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PATIENT SAFETY IN MATERNITY HOSPITALS IN FINLAND

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ACADEMIC DISSERTATION

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ABSTRACT

This study investigated the influence of delivery unit size and physician on-call arrangements on the outcomes of low-risk deliveries and evaluated the impact of time and day of birth on neonatal asphyxia and intrapartum and early neonatal mortality. Furthermore, the effect of increased hospital volume on maternal and perinatal outcome in a high-volume delivery unit was examined. Finally, by demonstrating the rate and causes of pregnancy-associated mortality the study provides information for all segments of the health care system to better respond to the medical needs of pregnant women.

The study of hospital volume and physician on-call arrangements (n=267 066) was based on Medical Birth Register data of hospital births in Finland in 2005–2009. The exclusion criteria were antepartum stillbirth, birthweight <2500 g, multiple pregnancy, and newborn with major congenital anomalies or birth defects. Odds ratios adjusted (AOR) for maternal age and parity demonstrated the effect of unit size and physician on-call arrangements on intrapartum and early neonatal mortality, neonatal asphyxia, newborn's transfer to special care nursery (SCN) or neonatal intensive care unit (NICU), and newborn's prolonged hospitalization.

In the study of influence of time of birth on perinatal outcomes (n=263 901), risk ratios adjusted (ARR) for maternal age and parity during office hours and outside office hours demonstrated the influence of time of birth on neonatal asphyxia and intrapartum and early neonatal mortality in different volume maternity units and with different physician on-call arrangements. The study was based on Medical Birth Register data of hospital births in Finland in 2005–2009. The exclusion criteria were antepartum stillbirth, gestational age

<37 weeks, multiple pregnancy, and newborn with major congenital anomalies or birth defects.

In the study of the effect of increased obstetric volume in a high-volume unit, the study hospital was Kätilöopisto Maternity Hospital in Helsinki, Finland. The number of deliveries temporarily increased significantly in Kätilöopisto Maternity Hospital due a construction project (began in May 2013) in Women´s Hospital, Helsinki, Finland. Thus, two different periods were created: 2011–2012 and 2014–2015. Population-based analysis of simultaneous variations in the outcome measures in the Helsinki region included all three Helsinki University Maternity Hospitals (Kätilöopisto Maternity Hospital, Jorvi Hospital, and Women´s Hospital). The study hospital had singleton hospital deliveries numbering 11 237 during the first period and 15 637 during the second period. The corresponding figures provided by the population-based analysis were 28 950 and 27 979.

To investigate the effect of the volume change, we compared AORs [adjusted for maternal age, parity, and pre-pregnancy body mass index (BMI)] of the following outcomes in different periods: induced delivery, Caesarean section, instrumental delivery, third- and fourth-degree perineal tear, and neonatal asphyxia, and the following neonatal outcomes: transfer to SCN or NICU, hospitalization >7 days, intubation, ventilator support, and antibiotic treatment.

The study of pregnancy-associated mortality in 2001–2012 combined data from several national registers and consisted of 10 427 deceased women, with 268 pregnancy-associated deaths (2.6%). We studied deaths by different causes in ongoing pregnancies and after deliveries, after termination of pregnancy, and after miscarriages. Furthermore, we calculated the mortality rates in non-pregnant, reproductive-age (15–49 years) women. To compare the results with earlier results from 1987–2000, we calculated ARRs using indirect

standardization and the age distribution of all pregnant and non-pregnant women.

Risk of asphyxia was lower in units having ≥ 2000 deliveries annually (17/1000) than in university hospitals (21/1000) (AOR 0.83, 95% CI 0.78–0.89). Compared with university hospitals, in units having 1000-1999 annual deliveries, intrapartum mortality rate was higher (2.4/1000 vs. 3.0/1000) (AOR 1.31, 95% CI 1.07–1.61); this was also the case for units in which physicians were at home when on-call (2.9/1000) (AOR 1.25, 95% CI 1.02–1.52).

The risk of asphyxia was higher (ARR 1.23, 95% CI 1.15–1.30) outside office hours (22.7/1000) than during office hours (18.4/1000). Compared with during office hours, risk of intrapartum and early neonatal mortality outside office hours was significantly elevated only in non-university hospitals having ≥ 2000 annual deliveries (2.2/1000 during office hours and 2.6/1000 outside office hours, ARR 1.51, 95% CI 1.07–2.14).

In emergency Caesarean sections, the risk of asphyxia was higher outside office hours (60.7/1000) than during office hours (52.9/1000, ARR 1.17, 95% CI 1.02–1.34). Instrumental vaginal delivery had higher risk of intrapartum and early neonatal mortality outside office hours (1.9/1000) than during office hours (0.6/1000, ARR 3.31, 95% CI 1.01–10.82).

Vaginal breech delivery had a lower risk of intrapartum and early neonatal mortality during office hours (24.0/1000) than outside office hours (7.3/1000, RR 0.31, 95% CI 0.11–0.87).

In Kätilöopisto Hospital between the two periods, the proportion of babies receiving 5-minute Apgar score < 7 increased from 1.2% to 2.1% (AOR 1.67, 95% CI 1.36–2.05), newborn transfers to SCN or NICU increased from 7.3% to 8.1% (AOR 1.11, 95% CI 1.02–1.22), and third- and fourth-

degree perineal tears increased from 1.4% to 2.0% (AOR 1.47, 95% CI 1.19–1.82).

Age-adjusted pregnancy-associated mortality decreased from 37.8/100 000 to 28.4/100 000 between the two periods. (ARR 0.75, 95% CI 0.65–0.88). In non-pregnant fertile-age females, the mortality rate decreased from 59.0/100 000 to 48.1/100 000 (ARR 0.82, 95% CI 0.79–0.84). Mortality rate for suicides was highest (21.8/100 000) after termination of pregnancy and lowest in ongoing pregnancies or right after birth (3.3/100 000).

Severe adverse obstetric outcomes are rare in Finnish maternity hospitals. Delivery units must have an on-call doctor present at all times. Risk of neonatal asphyxia is higher outside office hours than during office hours in all hospital volumes and in all on-call arrangements. Increasing obstetric volume in a high-volume unit can affect both maternal and perinatal outcomes. The high suicide mortality rate after induced abortion is alarming and the underlying reasons warrant further study.

SUOMENKIELINEN TIIVISTELMÄ

Turvallisen synnytyksen edellytyksenä on asiantunteva hoito synnyttäjän tarpeiden mukaan vuorokauden ajasta riippumatta. Jotta synnytystoiminnan turvallisuutta ja raskaana olevien naisten hoitoa voitaisiin edelleen kehittää Suomessa, tämän tutkimuksen tarkoituksena oli saada tietoa erikokoisten synnytysyksiköiden potilasturvallisuudesta ja vertailla eri tavoilla järjestettyä lääkärien päivystystoimintaa. Tutkimus vertaili myös virka-ajan ja päivystysajan vaikutusta vastasyntyneen vointiin. Lisäksi tutkittiin synnyttäjien määrän suuren nousun vaikutusta synnyttäjien ja syntyvien lasten turvallisuuteen Kätilöopiston sairaalassa ja raskauteen liittyviä kuolemia Suomessa.

Osatyö I, joka tutki synnytyssairaalan koon ja lääkärien päivystysjärjestelyjen vaikutusta syntyneen lapsen vointiin perustui syntymärekisteristä kerättyihin tietoihin sairaalassa syntyneistä lapsista vuosilta 2005-2009. Lopputulosmuuttujina tutkimuksessa olivat seuraavat lapsen voinnin mittarit: syntymänaikainen hapenpuute, syntymänaikainen kuolema, kuolema seitsemän vuorokauden kuluessa syntymästä, siirto eri hoitopaikkaan ja sairaalahoidon pituus. Todennäköisyyksien suhteet (AOR) laskettiin vakioimalla äidin ikä ja synnyttäneisyys. Koska tutkimus keskittyi niin kutsuttuihin matalan riskin synnytyksiin, käytössä olivat seuraavat poissulkukriteerit: syntymäpaino alle 2500g, raskauden aikana kuollut, monisikiöinen raskaus ja lapsen vaikea synnyynnäinen kehityshäiriö tai rakennevika. Näiden poistojen ja puuttuvien tietojen takia tehtyjen poistojen jälkeen osatyö käsitti 267 066 lasta.

Osatyö II vertaili päivystysajan ja virka-ajan merkitystä syntymänaikaiseen hapenpuutteeseen ja lapsen kuolemaan synnytyksenaikana tai seitsemän vuorokauden kuluessa

synnytyksestä. Lopputulosmuuttujia tarkasteltiin erikokoisissa sairaaloissa ja lääkäreiden eri päivystysjärjestelyjen mukaan. Suhteellinen riski (ARR) laskettiin vakioimalla äidin ikä ja synnyttäneisyys. Aineisto muodostui ajanjaksolla 2005-2009 yksisikiöisestä raskaudesta sairaalassa syntyneistä lapsista. Koska tutkimus keskittyi niin kutsuttuihin matalan riskin synnytyksiin, käytössä olivat seuraavat poissulkukriteerit: raskauden aikana kuollut, lapsen vaikea synnynnäinen kehityshäiriö tai rakennevika, syntymä ennen 37:ä täyttä raskausviikkoa ja monisikiöraskaus. Näiden poistojen ja puuttuvien tietojen takia tehtyjen poistojen jälkeen toinen osatyö käsitti 263 901 lasta.

Osatyöhön III, joka tarkasteli synnytysten määrän lisäystä Kättilöopiston sairaalassa kuului lisäksi väestötason vertailu koko pääkaupunkiseudun synnytysyksiköissä (Jorvi, Naistenklinikka, Kättilöopisto). Tutkimusajankohta valittiin toukokuussa 2013 aloitetun Helsingin Naistenklinikan remontin aiheuttamien synnyttäjä- ja henkilökuntamäärien muutosten perusteella. Yksisikiöisiä sairaalasyntyksiä tutkittiin kahtena ajanjaksona, 2011–2012 ja 2014–2015. Kättilöopiston aineisto muodostui ensimmäisenä ajanjaksona 11 237 vastasyntyneestä ja toisena ajanjaksona 15 637 vastasyntyneestä. Koko alueen väestötason analyysissä oli ensimmäisenä ajanjaksona 28 950 vastasyntynyttä ja toisena ajanjaksona 27 979 vastasyntynyttä.

Ajanjaksojen vertailua varten laskettiin todennäköisyyksien suhteita, jotka vakioitiin äidin iän, synnyttäneisyyden ja raskautta edeltävän painoindeksin mukaan. Lopputulosmuuttujia olivat synnytyksen käynnistys, päivystyskeisarileikkaus, pihti- tai imukuppisyntyminen, välilihan kolmannen tai neljännen asteen repeämä, syntymänaikainen hapenpuute, ja seuraavat vastasyntyneen vointia kuvaavat muuttujat: siirto valvonta- tai tehohoitoyksikköön, sairaalahoidon kesto vähemmän kuin

seitsemän päivää, intubaatio, hengitystukihoito, antibioottihoito, kuolleena syntynyt ja ensimmäisen seitsemän vuorokauden aikana kuollut.

Osatyö IV tutki raskauteen liittyviä kuolemia raskauden aikana ja vuoden kuluessa raskauden päättymisestä. Kuolemia tutkittiin erikseen raskauden aikana tai synnytyksen jälkeen sekä raskauden keskeytyksen ja keskenmenon jälkeen. Kuolinsyyt eriteltiin lääketieteellisiin syihin, onnettomuuksiin, itsemurhiin ja murhiin. Eri syistä johtuvia kuolemia tutkittiin myös niiden 15–49-vuotiaiden naisten joukossa, jotka eivät olleet raskaana viimeisen vuoden kuluessa. Tutkimuksen aineisto koostui 10 427 kuolleesta naisesta. Kuolemista 268 (2,6%) liittyi raskauteen. Tuloksia verrattiin aiemman vuosikymmenen tuloksiin laskemalla ikävakioituja suhteellisia riskejä.

Syntymänaikaisen hapenpuutteen riski oli pienempi yksiköissä, joissa oli ≥ 2000 synnytystä vuosittain (17/1000) kuin yliopistosairaaloissa 21/1000) (OR 0,83; 95% CI 0,78–0,89). Syntymänaikaisen kuoleman riski oli suurempi yksiköissä, joissa oli 1000–1999 synnytystä vuosittain (3,0/1000) (OR 1,31; 95% CI 1,07–1,61) verrattuna yliopistosairaaloihin (2,4/1000). Samoin riski oli suurempi yksiköissä, joissa lääkäri saattoi päivystää kotona (2,9/1000) (OR 1,25; 95 % CI 1,02–1,52).

Päivystysaikainen riski syntymänaikaiseen hapenpuutteeseen oli lisääntynyt (22,7/1000) riippumatta synnytystavasta tai päivystysmuodosta (ARR 1,23; 95% CI 1,15–1,30) verrattuna virka-aikaan (18,4/1000). Yli 2000 vuosittaisen synnytyksen yksiköt olivat ainoat, joissa oli päivystysaikana tilastollisesti merkittävästi korkeampi riski kuolemaan synnytyksen aikana tai seitsemän vuorokauden kuluessa syntymästä (2,6/1000) kuin virka-aikana (2,2/1000) (RR 1,51; 95% CI 1,07–2,14).

Perätilasynnytykseen alateitse liittyi päivystysaikana vähentynyt riski kuolemaan synnytyksen aikana tai seitsemän

vuorokauden kuluessa syntymästä (7,3/1000) verrattuna virka-aikaan (24,0/1000) (ARR 0,31; 95% CI 0,11–0,87).

Päivystyskeisarinleikkaukseen päivystysaikana liittyi lisääntynyt riski syntymänaikaiseen hapenpuutteeseen verrattuna virka-aikaan (52,9/1000 virka-aikana ja 60,7/1000 päivystysaikana) (ARR 1,17; 95% CI 1,02–1,34). Imukuppi- tai pihtiasvusteiseen alatiesynnytykseen liittyi päivystysaikana kohonnut riski kuolemaan synnytyksen aikana tai seitsemän vuorokauden kuluessa syntymästä (1,9/1000 päivystysaikana ja 0,6/1000 virka-aikana) (ARR 3,31; 95% CI 1,01–10,82).

Vertailtaessa kahta eri ajanjaksoa Kättilöopiston sairaalassa, niiden lasten osuus, jotka saivat viiden minuutin iässä Apgar-pisteitä alle seitsemän lisääntyi 1,2%:sta 2,1%:iin (AOR 1,67; 95% CI 1,36–2,05), vastasyntyneiden siirto valvonta- tai tehohoitoyksikköön lisääntyi 7,3%:sta 8,1%:iin (AOR 1,11; 95% CI 1,02–1,22) ja kolmannen ja neljännen asteen välilihan repeämien osuus nousi 1,4%:stä 2,0%:iin (AOR 1,47; 95% CI 1,19–1,82).

Vuosina 2001–2012 ikävakioitu raskauteen liittyvä kuolleisuus oli 28,4/100 000 synnytystä, mikä oli selkeästi matalampi kuin vuosina 1987–2000, jolloin kuolleisuus oli 37,8/100 000 (ARR 0,75; 95% CI 0,65–0,88). Kuolleisuus ei-raskaana olevien hedelmällisessä iässä olevien naisten keskuudessa laski ajanjaksojen välillä 59,0/100 000:sta 48,1/100 000:een (ARR 0,82; 95% CI 0,79–0,84). Itsemurhakuolleisuus oli korkein raskauden keskeytyksen jälkeen (21,8/100 000) ja matalin synnytyksiin päättyvissä raskauksissa ja raskaana olevien keskuudessa (3,3/100 000).

Vakavat synnytykseen liittyvät poikkeavat lopputulemat ovat harvinaisia suomalaisissa synnytyssairaaloissa. Löydösten perusteella voidaan suositella päivystävän lääkärin jatkuvaa

läsnäoloa synnytyssairaalassa. Päivystysaikaiseen synnytykseen liittyy lisääntynyt riski syntymänaikaiseen hapenpuutteeseen kaikissa synnytyssairaaloissa. Synnyttäjien määrän lisääminen suuressa synnytyssairaalassa voi lisätä sekä vastasyntyneeseen että synnyttäjään liittyvien ei-toivottujen tapahtumien suhteellista osuutta. Itsemurhia raskauden keskeytyksen jälkeen on hälyttävän paljon. Tämä vaatii tarkempaa tutkimusta syiden selvittämiseksi.

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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications:

- I. Karalis E, Gissler M, Tapper A-M, Ulander V-M. Effect of hospital size and on-call arrangements on intrapartum and early neonatal mortality among low-risk newborns in Finland. *Eur J Obstet Gynecol Reprod Biol* 2016; 198:116–119.
- II. Karalis E, Gissler M, Tapper A-M, Ulander V-M. Influence of time of delivery on risk of adverse neonatal outcome in different size of delivery units: a retrospective cohort study in Finland. *J Matern Fetal Neonatal Med* 2017; 20:1–7.
- III. Karalis E, Tapper A-M, Gissler M, Ulander V-M. The impact of increased number of low-risk deliveries on maternal and neonatal outcomes: A retrospective cohort study in Finland in 2011–2015. *Eur J Obstet Gynecol Reprod Biol* 2018; 223:30–34.
- IV. Karalis E, Ulander V-M, Tapper A-M, Gissler M. Decreasing mortality during pregnancy and for a year after while mortality after termination of pregnancy remains high: a population-based register study of pregnancy-associated deaths in Finland 2001-2012. *BJOG* 2017;124(7):1115–1121.

The publications are referred to in the text by their Roman numerals. These original publications are published with the

permission of their copyright holders. In addition, some unpublished material is presented.

ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
AIDS	Acquired Immunodeficiency Syndrome
AOR	Adjusted Odds Ratio
ARR	Adjusted Risk Ratio
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CP	Cerebral Palsy
HIE	Hypoxic ischaemic encephalopathy
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10 th edition
LGA	Large for Gestational Age
MMR	Maternal Mortality Ratio
NICU	Neonatal Intensive Care Unit
NNU	Neonatal Unit
OECD	Organisation for Economic Co-operation and Development
SCBU	Special Care Baby Unit
SCN	Special Care Nursery

SGA	Small for Gestational Age
SSI	Surgical Site Infection
THL	National Institute for Health and Welfare
Valvira	National Supervisory Authority for Welfare and Health
WHO	World Health Organization

1 INTRODUCTION

The annual number of babies born has been decreasing in recent years in Finland, now equivalent to the rate in the late 1980s. Fertility is often measured by calculating the total fertility rate, which indicates how many children a woman will give birth to during her lifetime (1). In 2016, the total fertility rate was lowest (1.30) in Helsinki and highest (1.87) in Seinäjoki, while the number for Finland overall was 1.57 (2). This means that on average every fertile woman will give birth to less than two children during her lifetime. However, the number of deliveries per hospital has increased because of closure of delivery units. In 1987, there were 53 delivery units in Finland with about 1120 deliveries per unit annually, whereas in 2016 there were 26 delivery units with about 2060 annual deliveries per unit (3). The lowest volume unit in continental Finland had 777 deliveries and the highest volume unit 7270 deliveries in 2016 (3).

Centralization of pre-term deliveries in Finland is based on several studies. Some studies demonstrate that risk for death is higher among pre-term and very low birthweight infants (<1500 g) in neonatal intensive care units (NICUs) having lower levels of care and less than 100 infants per year (4,5). In addition, a study by Rautava et al. (6) suggests that infants born at 22 to 28 gestational weeks in level II hospitals, instead of university hospitals, have higher risk for one-year mortality (OR 4.7, 95% CI 3.0–7.5). Furthermore, deliveries considered high risk because of maternal or foetal comorbidities are centralized to higher level hospitals with specialized care.

A consensus for safest place for low-risk deliveries does not exist. Some studies suggest that larger hospitals are safest (7-9), while other studies report that size of the delivery unit does not affect delivery outcome (10,11).

The aim of this study was to improve obstetric care in Finland. Patient safety of Finnish maternity hospitals was investigated by measuring the outcomes of newborns and pregnant women or recently pregnant women.

2 REVIEW OF THE LITERATURE

Numerous indicators are applied to measure quality of care and patient safety in obstetrics. No consensus exists on a single uniform set of indicators. Instead, indicators vary by country, region, or organization. Specialists and scientists have agreed that good obstetric quality indicators must have precise definitions and be easily accessible from data sources (12). Furthermore, good indicators have clinical importance and they can be affected by clinical practices (12). Currently, there are several projects trying to create an international consensus on the indicators, one of these being the Nordic Working Group on Patient Safety for the years 2013–2015. The group suggested frequent auditing of safety indicators related to resources and processes, maternal health, and newborn health (12).

2.1 FOUNDATIONS FOR SAFE MATERNAL AND PERINATAL CARE

Safety and quality in health care are bound together and consist of several factors that alone are insufficient but combined can ensure safe care (13). Essential components of care are as follows: involving the patient in decision-making, facility suitable for obstetric purposes, competent and motivated staff, availability of essential medicines, availability of safe equipment, compliance with evidence-based practices, comprehensive documentation, sufficient communication, good use of new information, and frequent auditing of practices (14). World Health Organization (WHO) has suggested national accreditation against selected safety standards to ensure that resources meet minimum standards for safe obstetric care (15).

Abundant evidence exists for the usefulness of simulation training in developing and maintaining obstetric skills (16-18). Simulation training can help low-level units to maintain the required skills and readiness for emergencies. Furthermore, many hospitals worldwide have successfully implemented high reliability organization principles to increase patient safety (19-21). These principles include preoccupation with failure, reluctance to simplify, sensitivity to operations, commitment to resilience, and deference to expertise (22).

2.2 SAFETY INDICATORS FOR MATERNAL OUTCOME

2.2.1 MATERNAL MORTALITY

The World Health Organization (WHO) defines maternal death as “death of woman while pregnant or within 42 days of the end of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes” (23). WHO has included all causes under the definition of pregnancy-related death as “a death occurring in woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of the death”. Maternal sepsis is one of the most common reasons for pregnancy-related deaths (24). Up to 70% of pregnancy-related deaths are preventable (25).

Late maternal death is defined by WHO as “death of a woman from direct or indirect obstetric causes more than 42 days but less than one year after the termination of pregnancy” (23). The most common way to report results is by considering maternal mortality and the direct and indirect obstetric causes. Direct obstetric causes are caused by pregnancy or its treatment, e.g. haemorrhage or eclampsia. Indirect obstetric causes arise from diseases that the woman already had before

pregnancy, e.g. diabetes or high blood pressure, and their suboptimal care (26). More than one-quarter of maternal death is due to indirect causes. One of the most common reasons worldwide for indirect maternal deaths is acquired immunodeficiency syndrome (AIDS) (27). In fact, AIDS is the most common cause of death among fertile-age women worldwide, albeit a very rare cause in Finland (28).

The term pregnancy-associated death considers deaths during pregnancy and up to one year after termination and from any cause, including accidents, homicides, and suicides. This term has been introduced by The American College of Obstetricians and Gynecologists (ACOG) and The Centers of Disease Control and Prevention (CDC) (29).

In an American study of pregnancy-related mortality, 22.7% of the women died before delivery, 16.6% died on the day of delivery or pregnancy termination, 20.8% died within days 1–6 postpartum, and 26.6% died within days 7–41 postpartum. After 42 days postpartum, 13.5% of the women died. (30) The most common causes of death on days 42–364 after the pregnancy are malignancies, suicides, and vascular diseases (31).

WHO advises reporting maternal mortality ratio (MMR) per 100 000 live births and publishes these results annually (23). The other method for reporting mortality is maternal mortality rate, which is calculated by dividing maternal deaths by number of women aged 15–49 years in the subject population (23). The latest published data demonstrate that MMR in Finland in 2015 was 3.0, in Sweden 4.0, in the USA 14.0, and in Sierra Leone 1360.0 (32).

The UK reports maternal mortality per maternities. This is calculated by dividing the number of indirect and direct maternal deaths by 100 000 maternities. A maternity is a pregnancy resulting in the delivery of a liveborn baby in any

pregnancy week or delivery of a stillborn baby after 24 completed pregnancy weeks. (33)

2.2.2 PERINEAL TEARS

According to the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), perineal tears during delivery have four groups by severity of the tear. First-degree tears affect the skin of the vulva and/or vaginal mucosa. Second-degree tears are tears that involve the pelvic floor, i.e. muscles of the perineum and vagina. Third-degree tears involve one or more anal sphincters and the rectovaginal septum. Fourth-degree tears include the rectal or anal mucosa. (34) Third- and fourth-degree tears may affect the woman's life long term by causing anal incontinence. The Organisation for Economic Co-operation and Development (OECD) has selected these injuries as patient safety indicators in obstetrics. Increased risk for anal sphincter injuries exists in units having less than 500 annual deliveries and in units having more than 5000 annual deliveries. (35) However, rate of severe perineal tears is not affected by time of birth or obstetric staffing (36). In Norway, perineal tears are the most common reason (30%) for patient injury compensation to the mother (37).

2.2.3 HAEMORRHAGE

Haemorrhage is the most common reason (27%) for maternal mortality worldwide. Better medical care could prevent 90% of these deaths. (38) Uterine artery embolization is an effective method to treat massive bleeding, and it can potentially prevent hysterectomy (39,40). Uterine artery embolization is available in many higher-level hospitals to treat massive bleeding after delivery. Estimating the blood loss is challenging and many guidelines advise on how to

recognize, avoid, and treat the loss. Blood loss of up to 500 ml postpartum is considered biological. Thus, the postpartum haemorrhage is defined as bleeding from the genital tract in excess of 500 ml. Need of blood transfusion and falling haematocrit have also been used to diagnose critical bleeding. For Caesarean section, the accepted blood loss is 1000 ml. (41) Since blood loss is often estimated and not measured, transfusion of four or more units of packed red blood cells is also used as a measure of severe maternal morbidity (42). For women requiring peripartum hysterectomy to control the blood loss, perioperative mortality is 71% lower at high-volume hospitals than at low-volume units (43).

2.2.4 INFECTIONS

In Norway, 23% of patient injury compensations to the mother are because of infections (37). The most common causes of puerperal infections are endometritis, wound infection, mastitis, urinary tract infection, and septic thrombophlebitis (44). Many hospitals maintain their own hospital-acquired infection registers, which enable a quick response and analysis of root causes when a change in the infection parameters is detected (45).

Reporting surgical site infections (SSI) is used in many countries as part of monitoring patient safety. The CDC defines gynaecological organ SSI as an infection occurring within 30 days of any operative procedure (e.g. Caesarean section) and it is divided into superficial incisional and deep incisional infections and organ/space SSI (46).

The National Institute for Health and Welfare in Finland (THL) uses the same classification. The European Centre for Disease Prevention and Control reported SSIs for 2.2% of Caesarean sections in 2013–2014 with an inter-country range from 0.6% to 7.7% (47). In the USA, infection rates do not

differ between different-sized maternity hospitals, but women with infections stay longer at lower-volume hospitals (48).

2.2.5 CAESAREAN SECTION RATE

Caesarean section rate is the number of Caesarean sections divided by 1000 live births. This is one of the OECD indicators for health care activities. Caesarean section can be a life-saving procedure for both mother and child, but it is a major surgery with risks. Caesarean section increases the risks for maternal and foetal morbidity in the current pregnancy as well as in future pregnancies. (49)

The Caesarean section rate has been increasing in developed countries due to multiple pregnancies, overweight, and convenience of the procedure for both the patient and obstetrician (49). Furthermore, factors associated with women's fears and societal and cultural beliefs likely contribute to the increase. For example, fear of childbirth increases the risk of Caesarean section fourfold (50).

In Finland, Caesarean section rate is 16.4 and in Germany 30.9 (51). In 2017 in Finland, Caesarean section rate was 16.0% in units having >1000 annual deliveries and 12.7% in units having <1000 annual deliveries. Furthermore, the rate was 15.6% in all university hospitals other than Helsinki University Hospital, where it was 19.0% (52). One explanation for the difference between university hospitals is the centralized care of the most severe congenital anomalies in Helsinki University Hospital.

WHO suggests that Caesarean section rate between 10% and 15% indicates optimal use. WHO has estimated that 32% of Caesarean sections in China, 15% in Brazil, and 11% in the USA are unnecessary, whereas in many African and Asian countries Caesarean sections should be increased to close to 100% for better maternal and perinatal outcomes. (49)

2.3 SAFETY INDICATORS FOR PERINATAL OUTCOME

2.3.1 PERINATAL MORTALITY

Figure 1 exemplifies the terminology for newborn deaths. Perinatal death is a death of a foetus after 22 completed pregnancy weeks or death of a child within seven days of delivery. This definition is used by WHO (53). Perinatal mortality is calculated by dividing perinatal deaths by 1000 newborns (54).

OECD uses a different definition for perinatal mortality: deaths of children within one week of birth, including foetal deaths of minimum gestation period of 28 weeks or minimum foetal weight of 1000 g, divided by 1000 births (51). The OECD criteria for gestational weeks are often considered too high because preterm birth is the main reason for perinatal mortality.

Different practices in recording very preterm livebirths, stillbirths, and terminations of pregnancy create variations in mortality rates between countries. An international collaborative study between the Euro-Peristat network and the Preterm Birth International Collaborative Epidemiology Working Group suggests that international comparisons of very preterm birth rates should exclude births at 22–23 weeks of gestation and terminations of pregnancy (55).

A previous Finnish study suggests that in different-volume hospitals perinatal mortality shows no statistically significant differences (10). Another study of babies born in pregnancy week 32 or later indicates that, relative to daytime, during the evenings there is a 1.3-fold higher risk and at night 1.5-fold higher risk for perinatal mortality in non-tertiary hospitals

(56). Perinatal mortality rate in unplanned out-of-hospital deliveries is twofold greater than in hospital deliveries (57).

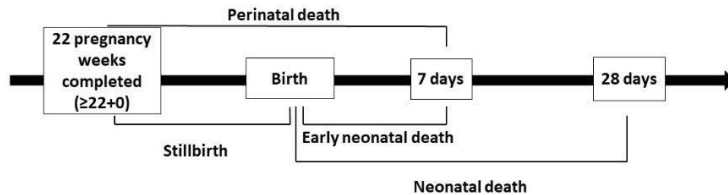


Figure 1. Terminology of newborn deaths.

2.3.2 EARLY NEONATAL MORTALITY

Early neonatal death is death during the first seven days after delivery. Early neonatal mortality is calculated by dividing early neonatal deaths by 1000 live births (54). A German study indicates that birthweight-specific early neonatal mortality risk is 3.5 times higher in hospitals with less than 500 births annually than in hospitals with a minimum of 1500 annual births (58). Furthermore, during night-time the risk for early neonatal death is 1.3-fold higher than during daytime (59).

2.3.3 NEONATAL MORTALITY

Neonatal death is a death of a live-born baby during the first 28 days of life. Neonatal mortality is calculated by dividing the deaths by 1000 live births (54). In 2015, neonatal mortality

rate (NMR) was 3.0 in Finland, 2.0 in the UK, and 46.0 in Pakistan (60).

Controversial results of neonatal mortality in maternity hospitals with different volumes have been reported. Some studies suggest lower neonatal mortality among infants born at minimum 32 gestational weeks in units with 100 to 999 annual deliveries relative to units with 1000 to 2499 annual deliveries (7,11). Furthermore, another study demonstrates that mortality is lowest in large hospitals with full access to neonatal care (9).

Time of birth has an effect on neonatal mortality; there is a 1.3-fold higher risk for neonatal death for term infants born outside of normal working hours (4.2/10 000 during office hours and 5.6/10 000 outside office hours) in Scottish hospitals (61).

2.3.4 ASPHYXIA

Perinatal asphyxia occurs when blood flow and gas exchange to the foetus are interrupted (62). Most infants exposed to perinatal hypoxia-ischaemia will recover quickly and will have normal survival. However, a proportion of infants will develop hypoxic-ischaemic encephalopathy (HIE), which affects the motor, sensory, cognitive, and behavioural outcome of the child. (62)

HIE is the most common reason (83%) for patient injury compensation to the child in Norway (37). For most newborns diagnosed with moderate or severe encephalopathy, the condition is attributed to asphyxia during labour (63). Children whose cerebral palsy (CP) is associated with birth asphyxia are three times more likely to have severe (grade IV and V) CP (64). Intrapartum foetal asphyxia occurs more often in low-risk mothers who have not received special prenatal care than in mothers considered at high risk (65).

Apgar scores are used worldwide to detect asphyxia. However, an analysis of 23 countries or regions in Europe states that Apgar scores cannot be used for international comparison of newborn health because of the variation in national scoring practices (66). Apgar scores <3 at 5 minutes and <7 at 10 minutes in term delivery are highly associated with CP and epilepsy in adolescence (67). Furthermore, HIE is diagnosed in 60% of term babies having a 5-minute Apgar score <4 (68). The Apgar score system is explained in Table 1.

Table 1. *Apgar Score. Modified from the American Academy of Pediatrics. (69)*

Indicator	0 points	1 point	2 points
Appearance (Colour)	Blue or pale	Blue extremities	Completely pink
Pulse	Absent	<100/minute	>100/minute
Grimace (reflex irritability)	No response	Minimal response	Cry or active withdrawal
Activity	None	Some flexion	Active motion
Respiration	Absent	Slow and irregular	Good, crying

Reported at 1 minute and 5 minutes after birth for all infants, and at 5-minute intervals thereafter until 20 minutes for infants with a score <7.

Umbilical artery pH level is another indicator used to define newborn asphyxia. The ideal pH is between 7.26 and 7.30 (70). However, risk of adverse neurological outcome varies between 3% and 18% in babies with umbilical artery pH<7.00, and the risk for adverse neurological outcomes starts to rise around pH 7.10 (70,71). Umbilical arterial lactate (>3.9 mmol/l) is more sensitive and specific for neonatal morbidity than low pH (72). Furthermore, umbilical artery pH cannot be

used in international comparison because countries apply different threshold levels for defining asphyxia (73).

2.4 OTHER INDICATORS FOR MATERNAL AND PERINATAL OUTCOME

In different countries, different safety indicators are used, and safety and quality control vary. Table 2 compares the indicators used in Australia and New Zealand combined, the UK, and the USA. Perineal tears, haemorrhage, and transfer to NICU are common indicators in all four countries, but for example low 5-minute Apgar score is defined below seven in the USA and Australia, but below six in the UK (74-76).

Transfer to NICU is a commonly applied parameter. However, the terminology and reporting are inconsistent, limiting its use. Instead, respiratory treatment of the newborn is often utilized as a safety indicator. This parameter also has limitations; it is more available in larger hospitals, thus being used in them more frequently. The same limitation is present when measuring transfers of mothers to the intensive care unit.

Risk for Erb's paralysis and fracture of the clavicle is used as a safety indicator; the risk is lower in larger delivery units. Furthermore, higher Caesarean section rate does not have a protective effect on the risk, and risk factors such as macrosomia do not predict the occurrence of the paralysis or the fracture. (77,78)

Prolonged hospital stay of a newborn is considered a better safety indicator than mother's hospital stay. However, duration of hospital stay is affected by availability of an intensive care bed, and thus, prolonged hospital stay is less likely in small maternity units than in larger ones (77). Between 2015 and 2016 in Finland, 7.4% of newborns stayed

at the hospital >7 days in university hospitals and 3.8% in units having <1000 annual deliveries (79).

Table 2. *Examples of obstetric safety indicators in three different continents.*

UK
Maternal infection
Urinary tract infection
Caesarean section/abdominal wound infection
Mastitis
Uterine infection
Perineal wound infection
Perineal trauma
1 st - 4 th degree tear
Episiotomy
Postpartum haemorrhage
499 ml or less
500-999 ml
1000-1999 ml
2000 ml+
5-minute Apgar score of term babies
< 7
Term baby treatment
Transfer/admission to SCBU/NNU/NICU
Mother and baby separation
Yes/No
Women's perception of safety questions
Were you ever separated from your baby?
Were you left alone by midwives or doctors at a time when it worried you?
If you raised a concern during labour and birth about safety, did you feel that it was taken seriously?
Would you like to talk about these questions with a midwife/doctor or another person now?

AUSTRALIA AND NEW ZEALAND

Spontaneous vaginal cephalic delivery

Maternal age 20-34 years at time of giving birth
First birth at ≥ 20 gestational weeks
Singleton pregnancy
Gestational age 37-40 weeks at delivery

Induction of labour

Yes/No

Instrumental vaginal birth

Yes/No

Vaginal birth after Caesarean section

Yes/No

Major perineal tears and/or surgical repair of the perineum

1st - 4th degree tear
Episiotomy

Antibiotic prophylaxis in Caesarean section

Yes/No

Pharmacological thromboprophylaxis in Caesarean section

Yes/No

Postpartum haemorrhage / blood transfusion

(No volume limits given)

Intrauterine growth restriction

Birth weight < 2500 g,
at ≥ 40 weeks of gestation

5-minute Apgar score < 7

Term babies, stillbirths excluded

Admission of term babies to SCN or NICU

Term babies transferred for reasons other than congenital abnormality

Peer review of serious adverse events

Number of serious adverse events that are addressed within a peer review process

USA

Maternal death

Yes/No

Intrapartum or neonatal death

For baby >2500 g

Uterine rupture

Yes/No

Maternal admission to intensive care unit

Yes/No

Birth trauma:

3rd /4th degree tear

Return to operating room or delivery unit

Yes/No

Admission to NICU

For baby >2500 g and staying for >24 h

Apgar score < 7 at 5 minutes

For baby >2500 g

Blood transfusion

Yes/No

NICU neonatal intensive care unit

SCN Special care nursery

SCBU Special care baby unit

NNU Neonatal unit

In addition to the safety indicators mentioned earlier, the data on patient injuries entitled to indemnity collected by the Finnish patient insurance centre can be used for improving patient safety in maternity hospitals. The centre handles all compensation procedures for patient injuries in Finland. After receiving the claim, the centre retrieves necessary information from the health care provider and hears the claimant before making the decision (80). The latest annual statement by the centre declares that there were 21 cases related to birth entitled to indemnity in 2017 in Finland (81). A previous Finnish study reported that 92% of the compensations were due to improper detection and management of foetal asphyxia (82). A Norwegian study on birth asphyxia has identified

human error as a main factor in 89% of the injuries and system error in 3% of the injuries entitled to indemnity due to substandard care (83). Even though the annual number of birth-related patient injuries is low, it is worth noting that the compensations are paid for a lifetime and can eventually reach two million euros (82).

2.5 EFFECT OF TIME OF DELIVERY ON OUTCOME

Sleep deprivation affects the hippocampus and impairs learning. (84). Interns returning home after an extended work shift have two times higher risk for motor vehicle accidents than interns returning from a normal-duration shift (85). Furthermore, compared with months with no extended shifts, during the months that interns had one to four extended shifts, the likelihood for fatigue-related preventable medical errors was almost ninefold higher (86).

There are only a few studies on surgical skills after sleep deprivation. Laparoscopic appendectomy conversion rate during weekends is lower than during weekdays, but risk for reoperations is higher, even though overall postoperative complications do not differ statistically (87). In gastrosurgery, fewer complications occur during weekdays than during weekends (88). Among surgical residents, an increased number of errors occurred after sleep deprivation in a test on a laparoscopic surgical simulator (89). Among gynaecologists, however, no such difference emerged after a night shift; only duration of the procedure increased, and the results were the same at all expertise levels (90).

Effect of night-time on obstetric events is presented in Table 3. Caesarean section or instrumental vaginal delivery is less probable outside of office hours (91,92). However, infants born in the evening or at night have an increased risk for low

Apgar score irrespective of the mode of delivery (93) and very low birthweight (<1500 g) infants have increased risk for neonatal mortality and major neonatal morbidity when born at night compared with daytime (94,95). Furthermore, a recent Austrian study found that babies born at ≥ 34 pregnancy weeks have a higher risk for asphyxia and neonatal mortality if born at night rather than during office hours (96).

Night-time delivery increases the risk of severe maternal morbidity (97). However, time of day has no effect on the incidence of postpartum haemorrhage after operative vaginal delivery or anal sphincter tears (97,98). Moreover, time of day has no impact on neonatal mortality or morbidity among term deliveries in academic hospitals (99).

Table 3. *Effect of night-time delivery on obstetric events (references 91-99).*

Night-time delivery has	
Lower likelihood for Caesarean section	OR 0.94, 95% CI 0.90–0.98
Lower likelihood for operative vaginal delivery	OR 0.92, 95% CI 0.89–0.96
Higher risk for low Apgar score	OR 1.38, 95% CI 1.17–1.63
Higher risk for neonatal mortality and morbidity for babies <1500 g	RR 2.18, 95% CI 1.37–3.47
Higher risk for asphyxia and neonatal mortality for babies born at ≥ 34 gestational weeks	OR 1.35, 95% CI 1.13–1.61
No effect on neonatal mortality at term in academic hospitals	OR 0.80, 95% CI 0.50–1.40
Higher risk for severe maternal morbidity	OR 1.30, 95% CI 1.20–1.41
No effect on postpartum haemorrhage after operative vaginal delivery	OR 1.15, 95% CI 0.75–1.78
No effect on anal sphincter tears	OR 1.34, 95% CI 0.70–2.55

Weekends entail a higher risk for postoperative haemorrhage, newborn trauma, and obstetric trauma in Caesarean sections (100). Birthweight-adjusted neonatal mortality between

weekends and weekdays does not differ, and weekend birth is not associated with an increased risk of any adverse perinatal outcome (93,101). A Welsh study indicates that neonatal mortality rate is higher in July and August (summer holiday months in the northern hemisphere) than in other months (102).

2.6 EFFECT OF DELIVERY UNIT VOLUME ON OUTCOME

In demanding surgery, the rates of postoperative complications are significantly reduced if the procedure is performed in a high-volume hospital compared with a small-volume hospital (103). Hospital stay is shorter, complications fewer, and mortality rate lower when operations are performed by a high-volume surgeon than by a low-volume surgeon (104). A high-volume surgeon is a more important factor in reducing adverse outcomes than hospital volume when measuring postoperative medical complications, length of stay, and lower transfusion requirements in gynaecological oncology (105,106).

Premature babies have better outcomes if born in tertiary units of a high-volume NICU than in low-volume units (94). The literature considering term deliveries is outdated and scarce (107,108). Units with smaller obstetrical volume have higher incidence rates of approved patient injury claims than units with higher volume (109).

In units with less than 1000 annual deliveries, there is a higher risk for asphyxia during weekends if the number of parturients exceeds 3/4 of the hospital's daily births (110). Furthermore, previous studies state that the smaller the delivery unit the higher the risk for maternal complications, such as perineal tears and haemorrhage and complications in operative delivery, while larger units have a higher risk for

infections (111,112). In academic medical units, which usually are the largest units as well, hospitalization is longer even among women with low-risk pregnancies, compared with non-academic hospitals (113). Mother's hospital stay has decreased from 6.6 days in 1987 to 2.7 days in 2016 in Finland (3).

3 AIMS OF THE STUDY

This study was devised to provide information on maternal health and performance of delivery units in Finland in order to improve obstetric care. Specific aims were to investigate the following:

- I. The effect of size of the maternity unit and physician on-call arrangements on the performance of maternity units (Study I)
- II. The impact of time of birth on perinatal outcome in different modes of delivery, in different-sized delivery units, and in different physician on-call arrangements (Study II)
- III. The effect of obstetric volume increase on maternal and perinatal outcome in a high-volume delivery unit (Study III)
- IV. The change in pregnancy-associated mortality in Finland from 1987 to 2012 (Study IV)

4 SUBJECTS AND METHODS

The subjects and methodological approaches for all four studies are presented in Table 4.

4.1 SUBJECTS

The population in Studies I and II comprised all hospital births in Finland in 2005–2009. After removing any cases meeting the exclusion criteria (see below) or for which data were missing, 267 066 births remained for statistical analysis in Study I, and 263 901 births in Study II.

In Study III, the study population was singleton hospital deliveries in Kätilöopisto Maternity Hospital, and population-based analysis consisted of singleton hospital deliveries in all three (Kätilöopisto Maternity Hospital, Jorvi Hospital and Women's Clinic) Helsinki University maternity hospitals. In 2015, Kätilöopisto Maternity Hospital had approximately 7500 annual deliveries, Jorvi Hospital approximately 3900 annual deliveries, and Women's Hospital approximately 2600 annual deliveries (114). Deliveries were analysed in two periods: 2011–2012 and 2014–2015. The study hospital population was 11 237 in the earlier period and 15 637 in the later period. In population-based analysis, the population was 28 950 in the earlier period and 27 979 in the later period.

In Study IV, the population comprised 10 427 deceased women of reproductive age (15-49 years) during 2001–2012 in Finland. The number of pregnancy-associated deaths was 268.

4.2 METHODS

4.2.1 REGISTERS USED

For Study III, the data were obtained from the hospital register of the Helsinki and Uusimaa Hospital District. All of the other registers used are introduced below. The data collected from different registers were linked to the mother's and child's identification numbers.

4.2.1.1 Medical Birth Register

THL maintains the Medical Birth Register. The birth hospitals in Finland submit data to the register for all live births and stillbirths with a gestational age of 22 weeks or more and a birthweight of 500 g or more. The person assisting during or after the birth submits the data when the birth takes place outside the hospital. The Population Register Centre supplements the register on live births and Statistics Finland on stillbirths and early neonatal deaths. The register includes information on mother's personal data, previous pregnancies and deliveries, present pregnancy and its monitoring, delivery, the infant, and data of the infant by the age of 7 days or at discharge, among others. (115) This register was used in Studies I, II, and IV.

4.2.1.2 National Register of Congenital Malformations

The National Register of Congenital Malformations contains data on congenital anomalies detected in stillbirths, live births, and fetuses in selective terminations of pregnancy. THL maintains the register. Hospitals, health care professionals, and cytogenetic laboratories submit the data. Data are also derived from the Medical Birth Register, the Care Registers for Health Care, the statistics on Information

on Outpatient Services in Specialized Health Care, the National Supervisory Authority for Welfare and Health (Valvira), and the Cause-of-Death Register. (116) This register was used in Studies I and II.

4.2.1.3 Finnish Cause-of-Death Register

The Finnish Cause-of-Death Register obtains data from death certificates, supplemented with data from the population information system of the Population Register Centre. The register covers persons who have died in Finland or abroad during the calendar year and who at the time of death were domiciled in Finland. Statistics Finland maintains the register. (117) This register was used in Study IV.

4.2.1.4 Register on Induced Abortions

THL maintains the Register on Induced Abortions. The register contains information on all legally induced abortions in Finland. The physician or hospital performing the procedure must report the case to THL within one month of the procedure. (118) The register covers 97% of the induced abortions (119). This register was used in Study IV.

4.2.1.5 Care Register for Health Care

The Care Register for Health Care maintained by THL contains data on the following: patients discharged from inpatient care, number of patients in inpatient care in health centres and hospitals, day surgeries, and specialized outpatient care. Health service providers (hospitals, health centres, and home-nursing service providers) are obliged to submit information to the register. (120) This register was used in Study IV.

Table 4. Objectives, subjects, and methods used in Studies I-IV.

	Study I	Study II	Study III	Study IV
Objective	To analyse the effect of the size of the maternity unit and physician on-call arrangements on neonatal outcomes	To analyse the impact of time of birth on neonatal outcomes in different-sized delivery units and in different physician on-call arrangements	To analyse the effect of obstetric volume increase on maternal and neonatal outcomes in a high-volume delivery unit	To analyse the change in the pregnancy-associated mortality in Finland from 1987 to 2012
Subjects	Singleton hospital births, birth weight > 2500 g, in Finland N= 267 066	Singleton hospital births, gestational age \geq 37 weeks, in Finland N= 263 901	Singleton hospital deliveries in Helsinki region Study hospital N= 11 237 (2011–2012) N= 15 637 (2014–2015) Population-based analysis N= 28 950 (2011–2012) N= 27 979 (2014–2015)	All deceased women of reproductive age in Finland N= 10 427
Periods	2005–2009	2005–2009	2011–2012 and 2014–2015	2001–2012
Registers used	Medical Birth Register National Register of Congenital Malformations	Medical Birth Register National Register of Congenital Malformations	Hospital Register of the Helsinki and Uusimaa Hospital District	Medical Birth Register Finnish Cause-of-Death Register Register on Induced Abortions Care Register for Health Care

	Study I	Study II	Study III	Study IV
Outcome measures	<p>Intrapartum mortality</p> <p>Early neonatal mortality</p> <p>Neonatal asphyxia</p> <p>Newborn's need for intensive care or transfer to another hospital</p> <p>Length of newborn's hospital stay</p>	<p>Neonatal asphyxia</p> <p>Combined intrapartum and early neonatal mortality</p>	<p>Induced delivery</p> <p>Mode of birth</p> <p>3rd or 4th degree perineal tears</p> <p>Perinatal death</p> <p>Stillbirth</p> <p>Early neonatal death</p> <p>Neonatal asphyxia</p> <p>Newborn</p> <ul style="list-style-type: none"> • Transfer • Antibiotic treatment • Intubation • Ventilator support • Hospitalization >7 days 	<p>Pregnancy-associated death</p> <p>Death of a non-pregnant fertile-age woman</p>
Methods	<p>Comparisons of delivery outcomes in different hospital volumes and on-call arrangements</p> <p>Odds ratios with 95% confidence intervals</p> <p>Multivariable logistic regression analysis adjusted for maternal age and parity</p>	<p>Comparisons of delivery outcomes during office hours and outside office hours in different hospital volumes and physician on-call arrangements</p> <p>Risk ratios with 95% confidence intervals</p> <p>Multivariable logistic regression analysis adjusted for maternal age and parity</p>	<p>Comparisons of outcomes before and after increased obstetric volume</p> <p>Odds ratios with 95% confidence intervals</p> <p>Multivariable logistic regression analysis adjusted for maternal age, parity, and pre-pregnancy BMI</p>	<p>Comparisons of mortality rates by cause of death after termination of pregnancy, after miscarriage, during pregnancy or after birth, and in non-pregnant fertile-age women in different periods</p> <p>Risk ratios with 95% confidence intervals</p> <p>Indirect standardization and age distribution of all pregnant and non-pregnant women</p>

4.2.2 STUDY DESIGN, SETTING, AND DATA COLLECTION

All included studies were register-based retrospective cohort studies. The study period in Studies I and II was 2005–2009. This period was selected because the number of delivery units did not change drastically, and no big changes occurred in care guidelines.

In Studies I and II, the hospitals were stratified into three categories of volume according to annual number of deliveries: units with ≥ 2000 births, units with 1000–1999 births, and units with < 1000 births. University hospitals were categorized separately and used as a reference in Study I because of the specialized care services that they provide. Finland has five university hospitals and the number of annual deliveries in these hospitals varied between 2500 and 5500 in 2009 (121). The volume limits were chosen according to the analyst's report of obstetric services at the national level. The report states that the optimal level of annual births must be over 2000 to maintain sufficient resources 24/7, and in units with less than 1000 annual deliveries the level is too low to maintain sufficient services for safe care 24/7 (122).

In Studies I and II, during the study period, physicians (obstetrician or resident in obstetrics and gynaecology) could stay at home while on-call in most of the units with less than 1000 births annually and in some of the units with 1000–1999 annual births. In university hospitals, the physician was always at the hospital. If the physician stayed at home when on-call, he/she had to be at the hospital within 30 minutes of receiving a phone call. A neonatologist was available only at university hospitals. In small units, paediatricians and anaesthetists could be at home while on-call, arriving 30 to 60 minutes after a phone call.

In Studies I and II, two groups were created according to physician on-call arrangements: hospitals where the physician was at the hospital when on-call, and hospitals where the

physician could be at home when on-call. University hospitals were stratified separately.

For Study II, two categories for time and day were created: office hours (8:00-15:59) during normal working days and outside office hours (16:00-7:59), including weekends (from Friday 16:00 until Monday 7:59) and national holidays. In addition, newborn outcomes in different times were observed in normal vaginal delivery, in vaginal breech delivery, in instrumental vaginal delivery, and in elective and emergency Caesarean sections.

Study III investigated how the increase in the number of deliveries in Kätilöopisto Maternity Hospital impacted maternal and neonatal outcome. Therefore, two periods were created: from the beginning of 2011 to the end of 2012 and from the beginning of 2014 to the end of 2015. The earlier period was used as a reference. Time periods were chosen because a construction project, which began in May 2013, decreased the capacity of deliveries in Women's Hospital. Kätilöopisto Maternity Hospital received supplementary resources to handle additional deliveries, but these were not measured in the study.

During both periods, deliveries of high-risk pregnancies (insulin-treated diabetes before pregnancy, pregnancies with more than two fetuses, and deliveries before the 32nd week of pregnancy, among others) were carried out in Women's Hospital. During the latter period, all elective Caesarean deliveries were performed in Women's Hospital.

In Study IV, the study period was from the beginning of 2001 to the end of 2012. Results from 1987 to 2000 were obtained for comparison. Deaths of the fertile-age female population were obtained from the Cause-of-Death Register. According to the CDC and the ACOG, pregnancy-associated death is defined as a death of a woman during pregnancy or up to one year after the end of pregnancy (123).

To detect all pregnancy-associated deaths, the following process was performed: first, with ICD-10 codes O00-O99, 35 deaths directly coded for a pregnancy-related condition and three deaths secondarily coded for a pregnancy-related condition were detected. Then, remaining deaths were identified by linking the deaths in women of reproductive age (15-49 years) with births, terminations of pregnancy, and ongoing pregnancies, miscarriages, and ectopic pregnancies. Patient's identification number linked the data from the Cause-of-Death Register to the data from the Medical Birth Register, the Register on Induced Abortions, and the Care Register for Health Care.

Cause of death was classified as medical causes (disease or medical condition) or external causes (including unintentional and intentional accidents). For study purposes, external causes were further classified as accidents, suicides, or homicides.

4.2.3 EXCLUSION CRITERIA APPLIED

The exclusion criteria in Study I were birth outside of a hospital, antepartum stillbirth, birthweight <2500 g, multiple pregnancy, and major congenital anomaly or birth defect of the newborn. Furthermore, deliveries outside the study period (1.1.2005 - 31.12.2009) were excluded, as were deliveries with missing outcome data. The exclusions are presented in Figure 2.

The exclusion criteria in Study II were delivery outside the study period (1.1.2005 - 31.12.2009), antepartum stillbirth, birth outside of a hospital, multiple pregnancy, gestational age <37 weeks, and newborn with major congenital anomalies or birth defects (as reported to the National Register on Congenital Anomalies). If information of gestational age was missing, the birthweight of <2500 g was used as an exclusion

criterion. If both gestational age and birthweight were missing, the newborn was excluded. Furthermore, deliveries with missing outcome data were excluded.

In the study population, 2.2% of the newborns with birthweight of ≥ 2500 g were born prematurely (between 34 and 36 gestational weeks). Gestational age of < 37 weeks was chosen to exclude also those premature babies that the weight limit of 2500 g would not have excluded.

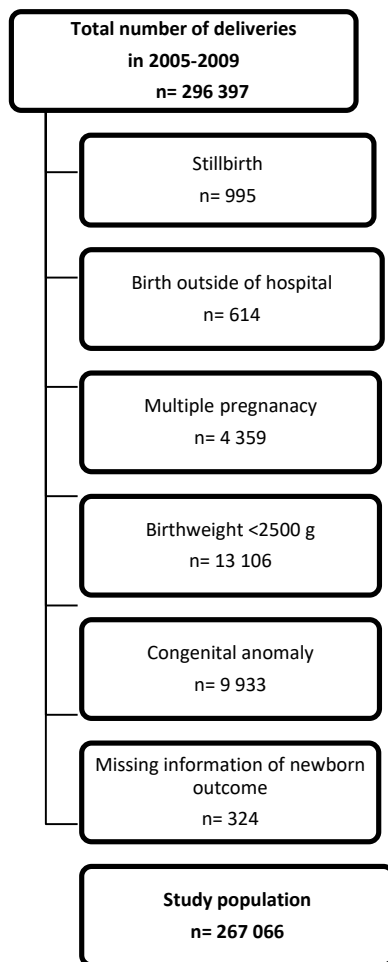


Figure 2. Data exclusion in Study I.

The exclusion criteria in Study III were multiple pregnancy, out-of-hospital delivery, and missing outcome data. In Study IV, the exclusion criteria were death outside of the study period (1.1.2001.31-12.2012), male sex, not of reproductive age (15-49 years), and missing outcome data.

4.2.4 OUTCOME MEASURES

In Study I, outcome measures were neonatal asphyxia, intrapartum death, early neonatal death, transportation of the newborn to a higher level of care, and duration of hospitalization of the newborn. Neonatal asphyxia was defined as the presence of any of the following: umbilical cord artery pH <7 at time of birth, 1-minute Apgar score 0-3, and 5-minute Apgar score 0-6. Neonatal asphyxia was defined according to the international consensus for defining an acute intrapartum hypoxic event (62).

Study II included the following outcomes measures: neonatal asphyxia (as defined in Study I) and intrapartum or early neonatal death. The outcome measures in Study III included induced delivery, emergency Caesarean section, instrumental delivery (vacuum and forceps), third or fourth degree perineal tear, perinatal death, stillbirth, early neonatal death, 5-minute Apgar score 0-6, 5-minute Apgar score 0-3, umbilical artery pH <7.00, newborn's transfer to a higher level of neonatal care, antibiotic treatment of a neonate, intubation of a neonate, ventilator support of a neonate, and hospitalization of a neonate for >7 days.

Furthermore, in Study III the following outcomes were measured to identify possible confounding factors: birthweight <2500 g, birthweight \geq 4500 g, large for gestational age (LGA), small for gestational age (SGA), duration of pregnancy <37 weeks, elective Caesarean section, and any congenital anomaly detected in the perinatal period.

The definitions used for large and small for gestational age are internationally accepted and widely used in the literature. Large for gestational age was defined as an infant whose birthweight was above the 90th percentile for gestational age. Small for gestational age was defined as an infant with a birthweight below the 10th percentile for gestational age. (124,125)

Outcomes in Study IV were pregnancy-associated death and death of a non-pregnant, reproductive-age (15-49 years) woman.

4.2.5 STATISTICAL ANALYSES

Statistical analyses were done with the statistical software package SAS 9.3 (SAS Institute Inc., Cary, NC, USA) Multivariable logistic regression was conducted in all studies because the incidence of the outcomes is low, and the studies used categorical dependent variables and continuous independent variables. The confounding factors selected for adjustment were chosen because they are widely used in similar studies worldwide.

In Study I, incidence rates and odds ratios (adjusted for maternal age and parity) (AORs) with 95% confidence intervals (CIs) were calculated. University hospitals served as a reference. In Study II, incidence rates and risk ratios (adjusted for maternal age and parity) (ARRs) with 95% CIs were calculated. Office hours served as a reference.

In Study III, incidence rates and AORs [adjusted for maternal age, parity, and pre-pregnancy body mass index (BMI)] with 95% CIs were calculated. Earlier period served as a reference. In Study IV, pregnancy-associated mortality rates were calculated per 100 000 pregnancies and mortality rate in non-pregnant women was calculated per 100 000 person-years. Then, ARR with 95% CIs were calculated and the earlier

period served as a reference. Indirect standardization and age distribution of all pregnant and non-pregnant women during the whole study period were used to calculate ARRs with 95% CIs.

4.2.6 ETHICS APPROVAL

THL approved the use of register data for Studies I and II. Helsinki and Uusimaa Hospital District granted permission to use data from the hospital register for Study III. THL and Statistics Finland approved the use of register data for Study IV. Register-based studies do not require authorization from a research ethics committee in Finland.

5 RESULTS

5.1 EFFECT OF SIZE OF MATERNITY UNIT AND PHYSICIAN ON-CALL ARRANGEMENTS ON THE PERFORMANCE OF MATERNITY UNITS (STUDY I)

Overall, intrapartum mortality rate in low-risk deliveries was 2.7/1000 newborns and early neonatal mortality rate was 0.2/1000 newborns during the study period in Finland. Risk of asphyxia (5-minute Apgar score <7 or umbilical artery pH <7.00) was lower (17/1000) in units having ≥ 2000 deliveries annually than in university hospitals (21/1000) (AOR 0.83, 95% CI 0.78–0.89). The asphyxia risk was also lower in units where physicians were at hospital when on-call (19/1000) (AOR 0.90, 95% CI 0.85–0.96). When comparing other unit volumes and on-call arrangements with university hospitals, no significant difference in the risk of asphyxia existed. The results are presented in Table 5.

Compared with university hospitals, in units where physicians were at home when on-call the intrapartum mortality rate was elevated, being 2.4/1000 in university hospitals and 2.9/1000 in units where physicians were at home when on-call (AOR 1.25, 95% CI 1.02–1.52). Intrapartum mortality rate was higher (3.0/1000) also in units having 1000-1999 annual deliveries (AOR 1.31, 95% CI 1.07–1.61). No significant difference emerged in early neonatal mortality when comparing volumes or on-call arrangements (Table 5).

Half of the newborns (56%) stayed in hospital for 2 to 3 days. In hospitals having less than 1000 annual deliveries, a larger proportion of babies stayed for more than three days (40.9%) than in university hospitals (30.9%) (Figure 3). As expected,

Results

infants were transferred to NICU more often in university hospitals than in smaller hospitals (Table 5).

Table 5. Outcomes of singleton hospital deliveries, excluding newborns of <37 pregnancy weeks or with congenital anomalies, in different-sized maternity units and with different physician on-call arrangements in Finland in 2005-2009.

	Absolute risk (incidence/1000)	Relative risk (AOR ^a)	95% CI	Absolute risk difference (%)
University hospital				
Neonatal asphyxia ^b	21	1.00		
Newborn transfer ^c	95	1.00		
Intrapartum death	2.4	1.00		
Early neonatal death	0.2	1.00		
≥ 2000				
Neonatal asphyxia ^b	17	0.83	0.78–0.89	-19
Newborn transfer ^c	72	0.74	0.72–0.77	-24
Intrapartum death	2.7	1.15	0.95–1.38	13
Early neonatal death	0.2	1.17	0.56–2.42	0
1000-1999				
Neonatal asphyxia ^b	2	1.02	0.95–1.10	-90
Newborn transfer ^c	89	0.95	0.91–0.98	-6
Intrapartum death	3	1.31	1.07–1.61	25
Early neonatal death	0.3	1.72	0.81–3.66	50
<1000				
Neonatal asphyxia ^b	19	0.99	0.91–1.08	-10
Newborn transfer ^c	54	0.57	0.54–1.59	-43
Intrapartum death	2.7	1.19	0.95–1.51	13
Early neonatal death	0.3	2.11	0.97–4.56	50
On-call at hospital^d				
Neonatal asphyxia ^b	19	0.90	0.85–0.96	-10
Newborn transfer ^c	75	0.773	0.75–0.80	-21
Intrapartum death	2.8	1.18	0.99–1.40	17
Early neonatal death	0.2	1.36	0.70–2.64	0
On-call at home				
Neonatal asphyxia ^b	19	0.95	0.88–1.02	-10
Newborn transfer ^c	70	0.74	0.71–0.77	26
Intrapartum death	2.9	1.25	1.02–1.52	21
Early neonatal death	0.3	1.85	0.91–3.76	50

^a Stratified by maternal age and parity.

^b 5-minute Apgar <7 or umbilical artery pH <7

^c To intensive care unit, observation unit, or other hospital.

^d Excluding university hospitals.

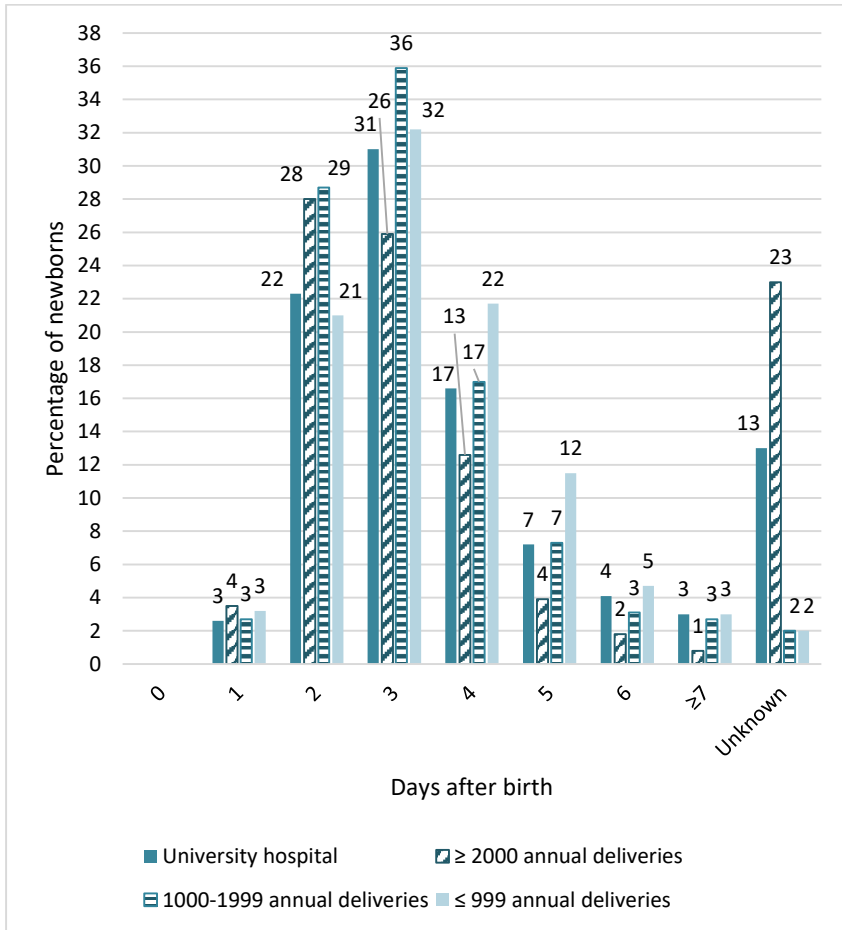


Figure 3. Duration of newborn hospital stay in different sizes of delivery units.

5.2 THE IMPACT OF TIME OF BIRTH ON PERINATAL OUTCOME IN DIFFERENT SIZE OF DELIVERY UNITS AND IN DIFFERENT PHYSICIAN ON-CALL ARRANGEMENTS (STUDY II)

Induction rate did not vary remarkably in different sizes of delivery units being 16-17% (Figure 4). Use of epidural analgesia was most common in university hospitals (46%) and was less used in large non-university units (32%) ($p < 0.001$) (Figure 5). More than 70% of the deliveries were vaginal deliveries. Emergency caesarean section rate was 8-9% in all hospital volumes. (Figure 6).

Regardless of time of delivery, the incidence rate of neonatal asphyxia was highest in spontaneous vaginal delivery, and lowest in instrumental vaginal delivery, vaginal breech delivery and elective caesarean sections. Intrapartum and early neonatal mortality was rare in all modes of delivery (Table 6).

Risk of asphyxia was elevated outside office hours in all hospital size-categories and in all on-call arrangements (22.7/1000 outside office hours and 18.4/1000 during office hours) (ARR 1.23, 95% CI 1.15–1.30). The risk remained higher even after excluding elective caesarean sections (20.9/1000 during office hours and 22.7/1000 outside office hours) (ARR 1.07, 95% CI 1.01-1.15). However, intrapartum and early neonatal mortality outside office hours compared to office hours was elevated only in hospitals having ≥ 2000 annual deliveries (2.2/1000 during office hours and 2.6/1000 outside office hours). (ARR 1.51, 95% CI 1.07–2.14) (Table 7)

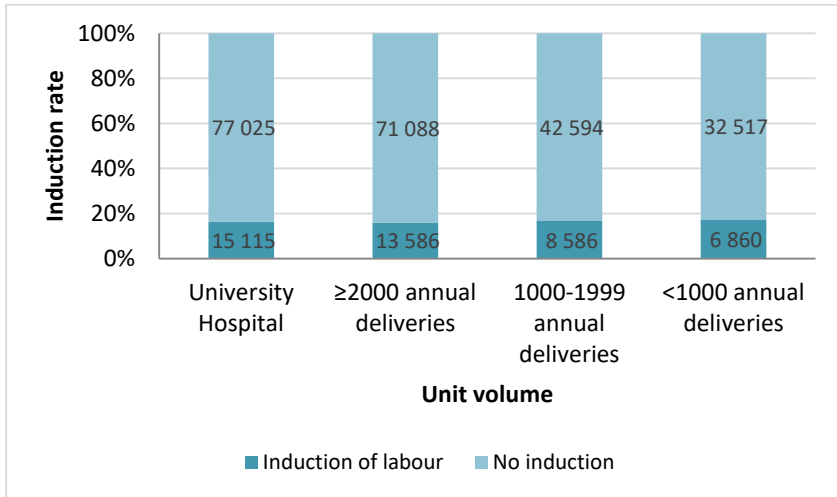


Figure 4. Induction of labour in different sizes of delivery units in Finland in 2005-2009, $p < 0.001$.

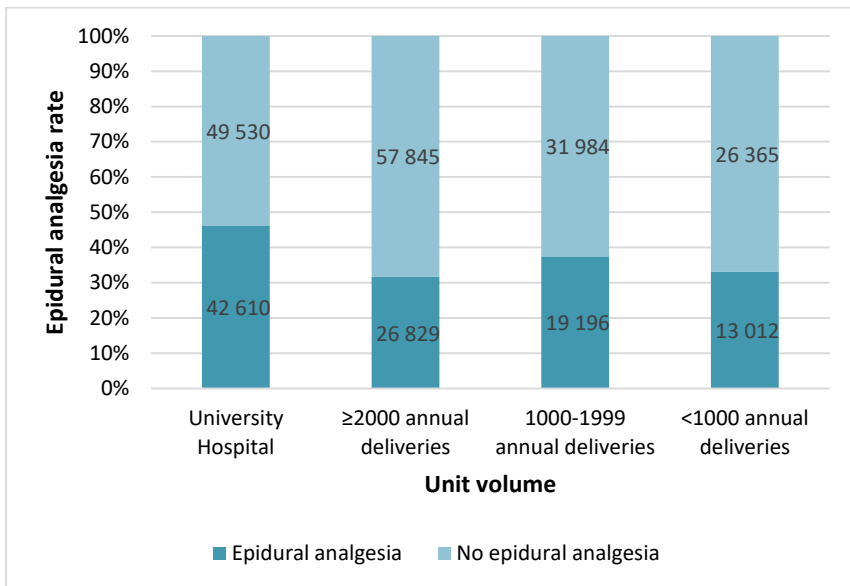


Figure 5. Use of epidural analgesia in different sizes of delivery units in Finland in 2005-2009, $p < 0.001$.

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Compared to office hours, spontaneous vaginal cephalic delivery had higher risk of asphyxia outside office hours (12.2/1000 during office hours and 13.8/1000 outside office hours) (ARR 1.12, 95% CI 1.02–1.23). Compared to office hours, vaginal breech delivery had a lower risk of asphyxia outside office hours (129.1/1000 during office hours and 95.3 /1000 outside office hours) (ARR 0.66, 95% CI 0.45–0.98). Vaginal breech delivery had also lower risk of intrapartum and early neonatal mortality outside office hours (24.0/1000 during office hours and 7.3/1000 outside office hours) (ARR 0.31, 95% CI 0.11–0.87).

Table 6. Adverse perinatal outcome in different modes of delivery in Finland in 2005-2009.

	Asphyxia		Intrapartum and early neonatal mortality			Total n	
	n	/1000	p	n	/1000		p
Spontaneous vaginal delivery	2699	10.2		496	1.9		201 410
Vaginal breech delivery	134	0.5	<0.001	15	0.1	<0.001	1288
Instrumental vaginal delivery	1362	5.2	<0.001	35	0.1	<0.001	22 010
Elective Caesarean section	156	0.6	<0.001	7	0.0	<0.001	16 696
Emergency Caesarean section	1321	5.0	<0.001	88	0.3	<0.001	22 478
Information missing							19

P-value in comparison with spontaneous vaginal delivery.

In instrumental vaginal delivery, risks of asphyxia did not change according to the time of birth, but risk for mortality increased, being 0.6/1000 during office hours and 1.9/1000 outside office hours (ARR 3.31, 95% CI 1.01–10.82). Emergency Caesarean section had increased risk of asphyxia outside office hours (52.9/1000 during office hours and 60.7/1000 outside office hours) (ARR 1.17, 95% CI 1.02–1.34), but no significant change in mortality (ARR 0.73, 95% CI 0.46–1.14) (Table 7).

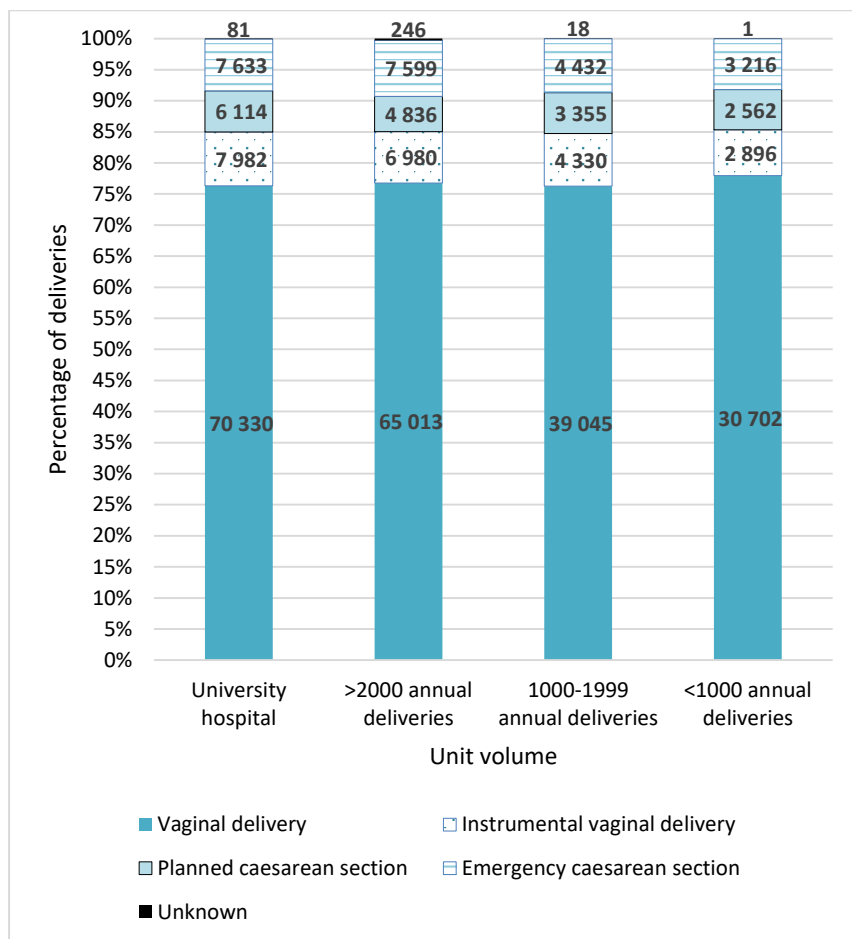


Figure 6. Modes of delivery in maternity units with different annual delivery rates in Finland in 2005-2009 ($p < 0.001$) in all delivery modes in each hospital category.

Results

Table 7. Effect of office hours on outcome in singleton hospital deliveries, excluding newborns born at <37 pregnancy weeks or with congenital anomalies, in Finland in 2005-2009.

	Absolute risk (incidence/1000)		Relative risk		Absolute risk difference (%)
	Office hours	Outside office hours	ARR*	95% CI	
University hospital					
Asphyxia**	19.4	23.4	1.21	1.09–1.34	17
Intrapartum and early neonatal mortality	2.2	2.2	1.01	0.74–1.38	0
≥2000 annual births					
Asphyxia**	16.6	21	1.25	1.12–1.41	21
Intrapartum and early neonatal mortality	2.2	2.6	1.51	1.07–2.14	15
1000-1999 annual births					
Asphyxia**	19.5	24	1.21	1.06–1.39	19
Intrapartum and early neonatal mortality	3	3	1.03	0.72–1.46	0
<1000 annual births					
Asphyxia**	18.6	23	1.25	1.07–1.46	19
Intrapartum and early neonatal mortality	2.0	2.4	1.20	0.74–1.93	17
On-call at hospital***					
Asphyxia**	18.4	22.8	1.23	1.14–1.32	19
Intrapartum and early neonatal mortality	2.1	2.5	1.19	0.96–1.46	16
On-call at home					
Asphyxia**	18.3	22.5	1.23	1.08–1.39	19
Intrapartum and early neonatal mortality	2.5	2.7	1.12	0.80–1.57	7

* Adjusted risk ratios for maternal age and parity.

** Either 1-minute Apgar score 0-3, 5-minute Apgar score 0-6, or umbilical artery pH < 7.00.

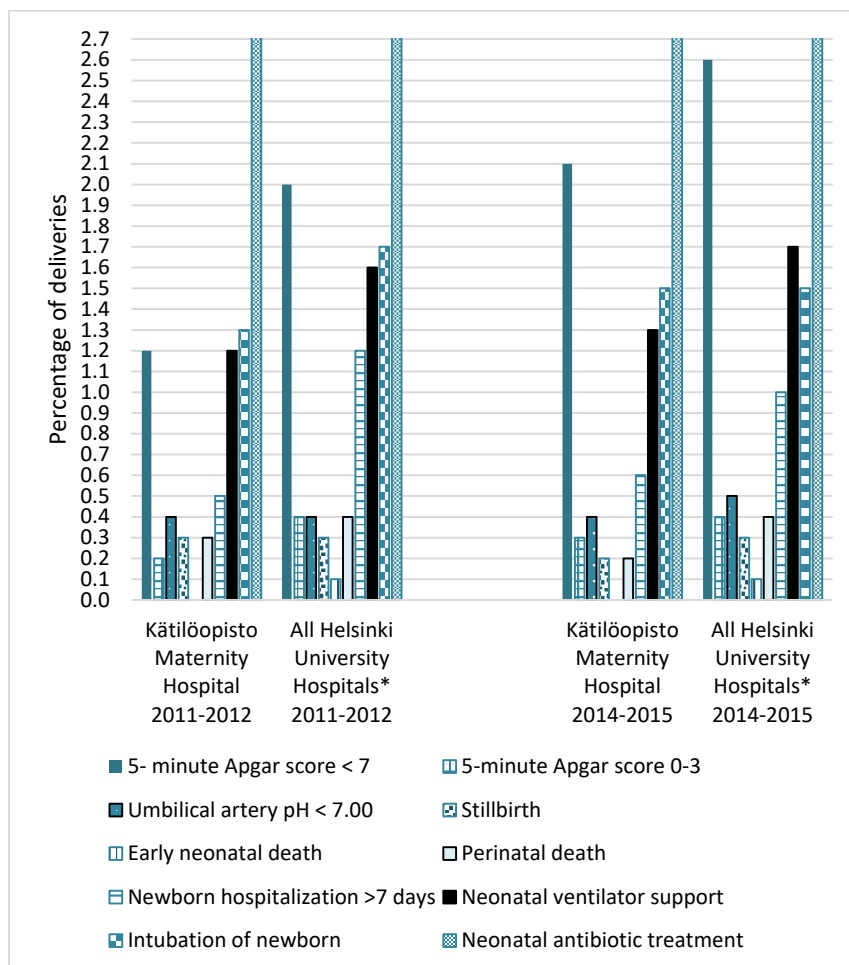
*** Excluding university hospitals.

5.3 EFFECT OF OBSTETRIC VOLUME INCREASE ON MATERNAL AND PERINATAL OUTCOME IN A HIGH-VOLUME DELIVERY UNIT (STUDY III)

5.3.1 MAIN OUTCOMES IN THE STUDY HOSPITAL

From 2011-2012 to 2014-2015, the number of singleton babies born increased from 11 237 to 15 637 (39%). The proportion of newborns receiving 5-minute Apgar score <7 increased from 1.2% to 2.1% (AOR 1.67, 95% CI 1.36–2.05). However, no significant difference was present in very low (0-3) Apgar scores. Transfers to NICU increased from 6.5% to 7.7% (AOR 1.17, 95% CI 1.06–1.29). Transfers to a higher level of neonatal care increased from 7.3% to 8.1% (AOR 1.11, 95% CI 1.02–1.22). No significant difference was detected in intubation rate or ventilator support of a newborn. The proportion of newborns receiving antibiotic treatment remained at 2.9%. Newborn hospitalization over seven days showed no significant change, being 0.5% during the first period and 0.6% during the second period.

Induction rate, instrumental deliveries, and emergency Caesarean sections showed no significant changes, but third- and fourth-degree perineal tears increased from 1.4% to 2.0% (AOR 1.47, 95% CI 1.19–1.82). The proportion of babies having umbilical artery pH <7 remained the same (0.4%), the number of perinatal deaths was low, and no significant changes were observed (Figures 7 and 8).



* Helsinki University hospitals are Kättilöopisto Maternity Hospital, Jorvi Hospital, and Women's Clinic.

Figure 7. Rate of adverse perinatal outcomes in 2011-2012 and 2014-2015 in Helsinki region.

5.3.2 OTHER OUTCOMES IN THE STUDY HOSPITAL

The proportion of babies born prematurely (before week 37) did not change significantly. Furthermore, there was no significant change in proportion of newborns with birthweight <2500 g, being 2.3% during the first period and 2.2% during the second period.

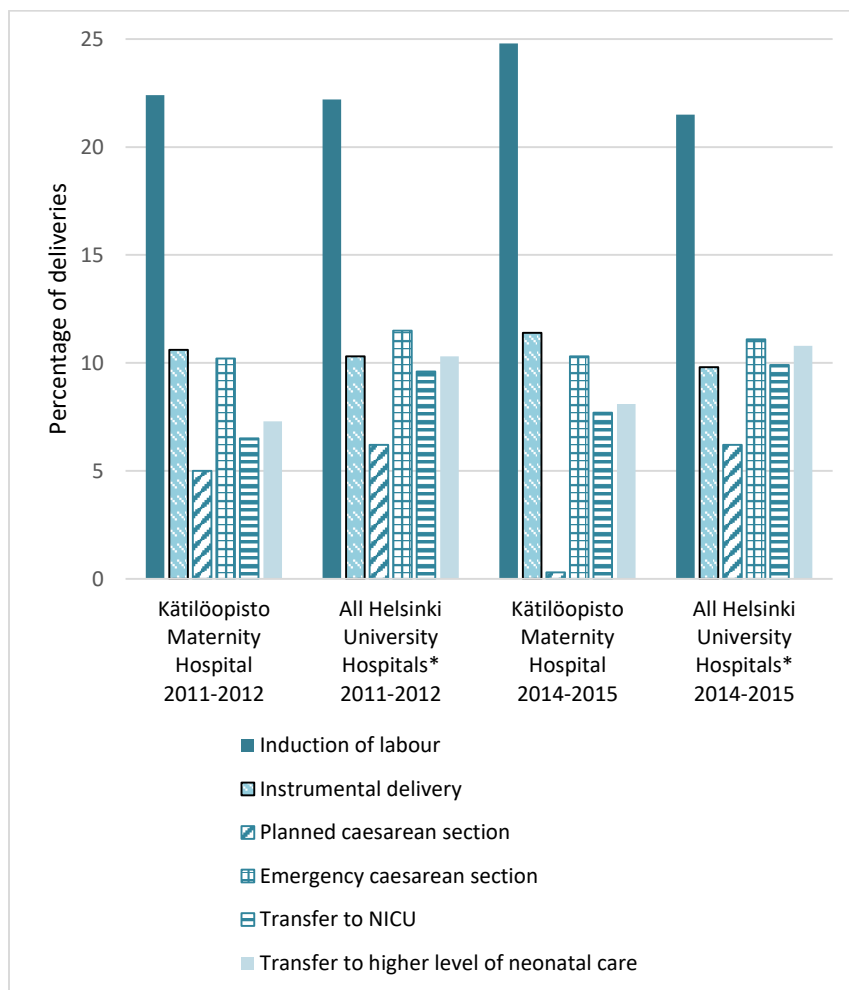
The proportion of babies with birthweight >4500 g decreased from 2.4% to 1.9% (AOR 0.84, 95% CI 0.71–0.99). The proportion of LGA babies decreased from 1.9% to 1.3% (AOR 0.67, 95% CI 0.55–0.81). There was no significant change in the proportion of SGA babies or in the proportion of newborns with congenital anomalies.

5.3.3 MAIN OUTCOMES IN POPULATION-BASED ANALYSIS

The total number of singleton babies born at the hospitals decreased by 3.4% (from 28 950 to 27 979) between the two periods. The proportion of newborns receiving 5-minute Apgar score <7 increased from 2.0% to 2.6% (AOR 1.27, 95% CI 1.18–1.42). However, neither the proportion of babies having 5-minute Apgar scores 0-3 nor the proportion of babies having umbilical artery pH <7.00 changed significantly. Newborn hospitalization over seven days decreased from 1.2% to 1.0% (AOR 0.84, 95% CI 0.71–0.98). The proportion of emergency Caesarean sections remained at 11%, the proportion of elective Caesarean sections remained at 6%, and the proportion of operative vaginal deliveries remained at 10%. The induction rate did not change, remaining at 22%.

The change in third- and fourth-degree perineal tears was not significant. Perinatal mortality was low, and the proportions remained unchanged. During both periods there occurred 35 early neonatal deaths (Figure 6).

No significant change was detected in transfers to a higher level of neonatal care, neonatal respiratory treatment, intubation, or antibiotic treatment (Figures 7 and 8).



* Helsinki University Hospitals are Kättilöopisto Maternity Hospital, Jorvi Hospital, and Women’s Clinic.

Figure 8. Rate of different delivery outcomes in 2011-2012 and 2014-2015 in the Helsinki region.

5.3.4 OTHER OUTCOMES IN POPULATION-BASED ANALYSIS

The number of LGA babies decreased by 18.5% (AOR 0.84, 95% CI 0.75–0.95). The changes in the proportions of babies with birthweight >4500 g, premature babies, SGA babies, and

babies with birthweight <2500 g were statistically insignificant. The proportion of congenital anomalies increased from 9.5% to 10.0% (AOR 1.07, 95% CI 1.01–1.13).

5.4 PREGNANCY-ASSOCIATED MORTALITY IN FINLAND (STUDY IV)

Age-adjusted, pregnancy-associated mortality decreased significantly from the end of the 20th century to the beginning of the 21st century, from 37.8/100 000 to 28.4/100 000 (ARR 0.75, 95% CI 0.65–0.88). In the non-pregnant population, mortality was 59.0/100 000 during the earlier period and 48.1/100 000 during the later period. Moreover, during the study period, mortality was highest among the eldest (45-49 years) non-pregnant women (176.1/100 000). Mortality rates in different age categories are presented in Figure 9.

Pregnancy-associated mortality due to medical causes decreased from 18.4/100 000 to 13.6/100 000 (ARR 0.74, 95% CI 0.59–0.92). Pregnancy-associated mortality due to external causes decreased from 19.4/100 000 to 14.8/100 000 (ARR 0.77, 95% CI 0.62–0.95).

The greatest decreases were in the risk for suicide during pregnancy or within one year of delivery, which decreased by 43% (from 5.8/100 000 to 3.3/100 000) (ARR 0.57, 95% CI 0.35–0.94), in homicides after miscarriage, which were reported as 4.4/100 000 during the earlier period and nil during the later period, and in medical causes in ongoing pregnancies or after birth, which decreased by 39% (from 18.7/100 000 to 11.4/100 000) (ARR 0.61, 95% CI 0.46–0.80).

Suicide mortality rate after termination of pregnancy did not change significantly, being 21.8/100 000 pregnancies during the later period.

Results

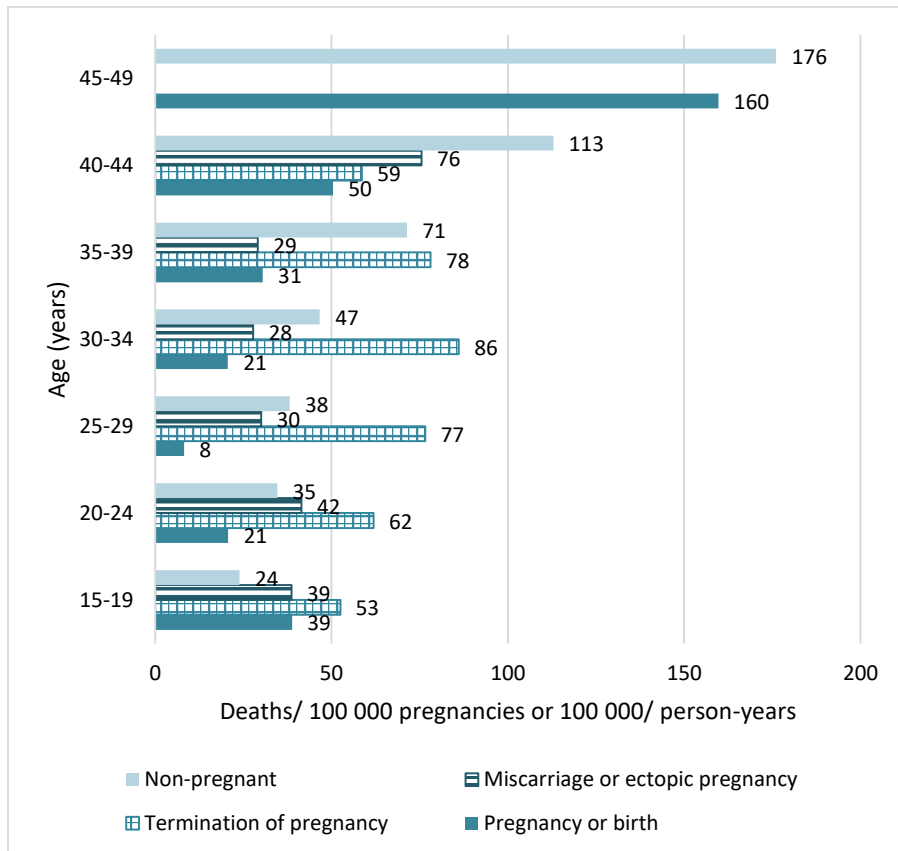


Figure 9. Pregnancy-associated mortality in Finland in 2001-2012.

6 DISCUSSION

All delivery units should provide safe and high-quality care. A study from New Zealand suggests that 55% of neonatal mortality and morbidity are potentially avoidable (126). The situation in Finnish delivery units is of interest because the number of delivery units in Finland has been slowly decreasing and care has been centralized to larger units. One of the main reasons for this has been the decreasing number of babies born annually (2). Furthermore, the legislation for 24/7 readiness for emergency Caesarean section resulted in closure of some delivery units. Later legislation led to most units with less than 1000 annual deliveries being closed (87). Characteristic of Finnish delivery units is that they are all publicly funded and there are no midwife-led units.

This thesis summarizes the situation in Finnish delivery units, thus providing insight on how to provide safe care and suggesting improvements. Special attention was given to how hospital volume, time of birth, and increased number of deliveries affect outcomes and how maternal mortality has changed in Finland.

6.1 EFFECT OF SIZE OF MATERNITY UNIT AND PHYSICIAN ON-CALL ARRANGEMENTS

Study I implied that higher risk for intrapartum death exists in units where the physician on-call is at home. This contradicts several studies demonstrating safety of midwife-led units (127,128). One explanation for this could be that most of the midwife-led units studied are not free-standing units, unlike the remote units in Finland where physicians can stay home when on-call. Furthermore, a German study demonstrated that neonatal asphyxia is best avoided if

emergency Caesarean section is performed within 20 minutes of the decision (129). This means that the operating team should be ready in the delivery hospital and the 30 minutes that a physician on-call at home was given to arrive at the hospital is too much. Thus, Study I confirmed that deliveries should happen in units where there is always a physician at the hospital.

This study indicated that factors other than the annual number of deliveries per unit also affect obstetric safety. One such factor could be the absence of a NICU or its low level in different hospitals. A British study demonstrates that the key to safe child birth is not so much the size of the delivery unit but how well the unit can meet the medical needs of the parturient and the newborn (130).

Compared with university hospitals, in smaller units the patient outcomes should not be worse since pregnancies with complications are directed to higher level delivery units. Interestingly, intrapartum foetal asphyxia occurs more often in low-risk mothers than in mothers considered at high risk (65), and this should be kept in mind when directing low-risk women to specific delivery units, planning the resources in those units, and making decisions about giving birth outside of delivery hospitals.

6.2 IMPACT OF TIME OF BIRTH

An increased risk of neonatal asphyxia in term deliveries outside office hours was detected in Study II. According to an American study as well as a Swedish study, night-time delivery is considered an independent risk factor for neonatal encephalopathy and the risk for foetal injury resulting in death is doubled at night (131,132). Neonatal mortality at night is even higher among preterm infants than among term infants (133,134).

One explanation for the higher risk of asphyxia outside office hours is different patient material during different times of the day. Induced deliveries are one reason for this variation. Most of the inductions are not timed so that the delivery would happen during office hours even though inductions are mainly (74%) done for medical reasons and induced deliveries are known to have a higher risk for adverse neonatal outcome (135-137).

Another factor influencing the outcomes outside office hours may be the staffing. The on-call obstetrician, anaesthetist, and paediatrician are each responsible for a larger patient group than the clinicians during office hours. This could cause a delay for the clinician to arrive when requested outside office hours compared with during office hours. However, a recent study from the UK states that the presence of a senior obstetrician is not a critical factor explaining the difference between outcomes during office hours and outcomes outside office hours (91). Furthermore, even though it is well known that sleep deprivation impacts human functioning (84), it is not proven to increase errors during night shifts (138).

Study II detected a lower risk of neonatal asphyxia in vaginal breech delivery outside office hours than during office hours. However, the risk was higher than in cephalic delivery. Breech delivery is considered to have up to twenty times higher risk of asphyxia than cephalic delivery (132). A possible explanation for our result is that breech deliveries are thoroughly planned, carefully monitored, and more readily converted to Caesarean section than vaginal cephalic deliveries (139).

6.3 EFFECT OF OBSTETRIC VOLUME INCREASE IN A HIGH-VOLUME DELIVERY UNIT

Number of deliveries increased in Kätilöopisto Maternity Hospital by 29%, from 5800 to 7500 deliveries annually. To ensure safe childbirth, the resources increased accordingly to support the increased work load. Furthermore, during peak hours at Kätilöopisto Maternity Hospital, women giving birth were directed to other hospitals in the Helsinki region. Kätilöopisto Maternity Hospital accepted mainly low-risk deliveries during both study periods. We recognize that high-volume tertiary units receive patients with severe medical conditions and are therefore likely have worse patient outcomes.

Between the two time periods, the proportion of babies with 5-minute Apgar score <7 increased, but no increase was detected in rate of SGA babies, low pH values, or induction rate. SGA and induction of labour are known risk factors for low Apgar scores (136,140). An increased rate of low Apgar scores was noted in all Helsinki region hospitals between the two periods.

The proportions of babies transferred to special care nursery (SCN) and NICU increased with the rising obstetric volume in Kätilöopisto Maternity Hospital. With regard to changes in neonatal outcome to explain this finding, rate of lower Apgar scores increased between the two periods with no significant change in the rate of SGA babies, babies with low umbilical artery pH, or preterm deliveries. The increased transfer rate to a higher level of neonatal care may reflect a change in the neonatal admission policy throughout the Helsinki region. During the later period neonates were transferred earlier to a paediatric unit that decided on therapeutic hypothermia treatment.

Even though the numbers of babies receiving low Apgar score and transfers to NICU and SCN increased, there was no significant change in the proportions of newborns receiving antibiotic treatment, respiratory support, or staying at hospital more than seven days. Thus, it is unlikely that the babies transferred to NICU or SCN were suffering from a severe medical condition.

During the study period the use of balloon catheter increased throughout the Helsinki region because of ongoing studies on its safety and efficacy (141). However, Study III did not detect any significant change in the induction rate, and thus, the use of balloon catheter is a highly unlikely explanation for the results. The induction of delivery is increasing worldwide. In the UK, 27% of deliveries are induced according the latest maternity statistics report (142). The use of balloon catheter is associated with a shorter length of stay in hospital, lower costs, and higher maternal satisfaction (143).

Operative vaginal delivery and infant birth weight are known risk factors for third and fourth degree perineal tears (144,145). Even though the rate of tears increased in Kätilöopisto Maternity Hospital, no significant change was observed in the rate of infants with birthweight >4500 g or operative vaginal delivery.

6.4 CHANGES IN PREGNANCY-ASSOCIATED MORTALITY

Study IV demonstrated that mortality among fertile-age women has decreased over the 15-year period. Mortality rates are lower among pregnant or previously pregnant women than among same-aged non-pregnant women. There are several reasons for this finding. Firstly, it is likely that most healthy women get pregnant (146). Secondly, pregnant women might have better access to health care facilities since

most of the pregnancies are followed up by a health care provider (3). Thirdly, health disorders might be treated more actively during pregnancy.

In Finland, ethnic minorities are so small in number that a separate evaluation of pregnancy-associated mortality is not feasible. Other countries publish alarming reports of higher maternal mortality rates among ethnic minorities (147,148). This might also be a risk in Finland and must be monitored since the number of immigrants is increasing steadily.

This study revealed that suicides are the most common external cause of pregnancy-associated deaths in Finland. The most common external cause of pregnancy-associated deaths varies between continents. Homicide is a leading cause in the USA (149). In Nordic countries, suicide is a common cause of pregnancy-related death, being the second most common external cause in Iceland and the third in Denmark (26,150). In low- and middle-income countries, only 1% of pregnancy-related deaths are due to suicide (151).

It is acknowledged worldwide that after termination of pregnancy suicidal behaviour increases dramatically (152). Most likely, there is no causality between termination of pregnancy and suicide. Instead, women are in a highly vulnerable state due to their socio-economic and mental health background and this triggers suicidal behaviour (153). Previous studies from Canada and the USA indicate that almost 60% of women undergoing their first termination of pregnancy have one or more pre-existing mental health disorders compared with 40% of women having their first childbirth (154,155). This indicates that further studies are required to elucidate the underlying reasons for suicidal behaviour after termination of pregnancy.

6.5 STUDY STRENGTHS AND LIMITATIONS

6.5.1 STRENGTHS

The results of this study are representative due to the accuracy of the register data in Finland (156,157). The results reflect actual intrapartum and early neonatal care better than many previous studies since antepartum stillbirths were excluded (Studies I and II).

The study of volume increase (Study III) focused on one unit only, thus excluding many confounding factors such as academic level, staff resources, medical equipment, and different obstetric practices. Simultaneous population-based analysis reflected variations in outcome measures in the same region, making the results more powerful. Organizational changes for the construction project in Women's Clinic happened during 2013. That entire year was excluded to allow personnel time to become accustomed to the new circumstances.

Study IV reported pregnancy-associated deaths per 100 000 pregnancies (and not per live births, as commonly used) because the study had as the numerator also those deaths occurring after termination of pregnancy, miscarriages, or ectopic pregnancies, which would not end in a live birth. Furthermore, the cut-off point of one year was used, instead of 42 days postpartum because more women live beyond the 42 days after delivery due to advances in medicine.

6.5.2 LIMITATIONS

Even though Studies I and II had many deliveries, the numbers of intrapartum and early neonatal deaths were low in this low-risk group. The low numbers prevented the stratification of deliveries into groups by mode of delivery during different hours of the day.

We acknowledge that differences in patient material impact our comparisons of different-sized obstetric units. In Studies I and II, adjustments only for maternal age and parity were made. However, we feel that our results reflect true differences between different-sized obstetric units; adverse perinatal outcomes should be less likely in smaller delivery units since pregnancies considered high risk due to maternal medical conditions, such as high blood pressure and insulin-treated diabetes, are directed to higher-level hospitals with more annual deliveries in Finland. We speculate that if maternal variables were adjusted in the statistical analyses the study results would indicate greater differences in outcomes between different-volume hospitals.

Many of the units where the physician could stay home when on-call were located far (>30 minutes' drive) from higher level hospitals. Thus, transportation to a higher-level hospital during delivery was not possible. The results therefore cannot be directly applied to other countries where midwife-led delivery units are in the same building or just a few kilometres away from specialist care.

Study III did not measure all factors that could have changed due to increased number of deliveries. For instance, no data on midwife-patient or physician-patient ratios were collected. Furthermore, neither maternal infections nor mortality were measured. Finally, a register-based study cannot collect information on patient or staff satisfaction if it is not previously collected in any database.

In Study IV, the number of deaths occurring after ectopic pregnancy or miscarriages might be underestimated if the pregnancy was at a very early stage and the women were never hospitalized or the pregnancy was not mentioned in the death certificate. Furthermore, the data were not stratified for socio-economic status, which could have influenced mortality results.

6.6 SIGNIFICANCE OF THIS STUDY AND FUTURE PROSPECTS

This study gives insights into patient safety in maternity hospitals and adds new information on the effect of increased number of deliveries in a large unit on pregnancy-associated mortality in Finland. These observations are particularly useful now, with deliveries being centralized to larger units and different strategies devised to control the escalating health care costs in Finland. Delivery units in Finland do not only offer delivery services but also antenatal and gynaecological care. Thus, sophisticated calculations of cost-effectiveness are required to determine whether centralization of deliveries saves public funds.

In Finland, perinatal/ maternal mortality is one of the lowest in the world. To improve maternal and neonatal care, future studies on patient safety in Finnish maternity hospitals should concentrate on maternal, perinatal, and neonatal morbidity. Furthermore, instead of comparing delivery volumes, research should focus on identifying other factors affecting delivery outcomes in Finnish hospitals. This would increase safety in all hospitals.

It would be ideal if staff could rotate between different obstetric units, thus gaining and sharing experience. Since this is highly unlikely due to private-life restrictions, simulation training could be used more, and new training models actively developed and implemented. Obstetricians should closely cooperate with professionals in information technology because developments in wearable devices and in virtual reality could be better deployed in providing safe and good-quality maternity care.

Leaders in obstetric units must be active in the change. Any major changes, such as increasing obstetric volume, should not be made without proper risk analysis and a contingency

plan. Furthermore, it would be wise to implement high reliability organization principles in maternity hospitals to diminish adverse obstetric events.

In order to better protect women against suicide after termination of pregnancy, the underlying circumstances should be elucidated. Future studies should analyse whether health care professionals can recognize the need for support, and whether they have the knowledge and skills to intervene and offer support. Furthermore, future studies should analyse in detail the backgrounds of these women and determine whether they try to seek help and what needs they have.

Finally, since Finland has good computerized patient registers, the creation of a national obstetric safety indicator list should be considered together with mandatory accreditation of all delivery units and units performing terminations of pregnancy against uniform safety and quality requirements.

7 CONCLUSIONS

This study provided useful information on maternal health and performance of delivery units in Finland. Based on Studies I-IV, our conclusions are the following:

1. Severe adverse obstetric outcomes are rare in Finland. Maternity unit volume affects obstetric outcomes. Higher intrapartum mortality in the units with physicians at home when on-call indicate that all delivery units should always have an on-call physician present in the hospital (Study I).
2. Risk of asphyxia is elevated at all unit volumes and with all on-call arrangements outside office hours compared with during office hours. Risk of asphyxia remains higher outside office hours even after excluding elective Caesarean sections. Relative to procedures performed during office hours, asphyxia risk is significantly elevated in instrumental vaginal deliveries and emergency Caesarean sections performed outside office hours. Thus, timing of induction of labour should be planned so that the deliveries with higher risk for operative delivery would occur during office hours (Study II).
3. Increase in obstetric volume in a high-volume maternity unit impacts both maternal and perinatal outcomes despite simultaneous increase in staffing, indicating that careful planning and risk estimation are required (Study III).
4. Mortality is lower in pregnant women than in age-matched non-pregnant women, and pregnancy-associated mortality has also decreased during the previous decades in Finland. However, pregnancy-

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associated mortality is highest after termination of pregnancy due to suicidal deaths, indicating a need for detailed research on the underlying mechanisms in order to support these women (Study IV).

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