status, chronic hypertension, diabetes, smoking, time period

Data from the Medical Birth Registry of Norway and Statistics Norway.

Study population Flow Diagram



Adapted from http://www.consort-statement.org/consort-statement/flow-diagram

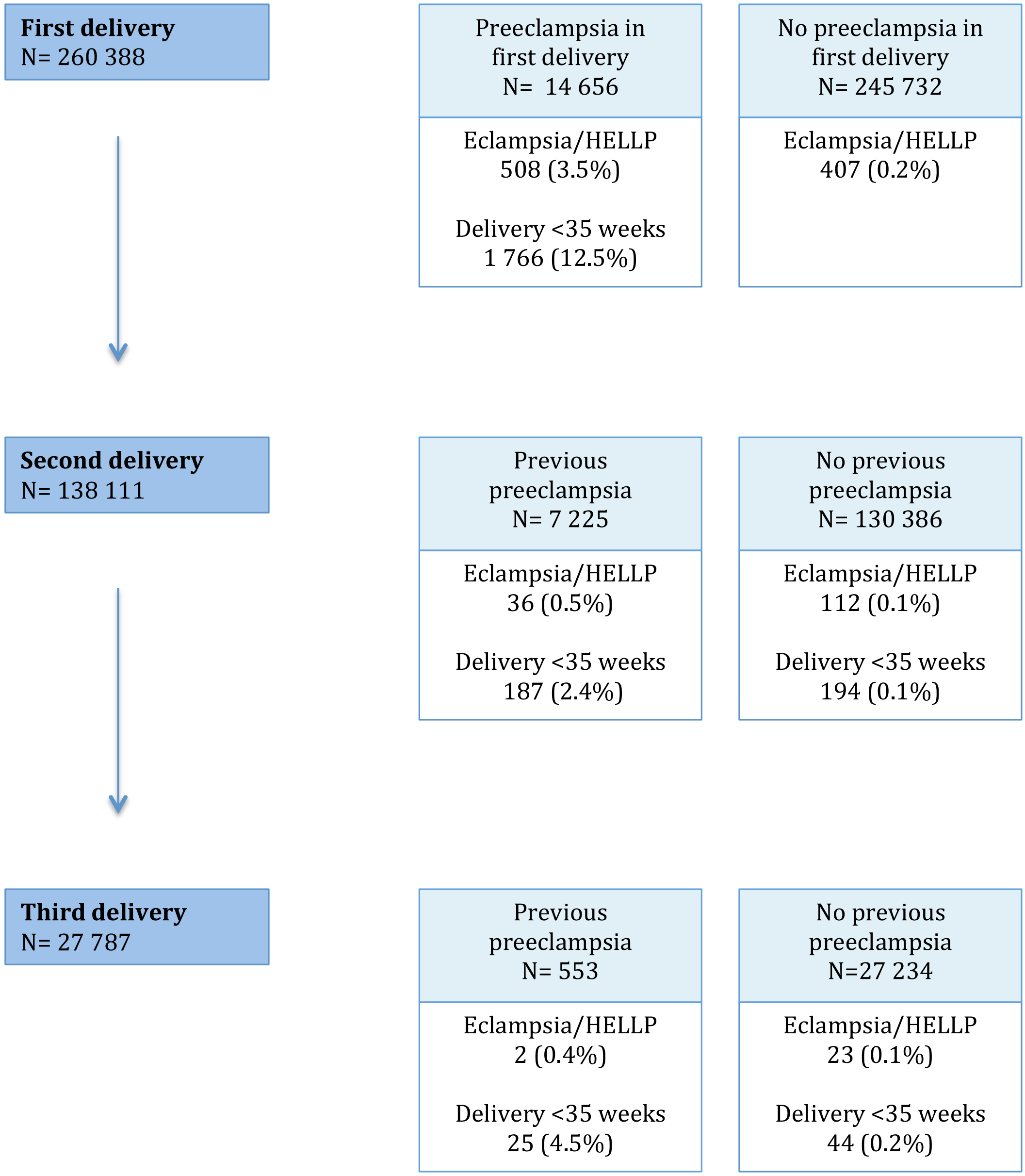


Figure 2. Successive deliveries for women who had a first delivery in the study period. Eclampsia or HELLP-syndrome, and delivery before 35 weeks in pregnancies with preeclampsia but no eclampsia or HELLP, by preeclampsia in first pregnancy or previous delivery with preeclampsia, eclampsia or HELLP. Norway 1999-2009.
Data from the Medical Birth Registry of Norway.

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